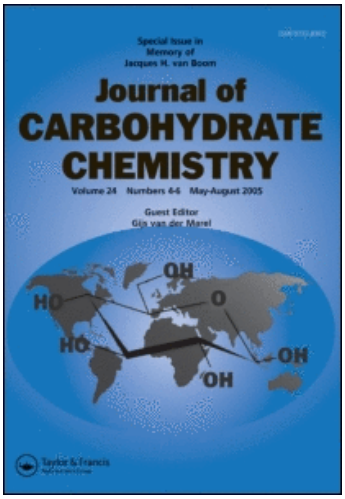

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SYNTHESIS OF MONOESTERS AS SURFACTANTS AND DRUGS FROM D-GLUCOSE

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ABSTRACT

We have synthesized a series of monoesters from **D**-glucose corresponding to the structures 3-*O*-acyl, 6-*O*-acyl-1,2-*O*-isopropylidene-α-**D**-glucofuranose and 3-*O*-acyl-**D**-glucose, following the sequence of reactions : **D**-glucose -> diacetone glucose -> acylation -> partial or total deprotection. These compounds were prepared as either potential non-ionic surfactants (fatty acid esters and perfluoroalkylated ester) or antitumour drugs (*n*-butyric esters). Results concerning surface activity, toxicity and antitumour effects are reported. A novel method for obtaining partially deprotected 6-*O*-acyl esters from their corresponding 3-*O*-acyl isomers is reported. Deprotection conditions have been studied and a higher selectivity in partial deprotection has been achieved. We have given particular attention to the choice of solvents and reagents in order not to limit the extent to which the products might be applied.

INTRODUCTION

Non-ionic surfactants can be synthesized by linking an alkyl chain to a polyhydroxylated molecule. Their amphiphilic properties are caused by the presence of the hydrophilic free OH groups and the hydrophobic alkyl chain. Most of the existing work in this field pertains to disaccharidic[1-6] and monosaccharidic[6-19] fatty acid esters.

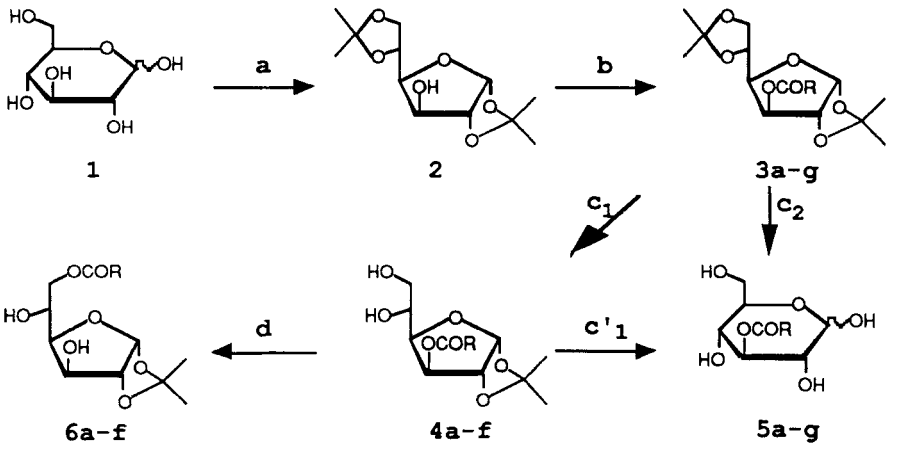
Direct acylation of saccharides with acid chlorides[8,20] leads to mixtures of mono-, di- and triesters which are difficult to separate. Such mixtures present limitations in the number of applications which might be sought since a well-defined compound is often required. Transesterifications using either natural triglycerides or methyl esters[3-5] of fatty acids also lead to mixtures. When transesterification is aided by an enzymatic catalyst,[12,13] selectivity is improved due to the discrete nature of primary OH groups. A mixture of isomeric monoesters is obtained when two vicinal OH groups are chelated in the presence of either the couple NaH-$CuCl_2$ or NaH-$CoCl_2$.[21-23] Regiospecific monoacylation of mono- and disaccharides can be effected when sophisticated acylating agents such as special amides or thioethers, are used in the presence of NaH in pyridine.[11,24]

Acylation of partially protected substrates is generally problematic since, for example, methyl 4,6-*O*-benzylidene-α-**D**-glucoside[8] upon acylation, gives a mixture of monoesters. However, there is no problem of selectivity when all OH groups on the substrate are protected except one: the condensation is thereby directed regiospecifically depending on the sites protected. This strategy has been applied to the synthesis of anomeric esters from 2,3,4,6-tetra-*O*-acetyl-**D**-glucopyranose using the method of Kœnigs-Knorr.[19] Also, di-*O*-acetal protection of hexoses and pentitols has been used to obtain unambiguous monoesters.[4,18] Herein we have used the latter methodology since protection and deprotection steps are easier than those involving either tetraacetates or tetraethers. Also the use of *O*-acetals permits selective deprotection in the presence of ester linkages.

The work described herein is the synthesis of alkylated esters derived from **D**-glucose which are non-ionic surfactants [*O*-acyl = *O*-octanoyl, *O*-lauroyl, *O*-palmitoyl, *O*-stearoyl, *O*-oleoyl; *O*-3'-(F-octyl)-propionyl] or drugs with a prolongated half-life in biological medium (*O*-acyl = *O*-n-butanoyl[25]). We carefully selected solvents and catalysts in order to avoid limiting the variety of applications to which the compounds might be put. We also give results on toxicity, surface activity of fatty acid esters and biological properties of some *n*-butyric esters prepared.

RESULTS AND DISCUSSION

A-Syntheses : The synthesis of **D**-glucose monoesters is outlined in Scheme 1 :



a) R = C_3H_7 ; b) R = C_7H_{15} ; c) R = $C_{11}H_{23}$; d) R = $C_{15}H_{31}$; e) R = $C_{17}H_{35}$; f) R = $C_{17}H_{33}$; g) R = $C_2H_4C_8F_{17}$

SCHEME 1

Step a : *The choice of acetalic group and the synthesis of diacetone glucose (**2**)*

The choice the protecting acetal group was guided by the selectivity of the partial deprotection (step c_1) which is in competition with total deacetalation (step c'_1; Scheme 1) and deacylations by routes k_A and k_B (Scheme 2).

In a preliminary study, we compared rate constants for the deprotection of the 5,6-*O*-acetal (k_1) and 1,2-*O*-acetal (k_2) in 1,2:5,6-di-*O*-isopropylidene-**α-D**-glucofuranose (**2**) (diacetone glucose), 1,2:5,6-di-*O*-cyclohexylidene-**α-D**-glucofuranose (**2'**) and 3,5-*O*-benzylidene-1,2-*O*-isopropylidene-**α-D**-glucofuranose (**2"**) respectively. The results showed that the k_1/k_2 ratios were similar, but the *O*-isopropylidene group deprotection was 5 to 7 times faster than that of the *O*-cyclohexylidene group depending to the site protected. Thus, the 3-*O*-acyl group will better be preserved in further deprotection steps in the case of **2**. We also observed that the 3,5-*O*-benzylidene group deprotection (**2"**) is approximately 50 times slower than that of the 5,6-*O*-isopropylidene group; however such a protecting group would incur a greater risk of deacylation during the preparation of deprotected 6-*O*-acyl esters.

Literature methods identify catalysts such as $ZnCl_2$,[26] $CuSO_4$,[27] I_2[28] or $FeCl_3$.[29] Sulfuric acid as the sole catalyst gives different yields depending on extraction conditions used.[26] We elected to use a recently reported and improved method[30] which is similar to the latter and which quotes a 70% yield of diacetone glucose.

Step b: *Synthesis of 3-O-acyl-1,2 : 5,6-di-O-isopropylidene-α-D-glucofuranose (**3**).*

An attempted transesterification of diacetone glucose with methyl palmitate using literature conditions[31] which involved reaction for 6 hours at 180 °C *in vacuo*, gave a residue which was black and partially caramelized and which contained 60% of the required ester. Esterification with acid chlorides is usually performed in pyridine which is present either as a solvent[8,18] or if used in stœchiometric amounts, as a base.[32] We opted not to use pyridine because of its noxious character[33] and its traces in the final products would likely compromise some of the potential applications. Thus, esterifications were performed in toluene in the presence of a stœchiometric amount of TEA in accordance with our recently published work.[34] Yields obtained were typically between 85 and 94%.

Step c_1: *Synthesis of 3-O-acyl-1,2-O-isopropylidene-α-D-glucofuranose (**4**)*

This step was studied in detail because of the interesting applications of the target products.

According to earlier work, there are numerous reaction media that enable selective deprotection of acetals ; for example : water-acetic acid,[35] methanol-HCl,[36] water-trifluoroacetic acid, water-acetic acid-trifluoroacetic acid.[37] We preferred a 0.2 N H_2SO_4 solution of ethanol-water 19:1 or Amberlite 15 H^+ acid resin, because its composition (mixture of solvents) is close to that of the azeotrope and therefore can be evaporated at a constant temperature. This limits the possibility of emulsification which appears with other water-co-solvent mixtures in which the proportion of water differs during evaporation.

Mono-deprotection (step c_1) is in competition with total deprotection (step c_2) and hence deacylation of substrate **3**. We therefore undertook preliminary kinetic studies in order to establish quantitatively the optimal conditions for the step c_1 performed in 19:1 ethanol-water using the conditions described in Table 1. The compounds studied have the following structure : 3-Y-1,2:5,6-di-O-isopropylidene-

Table 1 : *Deprotection rate constants of 5,6-O-acetal (k_1) and 1,2-O-acetal (k_2) with 0.1 N and 0.2 N H_2SO_4 solution of ethanol-water 19:1 at 50 °C.*

Substrate	$k_1 \times 10^5.s^{-1}$ (0.1 N)	$k_1^{0.2N}/k_1^{0.1N}$ (*)	k_1/k_1^2 (0.1 N)	$k_2 \times 10^5.s^{-1}$ (0.1 N)	$k_2^{0.2N}/k_2^{0.1N}$ (*)	k_1/k_2 (0.1 N)	k_1/k_2 (0.2 N)	k_2/k_2^2 (0.1 N)
2	110	2.7	1	1.13	1.8	97	146	1
3_a	71	2.6	0.65	1.77	1.7	40	64	1.6
3_b	36	2.7	0.33	1.50	1.7	24	39	1.3
$3'_b$	43	2.5	0.39	0.72	1.8	60	83	0.64
3_d	21	2.7	0.19	1.24	1.7	17	27	1.1
$3'_d$	24	2.7	0.22	0.59	1.7	41	65	0.52

(*) *ratio of rate constants obtained with* $[H^+]$ *= 0.1 N and 0.2 N*

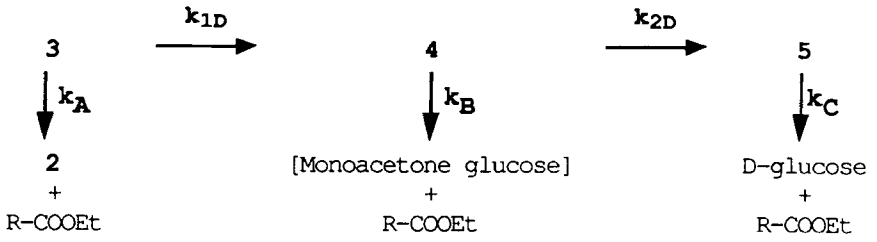
α-**D**-glucofuranose, including esters **3** and analoguous ethers with Y= *O*-C_8H_{17} (**3'$_b$**) and Y= *O*-$C_{16}H_{33}$ (**3'$_d$**).

The results presented in Table 1 give indications on parameters which influence the selectivity (k_1/k_2) in favour of producing type **4** compounds :

- the increase in acidity has more effect on the 5,6-*O*-acetal site ($k_1^{0.2N}/k_1^{0.1N}$) than on that of the 1,2-*O*-acetal ($k_2^{0.2N}/k_2^{0.1N}$) ; thus the selectivity is increased.

- the rates ratio k_1/k_2 decreases as the chain length increases one of the reasons for this result is the steric hindrance of the 3-*O*-acyl group which influences mainly the 5,6-*O*-acetal site on the substrate.

There is less selectivity in the deprotection of esters of glucose than in the analoguous ethers (see **3_b** and **3'$_b$**; **3_d** and **3'$_d$**); moreover experimental deprotection rate constants k_2 of such esters are higher than observed for the related diacetone glucose ($k_2/k_2^2 > 1$). The former result is due to the fact that esters of type **3** are deprotected under our conditions to give a proportion of ethyl ester resulting from the reactions depicted in the Scheme 2 :



SCHEME 2

For the palmitic ester $\mathbf{3_d}$, we determined deacylation rate constants k_A, k_B and k_C which are given in Table 1 along with the conditions used. The reaction was followed by examining the ethyl palmitate formation obtained from $\mathbf{3_d}$, $\mathbf{4_d}$ and $\mathbf{5_d}$ respectively :

$k_A = 0.55 \times 10^{-5}\ s^{-1}$; $k_B = 0.52 \times 10^{-5}\ s^{-1}$; $k_C = 0.47 \times 10^{-5}\ s^{-1}$ with $[H_2SO_4] = 0.1$ N.

The experimental rate constants k_1 and k_2, which are determined by following the consumption of substrates $\mathbf{3_d}$ and $\mathbf{4_d}$, express the overall process of deprotection by either the k_{1D} or k_{2D} route and the deacylation by either the k_A or k_B route :

$k_1 = k_{1D} + k_A$; $k_2 = k_{2D} + k_B$

Thus, for the palmitic ester $\mathbf{3_d}$ with 0.1 N H_2SO_4 solution at 50 °C, real deprotection rate constants are :

$k_{1D} = k_1 - k_A = (21-0.55) \times 10^{-5}\ s^{-1} = 20.45 \times 10^{-5}\ s^{-1}$ with $k_{1D}/k_A = 38$

$k_{2D} = k_2 - k_B = (1.24-0.52) \times 10^{-5}\ s^{-1} = 0.72 \times 10^{-5}\ s^{-1}$ with $k_{2D}/k_B = 1.4$

and deacetalation selectivity is given by the following ratio :

$k_{1D}/k_{2D} = 28.4$ instead of $k_1/k_2 = 17$.

Our study revealed that the yield of the partially deprotected ester **4** depends not only on the experimental k_1/k_2 ratio, but also on the k_{1D}/k_A and k_{2D}/k_B ratios. Calculations, based on the kinetic results of the reactions identified in Scheme 2, enabled us to determine the required reaction-time (t_M) to obtain the maximum percentage yield and corresponding mass of compound **4** (see Experimental). Thus, for $\mathbf{3_d}$, using the conditions identified in Table 1 with 0.1 N H_2SO_4, we found that for $t_M = 240$ minutes the reaction mixture contained :

5% of remaining **3d**; 76% of **4d** and 7.5% of ethyl palmitate stemming from **3d** by the routes k_{1D} and k_A; 11.5% of compounds stemming from **4d** by the routes k_{2D} and k_B.

When operating at 50 °C with 0.2 N H_2SO_4, we found that k_1/k_2 =27 instead of 17; k_{1D}/k_{2D} = 50 instead of 28.4; $k_A \approx k_B = 10^{-5}$ s^{-1} instead of 0.55 x 10^{-5} s^{-1}. These results gave a t_M = 100 minutes and a reaction mixture which contained :

3.3% of remaining **3d**; 82% of **4d** and 6% of ethyl palmitate stemming from **3d** by the routes k_{1D} and k_A; 8.7% of compounds stemming from **4d** by the routes k_{2D} and k_B.

These results encouraged us to prepare all esters of type **4** using the foregoing reaction conditions: the yields obtained were in the range 76 to 80%.

We paid careful attention to the acidity ($5 \leq pH \leq 6$) of the reaction mixture during neutralization in order to limit the possibility of transesterification in obtaining the corresponding 6-*O*-acyl-1,2-*O*-isopropylidene-α-D-glucofuranose **6** (step d, Table 2). Under these pH conditions, the partially deprotected ester fraction had 3 to 8% of the **6** isomer which was removed during purification.

We obtained results close to those obtained when H_2SO_4 was replaced by Amberlite 15H^+ acid resin.

Step d: *Preparation of 6-O-acyl-1,2-O-isopropylidene-α-D-glucofuranose (6)*

The synthesis of type **6** esters by esterification of 3,5-*O*-benzylidene-1,2-*O*-isopropylidene-α-D-glucofuranose **2"**, was not attempted because kinetic results failed to indicate a set of viable conditions for the selective deprotection of the 3,5-*O*-benzylidene group. Furthermore, we did not attempt to synthesize them from 1,2-*O*-isopropylidene-α-**D**-glucofuranose under the conditions defined in step b, due to the likelihood of significant proportions of -3,6 and -5,6 diesters being obtained as identified in Table 4.

Observations cited in the literature on internal monoester transesterifications[38] encouraged us to study transesterification reactions of partially deprotected esters of type **4**. We noted from our kinetic studies that during neutralization with an excess of either $NaHCO_3$ or TEA, the amount of the 6-O-acyl isomer increased with time between neutralization and HPLC analysis.

Therapeutic interest in the butyric ester **4a** influenced us to study its stability in a solution of 70 g/L in different basic and neutral media ; results presented in Table 2 show that 3-*O*-acyl ester

Table 2 : *Distribution of products formed in the course of time in solutions of 70 g/L of 3-O-n-butanoyl-1,2-O-isopropylidene-α-D-glucofuranose* $\mathbf{4_a}$.

Medium	Time	Isomers proportions (%)			deacylation %
		3-O-acyl	6-O-acyl	5-O-acyl	
pure water	1 month	95	5	< 1	< 1
(pH = 6.5)	3 months	94	6	< 1	3
4 °C	1 year	90	10	< 1	10
water	2 min	70	28	2	0
$[NaHCO_3]$ = 0.2 N	3 h	8	83	9	0
(pH = 8.1) 25 °C	95 h	6	94	4	20
water	2 min	7	89	4	5
[TEA] = 0.2 M	3 h	4	92	4	60
(pH = 12.1) 25 °C	24 h	0	0	0	100
ethanol-water 19:1	1 month	98	2	< 1	0
4 °C	3 months	96	4	< 1	2
ethanol-water 19:1	2 min	92	8	< 1	--
$[NaHCO_3]$ = 0.1 N	1 h	33	67	< 1	4
70 °C	2 h	5	95	< 1	5

Table 3: *Preparation of 6-O-acyl-1,2-O-isopropylidene-α-D-glucofuranose (6), by isomerisation of esters* **4** *with a 0.1 N* $NaHCO_3$ *solution of ethanol-water 19:1 at 70 °C.*

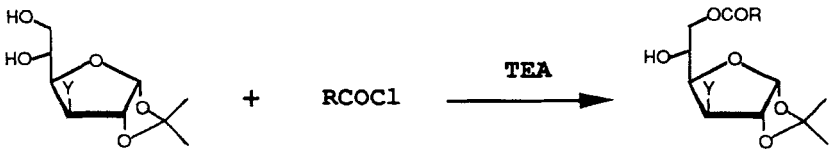
Substrate 4	t (min)	Products distribution (%)		deacylation (%)
		4	6	
$\mathbf{4_a}$	120	5	95	5
$\mathbf{4_b}$	180	4	96	4
$\mathbf{4_c}$	180	2	98	4
$\mathbf{4_d}$	180	1	99	3
$\mathbf{4_e}$	180	1	99	2
$\mathbf{4_g}$	180	3	97	3

Table 4 : *Selective esterification of 1,2-O-isopropylidene-α-D-glucofuranose and the 3-O-alkyl analoguous in step b conditions.*

Y	R	Products distribution (%)		
		6-O-acyl	3,6-di-O-acyl	5,6-di-O-acyl
OH	n-C_7H_{15}	70	20	10
	n-$C_{11}H_{23}$	70	20	10
	n-$C_{15}H_{31}$	70	20	10
O-n-C_8H_{17}	n-C_7H_{15}	96	-	4
O-n-$C_{16}H_{33}$	n-$C_{15}H_{31}$	94	-	6
O-n-$C_{18}H_{37}$	n-C_7H_{15}	95	-	5
	n-$C_{15}H_{31}$	94	-	6

isomerisation is favoured in basic media. The highest yield and fastest isomerisation were obtained with 0.1 N $NaHCO_3$ solution of ethanol-water 19:1 at 70 °C. The aforementionned conditions were applied to 3-O-acyl esters **4**; the results are shown in Table 3.

6-O-octanoyl (**6b**), 6-O-lauroyl (**6c**) and 6-O-palmitoyl (**6d**) esters were also synthesized by acylation in which the corresponding acid chlorides were reacted with 1,2-O-isopropylidene-α-D-glucofuranose, in order to make a quantitative comparison of its selectivity to acylation with that of 3-O-alkyl-1,2-O-isopropylidene-α-D-glucofuranoses :



4' **7**

7bb (Y= n-O-C_8H_{17} ; R = n-C_7H_{15}) ; **7dd** (Y= n-O-$C_{16}H_{33}$; R = n-$C_{15}H_{31}$) ; **7eb** (Y= n-O-$C_{18}H_{37}$; R = n-C_7H_{15}) ; **7ed** (Y= n-O-$C_{18}H_{37}$; R = n-$C_{15}H_{31}$)

In none of the reactions (Table 4) was the presence of a 5-O-acyl monoester identified. Esterification was found to occur preferentially

at site C-6 (95% of 6-*O*-acyl with 3-*O*-alkyl derivatives and 70% with monoacetone glucose). Acylation of secondary OH groups was found to occur in 3,6-di-*O*-acyl and 5,6-di-*O*-acyl derivatives. The relative proportions of these diesters show that site C-5 is less vulnerable to acylation than that of the C-3.

Such vulnerability at site C-5 is observed to an even greater extent with 3-*O*-alkyl derivatives; steric hindrance can explain the lower proportion of 5,6-diester in the latter case (5% instead of 10% for monoacetone glucose).

Step c_2 : *Synthesis of 3-O-acyl-D-glucose* ***5*** *by total deacetalation of type* ***3*** *esters.*

The analysis of the results outlined in Table 1 show that conditions used for step c_1 would lead to poor yields in totally deprotected esters (**5**), because deacylation rates (k_B and k_C) were found to be close to the 1,2-*O*-acetal deprotection rate (k_2). Moreover, we observed that some of the type **5** ester was transformed into ethyl 3-*O*-acyl-**D**-glucoside by reaction with ethanol. Mehltretter[18] prepared 3-*O*-stearoyl-**D**-glucose $\mathbf{5_e}$ in 52% yield using 12 N HCl ether-aqueous 1:1 solution. Glacet[34] obtained 3-*O*-palmitoyl-**D**-glucose ($\mathbf{5_d}$) in 78% yield by the same method, after filtration and washing of the cristallized product; however he could isolate neither the 3-*O*-*n*-octanoyl ($\mathbf{5_b}$) nor the 3-*O*-*n*-lauroyl ($\mathbf{5_c}$) homologue because they failed to precipitate.

We used a 12 N HCl dioxane-aqueous 4:1 solution and obtained total deacetalation of the esters in good yields (65-72%).

B- Surface activity and Bioactivity of some esters synthesized.

1/ Surface activity

Esters of type **4**, **5** and **6** with more than 8 carbon atoms on the alkyl chain have surfactant properties which are characterized, in particular, by their ability to form either emulsions (1 to 5% ester; 50 to 75% water; 45 to 25% vaseline fluid oil) or gels (4 to 8% ester; 50 to 70% water; 45 to 25% vaseline fluid oil), which are stable for several weeks at 20 °C and 40 °C.

Table 5:*Surface-active Characteristics of some esters in water at 25 °C.*

Esters	C.M.C. (10^{-4} M)	γ (mN/m)	H.L.B.	solubility (10^{-4} M)
4b	1.07	34	---	6.8
4c	0.39	30	7.8	0.8
4d	0.11	32	5.4	0.8
4e	0.06	34	4.0	0.6
5b	6.10	32	11.6	23.2
5c	2.29	29	10	11.7
5d	1.44	29	9.3	6.8
5e	1.99	31	8.9	7.0
5g	0.12	21	---	0.6

Table 5 gives, for some of the ester prepared, measurements of micellar critical concentration (C.M.C.), surface tension in water at 25 °C (γ) and hydrophile-lipophile balance (H.L.B.). This table shows that C.M.C. decreases with lipophilicity as it was shown in other works.[39-43]

2/ Acute toxicity

Acute toxicity on Mouse expressed in the dose (g/Kg) which causes mortality of 50% of a group of 10 Mice after 15 days (DL 50), was studied for most of the hereby synthesized esters, by oral way (O.W.) and intraperitoneal way (I.P.W.). Results are presented on Table 6.

Lethal doses of totally deprotected type **5** esters were found to be close to those found for the partially deprotected type **4** esters with the same acyl group.

3/ Antitumoral effects of *n*-butyric esters

It was shown that *n*-butyric acid and its sodium or arginine salts have antitumoral properties on murine and human cells.[44] The esters **3a**, **4a** and **6a** showed the same actvities when studied *in vitro* :

- growth inhibition of tumoral cells without affecting normal cells, and cell-differentiating effects;[45a]

Table 6 : *Lethal doses (DL 50) in g/Kg on a 20 g male weiss Mouse.*

Esters		3_a	4_a	5a	4_b	5_b	4_c	5_c	4_d	5_d	4_e
DL 50	O.W.	> 8	> 8	> 8	> 8	> 8	> 8	> 8	> 8	> 8	> 8
	I.P.W.	1.8	4.2	3	2.5	1.6	3.5	3	>8	> 8	> 8

- enhancement of antitumoral effects of α,β-interferon.[25,45b]

However, no antitumoral activity was observed *in vivo* with *n*-butyric salts because the seric half-life of such derivatives is lower than 5 minutes whereas *n*-butyric esters **3a, 4a** et **6a** have a seric half-life higher than 25 hours.[45c] Thus, low doses of *n*-butyric ester (10 to 20 mg/Kg/week) were found to raise prolonged antitumour effects *in vivo*.

EXPERIMENTAL

General Procedures. Reactions were monitored by HPLC (Waters 721) on reverse phase RP-18 (Merck) and PN 27-196 (Waters) with H_2O-Acetone mixture as eluent or CPG (Girdel) with columns OV 17 and SE 30. Preparative chromatography was performed on silica gel (Matrex 60 mesh) with a hexane-acetone gradient. Specific rotations were determined with a JASCO-DIP 970 polarimeter (Prolabo) and melting points with an Electrothermal automatic apparatus. ^1H NMR and ^{13}C NMR spectra were recorded using a Brucker WP 300 spectrometer. Surface tensions were determined using a Tensimat N° 3 (Prolabo) apparatus. Acetone, hexane, toluene and glucose monohydrate industrial grade were supplied by CINAS. 3'-(F-Octyl)-propionyl was kindly given by Professor A. CAMBON (Université de Nice).

Di-*O*-acetals of D-glucose

1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranose (**2**) was synthesized using the conditions described by Regnaut.[30]

1,2:5,6-Di-*O*-cyclohexylidene-α-D-glucofuranose (**2'**) was synthesized in accordance with the literature[46] procedure, mp 131 °C; $[\alpha]_D^{22}$ -2.4° (*c* 1.1, C_2H_5OH). Lit.[46] mp 131-132 °C; $[\alpha]_D^{25}$ -2.2° (C_2H_5OH).

3,5-*O*-Benzylidene-1,2-*O*-isopropylidene-α-D-glucofuranose (**2"**). To a solution of 1,2-*O*-isopropylidene-α-D-glucofuranose **4₀'**, (50 g, 0.27 mol) in benzaldehyde (106 g, 1 mol) was added $ZnCl_2$ (27 g, 0.2 mol) at room temperature. The mixture was stirred for 15 h during which the reaction was monitored by HPLC (eluent: H_2O-Acetone 1:1). HPLC analysis showed 3 peaks in the ratio 3:1:1, which remained constant after 4 h. The crude product was charged to a silica gel column eluted with a hexane-acetone gradient. The major product obtained (28 g, 40%) corresponded to the first eluted peak, mp 146-147 °C; $[\alpha]_D^{22}$ +22.9° (*c* 1.2, $CHCl_3$).

^{13}C NMR ($CDCl_3$) δ : 104.9 (C_1), 83.8 (C_2), 74.0 (C_3), 77.9 (C_4), 72.9 (C_5), 61.9 (C_6), 111.8 (Me_2C of -1,2), 94.4 (C_6H_5CH of -3,5), 26.7-26.1 (2 x CH_3), (C_6H_5 : 137.6 (C_{ipso}), 129.1 (C_{para}), 128.2 (2 x C_{ortho}), 126.1 (2 x C_{meta}).

Further resolution the reaction mixture was not achieved : a mixture of the *endo* and *exo* diastereoisomers of 5,6-*O*-benzylidene-1,2-O-isopropylidene-α-D-glucofuranose was obtained as an oil (18.7 g, 26%).

Synthesis of type 3 esters

To a stirred solution of dry diacetone glucose (**2**) in anhydrous toluene (120 g/L) was added, at room temperature, 1.1 equivalent of TEA followed by 1 equivalent of acid chloride. After 4 h the solution was filtrated and concentrated to yield, after purification on a silica gel column (100 g for 10 g of crude ester) eluted with a hexane-acetone gradient, the desired ester.

3-*O*-Butanoyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (3a). The above procedure as applied to **2** (26 g, 0.1 mol), TEA (15.4 mL 0.11 mol) and butanoyl chloride (10.5 g, 0.1 mol) yielded 29.5 g (90%) of **3a**. $[\alpha]_D^{22}$ -28.1° (*c* 1.2, $CHCl_3$).

^1H NMR ($CDCl_3$) δ : 5.87 (d, H_1, $J_{1,2}$= 3.6 Hz), 5.27 (d, H_2, $J_{2,3}$= 0 Hz), 4.47 (d, H_3, $J_{3,4}$= 3.1 Hz), 4.41 (dd, H_4, $J_{4,5}$= 7.5 Hz), 4.21 (m, H_5), 4.0-3.9 (2dd, H_6,$H_{6'}$), 1.52-1.31 (4s, 4 x CH_3), 2.33-2.34 (dt, OCOCH_2),

1.25 (m, $OCOCH_2CH_2$), 0.89 (t, CH_3). ^{13}C NMR ($CDCl_3$) δ : 105.2 (C_1), 83.4 (C_2), 75.75 (C_3), 79.8 (C_4), 72.4 (C_5), 67.2 (C_6), 111.6 (Me_2C of -1,2). 108.8 (Me_2C of -5,6), 26.8-25.3 (4 x CH_3), 172.3 (C=O), 34.2 ($OCOCH_2$), 31.8 ($OCOCH_2CH_2$), 14.04 (CH_3 -ω).

Anal. Calcd for $C_{16}H_{26}O_7$ (330.4): C, 58.17; H, 7.93. Found: C, 58.29; H, 8.02.

3-*O*-Octanoyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (3b). Likewise, **2** (19.5 g, 75 mmol), TEA (11.6 mL, 78 mmol) and octanoyl chloride (13.4 g, 75 mmol) gave 26.6 g (92%) of liquid **3b**. $[\alpha]_D^{22}$ -21.0° (*c* 1.25, $CHCl_3$). NMR spectra of the glucosyl moiety were identical to those of **3a**.

Anal. Calcd for $C_{20}H_{34}O_7$ (386.4): C, 62.16; H, 8.85. Found: C, 62.38; H, 8.76.

3-*O*-Lauroyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (3c). Likewise, **2** (13 g, 50 mmol), TEA (7.7 mL, 55 mmol) and lauroyl chloride (10.9 g, 50 mmol) gave 20.7 g (94%) of **3c**. $[\alpha]_D^{22}$ -24,5° (*c* 1.1, $CHCl_3$). NMR spectra of the glucosyl moiety were identical to those of **3a**.

Anal. Calcd for $C_{24}H_{42}O_7$ (442.6): C, 65.13; H, 9.56. Found: C, 65.22; H, 9.67.

3-*O*-Palmitoyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (3d). Likewise, **2** (13 g, 50 mmol), TEA (7.7 mL, 55 mmol) and palmitoyl chloride (10.9 g, 50 mmol) gave 23.4 g (94%) of **3d**. mp 30 °C; $[\alpha]_D^{22}$ -19.6° (*c* 1.2, $CHCl_3$). Lit.[8] mp 44-45 °C; $[\alpha]_J^{22}$ -18.5° (*c* 1.3, $CHCl_3$). NMR spectra of the glucosyl moiety were identical to those of **3a**.

Anal. Calcd for $C_{30}H_{54}O_7$ (526.7): C, 68.41; H, 10.33. Found: C, 68.44; H, 10.37.

3-*O*-Stearoyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (3e). Likewise, **2** (26 g, 0.1 mol), TEA (15.4 mL, 0.11 mol) and stearoyl chloride (30.2 g, 0 1 mol) gave 44.8 g (85%) of **3e**. mp 44-45 °C; $[\alpha]_D^{22}$ -18.5° (*c* 1.3, $CHCl_3$). NMR spectra of the glucosyl moiety were identical to those of **3a**.

Anal. Calcd for $C_{30}H_{54}O_7$ (526.7): C, 68.41; H, 10.33. Found: C, 68.44; H, 10.37.

3-*O*-Oleoyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (3f). Likewise, **2** (26 g, 0.1 mol), TEA (15.4 mL, 0.11 mol) and oleoyl

chloride (30 g, 0.1 mol) gave 44.6 g (85%) of **3f**. $[\alpha]_D^{22}$ -20.8° (*c* 1.2, $CHCl_3$). NMR spectra of the glucosyl moiety were identical to those of **3a**.

Anal. Calcd for $C_{30}H_{52}O_7$ (524.7): C, 68.67; H, 9.99. Found: C, 68.60; H, 9.88.

3-*O*-[3'-(F-Octyl)propionyl]-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (3g). Likewise, **2** (6.5 g, 25 mmol), TEA (3.8 mL, 27 mmol) and 3'-(F-octyl)propionyl chloride (12.7 g, 25 mmol) gave 8.3 g (90%) of **3g**. mp 69-70 °C; $[\alpha]_D^{22}$ -16.3° (*c* 1.1, $CHCl_3$). Lit.[32] mp 67 °C; $[\alpha]_D^{25}$ -15.3° (*c* 1.3, $CHCl_3$).

^{1}H-NMR ($CDCl_3$) δ : 5.87 (d, H_1, $J_{1,2}$= 3.6 Hz), 5.29 (d, H_2, $J_{2,3}$= 0 Hz), 4.47 (d, H_3, $J_{3,4}$= 3.1 Hz), 4.18 (dd, H_4, $J_{4,5}$= 7.5 Hz), 4.05 (m, H_5), 3.4-3.5 (2dd, H_6,$H_{6'}$), 1.52-1.31 (4s, 4 x CH_3), 2.33-2.34 (dt, $OCOCH_2$), 1.25 (m, $OCOCH_2CH_2$). ^{13}C NMR ($CDCl_3$) δ : 104.05 (C_1), 82.2 (C_2), 75.79 (C_3), 78.8 (C_4), 71.3 (C_5), 66.4 (C_6), 111.4 (Me_2C of -1,2), 108.4 (Me_2C of -5,6), 26.8-24.0 (4 x CH_3), 168.8 (C=O), 25.4 ($OCOCH_2$), 24.5 ($OCOCH_2CH_2$), 125-105 (C_8F_{17}).

Anal. Calcd for $C_{23}H_{23}O_7F_{17}$ (734.4): C, 37.61; H, 3.16; F, 43.98. Found: C, 37.80; H, 3.19; F, 44.10.

Kinetic Studies of Acid-catalyzed Deprotection and Deacylation

A solution of substrate (0.02 mole) in 0.1 N or 0.2 N H_2SO_4 of ethanol-water 19:1 prepared in a 100 mL volumetric flask was divided into 5 mL flasks and thermostated at 30 °C or 50 °C. Samples were neutralized with 0.5 N $NaHCO_3$ (2 mL) aqueous solution and then analyzed by HPLC (H_2O-Acetone eluent: from 70:30 for diacetone glucose to 15:85 for palmitic ester) using either 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose or its 6-*O*-alkyl derivatives as an internal standard. k_1 and k_2 were determined by monitoring the decrease in type **3** and **4** esters. k_A, k_B and k_C were determined by monitoring the increase in ethyl esters derived from the substrate types **3**, **4** and **5**. The calculations used to determine the maximum quantity of type **4** ester at t_M, the corresponding time, were based on classical equations applied to successive first order reactions identified in Scheme 2. If at t = 0 ,

$(\mathbf{3})_o = a$, at t, $(\mathbf{3})_t = a - x$, $(\mathbf{4})_t = y$, $(\mathbf{5})_t = z$ ($x = y + z$), compounds **3**, **4** and **5** concentrations at a defined time t is given by the following equations:

$$* \; x = a[1 - \exp(-k_1 t)] \quad (1)$$

$$* \; y = ak_1/(k_1 - k'_1) \; [\exp(-k'_1 t) - \exp(-k_1 t)] \quad (2)$$

$$* \; z = a \left[1 + [(k'_1 \exp(-k_1 t) - k_1 \exp(-k'_1 t)] / (k_1 - k'_1)\right] \quad (3)$$

$$\text{and } t_M = [\ln(k_1/k'_1)] / (k_1 - k'_1) \quad (4)$$

For type **3** compounds, the rates of deprotection k_{1D} and k_A are derived from the relationship $k_1 = k_{1D} + k_A$. For type **4** compounds, the rates of deprotection k_{2D} and k_B are derived from the relationship $k_2 = k_{2D} + k_B$.

Synthesis of type 4 esters

Type **3** ester (20 g) was melted with a 0.2 N H_2SO_4 solution of ethanol-water 19:1 (180 mL) at 50 °C. The reaction was monitored by HPLC (H_2O-Acetone eluent: from 40:60 for butyric ester to 15:85 for stearic ester) until a 95% conversion was achieved. After neutralization to pH 6 with aqueous sodium hydroxide (30%, w/w) Na_2SO_4 was filtered off and the solvent removed by evaporation *in vacuo*. The resulting crude product was purified on a silica gel column using a hexane-acetone gradient.

3-*O*-Butanoyl-1,2-*O*-isopropylidene-α-D-glucofuranose (4a). Application of the above procedure to **3a** (23 g, 70 mmol), yielded 16.3 g (80%) of **4a**. mp 45 °C; $[\alpha]_D^{22}$ +17.5° (*c* 1.1, $CHCl_3$).

^1H NMR ($CDCl_3$) δ: 5.87 (d, H_1, $J_{1,2}$= 3.6), 5.27 (d, H_2, $J_{2,3}$= 0), 4.47 (d, H_3, $J_{3,4}$= 3.1), 4.41 (dd, H_4, $J_{4,5}$= 7.5), 4.21 (m, H_5), 4.0-3.9 (2dd, H_6,$H_{6'}$), 1.52-1.31 (2s, 2 x CH_3), 2.33-2.34 (dt, $OCOCH_2$), 1.25 (m, $OCOCH_2CH_2$), 0.89 (t, CH_3). ^{13}C NMR ($CDCl_3$) δ : 105.2 (C_1), 83.4 (C_2), 75.75 (C_3), 79.8 (C_4), 72.4 (C_5), 67.2 (C_6), 111.6 (Me_2C of -1,2), 26.8-25.3 (2 x CH_3), 172.3 (C=O), 34.2 ($OCOCH_2$), 31.8 ($OCOCH_2CH_2$), 14.04 (CH_3, alkyl).

Anal. Calcd for $C_{13}H_{22}O_7$ (290.3): C, 53.78; H, 7.64. Found: C, 53.50; H, 7.61.

3-*O*-Octanoyl-1,2-*O*-isopropylidene-α-D-glucofuranose (4b). Likewise, **3b** (25 g, 65 mmol) gave 17.7 g (79%) of **4b**. mp 40 °C;

$[\alpha]_D^{22}$ +14.2° (*c* 1.3, $CHCl_3$). NMR spectra of the glucosyl moiety were identical to those of **4a**.

Anal. Calcd for $C_{17}H_{30}O_7$ (346.4): C, 58.94; H, 8.73. Found: C, 58.78; H, 8.59

3-*O*-Lauroyl-1,2-*O*-isopropylidene-α-D-glucofuranose (4c). Likewise, **3c** (25 g, 65 mmol) gave 20.9 g (80%) of **4c**. mp 42 °C; $[\alpha]_D^{22}$ +12.1° (*c* 1.1, $CHCl_3$). NMR spectra of the glucosyl moiety were identical to those of **4a**.

Anal. Calcd for $C_{21}H_{38}O_7$ (402.5): C, 62.66; H, 9.51. Found: C, 62.81; H, 9.59.

3-*O*-Palmitoyl-1,2-*O*-isopropylidene-α-D-glucofuranose(4d). Likewise, **3d** (20 g, 40 mmol) gave 14.3 g (78%) of **4d**. mp 55 °C; $[\alpha]_D^{22}$ +15.8° (*c* 1.1, $CHCl_3$). NMR spectra of the glucosyl moiety were identical to those of **4a**.

Anal. Calcd for $C_{25}H_{46}O_7$ (458.6): C, 65.47; H, 10.11. Found: C, 65.27; H, 10.08.

3-*O*-Stearoyl-1,2-*O*-isopropylidene-α-D-glucofuranose (4e). Likewise, **3e** (39.5 g, 75 mmol) gave 27.8 g (76%) of **4e**. mp 57 °C; $[\alpha]_D^{22}$ +18.9° (*c* 1.2, $CHCl_3$). NMR spectra of the glucosyl moiety were identical to those of **4a**.

Anal. Calcd for $C_{27}H_{50}O_7$ (486.7): C, 66.63; H, 10.35. Found: C, 66.79; H, 10.59.

3-*O*-[3'-(F-Octyl)propionyl]-1,2-*O*-isopropylidene-α-D-glucofuranose (4g). Likewise, **3g** (7 g, 9.5 mmol) gave 5.3 g (80%) of **4g**. mp 99 °C; $[\alpha]_D^{22}$ -12.5° (*c* 1.2, $CHCl_3$).

^{13}C NMR ($CDCl_3$) δ : 104.5 (C_1), 82.1 (C_2), 76.04 (C_3), 77.9 (C_4), 68.0 (C_5), 63.2(C_6), 110.9 (Me_2C of -1,2), 26.2-25.8 (2 x CH_3), 169.8 (C=O), 25.3 ($OCOCH_2$), 24.6 ($OCOCH_2CH_2$), 125-105 (C_8F_{17}).

Anal. Calcd for $C_{20}H_{19}O_7F_{17}$ (694.4): C, 34.59; H, 2.76; F, 46.52. Found: C, 34.78; H, 2.59; F, 46.29

Yields close to those above were obtained when the selective deprotection was undertaken in 19:1 ethanol-water using Amberlite $15H^+$ acid resin. In each case the reaction mixtures contained a type **3** ester (15 g), ethanol-water (100 mL), and resin (30 g). Reactions were undertaken at 60 °C over times ranging from 3 to 10 hours.

Synthesis of type 6 esters

Type **4** ester (10 g) was melted with a 0.2 N $NaHCO_3$ solution of 19:1 ethanol-water (90 mL) at 70 °C. The reaction was monitored by HPLC (H_2O–Acetone eluent: from 60:40 for diacetone glucose to 30:70 for stearic ester) until constant breakdown of isomeric products (120 to 180 min) was observed. After solvent evaporation under vacuum, the products of type **6** were each purified by silica gel chromatography using a hexane–acetone gradient.

6-*O*-Butanoyl-1,2-*O*-isopropylidene-α-D-glucofuranose (6a). Application of the above procedure to **4a** (14.5 g, 50 mmol) yielded 12.3 g (85%) of **6a**. mp 85 °C; $[\alpha]_D^{22}$ -1.1° (*c* 1.1, $CHCl_3$).

^1H NMR ($CDCl_3$) δ : 5.95 (d, H_1, $J_{1,2}$= 3.6 Hz), 4.53 (d, H_2, $J_{2,3}$= 0 Hz), 4.35 (d, H_3, $J_{3,4}$= 2.5 Hz), 4.07 (dd, H_4, $J_{4,5}$= 5.7 Hz), 4.22 (m, H_5), 4.42 (2dd, H_6,$H_{6'}$), 1.48-1.31 (2s, 2 x CH_3), 3.26 (s, OH), 2.36 (t, $OCOCH_2$), 1.63 (m, $OCOCH_2CH_2$), 0.89 (t, CH_3). ^{13}C NMR ($CDCl_3$) δ : 104.9 (C_1), 88.1 (C_2), 75.5 (C_3), 79.2 (C_4), 69.2 (C_5), 66.2 (C_6), 111.8 (Me_2C of -1,2), 26.7-26.1 (2 x CH_3), 174.4 (C=O), 34.1 ($OCOCH_2$), 31.8 ($OCOCH_2CH_2$), 14.04 (CH_3 -ω).

Anal. Calcd for $C_{13}H_{22}O_7$ (290.3): C, 53.78; H, 7.64. Found: C, 53.60; H, 7.61.

6-*O*-Octanoyl-1,2-*O*-isopropylidene-α-D-glucofuranose (6b). Likewise, **4b** (9.6 g, 25 mmol) gave 8.2 g (86%) of **6b**. mp 80 °C; $[\alpha]_D^{22}$ -0.5° (*c* 1.3, $CHCl_3$). NMR spectra of the glucosyl moiety were identical to those of **6a**.

Anal. Calcd for $C_{17}H_{30}O_7$ (346.4): C, 58.94; H, 8.73. Found: C, 58.78; H, 8.59.

6-*O*-Lauroyl-1,2-*O*-isopropylidene-α-D-glucofuranose (6c). Likewise, **4c** (12.5 g, 31 mmol) gave 11.2 g (90%) of **6c**. mp 86 °C, $[\alpha]_D^{22}$ -1.4° (*c* 1.1, $CHCl_3$). NMR spectra of the glucosyl moiety are identical to those of **6a**.

Anal. Calcd for $C_{21}H_{38}O_7$ (402.5): C, 62.66; H, 9.51. Found: C, 63.00; H, 9.70.

6-*O*-Palmitoyl-1,2-*O*-isopropylidene-α-D-glucofuranose(6d). Likewise, **6d** (11.4 g, 25 mmol) gave 10.5 g (92%) of **6d**. mp 82 °C; $[\alpha]_D^{22}$ -1.0° (*c* 1.1, $CHCl_3$). NMR spectra of the glucosyl moiety are identical to those of **6a**.

Anal. Calcd for $C_{25}H_{46}O_7$ (458.6): C, 65.47; H, 10.11. Found: C, 65.51; H, 10.20.

6-*O*-Stearoyl-1,2-*O*-isopropylidene-α-D-glucofuranose (6e). Likewise, **4e** (16.5 g, 35 mmol) gave 15.2 g (92%) of **6e**. mp 95 °C; $[\alpha]_D^{22}$ -0.9° (*c* 1.1, $CHCl_3$). NMR spectra of the glucosyl moiety are identical to those of **6a**.

Anal. Calcd for $C_{27}H_{50}O_7$ (486.7): C, 66.63; H, 10.35. Found: C, 66.90; H, 10.19.

6-*O*-[3'-(F-octyl)-propionyl]-1,2-*O*-isopropylidene-α-D-glucofuranose (6g). Likewise, **4g** (4 g, 5.8 mmol) gave 3.6 g (90%) of **6g**. mp 99 °C; $[\alpha]_D^{22}$ +1.1° (*c* 1.2, $CHCl_3$).

^{13}C NMR ($CDCl_3$) δ : 104.4 (C_1), 84.6 (C_2), 72.8 (C_3), 80.0 (C_4), 65.0 (C_5), 67.04(C_6), 110.4 (Me_2C of -1,2), 26.2-25.8 (2 x CH_3), 170.3 (C=O), 25.3 ($OCOCH_2$), 24.6 ($OCOCH_2CH_2$), 125-105 (C_8F_{17}).

Anal. Calcd for $C_{20}H_{19}O_7F_{17}$ (694.4): C, 34.59; H, 2.76; F, 46.52. Found : C, 34.69; H, 2.69; F, 46.39.

Esterification of 1,2-*O*-isopropylidene-α-D-glucofuranose (4_0') and the 3-*O*-alkyl ethers homologuous (4')

The 3-*O*-R-1,2-*O*-isopropylidene-α-D-glucofuranoses (**4'**) (R= *n*-octyl (**4_b'**), *n*-hexadecyl (**4_d'**) and *n*-octadecyl(**4_e'**)) were synthesized by Chellé.[47] To a stirred mixture of substrate (10 g) and of toluene (100 mL), was added 1.1 equivalent of TEA followed by 1 equivalent of acid chloride. The reaction was heated at 50 °C for 4 h and monitored by HPLC (H_2O-Acetone eluent: from 30:70 for **7bb** to 10:90 for **7ed**). The products of the reaction were extracted and purified using the same conditions as for esters of type **3**.

6-*O*-Acyl-1,2-*O*-isopropylidene-α-D-glucofuranose. The above procedure was applied to substrate **4_0'** (Y = OH) and *n*-octanoyl chloride to give, after purification, the product **6b** in 60% yield.

Likewise, substrate **4_0'** and *n*-lauroyl chloride gave **6c** in 58% yield.

Likewise, substrate **4_0'** and *n*-palmitoyl chloride gave **6d** in 59% yield.

6-*O*-Octanoyl-3-*O*-octyl-1,2-*O*-isopropylidene-α-D-glucofuranose (7bb). Likewise, **4'b** (8.3 g, 25 mmol) and octanoyl chloride (4.4 g, 27 mmol) gave 11 g (96%) of **7bb**. $[\alpha]_D^{22}$ -25.3° (*c* 1.2, $CHCl_3$).

^{1}H NMR ($CDCl_3$) δ : 5.92 (d, H_1, $J_{1,2}$= 3.8 Hz), 4.56 (d, H_2, $J_{2,3}$= 0 Hz), 3.98 (d, H_3, $J_{3,4}$= 3.1 Hz), 4.12 (dd, H_4, $J_{4,5}$= 3.3 Hz), 4.37 (m, H_5), 4.18 (2dd, H_6,$H_{6'}$), 1.48-1.31 (2s, 2 x CH_3), 5.3 (s, OH), 3.64 (m, OCH_2), 2.36 (t, $OCOCH_2$), 1.63-0.89(, 2 x alkyl). ^{13}C NMR ($CDCl_3$) δ : 105.03 (C_1), 82.9 (C_2), 81.9 (C_3), 79.1 (C_4), 68.1 (C_5), 66.3 (C_6), 111.1(Me_2C of -1,2), 26.7,26.2 (2 x CH_3), 174.1 (C=O), 34.1 ($OCOCH_2$), 70.5 (OCH_2), 31.8-13.9(2x alkyl).

Anal. Calcd for $C_{25}H_{46}O_7$ (458.6): C, 65.47; H, 10.11. Found: C, 65.17; H, 10.16

3-*O*-Hexadecyl-6-*O*-palmitoyl-1,2-*O*-isopropylidene-α-D-glucofuranose (7cc). Likewise, **4'c** (10.8 g, 25 mmol) and palmitoyl chloride (5.9 g, 27 mmol) gave 15.1 g (91%) of **7cc**. mp 46 °C; $[\alpha]_D^{22}$ -17.5° (*c* 1.3, $CHCl_3$). NMR spectra of the glucosyl moiety were identical to those of **7bb**.

Anal. Calcd for $C_{41}H_{78}O_7$ (683.1): C : 72.09; H, 11.51. Found: C, 71.59; H, 11.50

3-*O*-Octadecyl-6-*O*-Octanoyl-1,2-*O*-isopropylidene-α-D-glucofuranose (7eb). Likewise, **4'e** (9.3 g, 20 mmol) and octanoyl chloride (3.9 g, 22 mmol) gave 9.9 g (83%) of **7eb**. $[\alpha]_D^{22}$ -17.3° (*c* 1.3, $CHCl_3$). NMR spectra of the glucosyl moiety were identical to those of **7bb**.

Anal. Calcd for $C_{35}H_{66}O_7$ (599): C, 70.26; H, 11.03. Found: C, 69.82; H, 11.18.

3-*O*-Octadecyl-6-*O*-Palmitoyl-1,2-*O*-isopropylidene-α-D-glucofuranose (7eb). Likewise, **4'e** (11.6 g, 25 mmol) and palmitoyl chloride (5.9 g, 27 mmol) gave 16.3 g (92%) of **7eb**. $[\alpha]_D^{22}$ -14.4° (*c* 1.2, $CHCl_3$). NMR spectra of the glucosyl moiety were identical to those of **7bb**.

Anal. Calcd for $C_{43}H_{82}O_7$ (711.1): C, 72.7; H, 11.54. Found: C, 72.73; H, 11.76.

Synthesis of type 5 esters

Type **3** ester was added to a stirred mixture of dioxane (80 mL) and concentrated HCl (20 mL). A conversion of 90-95% was observed after 2 to 4 h at 30 °C. Saturated $NaHCO_3$ solution (10 mL) was added and final neutralization was achieved by small additions of solid $NaHCO_3$. The solution separated into two phases. The upper phase which contained the

ester of type **5**, was concentrated. The resulting residue gave 3-O-acyl-α-**D**-glucopyranose as crystals from either acetone or butanone. Further purification of the residue by silica gel column chromatography using a hexane-acetone gradient gave a mixture of anomers in which the α-anomer was found to be the major component.

3-*O*-Octanoyl-D-glucopyranose (5b). The above procedure was applied to **3b** (7.7 g, 20 mmol) to yield 4 g (65%) of **5b**. mp 140 °C; $[\alpha]_D^{22}$ +68.1° (*c* 1.1, CH_3OH).

^{13}C NMR ($CDCl_3$) δ : 92.2 ($C_{1\alpha}$), 71.6 ($C_{2\alpha}$), 76.7($C_{3\alpha}$), 69.9 ($C_{4\alpha}$), 67.8 ($C_{5\alpha}$), 60.6 ($C_{6\alpha}$), 96.4 ($C_{1\beta}$), 76.2 ($C_{2\beta}$), 79.5($C_{3\beta}$), 70.3 ($C_{4\beta}$), 68.8 ($C_{5\beta}$), 60.6 ($C_{6\beta}$), 174.4 (C=O), 34.1 ($OCOCH_2$), 31.8-14.04 (alkyl).

Anal. Calcd for $C_{14}H_{26}O_7$ (306.3): C, 54.89; H, 8.55. Found: C, 54.60; H, 8.61

3-*O*-Lauroyl-D-glucofuranose (5c). Likewise, **3c** (6.6 g, 15 mmol) gave 3.8 g (70%) of **5c**. mp 152 °C; $[\alpha]_D^{22}$ +59.7° (*c* 1.1, CH_3OH). NMR spectra of the glucosyl moiety are identical to those of **5b**.

Anal. Calcd for $C_{18}H_{34}O_7$ (362.4): C, 59.65; H. 9.45.
Found: C, 60.00; H, 9.30.

3-*O*-Palmitoyl-D-glucofuranose (5d). Likewise, **3d** (5 g, 10 mmol) gave 3 g (72%) of **5d**. mp 160 °C; $[\alpha]_D^{22}$ +48.7° (*c* 0.7, CH_3OH).

Lit.[8] mp 88 °C; $[\alpha]_D^{22}$ +48.7° (*c* 0.7, CH_3OH); lit.[18] mp 116 °C. NMR spectra of the glucosyl moiety were identical to those of **5b**.

Anal. Calcd for $C_{22}H_{42}O_7$ (418.6): C, 63.13; H, 10.11. Found: C, 63.41; H, 10.16.

3-*O*-Stearoyl-D-glucofuranose (5e). Likewise, **3e** (7.9 g, 15 mmol) gave 4.8 g (72%) of **5e**. mp 164°C; $[\alpha]_D^{22}$ +35.2° (*c* 1.0, pyridine). Lit.[34] $[\alpha]_D^{22}$ +59.6° (pyr.); lit.[18] mp 130 °C; $[\alpha]_D^{22}$ +66.5° (pyr., 10min). NMR spectra of the glucosyl moiety were identical to those of **5b**.

Anal. Calcd for $C_{24}H_{46}O_7$ (446.6): C, 64.54; H, 10.38. Found: C, 64.20; H, 10.59.

3-*O*-[3'-(F-Octyl)-propionyl]-D-glucofuranose (5g). Likewise, **3g** (7.3 g,10 mmol) gave 4.2 g (65%) of **5g**. mp 200 °C; $[\alpha]_D^{22}$ +33.7° (*c* 0.5, pyr. 1h->24h). Lit.[32] mp 102°C; $[\alpha]_D^{22}$ +35.0° (*c* 1.1, DMSO).

^{13}C NMR ($CDCl_3$) δ : NMR spectrum of the glucosyl moiety was identical to that of **5b**. 170.2 (C=O), 25.3 ($OCOCH_2$), 24.6 ($OCOCH_2CH_2$), 125-105 (C_8F_{17})

Anal. Calcd for $C_{17}H_{15}O_7F_{17}$ (654.4): C, 31.20; H, 2.31; F, 49.35. Found: C, 31.51; H, 2.39; F, 49.39.

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