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SUGAR CHEMISTRY WITHOUT PROTECTING GROUPS-III. A FACILE CHEMICAL SYNTHESIS OF 6-O-ACYL-D-GLYCOPYRANOSES AND METHYL-6-O-ACYL-D-GLYCOPYRANOSIDES.

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Abstract : Regioselective acylation of non protected glycopyranosides was performed using 3-acylthiazolidine-2-thiones **1** and the novel 3-acyl-5-methyl-1,3,4-thiadiazole-2(3H)-thiones **2** as the acylating reagents, yielding 6-O-acylated derivatives in high yields. Acylation of free α-D-glucose and α-D-galactose using the same conditions lead to the 6-O-acylglycoses. This reaction is compared with our previous synthesis of 1-O-acyl-β-D-glucoses from β-D-glucose.

Partially acylated sugars are of great importance as intermediates in carbohydrate chemistry or as biodegradable surface-active materials. However the numerous methods developed for selective acylation of these polyhydroxylic systems show that this fundamental reaction remains at present difficult to achieve and the purification of the expected products is generally tedious. Even selective acylation of primary hydroxyls over secondary ones can only be seldom achieved [1].

Esters in the 6 position of hexo-pyranoses and-pyranosides are generally obtained according to two main methods. The most used one involves multistep procedures, that is the preliminary synthesis of selectively protected intermediates, followed by esterification of the remaining free hydroxyl and subsequent removal of the protecting group [2].

Nevertheless, some chemical esterifications of free substrates have been already proposed. The selectivity of these reactions is based i) on the regioselective enhancement of the nucleophilicity of hydroxyl groups by the use of tributylstannyloxide [3] or via cobalt chelates [4] or ii) selectivity for primary hydroxyls associated with the use of bulky reagents, thus applying the Mitsunobu reaction in the carbohydrate field [5]

Enzyme-catalysed esterifications of glycosides and free sugars in organic solvents have been extensively studied recently. Indeed monoacylated sugars have been obtained by lipase [6] or protease-catalysed [7] esterifications or transesterifications in pyridine or in DMF. In these reactions, yields are often low in regard of the amounts of enzyme used. Moreover, the efficiency of the acylation is dramatically dependent on the substrate and on the acylating reagent.

To overcome these problems, we have developed a chemical methodology which applies to free hexopyranoses as well as to their glycosides and which is more convenient in matter of yields, reaction times and molar ratios of the reactants as well. In a preliminary communication [8] we have described a rapid and simple method for the preparation of 6-O-acylglucopyranosides and 6-O-acylglucopyranoses from the unprotected sugars and fatty acid derivatives. In the present work, we have generalized this method to various acid derivatives and have shown that it also applies in the manno- and galacto-series.

RESULTS

Our strategy for chemical acylation of unprotected sugars is argued as follows :

a) As acylating reagents, we have selected the 3-acylthiazolidine-2-thiones **1** and the new N-derivatives **2** of 2-mercapto-5-methyl-1,3,4-thiadiazole. We expected that thiazolidine-2-thione and 2-mercapto-5-methyl-1,3,4-thiadiazole formed in these reactions would not bring about intramolecular acyl migrations.

b) The selective activation of the more acidic hydroxyl of the substrate to the corresponding more nucleophilic alkoxide may be achieved by "gradually introducing" a strong base in the reaction mixture.

c) In some cases, we have used organic bases that can act as nucleophilic catalysts.

Preparation of the acylating reagents

N-acylthiazolidine-2-thiones have been previously prepared by the action of thiazolidine-2-thione or its thallium salt on carboxylic acids or acyl chlorides [9]. In our case, we have prepared compounds **1** (85-90 % yields) simply by reacting acyl chlorides on thiazolidine-2-thiones in the presence of triethylamine in dichloromethane [10].

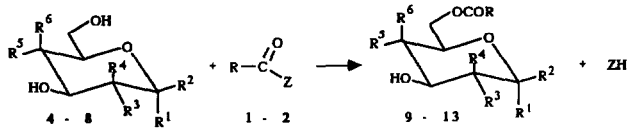
Under the same conditions, or in the presence of pyridine, the reaction of 2-mercapto-5-methyl-1,3,4-thiadiazole [11] with acyl chlorides was quantitative but afforded mixtures of compounds **2** and **3** in which the amides **2** were largely preponderant (**2**:**3** > 90:10). The former were easily purified by recrystallization and thus obtained in 80-95 % yields. The structures of these new compounds [12] were assigned from their spectrometric data. ^{13}C NMR peaks at δ 188-189 ppm supported the thione structures of compounds **2** whereas this peak did not show up in the ^{13}C spectra of thioesters **3**. In the IR spectra of **2**, the carbonyl group was characterized by an absorption band located at a very high frequency ($\nu_{C=O}$ 1750-1765 cm^{-1}) meaning that the nitrogen atom conjugates with the thiocarbonyl group rather than with the carbonyl one. This suggests that amides **2** could be regarded as acyl derivatives with a more effective leaving group than 3-acyl thiazolidine-2-thiones [10].

Selective acylations of methyl-D-glycopyranosides

In our preliminary experiments, we have tested various acylating reagents against glucopyranoside **4** in homogeneous conditions defined in table 1. Compared with the corresponding esters of 8-hydroxyquinoline or of N-hydroxysuccinimide and with palmitoylimidazolide, 3-palmitoylthiazolidine-2-thione **1f** appears to be more convenient in matter of selectivity and efficiency as well.

We demonstrated the generality of the reaction for the synthesis of various 6-O-acylglycopyranosides **9**-**11** (table 2). Reactions of 3-acylthiazolidine-2-thiones with **4** and **6** occurred within 0.5-2 hrs in anhydrous pyridine in the presence of a catalytic amount of NaH or of NaH:DMAP. The yield of 6-O-myristoyl methyl-α-D-

Fig - Synthesis of 6-O-acyl-D-glycopyranoses and 6-O-acyl-methyl-D-glycopyranosides



Methyl-α-D-glucoside	4 →	9	R^1 = OMe ; R^3 = R^5 = OH ; R^2 = R^4 = R^6 = H
Methyl-α-D-mannoside	5 →	10	R^1 = OMe ; R^4 = R^5 = OH , R^2 = R^3 = R^6 = H
Methyl-β-D-galactoside	6 →	11	R^2 = OMe , R^3 = R^6 = OH , R^1 = R^4 = R^5 = H
α-D-glucose	7 →	12	R^1 = OH , R^3 = R^5 = OH , R^2 = R^4 = R^6 = H
α-D-galactose	8 →	13	R^1 = OH , R^3 = R^6 = OH , R^2 = R^4 = R^5 = H

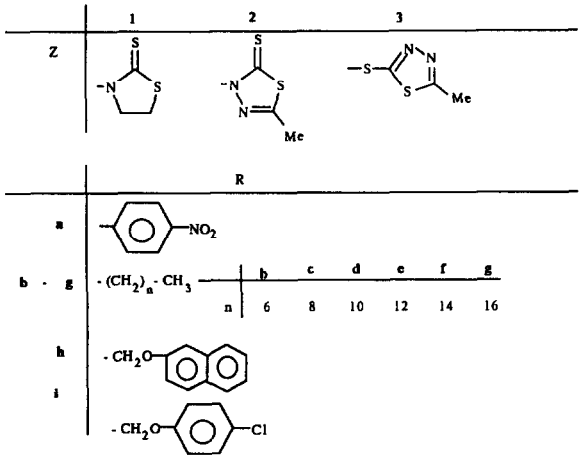
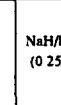


Table 1 Preparation of 6-O-acyl-methyl-α-D-glucopyranosides **9** using various reagents [a]

Run	Reagent	Catalyst (equiv.) [b]	Solvent	Temp (°C)	Reaction time (hr)	ester isolated-yield (%)
1	**1f**	NaH/DMAP (0.25/0.08)	C_5H_5N	r.t.	2	**9f** 88
2	CH_3-$(CH_2)_{16}CO_2$- 	NaH/DMAP (0.25/0.08)	C_5H_5N	r.t.	6	**9g** 44 [c]
2	CH_3-$(CH_2)_{14}CO_2$-N 	NaH/DMAP (0.25/0.08)	C_5H_5N	r.t.	27	**9f** 36 [c]
4	CH_3-$(CH_2)_{14}CO$-N 	NaH/DMAP (0.25/0.08)	C_5H_5N	r.t.	24	**9f** 38 [c]

a) Molar ratio of reagents/**4** 1/2

b) Molar ratio of catalysts to methyl α-D-glucoside **4**

c) Compounds **9** were purified by column chromatography for separating them from 20-30 % (overall yields) of 2-O-acyl and 3-O-acyl-α-D-glucopyranosides

glucopyranoside was only slightly affected by t BuOK, which is easier for use in large scale amounts (run 5). Esters **9a, c, g** and **11d** resulting from a selective acylation of primary hydroxyl were thus isolated in 55-88 % yields (table 2, runs 1-7 and 15) by column chromatography for separating them from small amounts of esters of secondary hydroxyls (yields 2-6 %).

As expected, amides **2** appeared to be more reactive than thiones **1**. Indeed, compound **2d** reacted with methyl-α-D-glucoside **4** at room temperature in pyridine without any additional initiator or catalyst (table 2, run 8) but required 16 hours. The addition of triethylamine and especially of DBU to mixtures of sugars **4-5** and reagents **2** in DMF solutions led to an improvement of the reaction times (table 2, runs 9-13). We thus obtained the expected 6-O-acyl methyl-α-D-gluco-(or manno-) pyranosides in good yields. Compared with acylations of compounds **4** and **6**, reactions with methyl-α-D-mannopyranoside **5** appeared nevertheless to be less selective. Along with the 6-O-acyl compounds **10**, we isolated mixtures of the 2-O-acyl and 3-O-acyl mannopyranosides in 10-12 % overall yields. Esters **9, 10** and **11** were completely analysed from their ^{1}H and ^{13}C NMR spectra. A large downfield shift of the carbon in the 6 position and a smaller upfield shift of the C-5 with respect to unmodified glycosides indicates clearly the position of the acyl group [13].

Selective acylations of free α-hexopyranoses

In a previous work [10], we have shown that 1-O-acyl-β-D-glycoses were at best prepared by reacting active esters of 8-hydroxyquinoline with the β-anomers of reducing sugars. In this work, we tried to acylate selectively α-D-glucose **7** and α-D-galactose **8**. As described in table 3, the α-anomers of free sugars were selectively acylated by the activated amides **1** or **2** in anhydrous pyridine in the presence of NaH : DMAP or in DMF using triethylamine or DBU as the base and/or catalyst (see below) within 0.1-3 hours at room temperature. The 6-O-acyl-D-glycoses **12** and **13** were isolated as mixtures of α and β anomers after column chromatography. The ^{1}H NMR spectra (DMSO-d_6) of these mixtures showed *inter alia* two doublets near δ 4.9 ppm ($J \cong 3.5$ Hz) and 4.3 ppm ($J \cong 7.5$ Hz) characteristic of the anomeric protons of each anomer. Compounds **12** and **13** generally crystallized from ethyl acetate/hexane mixtures, or acetone, or ethanol (see experimental part) as pure α-anomers. These esters did not anomerize within 24 hours in DMSO-d_6 solutions, which made it possible to run their ^{13}C NMR spectra in this solvent, but in deuterated pyridine the signals of the β-anomers could be detected by ^{1}H NMR after three hours at room temperature, which evidences that acylation did not take place at the anomeric hydroxyls.

DISCUSSION

Reactions of glycosides worked in the presence of NaH/DMAP are based on a preliminary activation of the most acidic hydroxyl followed by an acylation of the most nucleophilic oxyanion. In glycosides, the hydroxyl groups at the 2-position are considered as the most acidic ones with a pKa ≅ 12.5 [14]. This can be attributed to the stabilization of the 2-oxyanion by an hydrogen bond with the 3-OH and to the proximity of the electron-withdrawing heterocyclic oxygen. Acylation of the primary hydroxyl can thus be explained by i) acylation at the 2-position and subsequent intramolecular migration of the acyl group or ii) prototropic equilibria between the four oxyanionic forms favored by intramolecular hydrogen bounding in aprotic solvents. As a matter of fact we couldn't isomerize 2-O-lauroylmethyl-α-D-glucopyranoside (prepared by a conventional method [13]) to ester **9d** in the conditions of our

Table 2 : Syntheses of 6-O-monoesters of methyl-D-glycopyranosides using reagents 1 or 2

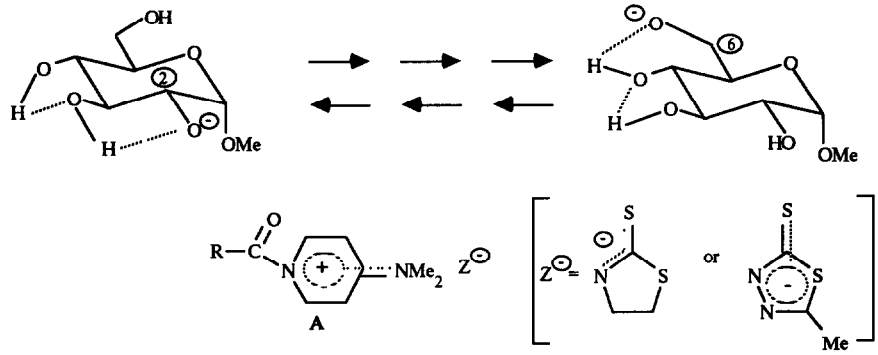
Run	sugar (1 equiv.)	Reagent (0.5 equiv.)	Catalyst (equiv.) [a]	Solvent	Temp. (°C)	Reaction time (hr)	ester isolated-yield (%)
1	4	1a	NaH (0.25)	C_5H_5N	r.t.	0.5	9a : 81
2	4	1c	NaH/DMAP (0.25/0.08)	C_5H_5N	r.t.	2	9c : 66
3	4	1d	NaH/DMAP (0.25/0.08)	C_5H_5N	r.t.	2	9d : 60
4	4	1e	NaH/DMAP (0.25/0.08)	C_5H_5N	r.t.	2	9e : 61
5	4	1e	t-BuOK/DMAP (0.25/0.08)	C_5H_5N	r.t.	2	9e : 55
6	4	1f	NaH/DMAP (0.25/0.08)	C_5H_5N	r.t.	2	9f : 88
7	4	1g	NaH/DMAP (0.25/0.08)	C_5H_5N	r.t.	2	9g : 70
8	4	2d		C_5H_5N	r.t.	16	9d : 60
9	4	2h	DBU (1)	DMF	r.t.	2	9h : 71
10	4	2h	Et_3N (1.5)	DMF	r.t.	2	9h : 32
11	5	2d	Et_3N (1.5)	DMF	r.t.	16	10d : 51
12	5	2h	Et_3N (1.5)	DMF	- 10	3	10h : 55
13	5	2h	DBU (1)	DMF	r.t.	2	10h : 45
14	5	2i	Et_3N (0.25)	DMF	r.t.	20	10i : 45
15	6	1d	NaH (0.25)	C_5H_5N	r.t.	2.5	11d : 75

a) Ratio (molar equiv.) of catalyst(s) to sugar.

Table 3 : Syntheses of 6-O-monoesters of α-D-glycopyranes using reagents 1 or 2

Run	sugar (1 equiv.)	Reagent (0.5 equiv.)	Catalyst (equiv.) [a]	Solvent	Temp. (°C)	Reaction time (hr)	ester isolated-yield (%)
1	7	1b	NaH/DMAP (0.25/0.08)	C_5H_5N	r.t.	1	12b : 60
2	7	1c	NaH/DMAP (0.25/0.08)	C_5H_5N	r.t.	1	12c : 67
3	7	1e	NaH/DMAP (0.25/0.08)	C_5H_5N	r.t.	1	12e : 63
4	7	1i	Et_3N (1.5)	DMF	r.t.	2	12i : 55
5	7	2h	——	C_5H_5N	r.t.	3	12h : 40
6	7	2h	Et_3N (1.5)	DMF	r.t.	2	12h : 60
7	7	2i	Et_3N (1.5)	DMF	r.t.	2	12i : 59
8	7	2i	DBU (1)	DMF	r.t.	0.1	12i : 64
9	8	1c	NaH/DMAP (0.25/0.08)	C_5H_5N	r.t.	2	13c : 66

reaction. Thus we think that acylation by the bulky loose ion pair A can only occure at the most electrophilic 6-oxygen.



Similar adducts can be expected with DBU and even with triethylamine to induce acylations. Moreover, at the same time, the anion Z^- participates to the reaction by a general base catalysis. More surprising is the formation of 6-monoesters of glucose and galactose from the free sugars. Indeed this implies that the anomeric hydroxyl lies in the relatively unreactive α-position, because we found [10] that β-glucose reacted with esters of 8-hydroxyquinoline to give selectively the 1β-monoesters. Although α-hexopyranoses are one-half as acidic as their β-anomers [16], the anomeric hydroxyl remains the most ionizable. But this α-alkoxide is well known to be less nucleophilic than the β one because of the anomeric stereoelectronic effect [17]. The 6-acylation of α-hexopyranoses is thus understandable in terms of prototropic equilibria and acylation of the most electrophilic 6-alkoxide. This reaction still implies that the acylating reagent is sufficiently reactive in order that esterification in the 6 position be faster than the anomerization of α-glycoses (or alkoxides) to β-glycoses.

CONCLUSION

The readily available 3-acylthiazolidine-2-thiones 1 and 3-acyl-5-methyl-1,3,4-thiadiazole-2-(3H)-thiones 2 reacted with unprotected α-hexopyranoses and their methyl glycosides in mild conditions to give good to high yields of 6-O-acylated sugars. Compared with other syntheses actually known, the interest of the present method lies in its generality and simplicity.

EXPERIMENTAL

All reagents were of commercially quality and were purchased from Janssen Chimica or Aldrich Chimie. Thin layer chromatography (TLC) was performed on Merck 60F 254 silica gel unactivated plates. As developers were used the UV light and a solution of 5 % H_2SO_4 in ethanol. For column chromatography, Merck 60H (5-40 μm) silica gel was used. Melting points were taken using a Reichert apparatus and are uncorrected. Optical rotations were measured using a Polartronic D polarimeter. Elemental analyses were made by the "Service de Microanalyse de l'ENSCR". IR spectra were taken using HCB (hexachlorobutadiene) on a Pye-Unicam SP_3-200 spectrophotometer. ^1H- and ^{13}C-NMR were obtained with TMS (tetramethylsilane) as internal standard ; using a Jeol FX 90Q (^1H-90 MHz and ^{13}C-22.5 MHz) spectrometer. All reactions were made under an inert atmosphere and solvents were purified according to general procedures.

8-Acyloxyquinolines, 1-acyloxysuccinimides and 1-acylimidazolides were prepared according to previously described procedures [10,18].

Preparation of 3-acylthiazolidine-2-thiones 1

3-acylthiazolidine-2-thiones were obtained from the appropriated acylchlorides by a method we have previously described [10]. We report here only the new products.

3-(4-nitrobenzoyl)-thiazolidine-2-thione **1a** : yield 85 % ; mp 163-164°C (CH_2Cl_2, n-Hexane) ; IR : $\nu_{C=O}$ 1670 cm^{-1} ; ^1H NMR ($CDCl_3$) δ (ppm) : 3,53 (t, 2H, S-CH_2, J = 7 Hz), 4.60 (t, 2H, N-CH_2, J = 7 Hz), 7.78-8.24 (2d, 4H, arom.) ; ^{13}C NMR ($CDCl_3$) δ (ppm) : 29.89 and 56.08 (C_4 and C_5), 123.95, 129.95, 139.92, 149.72 (arom.), 169.33 (C = O), 202.11 (C = S) ; anal. calcd for $C_{10}H_8NO_3S_2$: C 50.82, H 3.41 ; found : C 50.66, H 3.37.

3-(2-naphthoxyacetyl)-thiazolidine-2-thione **1h** : yield 89 % ; mp 162-164°C (CH_2Cl_2, n-Hexane) ; IR : $\nu_{C=O}$ 1715 cm^{-1} ; ^1H NMR ($CDCl_3$) δ (ppm) : 3,35 (t, 2H, S-CH_2, J = 7.7 Hz), 4.61 (t, 2H, N-CH_2, J = 7.7 Hz), 5.49 (s, 2H, O-CH_2), 7.39-7.79 (m, 7H, arom.) ; ^{13}C NMR ($CDCl_3$) δ (ppm) : 29.59 and 55.59 (C_4 and C_5), 70.17 (O-CH_2), 107.76, 118.68, 124.15, 126.56, 126.99, 127.73, 129.59, 129.78, 134.39, 155.84 (arom.), 169.79 (C = O), 201.54 (C = S) ; anal. calcd for $C_{15}H_{13}NO_2S_2$: C 59.38, H 4.32 ; found : C 59.32, H 4.45.

3-(4-chlorophenoxyacetyl)-thiazolidine-2-thione **1i** : yield 90 % ; mp 128-130°C (CH_2Cl_2, n-Hexane) ; IR : $\nu_{C=O}$ 1710 cm^{-1} ; ^1H NMR ($CDCl_3$) δ (ppm) : 3,40 (t, 2H, H_5, J = 7.6 Hz), 4.62 (t, 2H, H_4, J = 7.6 Hz), 5.49 (s, 2H, O-CH_2), 6.8-7.3 (2d, 4H, arom.) ; anal. calcd for $C_{11}H_{10}ClNO_2S_2$: C 45.90, H 3.68 ; found : C 45.86 ; H, 3.72.

Preparation of 3-acyl-5-methyl-1,3,4-thiadiazole-(3H)-2-thiones 2

To a stirred solution of 2-mercapto-5-methyl-1,3,4-thiadiazole (2.37 g, 18 mmol) and triethylamine (2.8 mL, 20 mmol) in CH_2Cl_2 (40 mL) at 0-5°C was added a solution of the appropriate acylchloride (20 mmol) in the same solvent. Stirring was continued for 2-12 hrs, and the solution was successively washed with 0.5 N HCl (2 x 10 mL), 5 % $NaHCO_3$ (3 x 20 mL) and water (2 x 10 mL). The organic phase was dried ($MgSO_4$) and the solvent evapored *in vacuum*. The residue was recrystallized to afford the amides 2.

amide **2d** : yellow needles ; yield 80 % ; mp 49-51°C (n-Hexane) ; IR : $\nu_{C=O}$ 1750 cm^{-1} ; ^1H NMR ($CDCl_3$) δ (ppm) : 0.88 (t, 3H), 1.26 (m, 16H), 1.73 (m, 2H), 2.47 (s, 3H, CH_3-C), 2.99 (t, 2H, CH_2-CO) ; ^{13}C NMR ($CDCl_3$) δ (ppm) : 13.94 ($\underline{C}H_3$-CH_2), 16.15 ($\underline{C}H_3$-C), 22.49, 23.98, 28.75, 29.16, 29.43, 31.73 [$(CH_2)_9$], 37.61 ($\underline{C}H_2$-CO), 154.89 (C = N), 171.34 (C = O), 188.21 (C = S).

amide **2f** : yellow needles ; yield 85 % ; mp 55-57°C (n-Hexane) ; IR : $\nu_{C=O}$ 1755 cm^{-1} ; ^1H NMR ($CDCl_3$) δ (ppm) : 0.88 (t, 3H), 1.26 (m, 24H), 1.68 (m, 2H), 2.47 (s, 3H, CH_3-C), 2.99 (t, CH_2-CO) ; anal. calcd for $C_{19}H_{34}N_2OS_2$: C 61.57, H 9.25 ; found : C 61.42, H 9.18.

amide **2g** : yellow needles ; yield 95 % ; mp 69-70°C (n-Hexane) ; IR : $\nu_{C=O}$ 1755 cm^{-1} ; ^1H NMR ($CDCl_3$) δ (ppm) : 0.88 (t, 3H), 1.25 (m, 28H), 1.67 (m, 2H), 2.46 (s, 3H, CH_3-C), 2.99 (t, 2H, CH_2-CO) ; ^{13}C NMR ($CDCl_3$) δ (ppm) : 14.02 ($\underline{C}H_3$-CH_2), 16.21 ($\underline{C}H_3$-C), 22.60, 24.06, 28.83, 29.16, 29.59, 31.84 [$(CH_2)_{15}$], 37.69 ($\underline{C}H_2$-CO), 154.92 (C = N), 171.39 (C = O), 188.24 (C = S).

amide **2h** : yellow needles ; yield 82 % ; mp 155-158°C (CH_2Cl_2, n-Hexane) ; IR : $\nu_{C=O}$ 1765 cm^{-1} ; ^1H NMR ($CDCl_3$) δ (ppm) : 2.50 (s, 3H, CH_3-C), 5.32 (s, 2H, CH_2-O), 7.33-7.73 (m, 7H, arom.) ; ^{13}C NMR ($CDCl_3$) δ (ppm) : 16.26 ($\underline{C}H_3$-C), 64.97 (CH_2-O), 107.19, 118.46, 124.07, 126.51, 126.97, 127.54, 129.60, 134.15, 155.57 (arom.), 159.31 (C = N), 171.28 (C = O), 189.30 (C = S) ; anal. calcd for $C_{15}H_{12}N_2O_2S_2$: C 56.94, H 3.82 ; found : C 56.79, H 3.80.

amide **2i** : yellow needles ; yield 88 % ; mp 143-146°C (CH_2Cl_2, n-Hexane) ; IR : $\nu_{C=O}$ 1760 cm^{-1} ; ^1H NMR ($CDCl_3$) δ (ppm) : 2.50 (s, 3H, CH_3-C), 5.20 (s, 2H, O-CH_2), 6.90-7.25 (2d, 4H, arom.) ; anal. calcd for $C_{11}H_9ClN_2O_2S_2$: C 43.92, H 3.02 ; found : C 43.77, H 3.25.

Preparation of 6-O-acylmethyl-α-D-glucopyranosides 9

Method A

Methyl-α-D-glucopyranoside **4** (1.9 g, 10 mmol) and the appropriate acylating reagent **1** or **3** (5 mmol) were dissolved in 30 mL of anhydrous pyridine. Sodium hydride (60 % dispersion in mineral oil, 2.5 mmol) along with DMAP (0.8 mmol, 0.1 g) were then added at room temperature. The solution was then stirred at the same temperature until decolorization had occured and the reaction was monitored by TLC (AcOEt, MeOH : 9/1, v/v). After addition of AcOH (0.5 mL), the solvent was removed *in vacuum* at 40°C. The residue was then shared between a phosphate buffer (pH 7 ; 30 mL) and a mixture containing EtOAc/n-BuOH (4/1, v/v ; 30 mL). The aqueous phase was extracted twice with the same mixture (2 x 20 mL) and the combined organic layers were washed with water (3 x 10 mL) and evaporated. The residue was chromatographied on a silica gel column (solvent : ethyl acetate and then ethyl acetate/methanol : 15/1 and 9/1).

Method B

Methyl-α-D-glucopyranoside **4** (1.9 g, 10 mmol), the acylating reagent **1** or **2** (5 mmol) and Et_3N (2.1 mL, 15 mmol) or DBU (1.5 mL, 10 mmol) were dissolved in dry DMF (25 mL). After the reaction had proceeded to completion, the mixture was worked as described in the above general procedure.

Ester **9a** : white needles ; yield 81 % ; mp 123-126°C (ethyl acetate, diethylether) ; TLC : Rf = 0,48 ; $[\alpha]^{20}_D$ + 90 (c = 0.5, methanol) ; IR : ν_{OH} 3520, 3350 and 3200, $\nu_{C=O}$ 1725 cm^{-1} ; ^1H NMR (DMSO-d_6) δ (ppm) : 3.32 (s, 3H, OCH_3), 3.40-4.50 (m, 6H, H_2-H_6), 4.60 (d, 1H, H_1, J = 3.2 Hz), 4.84, 4.85, 5.28 (3d, 3H, OH_2-OH_4),

8.20-8.50 (2d, arom.) ; ^{13}C NMR (DMSO-d_6) δ (ppm) : 54.51 (OCH_3), 65.18 (C_6), 69.51 (C_5), 70.43 (C_4), 71.87 (C_2), 73.25 (C_3), 99.85 (C_1), 123.90, 130.57, 135.12 and 150.29 (arom.), 164.18 (C = O).

Ester **9c** : yield 66 % ; mp 53-54°C (acetone) ; TLC : Rf = 0,49 ; $[\alpha]^{20}_D$ + 110 (c = 1, methanol) ; IR : ν_{OH} 3350 cm^{-1} (broad) , $\nu_{C=O}$ 1725 cm^{-1} ; ^1H NMR (DMSO-d_6) δ (ppm) : 0.89 (t, 3H, $C\underline{H}_3$-CH_2), 1.29 (m, 12H), 1.51 (m, 2H), 2.30 (t, 2H, CH_2-CO), 3.33 (s, 3H, O-CH_3), 2.70-3.80 (m, 6H, H_2-H_6), 4.56 (d, 1H, H_1, J = 3 Hz), 4.75, 4.85 and 5.10 (3d, 3H, OH_2-OH_4) ; ^{13}C NMR (DMSO-d_6) δ (ppm) : 13.88 (CH_3), 22.06, 24.47, 28.42, 28.64, 28.72, 28.83, 31.24 and 33.51 [CH_3-($\underline{C}H_2$)$_8$], 54.29 (O-CH_3), 63.58 (C_6), 69.59 (C_5), 70.46 (C_4), 71.84 (C_2), 73.22 (C_3), 99.71 (C_1), 172.69 (C = O) ; anal. calcd for $C_{17}H_{32}O_7$: C 58.60, H 9.26 ; found : C 58.42, H 9.38.

Ester **9d** : yield 60 % ; mp 70-72°C (acetone) ; TLC : Rf = 0,50 ; $[\alpha]^{20}_D$ + 108 (c = 1, methanol) ; IR : ν_{OH} 3350 cm^{-1} (broad) , $\nu_{C=O}$ 1730 cm^{-1} ; ^1H NMR (DMSO-d_6) δ (ppm) : 0.92 (t, 3H, $C\underline{H}_3$-CH_2-), 1.35 (m, 18H), 1.55 (m, 2H), 2.32 (t, 2H, CH_2-CO), 3.36 (s, 3H, O-CH_3), 2.80-4.50 (m, 6H, H_2-H_6), 4.56 (d, 1H, H_1, J = 3 Hz), 4.77, 4.86 and 5.10 (3d, 3H, OH_2-OH_4) ; ^{13}C NMR (DMSO-d_6) δ (ppm) : 13.82 (CH_3), 22.11, 24.47, 28.48, 28.75, 29.04, 31.32 and 33.51 [CH_3-($\underline{C}H_2$)$_{10}$], 54.26 (O-CH_3), 63.61 (C_6), 69.59 (C_5), 70.49 (C_4), 71.84 (C_2), 73.25 (C_3), 99.74 (C_1), 172.63 (C = O) ; anal. calcd for $C_{19}H_{36}O_7$: C 60.77, H 9.66 ; found : C 60.51, H 9.77.

Ester **9e** : yield 61 % ; mp 80-81°C (acetone) (lit.[13b]) ; ^{13}C NMR (DMSO-d_6) δ (ppm) : 13.86 (CH_3), 22.04, 24.42, 28.39, 28.66, 28.83, 28.97, 31.25 and 33.47 [CH_3-($\underline{C}H_2$)$_{12}$-], 54.25 (O-CH_3), 63.53 (C_6), 69.53 (C_5), 70.38 (C_4), 71.77 (C_2), 73.15 (C_3), 99.67 (C_1), 172.72 (C = O).

Ester **9f** : yield 88 % ; mp 86-89°C (acetone) (lit.[19]) ; ^{13}C NMR (DMSO-d_6) δ (ppm) : 13.85 (CH_3), 22.00, 24.41, 28.37, 28.61, 28.94, 31.21 and 33.46 [CH_3-($\underline{C}H_2$)$_{14}$-], 54.26 (O-CH_3), 63.50 (C_6), 69.54 (C_5), 70.38 (C_4), 71.76 (C_2), 73.14 (C_3), 99.66 (C_1), 172.69 (C = O).

Ester **9g** : yield 70 % ; mp 91-93°C (acetone) ; TLC : Rf = 0.50 ; IR : ν_{OH} 3350 cm^{-1} (broad) , $\nu_{C=O}$ 1725 cm^{-1} ; ^1H NMR (DMSO-d_6) δ (ppm) : 0.87 (t, 3H, $C\underline{H}_3$-CH_2-), 1.27 (m, 28H), 1.45 (m, 2H), 2.30 (t, 2H, CH_2-CO), 3.30 (s, 3H, O-CH_3), 2.90-4.45 (m, 6H, H_2-H_6), 4.56 (d, 1H, H_1, J = 3.5 Hz), 4.76, 4.87 and 5.11 (3d, 3H, OH_2-OH_4) ; ^{13}C NMR (DMSO-d_6) δ (ppm) : 13.84 ($\underline{C}H_3$-CH_2-), 22.00, 24.39, 28.34, 28.60, 28.92, 31.20 and 33.43 [CH_3-($\underline{C}H_2$)$_{16}$-], 54.24 (O-CH_3), 63.47 (C_6), 69.49 (C_5), 70.32 (C_4), 71.73 (C_2), 73.10 (C_3), 99.62 (C_1), 172.73 (C = O) ; anal. calcd for $C_{25}H_{48}O_7$: C 65.18, H 10.50 ; found : C 64.85, H 10.52.

Ester **9h** : yield 71 % ; mp 82-84°C (ethyl acetate) ; TLC : Rf = 0.47 ; IR : ν_{OH} 3400 cm^{-1} (broad) , $\nu_{C=O}$ 1760 cm^{-1} ; ^1H NMR (DMSO-d_6) δ (ppm) : 3.23 (s, 3H, O-CH_3), 3-4.40 (m, 6H, H_2-H_6), 4.53 (d, 1H, H_1, J = 3.5 Hz), 4.79, 4.89, 5.18 (3d, 3H, OH_2-OH_4), 4.95 (s, 2H, O-CH_2), 7.20-7.40 (m, 7H, arom.) ; ^{13}C NMR (DMSO-d_6) δ (ppm) : 54.72 (O-CH_3), 64.58 (C_6), 64.99 (O-CH_2), 69.70 (C_5), 70.34 (C_4), 71.92 (C_2), 73.33 (C_3), 99.93 (C_1), 107.52, 118.54, 124.23, 126.80, 127.02, 127.78, 129.08, 129.75, 134.25, 155.70 (arom.), 169.80 (C = O).

Preparation of 6-O-acylmethyl-α-D-mannopyranosides 10

Compounds **10** were prepared as described above for their epimers **9** (method B).

Ester **10d** : yield 51 % ; oily product ; TLC : Rf = 0.56 ; IR : ν_{OH} 3410 cm^{-1} (broad) , $\nu_{C=O}$ 1745 cm^{-1} ; ^1H NMR (DMSO-d_6) δ (ppm) : 0.88 (t, 3H, $\underline{C}H_3$-CH_2-), 1.26 (m, 18 H), 2.31 (t, 2H, CH_2-CO), 3.26 (s, 3H, OCH_3), 3.20-4.50 (m, 6H, H_2-H_6), 4.52 (d, 1H, H_1, J = 1.5 Hz), 4.57, 4.82, 4.97 (3d, 3H, OH_2-OH_4) ; ^{13}C NMR (DMSO-d_6) δ (ppm) : 14.12 ($\underline{C}H_3$-CH_2-), 22.65, 25.01, 29.16, 29.37, 29.61, 31.94 and 34.06 [(CH_3($\underline{C}H_2$)$_{10}$], 54.29 (O-CH_3), 64.50 (C_6), 67.54 (C_4), 70.46 (C_2), 71.16 (C_3 and C_5), 101.48 (C_1), 173.31 (C = O).

Ester **10h** : yield 55 % ; amorphous powder ; TLC : Rf = 0.54 ; IR : ν_{OH} 3340 cm^{-1} (broad) , $\nu_{C=O}$ 1755 cm^{-1} ; ^1H NMR (DMSO-d_6) δ (ppm) : 3.21 (t, 3H, OCH_3), 3.30-4.50 (m, 6H, H_2-H_6), 4.54 (d, 1H, H_1, J = 1.2 Hz), 4.73, 4.87, 5.06 (3d, 3H, OH_2-OH_4), 4.95 (s, 2H, O-CH_2), 7.30-7.83 (m, 7H, arom.) ; ^{13}C NMR (DMSO-d_6) δ (ppm) : 54.13 (O-CH_3), 64.66 (C_6), 64.83 (O-CH_2), 66.99 (C_4), 70.22 (C_2), 70.79 and 70.82 (C_3 and C_5), 101.20 (C_1), 107.35, 118.41, 123.99, 126.56, 126.86, 127.56, 128.89, 129.51, 134.14, 155.57 (arom.), 168.76 (C = O) ; anal. calcd for $C_{19}H_{22}O_8$: C 60.31, H 5.86 ; found : C 59.92, H 5.86.

Ester **10i** : yield 45 % ; oily product ; TLC : Rf = 0.54 ; IR : ν_{OH} 3400 cm^{-1} (broad) , $\nu_{C=O}$ 1750 cm^{-1} ; ^{13}C NMR (DMSO-d_6) δ (ppm) : 54.45 (O-CH_3), 64.83 (C_6), 65.23 (O-CH_2), 67.13 (C_4), 70.38 (C_2), 70.89 (C_3), 71.08 (C_5), 101.39 (C_1), 116.70, 125.50, 129.59, 156.81 (C arom.), 169.00 (C = O).

Preparation of 6-O-lauroylmethyl-β-D-galactoside 11d

Compound **11d** was obtained as described above for esters **9** (method A).

Ester **11d** : yield 75 % ; mp 84°C (ethyl acetate) ; TLC : Rf = 0.54 ; $[\alpha]^{20}_D$ - 8 (c = 0.5, MeOH) ; IR : ν_{OH} 3250 cm^{-1} (broad) , $\nu_{C=O}$ 1740 cm^{-1} ; ^1H NMR (DMSO-d_6) δ (ppm) : 0.88 (t, 3H, $C\underline{H}_3$-CH_2-), 1.26 (m, 18 H), 2.31 (t, CH_2-CO), 3.39 (s, 3H, O-CH_3), 3-4.25 (m, 6H, H_2-H_6), 3.99 (d, 1H, H_1, J = 8.1 Hz), 4.62, 4.79, 4.96 (3d, 3H, OH_2-OH_4) ; ^{13}C NMR (DMSO-d_6) δ (ppm) : 13.79 ($C\underline{H}_3$-CH_2-), 22.08, 24.47, 28.45, 28.72, 28.88, 29.02, 31.29 and 33.46 [(CH_3($\underline{C}H_2$)$_{10}$], 55.59 (O-CH_3), 63.47 (C_6), 68.43 (C_4), 70.22 (C_2), 72.17 (C_5), 73.03 (C_3), 104.30 (C_1), 172.58 (C = O) ; anal. calcd for $C_{19}H_{36}O_7$: C 60.77, H 9.66 ; found : C 60.45, H 9.84.

Preparation of 6-O-acyl-D-glucoses 12

6-O-acylglucoses were prepared as described for esters **9**. Compounds **12b, c** and **e** were obtained using method A, and compounds **12h-i** were synthesized usind method B.

Ester **12b** : yield 60 % ; crystallized as the α-anomer from ethyl acetate/n-hexane, mp 133-135°C (lit.[13a]) ; TLC : Rf = 0.31 ; $[\alpha]^{20}_D$ + 85 (c = 0.3, pyridine, measured after 2 hrs) ; IR : ν_{OH} 3450, 3320 and 3160 cm^{-1}, $\nu_{C=O}$ 1730 cm^{-1} ; ^1H NMR (DMSO-d_6) δ (ppm) : 0.88 (t, 3H, CH_3), 1.31 and 1.54 (m, 10H), 2.31 (t, 3H, $C\underline{H}_2$-CO), 2.85-4.60 (m, 6H, H_2-H_6), 4.93 (d after isotopic exchange with D_2O, 1H, H_1, J = 3.5 Hz), 4.53, 4.76, 5.04 (3d, 3H, OH_2-OH_4), 6.36 (d, 1H, OH_1) ; ^{13}C NMR (DMSO-d_6) δ (ppm) : 13.89 (CH_3), 22.04, 24.49, 28.40, 28.68,

31.12 and 33.50 [$(CH_3(\underline{C}H_2)_6$], 63.89 ($C_6$), 69.23 ($C_5$), 70.64 ($C_4$), 72.29 ($C_2$), 72.97 ($C_3$), 92.39 ($C_1$), 173.03 (C = O) ; anal. calcd for $C_{14}H_{26}O_7$: C 54.89, H 8.55 ; found : C 54.90, H 8.73.

Ester **12c** : yield 66 % ; crystallized as the α-anomer from ethyl acetate/n-hexane, mp 134-135°C (lit.[13a]) ; TLC : Rf = 0.31 ; $[\alpha]^{20}_D$ + 83 (c = 0.4, pyridine, measured after 2 hrs) ; IR : ν_{OH} 3470, 3330 and 3170 cm^{-1}, $\nu_{C=O}$ 1730 cm^{-1} ; ^1H NMR (DMSO-d_6) δ (ppm) : 0.89 (t, 3H, CH_3), 1.31 and 1.54 (m, 10H), 2.31 (t, 3H, CH_2-CO), 2.80-4.50 (m, 6H, H_2-H_6), 4.56, 4.78, 5.06 (3d, 3H, OH_2-OH_4), 4.96 (d after isotopic exchange with D_2O, 1H, H_1, J = 3.5 Hz), 6.40 (d, 1H, OH_1) ; ^{13}C NMR (DMSO-d_6) δ (ppm) : 13.88 (CH_3), 22.06, 24.17, 28.42, 28.64, 28.72, 28.83, 31.24 and 33.46 [$(CH_3(\underline{C}H_2)_8$], 63.82 ($C_6$), 69.13 ($C_5$), 70.57 ($C_4$), 72.19 ($C_2$), 72.90 ($C_3$), 92.27 ($C_1$), 172.85 (C = O) ; anal. calcd for $C_{16}H_{30}O_7$: C 57.46, H 9.04 ; found : C 57.05, H 9.11.

Ester **12e** : yield 63 % ; crystallized as the α-anomer from ethyl alcohol, mp 136-139°C (lit.[13a]) ; TLC : Rf = 0.33 ; IR : ν_{OH} 3440, 3320 and 3150 cm^{-1}, $\nu_{C=O}$ 1730 cm^{-1} ; ^{13}C NMR (DMSO-d_6) δ (ppm) : 13.98 (CH_3), 22.38, 24.74, 28.86, 29.07, 29.42, 31.65 and 33.81 [$(CH_3(\underline{C}H_2)_{12}$], 64.01 ($C_6$), 69.43 ($C_5$), 70.73 ($C_4$), 72.36 ($C_2$), 73.17 ($C_3$), 92.46 ($C_1$), 173.28 (C = O) ; anal. calcd for $C_{20}H_{38}O_7$ 1/2 H_2O : C 60,12, H 9.84 ; found : C 59.92, H 9.93.

Ester **12h** : yield 60 % ; crystallized as the α-anomer from acetone, mp 172-174°C ; TLC : Rf = 0.26 ; IR : ν_{OH} 3470, 3340 and 3250 cm^{-1}, $\nu_{C=O}$ 1755 cm^{-1} ; ^1H NMR (DMSO-d_6) δ (ppm) : 3.00-4.50 (m, 6H, H_2-H_6), 4.57, 4.80, 5.13 (3d, 3H, OH_2-OH_4), 4.92 (s, 2H, O-CH_2), 4.94 (d after isotopic exchange with D_2O, 1H, H_1), 6.41 (d, 1H, OH_1), 7.30-7.80 (m, 7H, arom.) ; ^{13}C NMR (DMSO-d_6) δ (ppm) : 64.58 (C_6), 64.75 (O-CH_2), 69.11 (C_5), 70.51 (C_4), 72.22 (C_2), 79.93 (C_3), 92.40 (C_1), 107.38, 118.35, 123.90, 126.45, 126.78, 127.51, 128.78, 129.43, 134.01, 155.46 (arom.), 168.80 (C = O).

Ester **12i** : yield 64 % ; obtained as a mixture of α and β anomers, mp 105-120°C ; TLC : Rf = 0.28 ; IR : ν_{OH} 3220 cm^{-1} (broad), $\nu_{C=O}$ 1760 cm^{-1} ; ^1H NMR (DMSO-d_6) δ (ppm) : α-anomer : 4.92 (d after isotopic exchange with D_2O, 1H, H_1, J = 3.8 Hz), 6.58 (d, 1H, OH_1) ; β-anomer : 4.37 (d after isotopic exchange with D_2O, 1H, H_1, J = 7.1 Hz), 6.71 (d, 1H, OH_1) ; ^{13}C NMR (DMSO-d_6) δ (ppm) : 64.75 (C_6 α and β), 65.21 (O-CH_2 α and β), 69.32 (C_5 α) ; 70.24 (C_4 β), 70.57 (C_4 α), 72.33 (C_2α), 73 09 (C_3 α), 73.63 (C_5 β), 74.90 (C_2β), 76.50 (C_3 β), 92.54 (C_1 α), 97.11 (C_1 β), 116.73, 125.45, 129.57, 156.73 (arom.), 168.92 (C = O α and β).

Preparation of 6-O-lauroyl-α-D-galactose

Compound **13d** was prepared using method A.

Ester **13d** : yield 66 % ; crystallized as the α-anomer from ethyl acetate, mp 113-116°C ; TLC : Rf = 0.35 ; IR : ν_{OH} 3400 cm^{-1} (broad), $\nu_{C=O}$ 1725 cm^{-1} ; ^{13}C NMR (DMSO-d_6) δ (ppm) : 13.88 (CH_3), 22.03, 24.39, 28.39, 28.58, 28.64, 28.77, 31.21, 33.41(CH_2), 63.91 (C_6), 67.59 (C_5), 68.48 (C_2), 69.00 (C_3), 69.21 (C_4), 92.59 (C_1), 172.82 (C = O) ; anal. calcd for $C_{16}H_{30}O_7$, 1/2 H_2O : C 55.96, H 9.10 ; found : C 55,69, H 9.19.

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