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A new synthesis of 6-*O*-acylsucroses and of mixed 6,6′-di-*O*-acylsucroses

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Abstract

Various 6-*O*-acylsucroses were synthesized in good yields from unprotected sucrose in *N,N*-dimethylformamide and the appropriate 3-acylthiazolidine-2-thiones **6** or 3-acyl-5-methyl-1,3,4-thiadiazole-2(3*H*)-thiones **7**. A selective ionization of the free sugar by sodium hydride or triethylamine, followed by acylation with **6**, gave 2-*O*-acylsucroses which were subjected in situ to intramolecular isomerizations using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) or an aqueous solution of triethylamine to yield 6-*O*-acylsucroses. The later were otherwise obtained directly when sucrose was acylated with **6** or **7** in the presence of DBU. Moreover, mixed 6,6′-di-*O*-acylsucroses were readily obtained from 6′-monoacylates by using a Mitsunobu reaction without involving the concomitant formation of the 3′,4′-epoxide.

Keywords: 6-*O*-Acylsucroses; 6,6′-Di-*O*-acylsucroses; Regiochemistry; Acylation

1. Introduction

We have previously reported on a new highly regioselective synthesis of 2-*O*-acylsucroses **1** based on a selective ionization of the free sugar to a more nucleophilic and stabilized 2-oxyanion [1]. We have otherwise shown that the ratio of base to

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substrate had to be maintained as low as possible in order to avoid the formation of other regioisomers, especially 6-*O*-acylsucroses **3** [1]. We now report on a new efficient synthesis of 6-*O*-acylsucroses which are useful intermediates for the introduction of a chlorine substituent at C-4 of the glucopyranosyl unit and thus in the synthesis of sucralose [2,3] a high intensity sweetener [4]. Such monoesters of sucrose and fatty acids become furthermore of primary interest owing to their surfactant properties [5–7], especially for the selective extraction of membrane proteins with retention of their native properties [8,9]. Besides, we have evaluated reactions of monoacyl sucroses under selected conditions designed to investigate the synthesis of sucrose diesters.

2. Results and discussion

Synthesis of 6-O-acylsucroses.—Acyl migrations through ortho acid intermediates are frequently observed in partially acylated carbohydrates and occur in various acidic, basic and even neutral media [10,11]. As they lead to complex mixtures, they are not generally used on a preparative scale [3]. We expected that carefully controlled isomerization of the readily available 2-*O*-acylsucroses **1** [1] could lead to 6-*O*-acylsucroses.

In a first experiment, we carried out the acylation of sucrose with 3-(naptht-2-oxyacetyl)-5-methyl-1,3,4-thiadiazole-2(3*H*)-thione (**7h**) in 95:5 *N,N*-dimethylformamide–water in the presence of triethylamine. Aliquots were removed at regular intervals and analyzed by LC. The data summarized in Table 1 show that a 2-*O*-acyl group in **1h**, initially formed, showed a tendency to migrate towards O-3 and that 3-*O*-acylsucrose **2h** isomerized to 6-*O*-acylsucrose **3h**, whereas migrations of the acyl group from the glucose moiety to the fructose ring appeared to be insignificant. However, isomerization was incomplete or partially reversible. We thus investigated other reaction conditions in order to increase the yields of 6-*O*-acylsucroses **3** through isomerization of 2-*O*- and 3-*O*-acylsucroses.

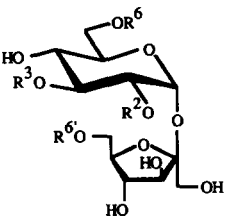
Table 1
Acylation of sucrose with thione **7h** in the presence of triethylamine in *N,N*-dimethylformamide containing 5% (v/v) of water [a]

Composition of mixtures of sucrose monoesters (LC, %) [b]				
Time (h)	**1h**	**2h**	**3h**	Others
3	56	9	27	
9	39	32	29	
24	22	27	46	4
48	14	20	60	7
120	14	20	60	7

[a] Sucrose (10 mmol) and thione **7h** (5mmol) were dissolved in *N,N*-dimethylformamide (30 mL) containing 5% of water (v/v). Triethylamine (20 mmol) was then added in one portion at room temperature and the mixture was stirred at the same temperature.

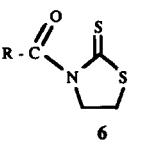
[b] The compositions of the mixtures of (naptht-2-oxyacetyl)sucroses were determined by LC analysis of aliquots using a 250×4.6 mm Spherisorb 5W column and a mixture containing 90:8.4:1.3:0.3 $CHCl_3$–MeOH–AcOH–H_2O as eluent.

Isomerization of 2-*O*-lauroylsucrose **1b** was found to occur quantitatively in *N,N*-dimethylformamide (DMF) in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) or 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) at room temperature within 2 h. Only trace amounts (< 1%) of sucrose or diesters were found by GLC or LC analyses in the mixtures, indicating that the migrations proceeded intramolecularly. 6-*O*-Lauroylsucrose **3b** was thus produced in a 60% yield along with 7–8% of ester **2b**, and small amounts of 6'- and/or 1'-acylates. Analogous results were obtained from 3-*O*-lauroylsucrose **2b**[1] either in DMF in the presence of DBU or in a mixture of DMF and a phosphate buffer at pH 9, indicating that the migration between O-2 and O-3 was irreversible. However, the acyl migration from O-3 to O-6 proceeded via a reversible pathway.

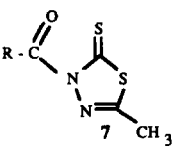


1 R^3, R^6, $R^{6'}$, H; R^2, CO-R **2** R^2, R^6, $R^{6'}$, H; R^3, CO-R

3 R^2, R^3, $R^{6'}$, H; R^6, CO-R **4** R^2, R^3, R^6, H; $R^{6'}$, CO-R



6



7

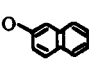
$R = (CH_2)_n - CH_3$

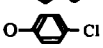
n	6	10	12	16
	a	b	c	d

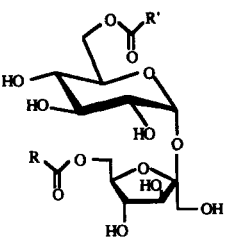
$R = (CH_2)_n - C_6H_5$

n	2	3
	e	f

$R = CH(C_6H_5)_2$ **g**

$R = CH_2 - O$  **h**

$R = CH_2 - O$  Cl **i**



R \ R'	$(CH_2)_3$-C_6H_5	CH=CH-C_6H_5	C_6H_5
$(CH_2)_6$-CH_3	**5j**	**5k**	**5l**
$(CH_2)_{10}$-CH_3	**5m**	**5n**	**5o**

The next step was to ascertain whether these intramolecular isomerizations were of general application. When the same reaction conditions were applied to octanoyl **1a**, stearoyl **1d**, and naptht-2-oxyacetyl **1h** derivatives, migrations of acyl groups took place, respectively, within 7, 24, and 0.25 h at room temperature.

In order to make the syntheses more practical, and to avoid the purification of intermediate 2-*O*-acylsucroses, acylations and isomerizations were performed in a one-pot procedure. Thus acylation of free sucrose with 3-octanoylthiazolidine-2-thione **6a**, 3-lauroylthiazolidine-2-thione **6b**, 3-(napthht-2-oxyacetyl)thiazolidine-2-thione **6g** and 3-stearoyl-5-methyl-1,3,4-thiadiazole-2(3*H*)-thione **7d** [12] in DMF and in the presence of triethylamine or of a catalytic amount of sodium hydride, followed by isomerization in the presence of DBU, yielded respectively 6-*O*-acylsucroses **3a**, **b**, **g**, and **d** in moderate to good yields (see Experimental). As an example, 6-*O*-octanoylsucrose **3a** was thus isolated in a 64% yield. When acylation was carried out in the presence of triethylamine, isomerization could be performed simply by adding water to the mixture and stirring the hydroorganic solution for 24 to 48 h at room temperature. Hydrolysis of esters under these conditions could be minimized, since esters of aryloxyacetic acids **3h–i** were obtained in 43% yields.

Furthermore, we successfully attempted the one-step synthesis of 6-*O*-acylsucroses by acylating free sucrose in anhydrous DMF in the presence of DBU. Again 6-*O*-octanoyl-, 6-*O*-palmitoyl-, and 6-*O*-stearoyl-sucroses **3a**, **3c**, and **3d** were isolated, after column chromatography, respectively, in 60, 56, and 58% yields.

The preferential reactivity of the 6-hydroxyl group with 3-acylthiazolidine-2-thiones **6** and 3-acyl-5-methyl-1,3,4-thiadiazole-2(3*H*)-thiones **7** in the presence of DBU is noteworthy. DBU is known to be a strong base and to work as a nucleophilic catalyst [13], whereas, as we previously described [14], selectivity was enhanced towards 6′-*O*-acylsucroses **4** when a weaker base, such as 1,4-diazabicyclo[2.2.2]octane (DABCO), was used [15].

The structures of 6-*O*-acylsucroses **3** were supported by the ^{13}C NMR data along with elemental analysis and mass spectrometry. In comparison with that of the parent sugar, a large downfield shift for the resonance of C-6 (ca. +3 ppm) along with an upfield shift for the resonance of C-5 (ca. −2 ppm) was in accord with the general trend observed by Yoshimoto et al. [24]. We have recently reported a structural characterization and a comparison of their ion spray mass spectra with those of other regioisomers[25]. Thus, the present methodology opens a straightforward approach to 6-*O*-acylsucroses under mild conditions[27] and makes it possible to synthesize a variety of compounds which are otherwise difficult to obtain[16,17].

*Synthesis of 6,6′-di-*O*-acylsucroses.*—Diesters of sucrose may be considered as non-ionic surfactants suitable for the preparation of biomimetic membranes[18,19].

In order to prepare such derivatives, we have first attempted to introduce a second acyl chain on derivatives **1** and **3** by using reagents **6** or **7**, either in DMF in the presence of organic bases such as DABCO, 1,8-bis(dimethylamino)napthtalene or 4-dimethylaminopyridine (DMAP), or in pyridine with a catalytic amount of sodium hydride. In such conditions, mixtures of di-, tri-, and poly-esters were revealed by chromatographic analyses, resulting from isomerizations, acylations, and/or transesterifications.

6,6′-Di-*O*-palmitoylsucrose has already been prepared from free sucrose by Bottle

and Jenkins [17] by using a Mitsunobu reaction[20]. Unfortunately, such substitution reactions generally proceed in addition with oxirane formation at the 3′ and 4′ positions [21,22].

Our first attempts to acylate derivatives **1** and **3** by octanoic or phenylbutyric acids, in the presence of triphenylphosphine and diisopropylazodicarboxylate (DIAD) in DMF, led to mixtures of monoesters with a poor overall conversion yield.

To overcome these problems, we therefore tried to apply the former reaction to 6′-acylates **4**[14] by using 2 molar equivalents of carboxylic acid and 2.5 molar equivalents of triphenylphosphine and DIAD. The substitution reaction occurred readily within 18–48 h at room temperature. The diesters turned out to be the 6,6′-di-*O*-acylsucroses **5**, which were isolated in 43–64% yields, and we never could reveal the presence of other regioisomers. Obviously, this method allows convenient access to a series of sucrose diesters bearing two different acyl groups respectively on the glucosyl and on the fructosyl moities. It is noteworthy that these reaction conditions are adapted to the introduction of an aliphatic acyl chain, a benzoyl group or even a functional group exhibiting polymerisation ability. Moreover, the use of 6′-*O*-acylsucroses as starting materials seems to prevent any formation of α-D-glucopyranosyl 3,4-anhydro-β-D-tagatofuranoside derivatives [21–23].

Relative to sucrose, the ^{13}C NMR spectra of the 6,6′-diesters revealed a downfield shift of +3.5 and +3.7 ppm, respectively, for the resonances of C-6 and C-6′, and an upfield shift of −2.6 and −3.5 ppm, respectively, for the resonances of C-5 and C-5′. Our attempts to obtain structural information on these novel diesters using EIMS were not conclusive. In contrast, the ion spray mass spectra gave abundant protonated molecules $[M + H]^+$ as well as adducts corresponding to $[M + H + H_2O]^+$. As an example, 6-*O*-benzoyl-6′-*O*-octanoyl sucrose **5l** gave ions at respectively m/z 573 and 591. The low energy CAD MS/MS spectra for the $[M + H]^+$ ion of this compound gave two different fragmentation pathways leading to either the $[MH - H_2O]^+$ at m/z 555 or the fragment Z^+ at m/z 289 [26].

3. Experimental

General methods.—All melting points were determined using a Reichert apparatus and are uncorrected. Elemental analyses were made by the Service Central d'Analyse du CNRS, Vernaison (France) or by the Service de Microanalyse de l'ENSCR, Rennes (France). Thin layer chromatography (TLC) was performed on Merck $60F_{254}$ Silica Gel nonactivated plates. UV light and a solution of 5% H_2SO_4 in EtOH were used to develop the plates. For column chromatography, Merck 60H (5–40 μm) Silica Gel was used. GC analyses were performed on a VEGA GC 6000 gas chromatograph using N_2 as carrier and an Altech column (15 m × 0.32 mm i.d.) coated with OV 1 (film thickness 0.5 μm). LC analyses were performed using a Spectra Physics SP 8800 apparatus, an LDC Spectromonitor III detector, and a 250 × 4.6 mm Spherisorb 5W column. Optical rotations were measured using a Polartronic D polarimeter. IR spectra were recorded using HCB (hexachlorobutadiene) on a Pye Unicam SP3-200 spectrophotometer. ^1H NMR spectra were recorded at 89.5 MHz using a Jeol FX90 Q spectrometer. ^{13}C NMR spectra were determined at 22.5 or at 75 MHz using a Jeol FX 90 Q or a Brucker AM

300 spectrometer. Electron impact (EI) mass spectra were determined on a Varian MAT 311 spectrometer at 70 eV.

Ion spray mass spectra were obtained using an API III triple quadrupole mass spectrometer (SCIEX, Thornhill, Ontario, Canada) equipped with an atmospheric pressure ionization (API) source operated in the ion spray mode.

All reagents were of commercially quality and were purchased from Janssen Chimica or Aldrich Chemical Co. Solvents were purified according to general procedures and reactions were performed under N_2. Compounds **1**, **2**, and **4** were prepared as previously described [1,14].

General procedures for the synthesis of 6-O-acylsucroses.—Method A. Sucrose(3.4 g, 10 mmol) was dissolved in anhyd DMF (30 mL) by heating at 80°C for 10 min. The solution was cooled to room temperature and 3-acylthiazolidine-2-thione **6**[12](5 mmol), followed by Et_3N (2.1 mL, 15 mmol), were added. The mixture was stirred at the same temperature for 15.5 h and DBU (1.5 mL, 10 mmol) was added. The mixture was stirred for another 7 h. After acidification with AcOH and evaporation of the DMF in vacuo, the solid residue was partitioned between a phosphate buffer (pH 7, 20 mL) and a mixture containing 1:1 EtOAc–*n*-butanol (40 mL). The aqueous phase was extracted twice with the same mixture (2 × 10 mL) and the combined organic layers were washed with water (3 × 10 mL) and concentrated. The crude mixtures were then chromatographied on a silica gel column using a 5:95 → 10:90 MeOH–EtOAc step-gradient mixture to give a 64% yield of **3a** and a 53% yield of **3d**.

6-O-Octanoylsucrose (**3a**).—From 3-octanoylthiazolidine-2-thione (**6a**, 1.23 g); amorphous powder (1.49 g, 64%); $[\alpha]_D^{20}$ + 36° (*c* 1, MeOH); IR (HCB): 3350 (br, OH) and 1730 (C = O) cm^{-1}. ^{13}C NMR (Me_2SO-d_6, 22.5 MHz): δ 13.90 (CH_3), 22.03, 24.41, 28.37, 28.45, 31.13, and 33.38 (CH_2), 62.28 (C-1′), 62.58 (C-6′), 63.53 (C-6), 70.05 (C-5), 70.16 (C-4), 71.54 (C-2), 72.71 (C-3), 74.55 (C-4′), 77.10 (C-3′), 82.73 (C-5′), 91.51 (C-1), 103.91 (C-2′), and 172.99 (C = O). EIMS (Me_3Si derivative): *m/z* 505 (1, $[M - 467]^+$), 451 (12, $[M - 521]^+$), 437 (15), 415 (16), 361 (100), 271 (65), 259 (6), 217 (55), 204 (3), 191 (6), 133 (3), 103 (17), 73 (68). Anal. Calcd. for $C_{20}H_{36}O_{12} \cdot H_2O$: C, 49.37; H, 7.87. Found: C, 49.36; H, 7.77.

6-O-Stearoylsucrose (**3d**).—From 3-stearoyl-5-methyl-1,3,4-thiadiazole-2(3*H*)-thione (**7d**, 1.99 g); amorphous powder (1.6 g, 53%); $[\alpha]_D^{20}$ + 39° (*c* 1, MeOH); lit. [28]; IR (HCB) 3380 (br, OH) and 1730 (C = O). ^{13}C NMR (Me_2SO-d_6, 22.5 MHz): δ 13.88 (CH_3), 22.03, 24.39, 28.48, 28.64, 28.99, 31.24, and 32.33 (CH_2), 62.20 (C-1′), 62.52 (C-6′), 63.50 (C-6), 69.97, and 70.11 (C-4 and C-5), 71.52 (C-2), 72.65 (C-3), 74.52 (C-4′), 77.04 (C-3′), 82.70 (C-5′), 91.45 (C-1), 103.86 (C-2′), and 172.93 (C = O). Anal. Calcd. for $C_{30}H_{56}O_{12} \cdot H_2O$: C, 57.48; H, 9.32. Found: C, 57.36; H, 9.24.

Method B. 6-*O*-Lauroylsucrose **3b** and 6-*O*-diphenylacetylsucrose **3g** were prepared from a solution of sucrose (3.4 g, 10 mmol) in anhyd DMF and using the appropriate 3-acylthiazolidine-2-thione [12], respectively, **6b** and **6g** (5 mmol) as acylating reagent and NaH (10 mg, 0.25 mmol). When decolorization had occurred, DBU (2.25 mL, 15 mmol) was added and isomerization was performed at room temp within 12 h. Compounds **3b** and **3g** were worked up as described in the above procedure.

6-O-Lauroylsucrose (**3b**).—From 3-lauroylthiazolidine-2-thione (**6b**, 1.5 g); hygroscopic powder from acetone (1.25 g, 48%); $[\alpha]_D^{20}$ + 46° (*c* 1, MeOH); lit. [28]; IR

(HCB) 3380 (br, OH) and 1735 (C = O) cm^{-1}. ^{13}C NMR (Me_2SO-d_6,22.5 MHz): δ 13.90 (CH_3), 22.06, 24.41, 28.48, 28.69, 28.99, 31.27 and 33.35 (CH_2), 62.28 (C-1′), 62.55 (C-6′), 63.55 (C-6), 70.03 (C-5), 70.14 (C-4), 71.54 (C-2), 72.71 (C-3), 74.55 (C-4′), 77.12 (C-3′), 82.70 (C-5′), 91.51 (C-1), 103.91 (C-2′), and 172.96 (C = O). EIMS (Me_3Si derivative): m/z 561 (24, $[M - 467]^+$), 451 (26, $[M - 577]^+$), 471 (18), 437 (27), 361 (100), 271 (39), 315 (3), 217 (91), 204 (9), 191 (7), 133 (4), 103 (14), 73 (82). Anal. Calcd. for $C_{24}H_{44}O_{12}$: C, 54.95; H, 8.45. Found: C, 55.30; H, 8.72.

6-O-Diphenylacetylsucrose (**3g**).—From 3-diphenylacetylthiazolidine-2-thione (**6g**, 1.56 g); white powder from acetone (0.69 g, 26%); mp 109–111°C; IR (HCB) 3400 (br, OH) and 1740 (C = O) cm^{-1}. ^{13}C NMR (D_2O and 1% 1,4-dioxane, 22.5 MHz): δ 57.46 (CH), 62.55 (C-1′), 63.09 (C-6′), 64.20 (C-6), 70.30 (C-4), 71.46 (C-5), 71.87 (C-2), 73.22 (C-3), 74.90 (C-4′), 77.67 (C-3′), 82.27 (C-5′), 92.97 (C-1), 104.56 (C-2′), 128.21, 129.46, and 139.15 (Ar), and 174.72 (C = O). Anal. Calcd. for $C_{26}H_{32}O_{12}$: C, 58.20; H, 6.01. Found: C, 57.95; H, 6.18.

Method C. Acylations of sucrose (3.4 g, 10 mmol) with thiones **7h** and **7i**[12] were performed in DMF (30 mL) and Et_3N (2.8 mL, 20 mmol) within 15 min at room temperature. Water (5 mL) was then added and the mixture was stirred for 24–48 h. Compounds **3h** and **3i** were worked up as described in Method A.

6-O-(Naptht-2-oxyacetyl)sucrose (**3h**).—From 3-(napthyt-2-oxyacetyl)-5-methyl-1,3,4-thiadiazole-2(3*H*)-thione (**7h**, 1.58 g); white crystals from acetone (1.1 g, 43%); mp 190–193°C; $[\alpha]_D^{20}$ + 47.8° (*c* 0.73, MeOH); IR (HCB) 3400 (br, OH) and 1740 (C = O) cm^{-1}. ^{13}C NMR (Me_2SO-d_6,22.5 MHz): δ 62.36 (C-1′), 62.55 (C-6′), 64.37 (C-6), 64.64 (OCH_2), 70.03 (C-4 and C-5), 71.54 (C-2), 72.74 (C-3), 74.58 (C-4′), 77.03 (C-3′), 82.68 (C-5′), 91.51 (C-1), 103.99 (C-2′), 107.33, 118.32, 123.90, 126.45, 126.83, 127.48, 128.78, 129.43, 134.03, and 155.46 (Ar), and 168.57 (C = O). EIMS (Me_3Si derivative): m/z 451 (31, $[M - 579]^+$), 437 (32), 361 (100), 271 (14), 217 (57), 204 (5), 191 (6), 133 (1), 103 (24), 73 (54). Anal. Calcd. for $C_{24}H_{30}O_{13}$: C, 54.75; H, 5.70. Found: C, 54.59; H, 5.82.

6-O-(4-Chlorophenoxyacetyl)sucrose (**3i**).—From 3-(4-chlorophenoxyacetyl)-5-methyl-1,3,4-thiadiazole-2(3*H*)-thione (**7i**, 1.5 g); white crystals from MeOH–$CHCl_3$ (1.05 g, 43%); mp 131–135°C; $[\alpha]_D^{20}$ + 49° (*c* 0.82, MeOH); IR (HCB) 3380 (br, OH) and 1740 (C = O) cm^{-1}. ^{13}C NMR (D_2O + 1% 1,4-dioxane, 22.5 MHz): δ 62.42 (C-1′), 63.23 (C-6′), 64.83 (C-6), 65.88 (OCH_2), 70.38 (C-4), 71.03 (C-5), 71.87 (C-2), 73.25 (C-3), 74.98 (C-4′), 77.53 (C-3′), 82.26 (C-5′), 92.92 (C-1), 104.59 (C-2′), 116.92, 127.13, 130.30, and 155.79 (Ar), and 171.20 (C = O). Anal. Calcd. for $C_{20}H_{27}O_{13}Cl \cdot H_2O$: C, 45.42; H, 5.52. Found: C, 45.70; H, 5.33.

Method D. 6-*O*-Octanoylsucrose **3a**, 6-*O*-palmitoylsucrose **3c** and 6-*O*-stearoylsucrose **3d** were obtained by acylation of sucrose (3.4 g, 10 mmol) in anhyd DMF (30 mL) using DBU (2.25 mL, 15 mmol) as a catalyst from the appropriate reagent [12], respectively, 3-octanoylthiazolidine-2-thione **6a** (1.23 g, 5 mmol), 3-palmitoyl-5-methyl-1,3,4-thiadiazole-2(3*H*)-thione **7c** (1.72 g, 5 mmol), and 3-stearoylthiazolidine-2-thione **6d** (1.99 g, 5 mmol). Reactions were performed at room temperature for 16–24 h and compounds **3a**, **3c**, and **3d** were isolated, through our usual purification procedure, respectively, in 60, 56, and 58% yields.

6-O-Palmitoylsucrose (**3c**).—Hygroscopic powder from EtOAc (1.54 g, 56%); $[\alpha]_D^{20}$

+ 42° (*c* 0.95, MeOH); lit. [17]; $[\alpha]_D$ + 40° (*c* 1, C_5H_5N); IR (HCB) 3400 (br, OH) and 1735 (C = O) cm^{-1}. ^{13}C NMR (Me_2SO-d_6, 22.5 MHz): δ 13.98 (CH_3), 22.25, 24.55, 28.69, 28.88, 29.33, 31.48, and 33.49 (CH_2), 62.44 (C-1'), 62.63 (C-6'), 63.63 (C-6), 70.24 (C-4 and C-5), 71.68 (C-2), 72.84 (C-3), 74.69 (C-4'), 77.31 (C-3'), 82.79 (C-5'), 91.70 (C-1), 104.02 (C-2'), and 173.09 (C = O). Anal. Calcd. for $C_{28}H_{52}O_{12} \cdot 2H_2O$: C, 54.52; H, 9.15. Found: C, 54.76; H, 8.98.

*General procedure for the synthesis of 6,6'-di-*O*-acylsucroses.*—6'-*O*-Acylsucrose (0.5 g) was dissolved in 20 mL of anhyd DMF at room temperature. The appropriate carboxylic acid was added followed by Ph_3P, respectively, 2.14 mmol and 2.67 mmol for the acylation of 6'-*O*-octanoylsucrose **4a**, and 1.91 mmol and 2.39 mmol for the acylation of 6'-*O*-lauroylsucrose **4b**. The solution was cooled to 0°C and DIAD was added: 2.67 mmol for the acylation of **4a**; 2.39 mmol for the acylation of **4b**. The mixture was stirred at room temperature for 18 to 48 h. The reaction was monitored by TLC using 40:8:1.6:0.4 EtOAc–MeOH–AcOH–H_2O. The solvent was removed in vacuo at 35–40°C. Then, the solid residue was subjected to column chromatography, eluting with 15:1 EtOAc–MeOH.

*6-*O*-(4-Phenylbutyryl)-6'-*O*-octanoylsucrose* (**5j**).—From 6'-*O*-octanoylsucrose (**4a**, 0.5 g); amorphous compound (0.28 g, 43%); $[\alpha]_D^{20}$ + 33° (*c* 0.97, MeOH); IR (HCB) 3400 (OH) and 1730 (C = O) cm^{-1}. ^{13}C NMR (Me_2SO-d_6, 22.5 MHz): δ 13.82 (CH_3), 21.95, 24.36, 28.29, 31.02, 33.27 [$(CH_2)_6$], 26.25, 32.78, 34.33 [$C_6H_5(CH_2)_3$], 61.90 (C-1'), 63.82 (C-6), 65.56 (C-6'), 70.00 and 70.22 (C-4 and C-5), 71.46 (C-2), 72.63 (C-3), 74.85 (C-4'), 76.45 (C-3'), 79.10 (C-5'), 91.48 (C-1), 104.10 (C-2'), 125.72, 128.21, 141.40 (Ar), 172.66 and 172.71 (C = O). EIMS (Me_3Si derivative): *m/z* 525 (2, $[M - 521]^+$), 505 (34, $[M - 541]^+$), 491 (31), 435 (8), 415 (30), 361 (27), 271 (100), 217 (45), 204 (14), 191 (9), 133 (4), 103 (14), 73 (79). Anal. Calcd. for $C_{30}H_{46}O_{13}$: C, 58.61; H, 7.54. Found: C, 58.35; H, 7.81.

*6-*O*-Cinnamoyl-6'-*O*-octanoylsucrose* (**5k**).—From 6'-*O*-octanoylsucrose (**4a**, 0.5 g); amorphous compound (0.3 g, 43%); $[\alpha]_D^{20}$ + 50.7° (*c* 0.83, MeOH); IR (HCB) 3400 (OH), 1730 (C = O) and 1640 (C = C) cm^{-1}. ^{13}C NMR (Me_2SO-d_6, 22.5 MHz): δ 13.85 (CH_3), 21.95, 24.36, 28.29,31.05, 33.27 (CH_2), 62.01 (C-1'), 64.42 (C-6), 65.50 (C-6'), 70.16 and 70.43 (C-4 and C-5), 71.46 (C-2), 72.71 (C-3), 74.88 (C-4'), 76.58 (C-3'), 79.07 (C-5'), 91.48 (C-1), 104.13 (C-2'), 117.89 (C = C), 128.29, 128.83, 130.38, 134.06 (Ar), 144.54 (C = C), 166.24 and 172.80 (C = O). EIMS (Me_3Si derivative): *m/z* 509 (5, $[M - 521]^+$), 505 (13, $[M - 525]^+$), 491 (8), 419 (14), 415 (13), 361 (15), 271 (100), 217 (22), 204 (6), 191 (3), 133 (3), 103 (8), 73 (44).

*6-*O*-Benzoyl-6'-*O*-octanoylsucrose* (**5l**).—From 6'-*O*-octanoylsucrose (**4a**, 0.5 g); amorphous compound (0.38 g, 63%); $[\alpha]_D^{20}$ + 35.3° (*c* 0.96, MeOH); IR (HCB) 3400 (OH) and 1730 (C = O) cm^{-1}. ^{13}C NMR (Me_2SO-d_6, 22.5 MHz): δ 13.88 (CH_3), 21.98, 24.36, 28.31, 31.05, and 33.27 (CH_2), 61.82 (C-1'), 64.42 (C-6), 65.31 (C-6'), 70.14 (C-4 and C-5), 71.63 (C-2), 72.76 (C-3), 75.04 (C-4'), 76.64 (C-3'), 79.07 (C-5'), 91.86 (C-1), 104.43 (C-2'), 128.64, 129.61, 129.73, 133.19 (Ar), 165.78 and 172.51 (C = O). EIMS (Me_3Si derivative): *m/z* 505 (20, $[M - 499]^+$), 483 (1, $[M - 521]^+$), 491 (25), 415 (28), 393 (15), 361 (27), 271 (100), 217 (35), 204 (13), 191 (9), 133 (4), 103 (11), 73 (84). Anal. Calcd. for $C_{27}H_{40}O_{13}$: C, 56.63; H, 7.04. Found: C, 56.32; H, 7.51.

6-O-(4-Phenylbutyryl)-6'-O-lauroylsucrose (**5m**).—From 6'-*O*-lauroylsucrose (**4b**, 0.5 g); amorphous compound (0.26 g, 41%); $[\alpha]_D^{20}$ + 34.8° (*c* 0.52, MeOH); IR (HCB) 3400 (OH) and 1740 (C = O) cm^{-1}. ^{13}C NMR (Me_2SO-d_6, 22.5 MHz): δ 13.88 (CH_3), 22.03, 24.36, 28.39, 28.64, 28.83, 28.94, 31.24, and 33.29 [$(CH_2)_{10}$], 26.28, 32.81, and 34.35 [$C_6H_5(CH_2)_3$], 61.93 (C-1'), 63.85 (C-6), 65.56 (C-6'), 70.03 and 70.24 (C-4 and C-5), 71.46 (C-2), 72.65 (C-3), 74.88 (C-4'), 76.47 (C-3'), 79.13 (C-5'), 91.51 (C-1), 104.13 (C-2'), 125.72, 128.21, and 141.40 (Ar), 172.66 and 172.74 (C = O). EIMS (Me_3Si derivative): *m/z* 561 (9, $[M - 541]^+$), 525 (2, $[M - 577]^+$), 547 (13), 471 (14), 435 (8), 361 (18), 271 (100), 217 (37), 204 (12), 191 (8), 133 (5), 103 (13), 73 (65). Anal. Calcd. for $C_{34}H_{54}O_{13} \cdot H_2O$: C, 59.29; H, 8.19. Found: C, 59.14; H, 8.22.

6-O-Cinnamoyl-6'-O-lauroylsucrose (**5n**).—From 6'-*O*-lauroylsucrose (**4b**, 0.5 g); amorphous compound (0.28 g, 45%); $[\alpha]_D^{20}$ +40.8° (*c* 0.91, MeOH); IR (HCB) 3400 (OH), 1730 (C = O) and 1640 (C = C) cm^{-1}. ^{13}C NMR (Me_2SO-d_6, 22.5 MHz): δ 13.88 (CH_3), 22.03, 24.33, 28.34, 28.64, 28.91, 31.24, 34.24 (CH_2), 61.93 (C-1'), 64.39 (C-6), 65.53 (C-6'), 70.14 and 70.41 (C-4 and C-5), 71.46 (C-2), 72.68 (C-3), 74.85 (C-4'), 76.42 (C-3'), 79.07 (C-5'), 91.48 (C-1), 104.13 (C-2'), 117.89 (C = C), 128.29, 128.81, 130.35, and 134.03 (Ar), 144.52 (C = C), 166.21 and 172.77 (C = O). EIMS (Me_3Si derivative): *m/z* 561 (12, $[M - 525]^+$), 509 (2, $[M - 577]^+$), 547 (19), 471 (22), 419 (6), 361 (27), 271 (100), 217 (34), 204 (9), 191 (8), 133 (3), 103 (14), 73 (78). Anal. Calcd. for $C_{33}H_{50}O_{13} \cdot 3/2H_2O$: C, 58.14; H, 7.84. Found: C, 58.44; H, 7.56.

6-O-Benzoyl-6'-O-lauroylsucrose (**5o**).—From 6'-*O*-lauroylsucrose (**4b**, 0.5 g); amorphous compound (0.38 g, 64%); $[\alpha]_D^{20}$ + 36.4° (*c* 0.96, MeOH); IR (HCB) 3400 (OH) and 1730 (C = O) cm^{-1}. ^{13}C NMR (Me_2SO-d_6, 22.5 MHz): δ 13.90 (CH_3), 22.06, 24.33, 28.37, 28.64, 28.94, 31.24, and 33.24 (CH_2), 61.82 (C-1'), 64.42 (C-6), 65.31 (C-6'), 70.11 (C-4 and C-5), 71.60 (C-2), 72.71 (C-3), 75.01 (C-4'), 76.58 (C-3'), 79.05 (C-5'), 91.83 (C-1), 104.40 (C-2'), 128.62, 129.19, 129.73, and 133.14 (Ar), 165.73 and 172.66 (C = O). EIMS (Me_3Si derivative): *m/z* 561 (15, $[M - 499]^+$), 483 (1, $[M - 577]^+$), 547 (26), 471 (19), 393 (6), 361 (15), 271 (100), 217 (47), 204 (13), 191 (9), 133 (4), 103 (14), 73 (77). Anal. Calcd. for $C_{31}H_{48}O_{13}$: C, 59.22; H, 7.69. Found: C, 59.01; H, 7.96.

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References

[1] C. Chauvin, K. Baczko, and D. Plusquellec, *J. Org. Chem.*, 58 (1993) 2291–2295.
[2] C.K. Lee, *Carbohydr. Res.*, 162 (1987) 53–63.
[3] P.J. Simpson, EP 0260979 (1988); *Chem. Abstr.*, 109 (1988) 110844e.

[4] L. Hough and R. Khan, in T.H. Grenby (Ed.), *Progress in Sweeteners*, Elsevier, New York, 1989, pp 97–120.
[5] L. Hough, *ACS Symp. Ser.*, 41 (1977) 9–21.
[6] J.R. Hurford, in C.K. Lee (Ed.), *Developments in Food Carbohydrates*, Applied Science Publishers, Barking, 1980, pp 327–350.
[7] R.W. Boggs, *Fette, Seifen, Anstrichm.*, 88 (1986) 154–158.
[8] D. Abran, F. Boucher, T. Hamanaka, K. Hiraki, Y. Kito, K. Koyama, R.M. Leblanc, H. Machida, G. Munger, M. Seidou, and M. Tessier, *J. Colloid Interface Sci.*, 128 (1989) 230–236.
[9] T. Katoh, M. Mimuro, and S. Takaichi, *Biochim. Biophys. Acta*, 976 (1989) 233–240.
[10] R. Khan, *Adv. Carbohydr. Chem. Biochem.*, 33 (1976) 235–254.
[11] A.H. Haines, *Adv. Carbohydr. Chem. Biochem.*, 33 (1976) 11–109.
[12] K. Baczko and D. Plusquellec, *Tetrahedron*, 47 (1991) 3817–3828.
[13] G. Häfelinger, in S. Pataï (Ed.), *The Chemistry of Functional Groups: The Chemistry of Amidines and Imidates*, Wiley, New York, 1975, pp 1–84.
[14] C. Chauvin and D. Plusquellec, *Tetrahedron Lett.*, 32 (1991) 3495–3498.
[15] D.A. Guzonas and D.E. Irish, *Can. J. Chem.*, 66 (1988) 1249–1257.
[16] R. Khan, *Pure Appl. Chem.*, 56 (1984) 833–844.
[17] S. Bottle and I.D. Jenkins, *J. Chem. Soc., Chem. Commun.*, (1984) 385.
[18] H. Ringsdorf, B. Schlarb, and J. Venzmer, *Angew. Chem., Int. Ed. Engl.*, 27 (1988) 113–158.
[19] Y. Ishigami and H. Machida, *J. Am. Oil Chem. Soc.*, 66 (1989) 599–603.
[20] O. Mitsunobu, *Synthesis*, (1981) 1–28.
[21] R.D. Guthrie, I.D. Jenkins, S. Thang, and R. Yamasaki, *Carbohydr. Res.*, 121 (1983) 109–117.
[22] S. Abouhilale, J. Greiner, and J.G. Riess, *Carbohydr. Res.*, 212 (1991) 55–64.
[23] G. Descotes, J. Mentech, and N. Roques, *Carbohydr. Res.*, 188 (1989) 63–70.
[24] K. Yoshimoto, Y. Itatani, Y. Shibata, and Y. Tsuda, *Chem. Pharm. Bull.*, 28 (1980) 208–219.
[25] C. Chauvin, P. Thibault, D. Plusquellec, and J. Banoub, *J. Carbohydr. Chem.*, 12 (1993) 459–475.
[26] B. Domon and C. Costello, *Glycoconjugate J.*, 5 (1988) 397–409.
[27] D. Plusquellec, K. Baczko, C. Chauvin, and P. Durand, Fr 2, 670,493 (1992); *Chem. Abstr.*, 118 (1992) 124955q.
[28] E. Reinefeld and S. Klaudinos, *Zücker*, 21 (1968) 330–338.