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Regioselective synthesis of new sucrose derivatives via 3-ketosucrose

Martina Pietsch, Martin Walter and Klaus Buchholz *

Institut für Technologie der Kohlenhydrate an der Technischen Universität Braunschweig-Sugar Institute, Langer Kamp 5, D-38106 Braunschweig (Germany)

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ABSTRACT

3-Ketosucrose (α-D-*ribo*-hexopyranosyl-3-ulose-β-D-fructofuranoside), obtained from sucrose via microbial oxidation with *Agrobacterium tumefaciens*, was shown to be an appropriate and versatile synthon for regioselective syntheses. Condensation with hydroxylamine and its derivatives with allyl and benzyl groups leads to the oxime and the corresponding substituted products. By reductive amination 3-amino-3-deoxy-α-D-allopyranosyl-β-D-fructofuranoside is obtained which can readily be submitted to further functionalization to methacryloyl and fatty acid derivatives. After silylation of 3-ketosucrose the 3-allyl and butylene-substituted as well as decyl- and dodecyl-substituted sucrose can be obtained via Grignard reaction, the side chains being C–C linked to the saccharide.

INTRODUCTION

Sucrochemistry has found much interest since sucrose (α-D-glucopyranosyl-β-D-fructofuranoside) is available on a large scale with high purity at low cost. However, the functionality with eight nearly equivalent hydroxyl groups makes selective synthesis of derivatives laborious and difficult. Furthermore, the preferential route for potential technical applications are reactions in water avoiding protecting groups which require highly selective catalysis. Enzymes offer the advantage of regioselectivity and *Agrobacterium tumefaciens* has a dehydrogenase which affords oxidation of sucrose and other disaccharides in the 3-position yielding 3-ketosucrose[1]. We already described the conditions of fermentation where sufficient enzymatic activity is formed, and optimized conditions for oxidation, in order to achieve good yields and low byproduct concentration levels for 3-keto-sucrose, -isomaltulose, and -leucrose[2–4]. The potential for further chemical steps is described in this article. Both routes, in aqueous solution to the oxime and the amino derivative with subsequent substitution, and C–C bond formation via

* Corresponding author.

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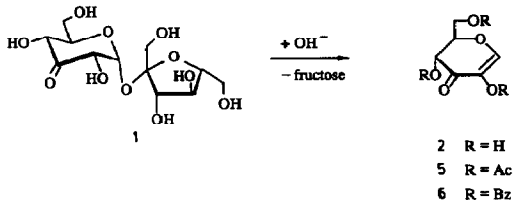

Fig. 1. β-Elimination of 3-ketosucrose.

the Grignard reaction with the protected 3-ketosucrose in organic solvents, are presented. The reactions in aqueous solution, fermentation and oxidation steps as well as the conversion via N-derivatives represent classical routes which may be scaled up to the technical level. The Grignard reaction offers a new approach to sucrose derivatives with C–C linked side chains.

RESULTS AND DISCUSSION

In a previous report[5] we presented results on the stability of 3-ketosucrose (**1**) in aqueous solution at various pH values. The instability of 3-ketosucrose in alkaline solution limits the range of classical organic reactions introduced in carbohydrate chemistry. Under alkaline conditions β-elimination occurs. When 3-ketosucrose (**1**) was treated with 1.2 N aqueous sodium hydroxide solution for 3 min, the free endiolone (**2**), which has been shown to be a key intermediate in the preparation of versatile chiral building blocks[6], could be obtained in 50% yield by the elimination of fructose (**3**) from 3-ketosucrose (**1**) [Fig. 1]. The free endiolone (**2**) was isolated first by Theander et al.[7] in low yields via the alkaline treatment of methyl β-D-3-oxo-*ribo*-hexopyranoside. Our investigations by ^{1}H NMR and ^{13}C NMR spectroscopy of **2** clearly demonstrated the existence mainly of the enol form in neutral aqueous solution. This is opposite to the assumption of Theander[7], who postulated that the dioxo form (**4**) exists in neutral aqueous solution [Fig. 2].

The free endiolone (**2**) underwent smooth acylation in pyridine with acetic anhydride or benzoyl chloride to afford the corresponding peracylated dihydropyranones (**5** and **6**) in rather good yields. Attempted condensation of **1** with amines such as allylamine and dodecylamine gave unstable products that could not be isolated. The reaction of **1** with hydroxylamine in water at pH 6 gave the oxime **7**. Stepwise deionisation of the mixture with strong acidic and strong basic ion-exchangers yielded a mixture of the oxime **7** and fructose as a degradation product.

Fig. 2. Keto–enol tautomerization of the endiolone (**2**).

Formation of the oxime was also performed in pyridine. Addition of acetic anhydride gave the peracetylated oxime **8** in 95% yield. The ^{13}C NMR spectrum showed the existence of two isomers. The ratio of the two forms, estimated by signal intensity, was ca. 45:55. In the major isomer the N-O-acetyl group is *syn* to C-4, which is indicated by the downfield shift of this signal (δ 62.2)[8]. Condensation reactions of **1** with substituted hydroxylamines were also successful. Thus both the *O*-allyl-oxime and the *O*-benzyl-oxime derivatives were obtained with yields of ca. 90%. The analysis of *O*-substituted oxime of **1**, namely *O*-allyl-oxime and *O*-benzyl-oxime, showed similar results. The predominating isomer with a percentage of at least 60% always had the substituent *syn* to C-4. The preference of this conformation is probably due to the sterically less hindered position of the N-O-group, which otherwise might interfere with the fructosyl unit at C-1.

Since the reaction with hydroxylamine was quite successful, the oxime **7** was expected to be a useful intermediate in the reductive amination of **1**. Synthesis of the 3-amino-3-deoxy derivative from 3-ketosucrose had been reported to be rather difficult, involving either chemical reduction or hydrogenation with metal catalysts[9,10]. Using the conditions of Kunz et al.[11], reductive amination of **1**, via the oxime provided 3-amino-3-deoxy-*allo*-sucrose (**9**) in 35% yield. Because of the second-order appearance of most of the resonances in the ^1H NMR spectrum it was not possible to establish the structure. The product **9** was peracetylated and a partial assignment of the signals was made via 2D ^1H NMR spectroscopy. The *allo* configuration was evident from the small $^3J_{H2,H3}$(4 Hz) and $^3J_{H3,H4}$(3.8 Hz) values[12]. As reductive amination of other 3-ketosugars always provided two isomers (*allo* and *gluco*)[11], it was surprising that 3-ketosucrose would give a single isomer. This might be explained by its specific molecular conformation, which may be similar to that of sucrose[13], in which the fructosyl unit is hydrogen bonded to the pyranoid ring. In this case, the contact of the molecule with the catalyst surface occurs only from one direction and the hydrogenation produces only the *allo* isomer.

Further functionalization of 3-amino-*allo*-sucrose (**9**) could easily be achieved by N-acylation. Different types of side chains were introduced by classical procedures. Thus the methacrylamide derivative, a polymer building block, was synthesized by the reaction of **9** with methacrylic anhydride in methanol at low temperature (−5°C), and **11** crystallized from acetone–ether in 60% yield.

A surfactant resulted from the attachment of a fatty acid residue to **9**. The acidic conditions of the reaction with lauroyl chloride led to complete hydrolysis of the glycosidic bond. Therefore, methyl laurate was chosen as the reactant because it afforded mild alkaline catalysis by sodium methanolate. Transesterification in methanol yielded laurylamide (**12**), purifiable by column chromatography on silica gel, as a yellowish syrup in 40% yield [Fig. 3].

Silylation of **1** with chlorotrimethylsilane in pyridine proved to offer a rather elegant access to Grignard reactions. The fully substituted derivative **13** was obtained as a syrup in 76% yield [Fig. 4]. An allyl side chain was introduced via the Grignard reaction with allylmagnesiumbromide to form the 3-*allo*-allyl-substituted

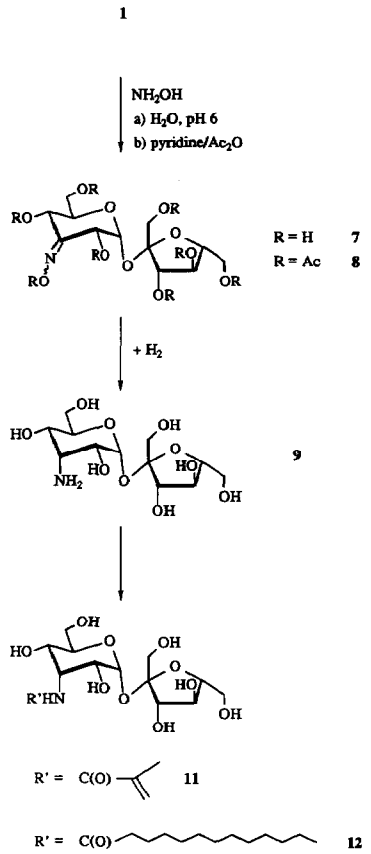

Fig. 3. Functionalization of 3-ketosucrose via reaction to the oxime and reductive amination.

sucrose derivative (**14**) as a crystalline product in 46% yield. The attack of the organometallic reagent is highly stereoselective and affords only the isomer with the *allo* configuration. The proposed *allo* configuration of **14** was confirmed by NOE difference spectroscopy[12]. Similarly the 1-butylene derivative (**15**) was isolated as a crystalline product. These monomers might be used to produce sucrose substituted polymers with different lengths of spacer groups between polymer and sucrose. In contrast to most other saccharide substituted polymers, the link is by C–C bonds, which has not to our knowledge been reported previously for disaccharide substituted polymers.

Alkyl side chains have similarly been introduced by Grignard reactions. The decyl-(**16**) and dodecyl-*allo*-sucrose derivatives (**17**) were obtained in 45 to 48% yield respectively. The silyl groups can easily be removed under mild alkaline conditions with potassium carbonate or ammonia in a mixture of methanol and water at room temperature without loss of the unprotected sugar derivatives (**18–21**). As expected, the alkyl-sucrose derivatives (**20** and **21**) exhibit good surface

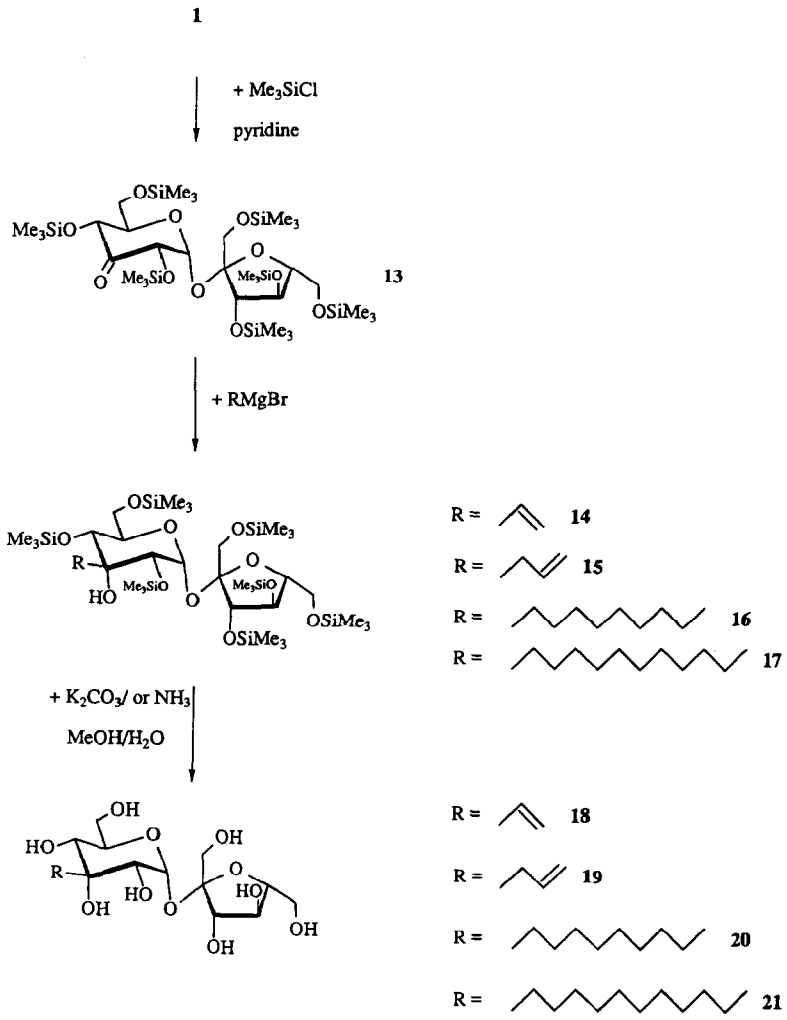

Fig. 4. Alkylation of 3-ketosucrose via the pertrimethylsilylated derivative.

active properties which compare favourably to other detergents based on saccharides[14]. Products **20** and **21** reduce the surface tension of water to 30 mN/m at a concentration of 5×10^{-5} mol/L. This type of C–C linked alkyl side chains to disaccharides also has not previously been reported, thus providing a new method to obtain specific sucrose derivatives.

EXPERIMENTAL

General methods.—Melting points were determined with a Sartorius apparatus and are uncorrected. Optical rotations were measured at 21°C with a Dr. Kernchen sucrometer. TLC was conducted on aluminum sheets, precoated with 0.2-mm

layers of Silica Gel 60F-254 (E. Merck, Darmstadt); the components were located either by exposure to UV light or by spraying with 0.2% napthoresorcin in EtOH–20% H_2SO_4 and followed by heating at 120°C. Column chromatography was performed on silica gel (230–400 mesh, Merck). NMR spectra were recorded with a Bruker AM-400 instrument; ^1H NMR spectra at 400 MHz and ^{13}C NMR spectra at 100 MHz. Mass spectra were recorded with a Finnigan MAT 8430 instrument. Microanalyses were performed by Analytisches Labor des Institutes für Pharmazeutische Chemie, Technische Universität, Braunschweig.

α-D-ribo-Hexopyranosyl-3-ulose-β-D-fructofuranoside (3-ketosucrose; **1**).—Biochemical oxidation of sucrose by *Agrobacterium tumefaciens* has been described elsewhere[2]. Pure **1** was isolated from the crude material by column chromatography (ion-exchanger, Amberlite CG 120II, Ca(II)-form, water, at 5°C); mp 62–65°C; $[\alpha]_D^{21}$ + 65.0° (*c* 4.2, H_2O); ^1H NMR (D_2O): δ 5.78 (d, 1 H, H-1), 4.60 (dd, 1 H, H-2), 4.44 (dd, 1 H, H-4), 4.17 (d, 1 H, H-3′), 4.01 (ddd, 1 H, H-5), 3.95 (dd, 1 H, H-4′), 3.92–3.73 (m, 7H), 3.62 (s, 2 H, H-1′a, 1′b); $J_{1,2}$ 4.6, $J_{2,4}$ 1.5, $J_{4,5}$ 9.8, $J_{3',4'}$ 8.6 Hz; ^{13}C NMR (D_2O): δ 208.13 (C-3), 104.82 (C-2′), 95.82 (C-1), 82.33 (C-5′), 76.89 (C-3′), 76.24 (C-5), 74.73, 74.67 (C-2,4′), 63.24 (C-6′), 62.15 (C-4), 63.24 (C-6′), 61.89 (C-1′), 61.06 (C-6); FABMS (neg): *m/z* 339 $[M - H]^-$, 431 $[M + glycerol - H]^-$. Anal. Calcd for $C_{12}H_{20}O_{11} \cdot H_2O$: C, 40.2; H, 6.2%. Found: C, 40.2; H, 6.2%.

*(+)-(2R,3R)-3,5-Dihydroxy-2-hydroxymethyl-2,3-dihydro-4*H*-pyran-4-one* (**2**).—A sample (1.2 g, 3.53 mmol) of **1** was treated with 10 mL 1.2 N NaOH at room temperature. After 3 min the solution was neutralized with N HCl, followed by concentration to dryness under reduced pressure. The solid was extracted with dry methanol, the resulting solution was filtered and concentrated under reduced pressure to a yellow syrup, which on column chromatography (4:1 acetonitrile–water) afforded 560 mg (50%) of **2** as a white amorphous powder; mp 58°C; $[\alpha]_D^{20}$ + 204° (MeOH); UV (water) λ_{max} (log ε) 293 (3100) at pH 7, λ_{max} (log ε) 340 (1380) at pH 12; ^1H NMR (D_2O): δ 7.30 (s, 1 H, H-6), 4.27 (d, 1 H, H-3), 4.01 (ddd, 1 H, H-2), 3.90 (dd, 1 H, H-7), 3.83 (dd, 1 H, H-7); $J_{2,3}$ 12, $J_{2,7}$ 2, $J_{2,7}$ 6, $J_{7,7}$ 12 Hz; ^{13}C NMR (D_2O): δ 192.97 (C-4), 151.52 (C-6), 133.67 (C-5), 83.26 (C-2), 68.05 (C-3), 60.65 (CH_2OH); FABMS: *m/z* 161 $[M + H]^+$, 143 $[M - OH]^+$, 131 $[M - CHO]^+$, 253 $[M + glycerol]^+$.

*(+)-(2R,3R)-3,5-Diacetoxy-2-acetoxymethyl-2,3-dihydro-4*H*-pyran-4-one* (**5**).—A sample of (200 mg, 1.25 mmol) **2** was dissolved in 2 mL pyridine and 1 mL acetic anhydride (10.6 mmol) was added. The solution was stirred for 30 min at room temperature, hydrolyzed with 2 mL ice–water, and concentrated to dryness under reduced pressure. Column chromatography (5:1 diethylether–cyclohexane) afforded 280 mg (78%) of **5** as a colorless syrup; $[\alpha]_D$ + 220° ($CHCl_3$); CIMS (NH_3, pos): *m/z* 304 $[M + NH_4]^+$, 287 $[M + H]^+$, 262 $[M + NH_4 - CH_3C{=}O]^+$.

*(+)-(2R,3R)-3,5-Bis(benzoyloxy)-2-benzoyloxymethyl-2,3-dihydro-4*H*-pyran-4-one* (**6**).—A sample (200 mg, 1.25 mmol) of **2** was dissolved in 2 mL pyridine and 2 mL benzoyl chloride (17.2 mmol) were added to the solution. The solution was

stirred for 3 h at room temperature, hydrolyzed with 2 mL ice–water, and extracted 3 times with CH_2Cl_2. The combined extracts were dried over Na_2SO_4 and concentrated to dryness under reduced pressure. Column chromatography (5 : 1 diethylether–cyclohexane) afforded 480 mg (81%) of **6** as colorness crystals; mp 73–74°C; $[\alpha]_D^{20}$ + 228° ($CHCl_3$); CIMS (NH_3, pos): *m/z* 490 $[M + NH_4]^+$, 473 $[M + H]^+$, 351 $[M - OBz]^+$, 231 $[M - 2OBz]^+$.

*3-(Hydroxyimino)-α-*D-ribo-*hexopyranosyl-β-*D-*fructofuranoside* (**7**).—A sample (240 mg, 3 mmol) of hydroxylamine hydrochloride was added to a stirred solution of 340 mg (1 mmol) **1** in water. The pH was adjusted to 6 with 1 N NaOH and maintained during the reaction. After standing for 16 h at room temperature the solution was deionized successively with 8 mL weak acid ion-exchanger (Serdolit CW 10) and 8 mL strong base ion-exchanger (Amberlite IRA 400). The resulting solution was freeze-dried to yield 160 mg of product (45%). However, it was a mixture of **7** and fructose; ^{13}C NMR (D_2O): δ 155.4 (C-3), 105.0 (C-2′), 92.1 (C-1), 82.3 (C-5′), 77.3 (C-3′), 75.4 (C-4′), 74.4 (C-5), 69.7 (C-2), 63.1 (C-6), 62.5 (C-4), 62.3 (C-1′), 61.3 (C-6′).

*3-(Acetoxyimino)-2,4,6-tri-*O*-acetyl-α-*D-ribo-*hexopyranosyl-1,3,4,6-tetra-*O*-acetyl-β-*D-*fructofuranoside.*—(**8**). A sample (340 mg, 1 mmol) of **1** and 210 mg (3 mmol) hydroxylamine hydrochloride were dissolved in 5 mL pyridine. The solution was stirred at room temperature for 14 h. Then acetic anhydride (3 mL) and further pyridine (5 mL) were added. The mixture was kept at room temperature for 20 h, then it was poured into satd $NaHCO_3$ and stirred vigorously. The mixture was extracted 3 times with CH_2Cl_2, and the combined extracts were dried over Na_2SO_4. The solvent was coevaporated with several portions of toluene. The resulting syrup was dried in vacuo (665 mg 96%); ^{13}C NMR ($CDCl_3$), the percentages of the two isomers were estimated by signal intensity; first isomer (55%): δ 169.9–166.7 ($COCH_3$), 151.5 (C-3), 103.6 (C-2′), 89.6 (C-1), 78.0 (C-5′), 75.2 (C-3′), 74.0 (C-4′), 69.3 (C-5), 67.5 (C-2), 63.4 (C-6), 62.9 (C-1′), 62.2 (C-4), 61.5 (C-6′), 21.4–19.1 (CH_3CO); second isomer (45%): δ 169.9–166.7 ($COCH_3$), 154.2 (C-3), 103.1 (C-2′), 90.5 (C-1), 78.5 (C-5′), 75.4 (C-3′), 74.3 (C-4′), 70.9 (C-5), 68.9 (C-4), 66.4 (C-2), 63.2 (C-6), 63.1 (C-1′), 61.6 (C-6′), 21.4–19.1 (CH_3CO); FABMS: *m/z* 692 $[M + H]^+$, 714 $[M + Na]^+$.

*3-Amino-3-deoxy-α-*D-*allopyranosyl-β-*D-*fructofuranoside [3-aminosucrose,* (**9**)*].*—A sample (5 g, 72 mmol) of hydroxylamine hydrochloride was dissolved in 150 mL water and the pH was adjusted to 6 with 10% NaOH. A solution (5 g, 14.7 mmol) of **1** in 50 mL water was added. The mixture was stirred at room temperature while the pH was held constant at 6 by titration with 1 N NaOH. After 16 h, 2 g Raney alloy were added and the suspension was added to a high pressure apparatus. Hydrogenation was carried out at 50°C and 120 bar H_2 pressure for 72 h. The alloy particles were filtered off and the filtrate was freeze dried. The crude material was passed through an ion-exchange column and the product isolated by chromatography (ion-exchanger in the NH_4^+ form, 0.5% aq NH_3 eluent) to yield 1.723 g (34%) of **9**; ^1H NMR (D_2O): δ 5.38 (d, 1H, H-1). 4.21

(d, 1 H, H-3'), 4.10 (dd, 1 H, H-4'), 3.96–3.57 (10 H), 3.40 (dd, 1 H, H-3); $J_{1,2}$ 3.7, $J_{3,4} = 4$, $J_{3',4'}$ 8.5 Hz; ^{13}C NMR (D_2O): δ 104.4 (C-2'), 92.7 (C-1), 82.0 (C-5'), 77.4 (C-3'), 74.2 (C-4'), 68.8, 67.5, 66.1 (C-2, 4, 5), 62.7 (C-6'), 62.4 (C-1'), 60.9 (C-6), 53.8 (C-3); FABMS: m/z 342 $[M + H]^+$, 434 $[M + \text{glycerol} + H]^+$.

*3-Acetamido-3-deoxy-2,4,6-tri-*O*-acetyl-α-*D*-allopyranosyl-1,3,4,6-tetra-*O*-acetyl-β-*D*-fructofuranoside* (**10**).—A sample (34 mg, 0.1 mmol) of **9** was peracetylated as for compound **2**. 60 mg (89%); ^1H NMR ($CDCl_3$): δ 6.67 (d, 1 H, NH), 5.55 (d, 1 H, H-1), 5.41 (d, 1 H, H-3'), 5.29 (dd, 1 H, H-4'), 4.91 (dd, 1 H, H-2), 4.85 (ddd, 1 H, H-3), 4.80 (dd, 1 H, H-4), 4.25–4.06 (8 H), 2.10-1.93 (24 H, CH_3); $J_{NH,3}$ 8.5 $J_{1,2} = J_{2,3} = 4$, $J_{3,4}$ 3.8, $J_{4,5}$ 10.1, $J_{3',4'} = J_{4',5'} = 6$ Hz; ^{13}C NMR ($CDCl_3$): δ 169.7, 169.6, 169.4, 169.1, 169.0, 168.5, 168.4, 168.3 (8 $COCH_3$), 103.1 (C-2'), 89.8 (C-1), 77.5 (C-5'), 74.6 (C-3'), 73.8 (C-4'), 65.3, 64.5, 64.1 (C-2,4,5), 62.4 (C-6'), 62.2 (C-1'), 61.2 (C-6), 46.4 (C-3), 22.5–19.6 (CH_3CO); FABMS: m/z 700 $[M + Na]^+$.

*3-Deoxy-3-(*N*-methacrylamido)-α-*D*-allopyranosyl-β-*D*-fructofuranoside* (**1**).—A sample (128 mg, 0.81 mmol) of methacrylic anhydride was added to a cooled (−10°C) suspension of 250 mg (0.73 mmol) **9** in MeOH. The mixture was stirred for 1 h at −10°C, 2 h at −5°C, and 2 h at 4°C. It was then warmed to room temperature and poured into 4:1 acetone–ether. The product **11** was filtered and washed with cold ether to yield 164 mg of **11** as white crystals (55%); mp 188–190°C; ^1H NMR (D_2O): δ 5.75 (d, 1 H, CH_a), 5.48 (d, 1 H, CH_b), 5.43 (dd, 1 H, H-1), 4.70 (dd, 1 H, H-2), 4.24 (d, 1 H, H-3'), 4.03 (dd, H-4'), 3.98–3.79 (8 H), 3.61 (s, 2 H, H-1'a, 1'b), 1.95 (s, 3 H, CH_3); $J_{CHa,b} < 1$, $J_{1,2}4$, $J_{3',4'}$ 8.5 Hz; ^{13}C NMR (D_2O): δ 174.2 (CO), 140.0 (–C=), 121.9 (=CH_2), 104.6 (C-2'), 92.4 (C-1), 82.5 (C-5'), 76.6 (C-3'), 74.4 (C-4'), 69.0 (C-5), 65.9, 65.8 (C-2, C-4), 63.1 (C-1'), 62.8 (C-6'), 60.8 (C-6), 53.4 (C-3), 18.7 (–CH_3); FABMS: m/z 410 $[M + H]^+$, 502 $[M + H + \text{glycerol}]^+$. Anal. Calcd for $C_{16}H_{27}NO_{11} \cdot H_2O$: C, 44.9; H, 6.8; N, 3.3%. Found: C, 44.9; H, 6.7; N, 3.2%.

*3-Deoxy-3-(*N*-laurylamido)-α-*D*-allopyranosyl-β-*D*-fructofuranoside* (**12**).—A suspension (250 mg, 0.73 mmol of **9** in 10 mL of MeOH was heated to 65°C. While boiling, 160 mg (0.73 mmol) methyl laurate in a solution of 2 N $NaOCH_3$ was added. After 4 h under reflux, the solvent was evaporated. The product was isolated by column chromatography (silica, 4:1 MeOH–5% aq NH_3) to yield 149 mg (40%) of **12**; ^1H NMR (D_2O): δ 5.43 (d, 1 H, H-1), 4.57 (d, 1 H, H-2), 4.22 (d, 1 H, H-3'), 4.07 (dd, 1 H, H-4'), 3.90–3.65 (10 H), 2.29 (OC–CH_2), 1.58 (OC–CH_2–CH_2–), 0.85 (–CH_3); $J_{1,2}$ 4, $J_{3',4'}$ 8.5 Hz; ^{13}C NMR (D_2O): δ 178.6 (CO), 104.6 (C-2'), 92.7 (C-1), 82.7 (C-5'), 77.9 (C-3'), 74.9 (C-4'), 66.4, 65.9 (C-2, 4, 5), 63.2 (C-1', 6'), 60.9 (C-6), 53.1 (C-3), 37.32 (OC-CH_2), 32.8–23.4 (–CH_2–), 14.5 (–CH_3); FABMS: m/z 524 $[M + H]^+$, 546 $[M + Na]^+$. Anal. Calcd for $C_{24}H_{45}NO_{11}$: C, 55.1; H, 8.7; N, 2.7%. Found: C, 55.6; H, 9.2; N, 2.4%.

*(2,4,6-Tri-*O*-trimethylsilyl)-α-*D*-*ribo*-hexopyranosyl-3-ulose-[1 → 2]-(1',3',4',6'-tetra-*O*-trimethylsilyl)-β-*D*-fructofuranoside* (**13**).—A sample (5 g, 14.7 mmol) of **1** was dissolved in 100 mL pyridine and 18.6 mL (147 mmol) chlorotrimethylsilane

was added to the solution. The mixture was kept at room temperature for 4 h, hydrolyzed with 50 mL ice-water, and extracted 3 times with CH_2Cl_2. The combined extracts were dried with Na_2SO_4 and then concentrated to dryness. Column chromatography (20:1 toluene–EtOAc) afforded 9.5 g (76%) of **13** as a colorless syrup. ^{1}H NMR ($CDCl_3$): δ 5.74 (d, 1 H, H-1), 4.34 (dd, 1 H, H-4), 4.25 (d, 1 H, H-3′), 4.22 (dd, 1 H, H-2), 4.14 (ddd, 1 H, H-5), 4.03 (dd, 1 H, H-4′), 3.83 (dd, 1 H, H-6), 3.47 (d, 1 H, H-1′), 3.35 (d, 1 H, H-1′), 0.14, 0.13, 0.13, 0.12, 0.11, 0.08, 0.07 (seven s, 7 · 9 H's, 7 · $SiMe_3$); $J_{1,2}$ 4.4, $J_{2,4}$ 1.6, $J_{4,5}$ 9, $J_{5,6}$ 2, $J_{6,6} = J'_{1,1} = 12$, $J_{3',4'} = J_{4',5'} = 8$ Hz; ^{13}C NMR ($CDCl_3$): δ 203.9 (C-3), 103.9 (C-2′), 94.0 (C-1), 81.9 (C-5′), 76.3 (C-3′), 75.3 (C-2), 74.6 (C-4′), 74.9 (C-5), 72.8 (C-4), 63.1 (C-6′), 63.0 (C-1′), 61.3 (C-6), (C-6), 1.0, 0.9, 0.7, 0.6, 0.0, 0.0, −0.1 (7 · $SiMe_3$); FABMS (neg): *m/z* 843 [M^-], 770 [M^- − $SiMe_3$], 467 [fructosyl residue].

3-C-Allyl-(2,4,6,6-tri-O-trimethylsilyl)-α-D-allopyranosyl-[1 → 2](1′,3′,4′,6′-tetra-O-trimethylsilyl)-β-D-fructofuranoside (**14**).—A sample (3.0 g, 3.55 mmol) of **13** in 30 mL dry diethyl ether was added to a freshly prepared solution of 3 g (20 mmol) allylmagnesiumbromide in 20 mL dry diethyl ether at −10°C. The reaction was carried out under an N_2 atmosphere. Allylmagnesiumbromide was freshly prepared from 0.5 g (20 mmol magnesium, 1.75 mL (20 mmol) allylbromide, and 20 mL diethyl ether by the standard method. The Grignard solution was stirred at room temperature for 2 h, then hydrolyzed with 50 mL ice–water, and diluted with satd aq NH_4Cl. The ether phase was separated and the aqueous phase was extracted 3 times with 20 mL diethyl ether. The combined ether solutions were washed successively with satd aq sodium disulfide, satd $NaHCO_3$, and water, followed by drying with Na_2SO_4, and concentration to dryness. Column chromatography (25:1 toluene–EtOAc) afforded 1.45 g (45%) of **14** as colorless crystals; mp 83–84°C; $[\alpha]_D^{20}$ 36° (MeOH); ^{1}H NMR ($CDCl_3$): δ 5.66 (m, 1 H, H-2″), 5.21 (d, 1 H, H-1), 5.03 (dd, 1 H, H-1b″), 4.99 (dd, 1 H, H-1a″), 4.21 (d, 1 H, H-3′), 3.96 (ddd, 1 H, H-5), 3.91 (dd, 1 H, H-4′), 3.72 (dd, 1 H, H-6), 3.58 (d, 1 H, H-4), 3.53–3.68 (m, 4 H, H-6, H-5′, H-6′, H-6′), 3.48 (d, 1 H, H-2), 3.41 (d, 1 H, H-1′), 3.33 (d, 1 H, H-1′), 2.41 (dd, 1 H, H-3″), 2.28 (dd, 1 H, H-3″), 0.07, 0.05, 0.04, 0.03, 0.02, 0.00, −0.02 (seven s, 7 · 9 H's, 7 · $SiMe_3$); $J_{1,2}$ 4.4, $J_{4,5}$ 10, $J_{5,6}$ 2, $J_{5,6}$ 3.5, $J_{6,6} = J_{1',1'} = 11$, $J_{3',4'} = J_{4',5'} = 9$, $J_{1a'',1b''}$ 1.8, $J_{1a'',2''}$ 11, $J_{1b'',2''}$ 17, $J_{2'',3''}$ 6, $J_{3'',3''}$ 13.5 Hz; ^{13}C NMR ($CDCl_3$): δ −0.3, −0.3, −0.1, 0.4, 0.7, 0.8, 1.9 (7 · $SiMe_3$), 37,3 (C-3″), 62,3 (C-6), 63,1 (C-1′), 63,2 (C-6′), 69,3 (C-2), 69,25 (C-5), 69,7 (C-4), 75,4 (C-4′), 76,0 (C-3′), 76,4 (C-3), 82,2 (C-5′), 92,3 (C-1), 104,0 (C-2′), 117,9 (C-1″), 133,7 (C-2″); FABMS (neg): *m/z* 885 [M − H]$^-$, 813 [M − $SiMe_3$]$^-$, 797 [M − $OSiMe_3$]$^-$.

3-C-(4-But-1-enyl)-(2,4,6-tri-O-trimethylsilyl)-α-D-allopyranosyl-[1 → 2]-(1′,3′,4′,6′-tetra-O-trimethyolsilyl)-β-D-fructofuranoside (**15**).—A sample (2.0 g, 2.37 mmol) of **13** in 30 mL dry diethylether was added to a freshly prepared solution of 3.2 g (20 mmol) but-1-enylmagnesiumbromide in 20 mL dry diethyl ether at −10°C. The reaction was carried out under an N_2 atmosphere. But-1-enylmagnesium-bromide was freshly prepared from 0.5 g (20 mmol) magnesium, 2.05 mL (20 mmol)

4-bromo-1-butene, and 20 mL diethyl ether by the standard method. The work up was performed similar to the procedure for the allylderivative. Column chromatography (80:1 toluene–EtOAc) afforded 0.98 g (46%) of **15** as colorless crystals; mp 43–46°C; $[\alpha]_D^{20}$ + 32° (MeOH); ^{1}H NMR ($CDCl_3$): δ 5.71 (m, 1 H, H-2″), 5.21 (d, 1 H, H-1), 4.94 (dd, 1 H, H-1b″), 4.86 (dd, 1 H, H-1a″), 4.21 (d, 1 H, H-3′), 3.96 (ddd, 1 H, H-5), 3.89 (dd, 1 H, H-4′), 3.88 (d, 1 H, H-4), 3.74 (dd, 1 H, H-6), 3.70–3.54 (m, 4 H, H-6, H-5′, H-6′, H-6′), 3.43 (d, 1 H, H-1′), 3.39 (d, 1 H, H-2), 3.33 (d, 1 H, H-1′), 2.02 (dd, 1 H, H-3″), 1.98 (dd, 1 H, H-3″), 1.71 (dt, 1 H, H-4″), 1.53 (dt, 1 H, H-4″), 0.08, 0.07, 0.05, 0.04, 0.03, 0.02, 0.00 (seven s, 7 · 9 H's, 7 · $SiMe_3$); $J_{1,2}$ 4.4, $J_{4,5}$ 10, $J_{5,6}$ 3.5, $J_{5,6}$ 2, $J_{6,6}$ 12, $J_{1',1'}$ 11, $J_{3',4'} = J_{4',5'} = 8$, $J_{1a'',1b''}$ 1.8, $J_{1a'',2''}$ 11, $J_{1b'',2''}$ 17, $J_{3'',4''}$ 5, $J_{4'',4''}$ 13 Hz; ^{13}C NMR ($CDCl_3$): δ 138.3 (C-2″), 114.3 (C-1″), 104.1 (C-2′), 92.3 (C-1), 82.4 (C-5′), 76.4 (C-3), 76.0 (C-3′), 75.7 (C-4′), 69.35 (C-5), 69.3 (C-2), 67.0 (C-4), 63.6 (C-6′), 63.1 (C-1′), 62.3 (C-6), 32.2 (C-3″), 28.4 (C-4″), 1.9, 1.1, 0.9, 0.8, 0.7, 0.0, 0.0 (7 · $SiMe_3$); FABMS (neg): *m/z* 899 $[M - H]^-$, 827 $[M - SiMe_3]^-$, 811 $[M - OSiMe_3]^-$.

3-C-Decyl-(2,4,6-tri-O-trimethylsilyl)-α-D-allopyranosyl-[1 → 2]-(1′,3′,4′,6′-tetra-O-trimethylsilyl)-β-D-fructofuranoside (**16**).—A sample (10 g, 11.8 mmol) of **13** in 60 mL dry diethyl ether was added to a freshly prepared solution of 10 g (40 mmol) decylmagnesiumbromide in 30 mL dry diethyl ether at −10°C. The reaction was carried out under an N_2 atmosphere. Decylmagnesiumbromide was freshly prepared from 1 g (40 mmol) magnesium, 8.4 mL (40 mmol) bromodecane, and 20 mL diethyl ether by the standard method. The work up was performed similar to the procedure for the allyl derivative. Column chromatography (80:1 toluene–EtOAc) afforded 5.24 g (46% of **16** as a colorless syrup; $[\alpha]_D^{20}$ + 22° (MeOH); ^{1}H NMR ($CDCl_3$): δ 5.26 (d, 1 H, H-1), 4.25 (d, 1 H, H-3′), 4.02 (ddd, 1 H, H-5), 3.93 (dd, 1 H, H-4′), 379 (dd, 1 H, H-6), 3.48 (d, 1 H, H-1′), 3.45 (d, 1 H, H-2), 3.38 (d, 1 H, H-1′), 1.30–1.20 (18 H, 9 · CH_2-decyl), 0.84 (t, 3 H, CH_3-decyl), 0.14, 0.13, 0.11, 0.10, 010, 0.08, 0.06 (seven s, 7 · 9 H's, 7 · $SiMe_3$),; $J_{1,2}$ 4.4, $J_{4,5}$ 10, $J_{5,6}$ 3.5, $J_{5,6}$ 2, $J_{6,6} = J_{1',1} = 11$, $J_{3',4'} = J_{4',5'} = 8$, $J_{1'',2''}$ 4 Hz; ^{13}C NMR ($CDCl_3$): δ = 104.1 (C-2′), 92.3 (C-1), 82.4 (C-5′), 76.7 (C-3), 76.0 (C-3′), 75.7 (C-4′), 69.8 (C-4), 69.3 (C-5), 68.9 (C-2), 63.6 (C-6′), 63.1 (C-1′), 62.5 (C-6), 33.1, 32.0, 30.2, 29.9, 29.7, 29.6, 29.3, 24.2, 22.7 (C-9″–C-1″), 14.1 (C-10″), 1.8, 0.9, 0.6, 0.5, −0.1, −0.2, −0.2, (7 · $SiMe_3$); FABMS (neg): *m/z* 985 $[M - H]^-$, 913 $[M - SiMe_3]^-$, 897 $[M - OSiMe_3)^-$.

3-C-Dodecyl-(2,4,6-tri-O-trimethylsilyl)-α-D-allopyranosyl-[1 → 2]-(1′,3′,4′,6′-tetraO-trimethylsilyl)-β-D-fructofuranoside (**17**).—A sample (10 g, 11.8 mmol) of **13** in 60 mL dry diethyl ether were added to a freshly prepared solution of 11 g (40 mmol) dodecylmagnesiumbromide in 30 mL dry diethyl ether at −10°C. The reaction was carried out under an N_2 atmosphere. Dodecylmagnesiumbromide was freshly prepared from 1 g (40 mmol) magnesium, 9.6 mL (40 mmol) bromododecane, and 20 mL diethyl ether by the standard method. The work up was performed similar to the procedure for the allyl derivative. Column chromatography (80:1 toluene–EtOAc) afforded 5.41 g (46%) of **17** as a colorless syrup; $[\alpha]_D^{20}$ + 24° (MeOH); ^{1}H NMR ($CDCl_3$): δ 5.26 (d, 1 H, H-1), 4.26 (d, 1 H, H-

3′), 4.02 (ddd, 1 H, H-5), 3.93 (dd, 1 H, H-4′), 3.79 (dd, 1 H, H-6), 3.48 (d, 1 H, H-1′), 3.45 (d, 1 H, H-2), 3.38 (d, 1 H, H-1′), 1.27–1.20 (22 H, 11 · CH_2-dodecyl), 0.83 (t, 3 H, CH_3-dodecyl), 0.15, 0.13, 0.12, 0.11, 0.10, 0.09, 0.07 (seven s, 7 · 9 H′s, 7 · $SiMe_3$); $J_{1,2}$ 4.4, $J_{4,5}$ 10, $J_{5,6}$ 3.5, $J_{5,6}$ 2, $J_{6,6} = J_{1',1'} = 11$, $J_{3',4'} = J_{4',5'} = 8$, $J_{1'',2''}$ 4 Hz; ^{13}C NMR ($CDCl_3$): δ 104.1 (C-2′), 92.3 (C-1), 82.4 (C-5′), 76.7 (C-3), 76.0 (C-3′), 75.7 (C-4′), 69.8 (C-4), 69.3 (C-5), 68.9 (C-2), 63.6 (C-6′), 63.1 (C-1′), 62.5 (C-6), 33.2, 32.0, 30.2, 29.9, 29.8, 29.7, 29.7, 29.7, 29.4, 24,2, 22.7 (C-11″–C-1″), 14.1 (C-12″), 1.8, 0.9, 0.6, 0.5, −0.1, −0.2, −0.2 (7 · $SiMe_3$); FABMS (neg): *m/z* 1013 $[M - H]^-$, 941 $[M - SiMe_3]^-$, 925 $[M - OSiMe_3]^-$.

3-C-Allyl-α-D-allopyranosyl-[1 → 2]-β-D-fructofuranoside (**18**).—A sample (500 mg 0.56 mmol) of **14** was treated with 50 mg K_2CO_3 dissolved in a mixture of 10 mL MeOH and 5 mL water for 10 min at room temperature. The solution was concentrated to dryness under reduced pressure and **18** was extracted with dry MeOH. The resulting solution was filtrated and concentrated to dryness to yield 214 g (0.56 mmol, 100%) of **18** as a white amorphous powder; mp 80°C; $[\alpha]_D^{20}$ + 29° (H_2O); ^{1}H NMR (D_2O): δ 5.69 (m, 1 H, H-2″), 5.27 (d, 1 H, H-1), 5.07 (m, 2 H, H-1a″, H-1b″), 4.09 (d, 1 H, H-3′), 3.94 (dd, 1 H, H-4′), 3.82 (ddd, 1 H, H-5), 3.71–3.65 (m, 4 H, H-6, H-6′, H6′, H-6′), 3.57 (d, 1 H, H-1′), 3.52 (d, 1 H, H-1′), 3.49 (d, 1 H, H-2), 3.41 (d, 1 H, H-4), 2.34 (d, 2 H, H-3″, H-3″); $J_{1,2}$ 4.4, $J_{4,5}$ 10, $J_{5,6}$ 3.5, $J_{5,6}$ 2, $J_{1',1'}$ 12, $J_{3',4'} = J_{4',5'} = 8$, $J_{2'',3''}$ 7.5 Hz; ^{13}C NMR (D_2O):δ 133.0 (C-2″), 120.1 (C-1″), 104.4 (C-2′), 93.0 (C-1), 82.0 (C-5′), 76.8 (C-3), 76.6 (C-3′), 74.2 (C-4′), 69.4 (C-5), 66.8 (C-2), 65.9 (C-4), 62.6 (C-6′), 61.8 (C-1′), 61.0 (C-6), 37.3 (C-3″); FABMS (neg): *m/z* 457 $[M - 3H + 2K]^-$, 419 $[M - 2H + K]^-$, 381 $[M - H]^-$.

3-C-(4-But-1-enyl)-α-D-allopyranosyl-[1 → 2]-β-D-fructofuranoside (**19**).—A sample (500 mg, 0.55 mmol) of **15** was treated with 50 mg K_2CO_3 dissolved in a mixture of 10 mL MeOH and 5 mL water for 10 min at room temperature. The solution was concentrated to dryness under reduced pressure and **19** was extracted with dry MeOH. The resulting solution was filtrated and concentrated to dryness to yield 217 g (0.55 mmol, 100%) of **19** as a white amorphous powder; mp 94°C; $[\alpha]_D^{20}$ + 34° (H_2O); ^{1}H NMR (D_2O): δ 5.78 (m, 1 H, H-2″), 5.29 (d, 1 H, H-1), 4.99 (dd, 1 H, H-1b″), 4.89 (dd, 1 H, H-1a″), 4.09 (d, 1 H, H-3′), 3.94 (dd, 1 H, H-4′), 3.82 (ddd, 1 H, H-5), 3.71–3.65 (m, 4 H, H-6, H-6′, H-6′, H-6), 3.59 (d, 1 H, H-2), 3.57 (d, 1 H, H-1′), 3.53 (d, 1 H, H-1′), 48 (d, 1 H, H-4), 1.95 (m, 2 H, H-3″, H-3″), 1.65 (dt, 2 H, H-4″, H-4″); $J_{1,2}$ 4.4, $J_{4,5}$ 11, $J_{5,6}$ 3.5, $J_{5,6}$ 2, $J_{1',1'}$ 11, $J_{3',4'} = J_{4',5'} =$ 8, $J_{1a'',1b''}$ 1.8, $J_{1a'',2''}$ 10, $J_{1b'',2''}$ 17, $J_{3'',4''}$ 8 Hz; ^{13}C NMR (D_2O):δ 139.2 (C-2″), 115.1 (C-1″), 104.4 (C-2′), 93.1 (C-1), 82.0 (C-5′), 76.8 (C-3), 76.7 (C-3′), 74.2 (C-4′), 69.5 (C-5), 67.0 (C-2), 66.1 (C-4), 62.6 (C-6′), 61.8 (C-1′), 62.0 (C-6), 31.8 (C-3″), 28.4 (C-4″); FABMS (neg): *m/z* 471 $[M - 3H + 2K]^-$, 433 $[M - 2H + K]^-$, 395 $[M - H]^-$.

3-C-Decyl-α-D-allopyranosyl-[1 → 2]-β-D-fructofuranoside (**20**).—A sample (4.5 g, 4.56 mmol) of **16** and 15 mL aq NH_3 (25%) was added to a mixture of 90 mL MeOH and 10 mL water. The solution was stirred for 20 min at room temperature

and then concentrated to dryness to yield 2.2 g (4.56 mmol, 100%) of **20** as a white amorphous powder; mp 145°C; $[\alpha]_D$ + 51° (Me_2SO); ^1H NMR (Me_2SO-d_6): δ 5.13 (d, 1 H, H-1′), 5.10 (d, 1 H, H-1), 4.85 (d, 1 H, H-1′), 4.80 (d, 1 H, H-4′), 4.70 (d, 1 H, H-3′), 4.32 (dd, 1 H, H-6), 4.25 (dd, 1 H, H-6), 1.15–1.05 (18 H, 9 · CH_2-decyl), 0.76 (t, 3 H, CH_3-decyl); $J_{1,2}$ 4.4, $J_{4,5}$ 10, $J_{5,6}$ 3.5, $J_{5,6}$ 2, $J_{6,6} = J_{1',1'} = 11$, $J_{3',4'} = J_{4',5'} = 8$ Hz; ^{13}C NMR (Me_2SO-d_6):δ 104.3 (C-2′), 92.6 (C-1), 82.9 (C-5′), 76.7 (C-3′), 75.6 (C-3), 74.1 (C-4′), 69.9 (C-5), 67.2 (C-2), 66.3 (C-4), 62.1 (C-6′), 61.9 (C-1′), 60.8 (C-6), 33.2, 31.5, 30.0, 29.3, 29.2, 28.9, 25.7, 23.8, 22.3 (C-9″–C-1″), 14.1 (C-10″); FABMS (neg): m/z 964 [2M], 481 [M − H]$^-$.

3-C-Dodecyl-α-D-allopyranosyl-[1 → 2]-β-D-fructofuranoside (**21**).—A sample (4.5 g, 4.44 mmol) of **17** and 15 mL aq NH_3 (25%) were added to a mixture of 90 mL MeOH and 10 mL water. The solution was stirred for 20 min at room temperature and then concentrated to dryness to yield 2.3 g (4.44 mmol, 100%) of **21** as a white amorphous powder; mp 110°C; $[\alpha]_D$ + 31° (Me_2SO); ^1H NMR (Me_2SO-d_6): δ 5.13 (d, 1 H, H-1′), 5.10 (d, 1 H, H-1), 4.85 (d, 1 H, H-1′), 4.80 (d, 1 H, H-4′), 4.70 (d, 1 H, H-3′), 4.32 (dd, 1 H, H-6), 4.25 (dd, 1 H, H-6), 1.15–1.05 (22 H H, 11 · CH_2-decyl), 0.76 (t, 3 H, CH_3-decyl); $J_{1,2}$ 4.4, $J_{4,5}$ 10, $J_{5,6}$ 3.5, $J_{5,6}$ 2, $J_{6,6} = J_{1',1'} = 11$, $J_{3',4'} = J_{4',5'} = 8$ Hz; ^{13}C NMR (Me_2SO-d_6):δ 104.3 (C-2′), 92.6 (C-1), 82.9 (C-5′), 76.8 (C-3′), 75.6 (C-3), 74.2 (C-4′), 69.9 (C-5), 67.3 (C-2), 66.4 (C-4), 62.1 (C-6′), 61.9 (C-1′), 60.9 (C-6), 33.2, 31.5, 30.0, 29.3, 29.28, 29.25, 29.23, 29.21, 28.9, 23.8, 22.3 (C-11″–C-1″), 14.1 (C-12″); FABMS (neg): m/z 509 [M − H]$^-$.

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