Towards C-2 symmetrical macrocyles with an incorporated sucrose unit[1]

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Abstract: The first C_2 symmetrical macrocyclic receptor containing two sucrose molecules has been prepared, albeit in low yield, by reaction of hexa-*O*-benzyl-6′-*O*-acroyl-6-*O*-allylsucrose in the presence of a second generation Grubbs catalyst (1,3-dimesityl-4,5-dihydroimidazol-2-ylidene ruthenium alkylidene complex). Highly selective protection of the 6′-OH group in 1′,2,3,3′,4,4′-hexa-*O*-benzylsucrose was a key step in the preparation of the precursor used under ring closing metathesis (RCM) conditions.

Key words: sucrose, macrocyclic receptors, metathesis, regioselective transformations.

Résumé : La réaction du hexa-*O*-benzyl-6′-*O*-acroyl-6-*O*-allylsucrose en présence du catalyseur de Grubbs de deuxième génération (complexe alkylidène 1,3-dimésityl-4,5-dihydroimidazol-2-ylidène ruthénium) nous a permis de préparer, avec un faible rendement, le premier récepteur macrocyclique de symétrie C_2 contenant deux molécules de sucrose. La protection hautement sélective du groupe OH en 6′ du 1′,2,3,3′,4,4′-hexa-*O*-benzylsucrose est l'étape clé dans la préparation du précurseur utilisé dans les conditions de fermeture de cycle par métathèse (RCM).

Mots clés : sucrose, récepteurs macrocycliques, métathèse, transformations régiosélectives.

[Traduit par la Rédaction]

Introduction

Sucrose, a cheap raw material, is available in more than 130 million tons per year; most of it is consumed on the food market. This chemical is very demanding to work with because of its very poor solubility in organic solvents (except DMF, pyridine, and DMSO), presence of eight hydroxyl groups that are difficult to differentiate, and the high sensitivity of the glycosidic bond in acidic media. However, this disaccharide is a subject of interest for several laboratories, which use it as a starting material for the preparation of fine chemicals (1–3), as well as biodegradable polymers or surfactants (4). Recently, a biocatalytic approach to sucrose analogs has been published (5).

As part of an on-going program, we elaborated a convenient route to 2,3,3′,4,4′-penta-*O*-benzylsucrose (6) (**1**), a useful starting material for the preparation of derivatives modified at the terminal (C1′, C6, C6′) positions. Differentiation of the primary hydroxyl groups in **1** is possible, which allows for the production of all three monoalcohols, as well as the 6,6′-diol **2**, in good yields (3, 7). Recently, we prepared another useful sucrose diol, compound **3** (8), and applied it in the preparation of a variety of crown ether analogs (**4**, Fig. 1) (9).

In this paper a methodology leading to complex sucrose macrocycles possessing higher symmetry will be described. Differentiation of the primary hydroxyl groups in **3** is required for regioselective introduction of the proper olefinic fragments needed for cyclization under ring closing metathesis (RCM) conditions.

Synthesis of selectively protected derivatives of hexa-*O*-benzylsucrose

Reaction of the free sucrose with 1 equiv. of silylating agent preferentially protects the 6′-OH group (10). Since the same feature applies for diol **2** (7), similar selective protection of **3** was also expected. Diol **3** was reacted with *tert*-butyldimethylsilyl chloride to afford alcohol **5** in 48% yield. Protection at the C-6′ position was confirmed by advanced NMR experiments performed on derivative **7** in which the COSY correlations between H-5 (glucose part) and both olefinic protons were visible. Since the yield of product **5** was not particularly impressive, we used the more bulky silyl reagent, *tert*-butyldiphenylsilyl chloride, and obtained alcohol **6** in 60% yield. Its structure was also confirmed by the NMR experiments performed on methyl uronate (**11**); the significant lowfield shift of the H-5 resonance (δ 4.56 ppm) proved that this proton is in close vicinity to the ester group, hence the 6-OH (and not 6′-OH) group in alcohol **7** was not protected (Scheme 1).

Synthesis of 6-*O*-allyl-6′-*O*-acroyl derivative **10**, the direct precursor of the C_2-symmetrical macrocycle, was achieved in 37% overall yield from **6** by allylation of the 6-

Received 30 August 2005. Published on the NRC Research Press Web site at http://canjchem.nrc.ca on 6 April 2006.

Dedicated to Professor Walter Szarek on the occasion of his 65th birthday.

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[1]This article is part of a Special Issue dedicated to Professor Walter A. Szarek.

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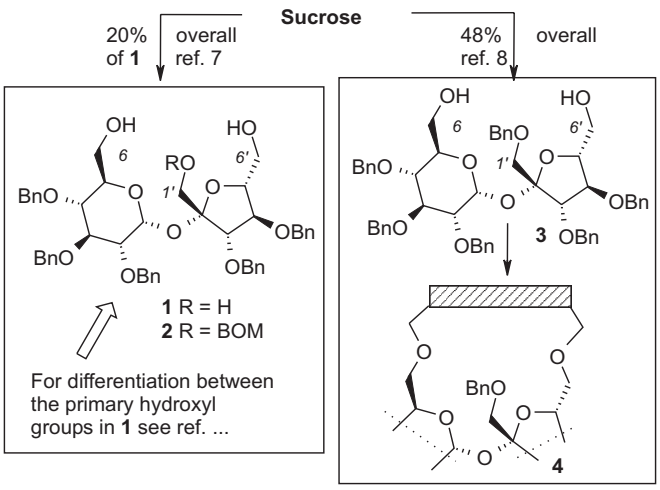
 doi:10.1139/V06-035

Fig. 1. Preparation of partially protected sucrose derivatives and synthesis of the crown ether analogs containing sucrose.



OH group with allyl bromide,[3] followed by removal of the silyl protection from the 6′-OH and subsequent acroylation (Scheme 1).

Cyclization of sucrose derivative 11 to the C_2-symmetrical receptor

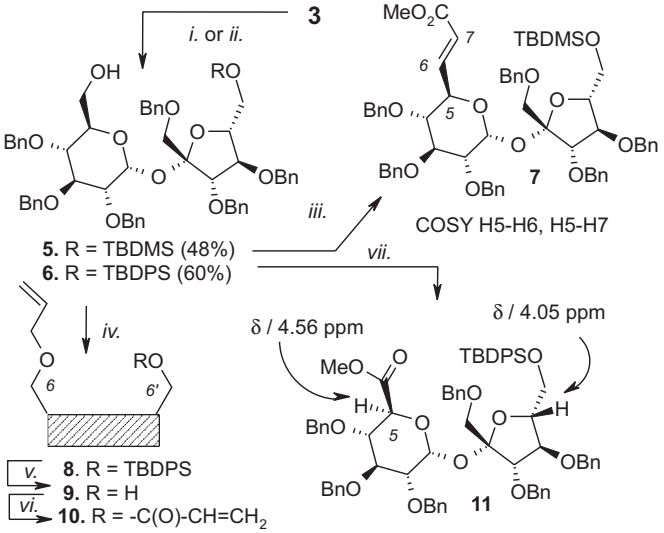
Reaction of **11** performed in the presence of a second generation Grubbs catalyst (1,3-dimesityl-4,5-dihydroimidazol-2-ylidene ruthenium alkylidene complex (11)) afforded a mixture of products in a total yield of about 35%. Four different compounds (**12**–**15**) were isolated by HPLC (Scheme 2).

Structures of all these products were established by MS and high-resolution NMR spectroscopy. The MS spectra of compounds **12** and **13** clearly pointed at the presence of only one molecule of sucrose (in both spectra, the signals *m*/*z* 971 [M($C_{58}H_{60}O_{12}$) + Na^+] and 987 [M($C_{58}H_{60}O_{12}$) + K^+] were seen). The geometry across the newly created double bonds was determined from the ^{1}H NMR spectra of these macrocycles. Thus, the large coupling constant (J = 16.1 Hz) pointed at the E geometry in **12**, while the smaller constant (J = 12.0 Hz) proved the Z geometry in **13**.

The MS data of one of the two remaining derivatives were in accordance with the dimeric structure; the signal at *m*/*z* 1919 [($C_{116}H_{120}O_{24}$) + Na^+] could be assigned to the expected cyclic derivative **14**. In the ^{13}C NMR spectrum of this compound, only one -CH=CH-C(O)- group was seen (δ 165.8, 145.6, and 120.0 ppm), which strongly supported the symmetrical structure. Further information was obtained from the ^{1}H NMR spectrum; the large coupling constant (J = 15.8 Hz) among two olefinic protons (at δ 6.83 and 5.96 ppm) clearly pointed at the E geometry across this double bond. This is consistent with the literature data reporting on a preferential synthesis of the E isomers under such conditions (12).

In the MS spectrum of the last identified product, the signal at *m*/*z* 1947 (differing by 28 Da (2 × CH_2 groups) from the dimer **14**) was detected. In the ^{13}C NMR spectrum, only

Scheme 1. (*i*) CH_2Cl_2, TBDMSCl (1 equiv.), DIPEA, DMAP, 48%; (*ii*) CH_2Cl_2, TBDPSCl (1 equiv.), DIPEA, DMAP, 60%; (*iii*) 1. Swern oxidation; 2. Ph_3P=CH-CO_2Me; (*iv*) CH_2Cl_2, 50% NaOH, AllBr, Bu_4NBr, rt, 66%; (*v*) Bu_4NF, THF, rt, 74%; (*vi*) CH_2Cl_2, Et_3N, DMAP, acroyl chloride, 75%; (*vii*) 1. Swern oxidation; 2. Jones oxidation; 3. CH_2N_2, 64% overall.



three olefinic carbon resonances (at δ 131.1 (=CH_2), 129.4, and ~128.2 ppm, respectively; assigned from the HETCOR correlations), one carbonyl resonance (at δ 165.9 ppm), and one set of signals connected with the sucrose skeleton (representative resonances at δ 104.7 (C-2′) and 90.3 (C-1)) were seen, which pointed at structure **15**. The geometry across the newly created double bond is most likely E (assumption based on the literature examples (12)), but because of the symmetry of **15**, it cannot be assigned by NMR.

We plan to assign this geometry by desymmetrization of the molecule; the results will be reported in a separate paper.

Conclusion

The first synthesis of a C_2-symmetrical macrocycle containing two sucrose units was realized by dimerization of the 6-*O*-allyl-6′-*O*-acroylsucrose monomer under RCM conditions with Grubbs II catalyst (1,3-dimesityl-4,5-dihydroimidazol-2-ylidene ruthenium alkylidene complex). Besides the expected receptor **14**, two compounds (with E and *Z* geometry, respectively, across the newly created double bond) resulting from the *intramolecular* cyclization and one dimeric open-chain product (from reaction among two allyl moieties) were produced. The overall yield of this process was low (ca. 35%).

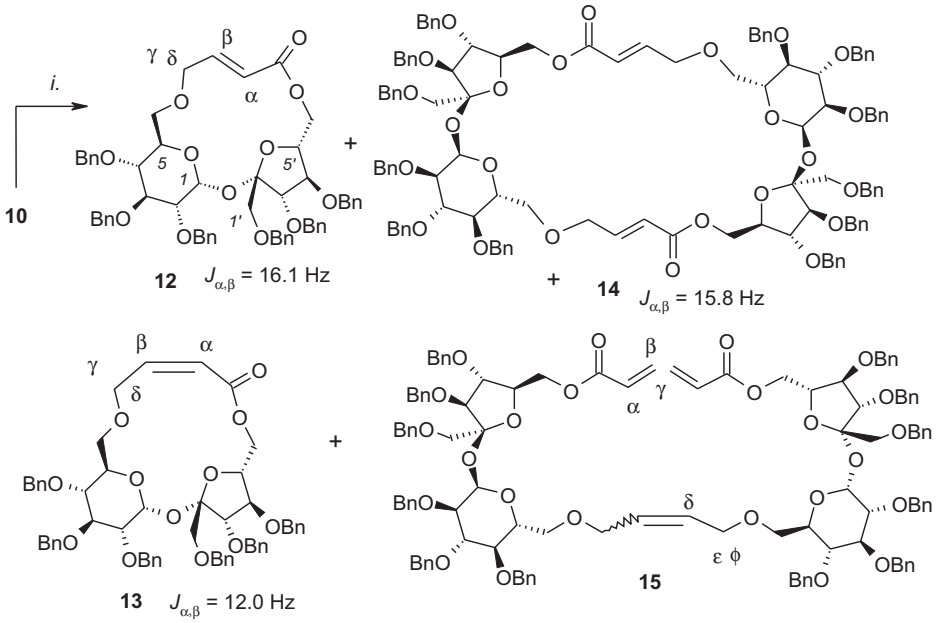
Experimental

General

NMR spectra were recorded with a Bruker AM 500 spectrometer for solutions in $CDCl_3$ (internal Me_4Si) unless otherwise stated. Most of the resonances were assigned by COSY (^{1}H–^{1}H) and (or) HETCOR and DEPT correlations.

[3] Interestingly, the reaction with allyl chloride was not effective under PTC conditions; removal of the silyl block from the C-6′ end, followed by allylation of both 6-OH and 6′-OH groups, led to known 6,6′-di-*O*-allyl-1′2,3,3′,4,4′-hexa-*O*-benzylsucrose (ref. 3).

Scheme 2. (*i*) CH_2Cl_2, second generation Grubbs catalyst, reflux, 3.5 h.



The ^1H and ^{13}C aromatic resonances occurring at the typical δ values were omitted for simplicity. Mass spectra were recorded with an ESI/MS Mariner (PerSeptive Biosystem) mass spectrometer. Optical rotations were measured with a Jasco P-1020 polarimeter for solutions in $CHCl_3$ (*c* = 1) at room temperature (rt). IR spectra (film) were recorded with a PerkinElmer Spectrum 2000 apparatus. Column chromatography was performed on silica gel (Merck, 70–230 or 230–400 mesh). Methylene chloride was distilled from CaH_2 and THF from potassium prior to use. Organic solutions were dried over anhydrous sodium sulfate.

1′,2,3,3′,4,4′-Hexa-*O*-benzyl-6′-*O*-*tert*-butyldimethylsilylsucrose (5)

To a solution of diol **3** (1.25 g, 1.4 mmol), DMAP (0.12 g), and diisopropylethylamine (0.8 mL) in CH_2Cl_2 (50 mL), a solution of *tert*-butyldimethylsilyl chloride (0.27 mL, 1.4 mmol) in CH_2Cl_2 (5 mL) was added over 60 min and the mixture was stirred for 24 h at rt. Water (70 mL) was added, the organic phase was separated, and the aqueous one extracted with ether (70 mL). The combined organic solutions were dried, concentrated, and the crude product was isolated by column chromatography (hexane – ethyl acetate, 7:1 to 1:1) to give the title compound (**5**) (0.48 g, 0.48 mmol, 48% calcd. on consumed **3**) as a colorless oil and unreacted alcohol **3** (0.36 g, 0.41 mmol). Data for **6**: $[\alpha]_D$ +33.5°. ^1H NMR (200 MHz) δ: 5.97 (d, 1H, $J_{1,2}$ = 3.8 Hz, H-1), 0.88 (s, 9H, 3×CCH_3), 0.06, 0.05 (2×s, SiMe_2). ^{13}C NMR (50 MHz) δ: 104.3 (C-2′), 88.6 (C-1), 83.6, 81.9, 80.7, 80.6, 80.1, 77.8 and 71.2 (C-2,3,3′,4,4′,5,5′), 75.6, 74.9, 73.5, 73.1, 72.6, 72.0, 71.8, and 62.9, 62.0 (C-1′,6,6′, 6×OCH_2Ph), 25.9 (CMe_3), 18.3 (CMe$_3$), –5.0 (SiMe_2). MS *m*/*z*: 1019 [M($C_{60}H_{72}O_{11}Si$) + Na^+]. Anal. calcd. for $C_{60}H_{72}O_{11}Si$: C 72.26, H 7.28; found: C 72.0, H 7.4.

Determination of the structure of 5 — Synthesis of the α,β-unsaturated ester 7

Alcohol **5** (80 mg, 0.08 mmol) in CH_2Cl_2 (2 mL) was added at –78 °C within 5 min to a solution of a Swern reagent (generated from 0.1 mL of oxalyl chloride and 0.3 mL DMSO in 5 mL of CH_2Cl_2). After stirring for 15 min at –78 °C, triethylamine (0.3 mL) was added and the mixture was allowed to attain rt. Water (3 mL) was added, the organic layer was separated, dried, and concentrated. The residue was dissolved in dry benzene (5 mL) to which methoxycarbonyl methylenetriphenylphosphorane (50 mg) was added; the mixture was stirred for 2 h at rt, filtered, and concentrated. The crude product was purified by column chromatography (hexane – ethyl acetate, 8:1) to afford ester **7** (67 mg, 0.064 mmol, 80%). IR (film, cm^{-1}) υ: 2929, 2858, 1725, 1675, 1454, 1090, 1028, 736, 698. ^1H NMR δ: 6.93 (dd, 1H, $J_{5,6}$ = 4.4 Hz, $J_{6,7}$ = 15.8 Hz, H-6), 6,04 (dd, 1H, $J_{5,7}$ = 1.8 Hz, H-7), 5.95 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1), 4.46 (d, 1H, $J_{3',4'}$ = 7.5 Hz, H-3′), 4.33 (dd, 1H, $J_{4',5'}$ = 7.5 Hz, H-4′), 3.96 (dd, 1H, $J_{2,3}$ = 7.4 Hz, $J_{3,4}$ = 8.9 Hz), 3.75 (s, 3H, OCH_3), 3.69 (d, 1H, $J_{1'A,1'B}$ = 10.9 Hz, H-1′A), 3.22 (dd, 1H, $J_{1,2}$ = 10.1 Hz, H-4), 0,93 (s, 9H, CMe_3), 0.10, 0.08 (2×s, SiMe_2). ^{13}C NMR δ: 166.7 (CO), 145.1 (C-6), 120.8 (C-7), 104.2 (C-2′), 88.8 (C-1), 83.8 (C-3′), 81.8 (C-4′), 81.7 (C-5′), 81.6 (C-4′), 81.0 (C-3), 79.9 (C-2), 75.6, 75.1, 73.4, 73.0, 72.7, 72.1 (6×CH_2Ph), 71.7 (C-1′), 69.7 (C-5), 63.4 (C-6′), 51.4 (OCH_3), 25.9 (CMe_3), 18.3 (CMe$_3$), –5.42, –5.44 (SiMe_2). MS *m*/*z*: 1073 [M($C_{63}H_{74}O_{12}Si$) + Na^+].

1′,2,3,3′,4,4′-Hexa-*O*-benzyl-6′-*O*-*tert*-butyldiphenylsilylsucrose (6)

To a solution of diol **3** (1.23 g, 1.39 mmol), DMAP (78 mg, 0.64 mmol), and diisopropylethylamine (0.5 mL) in CH_2Cl_2 (50 mL), *tert*-butyldiphenylsilyl chloride (0.36 mL, 1.4 mmol) was added over 30 min and the mixture was stirred overnight at rt. Water (70 mL) was added, the organic phase was separated, and the aqueous one extracted with CH_2Cl_2 (30 mL). The combined organic solutions were dried, concentrated, and the crude product was isolated by column chromatography (hexane – ethyl acetate, 5:1) to give the title compound (**6**) (0.93 g, 0.829 mmol, 60%) as a col-

orless oil. $[\alpha]_D$ +26.2°. IR (film, cm^{-1}) υ: 2930, 2859, 1497, 1454, 1089, 1028, 737, 698. ^1H NMR δ: 5.90 (d, $J_{1,2}$ = 3.8 Hz, 1H, H-1), 1.06 (s, 9H, CMe_3). ^{13}C NMR δ: 104.2 (C-2′), 88.7 (C-1), 83.6, 81.9, 80.7, 80.5, 80.1, 77.7, 71.3 (C-2,3,3′,4,4′,5,5′), 75.5, 74.9, 73.4, 73.1, 72.7, 72.3, 72.1 (C-1′ and 6×CH$_2$Ph), 63.9, 61.8 (C-6 and C-6′), 26.9 (Me_3C-Si), 19.2 (Me$_3$$C$Si). MS *m/z*: 1143.6 [M($C_{70}H_{76}O_{11}Si$) + Na^+]. Anal. calcd. for $C_{70}H_{76}O_{11}Si$: C 74.97, H 6.83; found: C 74.6, H 6.9.

(5*S*)-2,3,4-Tri-*O*-benzyl-5-*C*-metoxycarbonyl-α-D-xylopiranosyl-(1↔2)-6-*O*-*tert*-butyldiphenylsilyl-1,3,4-tri-*O*-benzyl-β-D-fructofuranoside (11)

DMSO (1 mL) was added dropwise to a solution of oxalyl chloride (0.4 mL) in CH_2Cl_2 (25 mL) at –78 °C under an argon atmosphere. After 5 min, alcohol **6** (1.2 g, 1.1 mmol in 15 mL CH_2Cl_2) was added and the mixture was stirred at –78 °C for 30 min. Triethylamine (1 mL) was added, stirring was prolonged for an additional 15 min at –78 °C, and the mixture was allowed to reach rt. It was then partitioned between water (40 mL) and ether (150 mL), the organic phase was separated, washed with water (2 × 50 mL) and brine (50 mL), dried, and concentrated. The oily residue was dissolved in acetone (20 mL) and titrated with Jones reagent (3 mL) until TLC (hexane – ethyl acetate, 1:1) indicated the disappearance of the starting material (ca. 20 min). The excess of the Jones reagent was decomposed with isopropanol (5 mL), most of the acetone was removed by vacuum, and the residue was partitioned between water (50 mL) and ethyl acetate (100 mL). The organic phase was separated, washed with brine (50 mL), dried, concentrated, and the crude acid was methylated with diazometane under standard conditions. Evaporation of the solvent left an oily residue, which was purified by column chromatography (hexane – ethyl acetate, 5:1) to give the title methyl uronate (**11**) (0.80 g, 0.698 mmol, 64%) as a colorless oil. $[\alpha]_D$ +19.9°. IR (film, cm^{-1}) υ: 2930, 2859, 1750 (CO), 1454, 1089, 1028, 737, 698. ^1H NMR δ: 5.77 (d, $J_{1,2}$ = 3.6 Hz, 1H, H-1), 4.78–4.40 (m, 14H, 12×CH_2Ph, H-3′, H-5), 4.30 (dd, $J_{3'4'}$ = 6.9 Hz, $J_{4'5'}$ = 6.9 Hz, 1H, H-4′), 4.07–4.03 (m, 1H, H-5′), 3.97–3.91 (m, 2H, both H-6′), 3.87 (dd, $J_{2,3}$ = 9.3 Hz, $J_{3,4}$ = 9.3 Hz, 1H, H-3), 3.69 (dd, $J_{4,5}$ = 9.4 Hz, 1H, H-4), 3.68 (d, $J_{1'A,1'B}$ = 11.2 Hz, 1H, H-1′A) 3.48 (d, 1H, H-1′B) 3.47 (dd, 1H, H-2), 3.469 (s, 3H, OCH_3), 1.05 (s, 9H, Me_3CSi). ^{13}C NMR δ: 170 (CO), 104.8 (C-2′), 90.1 (C-1), 83.8 (C-3′), 82.7 (C-4′), 81.6 (C-5′), 81.3 (C-3), 79.6 (C-4), 79.4 (C-2), 75.6, 74.9, 73.4, 73.0, 72.6, 72.3 (6×CH$_2$Ph), 70.9 (C-1′), 70.5 (C-5), 64.9 (C-6′), 51.9 (OCH$_3$), 26.9 (Me_3CSi), 19.3 (Me$_3$$C$Si). MS *m/z*: 1071.8 [M($C_{71}H_{76}O_{12}Si$) + Na^+].

6-*O*-Allyl-1′,2,3,3′,4,4′-hexa-*O*-benzylsucrose (9)

To a solution of **6** (1.71 g, 1.52 mmol) and allyl bromide (6 mL) in CH_2Cl_2 (40 mL), 50% NaOH (40 mL) and Bu_4NBr (0.15 g, 0.47 mmol) were added. The mixture was stirred vigorously for 24 h at rt. A second portion of allyl bromide (4 mL) was added, the stirring was continued overnight, and the mixture was then partitioned between water (30 mL) and ether (70 mL). The organic layer was separated, washed with water (40 mL), dried, concentrated, and the product was isolated by column chromatography (hexane – ethyl acetate, 7:1 to 4:1) to give 6-*O*-allyl-1′,2,3,3′,4,4′-hexa-*O*-benzyl-6′-*O*-*tert*-butyl-diphenylsilylsucrose (**8**) (0.91 g, 0.782 mmol, 52%; 66% calcd. on consumed **6**) as a colorless oil and unreacted alcohol **6** (0.38 g, 0.339 mmol). $[\alpha]_D$ +24.8°. IR (film, cm^{-1}) υ: 2929, 2859, 1453, 1090, 1027, 737, 698. MS *m/z*: 1184.6 [M($C_{73}H_{80}O_{11}Si$) + Na^+].

When the allyl bromide was replaced with allyl chloride, removal of the silyl protection from the C-6′ position was noted and the diallylated product was isolated from the reaction mixture in good yield.

To a solution of **8** (0.91 g, 0.782 mmol) in THF (20 mL), $Bu_4NF{\cdot}3H_2O$ (0.32 g, 1.0 mmol) was added and the mixture was stirred overnight at rt. The solvent was removed under reduced pressure and the residue was partitioned between ethyl acetate (40 mL) and water (40 mL). The organic layer was separated, dried, concentrated, and the residue was purified by column chromatography (hexane – ethyl acetate, 3:1 to 2:1) to give alcohol **9** (0.54 g, 0.58 mmol, 74%) as a colorless oil. $[\alpha]_D$ +35.2°. IR (film, cm^{-1}) υ: 2917, 2867, 1496, 1454, 1088, 1073, 1028, 736, 697. ^1H NMR δ: 5.93–5.83 (m, 1H, CH=CH$_2$), 5.52 (d, $J_{1,2}$ = 3.5 Hz, 1H, H-1), 5.27–5.22 (m, 1H, -CH$_2$-CH=CH_2, J = 17.2 Hz), 5.15 (1H, -CH$_2$-CH=CH_2, J = 10.4 Hz). ^{13}C NMR δ: 134.5 (-CH$_2$-CH=CH$_2$), 117.3 (-CH$_2$-CH=CH$_2$), 103.9 (C-2′), 91.1 (C-1), 83.7, 81.7, 81.3, 79.6, 79.4, 77.4, 71.3 (C-2,3,3′,4,4′,5,5′), 75.5, 74.9, 73.4, 73.3, 72.9, 72.49, 72.47, 71.2 (6×CH$_2$Ph, C-1′ and -CH$_2$-CH=CH$_2$), 67.9, 61.2 (C-6 and C-6′). MS *m/z*: 945 [M($C_{57}H_{62}O_{11}$) + Na^+]. Anal. calcd. for $C_{57}H_{62}O_{11}$: C 74.17, H 6.77; found: C 74.0, H 6.8.

6-*O*-Allyl-6′-*O*-acroyl-1′,2,3,3′,4,4′-hexa-*O*-benzylsucrose (10)

Alcohol **9** (0.355 g, 0.385 mmol) was dissolved in CH_2Cl_2 (20 mL) containing triethylamine (1 mL) and DMAP (ca. ~20 mg). Acroyl chloride (0.13 mL, 1.5 mmol) was added, the mixture was stirred for 1 h at rt and then partitioned between ether (70 mL) and water (50 mL). The organic phase was separated, dried, concentrated, and the residue was purified by column chromatography (hexane – ethyl acetate, 3:1) to give **10** (0.268 g, 0.29 mmol, 75%) as a yellowish oil. $[\alpha]_D$ +41.2°. IR (film): 3070, 3031, 2930, 2857, 1727, 1636, 1497, 1454, 1428, 1361, 821, 739, 700. ^1H NMR δ: 6.39 (dd, J = 1.3, 17.4 Hz, 1H, COCH=CH_2), 6.11 (dd, J = 10.5 Hz, 1H, second COCH=CH_2), 5.90–5.80 (m, 1H, CH$_2$CH=CH$_2$), 5.75 (dd, 1H, COCH=CH$_2$), 5.64 (d, $J_{1,2}$ = 3.6 Hz, 1H, H-1), 5.22 (dd, J = 17.2, 1.6 Hz, 1H, CH$_2$CH=CH_2), 5.12 (dd, J = 10.4 Hz, 1H, second CH$_2$CH=CH_2). ^{13}C NMR δ: 165.8 (CO), 134.7 (-CO$_2$$C$H=CH$_2$), 131.0 (-CO$_2$CH=$CH_2$), 128.5–127 (-CH$_2$$C$H=CH$_2$), 117.1 (-CH$_2$CH=$CH_2$), 104.7 (C-2′), 90.2 (C-1), 83.8, 82.2, 81.9, 79.7, 78.2, 77.7 and 70.7 (C-2,3,3′,4,4′,5,5′), 75.5, 74.8, 73.4, 72.9, 72.6, 72.5, 72.3, 70.9, 68.5, 65.3 (C-1′, C-6, C-6′, -CH$_2$CH=CH$_2$, and 6×OCH$_2$Ph). MS *m/z*: 999 [M($C_{60}H_{64}O_{12}$) + Na^+].

Metathesis reaction of 6-*O*-allyl-6′-*O*-acroyl-1′,2,3,3′,4,4′-hexa-*O*-benzylsucrose (10) catalyzed by Grubbs II catalyst

Compound **10** (0.250 g, 0.256 mmol) was dissolved in CH_2Cl_2 (7 mL) to which Grubbs II catalyst (13.1 mg, 0.015 mmol) was added and the mixture was boiled under reflux for 3.5 h. The mixture was then partitioned between

CH_2Cl_2 (20 mL) and water (30 mL), the organic phase was separated, and the aqueous one extracted with ether (10 mL). The combined organic layers were dried, concentrated, and the products were partially purified by column chromatography (hexane – ethyl acetate, 5:1 to 3:1) to afford unreacted compound **10** (30 mg) and a mixture of four compounds (76 mg) from which the individual products were isolated by HPLC (hexane – ethyl acetate, 5:2).

E-Isomer **12** was the first to be isolated. IR (film, cm^{-1}) υ: 2923, 2856, 1726 (CO), 1454, 1091, 1073, 1028, 736, 697. ^1H NMR (for numbering see Scheme 2) δ: 7.13 (ddd, $J_{\alpha,\beta}$ = 16.1 Hz, $J_{\beta,\delta}$ = 7.0 Hz, $J_{\beta,\gamma}$ = 5.2 Hz, 1H, H-β), 5.81–5.76 (m, 1H, H-α), 5.67 (d, $J_{1,2}$ = 3.8 Hz, H-1). ^{13}C NMR δ: 165.7 (CO), 147.8 (-CH_2*C*H=CHCO-), 22.3 (-CH=*CH*-CO-), 102.8 (C-2′), 88.6 (C-1), 84.2, 81.6, 79.9, 78.31, 78.25, 78.18, 71.2 (C-2,3,3′,4,4′,5,5″), 75.19, 75.13, 74.6, 73.3, 73.1, 72.4, 72.2, 69.9, 67.6, 60.0 (C-1′,6,6′, -*C*H_2CH=CH_2 and 6×O*C*H_2Ph). MS *m*/*z*: 971 (main signal) [M($C_{58}H_{60}O_{12}$) + Na^+] and 987 [M($C_{58}H_{60}O_{12}$) + K^+] (minor).

Z-Isomer **13** was the second to be isolated (contaminated with ca. 30% of **12**). ^1H NMR δ: 6.21 (ddd, $J_{\beta,\gamma}$ = 12.0 Hz, $J_{\beta,\delta}$ = 12.0 Hz, $J_{\alpha,\beta}$ = 5.2 Hz, 1H, H-β), 5.77 (ddd, $J_{\alpha,\gamma}$ = 1.8 Hz, $J_{\alpha,\delta}$ = 1.8 Hz, 1H, H-α), 5.54 (d, $J_{1,2}$ = 3.6 Hz, H-1). ^{13}C NMR δ: 166.1 (CO), 144.8 (-*C*H=CHCO-), 121.5 (-*C*H=CH-CO_2), 103.7 (C-2′), 90.2 (C-1), 83.7, 81.7, 80.7, 79.7, 79.0, 77.8, 71.6 (C-2,3,3′,4,4′,5,5′), 75.4, 74.6, 73.3, 73.1, 72.4, 72.3 (2×), 70.5, 67.2, 61.9 (C-1′,6′,6, -*C*H_2CH=CH_2 and 6×O*C*H_2Ph). MS *m*/*z*: 971 (minor signal) [M($C_{58}H_{60}O_{12}$) + Na^+] and 987 [M($C_{58}H_{60}O_{12}$) + K^+] (main).

Macrocyclic dimer **14** was the third to be isolated (contaminated with **12**, **13**, and **15**; ca. 5%–10% each). ^1H NMR δ: 6.83 (ddd, $J_{\alpha,\beta}$ = 15.8 Hz, $J_{\beta,\gamma}$ = 4.0 Hz, $J_{\beta,\delta}$ = 4.0 Hz, 1H, H-β), 5.96 (ddd, $J_{\alpha,\gamma}$ = 2.0 Hz, $J_{\alpha,\delta}$ = 2.0 Hz, 1H, H-α), 5.66 (d, $J_{1,2}$ = 3.7 Hz, H-1). ^{13}C NMR δ: 165.8 (CO), 145.6 (-CH_2*C*H=CHCO-), 120.0 (-CH_2CH=*C*HCO-), 104.6 (C-2′), 89.4 (C-1), 89.4, 83.6, 82.1, 81.3, 80.0, 77.7, 70.9 (C-2,3,3′,4,4′,5,5′), 75.5, 74.9, 73.5, 72.9, 72.5, 72.3, 71.6, 70.1, 69.3, 64.1 (C-1′,6,6′, -*C*H_2CH=CH_2 and 6×*C*H_2Ph). MS *m*/*z*: 1919 [M($C_{116}H_{120}O_{24}$) + Na^+] (strongest signal: 1920 [M + 1 + Na^+]).

Open-chain dimer **15** was the fourth to be isolated. ^1H NMR δ: 6.36 (dd, $J_{\alpha,\beta}$ = 17.4 Hz, $J_{\beta,\gamma}$ = 1.4 Hz, 1H, H-β), 6.09 (dd, $J_{\alpha,\gamma}$ = 10.4 Hz, 1H, H-α), 5.72 (dd, 1H, H-γ), 5.70 (dd, $J_{\delta,\phi}$ = 3.0 Hz, $J_{\delta,\varepsilon}$ = 3.0 Hz, 1H, H-δ), 5.62 (d, $J_{1,2}$ = 3.6 Hz, H-1). ^{13}C NMR δ: 165.9 (CO), 131.1 (-CO_2CH=*C*H_2), 129.5 (-CO_2*C*H=CH_2), 104.7 (C-2′), 90.3 (C-1), 83.9, 82.3, 81.8, 79.8, 78.3, 77.6, 70.70 (C-2,3,3′,4,4′,5,5′), 75.5, 74.8, 73.4, 72.9, 72.59, 72.50, 71.4, 70.8, 68.6, 65.4 (C-1′,6,6′, -*C*H_2CH=CH_2 and 6×*C*H_2Ph). MS *m*/*z*: 1947 [M($C_{118}H_{124}O_{24}$) + Na^+] (strongest signal: 1948 [M + 1 + Na^+]).

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