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Stereoselective (2-naphthyl)methylation of sugar hydroxyls by the hydrogenolysis of diastereoisomeric dioxolane-type (2-naphthyl)methylene acetals

Anikó Borbás,[a] Zoltán B. Szabó,[a] László Szilágyi,[b] Attila Bényei,[c] András Lipták[a,d,*]

[a]*Research Group for Carbohydrates of the Hungarian Academy of Sciences, Debrecen, PO Box 55, H-4010 Hungary*
[b]*Department of Organic Chemistry, Faculty of Science, University of Debrecen, Debrecen, PO Box 20, H-4010 Hungary*
[c]*Institute of Physical Chemistry, Faculty of Science, University of Debrecen, Debrecen, PO Box 7, H-4010 Hungary*
[d]*Department of Biochemistry, Faculty of Science, University of Debrecen, Debrecen, PO Box 55, H-4010 Hungary*

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Dedicated to Professor Derek Horton on the occasion of his 70th birthday

Abstract

The *cis* axial/equatorial OH groups of methyl α-L- and ethyl 1-thio-α-L-rhamnopyranoside, 1,6-anhydro-β-D-mannopyranose, and 1,6-anhydro-β-D-galactopyranose were reacted with 2-naphthaldehyde dimethyl acetal to diastereomeric dioxolane-type 2,3-*O*-(2-naphthyl)methylene or 3,4-*O*-(2-naphthyl)methylene acetals. The glycosides yielded the *exo*- and *endo*-isomers in nearly 1:1 ratio, 1,6-anhydro-β-D-mannopyranose gave predominantly the *endo*-, and 1,6-anhydro-β-D-galactopyranose exclusively *endo*-isomer. The acetals and some of their fully protected derivatives bearing benzyl or *tert*-butyldimethylsilyl groups were hydrogenolised with AlH_3 ($3LiAlH_4$-$AlCl_3$) or with $Me_3N{\cdot}BH_3$–$AlCl_3$ reagents. The *endo*-isomers were cleaved by both reagents to give *axial* NAP ethers, the *exo*-isomers of pyranosides furnished *equatorial* NAP ethers. However, the *exo*-isomers of pyranoses gave irregular *axial* ethers with a >30-fold enhancement of the reaction rates with respect to the *endo*-isomer.

1. Introduction

Although enormous progress has been made during the last two decades, the synthesis of complex oligosaccharides still remains difficult.[1] Conventional syntheses of the building blocks often require multiple protection and deprotection of various hydroxyl groups.[2] The introduction of acetals[3–5] and their transformation into hydroxy/ether derivatives are the most often used procedures. Reduction of dioxane type acetals of hexopyranosides with different mixed hydrides[6–11] result mainly in 4-*O*-alkyl/6-OH hexopyranosides, and the other type of solvents or reagents[8,9,12–15] give 6-*O*-alkyl/4-OH derivatives. The regioselectivity of the methods are attributed to preferential complexation at O-6 or O-4 leading to intermediary carbocations which are subsequently reduced to the hydroxy/ether derivatives.

From a preparative point of view, among the readily available hydroxy/ether derivatives the *O*-benzyl,[16,17] *O*-(*p*-methoxy)benzyl[16] and *O*-(2-naphthyl)methyl (NAP)[18] ethers are the most important. These can be obtained by the hydrogenolysis of 4,6-*O*-benzylidene,[16,17] 4,6-*O*-(*p*-methoxy)benzylidene[16] and 4,6-*O*-(2-naphthyl)methylene[18–21] acetals of hexopyranosides. 3,5-*O*-Benzylidene-xylofuranosides[22] were also cleaved with the $LiAlH_4$–$AlCl_3$ reagent to give 5-*O*-benzyl ethers.

In the case of the dioxolane type acetals of hexo-[23] and pentopyranosides,[24] the direction of the ring-cleavage reaction is determined by the configuration of the acetalic carbon. *Equatorial* ethers are obtained from the *exo*-(alkyl, aryl)-acetals; however, the *endo*-isomers react in an opposite way and the products are the *axial* ethers. This is a general rule and it was verified for all of the reagents above.[25]

* Corresponding author. Tel.: +36 52 512 900; fax: +36 52 512 913
E-mail address: liptaka@tigris.klte.hu (A. Lipták).

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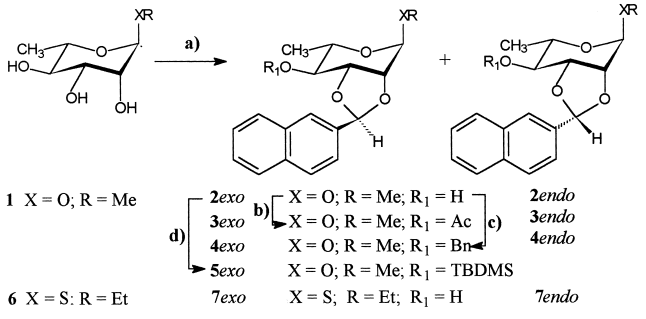
Most recently there have been some promising successful applications of sugar NAP ethers, mainly in the field of the synthesis of complex oligosaccharides.[26–35] Therefore, it was interesting to study the possibility of their preparation through the hydrogenolysis of both diastereomers of the hitherto unknown dioxolane type (2-naphthyl)methylene acetals.[19]

2. Results and discussion

To investigate the formation of dioxolane type (2-naphthyl)methylene acetals, two sets of starting compounds were selected: L-rhamnopyranosides and 1,6-anhydro-hexopyranoses.

Methyl α-L-rhamnopyranoside[36] (**1**) was reacted with 2-naphthaldehyde dimethyl acetal in the presence of *p*-toluenesulfonic acid (*p*TSA), and two diastereoisomeric forms of methyl 2,3-*O*-(2-naphthyl)methylene-α-L-rhamnopyranoside (***2exo*** and ***2endo***)[19] were obtained. The *exo*-isomer (42%) crystallised spontaneously, and in the mother liquor a ~2:1 ratio of the ***2exo*** and ***2endo*** isomers was detected by ^{1}H NMR (***2exo***: $\delta =$ 6.30 ppm; and ***2endo***: $\delta = 6.03$ ppm). Following acetylation of this mixture, the 4-*O*-acetyl derivatives were isolated in crystalline form (***3exo*** and ***3endo***). Similarly, treatment of the mixture of the ***2exo***/***2endo***-isomers with benzyl bromide/NaH in DMF solution gave the crystalline ***4exo***-isomer, and the syrupy ***4endo***-compound was obtained after column chromatographic purification. Deacetylation of compound **3***endo* yielded the **2***endo* derivative as a syrup. Compound **2***exo* was converted into 4-OTBDMS-ether (**5***exo*) by treatment with *tert*-butyldimethylsilyl chloride in the presence of imidazole. Since the protected thioglycosides are useful not only as glycosyl acceptors but also as glycosyl donors, treatment of ethyl 1-thio-α-L-rhamnopyranoside[37] (**6**) with 2-naphthaldehyde dimethyl acetal was also carried out, as described for the preparation of **2***exo*- and **2***endo*-compounds, to afford the crystalline **7***exo* (41%) and **7***endo* (47%) compounds (Scheme 1).

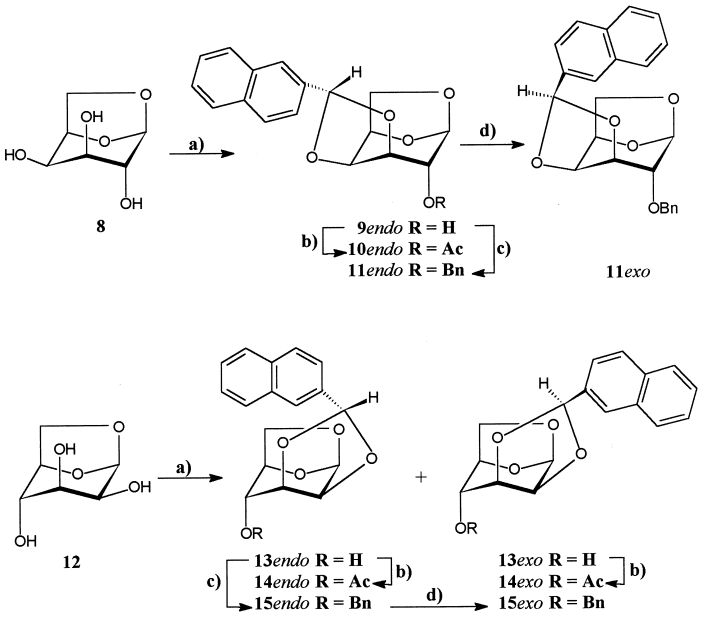


Scheme 1. Synthesis of dioxolane-type (2-naphthyl)methylene acetals of rhamnopyranosides. Reaction conditions: (a) 2-naphthaldehyde dimethyl acetal, TsOH, DMF; (b) acetic anhydride, pyridine; (c) benzyl bromide, NaH, DMF.

Acetalisation of 1,6-anhydro-β-D-galactopyranose[38] (**8**) required the same conditions as the L-rhamnopyranosides but only a single isomer was detected in the reaction mixture. It proved to be the *endo*-isomer (**9***endo*) which was acetylated (→**10***endo*) and benzylated (→**11***endo*); all of the three substances are crystalline. Compound **11***endo* was isomerised in dichloromethane with 0.05 equivalent of $AlCl_3$, and after 2 h, the **11***exo*:**11***endo* ratio was 1:2.36 (δ: 6.40 ppm and δ: 5.93 ppm).

Transformation of 1,6-anhydro-β-D-mannopyranose[39] (**12**) into the diastereoisomeric 2,3-*O*-(2-naphthyl)methylene acetals required a prolonged reaction time (5 days) and both isomers were isolated in crystalline form where the **13***endo*-isomer dominated (**13***endo*:**13***exo* = 6:1). This mixture was converted into the 4-*O*-acetyl derivatives (**14***endo* and **14***exo*). Compound **13***endo* was benzylated to **15***endo*. The **15***endo* diastereomer was converted into **15***exo* by isomerisation, and the ratio was 1.2:1 in favour of the *endo*-isomer as shown by ^{1}H-NMR measurements. Despite the fact that the *endo*-isomers of the 1,6-anhydro-2,3/3,4-*O*-(2-naphthyl)methylene-β-D-hexopyranoses are sterically extremely crowded, surprisingly they are the kinetic products, and the ratio of the two isomeric pairs in the equilibrium proves that the *endo*-isomers are more stable than the *exo* compounds (Scheme 2).

Comparison of the conditions of the ring-cleavage of benzylidene acetals to those of the (2-naphthyl)-methylene acetals revails that the latters require essentially milder conditions: the (2-naphthyl)methylene acetals can be opened by AlH_3 ($3LiAlH_4$–$AlCl_3$) instead of $AlClH_2$ ($LiAlH_4$–$AlCl_3$), the reaction time varies between 5 min to 2–3 hours at room temperature. Treatment of the *exo*-isomers of the methyl 2,3-*O*-(2-naphthyl)methylene-α-L-rhamnopyranoside derivatives (**2***exo*, **4***exo* and **5***exo*) with alane resulted in the 3-ONAP ethers (**16**–**18**) with isolated yields of 90, 93 and 93%. However, the *endo*-isomers (**2***endo*, **4***endo*) were cleaved to the 2-ONAP ethers (**19** and **20**) with a yield of 90 and 92%. Ring-opening proceeded with a complete stereoselectivity: the *exo*-isomers furnished *equatorial O*-NAP ethers, and the *endo*-isomers gave *axial O*-NAP ethers. The high stereoselectivity can be explained by two factors: under low temperature and in the presence of a soft Lewis acid (AlH_3) no isomerization was observed. The same reaction with high stereoselectivity were observed also in the case of the ethyl 2,3-*O*-(napthyl)methylene-1-thio-α-L-rhamnopyranoside isomers (**7***exo* and **7***endo*) affording ethyl 3-*O*-(2-naphthyl)methyl- (**21**) and ethyl 2-*O*-(2-naphthyl)-methyl-1-thio-α-L-rhamnopyranoside (**22**).



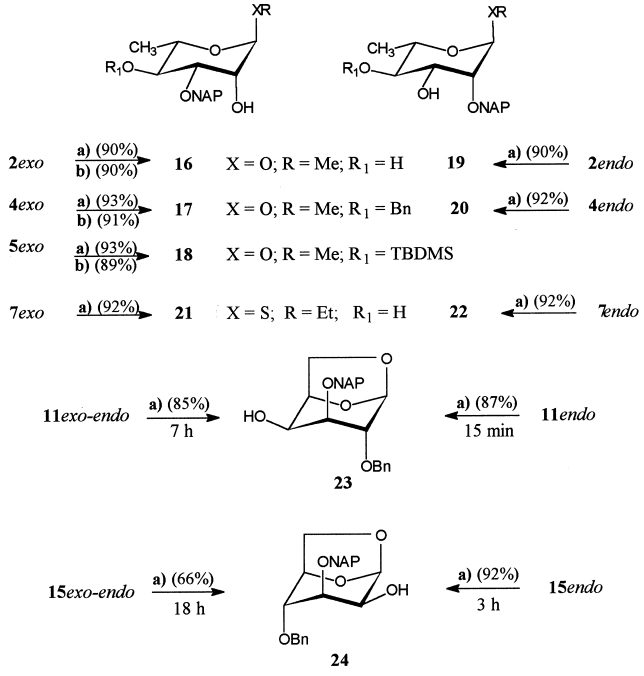
Scheme 2. Synthesis of dioxolane-type (2-naphthyl)methylene acetals of 1,6-anhydro-hexopyranoses. Reaction conditions: (a) 2-naphthaldehyde dimethyl acetal, TsOH, DMF; (b) acetic anhydride, pyridine; (c) benzyl bromide, NaH, DMF; (d) $AlCl_3$, CH_2Cl_2.

Compounds **2***exo*, **4***exo* and **5***exo* were treated with the $Me_3N{\cdot}BH_3$–$AlCl_3$ (4 equiv) reagent; the reaction was complete after 3 hours at room temperature and resulted in the same compounds (**16**–**18**) as with the alane reagent. The yields are also comparable to those of the alane-mediated reactions.

Cleavage of compounds **11***endo* and **15***endo* was stereoselective and fast reaction (84% isolated yield of **23** after 15 min, 89% yield of **24** after 3 h). The hydrogenolysis of the *exo*-isomers was studied with a mixture of the **11***exo*:**11***endo* (1:2.36) isomers and that of the **15***exo*:**15***endo* (1:1.2) isomers. The first reaction required 7 hours and gave only a single product: compound **23** was a characteristic cleavage product for the **11***endo*- but irregular for the **11***exo*-isomer. A completely similar reaction proceeded in the second reaction, resulting exclusively in the *axial O*-NAP ether again which was the regular cleavage product for the **15***endo*, but irregular for the **15***exo*-compound (Scheme 3). Similar irrregularities were also observed earlier for some benzylidene derivatives.[40–42]

We suppose that the hydrogenolysis, as well as the isomerisation of the dioxolane type benzylidene and (2-naphthyl)methylene acetals have common intermediates and these are the oxocarbonium ions. We assume that (i) the electrophylic attacks occur at different oxygens of the dioxolane skeleton; (ii) the reduction of the oxocarbonium ions is a faster reaction than the cleavage of the dioxolane ring.[43,44]

In the case of dioxolane type (2-naphthyl)methylene acetals the stereoselectivity of the hydrogenolysis of the *endo*-isomers is higher than in the case of benzylidene acetals. A probable explanation is that in the first case a very soft Lewis acid, AlH_3 is the electrophile, but it is a very hard hydride donor. In other words, the rate of the isomerisation is low, but the reduction is a fast process. The hydrogenolysis of the benzylidene acetals requires AlH_2Cl which enhances the rate of the isomeri-



Scheme 3. Hydrogenolysis of dioxolane-type (2-naphthyl)-methylene acetals of rhamnopyranosides and 1,6-anhydro-hexopyranoses. Reaction conditions: (a) AlH_3, CH_2Cl_2–Et_2O, r.t.; (b) $Me_3N{\cdot}BH_3$–$AlCl_3$, THF, r.t.

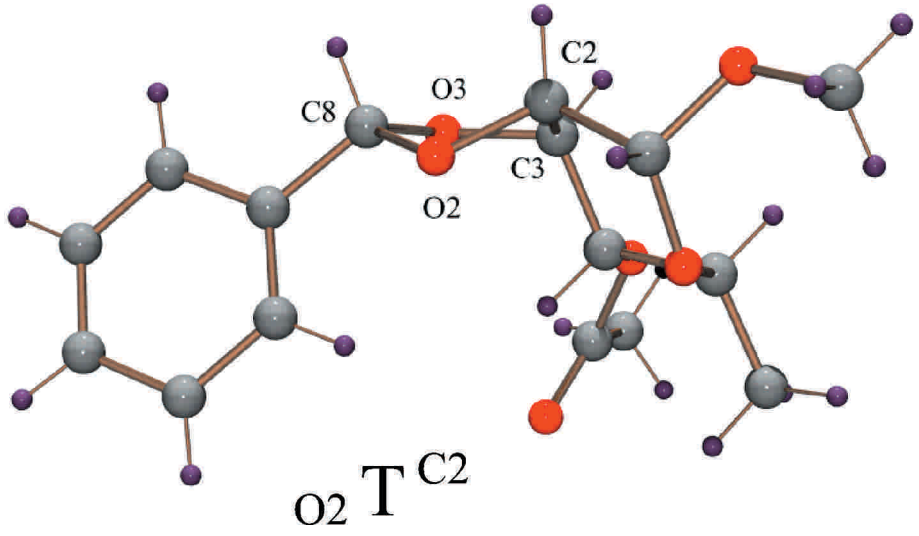


Fig. 1. X-ray structure of the methyl 4-*O*-acetyl-2,3-*endo*-benzylidene-α-L-rhamnopyranoside

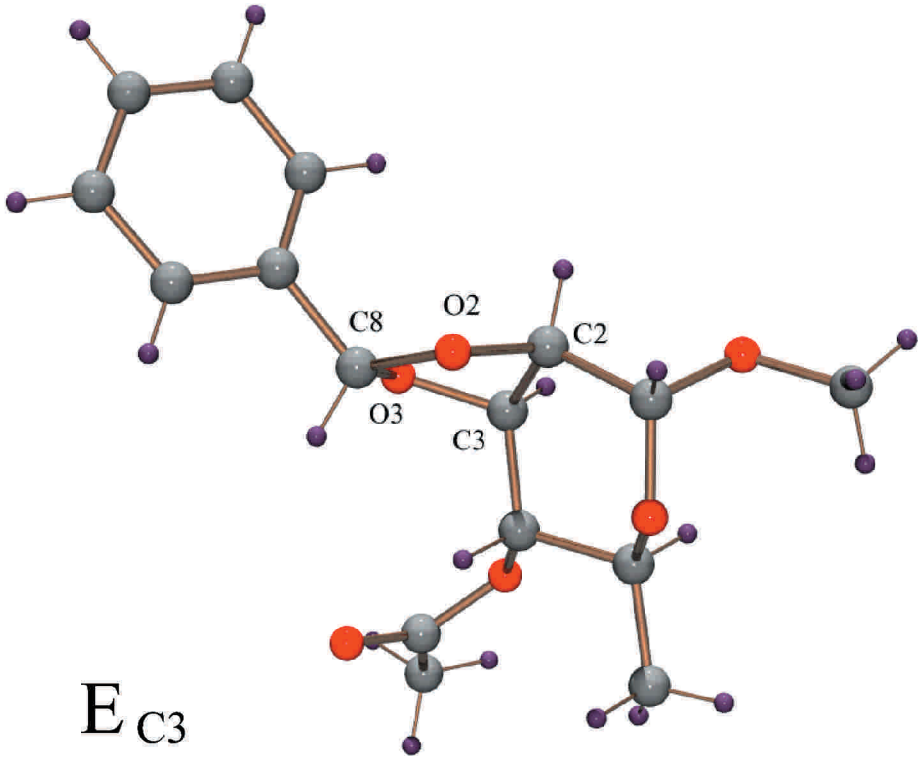


Fig. 2. X-ray structure of the methyl 4-*O*-acetyl-2,3-*exo*-benzylidene-α-L-rhamnopyranoside.

sation but decreases the rate of the reduction. X-ray crystallographic studies were performed on various *endo* and *exo* diastereoisomeric compounds in the rhamnopyranoside (methyl 4-*O*-acetyl-*exo*-[45] and methyl 4-*O*-acetyl-*endo*-2,3-*O*-benzylidene-α-L-rhamnopyranoside[45]) and mannopyranose (**14***exo* and **15***endo*) series[46] (Figs. 1–4). The main result of these investigations is that the dioxolane ring always adopts an envelope conformation in the *exo*-isomer, while it has a twist-like conformation in the *endo*-isomer. The angle of the planes of C2-C3-O3 and C8-O3-C3 for the *endo* isomers is in the region of 7–16°, while in the *exo* isomers it is in the region of 37–41°. The corresponding values for the C2-O2-C3 and O2-C8-O3 planes are 34-41°, and 0.6–12° for the *endo* and *exo* isomers, respectively. This means that the C8-O3-C3-C2 atoms are coplanar in the *endo* isomers, and the O2-C2-C3-O3 atoms are coplanar in the *exo* isomers. Detailed results

of the crystallographic studies will be published elsewhere.

Figs. 1–4 represent the conformation of the four studied molecules. In the case of both isomers the reagent (AlH_3) attacks at the oxygen located in the middle of the plane of the envelope or the twist skeleton. In the case of the *exo*-isomers the site of the attack cannot be the oxygen located at the carbon atom below or above the plane of the envelope. These observations suggest that the place of the attack of the reagent, or in other words, the electrophile on the oxygen depends on the conformation of the non-bonded electron pairs of the oxygen of the dioxolane-type skeleton. For more details on the hydrogenolysis of the dioxolane type acetal, investigations are under way in our laboratory.

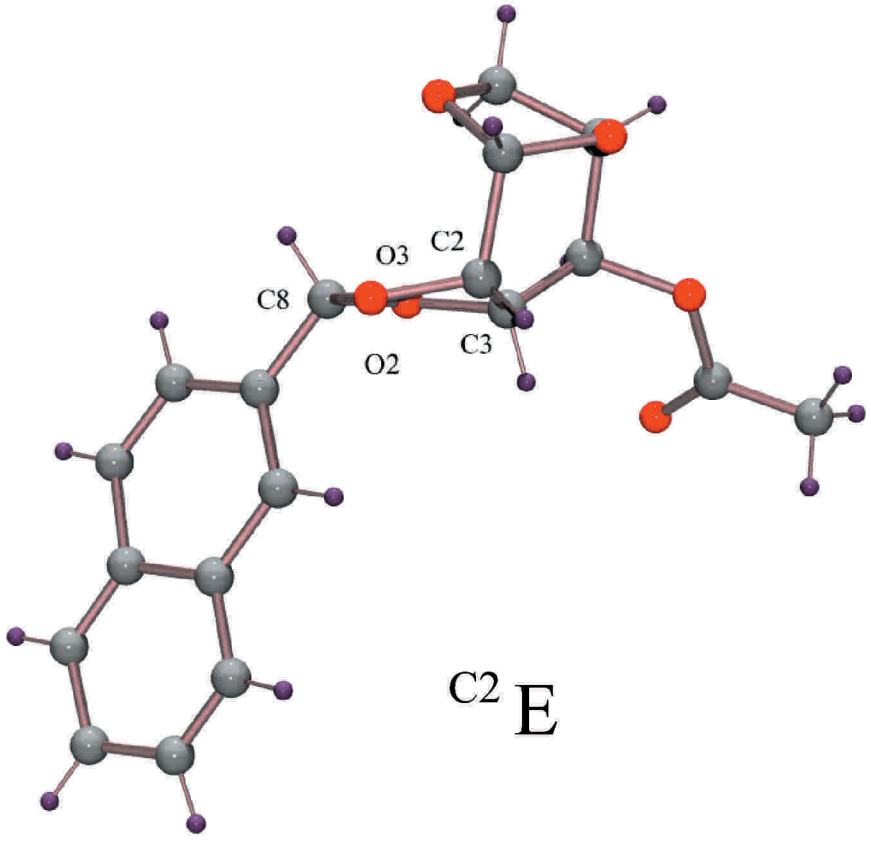


Fig. 3. X-ray structure of **14***exo*.

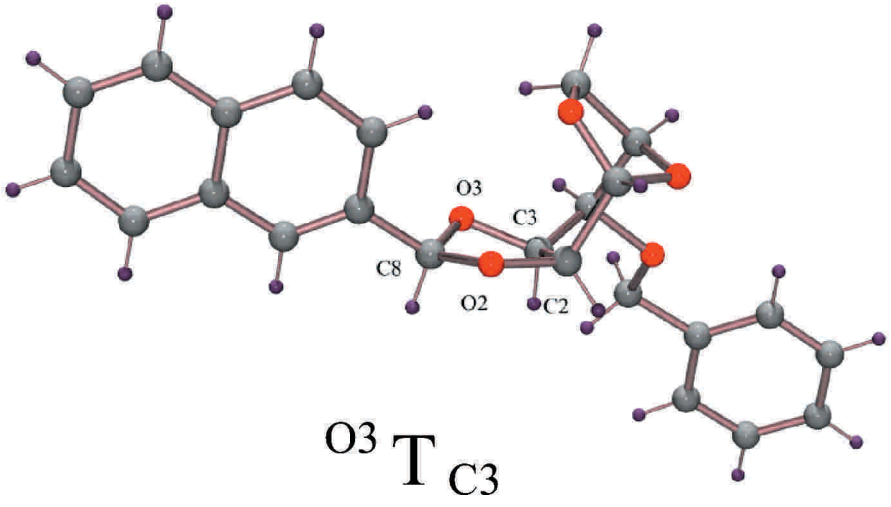


Fig. 4. X-ray structure of **15***endo*.

3. Experimental

General methods.—Optical rotations were measured at room temperature with a Perkin-Elmer 241 automatic polarimeter. Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. TLC was performed on Kieselgel 60 F_{254} (Merck) with detection by charring with 50% aqueous sulfuric acid. Column chromatography was performed on Silica Gel 60 (E. Merck 0.062–0.200 nm). The organic solutions were dried over $MgSO_4$, and concentrated in vacuum. The ^1H (200, 360 and 500 MHz) and ^{13}C NMR (50.3, 90.54, 125.76 MHz) spectra were recorded with Bruker WP-200SY, Bruker AM-360 and Bruker DRX-500 spectrometers for solutions in $CDCl_3$. Internal references: TMS (0.00 ppm for ^1H), $CDCl_3$ (77.00 ppm for ^{13}C). Single crystals of **14***exo* (from EtOAc-*n*hexane) and **15***endo* (from EtOH) suitable for X-ray diffraction measurement was obtained after recrystallization. X-ray diffraction data were collected at 293(1) K, Enraf Nonius MACH3 diffractometer, Mo Kα radiation $\lambda =$ 0.71073 Å.

*General method **A** for the hydrogenolysis of (2-naphthyl)methylene acetals of hexopyranosides with $LiAlH_4$-$AlCl_3$ to get compounds* **16**–**24**.—To a stirred solution of the starting acetal compound (1 mmol) and $LiAlH_4$ (3 equiv) in dry CH_2Cl_2:Et_2O (2:1, 6 mL) $AlCl_3$ in Et_2O (1 equiv in 3 mL) was added dropwise at room temperature. After complete conversion (10–15 min) 1–2 mL of EtOAc and 1–3 drops of water were added, the mixture was diluted with ethyl–acetate, washed with water (3 × 25 mL), dried and concentrated. The residue was purified by crystallization or column chromatography.

*General method **B** for the hydrogenolysis of (2-naphthyl)methylene acetals of hexopyranosides with $Me_3N.BH_3$-$AlCl_3$ to get compounds* **16**–**18**.—The mixture of the starting acetal compound (1 mmol), 4 Å molecular sieves (200 mg) and $Me_3N.BH_3$ (4 equiv) in dry THF (10 mL) was stirred for 30 min at room temperature, then $AlCl_3$ (4 equiv) was added. After complete conversion (2–3 h) the mixture was filtered through a layer of Celite, diluted with CH_2Cl_2, washed with water, dried, concentrated and co-evaporated 3 times with MeOH.

*Methyl 2,3-O-(2-naphthyl)methylene-α-L-rhamnopyranoside (**2**endo, **2**exo).*—To a solution of compound **1** (1.78 g, 10 mmol) in dry DMF (5 mL) 2-naphthaldehyde dimethyl acetal (2.6 g, 13 mmol) and catalytic amount of *p*-toluenesulfonic acid were added. The reaction mixture was stirred at room temperature for 24 h, then neutralized with triethylamine and evaporated in vacuo. The residue was dissolved in dichloromethane, washed with water (3 × 50 mL), dried and evaporated. The crude product was crystallized from *n*hexane–EtOAc to afford the title compound **2***exo* (1.35 g, 42%). The filtrate was a chromatographically unseparable mixture of the *exo* and *endo* isomers. Compound **2***exo*: mp 107–108 °C (white needles); $[\alpha]_D$ −2.4 (*c* 0.28, $CHCl_3$); R_f 0.25 (7:3 hexane–EtOAc); ^1H NMR δ (200 MHz, $CDCl_3$) 7.91–7.41 (7H, m, aromatic), 6.30 (1H, s, H acetalic), 4.93 (1H, s, H-1), 4.45 (1H, dd, $J_{2,3} = 5.2$, $J_{3,4} = 7.5$, H-3), 4.14 (1H, d, H-2), 3.53-3.80 (2H, m, H-4, H-5), 3.37 (3H, s, OCH_3), 2.79 (1H, d, $J_{4H,OH} =$ 4.1, 4-OH), 1.36 (3H, d, $J = 6.0$, CH_3-6); ^{13}C NMR δ (50 MHz, $CDCl_3$) 135.8 (2 ×), 133.6, 132.8, (C_q, aromatic), 128.4–123.4 (CH, aromatic), 103.1 (C acetalic), 98.0 (C-1), 79.6 (C-3), 75.4 (C-2), 71.9 (C-4), 65.3 (C-5), 54.9 (OCH_3), 17.4 (C-6). Anal. Calcd for $C_{18}H_{20}O_5$: C 68.34; H 6.37. Found: C 68.31; H 6.35.

Deacetylation of compound **3***endo* afforded the title compound **2***endo*, as a colorless syrup; $[\alpha]_D$ −23.1 (*c* 0.29, $CHCl_3$); R_f 0.25 (7:3 hexane–EtOAc). ^1H NMR δ (200 MHz, $CDCl_3$) 7.89–7.41 (7H, m, aromatic), 6.03 (1H, s, H acetalic), 5.01 (1H, s, H-1), 4.25 (1H, m, H-3), 4.14 (1H, d, $J_{2,3} = 2.1$, H-2), 3.73-3.45 (2H, m, H-4, H-5), 3.39 (3H, s, OCH_3), 3.14 (1H, br.s, 4-OH), 1.26 (3H, d, $J = 6.0$, CH_3-6); ^{13}C NMR δ (50 MHz, $CDCl_3$) 135.7-123.4 (C aromatic), 104.1 (C acetalic), 98.0 (C-1), 78.1 (C-3), 77.8 (C-2), 74.3 (C-4), 65.8 (C-5), 54.9 (OCH_3), 17.3 (C-6). Anal. Calcd for $C_{18}H_{20}O_5$: C 68.34; H 6.37. Found: C 68.30; H 6.34.

*Methyl 4-O-acetyl-2,3-O-(2-naphthyl)methylene-α-L-rhamnopyranoside (**3**endo, **3**exo).*—To a solution of the isomeric mixture of **2***exo* and **2***endo* (500 mg, 1.5 mmol) in dry pyridine (2 mL), acetic anhydride (1 mL) was added. After usual work-up procedure the title compounds were separated by column chromatography (7:3 hexane–EtOAc) yielding 250 mg (46%) of **3***endo* (R_f 0.42) and 230 mg (43%) of **3***exo* (R_f 0.50). Compound **3***endo* crystallized from EtOH, mp 122–123 °C (white crystals); $[\alpha]_D$ +49.3 (*c* 0.25, $CHCl_3$); ^1H NMR δ (200 MHz, $CDCl_3$) 7.95–7.80 (4H, m, aromatic), 7.57–7.41 (3H, m, aromatic), 6.07 (1H, s, H acetalic), 5.04 (1H, dd, $J_{3,4} = 7$, $J_{4,5} = 10$, H-4), 5.04 (1H, s, H-1), 4.40 (1H, t, $J_{2,3} = 7$, H-3), 4.27 (1H, d, H-2), 3.81 (1H, m, H-5), 3.40 (3H, s, OCH_3), 2.11 (3H, s, Ac), 1.20 (3H, d, $J = 6.0$, CH_3-6); ^{13}C NMR δ (50 MHz, $CDCl_3$) 169.9 (CO), 133.9–124.0 (C aromatic), 104.8 (C acetalic), 97.8 (C-1), 78.2 (C-3), 75.6 (C-2), 75.0 (C-4), 63.7 (C-5), 54.9 (OCH_3), 21.0 (Ac), 17.0 (C-6). Anal. Calcd for $C_{20}H_{22}O_6$: C 67.03; H 6.19. Found: C 66.97; H 6.15.

Compound **3***exo* crystallized from EtOH, mp 136–137 °C (white needles); $[\alpha]_D$ −6.6 (*c* 0.27, $CHCl_3$); ^1H NMR δ (200 MHz, $CDCl_3$) 7.95–7.76 (4H, m, aromatic), 7.57–7.43 (3H, m, aromatic), 6.38 (1H, s, H acetalic), 5.08 (1H, dd, $J_{3,4} = 8$, $J_{4,5} = 10$, H-4), 4.99 (1H, s, H-1), 4.54 (1H, dd, $J_{2,3} = 5.5$, H-3), 4.21 (1H, d, H-2), 3.81 (1H, m, H-5), 3.39 (3H, s, OCH_3), 2.14 (3H, s, Ac), 1.26 (3H, d, $J = 6.0$, CH_3-6); ^{13}C NMR δ (50 MHz, $CDCl_3$) 170.2 (CO), 135.5–123.5 (C aromatic), 103.1 (C acetalic), 98.0 (C-1), 77.2 (C-3), 75.6 (C-2),

71.6 (C-4), 63.5 (C-5), 54.9 (OCH_3), 20.9 (Ac), 17.0 (C-6). Anal. Calcd for $C_{20}H_{22}O_6$: C 67.03; H 6.19. Found: C 67.09; H 6.21.

*Methyl 4-O-benzyl-2,3-O-(2-naphthyl)methylene-α-L-rhamnopyranoside (**4**endo, **4**exo).*—To a solution of the isomeric mixture of **2***exo* and **2***endo* (500 mg, 1.5 mmol) in dry DMF (3 mL), 80% NaH was added at 0 °C (70 mg, 2.25 mmol) and stirred for 30 min. Then benzyl bromide (0.26 mL, 2.25 mmol) was added to the mixture and stirred for 2 h. After the usual work-up procedure the title compounds were separated by column chromatography (7:3 hexane–EtOAc) yielding 270 mg (44%) of **4***endo* (R_f 0.40) and 260 mg (43%) of **4***exo* (R_f 0.46). Compound **4***endo* isolated as colorless syrup, $[\alpha]_D$ −21.3 (*c* 0.34, $CHCl_3$); ^{1}H NMR δ (200 MHz, $CDCl_3$) 7.91–7.20 (12H, m, aromatic), 6.08 (1H, s, acetalic), 5.22 (1H, d, $J = 11.7$, CH_2a), 5.04 (1H, s, H-1), 4.82 (1H, d, CH_2b), 4.45 (1H, t, $J = 6.8$, H-3), 4.27 (1H, d, H-2), 3.75 (1H, m, H-5), 3.39 (3H, s, OCH_3), 3.34 (1H, m, H-4), 1.27 (3H, d, $J = 6.0$, CH_3-6); ^{13}C NMR δ (50 MHz, $CDCl_3$) 138.0-123.9 (C aromatic), 104.1 (C acetalic), 97.9 (C-1), 81.0 (C-4), 78.4 (2 ×, C-2, C-3), 72.6 (CH_2), 64.3 (C-5), 54.8 (OCH_3), 17.8 (C-6). Anal. Calcd for $C_{25}H_{26}O_5$: C 73.87; H 6.45. Found: C 73.98; H 6.40.

Compound **4***exo* crystallized from EtOH, mp 70–71 °C (white needles); $[\alpha]_D$ −69.7 (*c* 0.44, $CHCl_3$); ^{1}H NMR δ (500 MHz, $CDCl_3$) 7.91–7.20 (12H, m, aromatic), 6.14 (1H, s, acetalic), 4.93 (1H, d, $J = 11.7$, CH_2a), 4.89 (1H, s, H-1), 4.71 (1H, d, CH_2b), 4.60 (1H, t, $J = 5.1$, H-3), 4.13 (1H, d, $J = 5.1$, H-2), 3.71 (1H, m, H-5), 3.35 (1H, m, H-4), 3.31 (3H, s, OCH_3), 1.30 (3H, d, $J = 6.0$, CH_3-6); ^{13}C NMR δ (125 MHz, $CDCl_3$) 138.1, 135.9, 133.8, 132.9 (C_q, aromatic), 128.5, 128.3 (2x), 128.2 (2x), 128.1 (2x), 127.7, 126.5, 126.3, 125.8, 123.6 (CH, aromatic), 103.0 (C acetalic), 98.0 (C-1), 79.9 (C-3), 77.7 (C-4), 75.6 (C-2), 72.9 (CH_2), 64.1 (C-5), 54.9 (OCH_3), 17.9 (C-6). Anal. Calcd for $C_{25}H_{26}O_5$: C 73.87; H 6.45. Found: C 73.91; H 6.41.

*Methyl 4-O-tert-butyldimethylsilyl-2,3-O-(2-naphthyl)methylene-α-L-rhamnopyranoside (**5**exo).*—To a solution of **2***exo* (316 mg, 1 mmol) in dry DMF (3 mL), *tert*-butyldimethylsilyl chloride (210 mg, 1.2 mmol) and imidazole (163 mg, 2.4 mmol) were added and the mixture stirred overnight. After usual work-up procedure the title compound was purified by column chromatography (8:2 hexane–EtOAc, R_f 0.68) yielding 330 mg (77%) of **5***exo*, as colorless syrup, $[\alpha]_D$ −14.8 (*c* 0.37, $CHCl_3$); ^{1}H NMR δ (360 MHz, $CDCl_3$) 7.95–7.40 (7H, m, aromatic), 6.25 (1H, s, acetalic), 4.93 (1H, br.s, H-1), 4.36 (1H, dd, $J = 7.3$, 5.2, H-3), 4.13 (1H, d, $J = 5.2$, H-2), 3.66 (1H, m, H-5), 3.53 (1H, dd, $J = 9.3$, 7.3, H-4), 3.37 (3H, s, OCH_3), 1.32 (3H, d, $J = 6.1$, CH_3-6), 0.91 (9H, s, Bu^t), 0.19 (3H, s, Si–CH_3), 0.14 (3H, s, Si–CH_3); ^{13}C NMR δ (90 MHz, $CDCl_3$) 136.2, 133.8, 133.0 (C_q, aromatic), 128.4, 128.3, 127.7, 126.4, 126.2, 125.4, 123.6 (CH, aromatic), 102.7 (C-acetalic), 98.1 (C-1), 80.5 (C-3), 75.8, 72.8 (C-2, C-4), 65.6 (C-5), 54.8 (OCH_3), 25.9 (Bu^t), 18.3 (CH_3-6), 18.1 (Bu^t-C_q), −3.8, −4.5 (Si–CH_3). Anal. Calcd for $C_{24}H_{34}O_5Si$: C 66.94; H 7.96. Found: C 66.90; H 8.01.

*Ethyl 2,3-O-(2-naphthyl)methylene-1-thio-α-L-rhamnopyranoside (**7**endo, **7**exo).*—Compound **6** (700 mg, 3.3 mmol) was converted to compound **7** in a similar manner as described for the synthesis of **2**. The title compounds were purified by column chromatography (7:3 hexane–EtOAc) yielding 535 mg (47%) of **7***endo* (R_f 0.49) and 470 mg (41%) of **7***exo* (R_f 0.41). Compound **7***endo* crystallized from EtOAc-*n*hexane, mp 102–104 °C (white crystals); $[\alpha]_D$ −144.3 (*c* 0.24, $CHCl_3$); ^{1}H NMR δ (200 MHz, $CDCl_3$) 7.90–7.79 (4H, m, aromatic), 7.55–7.45 (3H, m, aromatic), 6.01 (1H, s, H acetalic), 5.68 (1H, s, H-1), 4.23 (1H, d, $J_{2,3} = 5.9$, H-2), 4.21 (1H, dd, $J_{3,4} = 10.5$, H-3), 4. (1H, m, H-5), 3.45 (1H, m, H-4), 2.72 (1H, d, $J_{4H,OH} = 4.1$, 4-OH), 2.61 (2H, m, SCH_2CH$_3$), 1.30 (3H, t, $J = 7.0$, SCH$_2$CH_3), 1.21 (3H, d, $J = 6.0$, CH_3-6); ^{13}C NMR δ (50 MHz, $CDCl_3$) 134.3-123.6 (C aromatic), 104.0 (C acetalic), 79.2 (C-1), 79.1 (C-3), 78.0 (C-2), 75.5 (C-4), 65.9 (C-5), 24.4 (SCH_2CH$_3$), 17.0 (C-6), 14.6 (SCH$_2$$CH_3$). Anal. Calcd for $C_{19}H_{22}O_4S$: C 65.87; H 6.40; S 9.25. Found: C 65.01; H 6.45; S 9.34.

Compound **7***exo* crystallized from EtOH, mp 135–137 °C (white needles); $[\alpha]_D$ −111.4 (*c* 0.34, $CHCl_3$); ^{1}H NMR δ (200 MHz, $CDCl_3$) 7.91–7.75 (4H, m, aromatic), 7.52–7.48 (3H, m, aromatic), 6.30 (1H, s, H acetalic), 5.60 (1H, s, H-1), 5.04 (1H, dd, $J_{2,3} = 5.1$, $J_{3,4} = 7.5$, H-3), 4.23 (1H, d, H-2), 4.18 (1H, m, H-5), 3.64 (1H, m, H-4), 2.79 (1H, d, $J_{4H,OH} = 4.5$, 4-OH), 2.60 (2H, m, SCH_2CH$_3$), 1.35 (3H, d, $J = 6.0$, CH_3-6); 1.28 (3H, t, $J = 7.0$, SCH$_2$CH_3), ^{13}C NMR δ (50 MHz, $CDCl_3$) 135.7–123.4 (C aromatic), 103.4 (C acetalic), 79.6 (C-1), 79.5 (C-3), 76.3 (C-2), 72.5 (C-4), 65.7 (C-5), 24.4 (SCH_2CH$_3$), 17.3 (C-6), 14.6 (SCH$_2$$CH_3$). Anal. Calcd for $C_{19}H_{22}O_4S$: C 65.87; H 6.40; S 9.25. Found: C 65.97; H 6.44; S 9.33.

*1,6-Anhydro-3,4-O-(2-naphthyl)methylene-β-D-galactopyranose (**9**endo).*—Compound **8** (2.1 g, 13.2 mmol) was converted to compound **9** in a similar manner as described for the synthesis of **2**. After 24 h TLC showed 70% conversion (7:3 hexane–EtOAc, R_f 0.49), the mixture was worked up and the solid crude product was crystallized from EtOAc yielding 2.18 g (55%) of **9***endo*: mp 260–262 °C (white needles); $[\alpha]_D$ +8.23 (*c* 0.12, $CHCl_3$); ^{1}H NMR δ (200 MHz, $CDCl_3 + Me_3OD$) 7.81–7.34 (7H, m, aromatic), 5.87 (1H, s, H acetalic), 5.42; ^{13}C NMR δ (50 MHz, $CDCl_3 + Me_3OD$) 103.2 (C acetalic), 100.1 (C-1), 74.3, 71.2, 70.4, 63.8 (C-2,3,4,5), 63.3 (C-6). Anal. Calcd for $C_{17}H_{16}O_5$: C 67.99; H 5.37. Found: C 68.04; H 5.31.

*2-O-Acetyl-1,6-anhydro-3,4-O-(2-naphthyl)methylene-β-D-galactopyranose (**10**endo).*—To a solution of **9***endo* (600 mg, 1.9 mmol) in dry pyridine (5 mL), acetic anhydride (3 mL) was added. After usual work-up procedure the solid residue was crystallized from EtOAc yielding 600 mg of **10***endo* (90%) as white needles; $[\alpha]_D$ +78.4 (*c* 0.49, $CHCl_3$); ^1H NMR δ (500 MHz, $CDCl_3$) 7.98–7.41 (7H, m, aromatic), 5.99 (1H, s, H acetalic), 5.51 (1H, s, H-1), 5.13 (1H, s, H-2), 4.54 (2H, m, H-3, H-5), 4.13 (1H, d, $J = 4.0$, H-4), 4.08 (1H, d, $J = 7.0$, H-6a), 3.35 (1H, d, H-6b), 2.12 (3H, s, Ac); ^{13}C NMR δ (125 MHz, $CDCl_3$) 133.5–123.2 (C aromatic), 102.8 (C acetalic), 98.6 (C-1), 75.7 (C-4), 71.9 (C-3), 70.5 (C-2), 69.1 (C-5), 63.3 (C-6) 20.6 (Ac). Anal. Calcd for $C_{19}H_{18}O_6$: C 66.66; H 5.30. Found: C 66.81; H 5.34.

*1,6-Anhydro-2-O-benzyl-3,4-O-(2-naphthyl)methylene-β-D-galactopyranose (**11**endo).*—To a solution of **9***endo* (300 mg, 1.0 mmol) in dry DMF (3 mL), 80% NaH was added at 0 °C (45 mg, 1.5 mmol) and stirred for 30 min. Then benzyl bromide (0.15 mL, 1.2 mmol) was added to the mixture and stirred for 2 h. After usual work-up procedure the residue was crystallized from EtOH yielding 340 mg (87%) of **11***endo*, as white needles: mp 128–130 °C $[\alpha]_D$ +32.7 (*c* 0.26, $CHCl_3$); ^1H NMR δ (200 MHz, $CDCl_3$) 8.08–7.35 (12H, m, aromatic), 5.93 (1H, s, H acetalic), 5.54 (1H, s, H-1), 4.83 (1H, d, $J = 12.0$, CH_2a), 4.70 (1H, d, $J = 12.0$, CH_2b) 4.65 (2H, m, H-4, 5), 4.38 (1H, d, $J_{3,4} = 7.0$, H–3), 4.16 (1H, d, $J = 7.0$, H-6a), 3.88 (1H, s, H-2), 3.54 (1H, dd, $J_{5,6} = 7.0$, H-6b), 3.81 (1H, s, H-5); ^{13}C NMR δ (50 MHz, $CDCl_3$) 137.2-123.4 (C aromatic), 102.9 (C acetalic), 99.8 (C-1), 76.6, 76.1, 72.1, 69.7 (C-2, 3, 4, 5), 72.2 (CH_2), 64.6 (C-6). Anal. Calcd for $C_{24}H_{22}O_5$: C 73.83; H 5.68. Found: C 73.81; H 5.64.

*1,6-Anhydro-2,3-O-(2-naphthyl)methylene-β-D-mannopyranose (**13**endo, **13**exo).*—To a solution of compound **12** (1.2 g, 7.4 mmol) in dry DMF (3 mL) 2-naphthaldehyde dimethyl acetal (1.9 g, 9.6 mmol) and catalytic amount of *p*-toluenesulfonic acid were added, and the mixture was stirred at room temperature. After 24 h TLC showed 50% conversion. The mixture stirred for 4 days, TLC showed 80% conversion (9:1 dichloromethane-acetone), the mixture was worked up and the solid crude product was crystallized from EtOH yielding 1.0 g of **13***endo*. The filtrate, containing the isomeric mixture of the title compounds was evaporated and separated by column chromatography (9:1 dichloromethane-acetone) yielding 200 mg of **13***endo* (over all yield 55%) and 200 mg of **13***exo* (9.2%). Compound **13***endo*: mp 220–221 °C (white needles); $[\alpha]_D$ −78.6 (*c* 0.11, $CHCl_3$); (R_f 0.23, 9:1 dichloromethane-acetone); ^1H NMR δ (200 MHz, $CDCl_3$) 7.98–7.81 (7H, m, aromatic), 5.95 (1H, s, H acetalic), 5.56 (1H, d, $J = 1.5$, H-1); ^{13}C NMR δ (50 MHz, $CDCl_3$) 134.1–124.4 (C aromatic), 104.8 (C acetalic), 99.3 (C-1), 78.7, 75.9 (C-3, 5), 71.6, 69. 2 (C-2, 4), 64.4 (C-6). Anal. Calcd for $C_{17}H_{16}O_5$: C 67.99; H 5.37. Found: C 68.01; H 5.33.

Compound **13***exo* crystallized from EtOH, mp 123–124 °C (white needles); $[\alpha]_D$ −43.5 (*c* 0.33, $CHCl_3$); (R_f 0.30, 9:1 dichloromethane-acetone); ^1H NMR δ (200 MHz, $CDCl_3$) 7.98–7.41 (7H, m, aromatic), 6.49 (1H, s, H acetalic), 5.59 (1H, d, $J = 2.5$, H-1); ^{13}C NMR δ (50 MHz, $CDCl_3$) 136.7-123.3 (C aromatic), 105.1 (C acetalic), 99.9 (C-1), 76.3, 75.8, 73.4, 69.2 (C-2, 3, 4, 5), 64.9 (C-6). Anal. Calcd for $C_{17}H_{16}O_5$: C 67.99; H 5.37. Found: C 66.71; H 5.32.

*4-O-Acetyl-1,6-anhydro-2,3-O-(2-naphthyl)methylene-β-D-mannopyranose (**14**endo, **14**exo).*—The isomeric mixture of **13***exo* and **13***endo* (300 mg, 1.0 mmol) was converted to compound **14***endo* and **14***exo* in a similar manner as described for the synthesis of **3**. Compound **14***endo* crystallized from EtOAc-*n*hexane, mp 160–162 °C (white crystals); $[\alpha]_D$ −111.5 (*c* 0.37, $CHCl_3$); (R_f 0.23, 9:1 dichloromethane-acetone); ^1H NMR δ (500 MHz, $CDCl_3$) 7.95–7.76 (4H, m, aromatic), 7.58–7.41 (3H, m, aromatic), 5.98 (1H, s, H acetalic), 5.51 (1H, s, H-1), 5.10 (1H, s, H-4), 4.68 (1H, m, H-5), 4.21 (2H, m, H-2, H-3), 4.10 (1H, m, H-6a), 3.85 (1H, m, H-6b), 2.18 (3H, s, Ac); ^{13}C NMR δ (125 MHz, $CDCl_3$) 133.9–124.1 (C aromatic), 104.5 (C acetalic), 98.8 (C-1), 75.7 (C-3), 73.1 (C-5), 71.3 (C-2), 70.8 (C-4), 64.4 (C-6) 20.7 (Ac). Anal. Calcd for $C_{19}H_{18}O_6$: C 66.66; H 5.30. Found: C 66.81; H 5.34.

Compound **14***exo* crystallized from EtOH, mp 83–85 °C (white needles); $[\alpha]_D$ +61.2 (*c* 0.29, $CHCl_3$); (R_f 0.30, 9:1 dichloromethane-acetone); Anal. Calcd for $C_{19}H_{18}O_6$: C 66.66; H 5.30. Found: C 66.73; H 5.26.

*1,6-Anhydro-4-O-benzyl-2,3-O-(2-naphthyl)methylene-β-D-mannopyranose (**15**endo).*—Compound **13***endo* (200 mg, 0.67 mmol) was converted to compound **15***endo* in a similar manner as described for the synthesis of **11***endo*. Compound **15***endo* crystallized from EtOH, mp 130–13 1°C (white needles); $[\alpha]_D$ +55.2 (*c* 0.34, $CHCl_3$); ^1H NMR δ (500 MHz, $CDCl_3$) 8.01–7.21 (12H, m, aromatic), 5.93 (1H, s, H acetalic), 5.59 (1H, d, $J = 2.9$, H-1), 4.78 (1H, d, $J = 12.0$, CH_2a), 4.69 (1H, d, $J = 12.0$, CH_2b) 4.71 (1H, s, H-4), 4.38 (1H, d, $J_{2,3} = 7.0$, H-3), 4.31 (1H, dd, H-2), 4.00 (1H, d, $J = 7.5$, H-6a), 3.87 (1H, d, H-6b), 3.81 (1H, s, H-5); ^{13}C NMR δ (125 MHz, $CDCl_3$) 137.0-124.3 (C aromatic), 104.6 (C acetalic), 98.9 (C-1), 75.7 2× (C-3, 5), 73.7 (C-4), 71.7 (C-2), 71.5 (CH_2), 64.6 (C-6). Anal. Calcd for $C_{24}H_{22}O_5$: C 73.83; H 5.68. Found: C 73.74; H 5.61.

Methyl 3-O-(2-naphthyl)methyl-α-L-rhamnopyranoside (**16**).—Compound **2***exo* (220 mg, 0.7 mmol) was converted to **16** following the general method A. The solid crude product was crystallized from EtOAc-*n*hexane yielding 200 mg (90%) of **16**: mp 74–76 °C (white needles); $[\alpha]_D$ −17.0 (*c* 0.27, $CHCl_3$); (Compound **2***exo* was also converted to **16** following the general method

B, with a yield of 90%). ^{1}H NMR δ (500 MHz, $CDCl_3$) 7.85–7.41 (7H, m, aromatic), 4.83 (1H, d, $J = 11.8$, CH_2a), 4.70 (1H, d, $J = 11.8$, CH_2b), 4.68 (1H, br.s, H-1), 4.02 (1H, br.s, H-2), 3.67 (1H, m, H-3), 3.61 (1H, m, H-5), 3.57 (1H, m, H-4), 3.32 (3H, s, OCH_3), 2.50 (1H, d, $J = 2.3$, OH-2), 2.32 (1H, d, $J = 2.5$, OH-3), 1.30 (3H, d, $J = 6.1$, CH_3-6); ^{13}C NMR δ (125 MHz, $CDCl_3$) 135.1, 133.2, 133.1 (C_q, aromatic), 128.6, 127.9, 127.7, 126.8, 126.3, 125.6 (CH, aromatic), 100.4 (C-1), 79.8 (C-3), 71.7 (CH_2), 71.6 (C-4), 67.8 (C-2), 67.5 (C-5), 54.8 (OCH_3), 17.6 (C-6). Anal. Calcd for $C_{18}H_{22}O_5$: C 67.91; H 6.97. Found: C 68.04; H 6.95.

Methyl 4-O-benzyl-3-O-(2-naphthyl)methyl-α-L-rhamnopyranoside (**17**).—Compound **4***exo* (86 mg, 0.2 mmol) was converted to **17** following the general method A. The crude product was purified by column chromatography (7:3 hexane-EtOAc) yielding 80 mg (93%) of **17** as a colorless syrup; $[\alpha]_D$ −30.3 (*c* 0.33, $CHCl_3$); (Compound **4***exo* was also converted to **17** following the general method B, with a yield of 91%). ^{1}H NMR δ (200 MHz, $CDCl_3$) 7.75–7.23 (12H, m, aromatic), 4.91 (1H, d, $J = 11.5$, CH_2a), 4.81 (2H, s, CH_2), 4.69 (1H, d, $J_{1,2} = 1.5$, H-1), 4.64 (1H, d, CH_2b), 4.05 (1H, m, H-2), 3.87 (1H, dd, $J_{2,3} = 3.5$, $J_{3,4} = 9.1$, H-3), 3.71 (1H, m, H-5), 3.48 (1H, t, $J_{4,5} = 9.1$, H-4), 3.32 (3H, s, OCH_3), 2.63 (1H, d, $J_{2H,OH} = 2.0$, 2-OH), 1.33 (3H, d, $J = 6.0$, CH_3-6); ^{13}C NMR δ (50 MHz, $CDCl_3$) 138.1-125.7 (C aromatic), 100.0 (C-1), 79.9 (2×, C-3, C-4), 75.3(CH_2-NAP), 72.0 (*CH_2*Ph), 68.4 (C-2), 54.7 (OCH_3), 17.8 (C-6). Anal. Calcd for $C_{25}H_{28}O_5$: C 73.51; H 6.91. Found: C 73.38; H 6.88.

Methyl 4-O-tert-butyldimethylsilyl-3-O-(2-naphthyl)methyl-α-L-rhamnopyranoside (**18**).—Compound **5***exo* (215 mg, 0.5 mmol) was converted to **18** following the general method A. The crude product was purified by column chromatography (8:2 hexane–EtOAc) yielding 200 mg (93%) of **18**. Compound **18** crystallized from EtOH: mp 74–76 °C (colorless crystals); $[\alpha]_D$ −53.8 (*c* 0.40, $CHCl_3$); (Compound **5***exo* was also converted to **18** following the general method B, with a yield of 89%). ^{1}H NMR δ (500 MHz, $CDCl_3$) 7.85–7.44 (7H, m, aromatic), 4.78 (1H, d, $J = 11.7$, CH_2a), 4.72 (1H, d, $J = 11.7$, CH_2b), 4.68 (1H, br.s, H-1), 3.98 (1H, br.s, H-2), 3.67-3.56 (3H, m, H-3, H-4, H-5), 3.34 (3H, s, OCH_3), 2.47 (1H, br.s, OH-2), 1.30 (3H, d, $J = 6.0$, CH_3-6), 0.91 (9H, s, Bu^t), 0.18 (2x3H, s, s, Si-CH_3); ^{13}C NMR δ (125 MHz, $CDCl_3$) 135.4, 133.2, 133.0 (C_q, aromatic), 128.3, 127.9, 127.7, 126.6, 126.2, 126.0, 125.7 (CH, aromatic), 100.1 (C-1), 80.4, 72.7, 6.84 (C-2, C-3, C-4), 71.8 (CH_2), 68.1 (C-5), 54.7 (OCH_3), 25.9 (Bu^t), 18.3 (CH_3-6), 18.1 (Bu^t-C_q), -3.8, −4.5 (Si-CH_3). Anal. Calcd for $C_{24}H_{36}O_5Si$: C 66.63; H 8.39. Found: C 66.48; H 8.30.

Methyl 2-O-(2-naphthyl)methyl-α-L-rhamnopyranoside (**19**).—Compound **2***endo* (220 mg, 0.7 mmol) was converted to **19** following the general method A. The crude product was purified by column chromatography (4:1 dichloromethane-acetone) yielding 200 mg (90%) of **19** as a colorless syrup; $[\alpha]_D$ +15.8 (*c* 0.53, $CHCl_3$); ^{1}H NMR δ (500 MHz, $CDCl_3$) 7.85–7.40 (7H, m, aromatic), 4.84 (d, 1H, 11.9, CH_2a), 4.66 (1H, br.s, H-1), 4.66 (1H, d, CH_2b), 3.70–3.75 (2H, m, H-2, H-3), 3.58 (1H, m, H-5), 3.45 (1H, t, $J = 9.0$, H-4), 3.30 (3H, s, OCH_3), 1.31 (3H, d, $J = 6.1$, CH_3-6); ^{13}C NMR δ (125 MHz, $CDCl_3$) 135.0, 133.2, 133.0 (C_q, aromatic), 128.4, 127.9, 127.7, 126.8, 126.2, 126.0, 125.7 (CH, aromatic), 99.1 (C-1), 78.1 (C-2), 73.8 (C-4), 73.1 (CH_2), 71.5 (C-3), 67.7 (C-5), 54.7 (OCH_3), 17.6 (CH_3-6). Anal. Calcd for $C_{18}H_{22}O_5$: C 67.91; H 6.97. Found: C 68.07; H 6.93.

Methyl 4-O-benzyl-2-O-(2-naphthyl)methyl-α-L-rhamnopyranoside (**20**).—Compound **4***endo* (130 mg, 0.32 mmol) was converted to **20** following the general method A. The crude product was purified by column chromatography (7:3 hexane–EtOAc) yielding 120 mg (92%) of **20** as a colorless syrup; $[\alpha]_D$ −11.3 (*c* 0.30, $CHCl_3$); ^{1}H NMR δ (200 MHz, $CDCl_3$) 7.91–7.21 (12H, m, aromatic), 4.90 (2H, d, $J = 12.0$, CH_2a, CH_2a‘), 4.75 (1H, d, $J_{1,2} = 1.5$, H-1), 4.73 (1H, d, CH_2b), 4.65 (1H, d, CH_2b‘), 3.94 (1H, m, H-3), 3.78 (1H, dd, $J_{2,3} = 4.0$, H-2), 3.66 (1H, m, H-5), 3.35 (1H, t, $J_{3,4} = 9.0$, H-4), 3.31 (3H, s, OCH_3), 2.35 (1H, d, $J_{3H,OH} = 9.0$, 3-OH), 1.35 (3H, d, $J = 6.0$, CH_3-6); ^{13}C NMR δ (50 MHz, $CDCl_3$) 138.4–125.7 (C aromatic), 97.9 (C-1), 82.2, 78.4 (C-2, C-4), 74.9 (CH_2-NAP), 73.1 (*CH_2*Ph), 71.6 (C-3), 66.9 (C-5), 54.7 (OCH_3), 18.0 (C-6). Anal. Calcd for $C_{25}H_{28}O_5$: C 73.51; H 6.91. Found: C 73.62; H 6.98.

Ethyl 3-O-(2-naphthyl)methyl-1-thio-α-L-rhamnopyranoside (**21**).—Compound **7***exo* (240 mg, 0.7 mmol) was converted to **21** following the general method A. The crude product was purified by column chromatography (3:2 hexane–EtOAc) yielding 220 mg (92%) of **21** as a colorless syrup; $[\alpha]_D$ −112.1 (*c* 0.69, $CHCl_3$); ^{1}H NMR δ (500 MHz, $CDCl_3$) 7.98–7.79 (4H, m, aromatic), 7.55–7.45 (3H, m, aromatic), 5.31 (1H, s, H-1), 4.78 (1H, d, $J = 12.0$, CH_2a),4.65 (1H, d, CH_2b), 4.19 (1H, d, $J_{2,3} = 4.0$, H-2), 4.09 (1H, m, H-5), 3.67 (2H, m, H-3, H-4), 3.11 (2H, s, 2-OH, 4-OH), 2.48 (2H, m, S*CH_2*CH_3),), 1.25 (3H, d, $J = 6.0$, CH_3-6), 1.15 (3H, t, $J = 7.0$, SCH_2CH_3); ^{13}C NMR δ (125 MHz, $CDCl_3$) 134.5-125.6 (C aromatic), 83.2 (C-1), 79.8 (C-2), 71.6 (CH_2), 75.1 (C-4), 69.2 (C-2), 68.1 (C-5), 24.9 (S*CH_2*CH_3), 17.5 (C-6), 14.7 (SCH_2*CH_3*). Anal. Calcd for $C_{19}H_{24}O_4S$: C 65.49; H 6.94; S 9.20. Found: C 65.57; H 6.95; S 9.31.

Ethyl 2-O-(2-naphthyl)methyl-1-thio-α-L-rhamnopyranoside (**22**).—Compound **7***endo* (130 mg, 0.32 mmol) was converted to **22** following the general method A. The crude product was purified by column chromatography (3:2 hexane–EtOAc) yielding 120 mg (92%) of **22**. Compound **22** crystallized from EtOAc-*n*hexane:

mp 75–76 °C (white needles); $[\alpha]_D$ −67.5 (*c* 0.49, $CHCl_3$); ^1H NMR δ (500 MHz, $CDCl_3$) 7.98–7.76 (4H, m, aromatic), 7.85–7.43 (3H, m, aromatic), 5.57 (1H, s, H-1), 4.81 (1H, d, $J = 12.0$, CH_2a),4.62 (1H, d, CH_2b), 3.98 (1H, m, H-5), 3.82 (1H, d, $J_{2,3} = 3.7$, H-2), 3.72 (1H, dd, $J_{3,4} = 9.5$, H-3), 3.51 (1H, t, H-4), 3.43 (2H, s, 3-OH, 4-OH), 2.49 (2H, m, SCH_2CH_3), 1.30 (3H, d, $J = 6.0$, CH_3-6), 1.19 (3H, t, $J = 7.0$, SCH_2CH_3); ^{13}C NMR δ (125 MHz, $CDCl_3$) 134.7-125.6 (C aromatic), 80.8 (C-1), 79.5 (C-2), 73.9 (C-4), 72.3 (CH_2), 71.8 (C-3), 68.1 (C-5), 24.9 (SCH_2CH_3), 17.5 (C-6), 14.7 (SCH_2CH_3). Anal. Calcd for $C_{19}H_{24}O_4S$: C 65.49; H 6.94; S 9.20. Found: C 65.38 H 6.88; S 9.32.

1,6-Anhydro-2-O-benzyl-3-O-(2-naphthyl)methyl-β-D-galactopyranose (**23**).—Compound **11***endo* (100 mg, 0.26 mmol) was converted to **23** following the general method A. The crude product was purified by column chromatography (7:3 hexane–EtOAc) yielding 87 mg (87%) of **23** as a colorless syrup; $[\alpha]_D$ −43.4 (*c* 0.42, $CHCl_3$); ^1H NMR δ (500 MHz, $CDCl_3$) 7.94–7.20 (12H, m, aromatic), 5.40 (1H, s, H-1), 4.68 (1H, d, $J = 11.5$, CH_2a-Bn), 4.53 (1H, d, $J = 12.0$, CH_2a-NAP), 4.46 (2H, d, CH_2b-Bn, CH_2b-NAP), 4.41 (1H, t, $J =$ 4.5, H-5), 4.19 (1H, d, $J = 7.2$, H-6a), 4.09 (1H, t, H-4), 3.79 (1H, d, H-3), 3.62 (1H, dd, H-6b), 3.58 (1H, s, H-2), 2.95 (H, br. s, 4-OH); ^{13}C NMR δ (125 MHz, $CDCl_3$) 1347.1-125.5 (C aromatic), 99.8 (C-1), 75.6 (C-3), 74.2 (C-5), 74.1 (C-2), 72.7 (CH_2-Bn), 72.1 (CH_2-NAP), 64.5 (C-4), 63.3 (C-6). Anal. Calcd for $C_{24}H_{24}O_5$: C 73.45; H 6.16. Found: C 73.53; H 6.21.

1,6-Anhydro-4-O-benzyl-3-O-(2-naphthyl)methyl-β-D-mannopyranose (**24**).—Compound **15** *endo* (130 mg, 0.32 mmol) was converted to **24** following the general method A, the rection was completed after 3 h. The crude product was purified by column chromatography (7:3 hexane–EtOAc) yielding 120 mg (92%) of **24** as a colorless syrup; $[\alpha]_D$ −35.2 (*c* 0.48, $CHCl_3$); ^1H NMR δ (500 MHz, $CDCl_3$) 7.95–7.12 (12H, m, aromatic), 5.39 (1H, s, H-1), 4.70 (1H, d, $J = 12.4$, CH_2a-Bn), 4.62 (1H, d, CH_2b-Bn), 4.39 (1H, d, $J = 12.5$, CH_2a-NAP), (1H, d, $J = 12.5$, CH_2a-NAP), 4.10 (1H, d, $J = 7.2$, H-6a), 4.19 (1H, d, $J = 7.2$, H-6a), 4.09 (1H, t, H-4), 3.79 (1H, d, H-3), 3.62 (1H, dd, H-6b), 3.58 (1H, s, H-2), 2.95 (H, br. s, 4-OH); ^{13}C NMR δ (125 MHz, $CDCl_3$) 1347.1–125.5 (C aromatic), 99.8 (C-1), 75.6 (C-3), 74.2 (C-5), 74.1 (C-2), 72.7 (CH_2-Bn), 72.1 (CH_2-NAP), 64.5 (C-4), 63.3 (C-6). Anal. Calcd for $C_{24}H_{24}O_5$: C 73.45; H 6.16. Found: C 73.37; H 6.11.

*Isomerisation of the 1,6-anhydro-2-O-benzyl-3,4-O-endo-(2-naphthyl)methylene-β-D-galactopyranose with $AlCl_3$ (**11***endo-exo).*—A mixture of **11***endo* (117 mg, 0.3 mmol) and 4Å molecular sieves in dry dichloromethane (3 mL) was stirred for 30 min., then 5 drops of Et_2O-solution of $AlCl_3$ ($\sim$100 μL, *c* 0.16 mol/l) was added. The reaction was monitored by TLC using different solvent systems (toluene–acetone, dichloromethane–acetone, hexane–EtOAc), but no changes could be detected. After 2 h the mixture was quenched with 0.1 mL of triethylamine, filtered, the filtrate was diluted with dichloromethane, washed with water (3 × 10 mL), dried and concentrated. The ^1H NMR spectrum of the residue showed an isomeric mixture of **11***exo* and *endo* in a ratio of 1:2.36; δ ^1H NMR (200 MHz, $CDCl_3$) 6.40 (H acetalic *exo*), 5.93 (H acetalic *endo*).

*Isomerisation of the 1,6-anhydro-4-O-benzyl-2,3-O-endo-(2-naphthyl)methylene-β-D-mannopyranose with $AlCl_3$ (**15***endo-exo).*—Compound **15***endo* (104 mg, 0.27 mmol) was isomerised in a similar manner as described for compound **11***endo*. The ^1H NMR spectrum of the residue showed an isomeric mixture of **15***exo* and *endo* in a ratio of 1:1.20; δ ^1H NMR (200 MHz, $CDCl_3$) 6.45 (H acetalic *exo*), 5.93 (H acetalic *endo*).

Hydrogenolysis of the isomeric mixture of 1,6-anhydro-2-O-benzyl-3,4-O-(2-naphthyl)methylene-β-D-galactopyranose with $LiAlH_4$-$AlCl_3$.—Isomeric mixture of compound **11***endo-exo* (100 mg, 0.26 mmol) was hydrogenolyzed following the general method A. The reaction was monitored by TLC, the reaction was completed after 7 h, formation of one product could be detected. The crude product was purified by column chromatography (7:3 hexane-EtOAc) yielding 83 mg (83%) of **23** as a colorless syrup.

Hydrogenolysis of the isomeric mixture of the 1,6-anhydro-4-O-benzyl-2,3-O-endo-(2-naphthyl)methylene-β-D-mannopyranose with $LiAlH_4$–$AlCl_3$.—Isomeric mixture of compound **15***endo-exo* (80 mg, 0.23 mmol) was hydrogenolyzed following the general method A. The reaction was monitored by TLC, after 18 h the conversion was $\sim$90%, and formation of one product could be detected. After the work-up procedure the crude product was purified by column chromatography (7:3 hexane–EtOAc) yielding 53 mg (66%) of **24**.

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