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STRATEGY AND PREPARATION OF SOME BUILDING BLOCKS FOR SYNTHESIS OF BRANCHED OLIGOSACCHARIDES

The importance of the role of oligosaccharides in biological processes relating to immunology, virology, cancer, antibiotic action has heightened the interest in accessibility and study of methods of their synthesis, including one-pot glycosidation, solid-phase synthesis, remote glycosilation and armed/disarmed glycosidation. Article discuss modern strategy of a glycoside bond formations based on the knowledge that a large disparity between the reactivities of the different glycosyl donors can be achieved by varying the protecting group and electron-donating or withdrawing character of the leaving group within the given classes of glycosyl donor. The synthetic approach designed in such pathway that the particular combination of protecting groups and anomeric substituents on sugar components would be selected. Several modern pathways for the design and the synthesis of branched oligosaccharides using various reactivity protective groups were discussed. A synthetic plan in which chosen protecting groups – acetyl (*Ac*), benzyl (*Bn*), 2-naphtyl (*2-Naph*), *p*-methoxybenzyl (*PMB*) and *p*-chlorobenzyl (*p-ClBn*) can be further selectively removed in high yields was represent in the article. Among the commonly used leaving groups in donor molecules thioglycosides were chosen as universal building block because they are stable under most reaction conditions often using for the construction building blocks of β-(1,3)-*D*-glucans. The methods of synthesis of some promising synthetic blocks for production of the corresponding branched oligo-derivatives were also outlined.

Key words: building blocks, protected monosaccharides, β-(1,3)-*D*-Glucans, synthesis.

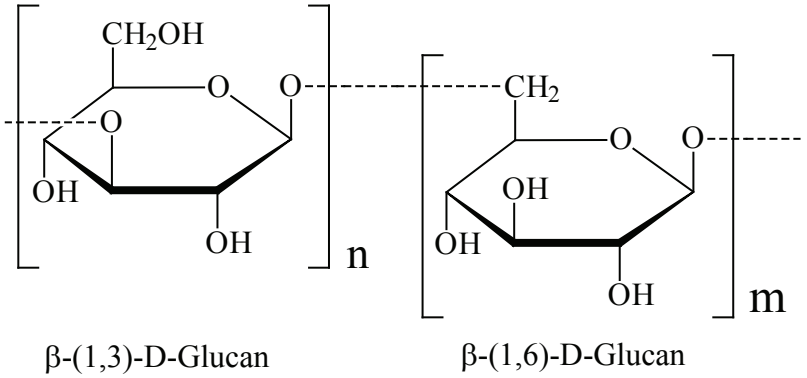
Carbohydrates besides they supply the largest part of the energy needed by the living cell, have been recognized in their involvement in various important biological functions [1, 2]. The study of carbohydrates has the fundamental scientific and medical importance [3 – 5].

Monosaccharides are fundamental biomolecules in that they are the building blocks of polysaccharides and they are the constitutional part of glycolipids, glycoproteins and nucleotides. While the biological importance of proteins and nucleic acids has been appreciated for a long time, oligosaccharides in form glycoconjugates are less understood and had only recently more generated interests [3 – 7]. Specific carbohydrate structures such as linear and branched oligosaccharides have been identified as markers for certain types of tumors [8], whiles others are binding sites for bacterial and viral pathogens [9].

Oligosaccharides are known to mediate cell-cell recognition, moderate the behavior of enzymes and other proteins, and fulfil various functions in the immune response. The recognition of saccharides is also important for carbohydrate metabolism and for the transport of these highly polar molecules across cell membranes [10]. These processes are intensively studied [11 – 14].

Homopolysaccharides, consisting of one sugar are described by use the suffix "an". Thus a polyglucose (polyglucopyranose) is termed "glucan". Others are heteropolysaccharides that may contain several various residues.

β-(1,3)-D-Glucans are the most commonly used terms for homopolysacharides that have β-(1,3)-D-linkages in the backbone and may possess β-D-glucosidic linkages at position 6 in different, repeating or branched units (Fig. 1). Glucans are wide spread in the nature and they are found in plants, bacteria, micro-algae, lichens, yeast and mushrooms [1, 2, 10].



β-(1,3)-D-Glucan β-(1,6)-D-Glucan

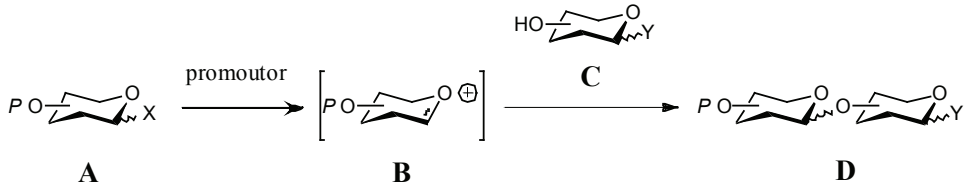
Fig. 1. General structure of β-(1,3)- and β-(1,6)-*D*-Glucans

The importance of the role of oligosaccharides in biological processes relating to immunology, virology, cancer, antibiotic action has heightened the interest in accessibility and study of methods of their synthesis [15 – 17], such as one-pot glycosidation [18 – 25], solid-phase synthesis [26 – 28], remote glycosilation [29] and armed/disarmed glycosidation [30, 31].

To date, the several methods directed toward the synthesis of branched β-(1,3)-D-glucans have been developed [15, 17, 25]. In order to avoid the laborious and time consuming multiple protection-deprotection and purification steps in the frames of the traditional procedure, methods based on programmable reactivity based one-pot strategy [22 – 25], and solid-phase synthesis [28] have been intensively studied.

For formation of a glycoside bond a living group X, (Scheme 1) which attached to the anomeric center of glycosyl donor **A** (where P are protecting groups), must be activated with a suitable Lewis acid (promoter) to leave the molecule giving rise to the oxonian ion **B**. This intermediate is then attacked by hydroxyl group of the glucose acceptor **C**. For an extension of the carbohydrate chain in both direction the formed disaccharide **D** must fulfil two demands: (1) it must be deprotectable selectively at single OH group and (2) it must carry a leaving group *Y* that can be activated in further glycosidation reaction without affecting the already formed glycoside bond.

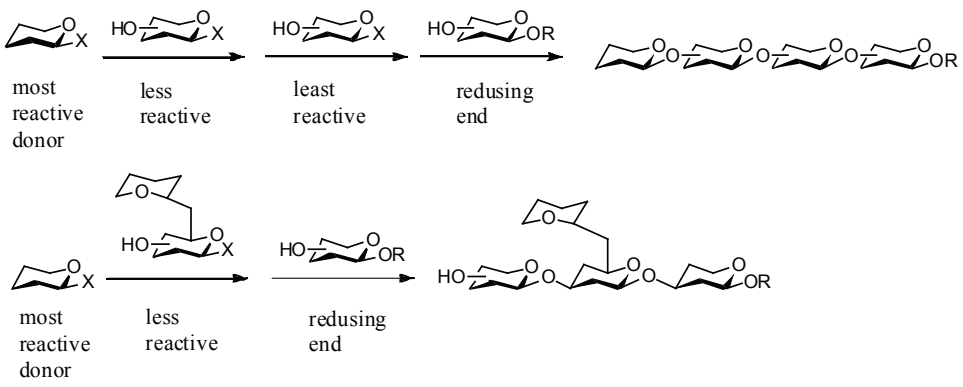
Scheme 1. The formation of a glycoside bond.



One-pot sequential glycosidation is based on the knowledge that a large disparity between the reactivities of the different glycosyl donors can be achieved by varying the protecting group and electron-donating or withdrawing character of the leaving group within the given classes of glycosyl donor [29]. The synthetic approach is designed in such pathway that the combination of protecting groups and anomeric substituents on sugar components would be selected [15, 30 – 37].

However, this methodology is not generally applicable because of the lack of knowledge about reactivity of useful glycosyl donors and acceptors. The relative reactivity value of glycosides can be measured in competition reactions between two donors to determine the relative rates of reactivity between them [22, 32, 38, 39]. The knowledge about quantitative relative reactivity value of glycosyl donors now is used in programmable one-pot oligosaccharide strategy (Scheme 2) [32, 40].

Scheme 2. Strategy for One-Pot Synthesis of Linear and Branched Oligosaccharides. [16]



For synthesis of branched oligosaccharides having β-(1,3)-*D*-glycosidic linkages, used building block must have free hydroxyl group at C-3 atom of β-glycopyranoside for linear glycosidation reactions and free hydroxyl group at C-6 for branching, which should be selectively deprotected in proper stages (Scheme 2).

Disaccharide building blocks obtained after glycosidation reaction can be used for following formation of tri-, tetra- and longer β-(1,3)-*D*-glucan building blocks.

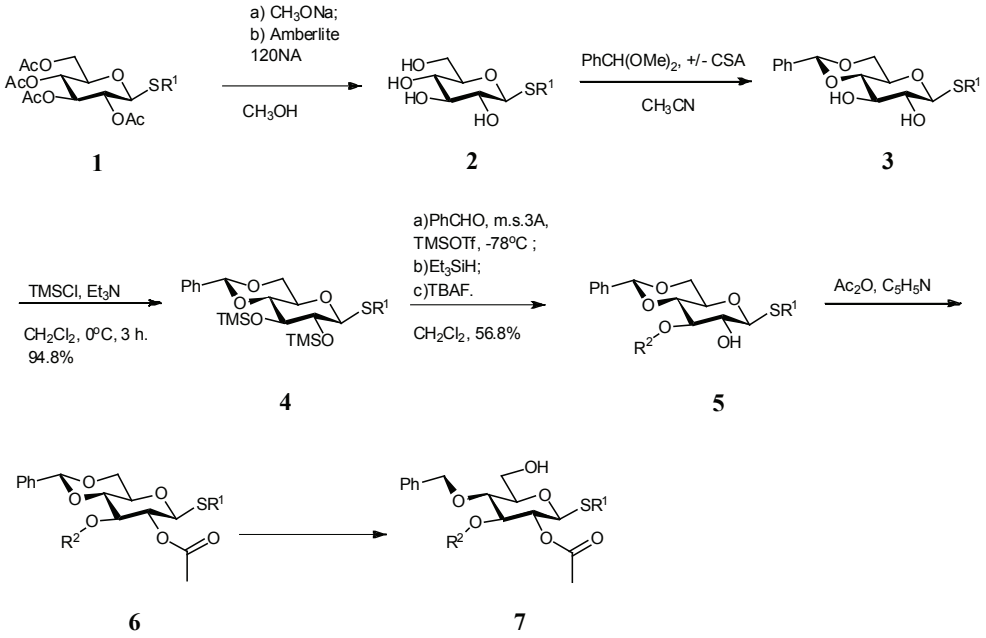
Results and Discussion

We have designed a synthetic plan in which chosen protecting groups – acetyl (*Ac*), benzyl (*Bn*), 2-naphtyl (*2-Naph*), *p*-methoxybenzyl (*PMB*) and *p*-chlorobenzyl (*p-ClBn*) can be selectively removed in high yields.

Among the commonly used leaving groups in donor molecules we chosen thioglycosides [41, 42] as universal building block because they are stable under most reaction conditions often using for the construction building blocks of β-(1,3)-*D*-glucans [19, 26]. Starting from Ethyl p-Methylphenyl-2,3,4,6-O-tetraacetyl-1-thio-β-D-glycopyranoside and after a row of transformation (Scheme 3): Zemplen deacetylation, the formation of benzyliden acetal protecting group for 4,6-hydroxy groups and

trimetylsilation of both C2, C3-hydroxy groups we designed Ethyl and *p*-Methylphenyl Thioglycosides (**4**). These compounds were used in synthesis of monosaccharides (**5**), in which from two free hydroxy groups only one at C-3 carbon atom was selectively protected by distinct substituted benzyl protecting groups. Next stages, the protection of last free hydroxy-group in the derivative (**5**) with formation acetate compound (**6**) and selective opening of 4,6-O-benzylidene acetal protecting groups should lead to target building blocks (**7**).

Scheme 3. Preparation of building blocks.



1 **2** **3**

4 **5**

6 **7**

1, 2, 3, 4 a) R^1 = Et; **b**) R^1 = *p*-MePh;
5 a) R^1 = Et; R^2 = Bn; **b**) R^1 = Et; R^2 = PMB; **c**) R^1 = *p*-MePh; R^2 = Bn;
d) R^1 = *p*-MePh; R^2 = PMB; **e**) R^1 = *p*-MePh; R^2 = *p*-ClPh;
6a) R^1 = Et; R^2 = Bn; **b**) R^1 = Et; R^2 = PMB.

Experimental Section

General Methods: THF, ether, and DME were distilled from sodium–benzophenone; acetonitrile and CH_2Cl_2 were distilled from P_2O_5 immediately prior use. The reactions were conducted under argon atmosphere. Melting points were determined on a Fargo melting point apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were determined on Bruker 400, 500 and 600 MHz spectrometers in $CDCl_3$ or DMSO-d_6 solution at 25 °C. Chemical shifts are expressed in ppm downfield from internal standard TMS. MS spectra were carried out on HP 5973 GC-MS instrument. Flash column chromatography was carried out over silica gel G60 (70-230 mesh, ASTM; Merck). Thin layer chromatography (TLS) was performed on silica gel G60 F_{254} (Merck) plates

with short wave length UV light for visualization. Elemental analyses were done on the Heraeus CHN-O Rapid instrument.

Ethyl 1-thio-β-*D*-glucopyranoside (2a). A solution of sodium methylate (65.6 mg, 1.2 mmol) in anhydrous CH_3OH (0.5 mL) was added to a stirring solution of **1a** (1.9605 g, 5.0 mmol) in anhydrous CH_3OH (10 ml) at room temperature. The mixture was stirred at room temperature for 2 h, the solution was neutralized with Amberlite IR-129 (H^+) resin, filtered, and concentrated. The residue was dried in high vacuum to give practically pure **2a** (1.2051 g, quantitatively) as amorphous mass, which was used without further purification.

Ethyl 4,6-O-benzyliden-1-thio-β-*D*-glucopyranoside (3a). To a solution of compound **2a** (1.1204 g, 5.0 mmol) and +/-CSA (1.9 mg, 0.008 mmol) in CH_3CN was added benzaldehyde dimethyl acetal (1.125 mL, 7.49 mmol). The mixture was stirred 2 h, until TLS showed that the reaction had been completed. Triethylamine (20 μL) was added to neutralize the acid and then concentrated. The residue was crystallized from EtOAc/Hexane and mother liquor was concentrated and chromatographed gave **3a** (1.2813 g, 81.7 %).

Ethyl 2,3-bis-O-trimethylsilil-4,6-O-benzyliden-1-thio-β-*D*-glucopyranoside (4a). To stirred and cooled to 0°C solution of **3a** (0.3124 g, 1 mmol) and Et_3N (1.054 mL, 7.5 mmol) in anhydrous CH_2Cl_2 (4 mL) was added TMSCl (380 μL, 3 mmol). After stirring at 0°C for 3 h TLC analysis (SiO_2, hexane/$CHCl_3$) was shown the absence of starting material. Solvent and abundance of reagents was removed *in vacuo*, and then residue was mixed with hexane (5 mL) and filtered. Solid was washed twice with hexane (3 mL) then hexane was removed under diminished pressure. The residue was dried *in vacuo* for overnight afforded **4a** (0.4223 g, 92.6 %) as oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.31-7.43 (m, 5H, ArH), 5.44 (s, 1H, Ph-CH), 4.42 (d, J = 9.6 Hz, 1H, H-1), 4.29 (m, 1H, H-4), 3.66-3-73 (m, 2H, H-3,H-6), 3.47 (dd, J = 4.4, 10.4 Hz, 1H, H-2), 3.42-3.40 (m, 2H, H-6, H-5), 2.70 (m, 2H, S$\underline{CH_2}CH_3$), 1.28 (t, J = 7.4 Hz, 3H, $SCH_2\underline{CH_3}$), 0.188 (s, 9H, $Si(CH_3)_3$), 0.043 (s, 9H, $Si(CH_3)_3$), ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.34 (C), 129.31 (CH), 128.54(CH), 126.64 (CH), 102.26 (CH), 87.34 (CH), 81.50 (CH), 76.38 (CH), 74.06 (CH), 70.55 (CH), 68.99 (CH), 25.31 (CH_2), 15.19 (CH_3), 1.35 (CH_3), 1.11 (CH_3) ppm; HRMS (FAB, M^+) calcd for $C_{21}H_{36}O_5SSi_2$ 456.1822, found 456.1836.

Ethyl 3-O-benzyl-4,6-O-benzyliden-1-thio-β-*D*-glucopyranoside (5a). To a mixture of freshly dried molecular sieves 3A (205 mg), compound **4a** (113.4 mg, 0.25 mmol), benzaldehyde (30.3 μL, 0.30 mmol) and anhydrous CH_2Cl_2 (2 mL) at -78°C was added TMSOTf (4 μL). After stirring at -78°C for 1 h triethylsilane (48 μL, 0.30 mmol) was added. The reaction was monitored by TLC for 5 h until a spot of starting material was disappeared and 1 M solution of TBAF in THF (597 μL, 0.60 mmol) was added. Then dry ice/acetone bath was removed and the reaction mixture was stirred for 1.5 h, quenched by adding aq. saturated solution of NH_4Cl (5 mL). The water layer was extracted with EtOAc (5 mL × 3). Organic layers were combined, dried over $MgSO_4$, filtered and concentrated. Flash column chromatography on silica gel (EtOAc/Hex = 1/10) gave **5a** (83 mg, 82.9 %) as a white solid. Analytically pure sample was crystallized from CHCl/Hex, mp 138-139 °C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.28-7.48 (m, 10H, ArH), 5.56 (s, 1H, Ph-CH), 4.96 (d, J = 11.7 Hz, Ph$\underline{CH_2}$), 4.79 (d, J = 11.7 Hz, Ph$\underline{CH_2}$), 4.45 (d, 1H, J = 9.7 Hz, H-1), 4.34 (dd 1H, H_{6e}, $^2J_{ae}$ = 10 Hz, $^3J_{5,6e}$ = 4.0 Hz), 3.76 (t, 1H, H-6a, $^2J_{ae}$ = 10 Hz, $^3J_{5,6e}$ = 10 Hz), 3.68 (m, 2H, H-3, H-4), 3.56 (m, 1H, H-2), 3.48 (m, 1H, H-5), 2.74 (m, 2H, S$\underline{CH_2}CH_3$), 1.30 (t, J = 7.4 Hz, 3H, $SCH_2\underline{CH_3}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.60 (C), 137.50 (C), 129.23 (CH), 128.68 (CH), 128.48 (CH),

128.28 (CH), 128.06 (CH), 126.22 (CH), 101.48 (CH), 86.80 (CH), 81.77 (CH), 81.45 (CH), 74.94 (CH), 73.20 (CH),70.98 (CH), 68.86 (CH), 24.80 (CH_2), 15.45 (CH_3) ppm.

Ethyl 3-O-*p*-methoxybenzyl-4,6-O-benzyliden-1-thio-β-*D*-glucopyranoside (5b). To a mixture of freshly dried molecular sieves 3A (205 mg), compound **4a** (123 mg, 0.27 mmol), p-methoxybenzaldehyde (39 μL, 0.32 mmol) and anhydrous CH_2Cl_2 (2 mL) at -78°C was added TMSOTf (4 μL). After stirring at -78°C for 1 h triethylsilane (52 μL, 0.32 mmol) was added. The reaction was monitored by TLC for 5 h until a spot of starting material was disappeared and 1 M solution of TBAF in THF (539 μL, 0.539 mmol) was added. Then dry ice/acetone bath was removed and the mixture was stirred for 1.5 h, quenched by adding aq. saturated solution of NH_4Cl (5 mL). The water layer was extracted with EtOAc (5 mL × 3). Organic layers were combined, dried over $MgSO_4$, filtered and concentrated. Flash column chromatography on silica gel (EtOAc/Hex = 1/5) gave **5** (83 mg, 72.2 %) as a white solid. Analytically pure sample was crystallized from CHCl/Hex, mp 128-129°C, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.36-7.49 (m, 5H, ArH), 7.29, 6.84 (dd, 4H, p-MeOArH, 5.56 (s, 1H, Ph-CH), 4.90 (d, *J* = 11.2 Hz, $PhCH_2$), 4.72 (d, *J* = 11.2 Hz, $PhCH_2$), 4.44 (d, *J* = 9.7 Hz, 1H, H-1), 4.33 (m, 1H, H-4), 3.77 (s, 3H, CH_3O), 3.44 – 3.79 (m, 5H, H-2, H-3, H-5, 2H-6,), 2.72 (m, 2H, S$\underline{CH_2}CH_3$), 1.29 (t, *J* = 7.4 Hz, 3H, $SCH_2\underline{CH_3}$) ppm.

Ethyl 2-O-acetyl-3-O-benzyl-4,6-O-benzyliden-1-thio-β-*D*-glucopyranoside (6a). To stirred and cooled to 0°C solution of **5a** (112.1 mg, 0.28 mmol) in anhydrous pyridine (0.5 mL) was added acetic anhydride (535 μL, 5.25 mmol). The mixture was stirred at room temperature for 15 h, when starting material was not found by TLC analysis. The mixture was co-evaporated with toluene (2 mL), EtOH (4 mL) and CH_2Cl_2 (2 mL) (each 3 times). The residue was purified by silica gel flash column chromatography (EtOAc/Hex = 1/10, then 1/5, 1/2) to give **6a** (109.8 mg, 88.7 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25-7.47 (m, 10H, ArH), 5.57 (s, 1H, Ph-CH), 5.04 (m, 1H, H-2), 4.86 (d, *J* = 12.0 Hz, $PhCH_2$), 4.66 (d, *J* = 12.0 Hz, $PhCH_2$), 4.44 (d, *J* = 10.8 Hz, 1H, H-1), 4.36 (m, 1H, H-4), 3.72 – 3.79 (m, 3H, H-3, 2H-6,), 3.48 (m, 1H, H-5), 2.68 (m, 2H, S$\underline{CH_2}CH_3$), 2.00 (s, 3H, CH_3CO), 1.23 (t, *J* = 7.4 Hz, 3H, $SCH_2\underline{CH_3}$) ppm.

Ethyl 2-O-acetyl-3-O-*p*-methoxybenzyl-4,6-O-benzyliden-1-thio-β-*D*-glucopyranoside (6b). To stirred and cooled to 0°C solution of **5b** (72.2 mg, 0.17 mmol) in anhydrous pyridine (0.5 mL) was added acetic anhydride (320 μL, 3.39 mmol). The mixture was stirred at room temperature for 16 h, when starting material was not detected by TLC analysis. The mixture was co-evaporated with toluene (2 mL), EtOH (4 mL) and CH_2Cl_2 (2 mL) (each 3 times). The residue was purified by silica gel flash column chromatography (EtOAc/Hex = 1/5) to give **6b** (74 mg, 93.4 %). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.36-7.49 (m, 5H, ArH), 7.18, 6.82 (dd, 4H, p-MeOArH, 5.56 (s, 1H, Ph-CH), 5.05 (m, 1H, H-2), 4.77 (d, *J* = 11.6 Hz, $PhCH_2$), 4.60 (d, *J* = 11.6 Hz, $PhCH_2$), 4.43 (d, *J* = 10.1 Hz, 1H, H-1), 4.35 (m, 1H, H-4), 3.77 (s, 3H, CH_3O), 3.70 – 3.79 (m, 3H, H-3, 2H-6,), 3.45 (m, 1H, H-5), 2.72 (m, 2H, S$\underline{CH_2}CH_3$), 2.01 (s, 1H, CH_3CO), 1.23 (t, *J* = 7.4 Hz, 3H, $SCH_2\underline{CH_3}$) ppm.

***p*-Methylphenyl 2,3,4,6-tetra-O-acetyl-1-thio-β-*D*-glucopyranoside (1b).** To a mixture of D-glucose pentaacetate **13** (1.9206 g, 4.92 mmol, dried in high vacuum for 24 h before the synthesis) and p-thiocresol (0.7453 g, 6 mmol) in anhydrous CH_2Cl_2 (20 mL) at 0°C was added boron trifluoride diethyl etherate. The mixture was stirred at room temperature 20 h. Reaction was quenched by adding sat. $NaHCO_3$ solution (20 mL) at 0°C. The mixture was diluted with CH_2Cl_2 (20 mL), organic layer was washed with $NaHCO_3$ solution (2 × 20 mL), water (20 mL) and brine (20 mL). The organic layer was

dried over $MgSO_4$, filtered and evaporated. The residue was crystallized from EtOAc/Hexane and a mother liquor was concentrated and chromatographed gave **1b** (1.8492 g, 82.7 %).

***p*-Methylphenyl 1-thio-β-*D*-glucopyranoside (2b).** A solution of sodium methylate (54.8 mg, 0.77 mmol) in anhydrous CH_3OH (2 mL) was added to a stirring solution of **1b** (1.4456 g, 3.18 mmol) in anhydrous CH_3OH (6 mL) at room temperature. The mixture was stirred at room temperature for 2 h, the solution was neutralized with Amberlite IR-129 (H^+) resin, filtered, and concentrated. The residue was dried over high vacuum to give practically pure **2b** (0.9253 g, quantitatively) as amorphous mass, which was used without further purification.

***p*-Methylphenyl 4,6-O-benzyliden-1-thio-β-*D*-glucopyranoside (3b).** To a solution of compound **2b** (0.9034 g, 3.15 mmol) and +/-CSA (1.2 mg, 0.005 mmol) in CH_3CN (15 mL) was added benzaldehyde dimethyl acetal (0.713 mL, 4.73 mmol). The mixture was stirred 4 h, until TLS showed that the reaction had been completed. Triethylamine (12 μL) was added to neutralize the acid and then concentrated. The residue was crystallized from EtOH and mother liquor was concentrated and purified by silica gel flash column chromatography (EtOAc/Hex = 1/2) gave **3b** (1.001 g, 84.7 %).

***p*-Methylphenyl 2,3-bis-O-trimethylsilil-4,6-O-benzyliden-1-thio-β-*D*-glucopyranoside (4b).** To stirred and cooled to 0°C solution of **3b** (0.4886 g, 1.30 mmol) and Et_3N (1.375 mL, 9.79 mmol) in anhydrous CH_2Cl_2 (8 mL) was added TMSCl (496 μL, 3.91 mmol). After stirring at 0°C for 6 h TLC analysis (SiO_2, Hex/Tol/EtOAc = 1/1/3) was shown the absence of starting material. Solvent and abundance of reagents was removed *in vacuo*, and then residue was mixed with hexane (5 mL) and filtered. Solid was washed with hexane (5 mL × 3) then hexane was removed under diminished pressure. The residue was dried *in vacuo* overnight afforded **4b** (0.6772 g, 99.6 %) as yellowish crystals. Analytically pure example was recrystallized from EtOH. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.34 (m, 7H, ArH), 7.10 (d, 2H, ArH), 5.45 (s, 1H, Ph-CH), 4.59 (d, J = 9.6 Hz, 1H, H-1), 4.30 (m, 1H, H-6), 3.70 (m, 2H, H-3, H-4,), 3.54 (m, 1H, H-2), 3.37-3.47 (m, 2H, H-5,H-6) 1.54 (s, 3H, CH_3) ppm.

***p*-Methylphenyl 3-O-benzyl-4,6-O-benzyliden-1-thio-β-*D*-glucopyranoside (5c).** To a mixture of freshly dried molecular sieves 3A (205 mg), compound **4b** (113.4 mg, 0.25 mmol), benzaldehyde (30.3 μL, 0.30 mmol) and anhydrous CH_2Cl_2 (2 mL) at -78°C was added TMSOTf (4 μL). After stirring at -78°C for 1 h triethylsilane (48 μL, 0.30 mmol) was added. The reaction was monitored by TLC for 5 h until a spot of starting material was disappeared and 1 M solution of TBAF in THF (597 μL, 0.60 mmol) was added. Then dry ice/acetone bath was removed and the mixture was stirred for 1.5 h, quenched by adding aq. saturated solution of NH_4Cl (5 mL). The water layer was extracted with EtOAc (5 mL × 3). Organic layers were combined, dried over $MgSO_4$, filtered and concentrated. Flash column chromatography on silica gel (EtOAc/Hex = 1/10) gave **5c** (83 mg, 82.9 %) as a white solid.

***p*-Methylphenyl 3-O-*p*-methoxybenzyl-4,6-O-benzyliden-β-*D*-glucopyranoside (5d).** To a mixture of freshly dried molecular sieves 3A (210 mg), compound **4b** (105.4 mg, 0.20 mmol), *p*-methoxybenzaldehyde (30 μL, 0.38 mmol) and anhydrous CH_2Cl_2 (2.2 mL) at -78°C was added TMSOTf (4 μL). After stirring at -78°C for 1 h triethylsilane (39 μL, 0.24 mmol) was added. The reaction was monitored by TLC for 6 h until a spot of starting material was disappeared and 1 M solution of TBAF in THF (406 μL, 0.406 mmol) was added. Then dry ice/acetone bath was removed and the mixture was stirred for 1.5 h, quenched by adding aq. saturated solution of NH_4Cl (5 mL). The water

layer was extracted with EtOAc (5 mL × 3). Organic layers were combined, dried over $MgSO_4$, filtered and concentrated. Flash column chromatography on silica gel (EtOAc/Hex = 1/10, then 1/5, 1/2) gave **5d** (70.6 mg, 70.0 %) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 6.81 (m, 13H, ArH), 5.54 (s, 1H, Ph-CH), 4.80 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.69 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.53 (d, *J* = 9.7 Hz, 1H, H-1), 4.36 (m, 1H, H-6), 3.73 – 3.80 (m, 4H, H-6 and CH_3O), 3.57 – 3.66 (m, 2H, H-3, H-4), 3.41 – 3.50 (m, 2H, H-2, H-5), 2.51 (br. s, 1H, OH), 2.33 (s, 3H, CH_3) ppm

***p*-Methylphenyl 3-O-*p*-chlorobenzyl-4,6-O-benzyliden-1-thio-β-*D*-glucopyranoside (5e).** To a mixture of freshly dried molecular sieves 3A (200 mg), compound **4b** (100.2 mg, 0.19 mmol), *p*-chlorobenzaldehyde (32.6 mg, 0.23 mmol) and anhydrous CH_2Cl_2 (2 mL) at -84°C was added TMSOTf (6 μL). After stirring at -84°C for 1 h triethylsilane (32 μL, 0.20 mmol) was added. The reaction was monitored by TLC for 6 h until a spot of starting material was disappeared and 1 M solution of TBAF in THF (386 μL, 0.39 mmol) was added. Then dry ice/acetone bath was removed and the mixture was stirred for 1.5 h, quenched by adding saturated aq. solution of NH_4Cl (5 mL). The water layer was extracted with EtOAc (5 mL×3). Organic layers were combined, dried over $MgSO_4$, filtered and concentrated. Flash column chromatography on silica gel (EtOAc/Hex = 1/10) gave **5c** (57.5 mg, 59.7 %) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.81 – 7.36 (m, 13H, ArH), 5.54 (s, 1H, Ph-CH), 4.80 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.69 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.53 (d, *J* = 9.7 Hz, 1H, H-1), 4.37 (m, 1H, H-6), 3.74 – 3.82 (m, 4H, H-6), 3.57 – 3.66 (m, 2H, H-3, H-4), 3.40 – 3.50 (m, 2H, H-2, H-5), 2.50 (br. s, 1H, OH), 2.32 (s, 3H, CH_3) ppm.

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СТРАТЕГІЯ ТА ОТРИМАННЯ ДЕЯКИХ СИНТЕТИЧНИХ БЛОКІВ ДЛЯ СИНТЕЗУ РОЗГАЛУЖЕНИХ ОЛІГОСАХАРИДІВ.

У статті обговорюються декілька сучасних дизайнерських рішень для планування синтезу разгалудженних олігосахаридів із застосуванням захисних функціональних груп різної реакційної здатності. Був представлений синтетичний план у якому застосовані такі захисні групи як ацетіл (*Ac*), бензіл (*Bn*), 2-нафтіл (*2-Naph*), *n*-метоксібензіл (*PMB*) і *n*-хлорбензіл (*p-ClBn*) та які у подальшому можуть бути селективно видалені з високим видобутком. Описано методи синтезу деяких перспективних синтетичних блоків призначених для отримання відповідних розгалужених оліго-похідних.

Ключові слова: синтетичні блоки, захищені моносахариди, β-(1,3)-*D*-глюкани, синтез.

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СТРАТЕГИЯ И ПОЛУЧЕНИЕ НЕКОТОРЫХ СИНТЕТИЧЕСКИХ БЛОКОВ ДЛЯ СИНТЕЗА РАЗВЕТВЛЕННЫХ ОЛИГОСАХАРИДОВ

В статье обсуждены несколько современных дизайнерских решений для планирования синтеза разветвленных олигосахаридов с применением защитных групп различной реакционной способности. Представлен синтетический план в котором используются такие защитные группы как ацетил (*Ac*), бензил (*Bn*), 2-нафтил (*2-Naph*), *n*-метоксибензил (*PMB*) и *n*-хлорбензил (*p-ClBn*) и которые в дальнейшем могут быть удалены с высоким выходом. Описаны методы синтеза некоторых перспективных синтетических блоков предназначенных для получения соответствующих разветвленных олиго-производных.

Ключевые слова: синтетические блоки, защищенные моносахариды, β-(1,3)-*D*-глюканы, синтез.