**Review**

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# Azidophenylselenylation of glycals towards 2-azido-2-deoxy-selenoglycosides and their application in oligosaccharide synthesis

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**Abstract:** 2-Amino-2-deoxy-pyranosyl units are important structural components of cell-wall polymers in prokaryotes, fungi and mammals. With respect to the need for development of novel and efficient vaccines and tools for serodiagnosis of infectious diseases, of particular interest are the oligosaccharide cell-wall antigens of pathogenic bacteria and fungi, which comprise 2-amino-2-deoxy-D-glucopyranose and 2-amino-2-deoxy-D-galactopyranose units as α- or β-anomers. Synthesis of N-acylated α-GlcN and α-GalN containing oligosaccharides is a special challenge due to the presence of a participating group at C2 which favors the formation of β- rather than α-glycoside bond. Herein we overview the efficient two-step approach for preparation of 1,2-*cis*-glycosides of 2-amino-2-deoxy-D-glucopyranose and 2-amino-2-deoxy-D-galactopyranose, which was recently developed in our laboratory. In the first step, an efficient and straightforward azidophenylselenylation procedure of glycals gives phenyl 2-azido-2-deoxy-1-selenoglycosides as versatile glycosyl donors. In the second step, these donors can be efficiently transformed into α- or β-glycosides depending on the choice of the solvent. In acetonitrile, total β-stereocontrol was achieved, and the use of diethyl ether as a solvent favouring α-stereoselectivity of glycosylations with phenyl 2-azido-2-deoxy-1-selenoglycosides. Besides, it was shown, that low reactivity and nucleophilicity of glycosyl acceptors which are glycosylated with phenyl 2-azido-2-deoxy-1-selenogalactosides facilitated the formation of α-GalN derivatives. To date, homogenous azidophenylselenylation of glycals and glycosylation with phenyl 2-azido-2-deoxy-1-seleno-α-D-glycopyranosides can be regarded as most useful tool for introduction of 2-amino-2-deoxy-D-glycopyranoside residues into complex synthetic oligosaccharides.

**Keywords:** 2-azido-2-deoxy-1-seleno-α-D-galactopyranoside; α-stereoselectivity; β-stereoselectivity; azidophenylselenylation; galactal; glucal; glycosylation; Mendeleev-21; trimethylsilyl azide.

## Introduction

2-Amino-2-deoxy-aldohexoses are known to be the principal structural and functional components of glycoproteins, proteoglycans [1], glycolipids, lipopolysaccharides and polysaccharides found in mammals, bacteria [2] and fungi [3]. The most abundant are 2-amino-2-deoxy-D-glucopyranosyl and 2-amino-2-deoxy-D-

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galactopyranosyl units which can be incorporated into natural glycosides as α- and β-anomers. This structural feature dramatically adds to the complexity of synthetic methods for the stereoselective synthesis of natural or related 2-amino-2-deoxyglycosides. Half-century long efforts were concentrated on elaboration of efficient stereospecific approaches towards 2-amino-2-deoxyglycosides, which indicated the substantial impact of the acyl-protected amino group at C-2 on the stereochemistry of glycosylation facilitating the formation of 1,2-*trans*-glycosides.To date, preparation of compounds of this type is very well designed [4–7].

On the contrary, the synthesis of 1,2-*cis*-glycosides (most often they have α-configuration) still represents a challenge and needs quite long sequences of synthetic steps [8–18]. Conventional synthetic strategy is based on the use of glycosyl donors with a non-participating azido group at C2 as a synthetic precursor of the amino- or amido-groups [17]. General method for the preparation of 2-azido-2-deoxy glycosyl donors is illustrated in Fig. 1 using the example of D-galactose as a starting compound. It includes first preparation of acetylated galactosyl bromide **1**, its conversion into galactal **2** followed by the laborious azidonitration according to Lemieux procedure [19] to give the mixture of 2-azido-2-deoxy glycosyl nitrates **3** and their further transformation into appropriate glycosyl donors. Simplification of this sequence can be achieved via direct transformation of glycal into 2-azido-2-deoxy glycosyl donors which is marked with a bold arrow in Fig. 1.

In this review, we describe recent works of our and others laboratories on the synthesis and application of phenyl 2-azido-2-deoxy-1-selenoglycosides as efficient starting materials for preparation of 2-amino-2-deoxy-glycosides. These compounds are directly used as glycosyl donors, which can be activated in different ways to control the formation 1,2-*cis* and 1,2-*trans* glycosides. Furthermore, they can be readily transformed into the corresponding 2-azido-2-deoxy-1-halides, imidates, and other types of glycosyl donors [15, 16].

After the description in 1991 by Tingoli et al. [20] of anti-Markovnikov one-step azidophenylselenylation (APS) of olefins with a mixture of $NaN_3$, $PhI(OAc)_2$, and $Ph_2Se_2$ in $CH_2Cl_2$, this reaction was applied by Czernecki et al. [21–25] to convert peracetylated and perbenzylated D-glucals and D-galactals into corresponding phenyl 2-azido-2-deoxy-1-seleno-α-D-gluco- and galactopyranosides. For galactals, complete stereocontrol was observed, and APS of glucals resulted in the mixture of *gluco*- and *manno*-adducts. Santoyo-Gonzalez et al. [26] confirmed poor stereoselectivity of APS of glucals and showed the inapplicability of this procedure to benzylidenated compounds. In contrast to monosaccharide glucals, APS of peracetylated glycals of lactose, maltose and cellobiose performed by Santoyo-Gonzalez et al. [27] afforded low yields of α,β-isomeric mixtures of phenyl 2-azido-2-deoxy-1-seleno-mannopyranosides.

As we reported before [28], the efficiency and selectivity of the procedure by Tingoli et al. [20] depends on the scale of the reaction. Presumably, the lower efficiency is connected with heterogeneity of the reaction mixture and low solubility of $NaN_3$ in $CH_2Cl_2$ in combination with high exothermicity of the chemical process. To avoid these obstacles and to make the APS procedure of glycals scalable and reproducible, we elaborated [28] a homogeneous procedure which involves trimethylsilylazide ($TMSN_3$) as a soluble azide donor to replace $NaN_3$. Treatment of a solution of triacetylgalactal **2** (1 mmol), $Ph_2Se_2$ (1 mmol) and diacetoxyiodobenzene

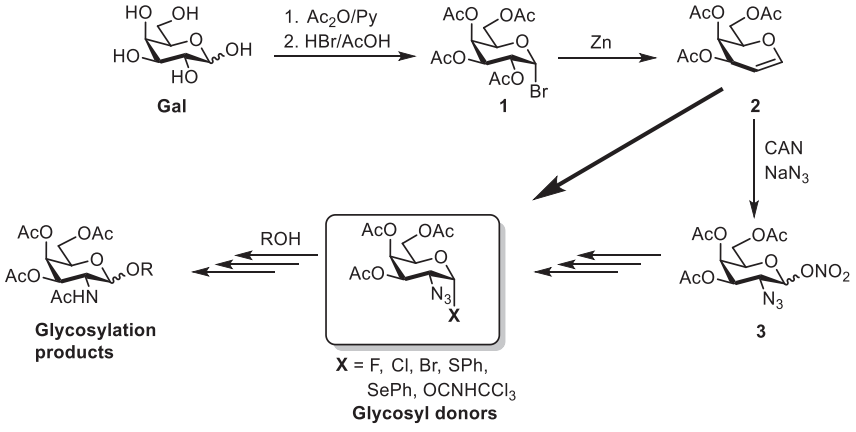



**Fig. 1:** Synthesis of 2-azido-2-deoxy galactosyl donors with the use of azidonitration of tri-O-acetyl-D-galactal **2**.

(1 mmol) in $CH_2Cl_2$ (5 ml) with $TMSN_3$ (2 mmol) at –10 °C in 4 h gave a 9:1:1 mixture of the target phenyl 3,4,6-tri-O-acetyl-2-azido-2-deoxy-1-seleno-α-D-galactopyranoside (**2a**), its regioisomer with a *talo*-configuration **2b**, and the corresponding 1,2-di-azide **2c** with *galacto*-configuration in 90 % overall yield. For a deeper insight into the mechanism of APS, we employed [29] a spin trap technique with nitrones and nitroso compounds as spin traps to confirm the presence of azido radicals in the reaction mixture, and demonstrated that these radicals are generated by decomposition of azidoiodinane derivatives.

Recently, with a view to an efficient and safe scale up, Guberman et al. [30] applied a continuous flow technology to homogeneous APS of triacetylgalactal **2** and optimized the conditions for a better yield of **2a**. The process was adapted to room temperature, and the production was scaled up to 5 mmol of galactal in 3 h, yielding 1.2 mmol/h of the target compound **2a**. Depending on the reaction conditions, up to six by-products [30] were detected in the reaction mixtures.

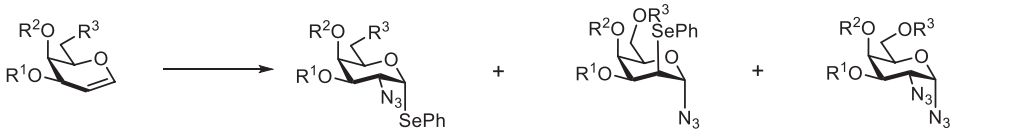
Differently to the Tingoli method [20], homogeneous APS of galactals (Fig. 2) proved to be compatible with a wide variety of protecting groups. Thus, 3,4,6-tri-O-benzyl-galactal **4** in these conditions was transformed [28] into corresponding phenyl 2-azido-2-deoxy-1-seleno-α-D-glycoside **4a** in 72 % yield. Homogeneous APS of 3,4-di-O-acetyl-D-fucal **5** gave 3,4-di-O-acetyl-2-azido-2-deoxy-1-seleno-α-D-fucopyranoside **5a** in good yield, as reported by Bedini et al. [31] and Hagen et al. [32].

Homogeneous APS was also successfully applied [28] to the transformation of 2,3,4-tri-O-acetyl-D-glucal. In different solvents and at varied temperature levels it afforded corresponding phenyl 2-azido-2-deoxy-1-selenoglycosides. The major products were phenyl 3,4,6-tri-O-acetyl-2-azido-2-deoxy-1-seleno-α-D-glucopyranoside (see *gluco*-isomer in Table 1) and phenyl 3,4,6-tri-O-acetyl-2-azido-2-deoxy-1-seleno-α-D-mannopyranoside (*manno*-isomer) with excellent yield (91 %) and ratio 2.7:1. We examined [33] the influence of the solvent, temperature and amount of azide source on the ratio of *gluco*- and *manno*-isomers formed in APS of **7**. In non-polar solvents (dichloromethane, hexafluorobenzene, tetrachloromethane, and toluene), the ratio of *gluco*- and *manno*-isomers was 2.7–3.2 to 1, in ethyl acetate and tetrahydrofuran it was substantially lower (1.3–1.5 to 1), while in polar solvents no regioselectivity was observed. Meanwhile, variation of the temperature in the range from –10 to –40 °C had no effect on regioselectivity of APS.

Further, we extended [33] the reaction conditions to a group of mono-, di-and trisaccharide glucals (Table 1) and studied the effect of the nature of protecting group on efficiency and regioselectivity of APS of these compounds. Variation of protecting groups showed that a combination of a non-polar protecting group (triisopropylsilyl, tributylsilyl, trimethylsilyl) at O3 and a bulky substituent at O4 (TBS, TIPS, mono- or disaccharide residue) facilitates the formation of a *gluco*-isomer (Table 1, entries 2, 4, 8, 10 and 12). High regioselectivity and efficiency of APS of lactal and sialyllactals provides an easy way towards derivatives of lactosamine, as in the synthesis of inhibitors of galectin-3 [34] and sialyllactosamine which are common glycoprotein motifs in bacteria and mammals.

## Phenyl 2-azido-2deoxy-1-selenoglycosides as glycosyl donors

Phenyl selenoglycosides were introduced as versatile glycosyl donors by Mehta and Pinto [35–37], and now are commonly used [38] in carbohydrate synthesis as glycosyl donors and glycosyl acceptors. In 2001,




**2** $R^1 = R^2 = Ac$, $R^3 = OAc$
**4** $R^1 = R^2 = Bn$, $R^3 = OBn$
**5** $R^1 = R^2 = Ac$, $R^3 = H$

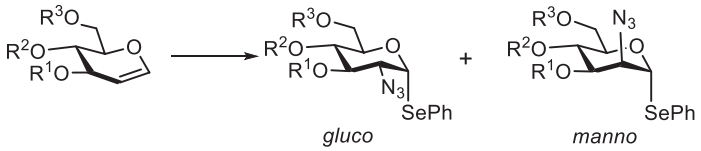
**2a** $R^1 = R^2 = Ac$, $R^3 = OAc$
**4a** $R^1 = R^2 = Bn$, $R^3 = OBn$
**5a** $R^1 = R^2 = Ac$, $R^3 = H$

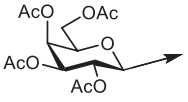
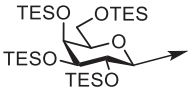
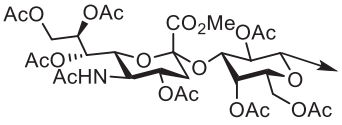
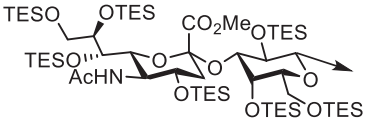
**2b** $R^1 = R^2 = R^3 = Ac$

**2c** $R^1 = R^2 = R^3 = Ac$

**Fig. 2:** APS of galactals **2**, **4**, and **5**.

**Table 1:** Examples of APS of variously protected glucals.



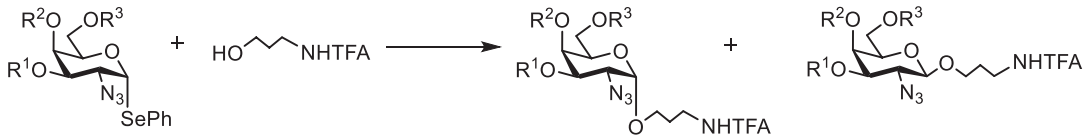

| Entry | $R^1$ | $R^2$ | $R^3$ | The ratio of *gluco* (a) and *manno* (b) products, yield | Ref. |
|---|---|---|---|---|---|
| 1 | Ac | Ac | Ac | 2.7:1 (91 %) | 28 |
| 2 | TIPS | –PhC– | | Only *gluco*, 77 % | 28 |
| 3 | Piv | $-CMe_2-$ | | 1:1 | 33 |
| 4 | TIPS | $-CMe_2-$ | | Only *gluco*, 85 % | 33 |
| 5 | Bz | Bz | Bz | 1:1 | 33 |
| 6 | Piv | Piv | Piv | 1.6:1 | 33 |
| 7 | TMS | TMS | TMS | 3:1 | 33 |
| 8 | TIPS | TIPS | TIPS | Only *gluco*, 81 % | 33 |
| 9 | Ac |  | Ac | 1.1:1, 89 % | 33 |
| 10 | TES |  | TES | Only *gluco*, 81 % [33], 56 % [34] | 33, 34 |
| 11 | Ac |  | Ac | 1:1, 75 % | 33 |
| 12 | TES |  | TES | Only *gluco*, 69 % | 33 |

Tseng et al. [39] performed glycosylation of a blocked derivative of threonine with phenyl 2-azido-4,6-benzylidene-3-O-chloroacetyl-2-deoxy-1-seleno-α-D-galactopyranoside promoted by AgOTf in the presence of $K_2CO_3$ or tetramethylurea. Notably, the α/β ratio substantially varied in these reactions from 1/1 to 7.5/1 depending on the type of the base and the temperature.

Per-O-acetylated 2-azido-2-deoxy-1-selenogalactoside **2a** was used as a glycosyl donor by Kärkkäinen et al. [40] in the presence of $I_2$ and DDQ or $I_2$ alone for glycosylation of simple aliphatic alcohols, L-serine and L-threonine. In these reactions, glycosides were produced with low to moderate yields, and the α/β ratio depended on the solvent and promoting compounds. On average, the mixture toluene – dioxane 1:3 facilitated α-glycosylation, but the yields were lower. However, under promotion with NIS/TfOH in $CH_2Cl_2$, the reaction of glycosyl donor **2a** with bis(2-chloroethoxy)ethanol showed no stereocontrol [41].

In 2016 we published [42] the results of a comprehensive study of glycosylation by per-O-acetylated (**2a**) and per-O-benzoylated (**6**) phenyl 2-azido-2-deoxy-1-seleno-α-D-galactopyranosides as glycosyl donors. It was found, that the stereoselectivity of glycosylation with these compounds depends on the reactivity of glycosyl acceptors and the reaction conditions. In acetonitrile, glycosylation of 3-trifluoroacetamidopropanol with **2a** and **6** was β-stereospecific (Table 2, entries 3 and 6). Glycosylation of 3-trifluoroacetamidopropanol with donors **2a** and **6** in the presence of NIS and TfOH at –35 °C in $CH_2Cl_2$ (Table 2, entries 1 and 4) and in diethyl ether (Table 2, entries 2 and 5) showed, that benzoyl protecting groups favored the formation of α-glycoside

**Table 2:** Glycosylation of 3-trifluoroacetamidopropanol with donors **2a** and **6** [42].



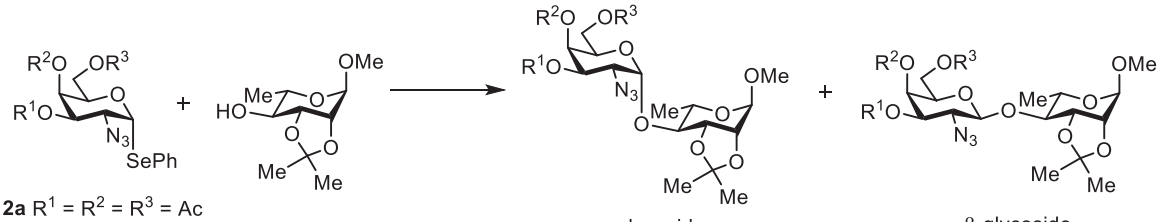

**2a** $R^1 = R^2 = R^3 = Ac$
**6** $R^1 = R^2 = R^3 = Bz$

| Entry | Donor | Promoter | Solvent | Temperature (°C) | The α/β ratio of glycosides, yield |
|---|---|---|---|---|---|
| 1 | **2a** | NIS, TfOH | $CH_2Cl_2$ | −35 | 1:2 (88 %) |
| 2 | **2a** | NIS, TfOH | $Et_2O$ | −35 | 1:3 (95 %) |
| 3 | **2a** | NIS, TfOH | MeCN | −35 | Only β (88 %) |
| 4 | **6** | NIS, TfOH | $CH_2Cl_2$ | −35 | 1:1 (92 %) |
| 5 | **6** | NIS, TfOH | $Et_2O$ | −35 | 1:1.3 (78 %) |
| 6 | **6** | NIS, TfOH | MeCN | −35 | Only β (75 %) |
| 7 | **6** | PhSeCl, AgOTf | $CH_2Cl_2$ | 0 | 2.4:1 (95 %) |
| 8 | **6** | PhSeCl, AgOTf | $Et_2O$ | 0 | 3.3:1 (95 %) |

as compared to acetylated donor **2a**. The use of PhSeCl/AgOTf for promotion of glycosylation with **6** substantially increased the proportion of α-glycoside (Table 2, entries 7 and 8).

Glycosylation of methyl 2,3-O-isopropylidene-α-L-rhamnopyranoside by donors **2a** and **6** demonstrated the α-directing effect of diethyl ether in comparison to $CH_2Cl_2$ (Table 3, entries 1 and 2 for donor **2a**; entries 4 and 5 for donor **6**), and confirmed the preferential formation of β-glycosides in MeCN (Table 3, entries 3 and 6). The highest α-selectivity was observed when PhSeCl/AgOTf system was used to promote glycosylation of methyl 2,3-O-isopropylidene-α-L-rhamnopyranoside with benzoylated donor **6** in diethyl ether (Table 3, entry 8). The results shown in Tables 2 and 3 provide the data needed for the choice of optimal solvents for

**Table 3:** Glycosylation of methyl 2,3-O-isopropylidene-α-L-rhamnopyranoside with donors **2a** and **6.**




**2a** $R^1 = R^2 = R^3 = Ac$
**6** $R^1 = R^2 = R^3 = Bz$

| Entry | Donor | Promoter | Solvent | Temperature (°C) | The α/β ratio of glycosides, yield |
|---|---|---|---|---|---|
| 1 | **2a** | NIS, TfOH | $CH_2Cl_2$ | −35 | 1:1.7 (80 %) |
| 2 | **2a** | NIS, TfOH | $Et_2O$ | −35 | 3.5:1 (87 %) |
| 3 | **2a** | NIS, TfOH | MeCN | −35 | 1:6 (87 %) |
| 4 | **6** | NIS, TfOH | $CH_2Cl_2$ | −35 | 2.5:1 (80 %) |
| 5 | **6** | NIS, TfOH | $Et_2O$ | −35 | 3.6:1 (88 %) |
| 6 | **6** | NIS, TfOH | MeCN | −35 | 1:3.8 (80 %) |
| 7 | **6** | PhSeCl, AgOTf | $CH_2Cl_2$ | 0 | 3:1 (72 %) |
| 8 | **6** | PhSeCl, AgOTf | $Et_2O$ | 0 | 4.7:1 (99 %) |

stereocontrolled α- or β-glycosylation with phenyl 2-azido-2-deoxy-1-seleno-α-D-glycopyranosides, as summarized in Fig. 3.

Stereoselectivity of 2-deoxy-2-azido-fucosylation was studied by Hagen et al. [32] on a series of phenyl 2-azido-2-deoxyselenofucosides as glycosyl donors in the presence of a diphenyl sulfoxide ($Ph_2SO$)/triflic anhydride ($Tf_2O$) reagent couple (Fig. 4). $^1$H NMR study of reactive intermediates generated from di-O-benzyl-fucosazide **7** upon treatment with $Ph_2SO$ and $Tf_2O$ in $CD_2Cl_2$ at −80 °C revealed the presence of corresponding covalent intermediate **15** as α-triflate (δ 6.06 ppm, J = 3.2 Hz) and α-oxosulfonium triflate (δ 6.10 ppm, J = 3.2 Hz), which are in equilibrium with the corresponding ionic intermediate **16**. Glycosylation of ethanol, 2-fluoroethanol, 2,2-difluoroethanol and 2,2,2-trifluoroethanol with donors **7**–**12** revealed the increase of α-stereoselectivity with the decrease of nucleophilicity of glycosyl acceptors. The authors [32] explained it with inability of weak nucleophiles to displace a covalent leaving group in covalent intermediates thus inhibiting the formation of β-glycoside and facilitating α-glycosylation of the ionic equilibrium partner. It is important to note, that intermediates generated from **7** started to decompose at –20 °C, and decomposition of similar intermediates generated from **8** began around 0 °C.

Glycosylation of cyclohexanol and two selectively protected model mannosides **13** and **14** unambiguously demonstrated that the benzoylated 2-azido-2-deoxy-fucosyl donors **8**, **9** and **10** were poor α-donors. On the contrary, selenoglycosides **7**, **11** and **12** favored the formation of 1,2-*cis*-glycosides. On the basis of this study, a straightforward synthesis of trisaccharide **TS1** (Fig. 5a) related to the repeating unit of the capsular polysaccharide (CPS) of *Staphylococcus aureus* type 5, which comprises both β-D-FucNAc and α-L-FucNAc residues, was fulfilled. Thus, phenyl selenoglycoside **17**, which is an enantiomer of the aforementioned compound **10**, was used as a glycosyl donor for stereoselective preparation of β-glycoside **19** (α/β ratio 1:7), which was 3-O-debenzoylated to give glycosyl donor **20** with a free 3-OH. Subsequent glycosylation of **20** with **11** was α-stereospecific and gave disaccharide **21** in 76 % yield.

Phenyl selenoglycosides **12** and **22**, which were prepared using the APS procedure, were the key synthetic blocks in the synthesis of protected disaccharides **24** and **27** related to repeating units of CPS of *S. aureus*

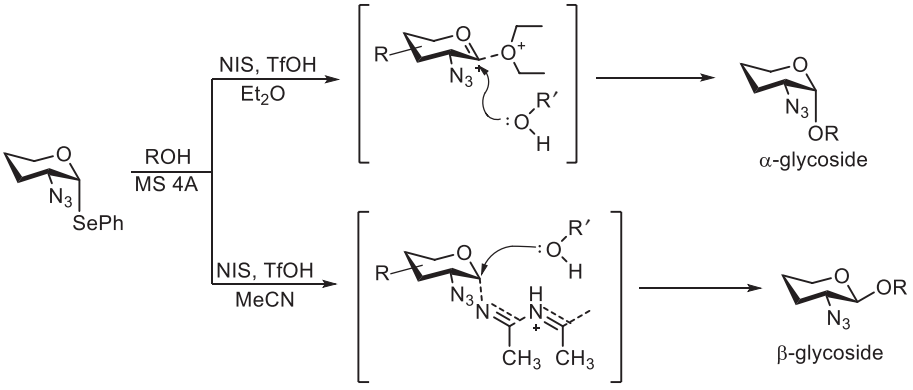



**Fig. 3:** Possible mechanisms of $Et_2O$ and MeCN effects on stereoselectivity of glycosylation.

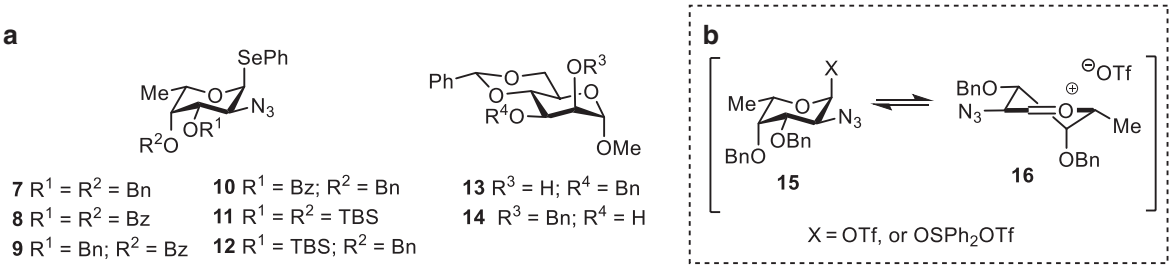



**Fig. 4:** (a) Structures of 2-azido-2-deoxy-L-fucosyl donors **7**–**12** and model acceptors **13** and **14**; (b) glycosylation intermediates.

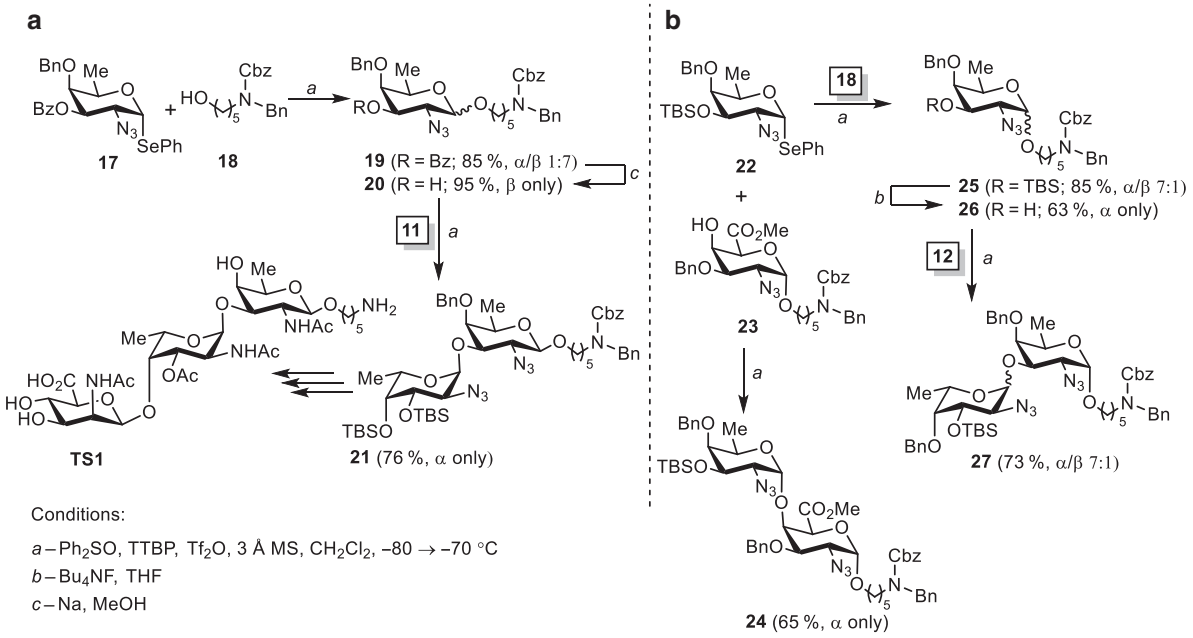



**Fig. 5:** (a) Synthesis of trisaccharide **TS1** related to the repeating unit of *S. aureus* type 5 CPS; (b) synthesis of disaccharides **24** and **27** related to CPS of *S. aureus* strain M and type 8 [32].

strain M and type 8. Monosaccharide **23** was glycosylated with selenoglycoside **22** to give α-linked disaccharide **24** as a sole product in 65 % yield (Fig. 5b). Disaccharide **27** was obtained in three steps, including two glycosylation steps. Glycosylation of **18** with selenoglycoside **22** yielded a mixture of glycosides **25** with α/β ratio 7:1 (85 %) (Fig. 5b). After deblocking, glycosylation of **26** with selenoglycoside **12** was conducted to afford disaccharides **27** with α/β ratio 7:1 (73 %).

Preparation of a spacered trisaccharide **TS2** (see Fig. 6) related to the repeating unit of *S. aureus* strain M CPS demanded the introduction of an additional α-galactosaminuronic acid residue. At first, phenyl selenoglycoside **28** was considered as a candidate glycosyl donor. However, model glycosylations by phenyl selenoglycoside **28** of a series of substituted ethanol derivatives in conditions described above [43] showed the prevalence of β-glycoside products even in the case of weak nucleophile – 2,2,2-trifluoroethanol. Alternatively, donor **29** [43] carrying an α-directing 4,6-O-bis-*tert*-butylsilylene (DTBS) group, which was suggested by Kiso et al. [44], showed excellent α-selectivity (α/β 19:1) in model experiments. Subsequently, donor **29** was successfully applied [43] in the synthesis of a spacered trisaccharide **TS2** (Fig. 6) related to the repeating unit of *S. aureus* strain M CPS. The glycosylation of N-benzyloxycarbonyl-N-benzyl-5-aminopentanol with donor **29** was α-stereospecific and afforded glycoside **30** in 82 % yield. Straightforward removal of DTBS protecting group, 6-O-regioselective oxidation, and methylation furnished glycosyl acceptor **23** in 85 % overall yield, which was glycosylated with **29** to give 88 % of α-glycoside **31** as a sole product. Its subsequent de-O-silylation, C-6-oxidation and methylation gave the acceptor **32**, which was glycosylated with **22**. Similarly to **30**, glycosylation of **32** was α-stereospecific and afforded trisaccharide **33** (79 %) as the precursor of **TS2** [43].

Phenyl 2-azido-2-deoxy-1-selenogalactosides were also successfully applied in our syntheses [45] of a series of biotinylated oligo-α-(1→4)-D-galactosaminides and their N-acetylated derivatives (Fig. 7) which are structurally related to galactosaminogalactan – the cell wall polysaccharide of fungal pathogen *Aspergillus fumigatus*, which is the most important airborne human fungal pathogen in industrialized countries. Thus, twelve α-(1→4)-D-galactosaminides composed of 1–6 α-GalN-units were readily obtained in a sequence of elongation steps using a versatile donor selenogalactoside **34** (Fig. 7) which was selected from a number of donor candidates. The pattern of O-substituents was tuned to manage α-stereoselectivity of glycosylation. Thus bulky DTBS protecting group at O4 and O6 was used to prevent the nucleophile attack from the β-site

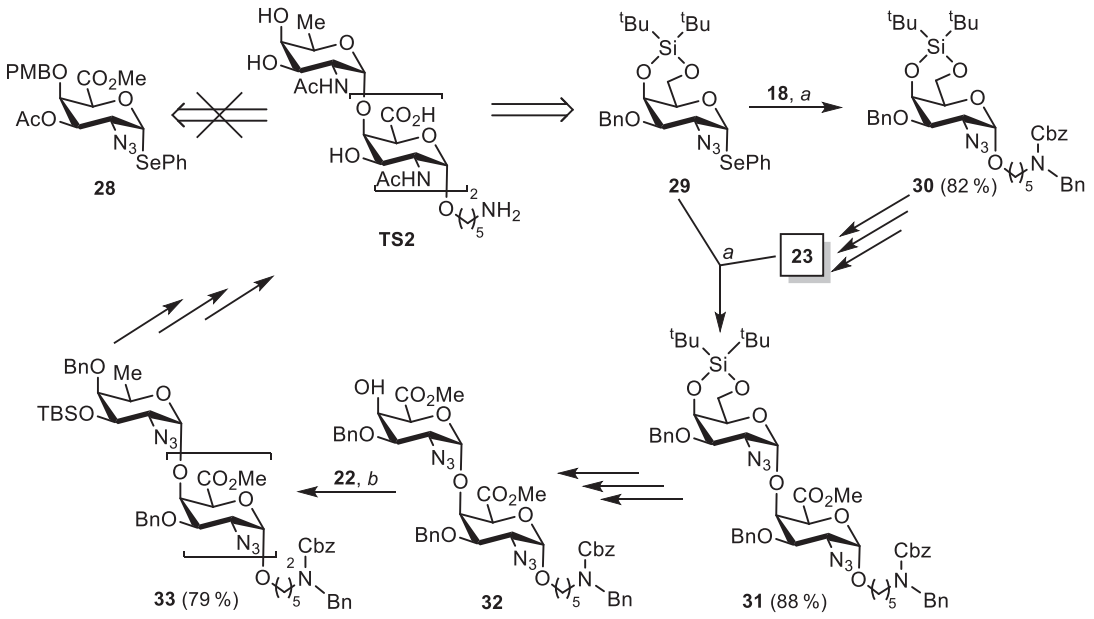



**Fig. 6:** Synthesis of a spacered trisaccharide related to the repeating unit of CPS of *S. aureus* strain M [43].

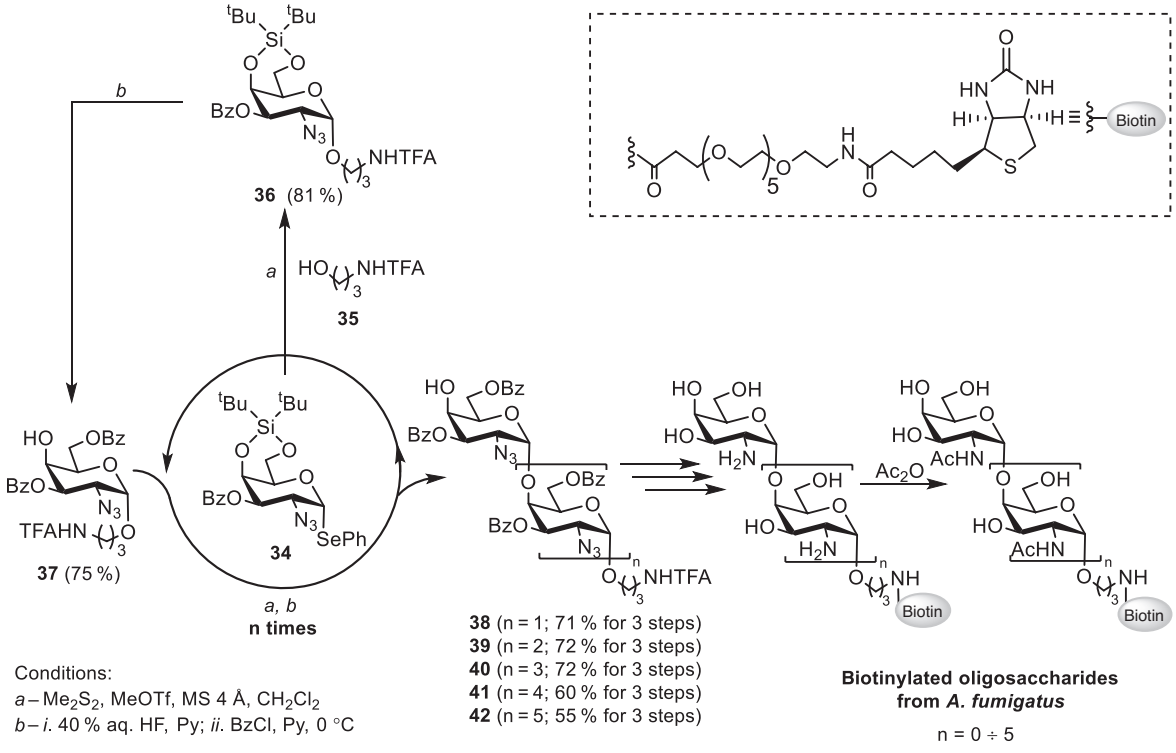



**Fig. 7:** Synthesis of neoglycoconjugates related to fragments of galactosaminogalactan from *A. fumigatus* [45].

[44, 46] while 3-O-benzoyl group was introduced to provide the remote anchimeric participation which favors α-stereoselectivity of glycosylation [17, 47–49]. This surprising but useful property of 3-O-benzoyl protecting group was already used by us in the synthesis of 1,2-*cis*-glycoside bond containing oligosaccharides related

to α-xylosylated Epidermal Growth Factor repeats of Notch [50–52], fucoidans [53–55], α-(1→3)-D-glucan of *A. fumigatus* [56, 57] and its α-(1→6)-linked isomer [58].

Thus, the glycosylation of 3-trifluoroacetamidopropanol **35** by donor **34** under the promotion with $Me_2S_2$-MeOTf as the optimal activation system afforded 81% of α-product **36.** Easy removal of DTBS group by the action of aqueous HF in pyridine followed by regioselective 6-O-benzoylation furnished glycosyl acceptor **37.** In a similar way, di-, tri- and tetrameric glycosyl acceptors **38–40** were obtained in 71–72% yields, and the yields of acceptors **41** and **42** in the last two chain elongation step were 60 and 55%, respectively. Thus obtained biotinyl-containing neoglycoconjugates were arrayed on streptavidin-coated plates and used to assess the epitopes of anti-galactosaminogalactan murine monoclonal antibodies and screen the human antibodies in the sera of patients with allergic bronchopulmonary and chronic pulmonary aspergillosis. The obtained data showed that the oligo-α-(1→4)-D-galactosamines and their N-acetylated derivatives allowed the first precise analysis of the specificity of the antibody responses to this extremely complex fungal polysaccharide [45].

## Conclusion and prospects

In conclusion, the efficient two-step approach for the preparation of 1,2-*cis*-glycosides of 2-amino-2-deoxy-D-glycopyranosides, which was recently proposed in our laboratory, is a handy tool for introduction of corresponding monosaccharide residues into complex synthetic oligosaccharides. Straightforward homogeneous regioselective APS of protected galactals opens the way to variously protected versatile glycosyl donors. β-Stereocontrol in glycosylation reactions with phenyl 2-azido-2-deoxyselenogalactosides is readily achieved by the use of acetonitrile as a reaction solvent. To attain α-stereocontrol, diethyl ether was shown to be effective as a reaction solvent. Furthermore, α-stereoselectivity of glycosylations with phenyl 2-azido-2-deoxy-1-selenoglycosides can be increased by taking advantage of stereocontrolling action of appropriate O-blocking groups. Thus, low reactivity and nucleophilicity of the acceptor and the presence of a bulky protecting group, which hinders β-glycosylation, favor the formation of 1,2-*cis*-glycosides. So far, homogenous APS of glycals and glycosylation with phenyl 2-azido-2-deoxy-1-seleno-α-D-glycopyranosides have been successfully used in preparation of complex oligosaccharides and neoglycoconjugates related to fragments of antigenic polysaccharides of *S. aureus* type 5, strain M and type 8 [32, 43], as well as to galactosaminogalactan of *A. fumigatus* [45].

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