On-water synthesis of glycosyl selenocyanate derivatives and their application in the metal free organocatalytic preparation of nonglycosidic selenium linked pseudodisaccharide derivatives†

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Glycosyl selenocyanate derivatives were prepared in very good yield by the treatment of glycosyl halide or triflate derivatives with potassium selenocyanate in water. A variety of selenium linked pseudodisaccharide derivatives were prepared in excellent yield using glycosyl selenocyanates as stable building blocks in the presence of hydrazine hydrate under metal-free organocatalytic reaction conditions.

Introduction

In order to support the increasing interest in glycobiology research for the development of novel carbohydrate based therapeutics, a large number of oligo- and polysaccharides as well as a diverse range of glycomimetics have been synthesized in the recent past.1–8 Pseudosugar derivatives (e.g. pseudodisaccharides) have been considered as useful glycomimetics for their use as stable enzyme inhibitors.7 One of the important techniques for the preparation of glycomimetics is to exchange the interglycosidic oxygen atom with other heteroatoms such as nitrogen, sulphur, selenium, etc.9–10 Due to their increased stability towards hydrolysis, a variety of thiosugars and thiglycosides have been prepared for their use in the biochemical investigations of the carbohydrate processing enzymes.11–13 Organoselenium chemistry has become an important topic of research due to the unique chemical behaviour of Se-containing compounds and their pharmacological potential.14–18 Although, selenium has been incorporated in different classes of molecules to improve their therapeutic index,19 the introduction of selenium within the carbohydrate framework has received less attention except for a few reports which include the synthesis of anomer selenoglycosides20–27 and their application in the preparation of oligosaccharides,28–30 glycal derivatives,31 glycosyl fluorides,32 C-glycosides33 and medicinally useful compounds.34 The synthesis of some cyclic sugar intermediates containing selenium in the ring has also been pursued.35 In addition, some reports also appeared on the synthesis of non-glycosidically selenium linked pseudodisaccharide derivatives.36–41 In most of the cases, elemental selenium, selenium oxide, selenourea or aryl selenol has been used as the source of selenium for its incorporation in the carbohydrate intermediates.23–37 Dialkyl or diaryldiselenides have also been used under reductive reaction conditions to furnish selenoglycosides.26,29 Obviously, there are several shortcomings associated with the above-mentioned reaction conditions such as use of obnoxious reagents, incompatibility of the base labile protecting groups, hazardous and special reaction conditions etc. Therefore, it is quite pertinent to develop reaction conditions avoiding earlier mentioned drawbacks. In the recent past, potassium p-methylselenobenzoate (KSeBz) has been successfully used as the selenium source in the preparation of several selenium containing carbohydrate derivatives.22,27,37 KSeBz has been prepared using a multistep reaction sequence starting from elemental selenium.22 As an alternative, a straightforward reaction condition has been reported for the synthesis of selenium linked glycosides using glycosyl selenoacetate as stable building blocks, prepared by the treatment of glycosyl halides with commercially available potassium selenocyanate (KSeCN) in acetonitrile avoiding the prerequisite preparation of the selenating agent.38 In a separate report, KSeCN has also been used as selenating agent for the preparation of unsymmetrical organoselenene and selenoglycosides.39 KSeCN has also been used as the selenating agent for the aqueous medium preparation di-alkyldiselenides.39 In order to extend the use of KSeCN in the preparation of selenium incorporated carbohydrate derivatives, attempts were made to prepare stable glycosyl selenocyanate derivatives and their utilization in the preparation of selenium linked pseudodisaccharides. Cumpstey and co-worker reported the synthesis of several non-glycosidically selenoether linked pseudodisaccharide derivatives using KSeBz as selenating agent, involving multistep reaction sequence via the formation of diiselenide derivatives.37 Lüdtke and co-workers synthesized selenium linked neoglycoconjugates and pseudodisaccharides using lithium

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diselenide using multistep reaction sequence. Expensive selenourea has been used as selenating agent in some studies. In this context, it would be beneficial to develop an environmentally benign aqueous reaction condition in the “Green chemistry” perspective for the preparation of glycosyl selenocyanate derivatives and their direct use in the synthesis of non-glycosidically selenoether linked pseudodisaccharide derivatives by the treatment of suitable glycosyl electrophiles. Inspired by the earlier studies on the use of KSeCN as efficient selenylating agent, a straightforward on-water synthesis of stable glycosyl selenocyanate derivatives and their application in the selenoether linked pseudodisaccharide derivatives under a metal-free organocatalytic reaction condition is reported herein (Scheme 1).

Results and discussion

In order to optimize the reaction condition for the preparation of glycosyl selenocyanate derivative, methyl 2,3,4-tri-O-benzoyl-6-deoxy-6-iodo-α-D-glucopyranoside (1) was treated with a varied quantity of KSeCN in the presence of tetrabutylammonium bromide (TBAB), a phase transfer catalyst (PTC) in water. The best yield of methyl 2,3,4-tri-O-benzoyl-6-deoxy-6-selenato-α-D-glucopyranoside (8) was obtained in 76% by using 1.5 equiv. KSeCN and 0.1 equiv. TBAB in H2O at 60 °C in 8 h. Reduction of the quantity of KSeCN and TBAB led to the incomplete reaction with low yield of product formation (Table 1). The reaction became sluggish at room temperature. The reaction did not proceed well in absence of TBAB and starting material decomposed under the reaction condition. Following the similar

Table 1 Optimization of the formation of glycosyl selenocyanate derivatives in H2O

| Sl no. | KSeCN (equiv.) | TBAB (equiv.) | Time (h) | Temp. (°C) | Yield (%) |
|-------|----------------|---------------|----------|------------|-----------|
| 1     | 1.2            | 0.1           | 10       | 60         | 60        |
| 2     | 1.5            | 0.1           | 8        | 60         | 76        |
| 3     | 1.5            | 0.1           | 8        | 80         | 70        |
| 4     | 1.5            | 0.05          | 12       | 60         | 66        |
| 5     | 1.5            | —             | 24       | 60         | 20        |
| 6     | 1.5            | 0.1           | 24       | RT         | 40        |

Starting material decomposed.

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Fig. 1 Glycosyl iodide and triflate derivatives used as electrophiles for the preparation of non-glycosidically selenium linked pseudodisaccharide derivatives.
Table 3  Optimization of the reaction of glycosyl selenocyanate with sugar electrophile at room temperature

| Sl no. | Comp. 8 (equiv.) | Comp. 3 (equiv.) | Base (equiv.) | Solvent | Time (min) | Yield (%) |
|--------|------------------|------------------|--------------|---------|-----------|-----------|
| 1      | 1.0              | 1.2              | NH₂NH₂•H₂O (4.0) | DMF     | 45        | 74        |
| 2      | 1.0              | 1.2              | NH₂NH₂•H₂O (4.0) | DMF     | 60        | 75        |
| 3      | 1.0              | 1.2              | NH₂NH₂•H₂O (4.0) | CH₃CN   | 60        | 77        |
| 4      | 1.0              | 1.2              | NH₂NH₂•H₂O (4.0) | CH₃CN   | 45        | 70        |
| 5      | 1.0              | 1.2              | NH₂NH₂•H₂O (3.0) | CH₃CN   | 60        | 70        |
| 6      | 1.0              | 1.2              | NH₂NH₂•H₂O (2.0) | CH₃CN   | 60        | 68        |
| 7      | 1.0              | 1.2              | NH₂NH₂•H₂O (4.0) | THF     | 60        | 45        |
| 8      | 1.0              | 1.2              | NH₂NH₂•H₂O (4.0) | CH₃OH   | 60        | 25        |
| 9      | 1.0              | 1.2              | NH₂NH₂•H₂O (4.0) | CH₃Cl   | 60        | 20        |
| 10     | 1.0              | 1.2              | NaBH₄ (2.0)     | CH₃CN   | 60        | 72        |
| 11     | 1.0              | 1.2              | K₂CO₃ (2.0)     | CH₃CN   |           |           |
| 12     | 1.0              | 1.2              | Pyrrolidine (4.0) | CH₃CN  | 120       | 20        |
| 13     | 1.0              | 1.2              | Pyrrolidine (4.0) | DMF     | 120       | 20        |
| 14     | 1.0              | 1.2              | Diethylamine (4.0) | CH₃CN  | 120       | 10        |

In this study, similar reaction condition has been applied for the preparation of a series of nonglycosidically selenoether linked pseudodisaccharide derivatives (18–32) in excellent yield (Table 4). The products were unambiguously characterized using NMR and mass spectral analysis.

Experimental

General methods

All reactions were monitored by thin layer chromatography over silica gel coated TLC plates. The spots on TLC were visualized by warming ceric sulphate (2% Ce(SO₄)₂ in 2 N H₂SO₄) sprayed plates on a hot plate. Silica gel 230–400 mesh was used for column chromatography. ¹H and ¹³C NMR spectra were recorded on Bruker Avance 500 MHz spectrometer using CDCl₃ as solvent and TMS as internal reference unless stated otherwise. Chemical shift values are expressed in δ ppm. HR-MS were recorded on a Micromass mass spectrometer.

General procedure for the preparation of glycosyl selenocyanate derivatives (8–14). To a solution of glycosyl halide or triflate derivative (1–7) (1 mmol) in H₂O (5 mL) was added K₃SeCN (1.5 mmol) and the reaction mixture was allowed to stir at 60 °C for appropriate time mentioned in Table 1. After complete consumption of the starting material, the reaction mixture was diluted with H₂O (25 mL) and extracted with EtOAc (2 × 20 mL). The organic layer was dried (Na₂SO₄) and concentrated under reduced pressure. The crude product was purified over SiO₂ using hexane–EtOAc as eluant to furnish pure product (8–14).

NMR spectral data of glycosyl selenocyanate derivatives (8–14):
Table 4 Preparation of selenium linked pseudodisaccharide derivatives using glycosyl selenocyanates in the presence of NH₂NH₂·H₂O in CH₃CN at room temperature

| Sl no. | Glycosyl selenocyanate | Glycosyl electrophile | Se-linked pseudodisaccharide derivative | Time (h) | Yield (%) |
|--------|------------------------|-----------------------|----------------------------------------|----------|-----------|
| 1      | 8                      | 3                     | ![Image](image1.png)                  | 60       | 77        |
| 2      | 8                      | 15                    | ![Image](image2.png)                  | 60       | 74        |
| 3      | 8                      | 16                    | ![Image](image3.png)                  | 60       | 65        |
| 4      | 9                      | 3                     | ![Image](image4.png)                  | 60       | 72        |
| 5      | 9                      | 15                    | ![Image](image5.png)                  | 60       | 76        |
| 6      | 10                     | 16                    | ![Image](image6.png)                  | 45       | 68        |
| 7      | 10                     | 17                    | ![Image](image7.png)                  | 45       | 70        |
| Sl no. | Glyosyl selenocyanate | Glyosyl electrophile | Se-linked pseudodisaccharide derivative | Time (h) | Yield (%) |
|-------|-----------------------|----------------------|-----------------------------------------|---------|-----------|
| 8     | 11 1                  | 60                   | 72                                      |         |           |
| 9     | 11 3                  | 60                   | 70                                      |         |           |
| 10    | 12 1                  | 80                   | 66                                      |         |           |
| 11    | 12 3                  | 80                   | 68                                      |         |           |
| 12    | 13 3                  | 60                   | 76                                      |         |           |
| 13    | 13 15                 | 60                   | 78                                      |         |           |
| 14    | 14 3                  | 60                   | 72                                      |         |           |
| 15    | 14 15                 | 60                   | 70                                      |         |           |

NCS<sub>e</sub> + R, I, OTf

NH<sub>4</sub>N<sub>2</sub>H<sub>4</sub>O (4.0 Equiv.)

CH<sub>3</sub>CN, RT

18-32

Time (h)  Yield (%)
Methyl 2,3,4-tri-O-benzoyl-6-deoxy-6-selenocyanato-α-D-glucopyranoside (8). Colorless oil; 1H NMR (500 MHz, CDCl3): δ 7.98-7.21 (m, 15H, Ar-H), 6.18 (d, J = 9.5 Hz, 1H, H-2), 5.41 (d, J = 10.0 Hz, 1H, H-3), 5.30-5.26 (m, 2H, H-6a, H-6b), 4.41-4.37 (m, 1H, H-5), 3.57 (s, 3H, OCH3), 3.42 (dd, J = 12.5 Hz, 3.0 Hz, 1H, H-6a), 3.31 (dd, J = 12.5 Hz, 8.0 Hz, 1H, H-6b); 13C NMR (125 MHz, CDCl3): δ 165.6, 165.5 (3 PhCO), 133.8-128.3 (Ar-C), 101.3 (SeC), 97.2 (C-1), 72.5 (C-5), 71.7 (C-2), 69.5 (C-3), 68.2 (C-4), 56.0 (OCH3), 31.0 (C-6); HRMS for C18H14NO3Se [M + H]+: calcd 596.0823; found: 596.0802.

Methyl 2,3,4-tri-O-benzoyl-6-deoxy-6-selenocyanato-α-D-glucopyranoside (9). Colorless oil; 1H NMR (500 MHz, CDCl3): δ 8.04-7.16 (m, 15H, Ar-H), 5.85 (dd, J = 10.0 Hz, 3.0 Hz, 1H, H-1), 5.68 (t, J = 10.0 Hz, 1H, H-4), 5.58 (br s, 1H, H-2), 4.91 (s, 1H, H-1), 4.32-4.29 (m, 1H, H-5), 3.51 (s, 3H, OCH3), 3.40 (dd, J = 12.5 Hz, 5.0 Hz, 1H, H-6a), 3.28 (dd, J = 12.5 Hz, 8.0 Hz, 1H, H-6b); 13C NMR (125 MHz, CDCl3): δ 166.0, 165.2, 165.1 (3 PhCO), 133.8-128.3 (Ar-C), 101.4 (SeC), 98.8 (C-1), 70.3 (C-2), 70.2 (C-5), 69.1 (C-3), 69.0 (C-4), 55.9 (OCH3), 31.4 (C-6); HRMS for C18H14NO3Se [M + H]+: calcd 596.0823; found: 596.0805.

Methyl 2,3,4-tri-O-benzoyl-6-deoxy-6-selenocyanato-α-D-mannopyranoside (10). Colorless oil; 1H NMR (500 MHz, CDCl3): δ 7.73-7.14 (m, 15H, Ar-H), 4.85 (d, J = 11.5 Hz, 1H, PhCH2), 4.60 (d, J = 12.0 Hz, 1H, PhCH), 4.54-4.50 (m, 3H, H-1, 2 PhCH2), 4.46 (brs H, 2 PhCH), 3.75 (dd, J = 8.5 Hz, 2.5 Hz, 1H, H-3), 3.70-3.66 (m, 2H, H-4, H-5), 3.64 (brs H, 1H, H-2), 3.33 (dd, J = 11.5 Hz, 3.0 Hz, 1H, H-6a, H-6b), 3.19 (s, 3H, OCH3), 3.03 (dd, J = 11.5 Hz, 7.0 Hz, 1H, H-6b); 13C NMR (125 MHz, CDCl3): δ 138.2-127.7 (Ar-C), 102.1 (SeC), 99.3 (C-1), 80.0 (C-5), 77.4 (C-2), 75.2 (PhCH2), 74.6 (C-3), 73.0, 72.1 (2 PhCH2), 70.5 (C-4), 55.2 (OCH3), 31.9 (C-6); HRMS for C18H14NO3Se [M + H]+: calcd 554.1445; found: 554.1430.

P-Methoxyphenyl-2-O-benzyl-3,4-isopropylidene-6-deoxy-6-selenocyanato-α-D-galactopyranoside (14). Colorless oil; 1H NMR (500 MHz, CDCl3): δ 7.25-7.15 (m, 5H, Ar-H), 6.91 (d, J = 8.5 Hz, 2H, Ar-H), 6.73 (d, J = 8.5 Hz, 2H, Ar-H), 5.26 (d, J = 3.5 Hz, 1H, H-1), 4.70 (d, J = 10 Hz, 1H, PhCH), 4.66 (d, J = 12.5 Hz, 1H, PhCH), 4.43 (t, J = 6.0 Hz, 1H, H-2), 4.29-4.28 (m, 1H, H-5), 4.15-4.14 (m, 1H, H-4), 3.65 (s, 3H, OCH3), 3.54-3.52 (m, 1H, H-1), 3.36 (dd, J = 12.0 Hz, 8.5 Hz, 1H, H-6a), 3.39 (dd, J = 12.5 Hz, 5.0 Hz, 1H, H-6b), 3.31 (s, 3H, CH3), 1.25 (s, 3H, CH3); 13C NMR (125 MHz, CDCl3): δ 155.3-114.6 (Ar-C), 109.7 (C(CH3)3), 102.0 (SeC), 96.5 (C-1), 75.7 (C-3), 75.6 (C-4), 74.2 (C-5), 72.5 (PhCH2), 67.2 (C-2), 55.5 (OCH3), 29.6 (C-6), 27.9, 26.3 (2 CH2); HRMS for C24H26NO5Se [M + H]+: calcd 506.1082; found: 506.1065.

General reaction condition for the preparation of non-glycosidically Se-linked pseudodisaccharides (18-32). To a solution of glycosyl selenoaciane derivative (8-14; 1.0 mmol) in anhydrous CH3CN (5 mL) was added glycosyl halide/triflate derivat (1.2 mmol) followed by NH4NH2·H2O (4.0 mmol) and allowed to stir the reaction mixture at room temperature for appropriate time as mentioned in Table 2. The reaction mixture was diluted with H2O (25 mL) and extracted with EtOAc (2 × 20 mL). The organic layer was dried (Na2SO4) and concentrated under reduced pressure. The crude product was purified using SiO2 using hexane–EtOAc as eluant to furnish pure product (18-32).

NMR spectral data of Se-linked pseudodisaccharide derivatis (18-32): (Methyl 2,3,4-tri-O-benzoyl-6-deoxy-α-D-glucopyranosid-6-yl)-methyl 2,3,4-tri-O-benzoyl-6-deoxy-α-D-mannopyranosid-6-yl selenide (18). Colorless oil; 1H NMR (500 MHz, CDCl3): δ 8.03-7.28 (m, 30H, Ar-H), 6.16 (t, J = 10 Hz, 1H, H-4a), 5.48 (s, J = 10.0 Hz, 1H, H-1a), 5.28 (dd, J = 10.5 Hz, 3.5 Hz, 1H, H-2a), 5.17 (d, J = 3.5 Hz, 1H, H-1a), 4.99 (d, J = 11.0 Hz, 1H, PhCH2), 4.68-4.65 (m, 3H, 3 PhCH2), 4.61 (s, 2H, 2 PhCH2), 4.59 (br s, 1H, H-1b), 4.30-4.26 (m, 1H, H-5a), 3.83-3.75 (m, 3H, 3H, 3-), 3.57 (d, J = 5.0 Hz, 1H, H-2b), 3.50 (s, 3H, OCH3), 3.25 (s, 3H, OCH3), 3.11 (d, J = 11.5 Hz, 1H, H-6a), 2.98-2.91 (m, 2H, H-6ab), 2.89-2.82 (m, 1H, H-6ab); 13C NMR (125 MHz, CDCl3): δ 165.7, 165.6, 165.3 (3 PhCO), 138.5-127.5 (Ar-C), 98.7 (C-1b), 96.7 (C-1a), 80.1 (C-5a), 78.5 (C-2a), 75.2 (PhCH2), 74.5 (C-5a), 73.1 (C-2a), 73.0 (C-3a), 72.5 (PhCH3), 72.2 (C-3a), 72.0 (PhCH3), 70.5 (C-4a), 70.3 (C-4b), 55.5, 54.6 (2 OCH3), 26.8 (C-6b), 25.4 (C-
methoxyphenyl 2,3-O-isopropylidene-4,6-di-deoxy-

(96.8 (C-1B), 81.8 (C-3A), 81.4 (C-4A), 80.1 (C-2B), 75.6, 75.1, 73.1 (3 PhC), 72.9 (C-2A), 71.5 (C-7A), 70.6 (C-3A), 70.2 (C-4A), 55.5, 55.0 (2 OCH3), 26.8 (C-6A), 25.6 (C-6B); HRMS for C56H56O13Se [M + H]+: calculated 1017.2964; found: 1017.2946.

(2,3,4,6-tetra-O-benzyl-6-deoxy-α-D-mannopyranosid-6-yl)-

NMR (125 MHz, CDCl3): δ 165.7, 165.6, 165.3 (3 PhCO), 138.7–127.5 (Ar-C), 98.4 (C-1A), 97.6 (C-1B), 81.8 (C-3A), 81.4 (C-5A), 80.1 (C-2A), 75.6, 75.0, 73.2 (3 PhC), 71.4 (C-2B), 71.3 (C-7A), 70.7 (C-3B), 70.5 (C-4A), 69.8 (C-4B), 55.4, 55.1 (2 OCH3), 26.7 (C-6A), 26.0 (C-6B); HRMS for C56H56O13Se [M + H]+: calculated 1017.2964; found: 1017.2946.

(3,4,6-tri-O-benzyl-3-deoxy-3-α-D-mannopyranosid-3-yl)

NMR (125 MHz, CDCl3): δ 154.6–112.9 (Ar-C), 107.0 (1C-7A), 98.8 (C-1A), 92.1 (C-1B), 86.0 (C-3A), 81.9 (C-5A), 80.2 (C-2A,C-5A), 78.7 (C-4A), 75.1 (PhCCH3), 74.8 (C-2A), 72.9 (C-7A), 72.7 (PhCCH3), 72.0 (PhCCH3), 55.4, 54.7 (2 OCH3), 37.8 (C-4A), 26.9, 25.4 (2 CH3), 25.3 (C-6B), 18.4 (CCH3); HRMS for C44H52O16Se [M + H]+: calculated 821.2804; found: 821.2785.

13C NMR (125 MHz, CDCl3): δ 165.5, 165.4, 165.3 (3 PhCO), 138.5–127.5 (Ar-C), 98.7 (C-1A), 98.5 (C-1B), 80.1 (C-5A), 78.5 (C-2A), 75.1 (PhCCH3), 74.6 (C-3A), 73.0 (C-2B), 72.5, 72.0 (2 PhCCH3), 71.4 (C-5A), 70.8 (C-3B), 70.6 (C-4B), 69.9 (C-5B), 55.4, 54.6 (2 OCH3), 26.7 (C-6A), 25.7 (C-6B); HRMS for C56H56O13Se [M + H]+: calculated 1017.2964; found: 1017.2945.

(3,4,6-tri-O-benzyl-3-deoxy-3-α-D-mannopyranosid-3-yl)

NMR (125 MHz, CDCl3): δ 138.8–126.3 (Ar-C), 101.4 (PhCCH3), 98.8 (C-1A), 98.3 (C-1B), 80.0 (C-5A), 79.7 (C-2A), 79.4 (C-7A), 75.1 (PhCCH3), 75.0 (C-4A), 74.1 (C-4B), 72.8 (PhCCH2), 72.7 (C-7A), 72.1 (PhCCH3), 70.1 (PhCCH3), 69.0 (C-6A), 59.9 (C-5A), 55.0, 54.8 (2 OCH3), 43.6 (C-3A), 28.6 (C-6B); HRMS for C44H52O16Se [M + H]+: calculated 883.2960; found: 883.2943.

13C NMR (125 MHz, CDCl3): δ 138.8–126.3 (Ar-C), 101.4 (PhCCH3), 98.8 (C-1A), 98.3 (C-1B), 80.0 (C-5A), 79.7 (C-2A), 79.4 (C-7A), 75.1 (PhCCH3), 75.0 (C-4A), 74.1 (C-4B), 72.8 (PhCCH2), 72.7 (C-7A), 72.1 (PhCCH3), 70.1 (PhCCH3), 69.0 (C-6A), 59.9 (C-5A), 55.0, 54.8 (2 OCH3), 43.6 (C-3A), 28.6 (C-6B); HRMS for C44H52O16Se [M + H]+: calculated 883.2960; found: 883.2943.
(1,2,3,4-Di-o-isopropyliden-6-deoxy-a-galactopyranosyl-6-yl)-(methyl 2,3,6-tri-O-benzyl-6-deoxy-a-mannopyranosyl-6-yl) selenide (29). Colorless oil; 1H NMR (500 MHz, CDCl3); δ 7.27–7.18 (m, 15H, Ar-H), 5.42 (d, J = 5.0 Hz, 1H, H-1A), 4.87 (d, J = 11.0 Hz, 1H, PhCH), 4.67–4.62 (m, 2H, 2 PhCH), 4.59 (s, 1H, H-1A), 4.57 (d, J = 11.0 Hz, 1H, PhCH), 4.51 (s, 2H, 2 PhCH), 4.50 (dd, J = 13.0 Hz, 5.5 Hz 1H, H-3A), 4.26 (d, J = 7.5 Hz, 1H, H-2A), 4.19–4.18 (m, 1H, H-4A), 3.85–3.81 (m, 1H, H-5A), 3.75–3.74 (m, 1H, H-5B), 3.71–3.67 (m, 3H, H-2B, H-3B, H-4B), 3.37 (s, 3H, OCH3), 2.96 (d, J = 12.5 Hz, 1H, H-6A), 2.76–2.75 (m, 7H, 3H, H-6B and H-6ab), 1.41, 1.33, 1.23, 1.22 (s, 12H, 4 CH3). 13C NMR (125 MHz, CDCl3); δ 138.5–127.5 (Ar-C), 109.0, 108.4 (2 (CH2)), 98.8 (C-1A), 96.6 (C-1A), 80.1 (C-5A), 78.7 (C-2B), 75.1 (PhCH3), 74.7 (C-3A), 72.7 (C-4A), 72.7, 72.0 (2 PhCH2), 71.8 (C-3A), 71.0 (C-4A), 70.5 (C-2A), 68.3 (C-5A), 54.7 (OCH3), 26.6 (C-6a), 26.1, 26.0, 24.9, 24.5 (4 CH3), 24.0 (C-6b); HRMS for C40H38O10Se [M + H]+: calcd 771.2647; found: 771.2629.

(1,2,3,4-Dio-isopropyliden-6-deoxy-a-galactopyranosyl-6-yl)-(methyl 2,3,6-tri-O-benzyl-6-deoxy-a-mannopyranosyl-6-yl)selenide (30). Colorless oil; 1H NMR (500 MHz, CDCl3); δ 7.25–7.17 (m, 15H, Ar-H), 5.40 (d, J = 4.5 Hz, 1H, H-1A), 4.89 (d, J = 11.0 Hz, 1H, PhCH), 4.81 (d, J = 11.0 Hz, 1H, PhCH), 4.71 (d, J = 11.0 Hz, 1H, PhCH), 4.69 (d, J = 11.0 Hz, 1H, PhCH), 4.58 (t, J = 11.5 Hz, 2H, 2 PhCH), 4.47 (d, J = 2.5 Hz, 2H, H-1A), 4.43 (d, J = 2.5 Hz, 1H, H-5A), 4.18–4.16 (m, 1H, H-1A), 3.88 (t, J = 9.5 Hz, 1H, H-3A), 3.80–3.73 (m, 2H, H-5a, H-5b), 3.42 (dd, J = 9.5 Hz, 3.5 Hz, 1H, H-2b), 3.33 (3H, OCH3), 2.36 (t, J = 9.5 Hz, 1H, H-5a), 2.91 (dd, J = 12.5 Hz, 2.0 Hz, 1H, H-6ab), 2.72–2.69 (m, 2H, H-6ab), 2.65 (dd, J = 12.5 Hz, 8.5 Hz, 1H, H-6ab); 13C NMR (125 MHz, CDCl3); δ 138.7–137.5 (Ar-C), 109.1, 108.4 (2 (CH2)), 97.8 (C-1A), 96.6 (C-1A), 81.8 (C-5A), 81.6 (C-3A), 80.1 (C-5B), 75.6, 75.1, 73.2 (3 PhCH3), 71.7 (C-4A), 71.1 (C-4B), 71.0 (C-4a), 68.5 (C-6a), 55.2 (OCH3), 26.5 (C-6a), 26.1, 26.0, 24.9, 24.5 (4 CH3), 24.0 (C-6b); HRMS for C40H38O10Se [M + H]+: calcd 771.2647; found: 771.2629.

(p-Methoxyphenyl-2-o-benzyl-3,4-isopropyliden-6-deoxy-a-galactopyranosyl-6-yl)-(methyl 2,3,6-tri-O-benzyl-6-deoxy-a-mannopyranosyl-6-yl)selenide (31). Colorless oil; 1H NMR (500 MHz, CDCl3); δ 7.77–7.13 (m, 20H, Ar-H), 6.96 (d, J = 8.5 Hz, 2H, Ar-H), 6.70 (d, J = 8.5 Hz, 2H, Ar-H), 5.18 (d, J = 3.0 Hz, 1H, H-1A), 4.83 (d, J = 11.0 Hz, 1H, PhCH), 4.69 (d, J = 12.5 Hz, 1H, PhCH), 4.63 (d, J = 12.5 Hz, 1H, PhCH), 4.60–4.59 (m, 2H, 2 PhCH), 4.47–4.44 (m, 4H, H-1B, 3 PhCH3) 4.32 (t, J = 7.0 Hz, 1H, H-2A), 4.23–4.18 (m, 2H, H-2B, H-2B), 3.69–3.68 (m, 2H, H-4a, H-5a), 3.62–3.58 (m, 5H, H-3a, H-3b, OCH3), 3.50 (dd, J = 8.0 Hz, 3.5 Hz, 1H, H-5b), 3.10 (3H, OCH3), 2.83–2.75 (m, 3H, H-6ab, H-6ab), 2.70 (dd, J = 12.5 Hz, 8.0 Hz, 1H, H-6ab), 1.29, 12.24 (s, 6H, 2 CH2); 13C NMR (125 MHz, CDCl3); δ 155.0–114.5 (Ar-C), 108.9 (C(CH3)2), 98.8 (C-1a), 96.8 (C-1a), 80.1 (C-5a), 78.2 (C-2a), 76.2 (C-3a), 75.9 (C-4a), 75.1 (PhCH3), 74.6 (C-4a), 74.3 (C-3a), 72.6 (C-2a), 72.3 (C-5a), 72.1, 72.0 (2 PhCH2), 68.6 (C-6a), 55.4, 54.7 (2 OCH3), 28.2 (CH2), 27.1 (C-6a), 26.4 (CH2), 24.8 (C-6b); HRMS for C35H34O13Se [M + H]+: calcd 927.3222; found: 927.3205.
(p-Methoxyphenyl-2-O-benzyl-3,4-O-isopropylidene-6-deoxy-α-L-galactopyranosid-6-yl)-(methyl 2,3,4-tri-O-benzyl-6-deoxy-β-D-gluco pyranosid-6-yl)selenide (32). Colorless oil; 1H NMR (500 MHz, CDCl3): δ 7.27–7.12 (m, 20H, Ar-H), 6.95 (d, J = 8.5 Hz, 2H, Ar-H), 6.71 (d, J = 8.5 Hz, 2H, Ar-H), 5.19 (d, J = 3.0 Hz, 1H, H-1A), 4.87 (d, J = 11.0 Hz, 1H, PhCH5), 4.79 (d, J = 11.0 Hz, 1H, PhCH5), 4.71–4.63 (m, 4H, H-1B, 3 PhCH5), 4.55 (dd, J = 12.0 Hz, 1H, H-2B), 4.46 (d, J = 11.0 Hz, 1H, PhCH5), 4.39–4.36 (m, 2H, H-5A, PhCH5), 4.21–4.20 (m, 1H, H-4A), 4.12–4.10 (m, 1H, H-5B), 3.85 (t, J = 9.0 Hz, 1H, H-4B), 3.65 (s, 3H, OCH3), 3.52 (dd, J = 7.5 Hz, 3.5 Hz, 1H, H-3B), 3.38 (dd, J = 9.5 Hz, 3.5 Hz, 1H, H-2A), 3.30 (d, J = 7.5 Hz, 1H, H-2A), 3.24 (s, 3H, OCH3), 3.21 (t, J = 9.0 Hz, 1H, H-4B), 2.80 (dd, J = 12.5 Hz, 2.0 Hz, 1H, H-6B), 2.74 (d, J = 7.5 Hz, 2H, H-6B), 2.54 (dd, J = 12.5 Hz, 8.0 Hz, 1H, H-6A), 1.30, 1.26 (s, 6H, 2 CH3); 13C NMR (125 MHz, CDCl3): δ 155.0–114.5 (Ar-C), 109.0 (C(CH3)2), 97.7 (C-1B), 96.7 (C-1A), 81.8 (C-5A), 81.3 (C-2A), 80.1 (C-3A), 76.0 (C-3B), 75.8 (C-4A), 75.6, 75.0 (2 PhCH3), 74.2 (C-4A), 73.2, 72.2 (2 PhCH3), 70.8 (C-5A), 68.5 (C-2A), 55.4, 55.0 (2 OCH3), 28.1 (CH3), 26.7 (C-6B), 26.4 (CH2), 24.6 (C-6B); HRMS for C53H58O11Se [M + H]+: calcd 927.3222; found: 927.3205.

Conclusions
In summary, an “on-water” reaction condition has been developed for the preparation of stable glycosyl selenocyanate derivatives using readily available KSeCN as selenium source under eco-friendly reaction condition. Furthermore, the glycosyl selenocyanate derivatives have been used as stable building blocks for the stereoselective preparation of nonglycosidically selenoether linked pseudodisaccharide derivatives in excellent yield under a meta-free organocatalytic reaction condition. This approach may be considered as a better alternative to those reported earlier for the preparation of selenoether linked sugars because of its simplicity and yield efficiency. To the best of our knowledge this is the maiden report on the synthesis and characterization of glycosyl selenocyanate derivatives and their application in the metal-free organocatalytic synthesis of selenoether linked disaccharide derivatives.

Author contributions
AKM conceived and designed the experiments; TM performed the experiments; AKM and TM analyzed the data; AKM and TM wrote the paper. All authors read and approved the final manuscript.

Conflicts of interest
There are no conflicts of interest to declare.

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