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Preparation of 5-Selenopentopyranose Sugars from Pentose Starting Materials by Samarium(II) Iodide or (Phenylseleno)formate Mediated Ring Closures

Mathew A. Lucas, Oanh T. K. Nguyen, Carl H. Schiesser* and Shi-Long Zheng†

School of Chemistry, The University of Melbourne, Victoria 3010, Australia

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Abstract—2,3,4-Tri-*O*-benzyl-1,5-dideoxy-5-seleno-D-pentopyranose sugars (**16**, **23**, **24**) are readily prepared by thermolysis of 2,3,4-tri-*O*-benzyl-5-benzylseleno-D-ribit-1-yl formate, 2,3,4-tri-*O*-benzyl-5-benzylseleno-D-xylit-1-yl formate and 2,3,4-tri-*O*-benzyl-5-benzylseleno-D-arabit-1-yl formate (**13**, **21**, **22**) in transformations which involve intramolecular nucleophilic attack of the benzylseleno moiety with concomitant loss of carbon dioxide and phenylselenoate. In a complementary procedure, treatment of 2,3,4-tri-*O*-benzyl-5-benzylseleno-5-deoxyribose (**19**) with samarium(II) iodide in THF affords 2,3,4-tri-*O*-benzyl-5-deoxy-5-seleno-D-ribopyranose (**26**) in 50% isolated yield in a process most likely involving intramolecular homolytic substitution at the selenium atom in the selenosugar.

Introduction

It is well accepted that carbohydrates play an important role in a vast array of biological processes. Modified carbohydrates such as nitrogen, phosphorus and sulfur containing monosaccharides are of interest due to their wide variety of pharmacological activity and physiochemical properties. Examples include 5-deoxy-5-thio-D-glucose (**1**) which has been shown to be a potent inhibitor of cellular D-glucose transport and also selectively toxic to hypoxic tumor cells,[1] *nojirimycin* (**2**), *deoxynojirimycin* (**3**) and the butylated analogue (**4**) which are well known to show antibacterial activity and have been proposed as chemotherapeutic agents to treat HIV infection.[2] Selenium analogues of these important compounds (e.g. **5**, **6**) may also be expected to show interesting properties.

There can be no doubt that selenium-containing organic molecules have played and continue to play an important role in biology and medicine.[3] The mythology surrounding the 'high toxicity' of organic selenides, which itself can be traced to the voyages of Marco Polo,[4] and, more recently, the American civil war,[5] has largely been dispelled, and a wide range of organic selenides are now accepted as useful antioxidants,[6] anti-inflammatory agents,[7] antibiotics[8] and anti-viral agents.[9] Examples include the diselenovaleric acid (**7**) which provides an effective treatment for Kwashiokor, a protein-malnutrition disorder,[10] selenacephalosporins (**8**) which were patented by Hoffman La Roche as antibiotics,[11] selenazine (**9**) which is reported to be effective against Methiciline resistant *Staphylococcus aureus*,[8] (MRS) and Ebselen (**10**), which is currently undergoing clinical trials as a non-steroidal antiinflammatory (Fig. 1).[7]

It is well established that selenium is an essential trace element and selenium dietary supplements are commonly available, especially in countries such as France and New Zealand, which are soil selenium deficient.[12]

There are very few reports of carbohydrates containing selenium in the ring position.[13] Those that have been reported (e.g. **6**) were prepared in very poor yield.[13] Given the biomedical importance of selenium-containing organic molecules, and the scarcity of (ring) selenium-modified carbohydrates, it is clear that a synthetically useful method for the preparation of selenium-containing carbohydrates is required.

As part of ongoing investigations, we were interested in the preparation of novel selenium-containing carbohydrates related to **5**. Given our recent successes in the preparation of selenium-containing higher heterocycles through the use of intramolecular free-radical homolytic substitution chemistry as well as ionic chemistry,[14,15] we began to explore the possibility of constructing the carbohydrates of interest through appropriate extensions of previous work.

We now report that 2,3,4-tri-*O*-benzyl-1,5-dideoxy-5-seleno-D-pentopyranose sugars (**16**, **23**, **24**) can be prepared by thermolysis of suitable selenoformate derivatives of pentose

Keywords: carbohydrate; selenium; free-radical; samarium iodide; ring closure.

* Corresponding author. Tel.: +61-3-8344-4180; fax: +61-3-9347-5180; e-mail: c.schiesser@chemistry.unimelb.edu.au

† Current address: West China University of Medical Sciences, Chengdu, China.

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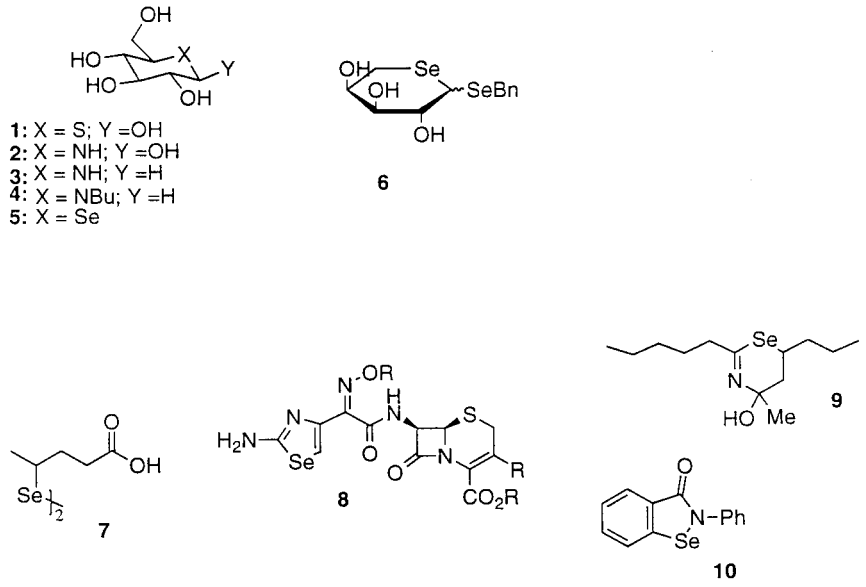


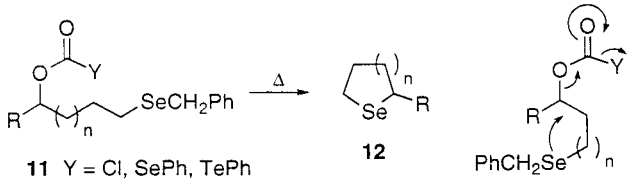
Figure 1.

carbohydrates, while 2,3,4-tri-*O*-benzyl-5-deoxy-5-seleno-D-pentopyranose analogues (**26**, **28**, **29**) can be prepared by treatment of suitable precursor aldopentose derivatives with samarium(II) iodide in THF/HMPA.

Results and Discussion

We reported recently that 1-(benzylseleno)alkyl (phenyltelluro)formates (**11**, Y=TePh), as well as the (phenylseleno)formate and chloroformate analogues, upon thermolysis, react to provide the selenium-containing rings (**12**) in excellent yield.[15] The mechanism of these transformations has been shown to involve intramolecular nucleophilic attack of the benzylseleno moiety with concomitant loss of carbon dioxide and phenylchalcogenide or chloride (Scheme 1).[15]

Given these previous observations, it seemed appropriate to explore similar chemistry involving aldopentose starting materials; selenoformate (**13**) derived from D-arabinose appeared to be a reasonable initial target. To that end D-arabinose was converted into 2,3,4-tri-*O*-benzyl-5-*O*-methanesulfonylarabinose (**14**) following the procedure of Barton and Quiclet-Sire.[16] Subsequent reduction with sodium borohydride followed by reaction with sodium benzylselenoate[14] afforded the benzylselenoarabitol (**15**) in 55% yield after flash chromatography (Scheme 2). Following our previously published procedure,[15] **15** was treated with a solution of phosgene in toluene followed by sodium phenylselenoate to give the required selenoformate (**13**) in 71% yield after chromatography.

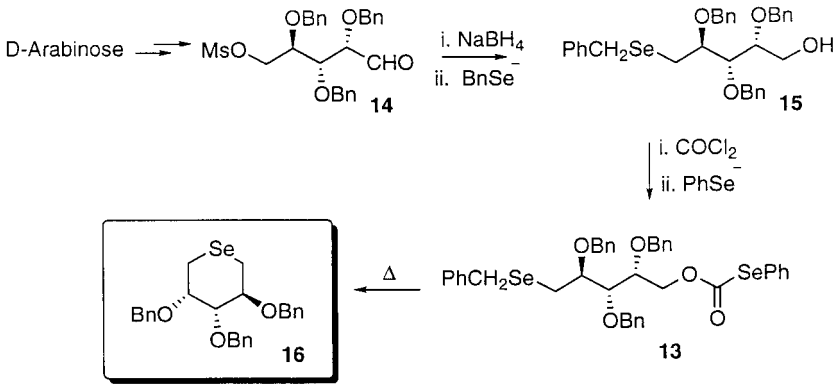


Scheme 1.

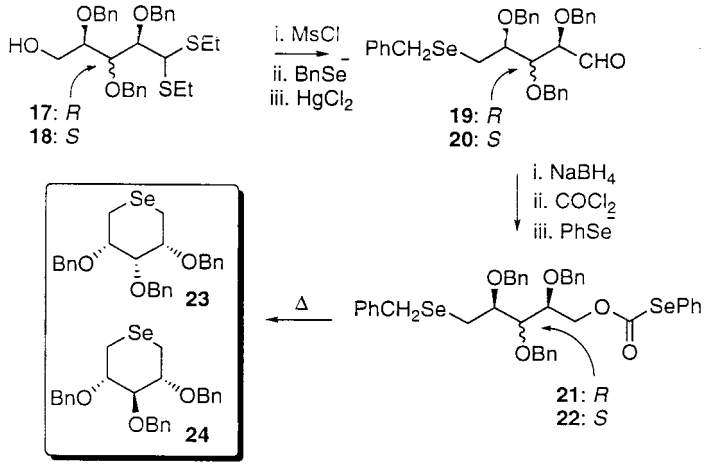
To our delight, when selenoformate (**13**) was heated to 150°C in benzene (0.27 M solution) in a sealed tube, ^{1}H NMR spectroscopy revealed an almost quantitative conversion into the required product; 2,3,4-tri-*O*-benzyl-1,5-dideoxy-5-seleno-D-arabinopyranose (**16**: $[\alpha]_D^{22}=-41$) was isolated in 81% yield after chromatography. Presumably, **16** is formed from **13** in an analogous manner to the transformations depicted in Scheme 1. When the complete sequence depicted in Scheme 2 was repeated using L-arabinose as starting material, 2,3,4-tri-*O*-benzyl-1,5-dideoxy-5-seleno-L-arabinopyranose, the enantiomer of **16** ($[\alpha]_D^{22}=+45$) was isolated in 74% yield from the corresponding L-selenoformate.

The procedure reported by Quiclet-Sire for the preparation of **14**,[16] when applied to the analogous ribose and xylose substrates, proved to be fraught with difficulties. In particular, the ribose and xylose analogues of **14** proved to be unstable and a preparative sequence that avoided their preparation was required. We found that the known dithioacetals[17] (**17**, **18**) derived from D-ribose and D-xylose respectively, are readily mesylated. Further treatment with sodium benzylselenoate followed by mercuric chloride deprotection afforded the benzylseleno aldehydes (**19**, **20**) in excellent yields (Scheme 3). Further sodium borohydride reduction and conversion of the resultant alcohols into the selenoformates (**21**, **22**) was achieved as described for the preparation of **13**. To our delight, both selenoformates (**21**, **22**) provided their respective (optically-inactive) cyclic selenosugar, namely 2,3,4-tri-*O*-benzyl-1,5-dideoxy-5-seleno-D-ribopyranose (**23**) and 2,3,4-tri-*O*-benzyl-1,5-dideoxy-5-seleno-D-xylopyranose (**24**) in 56 and 96% yield respectively (Scheme 3).

Given our recent successes in the application of intramolecular homolytic substitution chemistry to the synthesis of selenium and tellurium containing heterocycles,[6,14] we felt that this approach might be amenable to the preparation of selenosugars in which the 'anomeric' centre is oxygenated. Samarium (II) iodide mediated radical ring-closure seemed



Scheme 2.

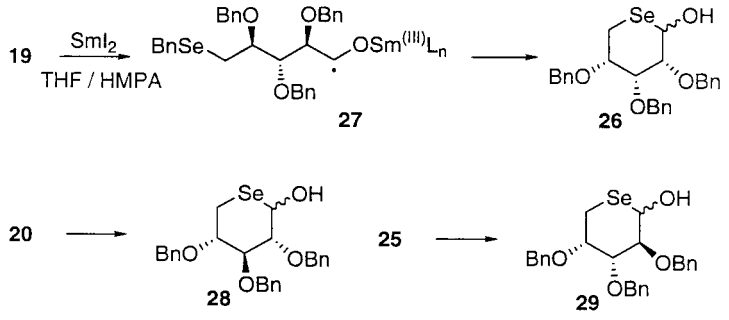


Scheme 3.

appropriate chemistry to explore,[18] although we were unaware of any reports of SmI_2 mediated homolytic substitution reactions at the outset of this work.

Aldehyde (**14**) was readily converted into the required benzylseleno derivative (**25**) by treatment with sodium benzylselenoate. With the required precursors (**19**, **20**, **25**) in hand, we began to explore the SmI_2 ring-closure chemistry. When **19** was treated with 2.5 equiv. of samarium(II) iodide in THF/HMPA, TLC analysis revealed the absence of starting material (**19**) after 20 min. To our delight, separation of the crude reaction mixture by flash chromatography afforded 2,3,4-tri-*O*-benzyl-5-deoxy-5-seleno-D-ribopyranose (**26**) in 50% yield. Presumably, **26** is formed by intramolecular homolytic substitution of the radical centre in **27**, generated by the reaction of the aldehyde moiety in **19** with SmI_2, at the selenium atom with expulsion of the benzyl group (Scheme 4). It should be noted that selenosugar (**26**) was isolated as a pair of anomers, as evidenced by ^1H NMR spectroscopy.

Unfortunately, treatment of 2,3,4-tri-*O*-benzyl-5-benzylseleno-5-deoxyxylose (**20**) and 2,3,4-tri-*O*-benzyl-5-benzylseleno-5-deoxyarabinose (**25**) with samarium(II) iodide in THF/HMPA gave a complex mixture of compounds as evidenced by TLC. Careful flash chromatography of each of these mixtures afforded impure samples 2,3,4-tri-*O*-benzyl-5-deoxy-5-seleno-D-xylopyranose (**28**)



Scheme 4.

and 2,3,4-tri-*O*-benzyl-5-deoxy-5-seleno-D-arabinopyranose (**29**). Despite the impurity of these samples, the formation of **28** and **29** was confirmed by HRMS in each case.[20]

To the best of our knowledge, these transformations represent the first examples of SmI_2 mediated homolytic substitution chemistry and complement the selenoformate mediated entry routes into rare 5-selenopentopyranose carbohydrates.

Experimental

All reagents used were obtained from commercial suppliers. Dibenzyl diselenide was prepared according to published procedure.[19] All melting points are uncorrected. Elemental analyses were carried out by Chemical and Micro Analytical Services Pty. Ltd.

2,3,4-Tri-*O*-benzyl-5-*O*-methanesulfonyl-D-arabitol. Sodium borohydride (180 mg, 4.8 mmol) was added with stirring at 0°C to a solution of 2,3,4-tri-*O*-benzyl-5-*O*-methanesulfonyl-arabinose (**14**)[16] (0.80 g, 1.6 mmol) in 4:1 dichloromethane–methanol (25 mL). The system was flushed with nitrogen. After stirring for 4 h at 0°C, the solvent was removed in vacuo, and the residue dissolved in ether (30 mL). The resultant solution was washed with water (5 mL), dried ($MgSO_4$), and the solvent removed. The title compound was isolated after flash chromatography (70:30 hexane–ethyl acetate) as a white crystalline solid of sufficient purity for further use (0.47 g, 59%), mp 58–59°C. ^{1}H NMR δ ($CDCl_3$) 1.79 (1H, sbr), 2.88 (3H, s), 3.66–3.81 (3H, m) 3.85 (1H, t, J=4.5 Hz), 3.94 (1H, m), 4.42 (1H, dd, J=5.8 Hz), 4.49–4.75 (7H, m), 7.29–7.34 (15H, m). ^{13}C NMR δ 36.83, 60.70, 69.25, 72.27, 72.31, 74.06, 77.43, 78.06, 78.71, 127.52, 127.62, 127.64, 127.86, 128.15, 137.29, 137.51, 137.81. IR(nujol) ν_{max} 3480 cm^{-1}. $[\alpha]_D^{27}$ (c=1.0, $CHCl_3$)=−4.2.

2,3,4-Tri-*O*-benzyl-5-*O*-methanesulfonyl-D-ribose diethyl dithioacetal. 4-Dimethylaminopyridine (12 mol%, 0.04 g, 0.334 mmol) was added to a solution of **17** in dry dichloromethane (15 mL) and dry pyridine (6 mL) at 0°C. After stirring at 0°C for 15 min, methanesulfonyl chloride (0.32 mL, 4.18 mmol) was added, and the mixture was stirred at room temperature for a further 4 h. The solvent was removed in vacuo, and the residue was dissolved in ethyl acetate (50 mL), washed with saturated $NaHCO_3$ (20 mL), dilute HCl (2×20 mL), water (2×50 mL) and saturated NaCl (20 mL), dried (Na_2SO_4), and the solvent removed in vacuo to afford the title compound as a green, unstable oil of sufficient purity for further use (1.45 g, 86%). ^{1}H NMR δ ($CDCl_3$) 1.17–1.26 (6H, m), 2.59–2.68 (4H, m), 2.77 (3H, s), 3.92 (1H, dd, J=3.9, 6.6 Hz), 4.09–4.17 (3H, m), 4.35 (2H, m), 4.60–4.78 (5H, m), 4.96 (1H, d, J=11 Hz), 7.29 (15H, m).

2,3,4-Tri-*O*-benzyl-5-*O*-methanesulfonyl-D-xylose diethyl dithioacetal was prepared by the procedure described above for the ribose analogue and isolated as an unstable orange viscous oil of sufficient purity for further use (85%) ^{1}H NMR δ ($CDCl_3$) 1.20 (6H, m), 2.61 (4H, m), 2.80 (3H, s), 3.85 (1H, m), 3.97 (2H, m), 4.16 (1H, t, J=4.6 Hz), 4.30 (1H, dd, J=6.6, 11 Hz), 4.41 (1H, dd, J=3.1, 11 Hz), 4.56–4.76 (5H, m), 4.90 (1H, m), 7.30–7.36 (15H, m).

Standard protocol A for the preparation of benzylseleno sugars: 2,3,4-tri-*O*-benzyl-5-benzylseleno-D-arabitol (15). Sodium borohydride (0.04 g, 1.06 mmol) was added to a solution of dibenzyl diselenide (0.12 g, 0.35 mmol) in dry ethanol (20 mL) and the solution was purged with nitrogen and allowed to react for 1 h. A solution of 2,3,4-tri-*O*-benzyl-5-*O*-methanesulfonyl-D-arabitol (0.34 g, 0.59 mmol) in ethanol (2 mL) was syringed into the benzylselenoate solution and the mixture was stirred for a further 18 h. The reaction solvent was removed in vacuo, and the residue dissolved in dichloromethane (40 mL). This organic solution was washed with saturated NaCl (10 mL) separated, dried (Na_2SO_4) and the solvent removed in vacuo. The title compound was purified by flash chromatography (hexane/ethyl acetate 80:20) affording **15** as a pale yellow solid, (0.24 g, 61%), mp 83–84°C. ^{1}H NMR δ ($CDCl_3$) 2.12 (1H, sbr), 2.91 (2H, d, J=5.4 Hz), 3.74 (2H, d, J=3.4 Hz), 3.57–3.85 (5H, m), 4.42–4.67 (6H, m), 7.23–7.32 (20H, m). ^{13}C NMR δ 25.18, 27.90, 61.80, 72.37, 72.89, 74.01, 79.81, 79.99, 80.18, 126.66, 127.68, 127.85, 127.90, 128.02, 128.33, 128.39, 128.44, 128.93, 138.05, 138.32, 138.37, 139.47. ^{77}Se NMR δ ($CDCl_3$) 222.36. IR(nujol) ν_{max} 3485 cm^{-1}. $[\alpha]_D^{27}$ (c=1.0, $CHCl_3$)=−4.1. Anal. Calcd for $C_{33}H_{36}O_4Se$: C, 68.9; H, 6.3. Found: C, 68.9; H, 6.4.

2,3,4-Tri-*O*-benzyl-5-benzylseleno-D-ribose diethyl dithioacetal was prepared from 2,3,4-tri-*O*-benzyl-5-*O*-methanesulfonyl-D-ribose diethyl dithioacetal following standard protocol A as a light yellow viscous oil (42%). ^{1}H NMR δ ($CDCl_3$) 1.18 (6H, m), 2.57–2.68 (5H, m), 2.89 (1H, dd, J=7.8, 13.0 Hz), 3.71 (2H, d, J=4.1 Hz), 3.93–3.98 (1H, m), 3.87 (1H, dd, J=3.2, 7.6 Hz), 4.17 (2H, m), 4.61 (4H, m), 4.76 (1H, m), 4.87 (1H, m), 7.19–7.34 (20H, m). ^{13}C NMR δ ($CDCl_3$) 14.42, 24.99, 26.35, 27.97, 53.94, 72.35, 73.41, 74.52, 79.84, 80.79, 82.41, 126.52, 127.48, 127.57, 127.85, 128.01, 128.25, 128.29, 128.37, 128.87, 138.07, 138.37, 139.58. ^{77}Se NMR δ ($CDCl_3$) 230.25. MS (ESI) m/z 703.4 $(M+Na)^+$. $[\alpha]_D^{28}$ (c=1.0, $CHCl_3$)=+5.1. Anal. Calcd for $C_{37}H_{44}O_3S_2Se$: C, 65.4; H, 6.5. Found: C, 65.5; H, 6.4.

2,3,4-Tri-*O*-benzyl-5-benzylseleno-D-xylose diethyl dithioacetal was prepared from 2,3,4-tri-*O*-benzyl-5-*O*-methanesulfonyl-D-xylose diethyl dithioacetal following standard protocol A as a light yellow viscous oil (40%). ^{1}H NMR δ ($CDCl_3$) 1.18 (6H, m), 2.51 (2H, m), 2.68 (2H, m), 2.82 (1H, dd, J=7.0, 12.5 Hz), 3.63 (1H, m), 3.74 (2H, s), 3.80 (1H, d, J=3.6 Hz), 4.01 (1H, dd, J=3.5, 6.8 Hz), 4.20 (1H, dd, J=3.6, 7.0 Hz), 4.40 (1H, m), 4.52–4.86 (6H, m), 7.27–7.34 (20H, m). ^{13}C NMR δ ($CDCl_3$) 14.33, 14.43, 23.44, 25.01, 25.34, 27.62, 53.54, 71.75, 74.96, 75.14, 78.66, 80.48, 82.83, 16.68, 127.17, 127.29, 127.50, 127.64, 127.68, 127.76, 127.83, 127.91, 128.04, 128.10, 128.20, 128.29, 128.43, 128.92, 137.88, 138.43, 138.55, 139.08. ^{77}Se NMR δ ($CDCl_3$) 224.28. MS (ESI) m/z 703.1 $(M+Na)^+$. $[\alpha]_D^{28}$ (c=1.0, $CHCl_3$)=−14.3. Anal. Calcd for $C_{37}H_{44}O_3S_2Se$: C, 65.4; H, 6.5. Found: C, 65.2; H, 6.5.

Standard protocol B for the deprotection of dithioacetals: 2,3,4-tri-*O*-benzyl-5-benzylseleno-aldehydo-D-ribose 19. Calcium carbonate (0.86 g, 8.56 mmol) and mercuric (II) chloride (2.32 g, 8.56 mmol) was added to a solution of 2,3,4-tri-*O*-benzyl-5-benzylseleno-D-ribose diethyl dithioacetal (1.18 g, 1.95 mmol) in acetonitrile-water (9:1, 15 mL). The mixture was stirred at room temperature for 4 h. The solution was then filtered through a Celite pad, and the filtrate was evaporated in vacuo. The residue was dissolved in dichloromethane and the solution was washed with 30% potassium iodide (20 mL), 30% sodium thiosulfate (20 mL) and saturated NaCl (20 mL) solutions. The organic phase was separated, dried (Na_2SO_4) and the solvent removed in vacuo to afford the title compound as a yellow viscous oil in quantitative yield. ^{1}H NMR δ ($CDCl_3$) 2.76 (1H, dd, J=4.5, 12.8 Hz), 2.96 (1H, dd, J=3.9, 12.9 Hz), 3.73 (2H, d, J=7.5 Hz), 3.92–4.01 (2H, m), 4.07 (1H, m), 4.43 (1H, m), 4.54 (2H, q, J=4.1 Hz), 4.64–4.71 (3H, m), 7.15–7.35 (20H, m), 9.47 (1H, s). ^{13}C NMR δ ($CDCl_3$) 25.32, 27.62, 72.17, 72.64, 72.96, 76.47, 81.93, 82.53, 126.55, 127.56, 127.69, 127.77, 127.80, 127.89, 128.23, 128.32, 128.39, 128.78, 137.22, 137.37, 137.50, 139.29, 201.04. ^{77}Se NMR δ ($CDCl_3$) 204.33. IR(neat) ν_{max} 1731 cm^{-1}. $[\alpha]_D^{29}$ ($CHCl_3$)=+16.0. HRMS (ESI) Calcd for $C_{33}H_{34}O_4SeNa$ $(M+Na)^+$ 597.1520. Found: 597.1518.

2,3,4-Tri-*O*-benzyl-5-benzylseleno-aldehydo-D-xylose 20 was prepared from 2,3,4-tri-*O*-benzyl-5-benzylseleno-D-xylose diethyl dithioacetal following standard protocol B as a yellow viscous oil (72%). ^{1}H NMR δ ($CDCl_3$) 2.54 (1H, dd, J=5.1, 12.7 Hz), 2.74 (1H, dd, J=8.5, 12.6 Hz), 3.68 (3H, m), 3.82 (d, 1H, J=5.3 Hz), 4.04 (1H, dd, J=3.2, 5.3 Hz), 4.31–4.76 (6H, m), 7.21–7.37 (20H, m), 9.65 (1H, s). ^{13}C NMR δ ($CDCl_3$) 23.10, 27.63, 72.41, 72.80, 73.84, 77.32, 79.34, 80.68, 126.74, 127.65, 127.93, 137.97, 128.0, 128.20, 128.27, 128.38, 128.40, 18.43, 128.81, 137.13, 137.15, 37.47, 138.82, 200.22. ^{77}Se NMR δ ($CDCl_3$) 219.90. IR(neat) ν_{max} 1729 cm^{-1}. $[\alpha]_D^{27}$ (c=1.0, $CHCl_3$)=−20.8. HRMS (ESI) Calcd for $C_{33}H_{34}O_4SeNa$ $(M+Na)^+$ 597.1520. Found: 597.1527.

2,3,4-Tri-*O*-benzyl-5-benzylseleno-D-ribitol was prepared from **19** following the same procedure as described for 2,3,4-tri-*O*-benzyl-5-*O*-methanesulfonyl-D-arabitol (above) as a light yellow viscous oil (82%). ^{1}H NMR δ ($CDCl_3$) 2.46 (1H, sbr), 2.80–3.00 (2H, m), 3.73–3.95 (6H, m), 4.03–4.06 (1H, m), 4.60–4.78 (6H, m), 7.33–7.45 (20H, m). ^{13}C NMR δ ($CDCl_3$) 24.61, 27.73, 61.12, 71.68, 72.17, 73.72, 78.6, 79.20, 79.62, 126.50, 17.56, 127.62, 127.66, 127.76, 127.82, 17.93, 128.21, 128.25, 128.29, 128.31, 137.81, 137.84, 137.94, 139.30. ^{77}Se NMR δ ($CDCl_3$) 224.28. IR(neat) ν_{max} 3466 cm^{-1}. MS (ESI) $(M+Na)^+$ m/z 599.4. $[\alpha]_D^{27}$ (c=1.0, $CHCl_3$)=−13.1. Anal. Calcd for $C_{33}H_{36}O_4Se$: C, 68.9; H, 6.3. Found: C, 68.9; H, 6.2.

2,3,4-Tri-*O*-benzyl-5-benzylseleno-D-xylitol was prepared from **20** following the same procedure as described for 2,3,4-tri-*O*-benzyl-5-*O*-methanesulfonyl-D-arabitol (above) as a light yellow viscous oil (67%). ^{1}H NMR δ ($CDCl_3$) 2.64 (1H, dd, J=6.1, 12.7 Hz), 2.80 (1H, dd, J=6.8 Hz), 3.48–3.84 (7H, m), 4.41–4.73 (6H, m), 7.24–7.33 (20H, m). ^{13}C NMR δ ($CDCl_3$) 23.91, 27.69, 61.58, 72.45, 72.69, 74.53, 78.63, 79.18, 79.35, 126.70, 127.73, 127.75, 127.80, 127.90, 128.04, 18.15, 128.15, 128.33, 128.35, 128.38, 128.43, 128.90, 137.78, 138.01, 138.12, 139.14. ^{77}Se NMR δ ($CDCl_3$) 224.71. IR(neat) ν_{max} 3466 cm^{-1}. MS (ESI) $(M+Na)^+$ m/z 599.0. $[\alpha]_D^{27}$ (c=1.0, $CHCl_3$)=−11.0. Anal. Calcd for $C_{33}H_{36}O_4Se$: C, 68.9; H, 6.3. Found: C, 68.9; H, 6.4.

Standard protocol C for the preparation of (phenylseleno) formates: (phenylseleno) 2,3,4-tri-*O*-benzyl-5-benzylseleno-D-arabit-1-yl formate 13. Sodium borohydride (16 mg, 38 mmol) was added with stirring to a solution of diphenyl diselenide (39 mg, 13 mmol), in dry THF (10 mL). The reaction vessel was purged with nitrogen and dry methanol (ca. 250 μL) was added dropwise until the yellow solution turned colorless (ca. 10 min). In a separate reaction vessel a 20% solution of phosgene in toluene (0.4 mL, 200 mmol) was added via syringe to a solution of **15** (120 mg, 21 mmol) in dry THF (10 mL) under nitrogen. The solution was stirred for 1 h and concentrated to approximately half the original volume in vacuo. After purging with nitrogen, the solution of the chloroformate was cannulated into the solution containing the sodium phenylselenoate and the resulting solution was stirred at room temperature under nitrogen overnight. The mixture was diluted with ether (30 mL) was washed with water (5 mL). The combined organic layers were dried (Na_2SO_4), and the solvent removed in vacuo. The selenoformate **13** was obtained as a yellow viscous oil after flash chromatography (hexane/ethyl acetate 90:10), (110 mg, 71%). ^{1}H NMR δ (C_6D_6) 2.86 (2H, m), 3.52 (2H, d, J=7.3 Hz), 3.79–3.89 (3H, m), 4.25–4.49 (8H, m), 6.69–7.33 (23H, m), 7.56 (2H, m). ^{13}C NMR δ (C_6D_6) 25.10, 27.64, 63.15, 71.92, 73.13, 74.02, 78.94, 79.11, 125.82, 126.54, 127.56, 127.61, 127.70, 127.74, 127.80, 127.90, 128.21, 128.32, 128.78, 129.03, 129.16, 135.66, 137.85, 137.87, 139.26, 160.39, 166.39. ^{77}Se NMR δ (C_6D_6) 219.69, 506.57. IR(neat) ν_{max} 1727 cm^{-1}. $[\alpha]_D^{29}$ (c=1.0, $CHCl_3$)=−12.4. Anal. Calcd for $C_{40}H_{40}O_5Se_2$: C, 63.3; H, 5.3. Found: C, 63.1; H, 5.3.

(Phenylseleno) 2,3,4-tri-*O*-benzyl-5-benzylseleno-D-ribit-1-yl formate 21 was prepared from 2,3,4-tri-*O*-benzyl-5-benzylseleno-D-ribitol following standard protocol C as a light yellow viscous oil, yield (71%). ^{1}H NMR δ ($CDCl_3$) 2.75 (2H, m), 3.72 (2H, d, J=7.5 Hz), 3.75–3.84 (3H, m), 4.34 (1H, dd, J=2.7, 12.0 Hz), 4.45–4.61 (7H, m), 7.21–7.36 (23H, m), 7.59 (2H, d, J=7.8 Hz). ^{13}C NMR δ ($CDCl_3$) 24.77, 27.79, 67.21, 72.09, 72.15, 73.68, 77.43, 78.75, 79.14, 125.91, 126.55, 127.59, 127.62, 127.84, 127.91, 127.97, 128.26, 128.34, 128.81, 129.02, 19.17, 135.74, 137.72, 137.89, 139.36, 166.61. ^{77}Se δ ($CDCl_3$) 219.90, 512.01. IR(neat) ν_{max} 1729 cm^{-1}. $[\alpha]_D^{26}$ (c=1.0, $CHCl_3$)=−15.6. HRMS (ESI) Calcd for $C_{40}H_{40}O_5Se_2Na$ $(M+Na)^+$ 783.1104. Found: 783.1115.

(Phenylseleno) 2,3,4-tri-*O*-benzyl-5-benzylseleno-D-xylit-1-yl formate 22 was prepared from 2,3,4-tri-*O*-benzyl-5-benzylseleno-D-ribitol following standard protocol C as a light yellow viscous oil (68%). ^{1}H NMR δ (C_6D_6) 2.55 (1H, dd, J=5.6, 12.5 Hz), 2.82 (1H, dd, J=6.9, 12.7 Hz), 3.47 (2H, d, J=5.4 Hz), 3.71 (1H, m), 3.82 (2H, m), 4.22–4.61 (8H, m), 6.92–7.26 (25H, m). ^{13}C NMR δ (C_6D_6) 27.71, 68.08, 72.52, 73.12, 74.74, 77.74, 79.23, 79.35,

126.93, 127.79, 18.08, 128.12, 128.55, 128.70, 129.10, 129.38, 129.40, 136.09, 138.75, 138.78, 138.84, 139.73, 166.32. ^{77}Se NMR δ (C_6D_6) 227.91, 509.02. IR(neat) ν_{max} 1728 cm^{-1} (C=O). MS (ESI) *m/z* $(M+Na)^+$ 783.9. $[\alpha]_D^{25}$ (*c*=1.0, $CHCl_3$)=−25.5. Anal. Calcd for $C_{40}H_{40}O_5Se_2$: C, 63.4; H, 5.3. Found: C, 63.5; H, 5.3.

Standard protocol D for the preparation of 2,3,4-tri-*O*-benzyl-1,5-dideoxy-5-selenopentopyranose sugars: 2,3,4-tri-*O*-benzyl-1,5-dideoxy-5-seleno-D-arabinopyranose 16. A solution of **13** (102 mg, 13.6 mmol) dissolved in dry benzene (0.5 mL, 0.27 M) in a vacuum sealed tube, was thermolised at 165°C in a silicon oil bath for 27 h, shielded from background light. Removal of the solvent in vacuo and purification via flash chromatography (hexane/ethyl acetate 90:10) afforded the title compound as a pale yellow viscous oil, (52 mg, 81%). ^{1}H NMR δ (C_6D_6) 2.19 (1H, dd, *J*=4.2, 13.2 Hz), 2.28 (1H, dd, *J*=3.4, 11.5 Hz), 3.07 (1H, dd, *J*=2, 13.2 Hz), 3.22 (1H, t, *J*=11 Hz), 3.70 (1H, m), 3.80 (1H, m), 4.09 (2H, m), 4.13–4.17 (1H, m), 4.30 (2H, m), 4.44 (1H, d, *J*=12 Hz), 4.70 (1H, d, *J*=12 Hz), 7.04–7.24 (15H, m) ^{13}C NMR δ (C_6D_6) 16.55, 17.84, 70.56, 70.846, 73.65, 76.49, 76.80, 77.78, 126.61, 126.76, 126.94, 127.25, 129.30, 133.07, 138.94, 139.42. ^{77}Se NMR δ (C_6D_6) 69.37. MS (ESI) *m/z* 491.5 $(M+Na)^+$. $[\alpha]_D^{22}$=−41. Anal. Calcd for $C_{26}H_{28}O_3Se$: C, 66.8; H, 6.1. Found: C, 66.8; H, 5.7.

2,3,4-Tri-*O*-benzyl-1,5-dideoxy-5-seleno-D-ribopyranose 23 was prepared from **21** following standard protocol D. Thermolysis at 180–190°C for 11 days afforded the title compound (after workup) as a light yellow viscous oil (32 mg, 56%). ^{1}H NMR δ (C_6D_6) 2.27 (2H, dd, *J*=3.2, 11.2 Hz), 3.52 (1H, dd, *J*=1.5, 3.9 Hz), 3.57 (1H, dd, *J*=1.5, 3.9 Hz), 4.13–4.35 (6H, m), 4.71 (1H, m), 4.97 (2H, m), 7.12–7.53 (15H, m). ^{13}C NMR δ (C_6D_6) 16.69, 7054, 74.73, 78.28, 81.78, 127.47, 127.79, 128.18, 128.35, 128.52, 128.58, 129.25, 129.31, 132.74, 139.16. ^{77}Se NMR δ (C_6D_6) 85.27. HRMS (ESI) Calcd for $C_{26}H_{28}O_3SeNa$ $(M+Na)^+$ 491.1101. Found: 491.1084.

2,3,4-Tri-*O*-benzyl-1,5-dideoxy-5-seleno-D-xylopyranose 24 was prepared from **22** following standard protocol D. Thermolysis at 165°C for 2 days afforded the title compound (after workup) as a light yellow viscous oil (47.9 mg, 96%). ^{1}H NMR δ (C_6D_6) 2.36 (4H, m), 3.19 (1H, t, *J*=8.7 Hz), 3.67 (2H, q, *J*=8.6 Hz), 4.42 (4H, q, *J*=11.7 Hz), 4.91 (2H, s), 7.12–7.27 (15H, m). ^{13}C NMR δ (C_6D_6) 22.07, 72.57, 76.29, 83.49, 87.23, 127.42, 127.63, 127.83, 128.11, 128.34, 128.47, 139.32, 139.94. ^{77}Se NMR δ (C_6D_6) 86.33. HRMS (ESI) Calcd for $C_{26}H_{28}O_3SeNa$ $(M+Na)^+$ 491.1101. Found: 491.1124.

2,3,4-Tri-*O*-benzyl-5-deoxy-5-seleno-D-ribopyranose 26. Dry HMPA (0.4 mL) was added to a stirred solution of SmI_2 in THF (5 mL, 0.1 M) and the solution flushed with nitrogen. 2,3,4-Tri-*O*-benzyl-5-benzylseleno-5-deoxyribose (**19**) (100 mg, 0.17 mmol) in THF (3 mL) was added via syringe and the resultant solution stirred for 4 h. A further aliquot of SmI_2 (5 mL) was added and the solution stirred overnight at which time TLC analysis indicated the absence of **19**. Saturated $NaHCO_3$ (20 mL) was added, the mixture extracted with ether, the combined organic layers dried ($MgSO_4$) and the solvent removed in vacuo. The residue was separated by flash chromatography (10% ethyl acetate in petrol) to afford **26** as a mixture of anomers (40 mg, 50%). ^{1}H NMR δ 2.4–2.9 (2H, m), 3.1–4.3 (4H, m), 4.5–4.9 (6H, m), 5.38 (0.5H, m, anomer A), 5.42 (0.5H, m, anomer B), 7.18–7.40 (15H, m). $[\alpha]_D^{25}$ (*c*=1.0, $CHCl_3$)=+11.4°C. HRMS (ESI) Calcd for $C_{26}H_{28}O_4SeNa$ $(M+Na)^+$ 507.1046. Found 507.1051.

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