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Novel cyclic tetraselenides of mannose: synthesis and mechanistic studies

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Dedicated to Professor K. Venkatesan on the occasion of his 75th birthday

Abstract—In this Letter, we disclose the synthesis of novel cyclic tetraselenides starting from mannose which are very unusual and rare and have been synthesised for the first time. The structures are confirmed by X-ray analysis. The reactivity of the reagent tetraethylammonium tetraselenotungstate, $(Et_4N)_2WSe_4$ has been compared with the well-known selenium transfer reagents Li_2Se_2 and Na_2Se_2. A tentative reaction mechanism has been proposed.

Selenium-containing compounds have found interesting and important roles as new generation pharmaceuticals, antioxidants, anti-inflammatory agents, etc.[1] Selenium-containing glycosides have also been identified as efficient antiviral and antitumour compounds.[2] In addition to the above, selenoglycosides have been efficiently used as glycosyl donors in various oligosaccharide syntheses.[3] Polychalcogenides are very attractive due to their chemical reactivity, oxidative properties and their occurrence in marine natural products.[4] There are only a few reports on the synthesis of polychalcogenide derivatives in aliphatic and aromatic systems.[5,6] To the best of our knowledge, there are no reports on polychalcogenide derivatives of carbohydrates. In this Letter, we report a class of novel cyclic tetraselenides **5**, **6** and **12** synthesised from D-mannose using tetraethylammonium tetraselenotungstate **1**, $(Et_4N)_2WSe_4$ as an efficient selenium transfer reagent.[7]

D-Mannose **2** was initially converted into its corresponding anomeric esters **3a–c** which on treatment with HBr/AcOH under standard conditions led to the formation of the corresponding bromides **4a–c**.[8] The mannosyl bromides **4a**,**b** were treated with tetraselenotungstate **1** (2 equiv, CH_3CN, 28 °C, 8 h) to furnish the novel, cyclic tetraselenides[9] **5a** and **5b**, respectively (Scheme 1).[10] The 1,5-trans-substituted structures of **5a** and **5b** were confirmed by X-ray crystallography (Fig. 1).[11]

These tetraselenides **5a** and **5b** are unusual and the first cyclic tetraselenides reported with a carbohydrate backbone. In the reaction of benzoyl-protected anomeric bromide **4c** with tetraselenotungstate **1**, apart from the formation of tetraselenide **6** as the major product, the formation of selenolevomannosan **7** (19%) as a minor product was also observed (Scheme 1).

A tentative mechanism for the formation of tetraselenide **5a** is given in Scheme 2. Participation of the axial acetate group in **4a** can lead to the formation of intermediate oxonium ion **8**. Nucleophillic attack of tetraselenotungstate **1** from the axial side results in the formation of intermediate **9**. It is possible to visualise displacement of the tosylate at C-5 with another molecule of **1** to give rise to the bis-alkylated species **10**.

It is believed that this intermediate **10**, in an internal redox process,[12a–d] can lead to the formation of 1,5-trans-substituted tetraselenide **5a**. A related cyclisation to form a polyselenide chain has been reported previously by Harpp et al.[5]

The reaction of bromo compound **11** synthesised from mannose **2**[13] (lacking neighbouring group participation) with **1** (CH_3CN, 28 °C, 8 h) gave exclusively the 1,5-cis-substituted cyclic tetraselenide **12** (Scheme 3) and not

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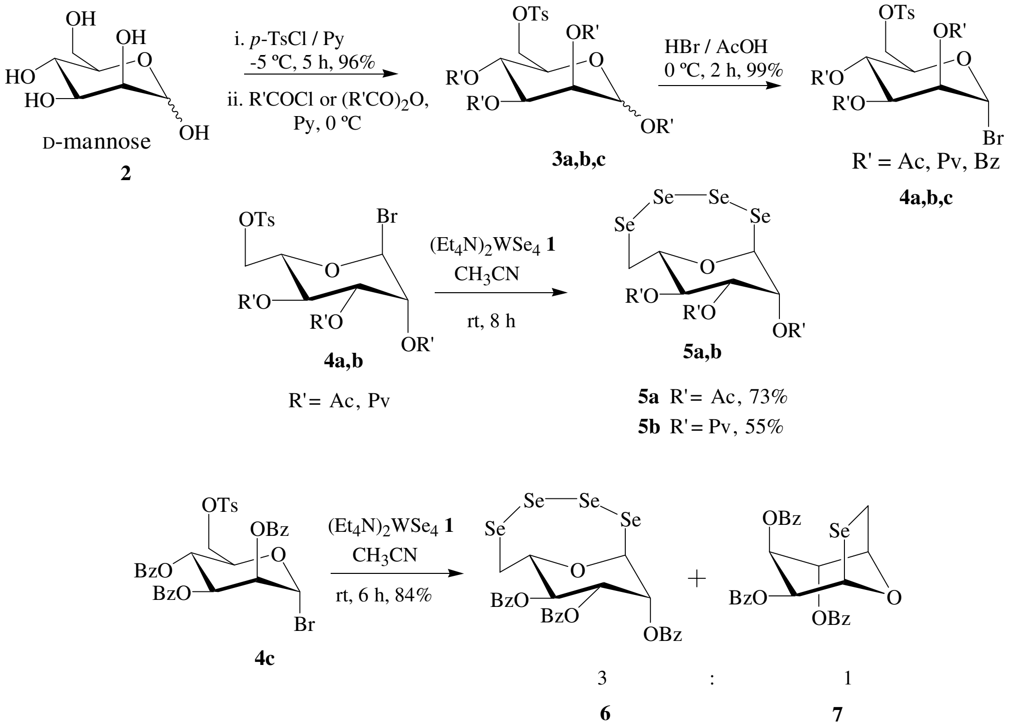


Scheme 1.

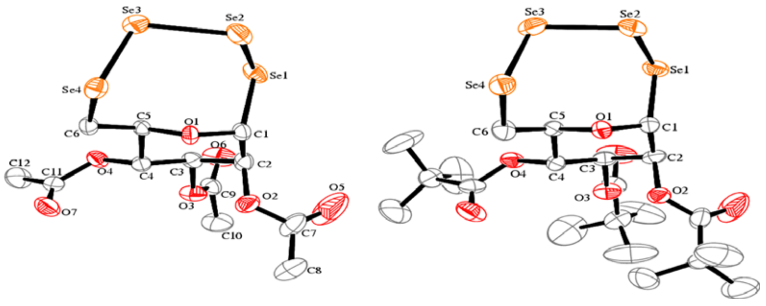


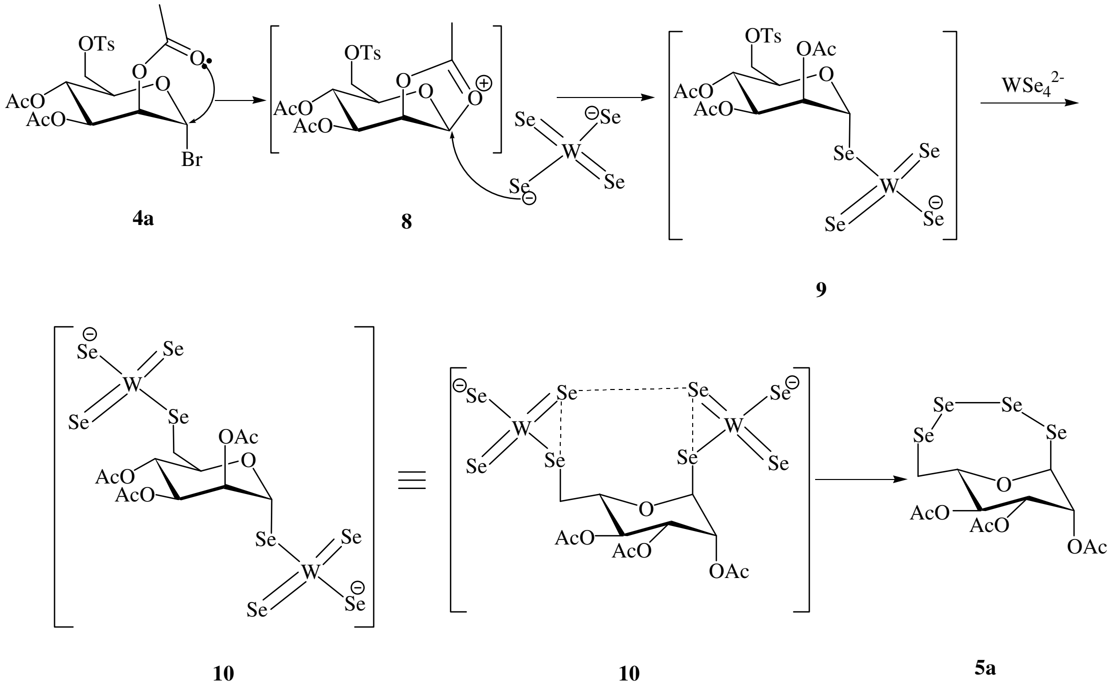
Figure 1. ORTEP diagrams of **5a** and **5b** (hydrogens are not shown for clarity).

product **13**. The proposed mechanism for the formation of **12** is given in Scheme 4. The 1,5-diaxially substituted structure of **12** was supported by the B3LYP method 6-31G* (6-31G(d)) level calculations.[14] Structure **12** was more stable than the equatorial structure **13** by 6 kcal/mol. The ^{77}Se NMR chemical shift value of the significant anomeric selenium atom (Se1) of the axial structure **12** is very similar to that of the other tetraselenides (Table 1). The selenium attached to the anomeric carbon in **12** shows a ^{77}Se NMR absorption at δ 714 which is close to the anomeric ^{77}Se signals for compounds **5a**; δ 720, **5b**; δ 716 and **6**; δ 720.

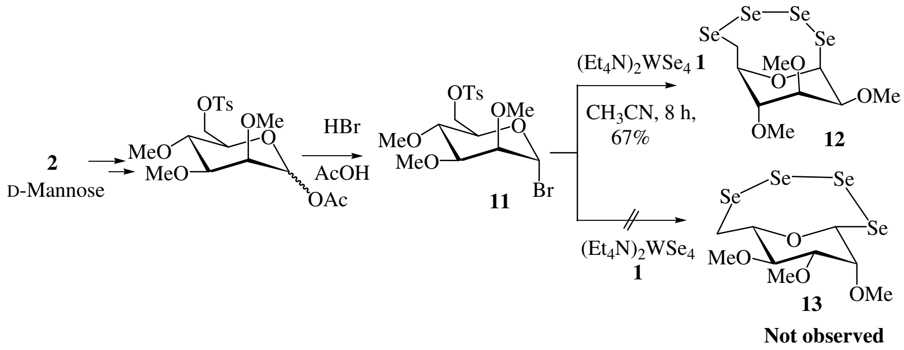
Reaction of mannosyl bromide **4c** with one equivalent of tetraselenotungstate **1** (CH_3CN, 4 h, 28 °C) led to the formation of a relatively unstable diselenide **16**[15] (Scheme 5). In order to compare the reactivity of the selenium transfer process, it was decided to react the mannosyl bromide **4c** with other selenium transfer reagents such as Na_2Se_2[16] and Li_2Se_2.[17] When bromide **4c** was treated with freshly prepared Li_2Se_2[17] (2 equiv, THF, 28 °C, 10 min) in the presence of a catalytic amount of *t*-BuOH, only diselenide **16**[15] (Scheme 5) was obtained, which was not very stable under the reaction conditions.

The above observations reveal that tungsten participates in the formation of tetraselenides **5** and **6**. In the reaction of **4c** with the reagents such as Na_2Se_2 and Li_2Se_2, not even a trace of tetraselenide **6** was detected in the product. To gain further insight into the reactions with tetraselenotungstate **1**, the reagent before and after reaction was studied by XPS, which showed the presence of at least two different oxidation states of tungsten [W(V) and W(VI)]. Since the powder patterns and XPS did not give any clear indications, there could possibly be formation of some kind of polymeric species derived from **1** after the reaction.

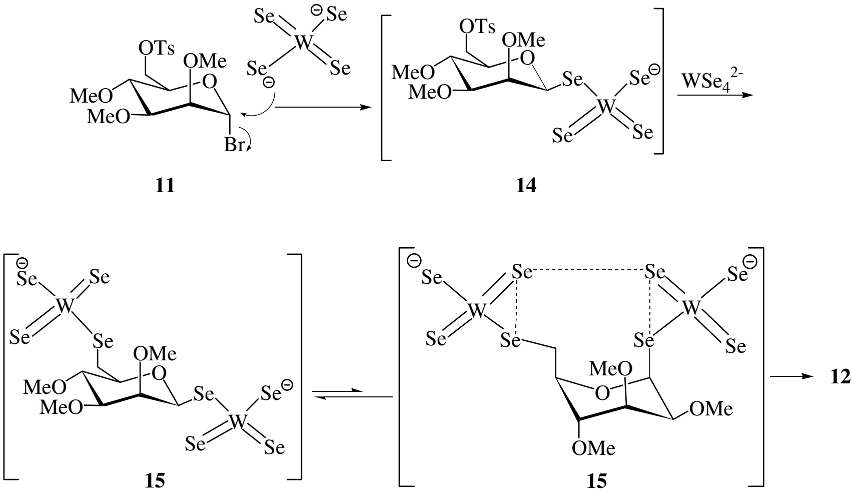
In summary, a new class of novel, cyclic tetraselenides has been synthesised in high yields using tetraselenotungstate **1** as an efficient selenium transfer reagent.



Scheme 2. Proposed mechanism for the formation of tetraselenides **5**.



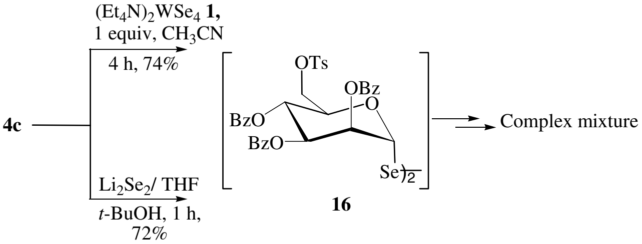
Scheme 3.



Scheme 4.

Table 1. ^{77}Se NMR Chemical shifts (76 MHz, $CDCl_3$)

Tetraselenide	^{77}Se NMR (δ ppm)
5a	720.2, 635.9, 472.8, 468.4
5b	715.6, 633.8, 469.7, 468.8
6	719.6, 634.1, 470.9, 466.8
12	714.0, 638.1, 472.4, 462.2



Scheme 5.

These tetraselenides are the first of their kind where all four selenium atoms are arranged in a cyclic manner as the backbone of mannose. The utility of these tetraselenides in carbohydrate chemistry is currently under investigation.

Acknowledgements

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9. *General experimental procedure for compound* **5a**: To a stirred solution of anomeric bromide **4a** (0.28 g, 0.395 mmol) in CH_3CN (3 ml), tetraethylammonium tetraselenotungstate **1** (2 equiv) was added and the reaction mixture was stirred for 8 h at 28 °C. After the disappearance of the starting material (TLC), the solvent was removed in vacuo and the resulting black residue was extracted with CH_2Cl_2–Et_2O (1:9, 5 × 20 ml) and filtered through a Celite pad. The filtrate was concentrated and the crude product was purified by flash column chromatography on silica gel (230–400 mesh, eluting with hexane–ethyl acetate 7:3). Compound **5a** was obtained as pale orange crystals (0.17 g, 0.25 mmol, 73%); $[\alpha]_D^{25}$ 10 (*c* 1, $CHCl_3$), mp: 185 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.78 (s, 1H), 5.52–5.35 (m, 3H), 4.13 (m, 1H), 3.15 (d, $J = 10.3$ Hz, 2H), 2.18 (s, 3H), 2.12 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.6, 170.4, 169.9, 78.2, 73.8, 72.7, 70.3, 67.3, 61.3, 25.6, 20.7, 20.6; ^{77}Se NMR (76 MHz, $CDCl_3$): δ 720.2, 635.9, 472.8, 468.4; HR-MS (*m*/*z*): calculated for $C_{12}H_{16}O_7Se_4$ ($M+Na^+$): 613.7376, observed ($M+Na^+$): 613.7427.
10. Tetraselenides **5a**, **5b**, **6** and **12** are stable at low temperature (4 °C). In solution over a period of time they gave rise to elemental selenium as one of the products. It is reported that polyselenide compounds decompose readily to give elemental selenium due to the lower bond energy of a Se–Se bond compared to a S–S bond.[6] In the present case where the polyselenide chain forms the backbone of a sugar it was found to be stable at low temperatures.
11. *Crystal structure data for* **5a**: $C_{18}H_{20}O_8Se_4$, MW = 613.7, crystal dimensions $0.25 \times 0.24 \times 0.17$ mm^3, $T = 293(2)$ K, Orthorhombic, space group *P* 21 21 21, $a = 8.057(5)$, $b = 8.640(5)$, $c = 26.858(16)$ Å, $\alpha = \beta = \gamma = 90.00°$, $Z = 4$, $V = 1869.6(19)$ cm^3, $\rho_{calcd} = 1.855$ g/cm^3, Mo K_α radiation ($\lambda v^\circ = 0.71073$ Å), $\mu = 4.001$ mm^{-1}, $2\theta = 1.52°$–26.37°; of 14,756 reflections collected, 3716 were independent (R(int) = 0.0328); GOF = 0.781, $R_1 = 0.0350$, $wR_2 = 0.0875$ ($\sigma > 2\sigma(I)$), absolute structure parameter 0.00(7), residual electron density 0.574/−0.487 e Å^{-3}. CCDC Number 282452. *Crystal structure data for* **5b**: $C_{21}H_{34}O_7Se_4$, MW = 740.9, crystal dimensions $0.38 \times 0.27 \times 0.22$ mm^3, $T = 293(2)$ K, trigonal, space group *P* 31, $a = 12.9677(14)$, $b = 12.9677(14)$, $c = 29.728(6)$ Å, $\alpha = \beta = 90.00°$, $\gamma = 120°$, $Z = 8$, $V = 4329.4(11)$ cm^3, $\rho_{calcd} = 2.192$ g/cm^3, Mo K_α radiation ($\lambda = 0.71073$ Å), $\mu = 6.824$ mm^{-1}, $2\theta = 1.81$–25.97°; of 33,534 reflections collected, 11,066 were independent (R(int) = 0.0480); GOF = 0.968, $R_1 = 0.0519$, $wR_2 = 0.1074$ ($\sigma > 2\sigma$(I)), absolute structure parameter −0.010(12), residual electron density 0.661/−0.362 e Å^{-3}. CCDC number 287584. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications. Copies of these data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(1223)336033 or e-mail: deposit@ccdc.cam.ac.uk or via www.ccdc.cam.ac.uk/conts/.
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