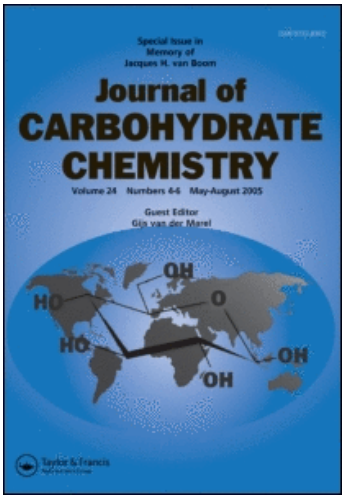

Journal of Carbohydrate Chemistry

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

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Online publication date: 07 September 2004

To cite this Article Rauter, Amélia P. , Canda, Tana , Justino, Jorge , Ismael, Maria I. and Figueiredo, José A.(2004) 'Synthesis of Phenylseleno Sugars from Epoxides and of α,β-Unsaturated Carbonyl Derivatives for the Study of Their Insecticidal Activity', Journal of Carbohydrate Chemistry, 23: 4, 239 — 251
To link to this Article: DOI: 10.1081/CAR-200030077
URL: http://dx.doi.org/10.1081/CAR-200030077

JOURNAL OF CARBOHYDRATE CHEMISTRY
Vol. 23, No. 4, pp. 239–251, 2004

Synthesis of Phenylseleno Sugars from Epoxides and of α,β-Unsaturated Carbonyl Derivatives for the Study of Their Insecticidal Activity

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CONTENTS

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DOI: 10.1081/CAR-200030077
0732-8303 (Print); 1532-2327 (Online)

ABSTRACT

This work reports the synthesis of sugar epoxides and their derivatives obtained by reaction with the dianion of phenyl selenoacetic acid. Approaches to the introduction of α,β-unsaturated carbonyl units in pyranoid systems were investigated. Preparation of a protected D-*glycero*-hex-3-enepyranosid-2-ulose and of a D-*erythro*-hex-2-enono-1,5-lactone is described. Some of the synthesized compounds possess insecticidal activity against fruit flies, house flies, and white flies.

Key Words: Sugar epoxides; Phenylseleno sugars; α,β-Unsaturated carbonyl moiety; Insecticidal activity.

INTRODUCTION

Sugar epoxides are versatile intermediates in organic synthesis,[1,2] due to the ease of their preparation from a variety of starting materials and to their susceptibility to reactions, for example, with electrophiles, nucleophiles, acids and bases. Furthermore, epoxides are part of a group of compounds recognized as active principles, with biological and pharmacological activities. Reference can be made to cytotoxic metabolites, namely crotepoxide, pipoxide, and senepoxide, the latter playing an important role as an antifeedant agent in plants.[3]

Methods for the preparation of epoxides use halohydrins as intermediate compounds,[4] and also alkenes,[5] vicinal diols,[6,7] glycals,[8,9] carbonyl compounds,[10] among others. Epoxides have been reported as starting materials for the synthesis of phenylseleno lactones, key intermediates for the preparation of butenolides.[11–13]

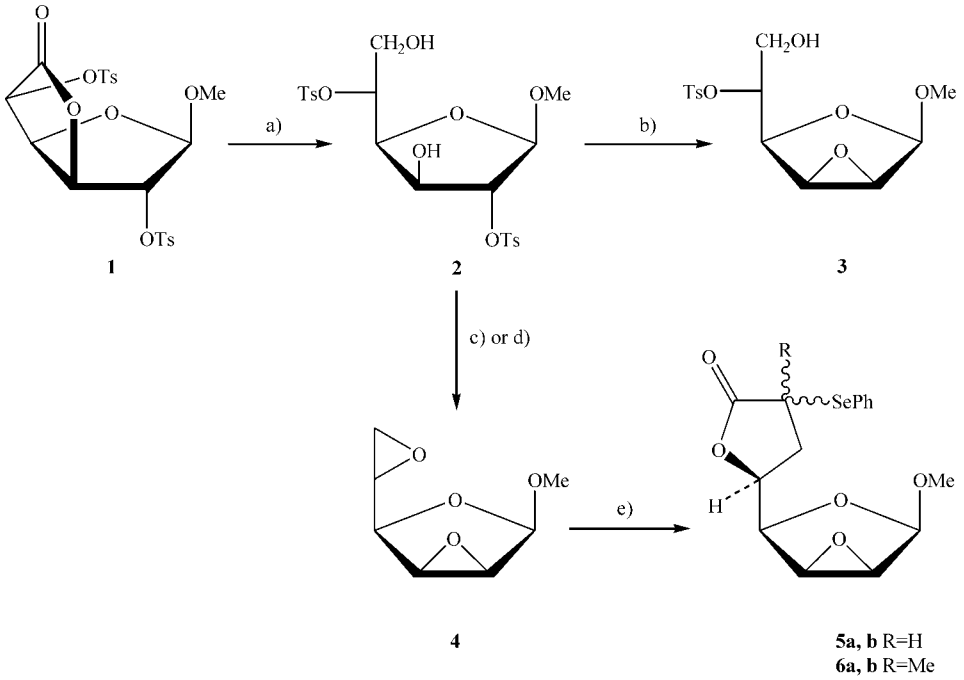
Recently, the sugar phenylseleno lactones **6a**, **b** and analogs to these compounds, their corresponding butenolides, as well as compound **22** have shown efficacy as insecticides with high toxicity to fruit fly (*Drosophila melanogaster*), white fly (*Trialeurodes vaporariorum*), and house fly (*Musca domestica*). The evaluation of the toxicity to fruit flies and house flies was determined by topical treatment, whereas the toxicity to the white fly was investigated by foliar treatment of glasshouse white fly. For fruit flies, the LD_{50} (μg per insect) $= 1.5 \times 10^{-4}$ (**6a**, **b**) and 1.6×10^{-4} (**22**) are interesting results, when compared to $LD_{50} = 1.25 \times 10^{-2}$ of imidacloprid, the reference insecticide for fruit flies. These compounds were not toxic to brine shrimps (*Artemia salina*), the reference organisms in assays to evaluate the potential toxicity hazard to organisms in ecosystems. These tests were performed using the immersion bioassay of brine shrimp larvae in brine.[14]

In this work, we report the synthesis of new epoxides, their phenylseleno sugar derivatives, and new pyranoid compounds, containing an α,β-unsaturated carbonyl moiety. The structural diversity of these compounds will enable a further investigation of the bioactive groups and of the structural units tolerated by the systems, in what concerns the influence of the presence of an oxirane, its orientation and position in the ring, the presence of a phenylselenolactone, or other phenylseleno groups and that of a α,β-unsaturated carbonyl unit in pyranoid structures.

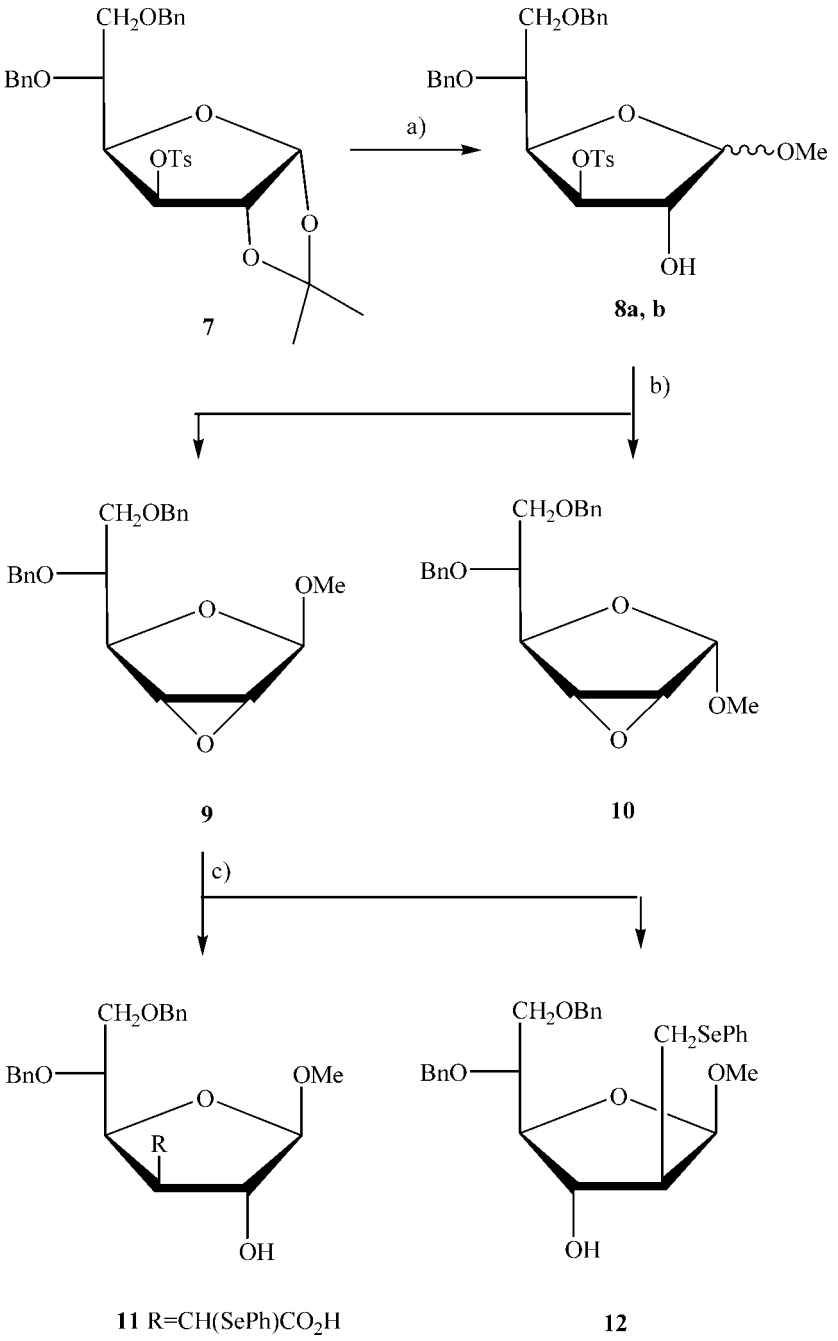
RESULTS AND DISCUSSION

The synthesis of the epimer in C-5 of the diepoxide **4** was accomplished starting from methyl 2,3-anhydro-β-D-mannofuranoside, which after partial tosylation at OH-6 and treatment with sodium methoxide gave the target molecule in 53% yield.[15] We have prepared the diepoxide **4** starting from methyl 2,5-di-*O*-tosyl-β-D-glucofuranoside (**2**),[13] which was obtained by reduction of **1**.[16] Reaction of **2** with potassium hydroxide in THF/H_2O solution at rt for 12 hr gave **4** in 97% yield.[13] In the presence of NaOH/dried methanol at rt,[17] compound **2** gave the epoxide **3** in 51% yield after 30 min, while the diepoxide **4** was formed in 61% yield by changing the reaction time to 1 hr 30 min (Sch. 1).

Reaction of diepoxide **4** with phenylselenoacetic acid or phenylselenopropionic acid/*n*-butyllithium, diisopropylamine in THF at 0°C gave the phenylselenolactones **5a**, **b** and **6a**, **b**[13] in 16% and 32%, yield respectively. The formation of the five-membered lactone in **5** was confirmed by the IR band of its carbonyl group at 1774 cm^{-1}. The presence of the oxirane ring was detected by the chemical shifts of C-2 and C-3 at δ 54.7 and 53.4, respectively, when compared to the corresponding C-2 at δ 83.3 and C-3 at δ 73.5 of the precursor molecule **2**. The bioactivity of the diastereoisomers **5a**, **b** will be investigated, since they are close related analogs to compounds **6a**, **b**, which showed potent insecticidal activity against fruit flies.



Scheme 1. Synthesis of sugar epoxides from methyl 2,5-di-*O*-tosyl-α-D-glucofuranurono-6,3-lactone (**1**):[16] (a) $LiBH_4$, THF, −10°C (1 hr), 14°C (16 hr), 94%;[16] (b) NaOH 4N, THF, rt, 30 min, 51%; (c) NaOH 4N, THF, rt, 1 hr 30 min, 61%; (d) KOH 1.25 N, THF, rt, 12 hr, 97%;[13] (e) LDA, $PhSeCHRCO_2H$, 0°C (1 hr), rt (16 hr), R = H, 16%, R = Me, 32%.

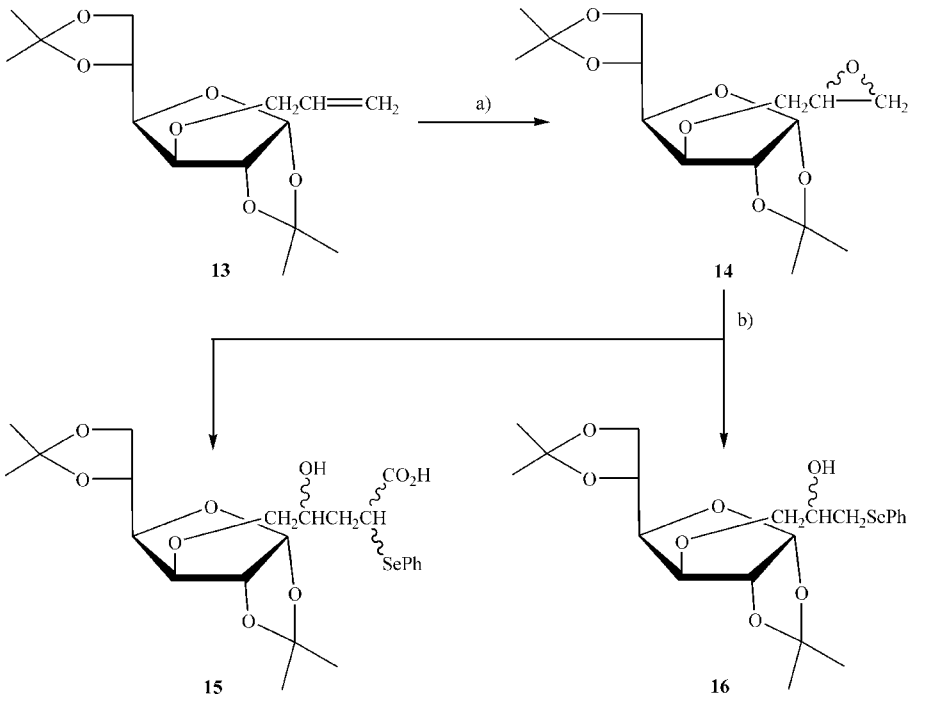


Scheme 2. Phenylseleno derivatives from a sugar epoxide: (a) MeCOCl, MeOH, 60°C, 48 hr, 96%; (b) NaOMe, MeOH, rt, 1 hr, 65% for **9**, 35% for **10**; (c) LDA, $PhSeCH_2CO_2H$, 0°C (1 hr), rt (16 hr), 40% for **11**, 17.5% for **12**, based upon the reacted starting material, recovered in 2.5% yield.

Preparation of 2,3-anhydroallofuranose derivatives was reported in the literature as early as 1976.[18] We report now the synthesis of the allofuranosides **9** and **10** by reaction of the 3-*O*-tosyl derivative **7** with acetyl chloride in methanol to give the 2-hydroxy derivatives **8a**, **b** in 96% yield (Sch. 2), which were treated with sodium methoxide in methanol at rt affording the target molecules **9** and **10** in 65% and 35% yield, respectively. The anomeric configuration of these compounds was established by NOESY, considering the interaction of the methyl group of **9** with H-2, H-3, H-5, H-6a, H-6b, while in compound **10** these interactions were not observed, being detected the interaction of H-1 with H-6a and H-6b.

Treatment of the epoxide **9** with the dianion of phenylselenoacetic acid gave the phenylselenoacid **11** in 40% yield, together with the secondary product **12**, obtained in 16% yield. The presence of the moieties bound to C-3 in **11** and C-2 in **12** was detected by the signal of H-3′ at δ 3.68 with $J_{3,3'} = 6.9$ Hz in **11**, while H-2′a, H-2′b of **12** are included in a multiplet at δ 3.73–3.56, as confirmed by COSY and NOESY experiments. ^{13}C NMR, DEPT, and HMQC spectra allowed to assign the signals corresponding to C-3′ at δ 50.6 in **11** and to C-2′ at δ 30.0 in **12**. The signal of the carbonyl group appeared at δ 167.7 in **11**. Both compounds presented IR bands confirming the presence of hydroxyl groups at 3432 cm^{-1}, while **11** showed the expected band due to the carbonyl group at 1728 cm^{-1}. The formation of secondary products such as **12** was previously reported by Fraser-Reid and Benkö.[19]

When the epoxide **14** (Sch. 3) was treated under the same reaction conditions as the epoxides **4** and **9**, the phenylseleno acid **15** and the secondary product **16** were obtained.

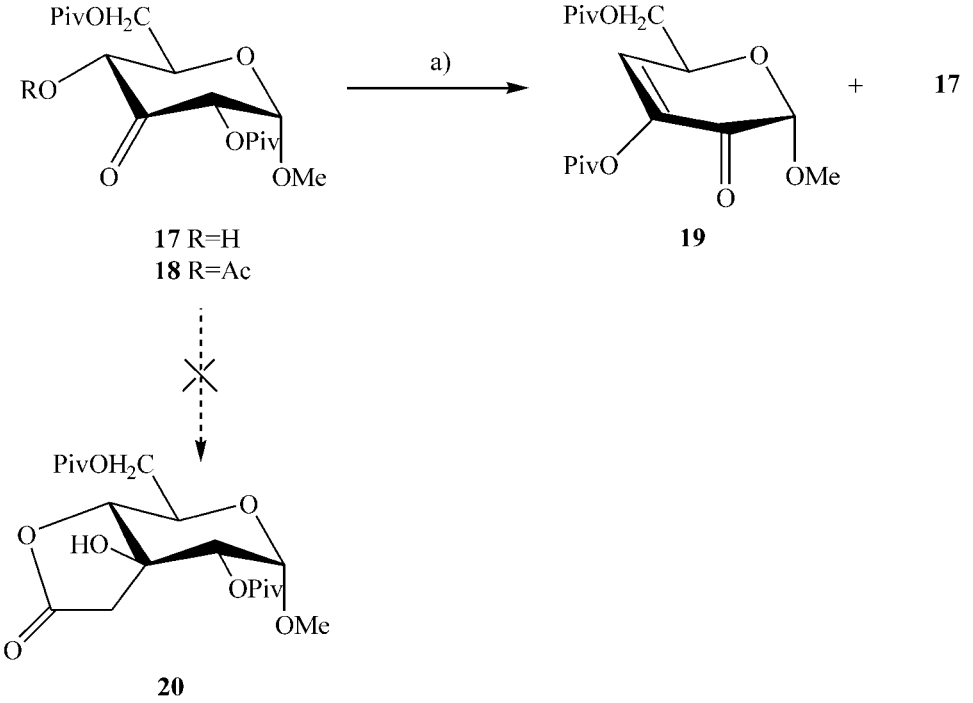


Scheme 3. Synthesis of phenylseleno sugars starting from the 3-*O*-allyl derivative **13**: (a) *m*-CPBA, NaOAc, CH_2Cl_2, rt, 45 hr, 58% based on reacted starting material, recovered in 5% yield; (b) LDA, $PhSeCH_2CO_2H$, 0°C (1 hr), rt (16 hr), 11% for **15**, 25% for **16**.

The synthesis of **14** was first accomplished by phase transfer catalyzed epoxy alkylation of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose with epichlorohydrin.[20] We have synthesized **14** by treatment of 3-*O*-allyl-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (**13**)[21] with *m*-chloroperbenzoic acid in dichloromethane at rt in 58% yield based on reacted starting material, recovered in 5% yield.

We have previously found that α,β-unsaturated five-membered ring lactones bound to sugars demonstrated fungicidal[12] and insecticidal activities.[14] We report now the synthesis of compounds **19** and **22**, which contain an α,β-unsaturated carbonyl group in their structure, in order to be able to evaluate the bioactivity of these pyranoid structures. The synthesis and reactions of sugar enolones were reported in the literature by Lichtenthaler.[22] We describe now the preparation of the keto sugar **19** in 33% yield by treating with the base $(Me_3Si)_2NLi$,[23] the α-acetoxy ketone **18** (Sch. 4), obtained by acetylation of methyl 2,6-di-*O*-pivaloyl-α-D-*ribo*-hexopyranosid-3-ulose.[24]

The expected intramolecular cyclization to give **20** did not occur and deacetylation gave **17** in 67% yield. The mechanism proposed for the synthesis of **19** is based on enolate formation, followed by transesterification to give the pyvaloate at position 3, tautomerism of the enol to the carbonyl compound, and elimination of acetic acid. The presence of the double bond was confirmed by the resonance of H-4 at δ 6.55 as a doublet with $J_{4,5} = 1.5$ Hz, together with ^{13}C NMR signals of C-3 and C-4 at δ 142.2 and 132.1, respectively. Two pivaloyl groups were detected by their resonances at δ 1.24 and 1.25 together with the signals of the corresponding carbonyl groups at δ 178.1



Scheme 4. Synthesis of the α,β-unsaturated keto sugar **19**: (a) $(Me_3Si)_2NLi$, −70°C, 1 hr 30 min, 33% for **19**, 67% for **17.**

and 175.7. H-1 appeared as a singlet at δ 4.89 and the signal of C-2 was assigned at δ 182.4.

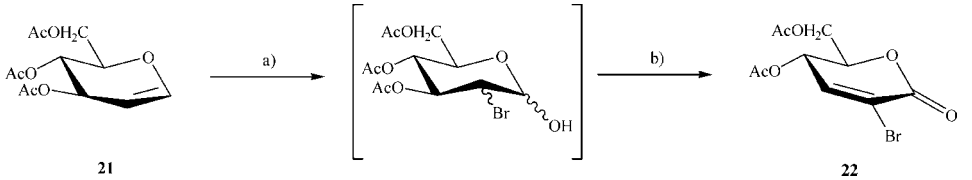
Reaction of the glycal **21** with NBS in THF/H_2O at rt, followed by oxidation of the intermediate 2-bromolactol with PCC in the presence of molecular sieve powder 3 Å, gave the biologically active α,β-unsaturated lactone **22** in 37% overall yield (Sch. 5). The lactone functionality was confirmed by the IR band at 1752 cm^{-1}, and by the signal of its carbonyl group at δ 157.1 in the ^{13}C NMR spectrum. The double bond gave the expected IR band at δ 1632 cm^{-1}. The ^1H NMR and ^{13}C NMR spectra exhibited the olefinic proton H-3 at δ 7.01 as a doublet with $J_{3,4} = 3.9$ Hz and the resonances of C-2 and C-3 at δ 116.4 and 142.3, respectively.

EXPERIMENTAL

General Methods

Reactions were monitored by TLC performed on aluminum sheets Kieselgel 60 F_{254} (Merck) with detection by UV light, than charring with 3% vanillin–sulfuric acid solution. Column chromatography (CC) was conducted under low pressure by elution of columns with silica gel (0.040–0.063 mm Merck). Melting points were determined with a Leica Galen III apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer 343 polarimeter, IR spectra were recorded with a Hitachi 270-50, and UV spectra with a Shimadzu UV-160 TCC-240 spectrophotometer. NMR spectra were carried out in $CDCl_3$ using a Varian Unity 300 MHz spectrometer and ^{13}C NMR spectra were recorded at 75.43 MHz. Chemical shifts are expressed in parts per million downfield from TMS.

Methyl 2,3-anhydro-5-*O*-tosyl-β-D-mannofuranoside (3). A solution of **2**[13] (1.78 g, 3.78 mmol) in THF (22 mL) was cooled to 0°C. Then NaOH 4 N (4.4 mL) was added dropwise and the mixture was stirred at rt for 30 min. Diethyl ether (225 mL) was added and the mixture was washed with water (155 mL). The organic phase was dried over sodium sulfate. Evaporation of the solvent under reduced pressure gave a residue which was purified by CC eluted with ethyl acetate/toluene (1 : 1) to give **3** as a syrup (600 mg, 51%); $[\alpha]_D^{20} = -5^\circ$ (c 1.0, CH_2Cl_2); IR (neat) 3404 cm^{-1} (OH), 1298 cm^{-1} (C-O, epoxide); ^1H NMR: δ 7.84 (d, 2H, Ph), 7.34 (d, 2H, Ph), 4.97 (s, 1H, H-1), 4.68–4.65 (m, 1H, H-5), 4.10 (d, 1H, H-4, $J_{4,5} = 8.0$ Hz), 3.89 (m, 1H, H-6a, $J_{6a,6b} = 11.4$ Hz), 3.78 (m, 1H, H-6b), 3.65, 3.51 (each d, 1H, H-2, H-3, $J_{2,3} = 2.7$ Hz),



Scheme 5. Synthesis of the α,β-unsaturated lactone **22**: (a) NBS, THF/H_2O, rt, 12 hr; (b) PCC, CH_2Cl_2, molecular sieve powder 3 Å, rt, 16 hr, 37% overall yield for (a) and (b).

2.49 (s, 3H, CH_3, Ts); ^{13}C NMR: δ 145.1, (Cq, Ph), 132.9 (Cq, Ph), 129.9, 127.8 (CH, Ph), 102.3 (C-1), 79.6 (C-5), 73.7 (C-4), 61.6 (C-6), 56.8 (OCH_3), 56.1, 54.5 (C-2, C-3), 21.5 (CH_3, Ts).

Anal. Calcd for $C_{14}H_{18}O_7S$ (330.35): C, 50.90; H, 5.49; S, 9.71. Found: C, 51.04; H, 6.00; S, 9.34.

Methyl 2,3:5,6-dianhydro-α-L-gulofuranoside (4). Methyl-2,5-di-*O*-tosyl-β-D-glucofuranoside (**2**) (3.12 g, 6.21 mmol) gave **4** (600 mg, 61%), following the experimental procedure described above for **3**, stirring the reaction mixture at rt for 1 hr 30 min; mp 127–128°C; physical and spectroscopy data were in full agreement with those given in literature.[13]

7(*R*)-, 7(*S*)-2,3-Anhydro-6,7-dideoxy-7-phenylselenyl-α-L-*gulo*-octofuranurono-8,5-lactone (5a, b). *n*-Butyl lithium 1.6 M in hexane (2.75 mL, 4.4 mmol) was added dropwise to a solution of diisopropylamine (0.62 mL, 4.4 mmol) in anhydrous THF (8 mL) at 0°C under argon. The reaction mixture was stirred at 0°C for 25 min. A solution of phenylselenoacetic acid (430 mg, 2 mmol) in anhydrous THF (2 mL) was added dropwise and the reaction mixture was stirred at 0°C for 1 hr. The solution of the diepoxide **4** (316 mg, 2 mmol) in anhydrous THF (1 mL) was dropped to the reaction mixture, which was stirred at 0°C for 1 hr and at rt for 16 hr. After acidification with 50% acetic acid (5 mL), the mixture was heated at 75°C for 6 hr, cooled to rt, neutralized with $NaHCO_3$ saturated solution, and extracted with diethyl ether (3 × 10 mL). The organic phase was washed with water, dried with sodium sulfate and evaporated. The residue was purified by CC with ethyl acetate/*n*-hexane (1 : 2) to give **5a**, **b** as a syrup (113.7 mg, 16%; ratio **5a**/**5b** = 1 : 1); IR (neat) 1774 cm^{-1}; ^1H NMR: δ 7.61–7.50 (m, 2H, Ph), 7.32–7.28 (m, 3H, Ph), 4.99 (s, 1H, H-1), 4.21 (d, 1H, H-4, $J_{4,5}$ = 4.8 Hz), 4.10–4.09 (m, 1H, H-5), 3.74–3.15 (m, 8H, OCH_3, H-6a, H-6b, H-2, H-3, H-7); ^{13}C NMR: δ 176.6 (C=O), 133.4, 129.3, 128.0 (CH, Ph), 102.0 (C-1), 77.1 (C-4), 70.4 (C-5), 59.0 (C-7), 55.8 (OCH_3), 54.7 (C-2), 53.4 (C-3), 27.4 (C-6).

Anal. Calcd for $C_{15}H_{16}O_5Se$ (355.24): C, 50.71; H, 4.54. Found: C, 49.76; H, 4.55.

Methyl 5,6-di-*O*-benzyl-3-*O*-tosyl-α,β-D-glucofuranoside (8a, b). A solution of 5,6-di-*O*-benzyl-1,2-*O*-isopropylidene-3-*O*-tosyl-α-D-glucofuranose (**7**) (600 mg, 1.08 mmol) in MeOH (3.25 mL) and AcCl (0.04 mL) was heated at 60°C and stirred for 30 hr.[25] The reaction mixture was cooled to rt, neutralized with $AgCO_3$, stirred for 2 hr, filtered and concentrated under vacuum. The residue was purified by CC eluted with ethyl acetate/*n*-hexane (1 : 3) to give **8a**, **b** (560 mg, 96%); $[\alpha]_D^{20} = -18°$ (*c* 1.0, $CHCl_3$); IR (neat): 3472 cm^{-1} (OH); ^1H NMR: δ 7.79–7.74 (m, 4H, Ph), 7.32–7.28 (m, 24H, Ph); 4.93–4.91 (m, 4H, H-1α, H-1β, H-3α, H-3β), 4.78–4.30 (m, 8H, 4 OCH_2Ph, H-2α, H-2β, H-4α, H-4β), 3.85–3.80 (m, 4H, H-5α, H-5β, H-6aα, H-6aβ), 3.66 (m, 2H, H-6bα, H-6bβ), 3.43, 3.34 (each s, 3H, OCH_3); 2.37, 2.36 (each s, 3H, CH_3, Ts); ^{13}C NMR: δ 145.0, 138.4 (each Cq, Ph), 129.8, 128.3, 128.2, 127.8, 127.5 (CH, Ph), 109.2 (C-1β); 101.4 (C-1α); 85.2, 83.3 (C-3α, C-3β); 78.9, 78.3 (C-5α, C-5β); 76.3, 76.0 (C-4α, C-4β), 75.4 (C-2α, C-2β), 73.4, 72.0 (OCH_2 Ph), 69.8 (C-6α, C-6β), 55.8 (OCH_3); 21.6 (CH_3, Ts).

Anal. Calcd for $C_{28}H_{32}O_8S$ (528.61): C, 63.62; H, 6.10; S, 6.07. Found: C, 63.19; H, 5.90; S, 5.83.

Methyl 2,3-anhydro-5,6-di-*O*-benzyl-β-D-allofuranoside (9) and methyl 2,3-anhydro-5,6-di-*O*-benzyl-α-D-allofuranoside (10). A solution of **8a**, **b** (940 mg, 1.78 mmol) in NaOMe 1 M in MeOH (28 mL) was stirred at rt for 1 hr. The reaction

mixture was diluted with water (55 mL) and concentrated in a rotary evaporator. The concentrated solution was extracted with $CHCl_3$ and the inorganic phase was dried and evaporated. The residue was purified by CC eluted with ethyl acetate/*n*-hexane (1 : 5) to give **9** (420 mg, 65%) and **10** (230 mg, 35%). Data for **9**: $[\alpha]_D^{20} = -88^\circ$ (*c* 1.0, $CHCl_3$); IR (neat): 1286 cm^{-1} (C–O, epoxide); ^1H NMR: δ 7.34–7.23 (m, 10H, 2Ph), 4.86 (s, 1H, H-1), 4.78, 4.74 (1H, part A of AB system, $J_{A,B} = 12$ Hz, OCH_2Ph), 4.54–4.48 (m, 3H, part B of AB, OCH_2Ph), 4.17 (d, 1H, H-4, $J_{4,5} = 9.3$ Hz), 3.84–3.77 (m, 2H, H-3, H-6a), 3.62-3.53 (m, 3H, H-2, H-5, H-6b), 3.25 (s, 3H, OCH_3); ^{13}C NMR: δ 137.9 (Cq, Ph), 128.0, 127.3, 127.2, 127.1 (CH, Ph), 102.4 (C-1), 78.1 (C-5), 76.5 (C-4), 72.8, 72.0 (OCH_2 Ph), 69.5 (C-6), 55.3 (C-2), 55.4 (OCH_3), 55.0 (C-3).

Anal. Calcd for $C_{21}H_{24}O_5$ (356.41): C, 70.77; H, 6.79. Found: C, 70.89; H, 6.97.

Data for **10**: $[\alpha]_D^{20} = -28^\circ$ (*c* 1.0, $CHCl_3$); IR (neat): 1296 cm^{-1} (C–O, epoxide);^1H NMR: δ 7.33–7.26 (m, 10H, 2Ph), 5.06 (s, 1H, H-1), 4.73, 4.69 (1H, part A of AB system, $J_{A,B} = 12$ Hz, OCH_2Ph), 4.56–4.52 (m, 3H, part B of AB system, OCH_2Ph), 4.37 (d, 1H, H-4, $J_{4,5} = 3.9$ Hz), 3.83 (d, 1H, H-3, $J_{2,3} = 2.7$ Hz), 3.70–3.57 (m, 4H, H-2, H-5, H-6a, H-6b), 3.45 (s, 3H, OCH_3); ^{13}C NMR: δ 137.8, 137.6 (Cq, Ph), 128.2, 127.5, 127.5, 127.4 (CH, Ph), 102.5 (C-1), 78.7 (C-5), 78.7 (C-4), 73.2, 72.4 (OCH_2Ph), 68.7 (C-6), 56.0 (C-2), 56.1 (C-3), 56.5 (OCH_3).

Anal. Calcd for $C_{21}H_{24}O_5$ (356.41): C, 70.77; H, 6.79. Found: C, 70.89; H, 6.97.

2(*R*)-, 2(*S*)-Phenylselenyl-2-(methyl 5,6-di-*O*-benzyl-3-deoxy-β-D-glucofurano-sid-3-yl)ethanoic acid (11) and methyl 5,6-di-*O*-benzyl-2-deoxy-2-*C*-phenylseleno-methyl-β-D-altrofuranoside (12). Starting from **9** (408 mg, 1.14 mmol), the experimental procedure described for **5a**, **b** gave **11** (255 mg, 40%) and **12** (103 mg, 17.5%) based on reacted starting material recovered in 2.5% yield, after purification by CC eluted with ethyl acetate/*n*-hexane 1 : 3. Data for **11**: IR (neat) 3432 cm^{-1} (OH), 1728 cm^{-1} (C=O); ^1H NMR: δ 7.53–7.49 (m, 2H, Ph), 7.33–7.08 (m, 13H, Ph), 4.78–4.74 (m, 2H, H-1′, part A of AB system, OCH_2Ph), 4.64–4.52 (m, 6H, H-2′, H-3′, H-4′, part B of AB system, OCH_2Ph), 4.04–3.92 (m, 2H, H-5′, H-6′a), 3.77 (dd, 1H, H-6′b, $J_{6'a,6'b} = 12.9$ Hz; $J_{5,6'b} = 5.4$ Hz), 3.68 (d, 1H, H-2, $J_{2,3'} = 6.9$ Hz); 3.34 (s, 3H, OCH_3); ^{13}C NMR: δ 167.7 (C=O), 138.3, 138.2 (Cq, Ph), 132.5, 128.9, 128.7, 128.2, 127.9 (CH, Ph), 109 (C-1′), 82.6 (C-4′), 79.8 (C-2′), 78.0 (C-5′, C-3′), 73.3, 71.7 (OCH_2 Ph), 70.1 (C-6′), 55.3 (OCH_3), 50.6 (C-2).

Anal. Calcd for $C_{29}H_{32}O_7Se$ (571.52): C, 60.94; H, 5.63. Found: C, 60.49; H, 6.01.

Data for **12**: IR (neat) 3432 cm^{-1} (OH); ^1H NMR: δ 7.69–7.65 (m, 2H, Ph), 7.34–7.23 (m, 13H, Ph), 4.97 (d, 1H, H-1, $J_{1,2} = 5.7$ Hz), 4.79, 4.75 (part A of AB system, $J_{AB} = 12$ Hz, OCH_2Ph), 4.68–4.58 (m, 4H, H-4 part B of AB system, OCH_2Ph), 3.89–3.79 (m, 2H, H-5, H-6a), 3.73–3.56 (m, 5H, H-6b, H-2, H-2′a, H-2′b, H-3), 3.32 (s, 3H, OCH_3); ^{13}C NMR: δ 138.3, 137.8 (Cq, Ph), 133.5, 129.0, 128.4, 127.7, 127.2 (CH, Ph), 104.9 (C-1), 83.5 (C-5), 80.3 (C-2, C-3), 78.9 (C-4), 73.6, 72.8 (OCH_2 Ph), 70.1 (C-6), 55.3 (OCH_3), 30.0 (C-2′).

Anal. Calcd for $C_{28}H_{32}O_5Se$ (527.51): C, 63.75; H, 6.14. Found: C, 63.51; H, 6.36.

3-*O*-[2′(*S*), 3′-, 2′(*R*), 3′-Anhydropropyl]-1,2:5,6-di-*O*-isopropylidene-α-D-gluco-furanose (14). A solution of **13** (1.07 mg, 3.56 mmol) in CH_2Cl_2 (75 mL) was treated with *m*-CPBA (2.85 g, 16.53 mmol) and sodium acetate (1.36 g, 16.53 mmol). The reaction mixture was stirred at rt for 45 hr. A saturated solution of $NaHCO_3$ was added and the mixture was extracted with CH_2Cl_2.The organic phase was washed with sodium thio-sulfate solution, then with NaCl solution and dried with sodium sulfate. Evaporation of

the solvent gave a residue which was purified by CC with ethyl acetate/toluene (1 : 1) to give **14** (550 mg, 58%, based on reacted starting material, recovered in 5% yield); ratio **14a/14b:** 2 : 1; IR (neat): 1380 cm^{-1} (C–O, isop.), 1262 cm^{-1} (C–O, epoxide); ^{1}H NMR: δ 5.89–5.87 (m, 2H, H-1), 4.60 (d, 1H, H-2, $J_{1,2} = 3.4$ Hz, minor), 4.55 (d, 1H, H-2, $J_{1,2} = 3.6$ Hz, major), 4.31 (m, 2H, H-4), 4.11–4.07 (m, 6H, H-3, H-6a, H-6b), 4.00–3.85 (m, 3H, H-5, H-1′a, minor), 3.88 (dd, 1H, H-1′a, $J_{1'a,\ 2'} = 3.0$ Hz, major), 3.63 (dd, 1H, H-1′b, $J_{1'a,\ 1'b} = 12.0$ Hz, $J_{1'b,2'} = 5.1$ Hz, major), 3.47 (dd, 1H, H-1′b, $J_{1'a,1'b} = 11.4$ Hz; $J_{1'b,2'} = 6.3$ Hz, minor), 3.15 (m, 2H, H-2′), 2.84–2.77 (m, 2H, H-3′a), 2.65–2.61 (m, 2H, H3′b), 1.49 (s, 6H, CH_3, isop.), 1.42 (s, 6H, CH_3, isop.), 1.35 (s, 6H, CH_3, isop.), 1.32 (s, 6H, CH_3, isop.); ^{13}C NMR: δ 111.6 (Cq, isop. 1, 2), 108.8 (Cq, isop. 5, 6), 105.0 (C-1), 82.6 (C-2, major), 82.4 (C-2, minor), 82.3 (C-5), 80.9 (C-3), 72.2 (C-4), 71.8 (C-1′, minor), 70.4 (C-1′, major), 67.1 (C-6), 50.5 (C-2′, minor), 50.3 (C-2′, major), 44.2 (C-3′, minor), 43.8 (C-3′, major), 26.6, 26.0, 25.2 (CH_3, isop.).

Anal. Calcd for $C_{15}H_{24}O_7$ (316.35): C, 56.95; H, 7.65. Found: C, 56.76; H, 7.70.

2(*R*,*S*)-Phenylselenyl-4(*R*,*S*)-hydroxy-5-(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranos-3-oxy)pentanoic acid (15) and 1,2;5,6-di-*O*-isopropylidene-3-*O*-[2′(*S*)-,2′(*R*)-hydroxy-3′-phenylselenyl]propyl-α-D-glucofuranose (16). Starting from **14** (536 mg, 1.7 mM) and following the procedure described for **5a**, **b**, compounds **15** (100 mg, 11%) and **16** (203 mg, 25%) were obtained after purification by CC eluted with ethyl acetate/*n*-hexane (1 : 2); Data for **15**: IR (neat) 3452 cm^{-1} (OH), 1382 cm^{-1} (C–O, isop.), 1736 cm^{-1} (C=O); ^{1}H NMR: δ 7.64–7.60 (m, 4H, Ph), 7.36–7.25 (m, 6H, Ph), 5.92–5.87 (m, 2H, H-1′), 4.54–4.52 (m, 2H, H-2′), 4.31–4.29 (m, 2H, H-4′), 4.17–3.52 (m, 20H, H-3′, H-5′, H-6′a, H-6′b, H-2, H-3a, H-3b, H-4 H-5a, H-5b), 1.53, 1.44 (each s, 12H, 4CH_3, isop.), 1.36, 1.32 (s, 12H, 4CH_3, isop.); ^{13}C NMR: δ ppm ($CDCl_3$): δ 177.6, 173.5 (C=O), 137.3 (Cq, Ph), 135.7, 131.5, 129.1, 128.6, 127.1 (CH, Ph), 112.0, 109.4 (Cq, isop.), 105.6 (C-1′), 84.4 (C-5′), 83.0, 82.5 (C-2′), 81.2 (C-3′), 73.0 (C-4′), 72.4, 70.7 (C-5a, C-5b), 69.2 (C-4), 67.7 (C-6′), 65.2 (C-3), 36.8 (C-2), 26.8, 26.2, 25.1 (CH_3, isop.).

Anal. Calcd for $C_{23}H_{32}O_9Se$ (531.45): C, 51.98; H, 6.06. Found: C, 51.40; H, 6.05.

Data for **16**: IR (neat) 3460 cm^{-1} (OH), 1380 cm^{-1} (C-O, isop.); ^{1}H NMR: δ 7.63–7.47 (m, 4H, Ph), 7.31–7.21 (m, 6H, Ph), 5.88–5.81 (m, 2H, H-1), 4.47 (d, 1H, H-2, $J_{1,2} = 3.6$ Hz), 4.42 (d,1H, H-2, $J_{1,2} = 3.6$ Hz), 4.28–3.80 (m, 16H, H-3, H-4, H-5, H-6a, H-6b, H-1′a, H-1′b, H-2′), 3.06–2.97 (m, 4H, H-3′a, H-3′b), 1.48, 1.43 (each s, 12H, 4CH_3, isop.), 1.42, 1.35 (s, 12H, 4CH_3, isop.); ^{13}C NMR: δ ppm ($CDCl_3$): δ 137.3 (Cq, Ph), 132.6, 129.1, 127.1 (CH, Ph), 111.9 (Cq, isop.), 109.3 (Cq, isop.), 105.6, 105.5 (C-1), 84.3 (C-5), 83.0, 82.4 (C-2), 81.3 (C-3), 74.6, 72.4 (C-1′), 72.8, 72.7 (C-4), 70.2, 69.2 (C-2′), 67.8 (C-6), 30.6, 30.4 (C-3′), 26.8, 26.2, 25.1 (CH_3, isop.).

Anal. Calcd for $C_{21}H_{30}O_7Se$ (473.39): C, 53.28; H, 6.38. Found: C, 53.39; H, 6.70.

Methyl 4-deoxy-3,6-di-*O*-pivaloyl-α-D-*glycero*-hex-3-enepyranosid-2-ulose (19). To a solution of $(Me_3Si)_2NLi$ 1 M in THF (1.43 mL), anhydrous THF (2.4 mL) was added and cooled to −70°C under argon atmosphere. A solution of **18**[24] (240 mg, 0.60 mmol) in THF (38 mL) was slowly added (35 min) and the reaction mixture was stirred at −70°C for 1 hr 30 min. The reaction mixture was then added to HCl 2N (1.9 mL), stirred until reaching the rt and extracted with ethyl acetate. A saturated solution of NaCl was added to the organic phase under stirring. Filtration and concentration of the filtrate gave a residue, which was solved in CH_2Cl_2 and dried with sodium sulfate. Evaporation

of the solvent and purification of the residue by CC eluted with ethyl acetate/toluene (1 : 8) gave **19** (36 mg, 33%) and **17** (80.5 mg, 67%), based on reacted starting material, recovered in 43% yield. The physical and spectroscopic data of **17** were in full agreement with those given in the literature.[19]

Data for **19**: $[\alpha]_D^{20} = +38^\circ$ (*c* 1.0, CH_2Cl_2); IR (neat) 1766 cm^{-1} (C═O), 1726 cm^{-1} (C═O), 1663 cm^{-1} (C═C); ^1H NMR: δ 6.55 (d, 1H, H-4, $J_{4,5} = 1.5$ Hz), 4.94 (td, 1H, H-5), 4.89 (s, 1H, H-1), 4.41 (dd, 1H, H-6a, $J_{5,6a} = 5.7$ Hz, $J_{6a,6b} = 11.7$ Hz), 4.23 (dd, 1H, H-6b, $J_{5,6} = 5.1$ Hz), 3.55 (s, 3H, OCH_3), 1.25 (s, 9H, CH_3, Piv), 1.24 (s, 9H, CH_3, Piv); ^{13}C NMR: δ 182.4 (C-2), 178.1, 175.7 (C═O, Piv), 142.2 (C-3), 132.1 (C-4), 99.1 (C-1), 67.6 (C-5), 64.3 (C-6), 56.9 (OCH_3), 39.0 (Cq, Piv), 27.1 (CH_3, Piv).

Anal. Calcd for $C_{17}H_{26}O_7$ (342.38): C, 59.64; H, 7.65. Found: C, 59.55; H, 7.87.

4,6-Di-*O*-acetyl-2-bromo-2,3-dideoxy-D-*erythro*-hex-2-enono-1,5-lactone (22). NBS (780 mg, 4.88 mmol) was added to a solution of 3,4,6-tri-*O*-acetyl-D-glucal (1 g, 3.67 mmol) in THF (370 mL) and water (92 mL) and the reaction mixture was stirred for 16 hr at rt, then it was poured in ice water, extracted with diethyl ether and the organic phase dried with sodium sulfate. Evaporation of the solvent gave a residue, which was added to a suspension of molecular sieve powder 3 Å (6.8 g) in a solution of PCC (4.37 g, 15.64 mmol). The reaction mixture was stirred at rt for 16 hr. Ethyl ether (100 mL) was added and the mixture stirred for 10 min and filtered. The filtrate was filtered over florisil and evaporated to give (**22**) as a syrup (760 mg, 67%); $[\alpha]_D^{20} = +121^\circ$ (*c* 1.0, CH_2Cl_2); IR (neat) 1752 cm^{-1} (C═O), 1632 cm^{-1} (C═C); ^1H NMR: δ 7.01 (d, 1H, H-3, $J_{3,4} = 3.9$ Hz), 5.30 (dd, 1H, H-4, $J_{4,5} = 6.6$ Hz), 4.194, 4.179, 4.152, 4.138 (H-6a, part of AB system, $J_{6a,6b} = 12.6$ Hz, $J_{5,6a} = 4.5$ Hz), 4.10, 4.08, 4.06, 4.04 (H-6b, part of AB system, $J_{5,6b} = 3.6$ Hz), 1.91 (s, 3H, Ac), 1.85 (s, 3-H, Ac); ^{13}C NMR: δ 170.1, 169.0 (C═O, Ac), 157.1 (C-1), 142.3 (C-3), 116.4 (C-2), 77.7 (C-4), 64.8 (C-5), 61.6 (C-6), 20.4 (CH_3, Ac).

Anal. Calcd for $C_{10}H_{11}BrO_6$ (307.09): C, 39.11; H, 3.61. Found: C, 39.13; H, 3.62.

ACKNOWLEDGMENT

This work was supported by the Treaty of Windsor Programme under the auspice of the British Council and the Ministério da Ciência e do Ensino Superior.

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