Chemistry of the Herbicidins. Reactivity of Silyl Enol Ethers Derived from Simple and Carbohydrate-based Tetrahydropyrans

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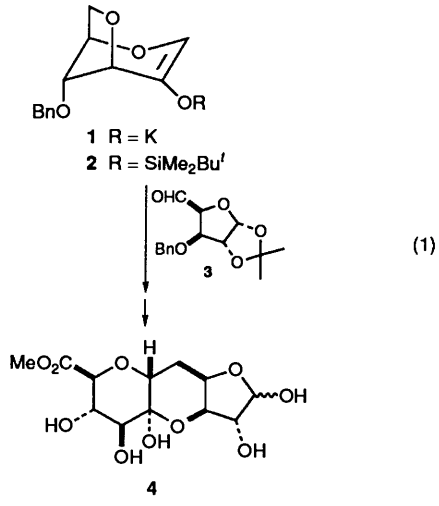
Details are described of preliminary synthetic studies, based on Lewis acid-mediated alkylation of a silyl enol ether, that were directed towards the C_{11} glycoside of the herbicidin class of nucleosides. The chemistry presented focuses on limitations encountered with the reactivity of both the electrophilic and nucleophilic components designed to serve this longer term synthetic objective. α-Chloro sulfide **6** readily undergoes a Lewis acid-promoted internal redox reaction leading to sulfide **8**; this is a consequence of the *O*-benzyl protecting group used at C-3 of chloro sulfide **6**. This pathway is avoided by use of *O*-silyl protection, and reaction of the silyl-protected α-chloro sulfide **11** with the simple heterocyclic silyl enol ether **5** gives the herbicidin models **13a** and **13b** incorporating the required *furano-pyrano-pyran* skeleton. Further experiments showed that the nucleophilic component required for the herbicidins, the carbohydrate-based silyl enol ether **2**, readily underwent Lewis acid-mediated rearrangement to give levoglucosenone **15**.

We recently described the coupling of the regiospecific enolate **1** with aldehyde **3** as the basis of a convergent synthetic approach to the C_{11}-glycoside **4** of the herbicidin class of nucleosides[1] [eqn. (1)]. Although a base-mediated aldol process proved



effective, an alternative aldol or alkylation sequence using a silyl enol ether, such as compound **2**,[2] under Lewis acid-mediated conditions, was also examined. The results of this latter study, together with supporting model work, are described in this paper and serve to highlight problems and limitations associated with both the reactivity of silyl enol ether **2** and electrophilic components related to aldehyde **3** that are of more general relevance to the convergent synthesis of complex carbohydrates.

Results and Discussion

(a) *Limitations on the Structure of the Electrophile.*—Our model studies were based on the simple, regiospecific silyl enol ether **5** which had previously been shown to undergo efficient Lewis acid-mediated coupling to both aldehydes and α-chloro sulfides.[3,4] For our longer term goal, the use of carbohydrate-derived α-chloro sulfides was especially attractive in view of the future manipulations required (see below).‡ The first substrate to be examined was the benzyl-protected furanoside **6**, which was prepared, as a diastereoisomeric mixture, by chlorination of the corresponding sulfide.[6] Under conditions ($ZnBr_2$, CH_2Cl_2, room temp.) that had been found to be successful with simpler α-chloro sulfides, silyl enol ether **5** failed to react with compound **6**. However, use of $TiCl_4$ (at −23 °C) did lead to a reaction but none of the expected adduct **7** was observed. The major product (isolated in 65% yield) was furanoside **8** where chloro sulfide **6** had clearly undergone both reduction at C-5 and loss of the C-3 benzyl residue (Scheme 1). Control experiments established that silyl enol ether **5** played no significant role in the conversion of chloro sulfide **6** into sulfide **8** and examination of the crude reaction mixture (from the process shown in Scheme 1) by ^1H NMR spectroscopy showed the presence of benzaldehyde, which was isolated as its 2,4-dinitrophenylhydrazone derivative (in 35% overall yield).

The above observations are consistent with the mechanism shown in Scheme 2, with Lewis acid activation of chloro sulfide **6** leading to the corresponding sulfonium ion **9**. The *cis* relationship between the two key functional groups at C-3 and C-4 of the furanoside ring — the C-3 *O*-benzyl moiety and the sulfonium ion unit — then permits intramolecular hydride

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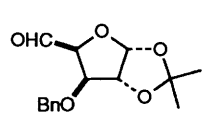
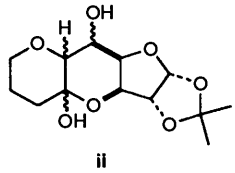
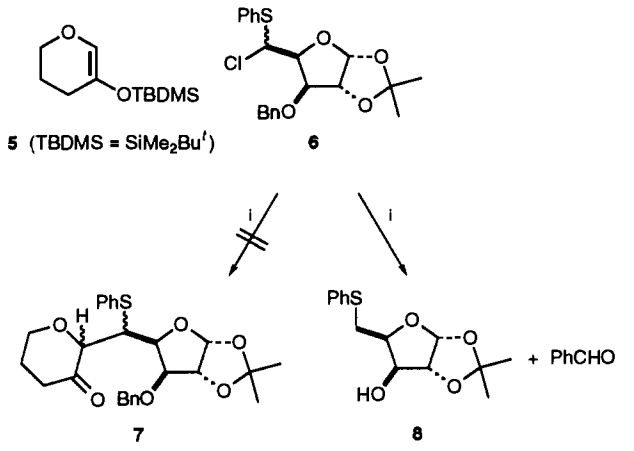
‡ Lewis acid-catalysed aldol reactions of enol ether **5** with aldehyde **i** (≡**3**)[5] have been successfully carried out but problems were encountered in the deoxygenation of the product adducts **ii**.



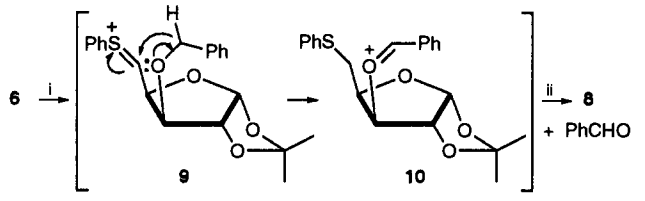
i (≡**3**)



ii



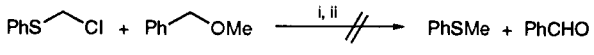
Scheme 1 *Reagents and conditions:* i, $TiCl_4$, CH_2Cl_2, −23 °C; then water



Scheme 2 *Reagents and conditions:* i, $TiCl_4$, CH_2Cl_2, −23 °C; ii, water

transfer to give oxonium ion **10**. This step must also derive a significant driving force as a result of formation of a benzylic oxonium ion. Hydrolytic work-up would then give the observed products, sulfide **8** and benzaldehyde.

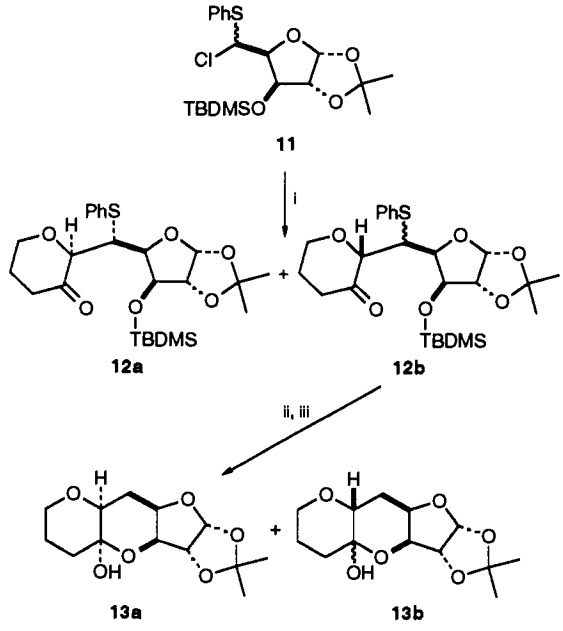
While related hydride transfers are known,*[7] two questions were raised. First, the synthesis of α-chloro sulfide **6**, by reaction of the corresponding sulfide with *N*-chlorosuccinimide (NCS), is expected to proceed *via* sulfonium ion **9**. However, we obtained no evidence for participation of the internal redox illustrated in Scheme 2 during the preparation of compound **6**. This result presumably reflects the reduced nucleophilicity of silyl enol ether **5**, relative to chloride ion, under the conditions used in Scheme 1. The second question raised by the formation of sulfide **8** relates to the nature of the hydride-transfer step itself. While the overall transformation represents an *internal* redox process, the hydride transfer need not be intramolecular in nature. We have, however, been unsuccessful in promoting a related intermolecular reaction: treatment of chloromethyl phenyl sulfide with either $TiCl_4$ or $ZnBr_2$ in the presence of methyl benzyl ether failed to give (by ^1H NMR spectroscopy) methyl phenyl sulfide or benzaldehyde (Scheme 3).



Scheme 3 *Reagents and conditions:* i, $TiCl_4$ or $ZnBr_2$, CH_2Cl_2, −23 °C to room temp.; ii, water

Although more elaborate experiments would be required to establish the intramolecular nature of the hydride-transfer step **9**→**10**, the favourable stereochemical relationship between the two participating centres makes this a likely pathway.

The complications associated with participation of the benzyl group were avoided by use of the silyl-protected α-chloro sulfide **11** (TBDMS = $SiMe_2Bu^t$). Coupling of silyl enol ether **5** to chloro sulfide **11** took place smoothly to give two major adducts **12a/b** in 70% combined yield as a 4:1 ratio of isomers (Scheme 4). Reductive desulfurisation of diastereoisomers **12a** and



Scheme 4 *Reagents and conditions:* i, **5**, $TiCl_4$, CH_2Cl_2, −70 °C; then water; ii, W-2 Raney Ni, EtOH; iii, Bu_4NF, THF

12b followed by desilylation then gave hemiketals **13a** and **13b** incorporating the *furano-pyrano-pyran* skeleton of the herbicidins.

The structures of both compounds **12a** and **13a** were established by X-ray crystallography[3b] but the stereochemistry of the phenylthio group in isomer **12b** has not been assigned. Although the structure of tricycle **13b**, at the epimerisable hemiketal centre (C-7, herbicidin numbering), is also not known with certainty, the data firmly established the viability of the *sequence* of transformations shown in Scheme 4.

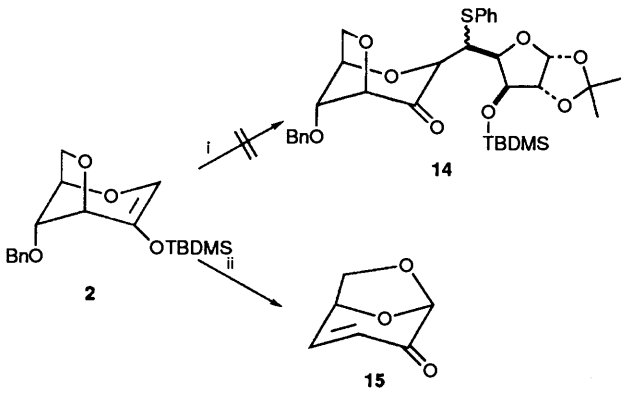
(b) *Reactivity of a Carbohydrate-derived Silyl Enol Ether. Limitation on the Structure of the Nucleophile.*—With the limitations associated with the compatibility of O-protecting groups and α-chloro sulfides/sulfonium ions identified, the silyl-protected electrophile **11** appeared to be a viable substrate for our purposes. The use of a fully substituted carbohydrate-based silyl enol ether, incorporating the functionality required for the herbicidins, was evaluated in order to extend the chemistry of the nucleophilic component. The synthesis of silyl enol ether **2**, readily available from D-mannitol, has already been described.[2] However, reaction of compound **2** with the 'stable' α-chloro sulfide **11** produced an unexpected twist. None of the desired adduct **14** was observed and the only product to be isolated was levoglucosenone **15** (Scheme 5).[8]

Control experiments showed that rearrangement of **2** in the presence of $TiCl_4$ gave levoglucosenone in essentially quantitative yield (by ^1H NMR spectroscopy) and in 40% yield when this rearrangement was carried out using $LiClO_4$ as Lewis acid.†

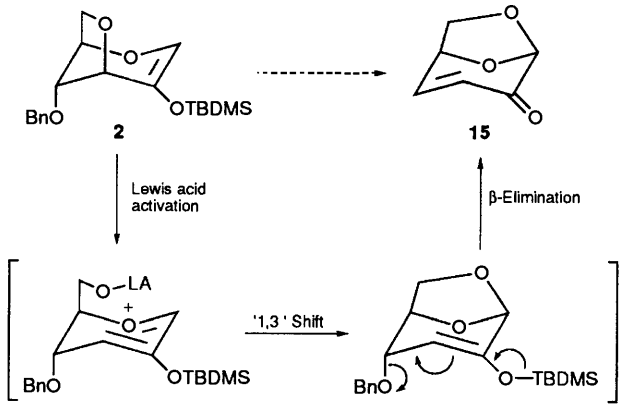
The favourable stereoelectronic arrangement associated with the relatively rigid bicyclic framework in silyl enol ether **2** is presumed to account for the simple nature of this process, which formally involves a three-step process (Scheme 6)—a 1,3-

* Sulfonium ions have also been shown to undergo intermolecular reduction using more conventional hydride reagents, such as $LiAlH_4$.[7b]

† The rearrangement of silyl enol ether **2** to give levoglucosenone **15** was also observed using the following Lewis acids (all reactions carried out in CH_2Cl_2): $TMSOSO_2CF_3$ (−78 °C); $AgOSO_2CF_3$ (−78 °C); $ZnBr_2$ (0 °C); $LiClO_4$[9] (20 °C).



Scheme 5 *Reagents and conditions:* i, **11**, $TiCl_4$, CH_2Cl_2, −70 to −23 °C; then water; ii, as i, but without compound **11**; *or*, $LiClO_4$, CH_2Cl_2, room temp.; then water



Scheme 6

shift, triggered by complexation of enol ether **2** to the Lewis acid, followed by β-elimination of benzyl alcohol.

All attempts to suppress the rearrangement of compound **2** and promote the intermolecular coupling step by pre-activation of chloro sulfide **11** with a selection of Lewis acids failed, and development of this chemistry as an alternative strategy to the herbicidins has been abandoned.

In summary, we have uncovered a number of structural features of both the electrophile and nucleophile that restrict an otherwise very useful coupling methodology. These limitations and undesired modes of reaction are most reasonably accounted for by the rigidity of the molecules involved—the *cis* and nearly coplanar disposition of the two key functional groups in chloro sulfide **6** and the favourable stereoelectronic arrangement associated with silyl enol ether **2**. Such problems, while specific to the tasks that we had undertaken, do, however, merit more general consideration in the design of synthetic strategies involving highly oxygenated molecules.

Experimental

General experimental methods have been described previously.[4] ^1H NMR spectra were all obtained at 270 MHz in $CDCl_3$ solution, and mass spectral data were obtained under electron impact unless otherwise stated, when chemical ionisation (with isobutane as the reagent gas) was employed.

3-O-*Benzyl*-1,2-O-*isopropylidene*-5-S-*phenyl*-5-*thio*-α-D-*xylofuranose*.—To a stirred emulsion of 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU) (218 mg, 1.43 mmol) and thiophenol (158 mg, 1.43 mmol) in dry benzene (5 cm^3) at room temperature, under nitrogen, was added 3-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-5-*o*-(*p*-tolylsulfonyl)-α-D-xylofuranose[10] (622 mg, 1.43 mmol). The resulting mixture was stirred for 12 h, then was diluted with dichloromethane (30 cm^3) and washed successively with hydrochloric acid (2 mol dm^{-3}; 20 cm^3) and saturated aq. sodium hydrogen carbonate (20 cm^3). The organic phase was dried (Na_2SO_4), concentrated, and purification by flash chromatography to give the *title compound* (460 mg, 86%) as a clear oil (Found: M^+, 372.1404. $C_{21}H_{24}O_4S$ requires *M*, 372.1393); ν_{max}(thin film)/cm^{-1} 1570, 1240 and 1200; δ_H 1.29 (3 H, s, Me), 1.42 (3 H, s, Me), 3.24 (2 H, d, *J* 7.5, 5-H_2), 3.99 (1 H, d, *J* 3, 3-H), 4.33 (1 H, td, *J* 7.5 and 3, 4-H), 4.44 (1 H, d, *J* 11.5), 4.59 (1 H, d, *J* 4, 2-H), 4.63 (1 H, d, *J* 11.5), 5.91 (1 H, d, *J* 4, 1-H) and 7.40–7.15 (10 H, m); *m/z* 372 (M^+).

3-O-*Benzyl*-5-*chloro*-1,2-O-*isopropylidene*-5-S-*phenyl*-5-*thio*-α-D-*xylofuranose* **6**.—To a stirred solution of 3-*O*-benzyl-1,2-*O*-isopropylidene-5-*S*-phenyl-5-thio-α-D-xylofuranose (252 mg, 0.68 mmol) in dry tetrachloromethane (1.5 cm^3), under nitrogen, was added NCS (95 mg, 0.7 mmol). The resulting suspension was stirred for 4 h at room temperature, then was filtered and evaporated to give the crude α-chloro sulfide **6** (273 mg, 99%) (as a mixture of diastereoisomers) as a clear yellow oil, which was used without further purification.

3-(O-tert-*Butyldimethylsilyl*)-1,2-O-*isopropylidene*-5-O-(p-*tolylsulfonyl*)-α-D-*xylofuranose*.—To a stirred solution of 1,2-*O*-isopropylidene-5-*O*-(*p*-tolylsulfonyl)-α-D-xylofuranose[10] (1.00 g, 2.9 mmol) and *tert*-butyldimethylsilyl chloride (TBDMSCl) (0.44 g, 2.99 mmol) in dry dichloromethane (25 cm^3) at room temperature was added DBU (0.53 g, 3.5 mmol). The resulting clear solution was stirred at room temperature for 17 h, then was diluted with dichloromethane (20 cm^3) and washed successively with water (40 cm^3), hydrochloric acid (2 mol dm^{-3}; 40 cm^3) and saturated aq. sodium hydrogen carbonate (40 cm^3). The organic phase was dried (Na_2SO_4), evaporated, and purified by flash chromatography to give the *title compound* (1.28 g, 98%) as a clear oil (Found: C, 54.9; H, 7.7. $C_{21}H_{34}O_7SSi$ requires C, 54.99; H, 7.47%); ν_{max}(thin film)/cm^{-1} 1595, 1285 and 1250; δ_H 0.07 (3 H, s), 0.11 (3 H, s), 0.85 (9 H, s), 1.29 (3 H, s), 1.40 (3 H, s), 2.45 (3 H, s), 4.07–4.29 (4 H, m, 3- and 4-H, and 5-H_2), 4.32 (1 H, d, *J* 3.5, 2-H), 5.84 (1 H, d, *J* 3.5, 1-H), 7.34 (2 H, d, *J* 8, part of AA'BB') and 7.80 (2 H, d, *J* 8, part of AA'BB'); *m/z* (CI) 459 (M^+ + H).

3-(O-tert-*Butyldimethylsilyl*)-1,2-O-*isopropylidene*-5-S-*phenyl*-5-*thio*-α-D-*xylofuranose*.—To a stirred emulsion of DBU (178 mg, 1.2 mmol) and thiophenol (129 mg, 1.2 mmol) in dry benzene (5 cm^3) at room temperature was added 3-(*O*-*tert*-butyldimethylsilyl)-1,2-*O*-isopropylidene-5-*O*-(*p*-tolylsulfonyl)-α-D-xylofuranose (535 mg, 1.2 mmol). The resulting mixture was heated at 50 °C for 16 h, then was diluted with dichloromethane (20 cm^3) and washed successively with hydrochloric acid (2 mol dm^{-3}; 15 cm^3) and saturated aq. sodium hydrogen carbonate (15 cm^3). The organic phase was dried (Na_2SO_4), evaporated, and purified by flash chromatography to give the *title compound* (288 mg, 61%) as a clear oil (Found: M^+, 396.1800. $C_{20}H_{32}O_4SSi$ requires *M*, 396.1789); ν_{max}(thin film)/cm^{-1} 1580 and 1290; δ_H 0.16 (3 H, s), 0.17 (3 H, s), 0.91 (9 H, s), 1.30 (3 H, s), 1.40 (3 H, s), 3.10 (1 H, dd, *J* 13 and 10, 5-H), 3.22 (1 H, dd, *J* 13 and 5, 5-H), 4.23–4.29 (2 H, m, 3- and 4-H), 4.38 (1 H, d, *J* 3.5, 2-H), 5.90 (1 H, d, *J* 3.5, 1-H) and 7.16–7.40 (5 H, m); *m/z* 396 (M^+).

3-(O-tert-*Butyldimethylsilyl*)-5-*chloro*-1,2-O-*isopropylidene*-5-S-*phenyl*-5-*thio*-α-D-*xylofuranose* **11**.—To a stirred solution of 3-(*O*-*tert*-butyldimethylsilyl)-1,2-*O*-isopropylidene-5-*S*-phenyl-5-thio-α-D-xylofuranose (422 mg, 1.1 mmol) in dry tetrachloromethane (5 cm^3) was added NCS (186 mg, 1.4 mmol).

The resulting suspension was stirred for 12 h at room temperature, then was filtered and evaporated to give chloro sulfide **11** (468 mg, 99%) (as a mixture of diastereoisomers) as a clear yellow oil, which was used without further purification.

6,10-*Anhydro*-3-O-(tert-*butyldimethylsilyl*)-8,9-*dideoxy*-1,2-O-*isopropylidene*-5-S-*phenyl*-5-*thio*-α-D-glycero-L-ido-*deco-furanos*-7-*ulose* **12a** *and Isomer* **12b**.—To a stirred solution of the crude α-chloro sulfide **11** (542 mg, 1.26 mmol) and silyl enol ether **5** (204 mg, 0.95 mmol) in dichloromethane (5 cm^3) at −78 °C was added $TiCl_4$ (1 mol dm^{-3} in dichloromethane; 1 cm^3, 1 mmol). After 0.5 h the reaction was quenched by rapid addition of saturated aq. sodium hydrogen carbonate (8 cm^3). The resulting emulsion was allowed to warm to room temperature, then was extracted with dichloromethane (4 × 15 cm^3). The combined organic extracts were dried (Na_2SO_4), and purification by flash chromatography gave diastereoisomers **12a** and **12b** (333 mg, 70%) as a 4:1 mixture (by ^1H NMR spectroscopy). Further purification by chromatography gave partial separation and provided the individual components.

Compound **12a** was isolated as crystals, m.p. 128–130 °C (from hexanes) (Found: C, 60.6; H, 7.8. $C_{25}H_{38}O_6SSi$ requires C, 60.69; H, 7.74%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1710; δ_H 0.05 (3 H, s), 0.14 (3 H, s), 0.90 (9 H, br s), 1.30 (3 H, s), 1.47 (3 H, s), 1.90–2.03 (1 H, m, 9-H), 2.26–2.37 (1 H, m, 9-H), 2.44 (1 H, dd, *J* 9 and 7, 8-H), 2.68–2.80 (1 H, m, 8-H), 3.63 (1 H, ddd, *J* 11.5, 10.5 and 4, 10-H^{ax}), 3.98 (1 H, dd, *J* 10.5 and 2, 5-H), 4.04 (1 H, br s, 6-H), 4.10–4.18 (2 H, m including d, *J* 2.5, 10-H^{eq} and 3-H), 4.38 (1 H, d, *J* 3.5, 2-H), 4.43 (1 H, dd, *J* 10.5 and 2.5, 4-H), 5.84 (1 H, d, *J* 3.5, 1-H) and 7.15–7.55 (5 H, m); *m/z* 494 (M^+).

Compound **12b** was isolated as an oil (Found: M^+, 494.2127. $C_{25}H_{38}O_6SSi$ requires *M*, 494.2156); $\nu_{max}(CHCl_3)/cm^{-1}$ 1720; δ_H 0.08 (3 H, s), 0.14 (3 H, s), 0.88 (9 H, s), 1.31 (3 H, s), 1.49 (3 H, s), 1.96–2.07 (1 H, m, 9-H), 2.11–2.29 (1 H, m, 9-H), 2.39–2.51 (1 H, m, 8-H), 2.62–2.72 (1 H, m, 8-H), 3.64 (1 H, td, *J* 11.5 and 3.5, 10-H^{ax}), 3.81 (1 H, dd, *J* 9.5 and 5, 5-H), 3.97 (1 H, d, *J* 5, 6-H), 4.04–4.14 (1 H, m, 10-H^{eq}), 4.17 (1 H, d, *J* 2.5, 3-H), 4.40 (1 H, d, *J* 3.5, 2-H), 4.41 (1 H, dd, *J* 9.5 and 2.5, 4-H), 5.90 (1 H, d, *J* 3.5, 1-H) and 7.19–7.58 (5 H, m); *m/z* 494 (M^+).

6,10-*Anhydro*-5,8,9-*trideoxy*-1,2-O-*isopropylidene*-β-L-glycero-D-gluco-*decofuranos*-7-*ulo*-7,3-*pyranose* **13a**.—A mixture of compound **12a** (88 mg, 0.18 mmol) and freshly prepared W-2 Raney nickel as a suspension in absolute ethanol (2 cm^3) was stirred vigorously for 0.5 h at room temperature. The catalyst was then removed by filtration through Celite and the product was quickly purified by flash chromatography to give the desulfurised product (28 mg, 40%) as an oil, which was used immediately.

The crude product prepared above was dissolved in tetrahydrofuran (THF) (2 cm^3), the solution was cooled to −23 °C and tetrabutylammonium fluoride (1 mol dm^{-3} in THF; 0.08 cm^3, 0.08 mmol) was added. After the mixture had been stirred at −23 °C for 5 min, saturated aq. ammonium chloride (2 cm^3) was added and the mixture was extracted with dichloromethane (4 × 5 cm^3). The combined extracts were dried (Na_2SO_4), and flash chromatography gave *title compound* **13a** (19 mg, 94%) as crystals, m.p. 146–148 °C (from diethyl ether–light petroleum) (Found: M^+, 272.1254. $C_{13}H_{20}O_6$ requires *M*, 272.1254); $\nu_{max}(CHCl_3)/cm^{-1}$ 3380; δ_H 1.33 (3 H, s), 1.49 (3 H, s), 1.45–1.94 (4 H, m, 8- and 9-H_2), 2.12–2.32 (2 H, m, 5-H_2), 3.23–3.33 (2 H, m, 6-H and 10-H^{ax}), 3.98–4.03 (1 H, m, 10-H^{eq}), 4.20 (1 H, quintet, *J* 2.5, 4-H), 4.31 (1 H, d, *J* 2.5, 3-H), 4.57 (1 H, d, *J* 4, 2-H) and 5.98 (1 H, d, *J* 4, 1-H); *m/z* 272 (M^+).

Decofuranos-7-*ulo*-7,3-*pyranose Isomer* **13b**.—By using the same procedure as described for the preparation of compound **13a**, sulfide **12b** (39.3 mg, 0.08 mmol) gave the furo-pyranopyranol **13b** as a viscous oil (6 mg, 25%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3400; δ_H 1.31 (3 H, s), 1.49 (3 H, s), 1.61–2.19 (6 H, m, 5-, 8- and 9-H_2), 3.48 (1 H, td, *J* 12 and 2.5, 10-H^{ax}), 3.52 (1 H, dd, *J* 12, 5, 6-H), 3.98 (1 H, dd, *J* 12 and 5, 10-H^{eq}), 4.30 (1 H, d, *J* 2, 3-H), 4.41 (1 H, dd, *J* 5.5 and 2, 4-H), 4.52 (1 H, d, *J* 4, 2-H) and 5.88 (1 H, d, *J* 4, 1-H); *m/z* (CI) 273 ($M^+ + 1$).

We were unable to obtain satisfactory high-resolution mass data for compound **13b**.

1,2-O-*Isopropylidene*-5-S-*phenyl*-5-*thio*-α-D-*xylofuranose* **8**.—To a stirred solution of the crude α-chloro sulfide **6** (215 mg, 0.53 mmol) in dichloromethane (2 cm^3) at −23 °C, under nitrogen, was added titanium tetrachloride (1 mol dm^{-3} in dichloromethane; 0.53 cm^3, 0.53 mmol). After 15 min at −23 °C, the reaction mixture was quenched by rapidly injecting saturated aq. sodium hydrogen carbonate (1 cm^3) into it. The resulting emulsion was allowed to warm to room temperature, then was extracted with dichloromethane (4 × 2 cm^3), dried (Na_2SO_4), and evaporated to give a clear yellow oil.

To a solution of the above yellow oil in methanol (2 cm^3) was added a solution of 2,4-dinitrophenylhydrazine (250 mg, 1.3 mmol) and conc. sulfuric acid (0.4 cm^3) in methanol (5 cm^3). After 15 min an orange precipitate formed, which was collected by filtration and recrystallised from ethyl acetate to give benzaldehyde 2,4-dinitrophenylhydrazone (50 mg, 35%) as orange needles, m.p. 239–242 °C, mixed m.p. 241–242 °C (lit.,[11] m.p. 237 °C).

Following filtration, the mother liquors were neutralised with saturated aq. sodium hydrogen carbonate and extracted with dichloromethane (4 × 10 cm^3). The extracts were dried (Na_2SO_4), evaporated, and purified by flash chromatography to give *title compound* **8** (97 mg, 65%) as crystals, m.p. 101–103 °C (from EtOAc–hexanes) (Found: C, 59.6; H, 6.5. $C_{14}H_{18}O_4S$ requires C, 59.55; H, 6.42%); ν_{max}(Nujol)/cm^{-1} 3400; δ_H 1.29 (3 H, s), 1.43 (3 H, s), 1.94 (1 H, br s, OH), 3.16 (1 H, dd, *J* 13.5 and 9, 5-H), 3.29 (1 H, dd, *J* 13.5 and 5, 5-H), 4.23–4.33 (2 H, m, 3- and 4-H), 4.51 (1 H, d, *J* 3.5, 2-H), 5.91 (1 H, d, *J* 3.5, 1-H) and 7.19–7.45 (5 H, m); *m/z* 282 (M^+).

Lewis Acid-mediated Rearrangement of Silyl Enol Ether **2**.—To a solution of compound **2**[2] (50 mg, 0.14 mmol) in dichloromethane (1 cm^3) was added anhydrous lithium perchlorate (0.5 mg, 3 mol%). The reaction mixture was stirred overnight at room temperature under nitrogen, then was quenched with saturated aq. sodium hydrogen carbonate. The organic phase was separated, dried (Na_2SO_4), and concentrated under reduced pressure. Purification of the residue by flash chromatography gave levoglucosenone **15** (7.2 mg, 40%) as an oil. The structure of the product was confirmed by direct comparison (TLC, IR, ^1H NMR) with an authentic sample and with data provided in the literature.[8]

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