A New Synthetic Approach to Pseudo-sugars by Asymmetric Diels–Alder Reaction. Synthesis of Optically Pure Pseudo-β-D-mannopyranose, 1-Amino-1-deoxypseudo-α-D-mannopyranose and Pseudo-α-L-mannopyranose Derivatives

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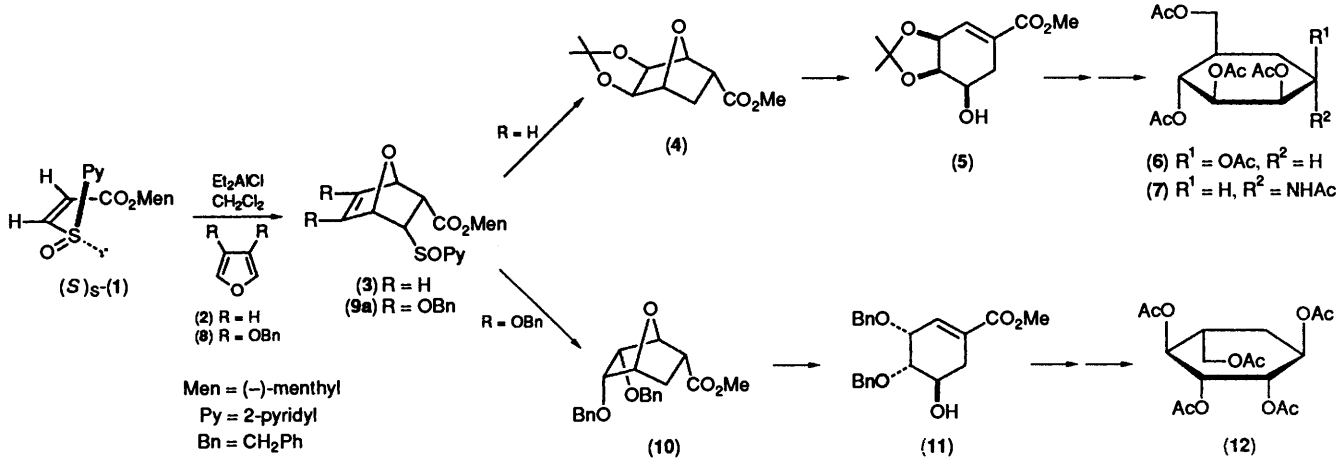
Synthesis of the optically pure title compounds has been achieved. The key features involved (i) construction of 7-*endo*-oxabicyclo[2.2.1]hept-5-ene-2-carboxylates **3** and **9a** by the asymmetric Diels–Alder reaction of $(S)_S$-3-(2-pyridylsulphinyl)acrylate **1** with furans **2** and **8**; (ii) stereoselective introduction of a 5,6-*exo* or -*endo* diol function to give the protected *exo* diol **4** and the protected *endo* diol **10**, respectively; (iii) formation of the shikimate derivatives **5** and **11** by cleavage of the oxide bridge of compounds **4** and **10**; (iv) conversion of compounds **5** and **11** to the pseudo-sugars **6** and **12**, and the pseudo-amino-sugar **7**.

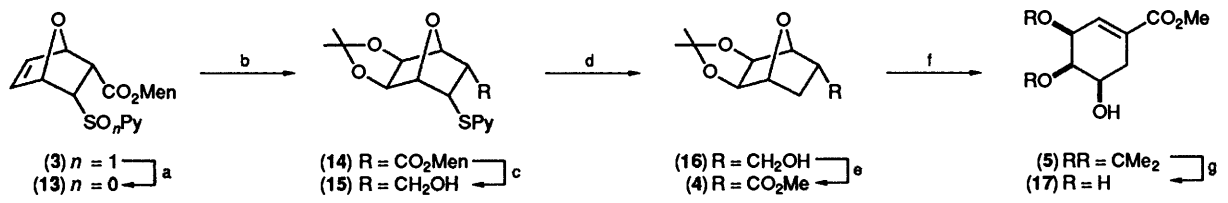
Pseudo-sugars are compounds in which a ring oxygen of a pyranoid sugar is replaced by a methylene group.[1] McCasland and co-workers are the first to synthesize a pseudo-sugar, namely (±)-pseudo-α-talopyranose. Pseudo-sugars have long been expected to be endowed with biological activities, because their structures are closely related to those of the parent sugars. This expectation was borne out when pseudo-α-D-galactopyranose was discovered as a natural antibiotic. Moreover, some pseudo-sugars and related compounds have been found to be components of some antibiotics. Interestingly, it has been demonstrated that (±)-pseudo-β-glucopyranose is as sweet as D-glucose[1] and that the α-anomer is effective in inhibiting both glucose-stimulated insulin release and islet glucokinase activity.[2] From these initial results, much attention has been focussed on the synthesis of enantiomeric pseudo-sugars. Suami and co-workers started their synthesis with (−)-7-*endo*-oxabicyclo[2.2.1]hept-5-ene-2-carboxylic acid, which was obtained by optical resolution of the racemate.[1] Other approaches relied on the use of natural carbohydrate precursors.[1,3,4] There has so far been no report on asymmetric synthesis of pseudo-sugars. We thus designed a synthetic route to these chemicals, involving an asymmetric Diels–Alder (D–A) reaction.

We have demonstrated that the asymmetric D–A reaction of $(S)_S$-3-(2-pyridylsulphinyl)acrylate **1** with furan **2** gave (−)-7-*endo*-oxabicyclo[2.2.1]hex-5-ene-2-carboxylate **3** with high diastereoselectivity (Scheme 1).[5] The cycloadduct **3**, of which the absolute stereochemistry has been determined as depicted in Scheme 1,[5] has been shown to be a valuable starting material for the chiral synthesis of D-showdomycin and D-anhydroallose derivatives.[6] This novel asymmetric reaction provides us with a powerful tool for the chiral synthesis of various kinds of polyoxygenated cyclohexane derivatives. Our approach to the chiral synthesis of pseudo-sugars by means of the asymmetric D–A reaction of **1** as a key step is outlined in Scheme 1. For stereoselective introduction of a 3,4-*cis* diol function of shikimic acid to the 7-oxabicyclo[2.2.1]heptene system, we chose furan **2** and 3,4-dibenzyloxyfuran **8** as dienes. Because of their bicyclic structure, the C=C bond of the D–A adducts **3** and **9a** is expected to react preferentially *via* its *exo* face,[7] thus ensuring good selectivity. *syn*-Hydroxylation of compound **3** and hydrogenation of compound **9a** give the protected *exo-cis* diol **4** and the protected *endo-cis* diol **10**, respectively. The diol derivatives **4** and **10** are transformed into the pseudo-sugars **6** and **12** *via* the shikimate derivatives **5** and **11**. Moreover, selective introduction of an amino group at C-5 of compound **5** gave the amino-sugar **7**. In our preliminary communications,[5,8,9] we have demonstrated an asymmetric synthesis of compounds **3** and **9a**, and further transformation of these into (−)-*epi*-shikimate **5** and (−)-shikimate **11**, respectively.

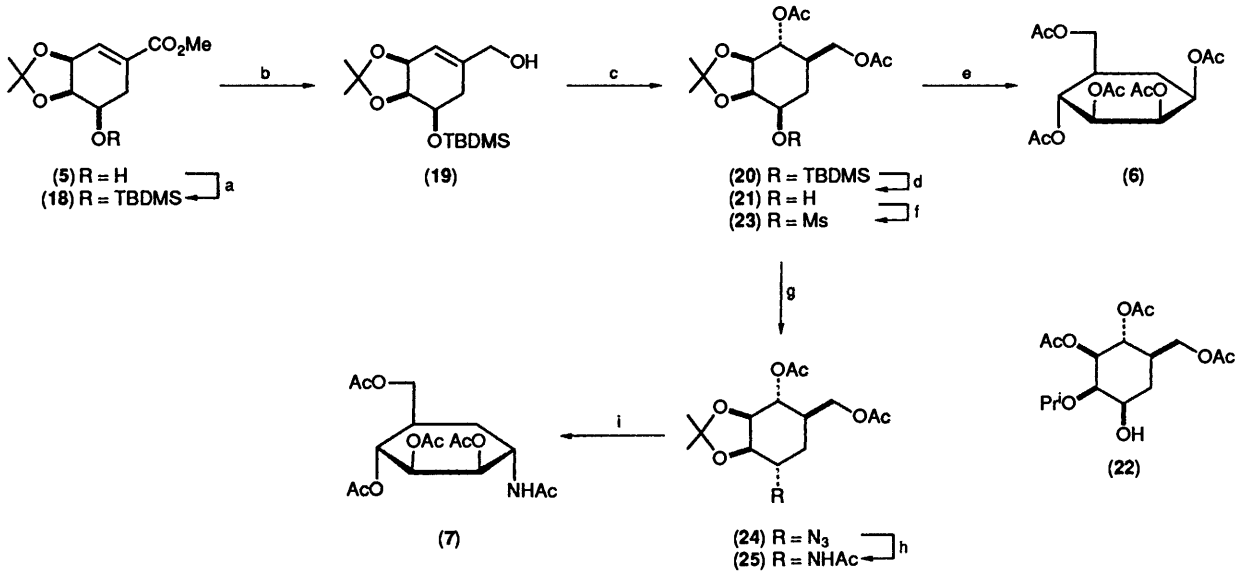
In this paper we describe, in detail, a chiral synthesis of penta-



Scheme 1.



Scheme 2. *Reagents and conditions:* a, $TiCl_3$, EtOH; b, Me_3NO, OsO_4, acetone; $Me_2C(OMe)_2$, TsOH, acetone, 65 °C; c, $LiAlH_4$, Et_2O; d, Raney-Ni (W-4), EtOH; e, Jones reagent, acetone; CH_2N_2, MeOH–Et_2O; f, $LiN(TMS)_2$, THF, −78 °C; g, aq. AcOH, 55 °C.



Scheme 3. *Reagents and conditions:* a, TBDMSOTf, Et_3N, CH_2Cl_2; b, $LiAlH_4$, THF, −18 °C; c, BH_3–THF; H_2O_2, OH^-; Ac_2O, py; d, Bu_4NF, THF; e, aq. AcOH, 55 °C; Ac_2O, py; f, MsCl, Et_3N, CH_2Cl_2, 0 °C; g, Bu_4NN_3, PhH, 80 °C; h, H_2, 3.4 atm, Raney-Ni (T-4), Ac_2O, EtOH; i, aq. AcOH, 60 °C; Ac_2O, py.

acetylpseudo-β-D-mannopyranose **6**, penta-acetyl-1-amino-1-deoxypseudo-α-D-mannopyranose **7**, and penta-acetylpseudo-α-L-mannopyranose **12** using an asymmetric D–A reaction of the sulphinylacrylate **1** *via* the shikimate derivatives **5** and **11**.

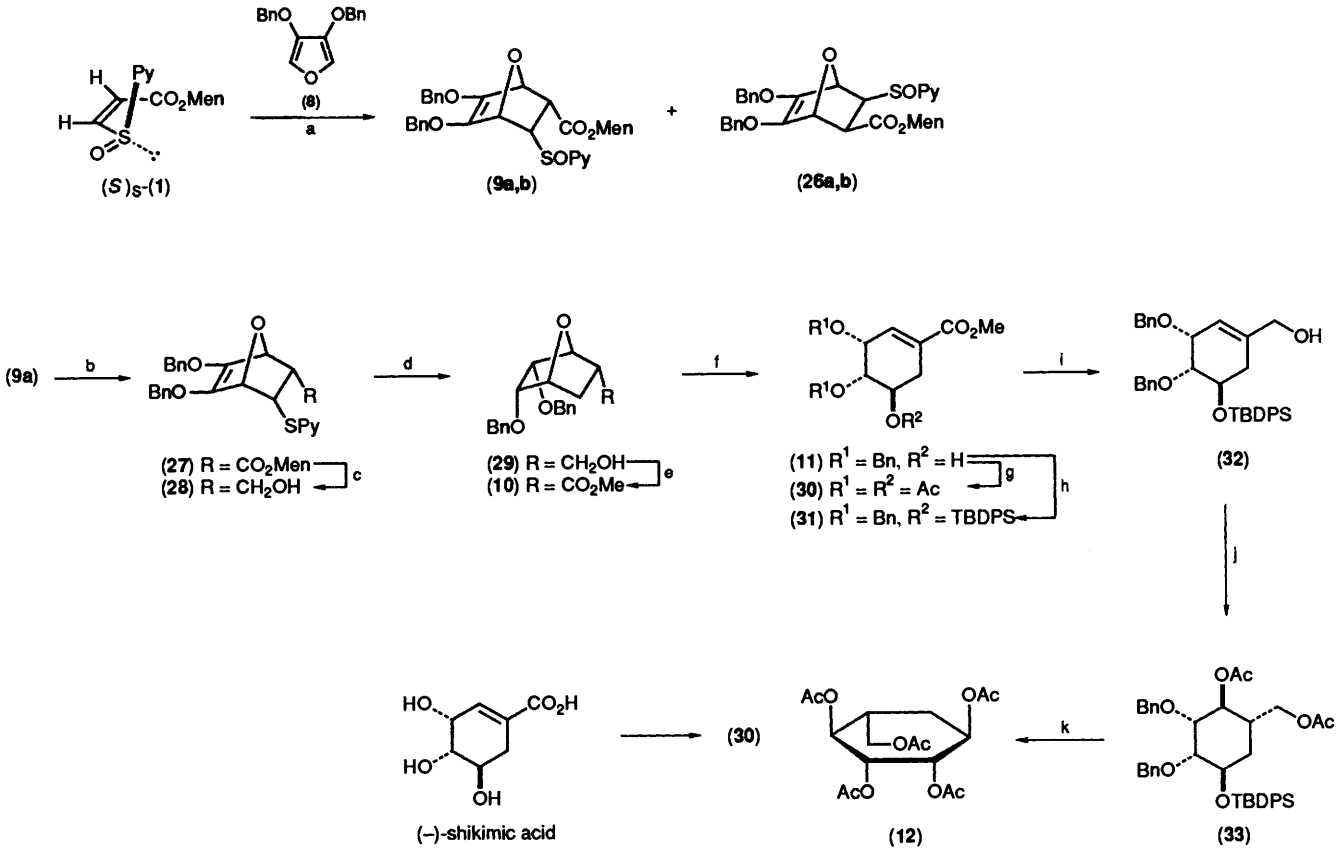
Results and Discussion

Synthesis of Pseudo-β-D-mannopyranose Penta-acetate **6** *and 1-Amino-1-deoxypseudo-α-D-mannopyranose Penta-acetate* **7**.—(−)-Methyl 5-*epi*-shikimate derivative **5** was prepared from the optically pure *endo* cycloadduct **3** in 26% overall yield as reported previously[9] (Scheme 2). The adduct **3** was reduced with $TiCl_3$ to give the sulphide **13**. *syn*-Hydroxylation of compound **13** with a catalytic amount of OsO_4 and successive protection of the two hydroxy groups afforded the desired *exo* acetonide **14**. Reduction of the ester group of compound **14** and desulphurisation of intermediate **15** gave the primary alcohol **16**, which was transformed into the methyl ester **4**. Following the procedure of Campbell,[10] ester **4** was converted into the *epi*-shikimate **5**. The enantiomeric excess (ee) was shown to be no less than 96% as determined by NMR spectroscopy.[9] The structure of compound **5** was further confirmed by transformation into (+)-5-*epi*-shikimate **17**. The spectral data of (−)-**5** and (+)-**17** were consistent with those of the racemic authentic compounds.[10]

The *epi*-shikimate **5** was transformed into pseudo-β-D-mannopyranose penta-acetate **6** as described in Scheme 3. Treatment of compound **5** with t-butyldimethylsilyl trifluoromethanesulphonate (TBDMSOTf)[11] gave the TBDMS ether **18** in 92% yield. The unsaturated ester **18** was converted into the allyl alcohol **19** by careful reduction with $LiAlH_4$ in tetrahydrofuran (THF) at −18 °C in 72% yield. For the introduction of a hydroxy group at C-2 in compound **19**, hydroboration was investigated. Thus treatment of compound **19** with BH_3–THF complex in THF and successive oxidation with H_2O_2, followed by acetylation,[3] gave an inseparable mixture (6:1) of a fully protected pseudo-β-D-mannopyranose **20** and 2,3-diacetoxy-1-(acetoxymethyl)-5-(t-butyldimethylsiloxy)-4-isopropoxycyclohexane (TBDMS ether of **22**). Hydroboration proceeded stereoselectively from the less hindered side, and opposite to the three protected hydroxy groups. The product ratio was dependent on reaction time and/or amounts of BH_3–THF complex. After desilylation of the mixture with Bu_4NF,[12] the resulting alcohol **21** was separated from 3,4-diacetoxy-5-(acetoxymethyl)-2-isopropoxycyclohexanol **22** in 53% yield (from the alcohol **19**). The ee of compound **21** was shown to be no less than 96% by 270 MHz NMR spectroscopy using a chiral shift reagent, Eu(hfc)$_3$.* Deprotection of compound **21** and subsequent acetylation afforded pseudo-β-D-mannopyranose penta-acetate **6** in 78% yield. The spectral data of compound (+)-**6** were consistent with those of an authentic sample.[13] The optical rotation value of **6** {$[\alpha]_D$ +2.53° (*c* 1.67 in $CHCl_3$)} coincided with that of the reported penta-acetate of pseudo-β-D-mannopyranose.

We then turned our attention to a chiral synthesis

* In the ^1H NMR spectrum, the acetonide methyl groups of (±)-**21** were resolved into a pair of singlets at δ 1.80 and 1.87 on using a chiral shift reagent, Eu(hfc)$_3$ (0.133 mol equiv.). By similar treatment, the spectrum of (−)-**21** showed the methyl signal at δ 1.87 and the corresponding enantiomer was not observed within the limit of detection (<2%).



Scheme 4. *Reagents and conditions:* a, Et_2AlCl, CH_2Cl_2, −20 °C; b, PBr_3, DMF, 0 °C; c, $LiAlH_4$, Et_2O; d, Raney-Ni (W-2), EtOH; e, Jones reagent, acetone; CH_2N_2, MeOH–Et_2O; f, $LiN(TMS)_2$, THF, −78 °C; g, TMSCl–NaI, MeCN; Ac_2O, py; h, TBDPSCl, imidazole, DMF; i, DIBAL-H, Et_2O, 0 °C; j, BH_3–THF; H_2O_2, OH^-; Ac_2O, py; k, Bu_4NF, THF; H_2, Pd/C, EtOH; Ac_2O, py.

of the pseudo-amino-sugar **7**. The best procedure for installing a nitrogen atom at C-1 involved activation of the hydroxy group of compound **21** as its corresponding mesyl ester **23** and successive azidation with Bu_4NN_3. Owing to its instability, the triflate of compound **21** could not be transformed into the azide **24**. The mesyl ester **23** reacted with Bu_4NN_3[14] in boiling benzene to afford a mixture (3:1) of the azide **24** and an unidentified compound. The product ratio was dependent on the reagents used, being 1:1 when the reaction was performed with LiN_3 or NaN_3 in hexamethylphosphoric triamide (HMPA) at 120 °C. The ^1H NMR spectrum of the azide **24** clearly showed inversion of configuration at C-1. The mixture (3:1) of the azide **24** and the unidentified compound was hydrogenated with Raney nickel T-4 in EtOH containing Ac_2O[15] to give the acetamide **25** in 52% yield from compound **23**. Deprotection and subsequent acetylation of the acetamide **25** furnished 1-amino-1-deoxypseudo-α-D-mannopyranose penta-acetate **7** in 83% yield. The spectral data of the product **7** were consistent with those of the racemic authentic compound.[15]

Synthesis of Pseudo-α-L-mannopyranose Penta-acetate **12**.—Our attempts were then focussed on a chiral synthesis of pseudo-α-L-mannopyranose derivative **12**, which has the unnatural L-absolute configuration, *via* the shikimate **11**. The D–A reaction of $(S)_S$-**1** with 3,4-dibenzyloxyfuran **8** in the presence of Et_2AlCl at −20 °C for 5 days gave the *endo* and *exo* cycloadducts **9** and **26** in 50 and 29% yield, respectively[8] (Scheme 4). The *endo* or *exo* stereochemistry of the products **9** and **26** was deduced by analogy with that of the *endo* and *exo* cycloadducts from $(S)_S$-**1** and furan **2**.[5] The absolute configuration of the major *endo* adduct **9a** and the major *exo* adduct **26a** was determined as shown in Scheme 4 based on our proposal in the cycloaddition of chiral sulphinylethenes.[16] The diastereoselectivity (ds) was calculated to be no less than 92% for compound **9** and 94% for compound **26** by NMR spectroscopy. The major *endo* adduct **9a** was reduced with PBr_3 in dimethylformamide (DMF)[17] to give the sulphide **27** in 84% yield. Treatment of sulphide **27** with $LiAlH_4$ afforded the primary alcohol (**28**) in 95% yield. Desulphenylation and hydrogenation of the 5,6-double bond were performed by reaction of compound **28** with Raney nickel W-2 to give the desired *endo-cis* dibenzyloxy derivative **29** in 45% yield. Oxidation of compound **29** with Jones reagent and successive treatment with CH_2N_2 furnished the methyl ester **10** in 67% yield. Ring opening of compound **10** by lithium hexamethyldisilazide (LHMDS) gave the unsaturated ester **11** in 56% yield. The structure of compound **11** was confirmed by its conversion into (−)-methyl triacetylshikimate **30**. Debenzylation with trimethylsilyl chloride (TMSCl)–NaI[18] and subsequent acetylation gave the triacetate **30**, $[\alpha]_D$ −162.2° (*c* 0.30, MeOH) {lit.,[19] $[\alpha]_D$ −168° (*c* 0.9, MeOH)}, in 53% yield. The spectral data of the synthetic triacetate **30** were identical with those of an authentic sample, $[\alpha]_D$ −161.7° (*c* 0.64, MeOH), prepared from natural (−)-shikimic acid.

A similar reaction sequence for the conversion of ester **5** into pseudo-sugar **6** was employed for the transformation of the shikimate **11** to pseudo-α-L-mannopyranose penta-acetate **12**. Protection of the hydroxy group of compound **11** was performed with t-butyldiphenylsilyl chloride (TBDPSCl) and imidazole in DMF to give the TBDPS ether **31** in 79% yield. Treatment of the ester **31** with diisobutylaluminium hydride (DIBAL-H) in Et_2O afforded the alcohol **32** in 88% yield. The allyl alcohol **32** was converted into a fully protected pseudo-α-L-mannopyranose **33** by hydroboration–oxidation and successive acetylation in 73% yield. The other possible isomer, a derivative of pseudo-β-D-

allopyranose, could not be detected in the reaction mixture. Hydroboration proceeded stereoselectively from the less hindered side of compound **32**. The mannopyranose derivative **33** was desilylated with Bu_4NF and debenzylated by catalytic hydrogenation. The resulting triol was acetylated to give pseudo-α-L-mannopyranose penta-acetate **12**, $[\alpha]_D$ −35.2° (*c* 0.56, $CHCl_3$) {lit.,[3] $[\alpha]_D$ −38.5° (*c* 1.04, $CHCl_3$)}, in 71% yield. The spectral data of compound **12** were consistent with those of an authentic sample.[3] According to the procedure developed in the synthesis of the pseudo-amino-sugar **7** from the TBDMS ether **20**, the TBDPS ether **33** may possibly be transformed into 1-amino-1-deoxypseudo-β-L-mannopyranose.

Thus, the first enantioselective preparation of pseudo-sugars by asymmetric synthesis has been achieved by employing the asymmetric D–A reaction of $(S)_S$-3-(2-pyridylsulphinyl)acrylate **1** with furans **2** and **8**. The most interesting feature of this method is that both the natural and the unnatural enantiomers of a target compound can, in principle, be synthesized by choosing $(S)_S$ or $(R)_S$ dienophile or by choosing the *endo* or *exo* cycloadduct. Studies along this line are now in progress in this laboratory.

Experimental

M.p.s were measured with a Yanaco melting point apparatus and are uncorrected. Spectroscopic measurements were performed with the following instruments: IR, JASCO A-102; ^1H NMR, JEOL JNM-GX 270 (270 MHz) for solutions in $CDCl_3$ with Me_4Si as internal standard; mass, JEOL JMS-D 200; optical rotations, JASCO DIP-140 digital polarimeter. Column chromatography and preparative TLC (PLC) were performed on Kieselgel 60 (Merck, Art. 9385 and Art. 7748, respectively).

(3S,4S,5R)-*Methyl* 5-(*t-Butyldimethylsiloxy*)-3,4-(*isopropylidenedioxy*)*cyclohex*-1-*ene*-1-*carboxylate* **18**.—TBDMSOTf[11] (50 μl, 0.22 mmol) was added dropwise to a solution of the alcohol **5**[9] (50 mg, 0.22 mmol) and triethylamine (46 μl, 0.33 mmol) in dry CH_2Cl_2 (4 ml) under nitrogen at 0 °C. The reaction mixture was stirred at room temperature for 2 h. The CH_2Cl_2 phase was washed with saturated aq. $NaHCO_3$ (0.5 ml). The aqueous layer was extracted with CH_2Cl_2 (4 ml × 3). The combined organic layer was washed with brine, dried ($MgSO_4$), and the solvent was evaporated off. The residue was chromatographed on silica gel [eluant hexane–AcOEt (3:1)] to give *compound* **18** as a syrup (69 mg, 92%) (Found: M^+ − Me, 327.1598. $C_{16}H_{27}O_5Si$ requires *m/z*, 327.1626); $[\alpha]_D^{26}$ −39.5° (*c* 1.73, $CHCl_3$); ν_{max}(neat) 1720 cm^{-1} (CO); δ_H 0.13 (6 H, s, $SiMe_2$), 0.92 (9 H, s, Bu^t), 1.35 (3 H, s, Me), 1.39 (3 H, s, Me), 2.48 (1 H, dddd, *J* 2.4, 2.7, 9.7, 16.8 Hz, 6β-H), 2.56 (1 H, ddd, *J* 0.9, 6.0, 16.8 Hz, 6α-H), 3.77 (3 H, s, OMe), 3.92 (1 H, ddd, *J* 2.2, 6.0, 9.7 Hz, 5-H), 4.35 (1 H, ddd, *J* 0.9, 1.0, 5.1 Hz, 4-H), 4.67 (1 H, m, 3-H) and 6.67 (1 H, m, 2-H); *m/z* 327 (M^+ − Me).

(3S,4S,5R)-5-(*t-Butyldimethylsiloxy*)-3,4-(*isopropylidenedioxy*)*cyclohex*-1-*enylmethanol* **19**.—$LiAlH_4$ (516 mg, 13.6 mmol) was added to a solution of the ester **18** (3.101 g, 9.07 mmol) in dry THF (20 ml) at −18 °C and the reaction mixture was stirred under argon at −18 °C for 25 min before being quenched with saturated aq. Na_2SO_4 (5 ml) at the same temperature. After 10 min at −18 °C, the precipitate was filtered off and washed with acetone. The combined organic layer was concentrated. The residue was purified by flash column chromatography on silica gel [eluant hexane–AcOEt (2:1)] to give the *alcohol* **19** (2.051 g, 72%) as an oil (Found: M^+ − Me, 299.1705. $C_{15}H_{27}O_4Si$ requires *m/z*, 299.1679); $[\alpha]_D^{24}$ −8.13° (*c* 1.37, $CHCl_3$); ν_{max}(neat) 3450 cm^{-1} (OH); δ_H 0.12 (6 H, s, $SiMe_2$), 0.92 (9 H, s, Bu^t), 1.38 (6 H, s, 2 × Me), 2.06 (1 H, dd, *J* 5.4, 15.9 Hz, 6α-H), 2.40 (1 H, dd, *J* 10.5, 15.9 Hz, 6β-H), 3.94 (1 H, ddd, *J* 2.2, 5.4, 10.5 Hz, 5-H), 4.04 (2 H, br s, CH_2OH), 4.31 (1 H, ddd, *J* 1.0, 5.4, 5.4 Hz, 4-H), 4.61 (1 H, m, 3-H) and 5.55 (1 H, br s, 2-H); *m/z* 299 (M^+ − Me).

(1R,2R,3S,4S,5R)-2-*Acetoxy*-1-(*acetoxymethyl*)-5-(*t-butyldimethylsiloxy*)-3,4-(*isopropylidenedioxy*)*cyclohexane* **20**.—A 1.0M solution of BH_3–THF complex in THF (18.2 ml, 18.2 mmol) was added dropwise to a solution of the allyl alcohol **19** (1.91 g, 6.08 mmol) in dry THF (30 ml) under nitrogen at 0 °C. The reaction mixture was stirred at room temperature for 3 h and quenched with water. 3M-Aq. NaOH (28.4 ml, 85.1 mmol) and then 30% aq. H_2O_2 (31.1 ml, 0.304 mol) were added to the reaction mixture at 0 °C. After being stirred at room temperature for 4 h, the reaction mixture was concentrated. The residue was extracted with Et_2O (200 ml × 3) and CH_2Cl_2 (200 ml × 3). The combined extracts were washed with brine, dried ($MgSO_4$) and the solvent was evaporated off. The residue was acetylated with pyridine (15 ml) and Ac_2O (15 ml) at room temperature. After the solvent was evaporated off, the residue was dissolved in CH_2Cl_2 (20 ml). The CH_2Cl_2 phase was washed successively with saturated aq. $NaHCO_3$ (40 ml) and brine. The aq. layer was extracted with CH_2Cl_2 (100 ml × 2) and the combined extracts were dried ($MgSO_4$) and the solvent was evaporated off. The residue was purified by flash column chromatography on silica gel [eluant hexane–AcOEt (1:1)] to give a mixture (1.891 g) (6:1, estimated by integration of the ^1H NMR spectrum) of the title compound **20** (calculated yield 63%) and 2,3-diacetoxy-1-(acetoxymethyl)-5-(t-butyldimethylsiloxy)-4-isopropoxycyclohexane (the TBDMS ether of **22**) as an oil; ν_{max}(neat) 1740 cm^{-1} (CO); for compound **20**: δ_H 0.12 (6 H, s, $SiMe_2$), 0.92 (9 H, s, Bu^t), 1.36 (3 H, s, Me), 1.59 (3 H, s, Me), 1.7–2.1 (3 H, m, 1-H, 6-H_2), 2.04 (3 H, s, Ac), 2.08 (3 H, s, Ac), 3.93 (1 H, dd, *J* 3.9, 10.9 Hz, *H*CHOAc), 4.00 (1 H, dd, *J* 4.9, 7.8 Hz, 3-H), 4.02 (1 H, dd, *J* 5.1, 10.9 Hz, HC*H*OAc), 3.95–4.05 (1 H, m, 5-H), 4.24 (1 H, dd, *J* 4.2, 4.3 Hz, 4-H) and 5.07 (1 H, dd, *J* 7.8, 10.5 Hz, 2-H).

(1R,2R,3S,4R,5R)-4-*Acetoxy*-5-(*acetoxymethyl*)-2,3-(*isopropylidenedioxy*)*cyclohexanol* **21**.—A 1.0M solution of Bu_4NF in THF (19.0 ml, 19.0 mmol) was added dropwise to a solution of the mixture of compound **20** and the TBDMS ether of compound **22** (6:1) (1.891 g) in dry THF (20 ml) under nitrogen at 0 °C. The reaction mixture was stirred at room temperature and the solvent was evaporated off. The residue was dissolved in $CHCl_3$ (20 ml) and the solution was washed with brine (5 ml). The aq. layer was extracted with $CHCl_3$ (50 ml × 3). The combined extracts were dried ($MgSO_4$) and the solvent was evaporated off. The residue was purified by flash column chromatography on silica gel [eluant hexane–AcOEt (1:1)] to give the *alcohol* **21** (980 mg, 53% from compound **19**) as an oil, and 3,4-*diacetoxy*-5-(*acetoxymethyl*)-2-*isopropoxycyclohexanol* **22** (96 mg, 5% from compound **19**) as an oil.

For *compound* **21** (Found: M^+, 302.1347. $C_{14}H_{22}O_7$ requires *M*, 302.1364); $[\alpha]_D^{24}$ −24.5° (*c* 0.56, $CHCl_3$); ν_{max}(neat) 3480 (OH) and 1740 cm^{-1} (CO); δ_H 1.38 (3 H, s, Me), 1.60 (3 H, s, Me), 1.69 (1 H, ddd, *J* 11.0, 11.5, 12.0 Hz, 6β-H), 1.83 (1 H, m, 5-H), 1.95 (1 H, m, 6α-H), 2.05 (3 H, s, Ac), 2.08 (3 H, s, Ac), 3.95 (1 H, dd, *J* 5.9, 11.0 Hz, *H*CHOAc), 4.04 (1 H, dd, *J* 4.4, 11.0 Hz, HC*H*OAc), 3.95–4.10 (1 H, m, 1-H), 4.10 (1 H, dd, *J* 5.4, 7.3 Hz, 3-H), 4.38 (1 H, dd, *J* 4.3, 4.4 Hz, 2-H) and 5.06 (1 H, dd, *J* 7.3, 10.0 Hz, 4-H); *m/z* 302 (M^+).

For *compound* **22** (Found: M^+, 346.1642. $C_{16}H_{26}O_8$ requires *M*, 346.1627); $[\alpha]_D^{26}$ −32.1° (*c* 0.10, $CHCl_3$); ν_{max}($CHCl_3$) 3500 (OH) and 1740 cm^{-1} (CO); δ_H 1.19 (3 H, d, *J* 6.1 Hz, *Me*CH), 1.28 (3 H, d, *J* 6.1 Hz, *Me*CH), 1.59–1.96 (3 H, m, 5-H, 6-H_2), 2.05 (3 H, s, Ac), 2.08 (6 H, s, 2 × Ac), 3.68–3.83 (1 H, m, 1-H), 3.77 (1 H, septet, *J* 6.1 Hz, Me_2CH), 3.93 (1 H, dd,

J 2.2, 2.4 Hz, 2-H), 3.98 (1 H, dd, *J* 4.1, 11.2 Hz, *H*CHOAc), 4.05 (1 H, dd, *J* 5.9, 11.2 Hz, HC*H*OAc), 4.84 (1 H, dd, *J* 2.5, 10.3 Hz, 3-H) and 5.27 (1 H, dd, *J* 10.3, 10.3 Hz, 4-H); *m/z* 346 (M^+).

(1R,2R,3S,4R,5R)-1,2,3,4-*Tetra-acetoxy*-5-(*acetoxymethyl*)-*cyclohexane* (*Pseudo*-β-D-*mannopyranose Penta-acetate*) **6**.—A solution of the alcohol **21** (43 mg, 0.14 mmol) in 50% aq. AcOH (1 ml) was heated at 55 °C for 3 h. After the solvent was evaporated off, the residue was acetylated with pyridine (1 ml) and Ac_2O (1 ml) at room temperature overnight. After usual work-up, the residue was purified by PLC [hexane–AcOEt (1:1)] to give the penta-acetate **6** (43 mg, 78%) as a syrup. Crystallisation from EtOH–Et_2O gave scales, m.p. 119 °C (lit.,[13] 119 °C) (Found: C, 52.8; H, 6.3. Calc. for $C_{17}H_{24}O_{10}$: C, 52.56; H, 6.23%); $[\alpha]_D^{26}$ +2.53° (*c* 1.67, $CHCl_3$) {lit.,[13] $[\alpha]_D^{20}$ + 2.9° (*c* 1.28, $CHCl_3$)}; ν_{max}($CHCl_3$) 1735 cm^{-1} (CO); δ_H(C_6D_6) 1.34–1.47 (1 H, m, 5-H), 1.64–1.78 (1 H, m, 6α-H), 1.64 (3 H, s, Ac), 1.68 (3 H, s, Ac), 1.70 (6 H, s, 2 × Ac), 1.71 (3 H, s, Ac), 1.87 (1 H, dd, *J* 12.5, 12.6 Hz, 6β-H), 3.76 (1 H, dd, *J* 3.4, 11.5 Hz, *H*CHOAc), 4.07 (1 H, dd, *J* 5.4, 11.5 Hz, HC*H*OAc), 4.76 (1 H, ddd, *J* 2.7, 4.9, 12.2 Hz, 1-H), 5.03 (1 H, dd, *J* 2.9, 10.3 Hz, 3-H), 5.46 (1 H, dd, *J* 10.5, 10.8 Hz, 4-H) and 5.86 (1 H, m, 2-H); *m/z* 389 (M^+ + 1), 346 (M^+ + 1 − Ac), 330 (M^+ + 1 − AcO) and 329 (M^+ − AcO).

(1R,2R,3S,4S,5R)-2-*Acetoxy*-1-(*acetoxymethyl*)-3,4-*isopropylidenedioxy*)-5-(*methylsulphonyloxy*)*cyclohexane* **23**.—Triethylamine (0.382 ml, 2.20 mmol) and MsCl (0.170 ml, 2.20 mmol) were added to a solution of the alcohol **21** (552 mg, 1.83 mmol) in dry CH_2Cl_2 (20 ml) under nitrogen at 0 °C. After the reaction mixture had been stirred at 0 °C for 5 h, cold water was added and the organic layer was separated. The aq. layer was extracted with CH_2Cl_2 (30 ml × 3). The combined extracts were washed with brine, dried ($MgSO_4$) and the solvent was evaporated off. The residue was purified by column chromatography on silica gel [eluant hexane–AcOEt (2:1)] to give the *triester* **23** (584 mg, 84%) as crystals, m.p. 126–127 °C (from AcOEt) (Found: C, 47.25; H, 6.4. Calc. for $C_{15}H_{24}O_9S$: C, 47.35; H, 6.36%); $[\alpha]_D^{25}$ −9.1° (*c* 1.00, $CHCl_3$); ν_{max}($CHCl_3$) 1740 (CO), 1360, 1335 and 1170 cm^{-1} (SO_2); δ_H 1.39 (3 H, s, Me), 1.61 (3 H, s, Me), 1.93 (1 H, m, 1-H), 2.01–2.13 (2 H, m, 6-H_2), 2.06 (3 H, s, Ac), 2.09 (3 H, s, Ac), 3.12 (3 H, s, OSO_2Me), 3.96 (1 H, dd, *J* 4.2, 11.2 Hz, *H*CHOAc), 4.05 (1 H, dd, *J* 5.9, 11.2 Hz, HC*H*OAc), 4.14 (1 H, dd, *J* 5.1, 7.1 Hz, 3-H), 4.54 (1 H, dd, *J* 3.9, 4.2 Hz, 4-H), 4.99 (1 H, ddd, *J* 3.9, 5.4, 11.1 Hz, 5-H) and 5.05 (1 H, dd, *J* 7.0, 9.9 Hz, 2-H); *m/z* 365 (M^+ − Me).

(1R,2R,3S,4R,5S)-2-*Acetoxy*-1-(*acetoxymethyl*)-5-*azido*-3,4-(*isopropylidenedioxy*)*cyclohexane* **24**.—Bu_4NN_3 (4.12 g, 14.5 mmol) was added to a solution of the mesyl ester **23** (550 mg, 1.45 mmol) in dry benzene (40 ml) and the reaction mixture was refluxed for 22 h under nitrogen. After the solvent was evaporated off, CH_2Cl_2 (40 ml) was added to the residue and the solution was washed with water (10 ml). The aq. phase was extracted with CH_2Cl_2 (40 ml × 2). The combined extracts were washed with brine, dried ($MgSO_4$) and the solvent was evaporated off. The residue was chromatographed on silica gel [eluant hexane–AcOEt (2:1)] to give a mixture (203 mg) of the azide **24** and an unknown compound (3:1, estimated by integration of the ^1H NMR spectrum). A part of the mixture was subjected to PLC [CH_2Cl_2–CCl_4 (10:1)] to give an analytical sample of *azide* **24** as a syrup (Found: M^+ − Me, 312.1187. $C_{13}H_{18}N_3O_6$ requires *m/z* 312.1194); $[\alpha]_D^{26}$ −19.0° (*c* 0.83, $CHCl_3$); ν_{max}($CHCl_3$) 2100 (N_3) and 1740 cm^{-1} (CO); δ_H 1.37 (3 H, s, Me), 1.55 (3 H, s, Me), 1.87–2.16 (3 H, m, 1-H, 6-H_2), 2.06 (3 H, s, Ac), 2.09 (3 H, s, Ac), 3.96 (1 H, dd, *J* 4.2, 11.5 Hz, *H*CHOAc), 4.04–4.17 (1 H, m, 5-H), 4.07 (1 H, dd, *J* 6.1, 11.5 Hz, HC*H*OAc), 4.11 (1 H, dd, *J* 5.5, 6.8 Hz, 3-H), 4.15 (1 H, dd, *J* 3.4, 5.5 Hz, 4-H) and 5.03 (1 H, dd, *J* 6.8, 10.5 Hz, 2-H); *m/z* 312 (M^+ − Me).

(1S,2R,3S,4R,5R)-1-*Acetamido*-4-*acetoxy*-5-(*acetoxy methyl*)-2,3-(*isopropylidenedioxy*)*cyclohexane* **25**.—A solution of the mixture of compound **24** and the unknown compound (3:1) (203 mg) in EtOH (20 ml), Ac_2O (0.5 ml) and Raney nickel T-4[20] (20 mg) was hydrogenated (3.4 atm starting pressure of hydrogen gas) at room temperature overnight in a Parr hydrogenation apparatus. The catalyst was removed by filtration and the filtrate was concentrated. CH_2Cl_2 (20 ml) was added to the residue and the solution was washed with saturated aq. $NaHCO_3$ (2 ml). The aq. layer was extracted with CH_2Cl_2 (30 ml × 3). The combined organic layer was washed with brine, dried ($MgSO_4$) and the solvent was evaporated off. The residue was purified by flash column chromatography on silica gel [eluant $CHCl_3$–MeOH (10:1)] to give the *amide* **25** (185 mg, 52% from **23**) as an oil. Crystallisation from AcOEt gave prisms, m.p. 160–161 °C (Found: C, 55.9; H, 7.3; N, 4.05. Calc. for $C_{16}H_{25}NO_7$: C, 55.95; H, 7.34; N, 4.08%); $[\alpha]_D^{26}$ −23.1° (*c* 0.93, $CHCl_3$) ν_{max}($CHCl_3$) 3300 (NH), 1 740 (CO) and 1650 cm^{-1} (CO); δ_H 1.34 (3 H, s, Me), 1.53 (3 H, s, Me), 1.7–2.1 (3 H, m, 1-H, 6-H_2), 2.02 (3 H, s, Ac), 2.07 (3 H, s, Ac), 2.10 (3 H, s, Ac), 4.00 (5 H, dd, *J* 4.9, 11.1 Hz, *H*CHOAc), 4.09 (1 H, dd, *J* 5.6, 10.3 Hz, HC*H*OAc), 4.12 (1 H, dd, *J* 5.8, 6.1 Hz, 3-H), 4.16 (1 H, dd, *J* 4.5, 5.4 Hz, 2-H), 4.36 (1 H, m, 1-H), 5.09 (1 H, dd, *J* 6.4, 9.0 Hz, 4-H) and 5.61 (1 H, d, *J* 7.6 Hz, NH); *m/z* 343 (M^+).

(1S,2R,3S,4R,5R)-1-*Acetamido*-5-(*acetoxymethyl*)-2,3,4-*triacetoxycyclohexane* (1-*Amino*-1-*deoxypseudo*-α-D-*mannopyranose Penta-acetate*) **7**.—A solution of the acetonide **25** (162 mg, 0.472 mmol) in 50% aq. AcOH (5 ml) was heated at 60 °C for 3 h. A small amount of pyridine was added to the reaction mixture and the solvent was evaporated off under reduced pressure. The residue was acetylated with Ac_2O (1 ml) and dry pyridine (1 ml) at room temperature overnight. The excess of reagents was evaporated off to give a yellow-brown oil (223 mg). The oil was chromatographed on silica gel (eluant AcOEt) to give *compound* **7** (151 mg, 83%) as a syrup (Found: M^+, 387.1483. $C_{17}H_{25}NO_9$ requires *M*, 387.1528); $[\alpha]_D^{26}$ +11.1° (*c* 1.45, $CHCl_3$); ν_{max}($CHCl_3$) 3400, 3300 (NH_2), 1730 (CO) and 1660 cm^{-1} (CO); δ_H 1.8–2.1 (3 H, m, 5-H, 6-H_2), 2.01 (3 H, s, Ac), 2.03 (3 H, s, Ac), 2.06 (3 H, s, Ac), 2.08 (3 H, s, Ac), 2.11 (3 H, s, Ac), 4.08 (1 H, dd, *J* 5.4, 11.2 Hz, *H*CHOAc), 4.14 (1 H, dd, *J* 6.1, 11.2 Hz, HC*H*OAc), 4.28 (1 H, m, 1-H), 5.11 (1 H, dd, *J* 2.7, 7.8 Hz, 3-H), 5.17 (1 H, dd, *J* 7.8, 8.1 Hz, 4-H), 5.27 (1 H, dd, *J* 2.7, 5.4 Hz, 2-H) and 5.89 (1 H, d, *J* 7.8 Hz, NH); *m/z* 387 (M^+), 328 (M^+ − OAc) and 327 (M^+ − AcOH).

Menthyl (1S,2R,3S,4S)-5,6-*Dibenzyloxy*-3-[(*S*)$_S$-2-*pyridylsulphinyl*]-7-*oxabicyclo*[2.2.1]*hept*-5-*ene*-2-*carboxylate* **9a**.—A 1.0M-solution of Et_2AlCl in hexane (0.11 ml, 0.11 mmol) was added dropwise to a solution of menthyl (*Z*)-3-[(*S*)$_S$-2-pyridylsulphinyl]acrylate **1**[5] (33.9 mg, 0.101 mmol) and 3,4-dibenzyloxyfuran **8**[21] (85.2 mg, 0.304 mmol) in dry CH_2Cl_2 (0.5 ml) under nitrogen at −20 °C. After 5 days at −20 °C, the reaction mixture was diluted with CH_2Cl_2 (3 ml). The pH was brought to 7 by addition of saturated aq. $NaHCO_3$ at 0 °C. The precipitate was filtered off and washed with CH_2Cl_2. The filtrate was separated and the aq. layer was extracted with CH_2Cl_2 (5 ml × 3). The combined CH_2Cl_2 phase was washed with brine, dried ($MgSO_4$) and the solvent was evaporated off. The residue was subjected to PLC [AcOEt–hexane (2:1)] to give compound **9a** (29.6 mg, 48%) and a mixture (19.0 mg, 31%) of compounds **9b**, **26a** and **26b** (6:91:3, estimated by integration of the ^1H NMR spectra). The starting dienophile **1** (5.2 mg, 15%) was recovered.

For *compound* **9a** (Found: M^+ − $C_{18}H_{25}NO_3S$, 280.1060. $C_{18}H_{16}O_3$ requires *m/z*, 280.1098); $[\alpha]_D^{24}$ +93.1° (*c* 1.00,

$CHCl_3$); $\nu_{max}(CHCl_3)$ 1728 (CO), 1685 (C=C) and 1025 cm^{-1} (SO); δ_H 0.45 (3 H, d, *J* 6.8 Hz, Me), 0.76 (3 H, d, *J* 6.8 Hz, Me), 0.83 (3 H, d, *J* 6.4 Hz, Me), 0.71–0.80 (9 H, m, 3 × CH_2, 3 × CH), 3.57 (1 H, dd, *J* 4.3, 8.4 Hz, 2-H), 4.20 (1 H, dd, *J* 3.8, 8.4 Hz, 3-H), 4.41 (1 H, ddd, *J* 4.2, 10.8, 10.8 Hz, 1′-H), 4.88 (1 H, dd, *J* 1.5, 4.3 Hz, 1-H), 4.92 (1 H, d, *J* 11.5 Hz, PhC*H*H), 4.97 (1 H, d, *J*, 12.0 Hz, PhC*H*H), 5.18 (1 H, d, *J* 12.0 Hz, PhCH*H*), 5.23 (1 H, d, *J* 11.5 Hz, PhCH*H*), 5.30 (1 H, dd, *J* 1.5, 3.8 Hz, 4-H), 7.25–7.44 (11 H, m, 11 × ArH), 7.85 (1 H, ddd, *J* 1.7, 7.7, 7.8 Hz, ArH), 7.95 (1 H, ddd, *J* 1.0, 1.1, 7.8 Hz, ArH) and 8.95 (1 H, ddd, *J* 1.0, 1.7, 4.9 Hz, ArH); *m/z* 335 (M^+ − 3,4-dibenzyloxyfuran) and 280 (3,4-dibenzyloxyfuran).

For *compound* **26a**: $[\alpha]_D^{26}$ −19.6° (*c* 1.06, $CHCl_3$); $\nu_{max}(CHCl_3)$ 1728 (CO), 1683 (C=C) and 1011 cm^{-1} (SO); δ_H 0.77 (3 H, d, *J* 6.8 Hz, Me), 0.87 (3 H, d, *J* 6.8 Hz, Me), 0.89 (3 H, d, *J* 7.6 Hz, Me), 0.59–2.05 (9 H, m, 3 × CH_2, 3 × CH), 3.02 (1 H, d, *J* 8.5 Hz, 2-H), 3.71 (1 H, d, *J* 8.5 Hz, 3-H), 4.67 (2 H, s, PhCH_2), 4.71 (1 H, ddd, *J* 4.2, 11.0, 11.0 Hz, 1′-H), 4.90 (1 H, d, *J* 11.7 Hz, PhC*H*H), 4.96 (1 H, d, *J* 11.7 Hz, PhCH*H*), 4.96 (1 H, d, *J* 1.2 Hz, 1-H), 5.18 (1 H, d, *J* 1.2 Hz, 4-H), 7.15–7.41 (11 H, m, 11 × ArH), 7.91 (1 H, ddd, *J* 1.2, 7.8, 7.8 Hz, ArH), 8.03 (1 H, d, *J* 7.8 Hz, ArH) and 8.62 (1 H, dd, *J* 1.2, 3.9 Hz, ArH); *m/z* 280 (3,4-dibenzyloxyfuran).

The structure of compound **26a** was confirmed by transformation into the corresponding sulphide (an oil) according to the procedure for the preparation of the sulphide **27** (*vide infra*) (Found: C, 72.2; H, 7.1; N, 2.6. Calc. for $C_{36}H_{41}NO_5S$: C, 72.09; H, 6.89; N, 2.34%); $[\alpha]_D^{25}$ −5.4° (*c* 0.95, $CHCl_3$); $\nu_{max}(CHCl_3)$ 1720 (CO) and 1687 cm^{-1} (C=C); δ_H 0.67–2.05 (9 H, m, 3 × CH_2, 3 × CH), 0.75 (3 H, d, *J* 6.7 Hz, Me), 0.83 (3 H, d, *J* 6.7 Hz, Me), 0.88 (3 H, d, *J* 7.1 Hz, Me), 3.08 (1 H, d, *J* 8.7 Hz, 2-H), 4.60 (1 H, d, *J* 8.7 Hz, 3-H), 4.67 (1 H, ddd, *J* 4.4, 10.7, 10.7 Hz, 1′-H), 4.84 (1 H, d, *J* 1.5 Hz, 1-H), 4.88 (1 H, d, *J* 1.5 Hz, 4-H), 4.95 (1 H, d, *J* 11.7 Hz, PhC*H*H), 4.96 (1 H, d, *J* 11.7 Hz, PhCH*H*), 5.03 (1 H, d, *J* 11.5 Hz, PhC*H*H), 5.08 (1 H, d, *J* 11.5 Hz, PhCH*H*), 6.98 (1 H, ddd, *J* 1.0, 4.9, 7.3 Hz, ArH), 7.14 (1 H, ddd, *J* 1.0, 1.0, 8.1 Hz, ArH), 7.19–7.50 (11 H, m, 11 × ArH) and 8.39 (1 H, ddd, *J* 1.0, 1.8, 4.9 Hz, ArH); *m/z* 599 (M^+).

Menthyl (1S,2R,3S,4S)-5,6-*Dibenzyloxy*-3-[(*S*)$_S$-2-*pyridylthio*]-7-*oxabicyclo*[2.2.1]*hept*-5-*ene*-2-*carboxylate* **27**.—Phosphorus tribromide (0.227 ml, 2.39 mmol) was added to a solution of compound **9a** (183.7 mg, 0.299 mmol) in DMF (10 ml) under nitrogen at 0 °C. After being stirred at 0 °C for 40 min, the reaction mixture was treated with cold, saturated aq. $NaHCO_3$ (20 ml) at 0 °C and the pH was brought to 7. The solvent was evaporated off and water (10 ml) was added to the residue. The aq. layer was extracted with CH_2Cl_2 (20 ml × 6). The combined extracts were washed with brine, dried ($MgSO_4$) and the solvent was evaporated off. The residue was purified by flash column chromatography on silica gel [eluant hexane–Et_2O (3:1)] to give the sulphide **27** (145.6 mg, 84%) as an oil (Found: M^+, 599.2655. Calc. for $C_{36}H_{41}NO_5S$: *M*, 599.2703); $[\alpha]_D^{27}$ −12.2° (*c* 0.89, $CHCl_3$); $\nu_{max}(CHCl_3)$ 1724 (CO) and 1685 cm^{-1} (C=C); δ_H 0.65 (3 H, d, *J* 6.6 Hz, Me), 0.81 (3 H, d, *J* 6.6 Hz, Me), 0.83 (3 H, d, *J* 7.1 Hz, Me), 0.74–1.95 (9 H, m, 3 × CH_2, 3 × CH), 3.65 (1 H, dd, *J* 4.0, 9.2 Hz, 2-H), 4.65 (1 H, ddd, *J* 4.4, 10.9, 10.9 Hz, 1′-H), 4.83 (1 H, d, *J* 11.7 Hz, PhC*H*H), 4.88 (1 H, dd, *J* 4.1, 9.2 Hz, 3-H), 4.89 (1 H, dd, *J* 1.2, 4.0 Hz, 1-H), 4.92 (1 H, d, *J* 11.7 Hz, PhCH*H*), 4.97 (1 H, d, *J* 11.7 Hz, PhC*H*H), 5.10 (1 H, dd, *J* 1.2, 4.1 Hz, 4-H), 5.12 (1 H, d, *J* 11.7 Hz, PhCH*H*), 6.98 (1 H, ddd, *J* 1.0, 1.1, 8.1 Hz, ArH), 7.18 (1 H, ddd, *J* 1.1, 5.0, 7.3 Hz, ArH), 7.25–7.36 (10 H, m, 10 × ArH), 7.44 (1 H, ddd, *J* 1.9, 7.3, 8.1 Hz, ArH) and 8.42 (1 H, ddd, *J* 1.0, 1.9, 5.0 Hz, ArH); *m/z* 508 (M^+ − Bn).

{(1S,2S,3S,4S)-5,6-*Dibenzyloxy*-3-(2-*pyridylthio*)-7-*oxabicyclo*[2.2.1]*hept*-5-*en*-2-*yl*}*methanol* **28**.—$LiAlH_4$ (7.0 mg, 0.19 mmol) was added to a solution of ester **27** (73.7 mg, 0.123 mmol) in dry Et_2O (4 ml) at 0 °C and the reaction mixture was stirred under argon at room temperature for 55 min. The reaction mixture was quenched with saturated aq. Na_2SO_4 at 0 °C. After 10 min at 0 °C, the precipitate was filtered off and washed with $CHCl_3$ and acetone. The solvent was then evaporated off and the residue was purified by flash column chromatography on silica gel [eluant hexane–AcOEt (1:1)] to give compound **28** (55.7 mg, 95%) as an oil (Found: M^+, 447.1490. Calc. for $C_{26}H_{25}NO_4S$: *M*, 447.1502); $[\alpha]_D^{25}$ −12.7° (*c* 1.01, $CHCl_3$); $\nu_{max}(CHCl_3)$ 3380 (OH) and 1680 cm^{-1} (C=C); δ_H 2.95–3.05 (1 H, m, 2-H), 3.11 (1 H, br s, OH), 3.72 (1 H, dd, *J* 6.4, 11.2 Hz, C*H*H), 3.81 (1 H, dd, *J* 7.8, 11.2 Hz, CH*H*), 4.44 (1 H, dd, *J* 4.2, 8.3 Hz, 3-H), 4.81 (1 H, dd, *J* 1.2, 4.1 Hz, 1-H), 4.86 (1 H, d, *J* 11.7 Hz, PhC*H*H), 4.93 (1 H, d, *J* 11.4 Hz, PhC*H*H), 4.99 (1 H, d, *J* 11.4 Hz, PhCH*H*), 5.00 (1 H, d, *J* 11.7 Hz, PhCH*H*), 5.01 (1 H, dd, *J* 1.2, 4.2 Hz, 4-H), 7.04 (1 H, ddd, *J* 1.0, 5.0, 7.3 Hz, ArH), 7.25–7.39 (11 H, m, 11 × ArH), 7.50 (1 H, ddd, *J* 1.8, 7.3, 7.7 Hz, ArH) and 8.43 (1 H, ddd, *J* 1.0, 1.8, 4.9 Hz, ArH); *m/z* 447 (M^+).

{(1S,2S,4R,5S,6R)-5,6-*Dibenzyloxy*-7-*oxabicyclo*[2.2.1]-*heptan*-2-*yl*}*methanol* **29**.—Raney Ni (W-2, 5.9 ml) was added to a solution of compound **28** (283.0 mg, 0.633 mmol) in EtOH (8.5 ml) and the mixture was stirred under argon at room temperature for 6 days. The metal powder was filtered off and washed with EtOH and the filtrate was concentrated. The residue was passed through a short column of silica gel (eluant $CHCl_3$) to give the alcohol **29** (95.5 mg, 45%) as an oil (Found: M^+, 340.1673. Calc. for $C_{21}H_{24}O_4$: *M*, 340.1673); $[\alpha]_D^{27}$ +55.4° (*c* 2.14, $CHCl_3$) $\nu_{max}(CHCl_3)$ 3470 cm^{-1} (OH); δ_H 1.75 (1 H, ddd, *J* 5.3, 11.3, 12.0 Hz, *exo*-3-H), 2.11 (1 H, dd, *J* 5.6, 12.0 Hz, *endo*-3-H), 2.48–2.58 (1 H, m, 2-H), 2.94 (1 H, br dd, *J* 6.0, 7.4 Hz, OH), 3.80–4.02 (4 H, m, CH_2, 5- and 6-H), 4.40 (1 H, dd, *J* 4.8, 5.3 Hz, 4-H), 4.44 (1 H, d, *J* 10.6 Hz, PhC*H*H), 4.52 (1 H, d, *J* 10.6 Hz, PhCH*H*), 4.57 (1 H, d, *J* 11.4 Hz, PhC*H*H), 4.62 (1 H, dd, *J* 5.1, 5.1 Hz, 1-H), 4.78 (1 H, d, *J* 11.4 Hz, PhCH*H*) and 7.25–7.38 (10 H, m, 10 × ArH); *m/z* 341 (M^+ + 1).

(1S,2R,4R,5S,6R)-*Methyl* 5,6-*Dibenzyloxy*-7-*oxabicyclo*-[2.2.1]*heptane*-2-*carboxylate* **10**.—Jones reagent[22] (2.67M; 0.11 ml) was added dropwise to a solution of the alcohol **29** (35.8 mg, 0.106 mmol) in acetone (1 ml) at 0 °C and the reaction mixture was stirred under nitrogen at room temperature for 2.5 h. After dilution with Et_2O (10 ml), the organic layer was washed with 1M aq. HCl and separated. The aq. layer was extracted with Et_2O (5 ml × 10). The combined organic phase was dried ($MgSO_4$) and concentrated. The residue was dissolved in MeOH–Et_2O (2.0 ml–0.5 ml) and treated with a diazomethane–Et_2O solution (6.0 ml) at 0 °C. After 50 min at 0 °C, the solvent was evaporated off. The residue was purified by PLC [hexane–Et_2O (1:1)] to give the ester **10** (25.9 mg, 67%) as a pale yellow oil (Found: $M^+ - C_7H_7$, 277.1105. $C_{15}H_{17}O_5$ requires *m/z* 277.1075); $[\alpha]_D^{25}$ −2.1° (*c* 0.79, $CHCl_3$); $\nu_{max}(CHCl_3)$ 1737 cm^{-1} (CO); δ_H 1.83 (1 H, dddd, *J* 1.2, 6.0, 11.8, 12.3 Hz, *exo*-3-H), 2.76 (1 H, dd, *J* 5.6, 12.3 Hz, *endo*-3-H), 3.04 (1 H, ddd, *J* 5.5, 5.6, 11.8 Hz, 2-H), 3.36 (3 H, s, OMe), 3.81 (1 H, ddd, *J* 1.2, 4.7, 8.3 Hz, 6-H), 3.91 (1 H, dd, *J* 5.0, 8.3 Hz, 6-H), 4.48 (1 H, d, *J* 10.1 Hz, PhC*H*H), 4.50 (1 H, dd, *J* 4.7, 6.0 Hz, 4-H), 4.52 (1 H, d, *J* 10.1 Hz, PhCH*H*), 4.63 (1 H, d, *J* 12.0 Hz, PhC*H*H), 4.65 (1 H, d, *J* 12.0 Hz, PhCH*H*), 4.82 (1 H, dd, *J* 5.0, 5.5 Hz, 1-H) and 7.24–7.38 (10 H, m, 10 × ArH); *m/z* 368 (M^+) and 277 (M^+ − Bn).

(3R,4S,5R)-*Methyl* 3,4-*Dibenzyloxy*-5-*hydroxycyclohex*-1-*ene*-1-*carboxylate* **11**.—A 1.59M-solution of BuLi in hexane (0.14 ml, 0.22 mmol) was added to a solution of hexamethyldisilazane (0.05 ml, 0.22 mmol) in dry THF (1 ml) and the

mixture was maintained at −78 °C for 0.5 h under argon. A solution of bicyclic ester **10** (33.0 mg, 0.090 mmol) in dry THF (0.8 ml) was introduced and the reaction mixture was stirred at −78 °C for 0.5 h. The solvent was evaporated off and the residue was dissolved in CH_2Cl_2 (20 ml). The organic layer was washed with 1M-HCl (1 ml). The aq. layer was extracted with CH_2Cl_2 (10 ml × 3) and the combined organic phase was washed with brine, dried ($MgSO_4$), and concentrated. The residue was purified by PLC [Et_2O–hexane (2:1)] to give compound **11** (18.4 mg, 56%) as an oil (Found: M^+, 368.1642. Calc. for $C_{22}H_{24}O_5$: M, 368.1622); $[\alpha]_D^{25}$ −168.7° (*c* 1.02, $CHCl_3$); ν_{max}($CHCl_3$) 3600 (OH), 1715 (CO) and 1650 cm^{-1} (C=C); δ_H 2.21 (1 H, dddd, *J* 1.0, 2.4, 8.2, 18.2 Hz, 6β-H), 2.48 (1 H, br s, OH), 2.96 (1 H, dd, *J* 5.7, 18.2 Hz, 6α-H), 3.47 (1 H, dd, *J* 3.9, 9.3 Hz, 4-H), 3.75 (3 H, s, OMe), 4.19–4.27 (2 H, m, 3- and 5-H), 4.55 (1 H, d, *J* 11.8 Hz, PhC*H*H), 4.66 (1 H, d, *J* 11.8 Hz, PhCH*H*), 4.71 (1 H, d, *J* 12.0 Hz, PhC*H*H), 4.72 (1 H, d, *J* 12.0 Hz, PhCH*H*), 6.93 (1 H, ddd, *J* 1.2, 2.4, 4.8 Hz, 2-H) and 7.25–7.40 (10 H, m, 10 × ArH); *m/z* 368 (M^+).

(−)-*Methyl Triacetylshikimate* **30**.—To a stirred solution of compound **11** (15.3 mg, 0.042 mmol) and NaI (26.4 mg, 0.175 mmol) in MeCN (0.5 ml) was slowly added TMSCl (0.021 ml, 0.165 mmol) at 0 °C. After being stirred at room temperature for 19 h, the reaction mixture was quenched with water (3 drops) at 0 °C and the solvent was evaporated off. 20% aq. $Na_2S_2O_3$ was added to the residue. The aq. layer was washed with Et_2O (5 ml × 1) and was extracted with AcOEt (8 ml × 5). The AcOEt phase was dried ($MgSO_4$) and the solvent was evaporated off. The residue was acetylated with Ac_2O (0.3 ml) and dry pyridine (0.3 ml) at room temperature overnight. After usual work-up, the residue was purified by PLC [benzene–Et_2O (4:1)] to give the triacetate **30** (6.9 mg, 53%) as an oil (Found: C, 53.5; H, 6.1. Calc. for $C_{14}H_{18}O_8$: C, 53.50; H, 5.77%); $[\alpha]_D^{25}$ −162.2° (*c* 0.30, MeOH), for compound **30** from natural (−)-shikimic acid $[\alpha]_D^{24}$ −161.7° (*c* 0.64, MeOH) {lit.,[19] $[\alpha]_D^{22}$ −168° (*c* 0.9, MeOH)}; ν_{max}($CHCl_3$) 1741 (CO) and 1659 cm^{-1} (C=C); δ_H 2.06 (3 H, s, Ac), 2.07 (3 H, s, Ac), 2.09 (3 H, s, Ac), 2.44 (1 H, ddd, *J* 1.8, 4.2, 19.3 Hz, 6α-H), 2.93 (1 H, dddd, *J* 1.7, 1.9, 6.4, 19.3 Hz, 6β-H), 3.78 (3 H, s, OMe), 5.25 (1 H, dd, *J* 3.8, 7.9 Hz, 4-H), 5.29 (1 H, ddd, *J* 4.2, 6.4, 7.9 Hz, 5-H), 5.74 (1 H, ddd, *J* 1.7, 3.8, 3.9 Hz, 3-H) and 6.76 (1 H, ddd, *J* 1.8, 1.9, 3.9 Hz, 2-H); *m/z* 314 (M^+).

(3R,4R,5R)-*Methyl* 3,4-*Dibenzyloxy*-5-(*t-butyldiphenylsiloxy*)*cyclohex*-1-*ene*-1-*carboxylate* **31**.—A solution of compound **11** (20 mg, 0.054 mmol) in dry DMF (0.5 ml) was added to a solution of TBDPSCl (28 μl, 0.11 mmol) and imidazole (13.5 mg, 0.217 mmol) in dry DMF (0.5 ml). The reaction mixture was stirred under nitrogen at room temperature for 24 h. The reaction mixture was chromatographed on silica gel [eluant hexane–AcOEt (6:1)] to give *compound* **31** (26 mg, 79%) as an oil (Found: M^+, 606.2791. $C_{38}H_{42}O_5Si$ requires M, 606.2801); $[\alpha]_D^{26}$ −37.4° (*c* 0.69, $CHCl_3$); ν_{max}($CHCl_3$) 1710 (CO) and 1650 cm^{-1} (C=C); δ_H 0.92 (9 H, s, Bu^t), 2.29–2.50 (2 H, m, 6-H_2), 3.55 (1 H, m, 5-H), 3.73 (3 H, s, Me), 4.18 (1 H, m, 4-H), 4.35 (1 H, d, *J* 12.2 Hz, PhC*H*H), 4.46 (1 H, d, *J* 12.2 Hz, PhCH*H*), 4.48 (1 H, m, 3-H), 4.53 (1 H, d, *J* 12.2 Hz, PhC*H*H), 4.59 (1 H, d, *J* 12.2 Hz, PhCH*H*), 6.98 (1 H, m, 2-H) and 7.10–7.73 (20 H, m, 20 × ArH); *m/z* 606 (M^+).

(3R,4R,5R)-3,4-*Dibenzyloxy*-5-(*t-butyldiphenylsiloxy*)*cyclohex*-1-*enylmethanol* **32**.—A 1.0M-solution of DIBAL-H in toluene (0.678 ml, 0.678 mmol) was added to a solution of the ester **31** (137 mg, 0.226 mmol) in dry Et_2O (7 ml) at 0 °C. The reaction mixture was stirred under nitrogen at 0 °C for 7 h and quenched with saturated aq. Na_2SO_4 at 0 °C. After 30 min at 0 °C, the precipitate was filtered off and washed with acetone (10 ml). The combined organic layer was concentrated. The residue was purified by column chromatography on silica gel [eluant hexane–AcOEt (3:1)] to give the *alcohol* **32** (115 mg, 88%) as an oil (Found: M^+, 578.2810. $C_{37}H_{42}O_4Si$ requires M, 578.2850); $[\alpha]_D^{27}$ −15.0° (*c* 0.62, $CHCl_3$); ν_{max}($CHCl_3$) 3400 (OH), 1620 and 1590 cm^{-1} (C=C); δ_H 0.97 (9 H, s, Bu^t), 1.87–2.23 (2 H, m, 6-H_2), 3.63 (1 H, dd, *J* 4.0, 6.2 Hz, 4-H), 3.92 (2 H, br s, CH_2OH), 4.24 (1 H, ddd, *J* 4.0, 4.0, 5.8 Hz, 5-H), 4.35 (1 H, m, 3-H), 4.48 (1 H, d, *J* 12.2 Hz, PhC*H*H), 4.541 (1 H, d, *J* 12.2 Hz, PhCH*H*), 4.544 (1 H, d, *J* 12.2 Hz, PhC*H*H), 4.61 (1 H, d, *J* 12.2 Hz, PhCH*H*), 5.75 (1 H, m, 2-H) and 7.19–7.61 (20 H, m, 20 × ArH); *m/z* (577 (M^+ − 1), 561 (M^+ + 1 − H_2O) and 521 (M^+ − Bu^t).

(1S,2S,3R,4R,5R)-2-*Acetoxy*-1-(*acetoxymethyl*)-3,4-*dibenzyloxy*-5-(*t-butyldiphenylsiloxy*)*cyclohexane* **33**.—A 1.0M-solution of BH_3–THF complex (1.96 ml, 1.96 mmol) was added dropwise to a solution of the allyl alcohol **32** (113 mg, 0.196 mmol) in dry THF (6 ml) under nitrogen at 0 °C. The reaction mixture was stirred at room temperature for 8 h and quenched with water. 3M-Aq. NaOH (1 ml) and then 30% aq. H_2O_2 (1.5 ml) were added to the reaction mixture at 0 °C. After being stirred at room temperature for 12 h, the reaction mixture was concentrated. The residue was extracted with CH_2Cl_2 (12 ml × 5). The combined extracts were washed with brine, dried ($MgSO_4$), and the solvent was evaporated off. The residue was acetylated with dry pyridine (1 ml) and Ac_2O (1 ml) at room temperature. After usual work-up, the residue was purified by column chromatography on silica gel [eluant hexane–AcOEt (3:1)] to give the *diacetate* **33** (96.9 mg, 73%) as an oil (Found: M^+ − Bu^t, 623.2489. $C_{37}H_{39}O_7Si$ requires *m/z* 623.2464); $[\alpha]_D^{27}$ +7.0° (*c* 0.42, $CHCl_3$) ν_{max}($CHCl_3$) 1730 cm^{-1} (CO); δ_H 1.02 (9 H, s, Bu^t), 1.48–2.37 (3 H, m, 1-H, 6-H_2), 2.02 (3 H, s, Ac), 2.06 (3 H, s, Ac), 3.57 (1 H, dd, *J* 2.9, 2.9 Hz, 4-H), 3.88 (1 H, dd, *J* 2.9, 9.8 Hz, 3-H), 3.93–3.98 (1 H, m, 5-H), 3.96 (1 H, dd, *J* 4.2, 11.2 Hz, *H*CHOAc), 3.99 (1 H, dd, *J* 5.9, 11.2 Hz, HC*H*OAc), 4.25 (1 H, d, *J* 12.2 Hz, PhC*H*H), 4.47 (1 H, d, *J* 12.5 Hz, PhCH*H*), 4.47 (2 H, s, PhCH_2), 5.30 (1 H, dd, *J* 10.4, 10.4 Hz, 2-H) and 7.04–7.61 (20 H, m, 20 × ArH); *m/z* 637 (M^+ − Ac) and 623 (M^+ − Bu^t).

(1R,2S,3R,4S,5S)-1,2,3,4-*Tetra-acetoxy*-5-(*acetoxymethyl*)-*cyclohexane* (*Pseudo*-α-L-*mannopyranose Penta-acetate*) **12**.—A 1.0M-solution of Bu_4NF in THF (0.375 ml, 0.375 mmol) was added dropwise to a solution of the TBDPS ether **33** (51 mg, 0.075 mmol) in dry THF (6 ml) at 0 °C. The reaction mixture was stirred at room temperature for 5 h and the solvent was evaporated off. The residue was dissolved in $CHCl_3$ (6 ml) and the solution was washed with brine (1 ml). The aq. layer was extracted with $CHCl_3$ (8 ml × 3). The combined extracts were dried ($MgSO_4$) and the solvent was evaporated off. The residue was purified by column chromatography on silica gel [eluant hexane–AcOEt (5:1)] to give 4-acetoxy-5-(acetoxymethyl)-2,3-dibenzyloxycyclohexanol (26.7 mg) as an oil. A solution of the alcohol (21.5 mg) in EtOH (10 ml), AcOH (one drop), and 5% Pd–C (30 mg) was hydrogenated (3.5 atm starting pressure of hydrogen gas) at room temperature overnight in a Parr hydrogenation apparatus. The catalyst was removed by filtration and the filtrate was concentrated. The residue was acetylated with Ac_2O (1 ml) and dry pyridine (1 ml) at room temperature overnight. After usual work-up, the residue was purified by PLC [hexane–AcOEt (2:1)] to give compound **12** (16.5 mg, 71%) as a white solid. Crystallisation from EtOH–Et_2O gave plates, m.p. 92 °C (lit.,[3] 84–86 °C) (Found: C, 52.3; H, 6.3. Calc. for $C_{17}H_{24}O_{10}$: C, 52.56; H, 6.23%); $[\alpha]_D^{27}$ −35.2° (*c* 0.56, $CHCl_3$) {lit.,[3] $[\alpha]_D^{28}$ −38.5° (*c* 1.04, $CHCl_3$)}; ν_{max}($CHCl_3$) 1 740 cm^{-1} (CO); δ_H 1.99 (3 H, s, Ac), 2.05 (3 H, s, Ac), 2.07 (3 H, s, Ac), 2.13 (3 H, s, Ac), 2.15 (3 H, s, Ac), 1.81–2.30 (3 H, m, 5-H, 6-H_2), 3.95 (1 H, dd, *J* 3.8, 11.4 Hz, *H*CHOAc),

4.12 (1 H, dd, *J* 5.5, 11.4 Hz, HC*H*OAc), 5.04 (1 H, ddd, *J* 2.9, 2.9, 6.4 Hz, 1-H) and 5.21–5.34 (3 H, m, 2-, 3- and 4-H); *m/z* 389 ($M^+ + 1$), 346 ($M^+ + 1 - Ac$), 330 ($M^+ + 1 - OAc$) and 329 ($M^+ - OAc$).

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