

# Synthesis of spirocycles *via* ring closing metathesis of heterocycles carrying *gem*-diallyl substituents obtained *via* ring opening of (halomethyl)cyclopropanes with allyltributyltin

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In the presence of allyl tri-*n*-butyltin–AIBN, cyclopropylmethyl bromides/xanthates undergo ring-opening reaction with concomitant formation of geminal diallyl derivatives in good yields. The ring closing metathesis reactions on geminal diallyl derivatives with Grubbs' catalyst provided spirocyclopentenyl products. Combination of these two methodologies has been applied to the synthesis of mono-, bis-cyclopentyl-carbohydrates as well as spirocyclopentylproline derivatives.

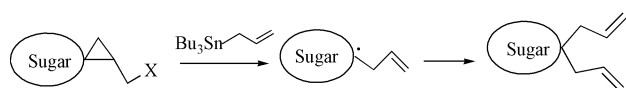
## Introduction

Interest in developing new protocols that can give rise to spiro derivatives has risen considerably, primarily due to the inherent rigidity displayed by the spiro functionality.<sup>1</sup> Molecules containing a spiro group find innumerable applications particularly in peptides,<sup>2</sup> nucleosides<sup>3</sup> and carbohydrates.<sup>4</sup> The synthesis of spiro derivatives was difficult until the advent of novel catalysts by Schrock<sup>5</sup> and Grubbs<sup>6</sup> used in ring closing metathesis (RCM). The RCM based approaches<sup>7</sup> have made the introduction of a spiro group in the structural framework of an organic molecule an easy proposition.<sup>8</sup> For instance, *gem*-diallyl containing substrates undergo RCM to produce spirocyclopentene derivatives.<sup>9</sup>

The synthesis of *gem*-diallyl derivatives can be realized by double alkylation of an active methylene group.<sup>10</sup> We realized that the introduction of a *gem*-diallyl functionality on a carbon atom not activated by any electron-withdrawing group, is a difficult proposition. The problem becomes insurmountable when a carbohydrate precursor is involved because base catalysed reactions lead to tandem elimination of water molecules, resulting in the formation of a mixture of compounds.

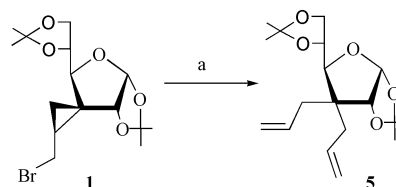
Some years ago, we observed interesting reactions<sup>11</sup> with carbohydrate cyclopropyl precursors. For example, the radical mediated cyclopropyl scission of the spirocyclopropyl bromide **1** with *n*-Bu<sub>3</sub>SnH gave the *C*-allyl derivative **2** in a stereo-controlled fashion. On the other hand, hydrogenation of the cyclopropyl-aldehyde derivative **3** over Pd/C provided **4** with a quaternary chiral center (Scheme 1).

We were particularly impressed by the radical ring opening reaction as described above because we envisaged that *in situ* quenching of the homoallyl radical formed (Fig. 1) with allyltri-*n*-butyltin<sup>12</sup> should lead to the formation of a *gem*-diallyl derivative. This study forms the main objective of this manuscript.<sup>13</sup>



Scheme 1

and catalytic AIBN to give the *gem*-diallyl derivative **5** in 76% yield (Scheme 2). The structure of **5** was proven, beyond any doubt, by <sup>1</sup>H, <sup>13</sup>C, mass spectroscopy and elemental analysis.



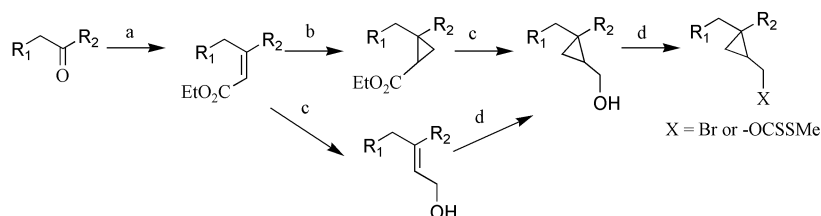
Scheme 2 Reagents and conditions: (a) allyltri-*n*-butyltin, C<sub>6</sub>H<sub>6</sub>, AIBN, 80 °C, 76%.

In order to establish the versatility of this reaction, a number of spirocyclopropylmethyl bromides were prepared (Table 1), according to the general strategy depicted in Scheme 3. The carbonyl derivative was subjected to the Wittig reaction with Ph<sub>3</sub>P=CHCO<sub>2</sub>Et in refluxing benzene. For entries 1–3, the resulting unsaturated ester was cyclopropanated<sup>14</sup> with Me<sub>3</sub>S(O)I–NaH in DMSO and then reduced with DIBAL–H in CH<sub>2</sub>Cl<sub>2</sub> at –78 °C to afford the cyclopropylmethanol derivatives. For entry 4, the unsaturated ester was first reduced with DIBAL–H in CH<sub>2</sub>Cl<sub>2</sub> at –78 °C to provide an allylic alcohol which was subsequently cyclopropanated (entry 5 as well) using the modified Simmons–Smith method<sup>15</sup> by using Et<sub>2</sub>Zn–CH<sub>2</sub>I<sub>2</sub> in CH<sub>2</sub>Cl<sub>2</sub> at –20 °C. Conversion of the cyclopropyl-

Fig. 1

## Results and discussion

The requisite precursor **1**, earlier reported<sup>11</sup> from our laboratory, was treated with allyltri-*n*-butyltin in refluxing benzene



**Scheme 3** Reagents and conditions: (a)  $\text{PPh}_3=\text{CHCO}_2\text{Et}$ ,  $\text{C}_6\text{H}_6$ ,  $80^\circ\text{C}$ ; (b)  $\text{Me}_3\text{SOI}$ ,  $\text{DMSO}$ ,  $\text{NaH}$ ; (c)  $\text{DIBAL-H}$ ,  $\text{CH}_2\text{Cl}_2$ ,  $-78^\circ\text{C}$ ; (d)  $\text{CBr}_4$ ,  $\text{PPh}_3$ ,  $\text{CH}_2\text{Cl}_2$ ,  $\text{py}$  or  $\text{NaH}$ ,  $\text{CS}_2$ ,  $\text{MeI}$ ,  $\text{THF}$ ; (e)  $\text{Et}_2\text{Zn}$ ,  $\text{CH}_2\text{I}_2$ ,  $\text{CH}_2\text{Cl}_2$ ,  $-20^\circ\text{C}$ .

**Table 1** Synthesis of *gem*-diallyl compounds from (halomethyl)cyclopropanes

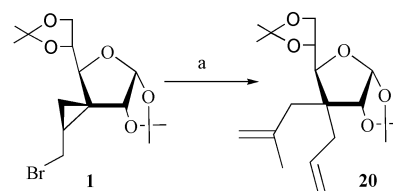
Entry	Substrate	Product	Yield (%)
1			76
2			44
3			81
4			60
5			53
6			62

methanol to the corresponding cyclopropylmethyl bromide was accomplished with  $\text{CBr}_4\text{-Ph}_3\text{P}$ -pyridine in  $\text{CH}_2\text{Cl}_2$  at room temperature.

The preparation of the xanthate derivative (entry 6) from the cyclopropylmethanol was accomplished using a well-defined protocol using  $\text{CS}_2\text{-NaH-MeI}$  in  $\text{THF}$ . The bromoxanthate derivatives (entries 1–6) were treated with allyltri-*n*-butyltin-AIBN in refluxing benzene to provide the *gem*-diallyl product in good yields. The diallyl derivatives were fully characterized by spectroscopic methods.

Application of this concept to install two different allylic functionalities on the same carbon was also explored when methallyltri-*n*-butyltin was treated with **1** to give rise to 3-deoxy-3-*C*-allyl-3-*C*-methallyl derivative **20** (Scheme 4). The absolute stereochemistry of **20** was established by NOE studies as indicated in Fig. 2.

Having in hand the *gem*-diallyl derivatives, our next target



**Scheme 4** Reagents and conditions; (a) methallyltri-*n*-butyltin,  $\text{C}_6\text{H}_6$ , AIBN,  $80^\circ\text{C}$ , 12 h, 52%.

was to perform ring closing metathesis reactions<sup>7</sup> in order to convert them to novel spirocyclopentyl derivatives. For instance, compound **5** was treated with Grubbs' catalyst in  $\text{CH}_2\text{Cl}_2$  at room temperature to provide the spirocyclopentyl derivative **21** whose structure was supported by spectroscopic data. Interestingly the RCM reaction of **20** gave **22** in 75% yield (Scheme 5).

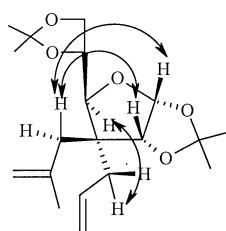
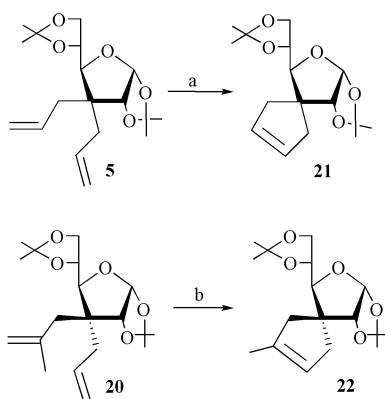
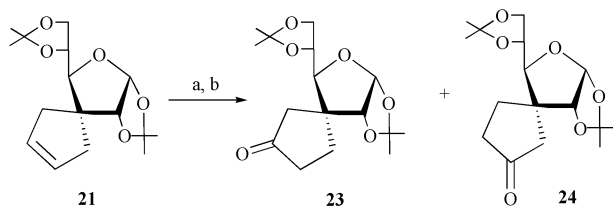


Fig. 2



Scheme 5 Reagents and conditions; (a) Grubbs' catalyst,  $\text{CH}_2\text{Cl}_2$ , rt, 80%; (b) Grubbs' catalyst,  $\text{CH}_2\text{Cl}_2$ , rt, 75%.

Our next plan was to adopt an iterative approach of the above two strategies and prepare some novel bis-spirocyclopentyl derivatives of carbohydrates. For this endeavor, compound **21** was subjected to hydroboration–oxidation reaction, which led to the formation of a complex mixture of diastereomers (Scheme 6). The mixture as such was oxidized under Swern oxidation conditions to give two products (**23** and **24**), separated by silica gel chromatography. The correct assignment of the structures of **23**<sup>4</sup> and **24** was performed by NOE experiments (Fig. 3).



Scheme 6 Reagents and conditions; (a)  $\text{BH}_3 \cdot \text{SMe}_2$ , NaOAc, 30%  $\text{H}_2\text{O}_2$ , THF, 0 °C, 1 h; (b)  $(\text{COCl})_2$ ,  $\text{Me}_2\text{SO}$ ,  $\text{CH}_2\text{Cl}_2$ ,  $\text{Et}_3\text{N}$ , -78 °C, 2 h, 56%.

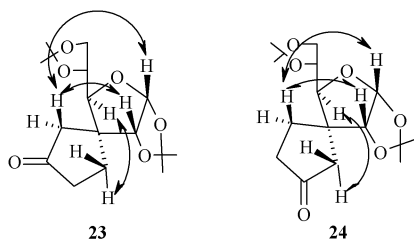
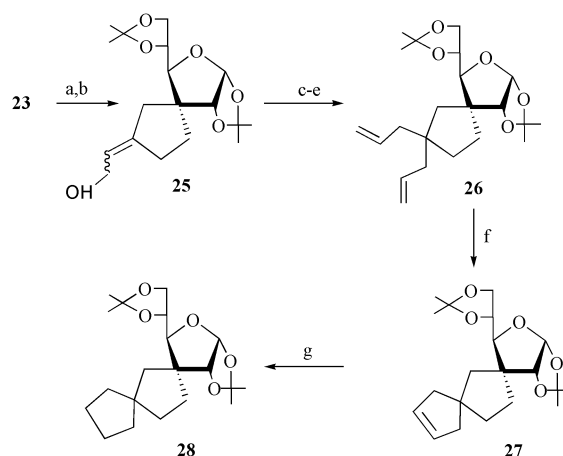


Fig. 3

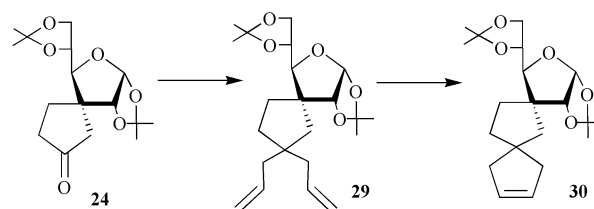
Compound **23** was subjected to the following sequence of reactions: Wittig olefination with  $(\text{EtO})_2\text{P}(\text{O})\text{CH}_2\text{CO}_2\text{Et}$ , reduction of ester group with DIBAL-H to obtain **25**, Simmons–Smith cyclopropanation and the corresponding xanthate preparation with  $\text{NaH}-\text{CS}_2-\text{MeI}$  in THF (Scheme 7).

The radical induced diallylation of xanthate gave **26** whose RCM reaction and catalytic hydrogenation produced the bis-spiro-derivative **28**.



Scheme 7 Reagents and conditions; (a)  $(\text{EtO})_2\text{P}(\text{O})\text{CH}_2\text{CO}_2\text{Et}$ , NaH, THF, 0 °C  $\rightarrow$  rt, 80%; (b) DIBAL-H,  $\text{CH}_2\text{Cl}_2$ , -78 °C, 0.5 h, 88%; (c)  $\text{Et}_2\text{Zn}$ ,  $\text{CH}_2\text{I}_2$ ,  $\text{CH}_2\text{Cl}_2$ , -20 °C, 14 h, 60%; (d) NaH,  $\text{CS}_2$ , MeI, THF, 0.5 h, 90%; (e) allyltributyltin,  $\text{C}_6\text{H}_6$ , AIBN, 80 °C, 34%; (f) Grubbs' catalyst,  $\text{CH}_2\text{Cl}_2$ , rt, 4 h, 88%; (g) 10% Pd/C- $\text{H}_2$ , MeOH, 82%.

In a similar manner, the other isomer (**24**) was also converted to the diallyl derivative **29** and the bis-spiro-derivative **30** (Scheme 8).



Scheme 8

Spiroproline derivatives are of interest in biological studies with potential applications as an inhibitor and mechanistic probe of prolyl-4-hydroxylase.<sup>20</sup> In pursuit of the development of potent inhibitors of angiotensin converting enzyme (ACE), lipophilic and sterically hindered spiroproline derivatives have been substituted in the structural framework of peptides. In addition, spiroprolines could offer interesting scaffold precursors, particularly in the synthesis of combinatorial libraries of peptides. The earlier synthetic efforts aimed at spiroproline analogues involved building the proline nucleus on the structural backbone of the alicyclic system followed by resolution. We decided to try to expand the potential of our synthesis of spirocyclic compounds to proline derivatives, with the hitherto unknown 2-azaspiro[4.4]nonanecarboxylic acid derivative **39** as the target.

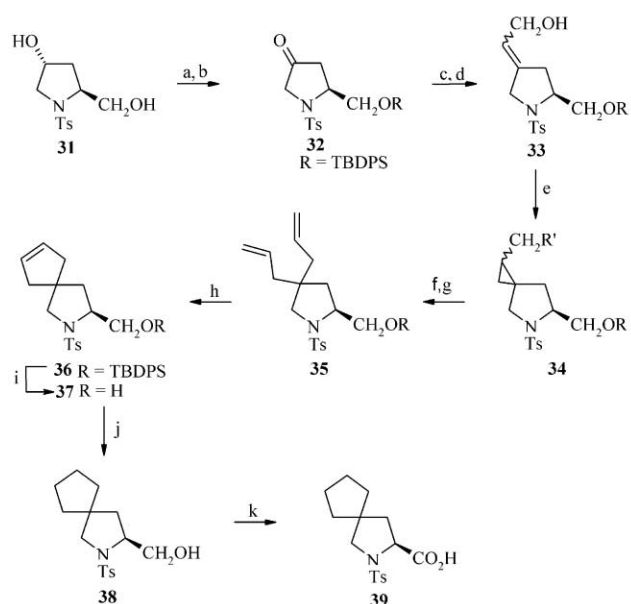
The known *trans*-*N*-(*p*-toluenesulfonyl)-4-hydroxy-L-prolinol (**31**)<sup>21</sup> was converted into 4,4'-cyclopentyl-L-proline derivative by essentially following the route already discussed and shown in Scheme 9. The purity of the final product was determined by chiral HPLC (95%). The structure of **39** was supported by its <sup>1</sup>H-NMR, <sup>13</sup>C-NMR, and mass spectral data.

## Conclusions

We have derived a simple protocol to introduce a *gem*-diallyl group. The RCM reaction provided a strategy for the preparation of spirocyclopentyl derivatives of sugars and L-proline.

## Experimental

NMR spectra were recorded on Bruker AC 200, MSL 300 or DRX 500 MHz instruments in  $\text{CDCl}_3$  or acetone- $\text{D}_6$  using TMS as internal standard. IR spectra were recorded on a Perkin–Elmer 16 PC-FT IR spectrometer. Electron impact mass spectra (EIMS) were recorded on a Finnigan MAT-1020.



**Scheme 9** Reagents and conditions: (a) TBDPSCl, imidazole, DMF, rt, overnight; (b) PDC, 4 Å mol sieves, CH<sub>2</sub>Cl<sub>2</sub>, 4 h, 60%; (c) Ph<sub>3</sub>P=CHCO<sub>2</sub>Et, C<sub>6</sub>H<sub>6</sub>, 80 °C, 24 h; (d) DIBAL-H, CH<sub>2</sub>Cl<sub>2</sub>, -78 °C, 45 min, 85%; (e) Et<sub>2</sub>Zn, CH<sub>2</sub>I<sub>2</sub>, CH<sub>2</sub>Cl<sub>2</sub>, overnight, 78%; (f) Ph<sub>3</sub>P, CBr<sub>4</sub>, CH<sub>2</sub>Cl<sub>2</sub>, pyridine, 0 °C, 30 min.; (g) allyltri-*n*-butyltin, AIBN, C<sub>6</sub>H<sub>6</sub>, 8 h, 66%; (h) Grubbs' catalyst, CH<sub>2</sub>Cl<sub>2</sub>, rt, 1.5 h, 96%; (i) TBAF, THF, rt, 2 h, 93%; (j) Pd/C, H<sub>2</sub>, MeOH, 3 h, 96%; (k) RuCl<sub>3</sub>·(H<sub>2</sub>O)<sub>n</sub>, NaIO<sub>4</sub>, CCl<sub>4</sub>, CH<sub>3</sub>CN, H<sub>2</sub>O, rt, 2 h, 77%.

Microanalysis was carried out on a Carlo-Elba elemental analyzer. Melting points were measured on a Buchi B-540 apparatus and are uncorrected. Optical rotations were recorded on a JASCO DIP-1020 digital polarimeter. Solvents were distilled over drying agents under argon or nitrogen. All reactions were monitored by thin-layer chromatography carried out on 0.25 m E. Merck silica gel plates (60F-254) using UV light as visualizing agent and anisaldehyde in ethanol as developing agent. Silica gel (60-120) was purchased from Acme Chemical Company.

#### General procedure for cyclopropanation with Me<sub>3</sub>S(O)I

To the mixture of Me<sub>3</sub>S(O)I (2.0 eq.) and NaH (2.0 eq.) in DMSO at 0 °C was added a solution of  $\alpha,\beta$ -unsaturated ester in dry DMSO under argon. After 2 h, the reaction was quenched with water and extracted with ether, washed with brine, dried and concentrated. The residue was purified by column chromatography on silica gel.

#### General procedure for cyclopropanation with Et<sub>2</sub>Zn

To a solution of the allylic alcohol in dry CH<sub>2</sub>Cl<sub>2</sub> under argon at -20 °C was added a 1 M solution of Et<sub>2</sub>Zn (3.0 eq.) and CH<sub>2</sub>I<sub>2</sub> (6.0 eq.). After 12 h, the reaction was quenched with ice and partitioned between CH<sub>2</sub>Cl<sub>2</sub> and water. The organic layer was dried, concentrated and the residue passed through a short column of silica gel.

#### General procedure for the preparation of cyclopropylmethyl bromides

To the stirred solution of the cyclopropylmethanol in dry CH<sub>2</sub>Cl<sub>2</sub> at rt was added pyridine, triphenylphosphine (2.2 eq.) and CBr<sub>4</sub> (1.1 eq.) successively. After 30 min solvent was removed *in vacuo* and the residue was passed through a short bed of silica gel.

#### General procedure for the preparation of xanthates

CS<sub>2</sub> (4.0 eq.) was added to a previously stirred solution of the cyclopropylmethanol and NaH (2.0 eq.) in dry THF at 0 °C

under N<sub>2</sub> followed by CH<sub>3</sub>I (5.0 eq.). After 30 min the reaction was quenched with saturated aq. NH<sub>4</sub>Cl, extracted with CH<sub>2</sub>Cl<sub>2</sub> and washed with water, brine and dried. The crude product was purified by column chromatography on silica gel.

#### General procedure for diallylation

A solution of the cyclopropylmethyl bromide/xanthate, allyltri-*n*-butyltin (2.0 eq.) and AIBN (cat.) in benzene was degassed and refluxed under argon for 12 h. The reaction mixture was concentrated, diluted with ether and stirred with an aq. solution of KF for 3 h and then filtered. The filtrate was washed with water, dried (Na<sub>2</sub>SO<sub>4</sub>), concentrated and the residue purified by column chromatography on silica gel.

#### General procedure for RCM

A solution of the *gem*-diallyl compound and Grubbs' catalyst (5 mol%) in CH<sub>2</sub>Cl<sub>2</sub> was stirred at rt for 3 h. Solvent was removed and the crude product purified by column chromatography on silica gel.

#### 3-Deoxy-1,2:5,6-di-*O*-isopropylidene-3,3-*C*-diallyl- $\alpha$ -*D*-ribohexofuranose (5)

Following the general procedure for diallylation, compound **1**<sup>11</sup> (0.19 g, 0.52 mmol), allyltri-*n*-butyltin (0.35 mL, 1.0 mmol) and AIBN (10 mg) in benzene (6 mL) gave compound **5** (0.13 g, 76%); [a]<sub>D</sub> + 36 (*c* 2.1 in CHCl<sub>3</sub>);  $\delta$ <sub>H</sub> (300 MHz; CDCl<sub>3</sub>) 1.27, 1.33, 1.45, 1.50 (4 s, 12 H), 2.15–2.45 (m, 4 H), 3.72 (m, 1H), 3.78 (m, 1 H), 4.09 (m, 2 H), 4.24 (d, 1 H, *J* 3.4 Hz), 5.03 (m, 4 H), 5.57 (d, 1 H, *J* 3.4 Hz), 5.90 (m, 2 H);  $\delta$ <sub>C</sub> (50 MHz; CDCl<sub>3</sub>) 25.5, 26.4, 26.8, 27.1, 36.1, 37.0, 50.6, 69.0, 73.5, 85.2, 86.0, 104.4, 109.5, 111.3, 117.6, 134.8, 135.5 (Found: C, 66.46; H, 8.92. C<sub>18</sub>H<sub>28</sub>O<sub>5</sub> requires C, 66.64; H, 8.70%).

#### Methyl 3-*O*-benzyl-5,6-*O*-cyclohexylidene-2-deoxy-2,2-*C*-[(hydroxymethyl)ethylene]- $\beta$ -*D*-*arabino*-hexofuranoside (8)

A mixture of compound **7**<sup>16</sup> (3.6 g, 10.0 mmol) and PPh<sub>3</sub>=CHCO<sub>2</sub>Et (5.2 g, 15.0 mmol) was refluxed in benzene (20 mL) for 4 h and concentrated. The residue was purified by passing through a bed of silica gel (light petroleum–EtOAc 20 : 1) to afford the unsaturated ester (3.2 g) which was treated with Me<sub>3</sub>S(O)I (3.2 g, 14.8 mmol) and NaH (0.6 g, 14.8 mmol) in dry DMSO (10 ml), as per general procedure, to give the cyclopropyl derivative (1.3 g). It was dissolved in dry CH<sub>2</sub>Cl<sub>2</sub> (10 mL) and cooled to -78 °C. DIBAL-H solution (2.0 molar solution, 3.7 mL, 7.4 mmol) was introduced, stirred for 1 h, and treated with saturated solution of sodium potassium tartrate. The organic layer was separated, dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated. The resulting residue was purified on silica gel with ethyl acetate–light petroleum (2 : 3) to give methyl 3-*O*-benzyl-5,6-*O*-cyclohexylidene-2-deoxy-2,2-[(hydroxymethyl)ethylene]- $\beta$ -*D*-*arabino*-hexofuranoside **8** (0.93 g, 23%); [a]<sub>D</sub> + 82 (*c* 0.5 in CHCl<sub>3</sub>);  $\delta$ <sub>H</sub> (200 MHz; CDCl<sub>3</sub>) 0.75 (dd, 1 H, *J* 5.8, 8.8 Hz), 0.9 (t, 1 H, *J* 5.8 Hz), 1.39–1.75 (m, 11 H), 2.31 (br s, 1 H), 3.26 (dd, 1 H, *J* 8.8, 11.7 Hz), 3.34 (s, 3 H), 3.59 (d, 1 H, *J* 3.8 Hz), 3.71 (dd, 1 H, *J* 5.9, 11.7 Hz), 3.97–4.21 (m, 4 H), 4.38 (m, 1 H), 4.64 (d, 1 H, *J* 11.6 Hz), 4.79 (d, 1 H, *J* 11.6 Hz), 4.86 (s, 1 H), 7.32 (m, 5 H) (Found: C, 68.40; H, 7.68. C<sub>23</sub>H<sub>32</sub>O<sub>6</sub> requires C, 68.29; H, 7.97%).

#### Methyl 3-*O*-benzyl-5,6-*O*-cyclohexylidene-2-deoxy-2,2-*C*-diallyl- $\beta$ -*D*-*arabino*-hexofuranoside (9)

Following the general procedure, compound **8** (1.6 g, 4.0 mmol), PPh<sub>3</sub> (2.3 g, 8.8 mmol), CBr<sub>4</sub> (1.5 g, 4.4 mmol) and pyridine (0.3 mL) gave the corresponding cyclopropylmethylbromide (purified by passing through a short bed of silica gel, eluting with ethyl acetate–light petroleum–1:9, 1.3 g). Following the general procedure for diallylation, the cyclo-

propylmethyl bromide (1.3 g, 2.8 mmol), allyltri-*n*-butyltin (1.8 ml, 5.6 mmol) and AIBN (10 mg) gave **9** (0.75 g, 44%);  $[\alpha]_D + 66$  (*c* 0.41 in CHCl<sub>3</sub>);  $\delta_H$  (500 MHz; CDCl<sub>3</sub>) 1.58 (m, 10 H), 2.05–2.40 (m, 4 H), 3.31 (s, 3 H), 3.90 (d, 1 H, *J* 4.4 Hz), 3.95 (dd, 1 H, *J* 5.9, 8.3 Hz), 4.08 (m, 2 H), 4.31 (m, 1 H), 4.49 (d, 1 H, *J* 11.0 Hz), 4.71 (s, 1 H), 4.74 (d, 1 H, *J* 11.0 Hz), 5.06 (m, 4 H), 5.77 (m, 2 H), 7.31 (m, 5 H);  $\delta_C$  (125 MHz; CDCl<sub>3</sub>) 23.9, 24.1, 25.2, 35.0, 35.3, 36.5, 52.6, 55.9, 67.2, 73.2, 74.2, 80.4, 84.4, 109.2, 109.6, 117.5, 117.7, 127.6–128.3, 135.0, 138.5 (Found: C, 72.73; H, 8.44. C<sub>26</sub>H<sub>36</sub>O<sub>5</sub> requires C, 72.87; H, 8.47%).

**(E)-5-O-(tert-Butyldiphenylsilyl)-3-deoxy-1,2-O-isopropylidene-3,3-C-[(hydroxymethyl)ethylene]- $\alpha$ -D-threo-pentofuranose (11)**

Cyclopropanation of **10**<sup>17</sup> (3.5 g, 7.0 mmol) was carried out as per the general procedure using NaH (0.56 g, 14.1 mmol) and Me<sub>3</sub>S(O)I (3.1 g, 14.1 mmol) in DMSO (10 mL). The cyclopropanated product (2.1 g, 4.2 mmol) was reduced with DIBAL-H (2 M solution, 4.7 mL, 9.4 mmol) at –78 °C as reported before to obtain **11** (1.6 g, 48%);  $[\alpha]_D + 11.1$  (*c* 2.1 in CHCl<sub>3</sub>);  $\delta_H$  (300 MHz; CDCl<sub>3</sub>) 0.5 (t, 1H, *J* 5.1 Hz), 0.97 (s, 9H), 1.08 (m, 2H), 1.26, 1.52 (2s, 6H), 3.16 (t, 1H, *J* 11.4 Hz), 3.29 (dd, 1H, *J* 6.2, 10.6 Hz), 3.56 (dd, 1H, *J* 4.7, 10.6 Hz), 4.36 (m, 2H), 5.79 (d, 1H, *J* 3.6 Hz), 7.40 (m, 5H), 7.65 (m, 5H);  $\delta_C$  (75 MHz; CDCl<sub>3</sub>) 12.5, 19.1, 20.7, 26.6, 26.8, 27.1, 33.8, 63.5, 65.1, 78.5, 86.4, 104.6, 111.7, 127.7, 129.8, 133.0, 135.6; MS (EI) *m/z* 255 (M<sup>+</sup> – O<sup>t</sup>BuSiPh<sub>2</sub>) (Found: C, 68.96; H, 7.87. C<sub>27</sub>H<sub>36</sub>O<sub>5</sub>Si requires C, 69.20; H, 7.74%).

**5-O-(tert-Butyldiphenylsilyl)-3-deoxy-3,3-C-diallyl-1,2-O-isopropylidene- $\alpha$ -D-threo-pentofuranose (12)**

As per the general procedure, **11** (0.6 g, 1.3 mmol) was converted to the corresponding cyclopropylmethyl bromide using Ph<sub>3</sub>P (0.7 g, 2.8 mmol), CBr<sub>4</sub> (0.5 g, 1.4 mmol) and pyridine (0.5 mL) in CH<sub>2</sub>Cl<sub>2</sub> (25 mL). The cyclopropylmethyl bromide thus obtained (0.61 g, 1.2 mmol) was treated with allyltri-*n*-butyltin (0.74 mL, 2.4 mmol) and AIBN (5 mg) by following the general procedure for diallylation, to afford **12** (0.45 g, 81%);  $[\alpha]_D + 22$  (*c* 1.0 in CHCl<sub>3</sub>);  $\delta_H$  (200 MHz; CDCl<sub>3</sub>) 1.08 (s, 9 H), 1.29 (s, 3 H), 1.54 (s, 3 H), 1.87–2.54 (m, 4 H), 3.82 (m, 2 H), 4.03 (t, 1 H, *J* 6.5 Hz), 4.25 (d, 1 H, *J* 3.4 Hz), 5.0 (m, 4 H), 5.70 (d, 1 H, *J* 3.4 Hz), 5.80 (m, 2 H), 7.35–7.77 (m, 10 H);  $\delta_C$  (50 MHz; CDCl<sub>3</sub>) 19.3, 26.5, 27.0, 35.6, 36.5, 50.0, 62.9, 84.7, 85.6, 104.2, 111.0, 117.7, 127.8, 129.8, 133.3–135.7; MS (EI) *m/z* 257 (M<sup>+</sup> – *t*-BuSiPh<sub>2</sub>) (Found: C, 73.19; H, 8.28. C<sub>30</sub>H<sub>40</sub>O<sub>4</sub>Si requires C, 73.13; H, 8.18%).

**(4-Methoxyspiro[2.5]octan-1-yl)methanol (14)**

To a solution of **13**<sup>18</sup> (0.6 g, 3.0 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (25 mL) under argon atmosphere at –78 °C was added a 2.1 M solution of DIBAL-H (3.6 mL, 7.6 mmol). After stirring for 1 h at –78 °C, the reaction mixture was worked up in the usual fashion to give a residue, which was purified by silica gel chromatography (EtOAc–light petroleum 1 : 9) to give 2-(2-methoxycyclohexylidene)ethanol (0.4 g). Following the general procedure for cyclopropanation, 2-(2-methoxycyclohexylidene)ethanol (0.4 g, 2.6 mmol), a 1 M solution of Et<sub>2</sub>Zn (7.8 mL, 7.8 mmol) and CH<sub>2</sub>I<sub>2</sub> (1.2 mL, 15.6 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (25 mL) gave **14** (0.29 g, 56%);  $\delta_H$  (200 MHz; CDCl<sub>3</sub>) 0.14 (t, 1 H, *J* 5.1 Hz), 0.47 (dd, 1 H, *J* 5.1, 8.8 Hz), 1.25–1.95 (m, 9 H), 2.53 (s, 1 H), 2.96 (br s, 1 H), 3.34 (s, 3 H), 3.53 (dd, 1 H, *J* 8.8, 11.0 Hz), 3.68 (m, 1 H);  $\delta_C$  (50 MHz; CDCl<sub>3</sub>) 13.7, 21.0, 24.9, 25.4, 25.9, 26.0, 28.7, 56.1, 62.2, 83.9; MS (EI) *m/z* 170 (M<sup>+</sup>).

**1,1-Diallyl-2-methoxycyclohexane (15)**

Following the general procedure of bromination, compound **14** (0.25 g, 1.5 mmol), Ph<sub>3</sub>P (0.85 g, 3.2 mmol), CBr<sub>4</sub> (0.54 g,

1.6 mmol) and pyridine (0.5 mL) gave the corresponding cyclopropylmethyl bromide (0.27 g). As per general procedure, the cyclopropylmethyl bromide (0.27 g, 1.2 mmol), allyltri-*n*-butyltin (0.7 mL, 2.4 mmol) and AIBN (20 mg) gave **15** (0.17 g, 60%);  $\delta_H$  (200 MHz; CDCl<sub>3</sub>) 1.10–1.80 (m, 8 H), 1.92–2.30 (m, 4 H), 2.94 (dd, 1 H, *J* 3.4, 7.8 Hz), 3.27 (s, 3 H), 4.94 (m, 4 H), 5.77 (m, 2 H);  $\delta_C$  (50 MHz; CDCl<sub>3</sub>) 21.0, 22.9, 24.1, 31.4, 36.8, 39.8, 40.9, 56.3, 82.3, 117.0, 117.2, 135.1; MS (EI) *m/z* 194 (M<sup>+</sup>) (Found: C, 80.62; H, 11.53. C<sub>13</sub>H<sub>22</sub>O requires C, 80.35; H, 11.41%).

**{2-(Benzyloxymethyl)cyclopropyl}methanol (17)**

Cyclopropanation of **16**<sup>19</sup> (1.4 g, 7.8 mmol) was achieved by following the general procedure using Et<sub>2</sub>Zn (1 M solution, 23.5 mL, 23.5 mmol) and CH<sub>2</sub>I<sub>2</sub> (3.8 mL, 47.2 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (50 mL) at –20 °C to yield **17** (0.79 g, 52%);  $\delta_H$  (300 MHz; CDCl<sub>3</sub>) 0.20 (dd, 1 H, *J* 2.9, 7.0 Hz), 0.8 (m, 1 H), 1.33 (m, 2 H), 2.96 (s, 1 H), 3.14 (m, 2 H), 3.90 (m, 2 H), 4.55 (m, 2 H), 7.33 (m, 5 H);  $\delta_C$  (50 MHz; CDCl<sub>3</sub>) 8.6, 14.8, 18.5, 62.9, 70.7, 73.1, 127.9, 128.5, 137.5; MS (EI) *m/z* 161 (M<sup>+</sup> – CH<sub>2</sub>OH), 101 (M<sup>+</sup> – OBn).

**2-Allylpent-4-enyl benzyl ether (18)**

Compound **17** (0.4 g, 2.1 mmol) was treated with PPh<sub>3</sub> (1.2 g, 4.6 mmol), CBr<sub>4</sub> (0.76 g, 2.3 mmol) and pyridine (1.5 mL) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) as per the general procedure for bromination. The resulting cyclopropylmethyl bromide derivative (0.4 g, 1.6 mmol) was reacted with allyltri-*n*-butyltin (1.0 mL, 3.2 mmol) according to the general procedure for diallylation, to give **18** (0.24 g, 53%);  $\delta_H$  (200 MHz; CDCl<sub>3</sub>) 1.76 (m, 1 H), 2.10 (m, 4 H), 3.33 (dd, 2 H, *J* 5.9, 11.2 Hz), 4.46 (d, 2 H, *J* 11.7 Hz), 5.00 (m, 4 H), 5.73 (m, 2 H), 7.26 (m, 5 H);  $\delta_C$  (50 MHz; CDCl<sub>3</sub>) 35.4, 38.3, 72.4, 73.1, 116.3, 127.5, 128.3, 136.7; MS (EI) *m/z* 216 (M<sup>+</sup>) (Found: C, 83.35; H, 9.47. C<sub>15</sub>H<sub>20</sub>O requires C, 83.29; H, 9.32%).

**3-Deoxy-1,2:5,6-di-O-isopropylidene-3,3-C-[S-methylthio-carbonylmethylethylene]- $\alpha$ -D-ribo-hexofuranose (19)**

Following the general procedure for the preparation of xanthate, **6** (0.22 g, 0.73 mmol), NaH (0.059 g, 1.5 mmol) and CH<sub>3</sub>I (0.3 mL, 4.9 mmol) gave compound **19** (0.26 g, 92%);  $[\alpha]_D + 97$  (*c* 1.0 in CHCl<sub>3</sub>);  $\delta_H$  (200 MHz; CDCl<sub>3</sub>) 0.71 (t, 1 H, *J* 5.6 Hz), 1.27 (s, 6 H), 1.33 (m, 1 H), 1.36, 1.52 (2 s, 6 H), 1.81 (m, 1 H), 2.57 (s, 3 H), 3.72 (ddd, 1 H, *J* 9.3, 5.2, 6.4 Hz), 3.92 (dd, 1 H, *J* 5.2, 8.8 Hz), 4.05 (dd, 1 H, *J* 6.4, 8.8 Hz), 4.16 (d, 1 H, *J* 9.3 Hz), 4.32 (d, 1 H, *J* 3.9 Hz), 4.48 (dd, 1 H, *J* 9.3, 11.8 Hz), 4.97 (dd, 1 H, *J* 5.4, 11.8 Hz), 5.97 (d, 1 H, *J* 3.9 Hz);  $\delta_C$  (50 MHz; CDCl<sub>3</sub>) 13.7, 16.4, 18.8, 25.3, 26.7 (2C), 27.0, 34.5, 68.1, 75.0, 75.5, 79.0, 86.3, 104.7, 109.5, 111.9, 215.7 (Found: C, 52.23; H, 6.87; S, 16.63. C<sub>17</sub>H<sub>26</sub>O<sub>6</sub>S<sub>2</sub> requires C, 52.29; H, 6.71; S, 16.42%).

**3-Deoxy-1,2:5,6-di-O-isopropylidene-3-C-allyl-3-C-methylallyl- $\alpha$ -D-ribo-hexofuranose (20)**

By following the general procedure for diallylation, compound **1**<sup>11</sup> (0.2 g, 0.55 mmol), methylallyltri-*n*-butyltin (0.5 g, 1.4 mmol) and AIBN (5 mg) gave **20** (97 mg, 52%);  $[\alpha]_D + 57$  (*c* 0.7 in CHCl<sub>3</sub>);  $\delta_H$  (200 MHz; CDCl<sub>3</sub>) 1.32 (s, 3 H), 1.36 (s, 3 H), 1.43 (s, 3 H), 1.54 (s, 3 H), 1.86 (s, 3 H), 2.10 (d, 1 H, *J* 13.3 Hz), 2.35 (d, 1 H, *J* 13.3 Hz), 2.47 (d, 2 H, *J* 7.8 Hz), 3.89 (m, 2 H), 4.09–4.33 (m, 2 H), 4.49 (d, 1 H, *J* 3.9 Hz), 4.76 (s, 1 H), 4.91 (s, 1 H), 5.05 (s, 1 H), 5.11 (m, 1 H), 5.61 (d, 1 H, *J* 3.5 Hz), 6.02 (m, 1 H); MS (EI) *m/z* 338 (M<sup>+</sup>) (Found: C, 67.51; H, 8.90. C<sub>19</sub>H<sub>30</sub>O<sub>5</sub> requires C, 67.43; H, 8.93%).

**3-Deoxy-1,2:5,6-di-O-isopropylidene- $\alpha$ -D-ribo-hexofuranose-3-spiro-3-cyclopentene (21)**

Following the general procedure for RCM, compound **5** (0.10 g, 0.3 mmol) and Grubbs' catalyst (5 mg) in CH<sub>2</sub>Cl<sub>2</sub> (8 mL) gave

**21** (73 mg, 80%),  $[\alpha]_{\text{D}} + 43$  (*c* 0.9 in  $\text{CHCl}_3$ );  $\delta_{\text{H}}$  (200 MHz;  $\text{CDCl}_3$ ) 1.31 (s, 6 H), 1.40 (s, 3 H), 1.50 (s, 3 H), 1.79 (m, 1 H), 2.57 (m, 3 H), 3.96 (m, 2 H), 4.10 (m, 2 H), 4.24 (d, 1 H, *J* 3.7 Hz), 5.69 (m, 3 H);  $\delta_{\text{C}}$  (50 MHz;  $\text{CDCl}_3$ ) 25.4, 26.4, 26.7, 27.0, 34.9, 36.3, 55.1, 68.3, 74.5, 81.6, 87.2, 103.9, 109.2, 111.7, 127.3, 130.2; MS (EI) *m/z* 281 ( $\text{M} - \text{Me}$ )<sup>+</sup> (Found: C, 64.75; H, 8.23.  $\text{C}_{16}\text{H}_{24}\text{O}_5$  requires C, 64.84; H, 8.16%).

**3-Deoxy-1,2,5,6-di-O-isopropylidene- $\alpha$ -D-ribo-hexofuranose-3-spiro-3-(3-methylcyclopentene) (22)**

Following the general procedure for RCM, compound **20** (75 mg, 0.22 mmol) and Grubbs' catalyst (5 mg) in  $\text{CH}_2\text{Cl}_2$  (5 mL) gave **22** (52 mg, 75%)  $[\alpha]_{\text{D}} + 46$  (*c* 0.45 in  $\text{CHCl}_3$ );  $\delta_{\text{H}}$  (200 MHz;  $\text{CDCl}_3$ ) 1.25 (s, 3 H), 1.32 (s, 3 H), 1.41 (s, 3 H), 1.53 (s, 3 H), 1.73 (s, 3 H), 2.57 (m, 4 H), 3.97 (m, 2 H), 4.12 (m, 2 H), 4.26 (d, 1 H, *J* 3.4 Hz), 5.31 (br s, 1 H), 5.70 (d, 1 H, *J* 3.4 Hz);  $\delta_{\text{C}}$  (50 MHz;  $\text{CDCl}_3$ ) 25.4, 26.4, 26.7, 27.0, 29.7, 34.9, 40.7, 55.8, 68.2, 74.7, 81.8, 87.4, 104.1, 109.3, 111.8, 123.6, 136.9; MS (EI) *m/z* 295 ( $\text{M} - \text{Me}$ )<sup>+</sup> (Found: C, 65.82; H, 8.63.  $\text{C}_{17}\text{H}_{26}\text{O}_5$  requires C, 65.78; H, 8.44%).

**(3R)-3-Deoxy-1,2,5,6-di-O-isopropylidene- $\alpha$ -D-ribo-hexofuranose-3-spiro(3-oxocyclopentane) (23) and (3S)-3-deoxy-1,2,5,6-di-O-isopropylidene- $\alpha$ -D-ribo-hexofuranose-3-spiro-(3-oxocyclopentane) (24)**

To a solution of compound **21** (1.8 g, 6.1 mmol) in THF (10 mL) under  $\text{N}_2$ , was added  $\text{BH}_3 \cdot \text{SMe}_2$  (0.6 mL, 6.7 mmol) at 0 °C. After 2 h, a saturated aq. solution of sodium acetate and  $\text{H}_2\text{O}_2$  (30% solution, 0.8 mL, 7.3 mmol) were added at -15 °C. Solvent was removed and the residue extracted with EtOAc, washed with brine, dried ( $\text{Na}_2\text{SO}_4$ ), and concentrated. The crude product was purified on silica gel using light petroleum–EtOAc (3 : 2) to give a residue (1.6 g, 5.1 mmol) which was added to a solution of  $(\text{COCl})_2$  (1.0 mL, 10.2 mmol) and  $\text{Me}_2\text{SO}$  (1.6 mL, 20.4 mmol) in  $\text{CH}_2\text{Cl}_2$  (10 mL) under nitrogen at -78 °C. After 1 h at -78 °C,  $\text{Et}_3\text{N}$  (4.4 mL, 30.6 mmol) was added and allowed to attain rt. The reaction mixture was diluted with  $\text{CH}_2\text{Cl}_2$ , washed with water, brine, dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated. The crude product was purified on silica gel with light petroleum–EtOAc (5 : 1) to afford **23** (0.59 g),  $[\alpha]_{\text{D}} + 89.11$  (*c* 1.0 in  $\text{CHCl}_3$ );  $\delta_{\text{H}}$  (500 MHz;  $\text{CDCl}_3$ ) 1.33 (s, 6 H), 1.42, 1.55 (2 s, 6 H), 1.95 (d, 1 H, *J* 17.8 Hz), 2.17–2.32 (m, 2 H), 2.35–2.47 (m, 2 H), 2.50 (d, 1 H, *J* 17.8 Hz), 3.88 (dt, 1 H, *J* 8.9, 3.2 Hz), 3.95 (m, 2 H), 4.16 (m, 1 H), 4.24 (d, 1 H, *J* 3.7 Hz), 5.73 (d, 1 H, *J* 3.7 Hz);  $\delta_{\text{C}}$  (50 MHz;  $\text{CDCl}_3$ ) 25.1, 26.4, 26.7, 26.9, 36.4, 43.0, 53.1, 68.8, 74.2, 82.2, 86.1, 104.1, 109.7, 112.2, 216.2; MS (EI) *m/z* 297 ( $\text{M}^+ - \text{CH}_3$ ) (Found: C, 61.65; H, 7.46.  $\text{C}_{16}\text{H}_{24}\text{O}_6$  requires C, 61.52; H, 7.74%). Further elution afforded compound **24** (0.7 g),  $[\alpha]_{\text{D}} + 32.3$  (*c* 1.0 in  $\text{CHCl}_3$ );  $\delta_{\text{H}}$  (500 MHz;  $\text{CDCl}_3$ ) 1.31 (s, 6 H), 1.38 (s, 3 H), 1.52 (s, 3 H), 1.65 (m, 1 H), 2.17–2.32 (m, 2 H), 2.46 (m, 1 H), 2.54 (ABq, 2 H, *J* 17.5 Hz), 3.87 (d, 1 H, *J* 9.4 Hz), 3.95 (dd, 1 H, *J* 5.2, 8.6 Hz), 4.07 (ddd, 1 H, *J* 9.4, 5.2, 6.2 Hz), 4.18 (dd, 1 H, *J* 6.2, 8.6 Hz), 4.30 (d, 1 H, *J* 3.2 Hz), 5.79 (d, 1 H, *J* 3.2 Hz);  $\delta_{\text{C}}$  (50 MHz;  $\text{CDCl}_3$ ) 24.9, 25.5, 26.1, 26.4, 26.6, 36.7, 41.8, 52.6, 68.6, 73.8, 81.8, 86.6, 103.9, 109.6, 111.9, 215.8; MS (EI) *m/z* 297 ( $\text{M}^+ - \text{CH}_3$ ) (Found: C, 61.38; H, 7.54.  $\text{C}_{16}\text{H}_{24}\text{O}_6$  requires C, 61.52; H, 7.74%).

**(3R)-3-Deoxy-1,2,5,6-di-O-isopropylidene- $\alpha$ -D-ribo-hexofuranose-3-spiro[3-(hydroxyethylidene)cyclopentane] (25)**

Compound **23** (0.31 g, 1.0 mmol) in THF (4 mL) was added to a previously stirred solution of triethyl phosphonoacetate (0.25 mL, 1.3 mmol) and NaH (0.048 g, 1.2 mmol) in THF (5 mL) at 0 °C under  $\text{N}_2$ . After 0.5 h at rt, saturated aq.  $\text{NH}_4\text{Cl}$  was added and the solvent removed. The residue was extracted with EtOAc, washed with water, brine, dried and concentrated. The crude product was purified on silica gel by using light

petroleum–EtOAc (3 : 2). The resulting product (0.32 g) was added to DIBAL-H (2 M solution in toluene, 1.0 mL, 2 mmol) in  $\text{CH}_2\text{Cl}_2$  (8 mL) at -78 °C. After 0.5 h, saturated aq.  $\text{NH}_4\text{Cl}$  was added at -78 °C and the product diluted with  $\text{CH}_2\text{Cl}_2$ , washed with brine, dried and evaporated. The residue was passed through a short bed of silica gel eluting with EtOAc–light petroleum (1 : 1) to give **25** (0.26 g, overall yield for two steps 77%);  $\delta_{\text{H}}$  (200 MHz;  $\text{CDCl}_3$ ) 1.30, 1.32, 1.40, 1.52 (4 s, 12 H), 1.88–2.07 (m, 3 H), 2.29–2.60 (m, 3 H), 3.85–4.17 (m, 7 H), 5.58 (m, 1 H), 5.70 (m, 1 H);  $\delta_{\text{C}}$  (50 MHz;  $\text{CDCl}_3$ ) 25.2, 25.9, 26.3, 26.6, 26.8, 27.2, 27.5, 30.2, 32.6, 37.4, 55.0, 55.8, 59.9, 60.1, 68.4, 74.2, 81.1, 85.2, 85.4, 103.9, 109.2, 111.5, 121.5, 143.6; MS (EI) *m/z* 340 ( $\text{M}^+$ ) (Found: C, 63.59; H, 8.13.  $\text{C}_{18}\text{H}_{28}\text{O}_6$  requires C, 63.51; H, 8.29%).

**(3R)-3-Deoxy-1,2,5,6-di-O-isopropylidene- $\alpha$ -D-ribo-hexofuranose-3-spiro(3,3-diallylcyclopentane) (26)**

Following the general procedure for cyclopropanation, **25** (0.13 g, 0.38 mmol), a 1 M solution of  $\text{Et}_2\text{Zn}$  (1.1 mL, 1.14 mmol) and  $\text{CH}_2\text{I}_2$  (0.18 mL, 2.28 mmol) in dry  $\text{CH}_2\text{Cl}_2$  (5 mL) gave the cyclopropylmethanol derivative (85 mg) which was converted into the xanthate derivative with NaH (19 mg, 0.48 mmol),  $\text{CS}_2$  (0.06 mL, 0.96 mmol) and MeI (0.08 mL, 1.2 mmol). By following the general procedure for diallylation, the xanthate derivative (90 mg, 0.3 mmol), allyltri-*n*-butyltin (0.2 mL, 0.6 mmol) and AIBN (5 mg) gave **26** (26 mg, overall yield 19%),  $[\alpha]_{\text{D}} + 22.8$  (*c* 1.1 in  $\text{CHCl}_3$ );  $\delta_{\text{H}}$  (200 MHz;  $\text{CDCl}_3$ ) 0.97 (d, 1 H, *J* 14.4 Hz), 1.32, 1.34, 1.40, 1.50 (4 s, 12 H), 1.55–1.67 (m, 2 H), 1.75 (d, 1 H, *J* 14.4 Hz), 1.83–2.03 (m, 2 H), 2.15 (d, 4 H, *J* 6.4 Hz), 3.80–3.93 (m, 2 H), 4.01–4.20 (m, 2 H), 4.26 (d, 1 H, *J* 3.4 Hz), 4.94–5.10 (m, 4 H), 5.62 (d, 1 H, *J* 3.4 Hz), 5.66–5.92 (m, 2 H);  $\delta_{\text{C}}$  (50 MHz;  $\text{CDCl}_3$ ) 25.5, 26.5, 26.8, 27.1, 27.9, 35.5, 39.2, 43.3, 43.9, 45.7, 56.2, 69.1, 74.0, 82.8, 87.8, 104.1, 109.4, 111.9, 117.4, 135.4 (Found: C, 70.03; H, 9.13.  $\text{C}_{22}\text{H}_{34}\text{O}_5$  requires C, 69.81; H, 9.05%).

**(3R)-3-Deoxy-1,2,5,6-di-O-isopropylidene- $\alpha$ -D-ribo-hexofuranose-3-spirocyclopentane-3-spiro(3-cyclopentene) (27)**

Following the general procedure for RCM, compound **26** (22 mg, 0.06 mmol), and Grubbs' catalyst (3 mg) in  $\text{CH}_2\text{Cl}_2$  (5 mL) gave **27** (18 mg, 88%),  $[\alpha]_{\text{D}} + 22.7$  (*c* 0.5 in  $\text{CHCl}_3$ );  $\delta_{\text{H}}$  (200 MHz;  $\text{CDCl}_3$ ) 1.22 (d, 1 H, *J* 15.1 Hz), 1.32, 1.35, 1.41, 1.51 (4 s, 12 H), 1.55–1.74 (m, 2 H), 1.82–2.13 (m, 3 H), 2.34 (m, 4 H), 3.88 (m, 2 H), 4.11 (m, 2 H), 4.29 (d, 1 H, *J* 3.5 Hz), 5.62 (d, 1 H, *J* 3.5 Hz), 5.65 (s, 2H);  $\delta_{\text{C}}$  (50 MHz;  $\text{CDCl}_3$ ) 25.6, 26.6, 26.8, 27.2, 28.8, 39.5, 43.7, 47.0, 47.3, 50.3, 55.9, 69.1, 74.2, 83.1, 88.4, 104.3, 109.4, 111.8, 129.5, 130.0 (Found: C, 68.30; H, 8.69.  $\text{C}_{20}\text{H}_{30}\text{O}_5$  requires C, 68.55; H, 8.63%).

**(3S)-3-Deoxy-1,2,5,6-di-O-isopropylidene- $\alpha$ -D-ribo-hexofuranose-3-spiro(3,3-diallylcyclopentane) (29)**

Compound **29** was prepared from **(24)** (overall yield 8%) by following the same procedure described for **23**,  $[\alpha]_{\text{D}} + 47.5$  (*c* 1.0 in  $\text{CHCl}_3$ );  $\delta_{\text{H}}$  (200 MHz;  $\text{CDCl}_3$ ) 1.31, 1.33, 1.39, 1.49 (4 s, 12 H), 1.57 (m, 3 H), 1.76–1.92 (m, 3 H), 2.11 (d, 4 H, *J* 7.3 Hz), 3.75–3.93 (m, 2 H), 3.98–4.17 (m, 3 H), 4.98–5.08 (m, 4 H), 5.63 (d, 1 H, *J* 3.4 Hz), 5.72–5.93 (m, 2 H);  $\delta_{\text{C}}$  (50 MHz;  $\text{CDCl}_3$ ) 25.7, 26.5, 26.8, 27.2, 29.0, 35.9, 38.0, 43.9, 44.1, 44.3, 55.9, 69.1, 74.2, 82.6, 87.7, 104.4, 109.4, 111.6, 117.0, 117.3, 135.7, 135.9 (Found: C, 69.82; H, 9.15.  $\text{C}_{22}\text{H}_{34}\text{O}_5$  requires C, 69.81; H, 9.05%).

**(3S)-3-Deoxy-1,2,5,6-di-O-isopropylidene- $\alpha$ -D-ribo-hexofuranose-3-spirocyclopentane-3-spiro(3-cyclopentene) (30)**

Following the general procedure for RCM, compound **29** (30 mg, 0.08 mmol) and Grubbs' catalyst (4 mg) in  $\text{CH}_2\text{Cl}_2$  (5 mL) gave **30** (24 mg, 87%),  $[\alpha]_{\text{D}} + 38.9$  (*c* 0.85 in  $\text{CHCl}_3$ );  $\delta_{\text{H}}$  (200 MHz;  $\text{CDCl}_3$ ) 1.32, 1.34, 1.40, 1.49 (4 s, 12 H), 1.55–

1.87 (m, 4 H), 1.93 (d, 1 H, *J* 14.2 Hz), 2.11 (d, 1 H, *J* 14.2 Hz), 2.20–2.41 (m, 4 H), 3.79–3.94 (m, 2 H), 4.04–4.20 (m, 3 H), 5.63 (m, 3 H);  $\delta_C$  (50 MHz; CDCl<sub>3</sub>) 25.6, 26.5, 26.8, 27.1, 30.0, 39.9, 42.2, 46.6, 47.3, 49.0, 55.5, 69.0, 74.1, 82.9, 88.8, 104.3, 109.4, 111.6, 129.4, 130.0 (Found: C, 68.80; H, 8.78. C<sub>20</sub>H<sub>30</sub>O<sub>5</sub> requires C, 68.55; H, 8.63%).

**(5S)-(5-tert-Butyldiphenylsilyloxymethyl)-1-(toluene-4-sulfonyl)pyrrolidin-3-one (32)**

A mixture of compound **31** (2.3 g, 8.5 mmol), TBDPSCI (2.4 mL, 9.35 mmol) and imidazole (0.64 g, 9.35 mmol) in DMF (15 mL) was stirred overnight. The reaction mixture was diluted with water, extracted with EtOEt, dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated. The residue was passed through a short column of silica gel with light petroleum–ethyl acetate (4 : 1). The product (3.0 g, 5.9 mmol) was treated with PDC (3.0 g, 8.0 mmol) and powdered molecular sieves 4 Å (3.0 g) in CH<sub>2</sub>Cl<sub>2</sub> (100 mL). After stirring at rt for 4 h, the mixture was filtered through a bed of silica gel with EtOEt as eluent. The filtrate was concentrated and crystallized from CHCl<sub>3</sub> to give **32** (2.6 g, 60%); mp 144 °C;  $[a]_D^{25} + 34$  (*c* 1.0 in CHCl<sub>3</sub>); IR (CHCl<sub>3</sub>) 1764 cm<sup>-1</sup> (C=O);  $\delta_H$  (200 MHz; CDCl<sub>3</sub>) 1.00 (s, 9 H), 2.3 (m, 2 H), 2.42 (s, 3 H), 3.58 (dd, 1 H, *J* 2.3, 10.3 Hz), 3.82 (ABq, 2 H, *J* 18.7 Hz), 4.00 (dd, 1 H, *J* 3.3, 10.3 Hz), 4.32 (m, 1 H), 7.55 (m, 14 H);  $\delta_C$  (50 MHz; CDCl<sub>3</sub>) 19.0, 21.5, 26.6, 40.0, 54.0, 58.0, 67.9, 127.0–143.8, 208.6; MS (EI) *m/z* 450 (M<sup>+</sup> – 'Bu) (Found: C, 66.03; H, 6.68; N, 2.66; S, 6.46. C<sub>28</sub>H<sub>33</sub>NO<sub>4</sub>SSi requires C, 66.24; H, 6.55; N, 2.76; S, 6.32%).

**(5S,2E,Z)[(5-tert-Butyldiphenylsilyloxymethyl)-1-(toluene-4-sulfonyl)pyrrolidin-3-ylidene]ethanol (33)**

A solution of compound **32** (4.0 g, 7.9 mmol), Ph<sub>3</sub>P=CHCO<sub>2</sub>Et (5.48 g, 15.8 mmol) in benzene (25 mL) was heated under reflux for 24 h. Solvent was removed and the residue passed through a short column of silica gel with light petroleum–ethyl acetate (19 : 1) to give the  $\alpha,\beta$ -unsaturated ester (4.18 g) which was taken in CH<sub>2</sub>Cl<sub>2</sub> (50 mL) and cooled to –78 °C. DIBAL-H (2 M solution in toluene, 8.3 mL, 16.6 mmol) was introduced. After stirring at –78 °C for 45 min., excess DIBAL was quenched by addition of saturated solution of sodium potassium tartrate. The mixture was stirred at rt for 3 h, filtered, and concentrated. The product was purified on silica gel by using light petroleum–ethyl acetate (4 : 1) to give **33** (3.6 g, 85%);  $\delta_H$  (200 MHz; CDCl<sub>3</sub>) 1.08 (s, 9 H), 2.14–2.69 (m, 2 H), 2.43 (s, 3 H), 3.48–4.0 (m, 7 H), 5.43 (m, 1 H), 7.20–7.74 (m, 14 H);  $\delta_C$  (50 MHz; CDCl<sub>3</sub>) 19.0, 21.2, 26.6, 30.2, 34.6, 49.1, 52.7, 59.6, 60.6, 65.7, 66.1, 121.5–137.4, 143.1; MS (EI) *m/z* 478 (M<sup>+</sup> – 'Bu) (Found: C, 67.59; H, 7.12; N, 2.44; S, 5.78. C<sub>30</sub>H<sub>37</sub>NO<sub>4</sub>SSi requires C, 67.25; H, 6.96; N, 2.61; S, 5.98%).

**(2S)-(2-tert-Butyldiphenylsilyloxymethyl)-4,4'-diallyl-1-(toluene-4-sulfonyl)pyrrolidine (35)**

Cyclopropanation of **33** was done as described earlier using Et<sub>2</sub>Zn–CH<sub>2</sub>I<sub>2</sub> to give **34** (0.8 g, 78%);  $\delta_H$  (200 MHz; CDCl<sub>3</sub>) 0.10 (m, 1 H), 0.45 (m, 1 H), 0.75–2.0 (m, 3 H), 1.11 (s, 9 H), 2.44 (s, 3 H), 3.0–4.25 (m, 7 H), 7.30 (m, 14 H);  $\delta_C$  (50 MHz; CDCl<sub>3</sub>) 19.0, 21.2, 24.1, 24.6, 26.8, 30.6, 37.0, 51.0, 56.6, 60.5, 60.7, 62.5, 63.1, 65.5, 127.5–135.4, 143.0; MS (EI) *m/z*: 548 (M<sup>+</sup> – 1). Subsequent bromination and allylation reactions as per general procedure, afforded **35** (0.55 g, 66%) (contaminated with trace amount of tin reagent and used as such for the next reaction);  $\delta_H$  (200 MHz; CDCl<sub>3</sub>) 1.05 (s, 9 H), 1.59 (m, 3 H), 1.81 (dd, 1 H, *J* 3.1, 6.3 Hz), 2.06 (d, 2 H, *J* 6.3 Hz), 2.38 (s, 3 H), 3.16 (ABq, 2 H, *J* 10.9 Hz), 3.66 (m, 1 H), 3.79 (dd, 1 H, *J* 6.7, 10.1 Hz), 4.01 (dd, 1 H, *J* 3.3, 10.1 Hz), 4.8 (m, 4 H), 5.7 (m, 2 H), 7.1–7.6 (m, 14 H);  $\delta_C$  (75 MHz; CDCl<sub>3</sub>) 19.25, 21.4, 26.9, 38.85, 39.4, 40.7, 43.7, 58.2, 60.0, 66.3, 118.2, 127.3–136.0, 142.9; MS (EI) *m/z* 516 (M<sup>+</sup> – 'Bu).

**(3S)-[2-(Toluene-4-sulfonyl)-2-azaspiro[4.4]non-7-en-3-yl]-methanol (37)**

Compound **35** was subjected to RCM reaction to afford **36** (0.31 g, 96%);  $\delta_H$  (200 MHz; CDCl<sub>3</sub>) 1.06 (s, 9 H), 1.7–2.3 (m, 6 H), 2.43 (s, 3 H), 3.19 (ABq, 2 H, *J* 9.5 Hz), 3.60 (m, 1 H), 3.69 (t, 1 H, *J* 9.5 Hz), 4.11 (dd, 1 H, *J* 3.2, 9.5 Hz), 5.50 (m, 2 H), 7.2–7.7 (m, 14 H);  $\delta_C$  (50 MHz; CDCl<sub>3</sub>) 19.8, 22.1, 27.5, 42.6, 43.8, 44.8, 48.0, 61.2, 61.7, 67.0, 128.1–136.1, 141.7} and then treated with n-Bu<sub>4</sub>NF (1 M solution in THF, 1.5 mL, 1.5 mmol) in THF (5 mL) at rt for 1 h. Solvent was removed and the residue purified on a short silica gel column using light petroleum–ethyl acetate (4 : 1) to give **37** (0.16 g, 93%),  $[a]_D^{25} - 38$  (*c* 0.7 in CHCl<sub>3</sub>);  $\delta_H$  (200 MHz; CDCl<sub>3</sub>) 1.5–2.0 (m, 4 H), 2.32 (m, 2 H), 2.48 (s, 3 H), 3.32 (ABq, 2 H, *J* 9.7 Hz), 2.64 (m, 1 H), 2.76 (br d, 2 H), 5.42 (m, 1 H), 5.58 (m, 1 H), 7.35 (d, 2 H, *J* 7.7 Hz), 7.74 (d, 2 H, *J* 7.7 Hz);  $\delta_C$  (50 MHz; CDCl<sub>3</sub>) 21.3, 42.1, 42.5, 43.4, 46.8, 61.4, 62.1, 65.5, 127.4–129.4, 143.4; MS (EI) *m/z* 292 (M<sup>+</sup> – 1) (Found: C, 62.70; H, 7.02; N, 4.19; S, 10.26. C<sub>16</sub>H<sub>21</sub>NO<sub>3</sub>S requires C, 62.51; H, 6.89; N, 4.56; S, 10.43%).

**(3S)-[2-(Toluene-4-sulfonyl)-2-azaspiro[4.4]nonan-3-yl]-methanol (38)**

Compound **37** (0.155 g, 0.5 mmol) and 10% Pd/C (0.02 g) in methanol (5 mL) were stirred under hydrogen atmosphere at normal temperature and pressure (ntp) for 3 h. The catalyst was filtered and the filtrate concentrated to give **38** (0.15 g, 96%);  $[a]_D^{25} - 15$  (*c* 0.7 in CHCl<sub>3</sub>);  $\delta_H$  (200 MHz; CDCl<sub>3</sub>) 0.86 (m, 2 H), 1.52 (m, 6 H), 1.75 (m, 2 H), 2.46 (s, 3 H), 3.23 (ABq, 2 H, *J* 9.5 Hz), 3.58 (m, 1 H), 3.78 (br s, 2 H), 7.35 (d, 2 H, *J* 7.6 Hz), 7.73 (d, 2 H, *J* 7.6 Hz);  $\delta_C$  (50 MHz; CDCl<sub>3</sub>) 21.3, 24.1, 35.9, 36.4, 41.2, 48.0, 60.5, 62.2, 65.7, 127.3, 129.4, 133.9, 143.5 (Found: C, 61.93; H, 7.76; N, 4.39; S, 10.39. C<sub>16</sub>H<sub>23</sub>NO<sub>3</sub>S requires C, 62.11; H, 7.49; N, 4.53; S, 10.36%).

**(3S)-2-(Toluene-4-sulfonyl)-2-azaspiro[4.4]nonane-3-carboxylic acid (39)**

A mixture of **38** (0.13 g, 0.42 mmol), CH<sub>3</sub>CN (2 mL), CCl<sub>4</sub> (2 mL), H<sub>2</sub>O (2 mL), NaIO<sub>4</sub> (0.1 g, 1.32 mmol) and RuCl<sub>3</sub>(H<sub>2</sub>O)<sub>n</sub> (0.02 g) was vigorously stirred at rt for 2 h. The reaction mixture was filtered through a pad of celite, the filtrate concentrated and the residue purified on silica gel by using ethyl acetate afforded **39** (0.1 g, 77%);  $[a]_D^{25} - 67$  (*c* 0.7 in CHCl<sub>3</sub>); IR (CHCl<sub>3</sub>) 1726 (C=O), 3012 cm<sup>-1</sup> (OH);  $\delta_H$  (200 MHz; CDCl<sub>3</sub>) 1.18 (m, 2 H), 1.52 (m, 6 H), 2.05 (m, 2 H), 2.41 (s, 3 H), 3.18 (ABq, 2 H, *J* 9.1 Hz), 4.20 (t, 1 H, *J* 8.2 Hz), 7.29 (d, 2 H, *J* 9.1 Hz), 7.73 (d, 2 H, *J* 9.1 Hz), 10.7 (br. s, 1 H);  $\delta_C$  (50 MHz; CDCl<sub>3</sub>) 21.4, 24.3, 24.5, 35.8, 36.3, 42.5, 49.7, 59.1, 60.4, 127.6, 129.6, 134.7, 143.6, 177.0; MS (EI) *m/z* 278 (M<sup>+</sup> – CO<sub>2</sub>) (Found: C, 59.06; H, 6.80; N, 4.15; S, 9.63. C<sub>16</sub>H<sub>21</sub>NO<sub>4</sub>S requires C, 59.42; H, 6.54; N, 4.33; S, 9.91%).

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