

# Ring closing metathesis of a 4,6-diallyl-*myo*-inositol orthoformate as a model for an inositol cyclopolymer

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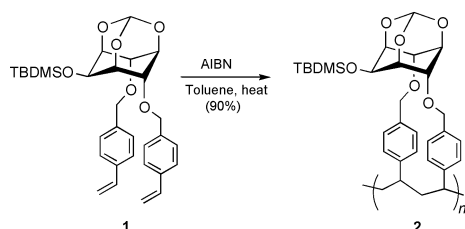
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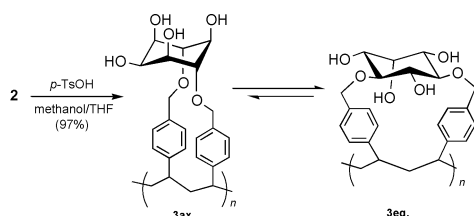
Ring closing metathesis (RCM) of the diallyl inositol derivative **5** gave the product **6** which after cleavage of the orthoester served as a model for assignment of the preferred conformation of the analogous deprotected inositol cyclopolymer **3**.

In the preceding Communication the cyclopolymerisation of the conformationally locked 4,6-bis(4-vinylbenzyl)-*myo*-inositol **1** to the novel cyclopolymer **2** was reported (Scheme 1).<sup>1</sup>



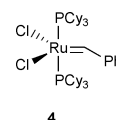
Scheme 1 Polymerisation of the monomer **1** to cyclopolymer **2**.

The rigid inositol unit of the monomer **1** acts as a template to bring both polymerisable styryl groups into close proximity for cyclopolymerisation. The monomer **1** was polymerised at high dilution (0.1 mmol ml<sup>-1</sup>) in toluene with 2–3 wt% of AIBN as a radical initiator to give a soluble linear cyclic polymer **2** in high yield (80–90%) with molecular weight  $M_n$  of 10 000–20 000 as determined by GPC.<sup>†</sup> It was hoped that removal of the orthoester and silyl groups would release a hydrophilic polymer with oriented functionality. Thus the polymer **2** was heated in a mixture of THF and methanol in the presence of toluene-*p*-sulfonic acid to give the hydroxylated polymer **3** (Scheme 2). The polymer **3** would be expected to exhibit interesting hydrophilic and metal binding properties if all five hydroxy groups remained axial **3ax**.<sup>2,3</sup> However, the alternative conformation **3eq**, would also be feasible. Unfortunately the polymer **3** shows very broad <sup>1</sup>H and <sup>13</sup>C NMR spectra, making the full conformational interpretation difficult, and hence conformational studies using model small molecules were carried out to gain insight into this feature.

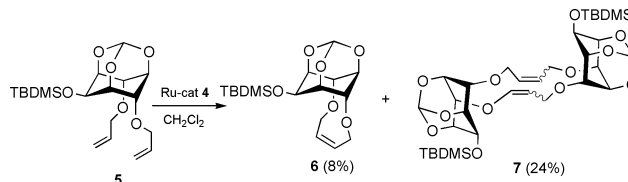


Scheme 2 Deprotection of polymer **2** to give two alternative conformations of **3**.

The model compounds were thought to be accessible by ring closing metathesis (RCM)<sup>4,5</sup> of the monomer **1** using the ruthenium based alkylidene catalyst **4**.<sup>6</sup> However, attempted ring closure of the monomer **1**, under high dilution (11.2 mM),



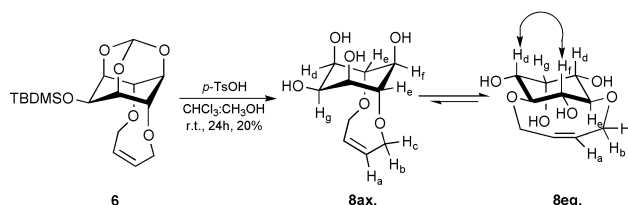
failed and gave only oligomeric products. This was ascribed to the rigid steric arrangement of the two styryl groups in a single unit of **1**, making the formation of another ring difficult. RCM of an alternative monomer with flexible alkyl linking groups was therefore carried out. The diallyl inositol **5** was formed in 78% yield by treating **1** with allyl bromide and sodium hydride in DMF. On treatment of the monomer **5** with the ruthenium initiator **4**, the ring closed product **6** and 'dimer' **7** were obtained, together with starting material (35%) and oligomeric products (Scheme 3). The double bond stereochemistry of these symmetrical products has not been assigned, but it is reasonable to assume that compound **6** has the *Z*-double bond configuration.



Scheme 3 RCM of the diallyl inositol **5**.

The RCM product **6** was deprotected to give the model compound **8** (Scheme 4).<sup>‡</sup>

Analysis of the <sup>1</sup>H NMR spectrum of the deprotected product **8** indicated that the preferred ring conformation was **8eq**. The protons H<sub>d</sub> (δ 3.20, dd, *J* 9 and 3), H<sub>e</sub> (δ 3.31, br t, *J* 9, 9) and H<sub>f</sub> (δ 2.92, dt, *J* 6 and 9) were all axial and the measured coupling constants were in good agreement with those predicted by computer modelling.<sup>7</sup> A strong <sup>1</sup>H NMR NOE effect was also observed between the signals due to H<sub>d</sub> and H<sub>f</sub> (see Scheme 4) and between H<sub>a</sub> (δ 5.75, br s) and H<sub>e</sub>.

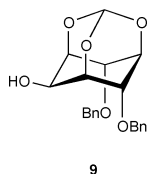


Scheme 4 Deprotection of the ring closed product **6** showing the observed NOE for **8eq**.

Variable temperature (VT) <sup>1</sup>H NMR experiments were carried out for both the deprotected RCM product **8** and the analogous 'dimer' in DMSO over the temperature range 300–330 K. However, although the signals due to the OH peaks altered as a result of the breaking of hydrogen bonds, there were

no dramatic changes in the other signals. This demonstrates the rigidity of the structure in inhibiting inositol ring-flipping.

The  $^1\text{H}$  NMR signals of the inositol ring protons of the 4,6-dibenzyl-*myo*-inositol orthoformate **9**<sup>5</sup> occurred at  $\delta$  4.45



(1H, m), 4.30 (2H, m) and 4.23 (3H, m) and resembled closely the analogous signals in the polymer **2** ( $\delta$  4.5–4.2, br multiplet), indicating that the ring conformation was maintained, as expected, in the polymer. The  $^1\text{H}$  NMR chemical shifts ( $\delta$  3.60–2.92) of the ring protons of the deprotected metathesis product **8eq**, are shifted upfield compared with those in the model **9**. Similarly the inositol ring protons of the deprotected polymer **3** ( $\delta$  3.7–3.0) are shifted upfield from which it is concluded that the inositol ring in **3** has the conformation **3eq**. The  $^{13}\text{C}$  NMR spectra peaks of **3** were too broad to be assigned.

In conclusion, we have established the conformation of the novel inositol polymer **3** using the model compound **8** prepared by ring closing metathesis. The  $^1\text{H}$  NMR analysis strongly

suggests that the polymer **3ax** is converted into **3eq** when deprotected.

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## Notes and references

† Full details of the synthesis and properties of polymers based on the monomer **1** will be described in a full paper.

‡ A similar sequence of reactions was carried out using 'dimer' **7**, and the spectroscopic properties of the inositol ring atoms were very similar to those discussed for the small ring analogue **6**.

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