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A formal synthesis of valiolamine from *myo*-inositol

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ABSTRACT

An efficient formal synthesis of racemic valiolamine starting from readily available *myo*-inositol is reported. In all the synthetic steps only one regioisomer is formed, which circumvents laborious purification of products. Regioselective benzylation of *myo*-inositol orthoformate, super-hydride mediated deoxygenation of a cyclitol derivative and stereoselective addition of dichloromethyllithium to an inosose are the key reactions in the synthesis.

1. Introduction

myo-Inositol (**1**), the most abundant cyclitol occurring in nature, plays an important role as structural basis for a number of secondary messengers in eukaryotic cells.[1] The cyclic polyol core as well as the well investigated regioselective reactions of *myo*-inositol and its derivatives[2] would be useful for the synthesis of compounds with potential biological, medicinal and material properties. *myo*-Inositol has been used as a starting material for the synthesis of natural products,[3] such as phosphatidyl inositol 3,4,5-trisphosphate (PIP_3), racemic tetrodotoxin, polyoxin J, and nojirimycin.

The attempts to synthesize useful products from *myo*-inositol and its derivatives, have been hampered by the formation of regioisomeric products due to the subtle differences in the reactivity of their hydroxyl groups as well as the *meso* configuration of *myo*-inositol, which requires either desymmetrization or resolution at some stage in the synthesis for accessing optically active products. We have addressed the former issue in our work, which resulted in the development of efficient methods for the synthesis of a diverse group of diastereomeric cyclitol derivatives and analogs from *myo*-inositol.[4] The regioselectivity in the O-alkylation of inositol derivatives was attributed to the chelation of the counter ion (lithium or sodium) used in the base, with the inositol derivatives

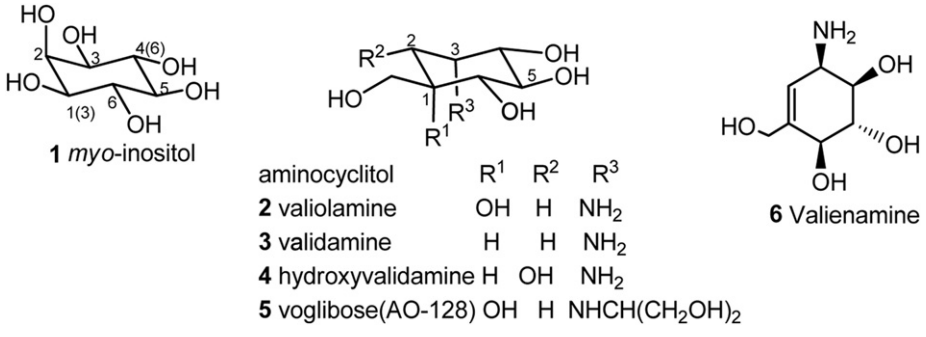

Fig. 1. Structure of *myo*-inositol and few aminocyclitols.

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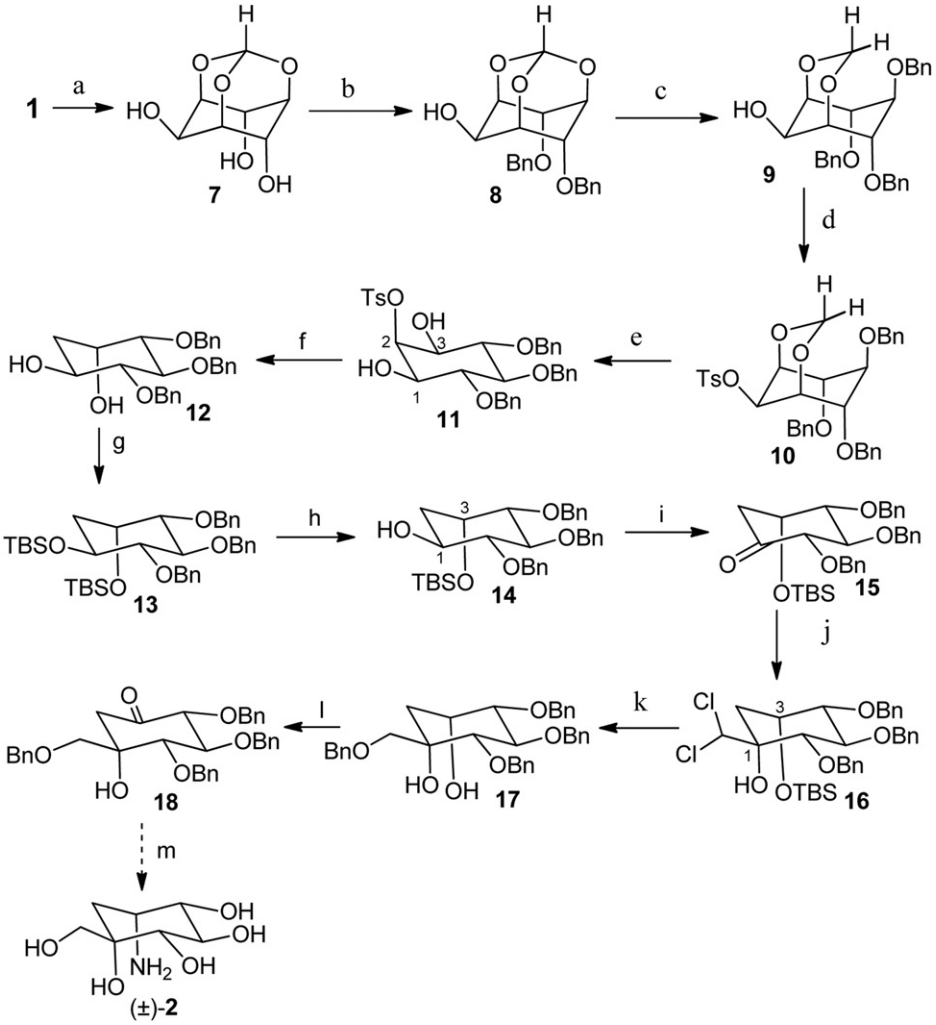
undergoing reactions. The aim of the current work is to demonstrate the flexibility, adaptability and utility of the reactions and synthetic methods developed earlier,[4] for the targeted synthesis. Accordingly we herein present results on the formal synthesis of valiolamine from *myo*-inositol.

2. Results and discussion

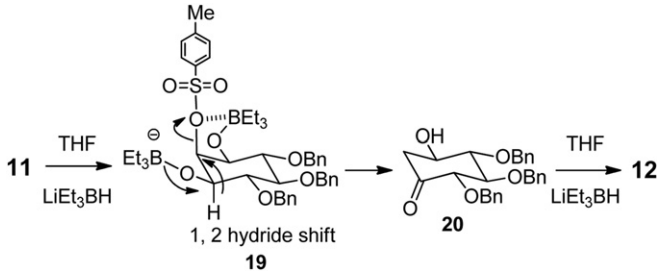
Valiolamine[5] (**2**, Fig. 1) is a pseudo-amino sugar first isolated from the fermentation broth of *Streptomyces hygroscopicus* subsp. *Limoneus* and was found to be more potent against α-glucosidase, maltase, *iso*-maltase and sucrase compared to valienamine, validamine, and hydroxyvalidamine. This subsequently resulted in extensive chemical modification of valiolamine and led to the preparation of voglibose **5** (coded as AO-128),[6] an orally active antidiabetic agent. A comparison of the structure of valiolamine and *myo*-inositol reveals that the relative orientation of the C4-, C5-, and C6-hydroxyl groups is same in both the molecules. To convert *myo*-inositol to racemic valiolamine, (a) the C2-hydroxyl group has to be replaced by a hydrogen; (b) C3(1)-hydroxyl group must be converted to an amino group with inversion of configuration at the C3(1)–carbon; (c) the C1(3)-hydroxyl group must be replaced by a hydroxymethyl group; and (d) the C1(3)-hydrogen must be replaced by a hydroxyl group. Key reactions in our synthetic approach to achieve these changes in *myo*-inositol were (i) lithium hydride mediated selective benzylation of the C4- and C6-hydroxyl groups of *myo*-inositol orthoformate **7**; (ii) a novel deoxygenation reaction of the tosylate **11**,[7] and (iii) stereospecific nucleophilic addition of dichloromethyllithium to the inosose **15** (Scheme 1).[3e]

myo-Inositol orthoformate **7** was obtained from *myo*-inositol using a known procedure;[8] the C4- and C6-hydroxyl groups were selectively benzylated using lithium hydride and benzyl bromide.[10] The dibenzyl ether **8** was converted to the tribenzyl ether **9** by transient protection of the C2-hydroxyl group to enable selective cleavage, of the orthoformate moiety[2e,f] (with DIBAL-H) to the corresponding formaldehyde acetal. Good yield could be obtained consistently for both the O-alkylation reactions (preparation of **8** and its PMB ether) on 10 g scale. The tribenzyl ether **9** was obtained in a yield of 90% over four steps from **8**. The free hydroxyl group in **9** was converted to the corresponding tosylate **10**, by heating with tosyl chloride in pyridine. Although tosylates of secondary alcohols are known to quaternize tertiary amines, such as pyridine, the tosylate **10** was stable at elevated temperatures in the presence of pyridine (Scheme 1, step 'd'), perhaps because of the rigidity imparted by the 1,3-acetal bridge on the molecule. Subjecting **10** to acetolysis using trifluoroacetic anhydride and acetic acid[11] resulted



Scheme 1. Reagents and conditions: (a) as in Ref. 8; (b) DMF, LiH, BnBr, rt, 25 h 30 min, 65%; (c) i. DMF, NaH, PMBCl, 0 °C to rt, 3 h; ii. DCM, DIBAL-H, 0 °C to rt, 4 h; iii. DMF, NaH, BnBr, 0 °C to rt, 1 h; iv DCM/H_2O, DDQ, 0 °C to rt, 5 h; 90% (over four steps); (d) Pyridine TsCl, DMAP, 80 °C, 9 h, 93%; (e) i. DCM, TFAA, AcOH, 0 °C to rt, 12 h; ii. K_2CO_3, MeOH, rt, 8 h, 90%; (f) THF, $LiEt_3BH$, 0 °C to rt; 4 h, 85%; (g) DCM, 2,6-lutidine, TBSOTf, 0 °C to rt, 90 min, 95%; (h) CSA, MeOH, 0 °C to rt; 35 min, 95%; (i) AcOEt, IBX, reflux, 8 h, 95%; (j) THF, LDA (2.0 equiv), CH_2Cl_2, −78 °C to 0 °C, 4 h, 82%; (k) i. DMSO, aq (nBu)$_4$NOH, rt, 8 min, then MeOH, $NaBH_4$, 0 to 5 °C, 20 min; ii. Bu_2SnO, MeOH, toluene, reflux, 24 h then BnBr, n-Bu_4NBr, toluene, reflux, 5 h, 43%; (l) AcOEt, IBX, reflux, 7 h, 65%; (m) as in Ref. 9.

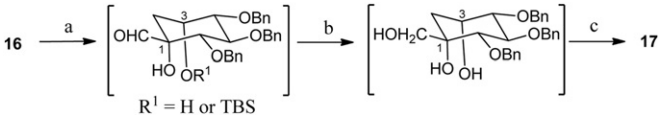
in cleavage of the methylidene acetal (with concomitant flipping of the carbocyclic ring[2e,f]) to furnish the diol **11** in good yield. Acid catalyzed solvolysis or hydrolysis of the acetal **10** (with HCl or TsOH in MeOH or THF) was very sluggish (50% conversion to **11** after boiling for 4–5 days). This indicated that protic acids are not strong enough to bring about cleavage of the acetal. Hence we had to use a stronger (Lewis) acid, acylium ion, to cleave the methylidene acetal in **10**. Reaction of the tosylate **11** with excess lithium triethylborohydride (super-hydride)[7] in THF resulted in the reduction of the tosylate and inversion of one of the hydroxyl groups through the in situ stereoselective reduction of the intermediate ketone **20** (Scheme 2), to give the protected racemic *vibo*-quercitol **12**.[12,13]



Scheme 2. Mechanism for the formation of the diol **12**.

In order to gain access to the axial TBS protected ketone **15**, the diol **12** was converted into the bis-silyl derivative **13** in quantitative yield using excess of TBSOTf and 2,6-lutidine in dichloromethane. The bis-silyl ether **13** was then subjected to regioselective deprotection of the equatorial TBS ether using an equimolar amount of camphorsulphonic acid in methanol, leaving the axial TBS ether unaffected. The free hydroxyl group in **14** was oxidized using IBX (2-iodoxy benzoic acid)[14] in refluxing ethyl acetate to give the desired ketone **15** in excellent yield. For the introduction of the equatorial hydroxymethyl group, the ketone **15** was reacted with dichloromethyllithium (generated by reacting lithium diisopropylamide with dichloromethane in THF at −78 °C)[3e,15] to get exclusively the dichloromethyl derivative **16**. The selectivity observed for the addition of dichloromethyllithium to the ketone **15**, is perhaps due to the presence of the bulky axial silyl ether, which restricts the approach of the nucleophile to one face of the ketone. It is also possible that the lithium ion chelates between the axial oxygen (of the TBS ether) and the carbonyl oxygen to aid in the formation of the product carrying an equatorial dichloromethyl group. This line of thought is supported by the fact that addition of dichloromethyllithium to the epimer of **15** (**26**, see below), which has an equatorial TBS ether resulted in the formation of a mixture of isomeric chlorooxiranes.

The dichloromethyl group in **16** was hydrolyzed with aqueous tetrabutylammonium hydroxide[3e,15] to get the corresponding aldehyde, which was reduced with sodium borohydride to obtain the hydroxymethyl derivative with concomitant cleavage of the TBS group. However, it is not clear whether the TBS ether was cleaved during the hydrolysis of the dichloromethyl derivative to the corresponding aldehyde or during the borohydride reduction of the aldehyde to the corresponding alcohol (Scheme 3). This hydroxymethyl derivative was converted to benzyloxymethyl derivative **17**[16] by its reaction with dibutyltin oxide (MeOH/toulene) followed by benzyl bromide. The secondary hydroxyl group in **17** was oxidized with IBX to obtain the racemic ketone **18**.[16] Synthesis of (+)-valiolamine as well as voglibose (AO-128) from (+)-**18** is reported in the literature.[9]

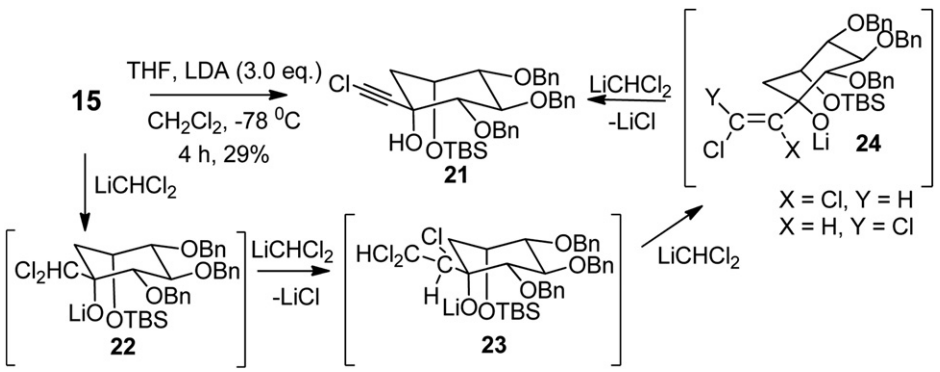


Scheme 3. Intermediates involved in the conversion of **16** to **17**. (a) DMSO, aq (*n*Bu)NOH, rt, 8 min; (b) MeOH, $NaBH_4$, 0–5 °C, 20 min; (c) Bu_2SnO, MeOH, toluene, reflux, 24 h then BnBr, *n*-Bu_4NBr, toluene, reflux, 5 h.

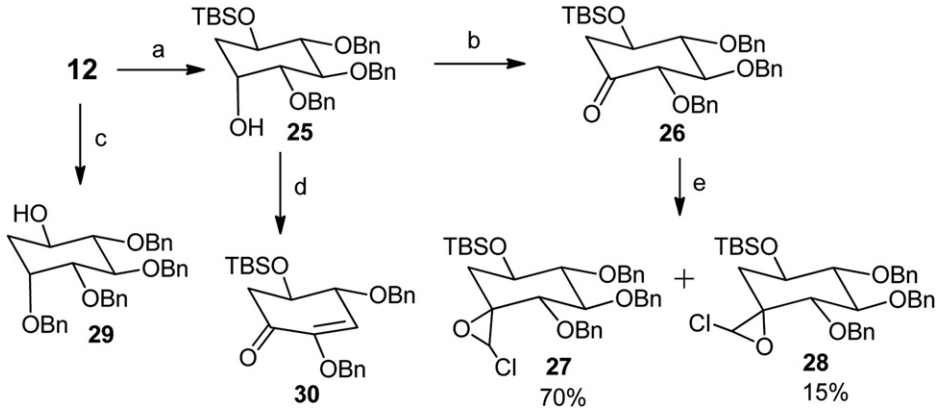
Initially, we carried out addition of dichloromethyllithium to the ketone **15** using 3 equiv of dichloromethyllithium. However results of these experiments were not consistent and in some trials we observed the formation of the alkyne **21** (29%), while major amount of **15** remained unreacted (Scheme 4). Formation of the chloroalkyne **21** (from **15** and dichloromethyllithium) is quite surprising and to the best of our knowledge this seems unprecedented in the literature. A plausible mechanism is depicted in Scheme 4. To circumvent this problem, amount of dichloromethyllithium was lowered to 2 M equiv, which produced the dichloromethyl derivative **16** consistently in good yield.

We also carried out silylation of **12** with 1 equiv of TBSOTf and its benzylation with sodium hydride and benzyl bromide (Scheme 5). The former reaction resulted in the formation of the equatorial TBS ether **25** exclusively, and benzylation gave the axial benzyl ether **29** as the major product. Similar instances of reversal of selectivity during the O-substitution reactions of cyclitol derivatives have been observed earlier.[4,10,17] Extensive investigation of the O-alkylation reaction of inositol derived diols and triols in our laboratory[4,10,17] had revealed that predominant O-alkylation occurs at a hydroxyl group situated adjacent to a *cis*-oxygen atom. Predominant formation of **29** from **12** is in agreement with our prior observations.[4,10,17]

Reaction of the ketone **26** with dichloromethyllithium (Scheme 5) resulted in the formation of two isomeric chlorooxiranes **27** and



Scheme 4. Unexpected formation of the alkyne **21** from the ketone **15**.



Scheme 5. Reagents and conditions: (a) DCM, 2,6-lutidine, TBSOTf, 0 °C to rt, 3 h, 83%; (b) AcOEt, IBX, reflux, 8 h, 85%; (c) NaH, BnBr, DMF, 0 °C to rt, 17 h, 60%; (d) i. AcOEt, IBX, reflux, 8 h; ii. silica gel, Et_3N, 79%; (e) THF, LDA, CH_2Cl_2, −78 °C to rt, 3 h 30 min.

28 (in the ratio 4.7:1), which were separable by column chromatography. The minor product, chlorooxirane **28**, could be crystallized from acetonitrile at room temperature. Single crystal X-ray diffraction analysis of these crystals revealed the axial disposition of the oxirane oxygen in **28** (see ESD). The ketone **26** was obtained by the oxidation of **25** with IBX and was purified by passing it through a small column of silica gel (in less than 2 h). Initially, we used silica gel pre-treated with triethylamine for the column chromatographic purification of the ketone **26**, since we were concerned that the acidity of the silica gel used, could cleave the TBS ether in **26**. However, this procedure resulted in the formation of the α,β-unsaturated ketone **30** probably through its enol form.

Although there are several reports[9,18] on the synthesis of valiolamine, only one report used *myo*-inositol as the starting material.[19] This synthesis involved the bio-deoxygenation of *myo*-inositol employing bacterial strains to produce mainly (−)-*vibo*-quercitol,[20] together with (−)-*epi*- and (−)-*proto*-quercitol. These quercitols (deoxyinositols) were then separated and purified by a combination of chromatography on ion-exchange-resin columns and subsequent recrystallization. (−)-*vibo*-Quercitol was then biochemically oxidized under the influence of *Gluconobacter* sp. AB10277. Apart from these laborious procedures, the synthesis also relies on the protection of *myo*-inositol hydroxyl groups as acetal/ketal, which leads to the formation of unwanted regioisomeric products during the synthesis.

3. Conclusion

A formal synthesis of racemic valiolamine from *myo*-inositol presented here demonstrates the utility and potential of the synthetic methods developed in our laboratory[4,10,17b,c] (for the selective reactions of inositol hydroxyl groups), for the targeted synthesis of cyclitol derivatives. Although we have used one type of protecting group (benzyl) for C4-, C5-, C6-hydroxyl groups (see **9**, Scheme 1), one can use orthogonal protection at these positions based on the chemistry developed earlier in our laboratory.[4] Use of orthogonal protection could in principle give access to a variety of derivatives or analogs of natural product, which has implications from structure–activity relationship point of view. Development of efficient methods for the desymmetrization of inositol derivatives is currently being investigated in our laboratory.

4. Experimental section

4.1. General methods

All the solvents were purified according to literature procedures[21] before use. All air or moisture sensitive reactions were carried out in an atmosphere of argon. Sodium hydride used in experiments was 60% suspension in mineral oil. In thin layer chromatography (TLC) spots were rendered visible either by shining UV light or by charring the plates with chromic acid solution. Column chromatographic separations (silica gel, 100–200 mesh) and flash column chromatographic separations (silica gel, 230–400 mesh) were carried out with light petroleum/ethyl acetate mixtures as eluent. For column chromatographic separation of compounds containing the PMB/TBS group (except for ketones **15** and **26**), the silica gel used was pre-eluted with a triethylamine/light petroleum (1:49, 3–5 mL/g) mixture. Work-up 'as usual' implies washing of the organic layer with water followed by brine, drying the organic extract over anhydrous sodium sulfate, and removal of the solvent under reduced pressure using a rotary evaporator. All the melting points reported are uncorrected. All the asymmetrically substituted *myo*-inositol derivatives reported are racemic; however only one of the enantiomers is shown in all the schemes.

4.2. Experimental procedure and characterization data for compounds

*4.2.1. 4,6-Di-O-benzyl-myo-inositol-1,3,5-orthoformate (**8**).* To a solution of the orthoformate **7** (10.0 g, 52.63 mmol) in DMF (500 mL) was added lithium hydride (1.68 g, 210.52 mmol) at ambient temperature and stirred for 90 min. To the above thick slurry, benzyl bromide (13.77 mL, 115.78 mmol) was added and stirred for 24 h. Ice was added to reaction mixture and stirred for 5 h, solvents were removed under reduced pressure and the residue worked up with ethyl acetate 'as usual'. The crude product was crystallized from ethyl acetate to afford the dibenzyl ether **8** (12.7 g, 65%). Mp 122–124 °C (lit.[8c] Mp 124–125 °C).

*4.2.2. 4,5,6-Tri-O-benzyl-1,3-methylidene-myo-inositol (**9**).* To an ice cooled solution of the dibenzyl ether **8** (10.1 g, 27.27 mmol) in DMF (100 mL) was added sodium hydride (2.18 g, 54.53 mmol) followed by 4-methoxybenzyl chloride (5.55 mL, 40.9 mmol) and the reaction mixture was stirred for 3 h at ambient temperature. Ice was added to reaction mixture and solvents were removed under reduced pressure and the residue worked up 'as usual' with ethyl acetate to obtain crude PMB ether (16 g).

This crude PMB ether (16 g) was taken in dichloromethane (70 mL), cooled using ice bath and DIBAL-H (68.2 mL, 1.0 M soln in toluene) was added and the resulting mixture was stirred at ambient temperature for 4 h. The reaction mixture was poured onto a rapidly stirred, cooled solution of saturated aq ammonium chloride (200 mL) and sodium potassium tartarate (150 g in 250 mL of water). Ethyl acetate (400 mL) was added to it and stirred for 12 h at

ambient temperature. The two layers were separated and the aqueous layer was extracted with ethyl acetate (3×300 mL); the combined organic layers were washed with brine, dried over anhydrous sodium sulfate, solvent was evaporated under reduced pressure to afford the crude benzylidene acetal (17 g).

The crude acetal (17 g) was taken in DMF (100 mL) cooled using an ice bath and sodium hydride (2.18 g, 54.53 mmol) was added followed by benzyl bromide (4.86 mL, 40.9 mmol), and the mixture was stirred for 1 h at ambient temperature. Ice was added to the reaction mixture, solvents were removed under reduced pressure; the residue obtained was taken in ethyl acetate and worked up 'as usual' to afford the crude tribenzyl ether (18 g).

To an ice cooled solution of the crude tribenzyl ether (9 g) in DCM/H_2O (300:3 mL), DDQ (4.64 g, 20.45 mmol) was added and stirred at ambient temperature for 5 h. The reaction mixture was diluted with DCM (200 mL) and washed with 40% aq sodium hydrogen carbonate solution (2×400 mL), followed by brine and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (gradient elution: ethyl acetate/light petroleum 2:8–3:7) to afford **9** (5.68 g, 90%) as a solid. Mp 76–78 °C; IR ($CHCl_3$): $\bar{\nu}$ 3250–3550 (OH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.40–7.26 (m, 15H), 4.92 (d, J=7.0 Hz, 1H), 4.84 (d, J=7.0 Hz, 1H), 4.77 (s, 2H), 4.71 (d, J=11.6 Hz, 2H), 4.57 (d, J=11.6 Hz, 2H), 4.09 (d, J=2.5 Hz, 2H), 3.97 (d, J=7.6 Hz, 2H), 3.83 (m, which becomes t, J=2.3 Hz on D_2O exchange, 1H), 3.68 (t, J=7.7 Hz, 1H), 3.21 (d, J=10.7 Hz, OH, 1H) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 138.2, 137.2, 128.4, 128.2, 127.89, 127.86, 127.8, 127.6, 127.5, 85.2, 81.3, 75.2, 74.5, 71.5, 62.9 ppm. Elemental Anal. $C_{28}H_{30}O_6$ (462.53) calcd C, 72.71; H, 6.54 found C, 72.74; H, 6.65%.

*4.2.3. 4,5,6-Tri-O-benzyl-1,3-methylidene-2-O-tosyl-myo-inositol (**10**).* The *myo*-alcohol **9** (9.5 g, 20.54 mmol), pyridine (25 mL), tosyl chloride (9.79 g, 51.35 mmol), and DMAP (0.1 g) were heated at 80 °C for 9 h. The reaction mixture was cooled to ambient temperature, ice was added and the solvent was removed under reduced pressure, the residue was taken in ethyl acetate and worked up as usual. The crude product was purified by flash column chromatography (eluent: ethyl acetate/light petroleum 1:4) to afford the tosylate **10** (11.8 g, 93%) as a gum. In a few trials on a lower scale (3 g of **9**) the tosylate **10** was obtained as a solid, Mp 76–77 °C (crystals from ethyl acetate/light petroleum); ^1H NMR (200 MHz, $CDCl_3$): δ 7.87–7.73 (m, 2H), 7.40–7.15 (m, 17H), 5.03 (d, J=6.0 Hz, 1H), 4.92–4.83 (m, 2H), 4.58 (s, 2H), 4.50 (d, J=11.7 Hz, 2H), 4.41 (d, J=11.7 Hz, 2H), 4.15 (br s, 2H), 3.90 (br d, J=4.4 Hz, 2H), 3.63 (t, J=4.5 Hz, 1H) 2.36 (s, 3H) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 145.0, 137.8, 137.2, 133.4, 129.8, 128.3, 127.9, 127.8, 127.72, 127.67, 85.3, 80.8, 78.7, 73.0, 72.6, 71.7, 71.4, 21.5 ppm. Elemental Anal. $C_{35}H_{36}O_8S$ (616.72): calcd C, 68.16; H, 5.88 found C, 67.80; H, 5.86%.

*4.2.4. 4,5,6-Tri-O-benzyl-2-O-tosyl-myo-inositol (**11**).* To an ice cooled solution of the tosylate **10** (7.0 g, 11.35 mmol) in dichloromethane (15 mL), trifluoroacetic anhydride (6.31 mL, 45.40 mmol) was added followed by glacial acetic acid (2.6 mL, 45.40 mmol) and stirred at ambient temperature for 12 h. The reaction mixture was cooled (ice bath), and potassium carbonate was added and stirred for 4 h (till the pH was neutral, as indicated by pH paper). The resulting mixture was passed through a bed of Celite and the filtrate was concentrated. The residue obtained (10 g) was taken in THF/MeOH (1:1, 20 mL) and potassium carbonate (6.3 g, 45.40 mmol) was added, stirred for 8 h. Ice was added to the reaction mixture, solvents were removed under reduced pressure and the residue was worked up with ethyl acetate 'as usual'. The crude product was flash column chromatoghraphed (eluent: ethyl acetate/light petroleum, 2:3) to afford the diol **11** (6.17 g, 90%) as a colorless solid. Mp 133.5–135.5 °C; IR ($CHCl_3$): $\bar{\nu}$ 3550–3500, 3500–3400 (OH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.85–7.75 (m, 2H), 7.40–7.27 (m, 17H), 5.08 (t, J=2.0 Hz, 1H), 4.86 (s, 2H), 4.87 (d, J=11.1 Hz, 2H), 4.72 (d, J=11.1 Hz, 2H), 3.75–3.60 (m, 4H), 3.55–3.43 (m, 1H), 2.45 (s, CH_3, 3H), 2.40 (d, J=2.0 Hz, OH, 2H) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 144.5, 138.1, 133.6, 129.4, 128.4, 128.3, 128.1, 127.9, 127.8, 127.7, 127.6, 82.8, 82.1, 81.4, 75.5, 75.4, 69.9, 21.6 ppm. Elemental Anal. $C_{34}H_{36}O_8S$ (604.71): calcd C, 67.53; H, 6.00 found C, 67.28; H, 6.04%.

*4.2.5. Racemic 1,5,6-tri-O-benzyl-3-deoxy-myo-inositol (2,3,4-tri-O-benzyl-vibo-quercitol, **12**).* To an ice cooled solution of the tosylate **11** (3.0 g, 4.96 mmol), in THF (20 mL) was added lithium triethylborohydride (super-hydride) (19.8 mL, 1.0 M soln in THF, 19.8 mmol) and stirred at ambient temperature for 4 h. Ice was added to the reaction mixture and the solvent evaporated under reduced pressure; the residue obtained was worked up with ethyl acetate 'as usual'. The crude product was purified by flash column chromatography (eluent: ethyl acetate/light petroleum, 2:3) to afford the racemic diol **12**[12] (1.83 g, 85%) as a colorless solid. Mp 100.5–102.5 °C; IR (Neat): $\bar{\nu}$ 3600–3200 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.45–7.27 (m, 15H), 5.01 (d, J=11.4 Hz, 1H), 4.92 (d, J=10.7 Hz, 1H), 4.82 (d, J=10.7 Hz, 1H), 4.78–4.63 (m, 3H), 4.17–4.08 (m, 1H), 4.05–3.90 (m, 1H), 3.84 (t, J=9.3 Hz, 1H), 3.50 (dd, J=9.3 and 3.1 Hz, 1H), 3.27 (t, J=9.3 Hz, 1H), 2.48 (br s, OH, 1H), 2.40–2.17 (m, 1OH, 2H), 1.48–1.28 (m, 1H) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 138.5, 137.8, 128.4, 128.3, 127.8, 127.7, 127.5, 86.1, 83.1, 81.4, 75.6, 75.3, 72.6, 67.8, 65.8, 33.7 ppm. Elemental Anal. $C_{27}H_{30}O_5$ (434.52): calcd C, 74.63; H, 6.96 found C, 74.29; H, 6.71%.

*4.2.6. Preparation of diTBS ether **13**.* To an ice cooled solution of the diol **12** (3.0 g, 6.90 mmol) in dichloromethane (10 mL), 2,6-lutidine (2.0 mL, 17.26 mmol) was added followed by TBSOTf (3.65 mL, 15.88 mmol). Resulting reaction mixture was stirred at room temperature for 90 min. Ice was added to the reaction mixture, and worked up 'as usual' with dichloromethane. The crude product was purified by column chromatography (eluent: ethyl acetate/light petroleum, 1:9) to afford racemic **13** (4.34 g, 95%) as a gum. ^1H NMR (200 MHz, $CDCl_3$): δ 7.40–7.20 (m, 15H), 4.92–4.72 (m, 4H), 4.68 (s, 2H), 4.20–4.00 (m, 2H), 3.86 (t, J=9.5 Hz, 1H), 3.38–3.24 (m, 2H), 2.05–1.87 (m, 1H), 1.50–1.30 (m, 1H), 0.89 (s, 18H), 0.08 (s, 3H), 0.06 (s, 6H), 0.04 (s, 3H) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 139.1, 139.0, 138.6, 128.2, 128.1, 127.9, 127.7, 127.5, 127.3, 127.2, 87.0, 83.3, 81.4, 75.8, 75.7, 72.9, 70.4, 67.6, 38.4, 25.9, 25.8, 18.1, 18.0, −4.4, −4.5, −4.6, −5.2 ppm. Elemental Anal. calcd $C_{39}H_{58}O_5Si_2$ (663.05) C, 70.65; H, 8.82 found C, 70.58; H, 8.66%.

*4.2.7. Preparation of the racemic TBS ether **14**.* To an ice cooled solution of the diTBS ether **13** (1.54 g, 2.32 mmol) in methanol (16 mL) was added camphorsulphonic acid (0.54 g, 2.32 mmol) and stirred at ambient temperature for 35 min. The acid was neutralized by the addition of triethylamine (0.5 mL), the reaction mixture was concentrated under reduced pressure and the residue was worked up with ethyl acetate 'as usual'. The crude product was purified by column chromatography (eluent: ethyl acetate/light petroleum, 1:6) to afford the racemic TBS ether **14** (1.21 g, 95%) as a gum. IR ($CHCl_3$): $\bar{\nu}$ 3300–3600 (OH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.41–7.23 (m, 15H), 5.08–4.90 (m, 2H), 4.85–4.57 (m, 4H), 4.25–4.15 (m, 1H), 4.05–3.85 (m, 2H), 3.43–3.20 (m, 2H), 2.26 (br s, OH, 1H), 2.15–1.95 (m, 1H), 1.45–1.22 (m, 1H), 0.88 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 138.71, 138.67, 138.5, 128.6, 128.3, 128.2, 128.1, 128.0, 127.9, 127.5, 127.4, 86.6, 83.6, 81.4, 75.5, 72.6, 68.4, 67.2, 35.9, 25.8, 18.1, −4.6, −5.0 ppm. Elemental Anal. calcd for $C_{33}H_{44}O_5Si$ (548.78) C, 72.22; H, 8.08 found C, 71.93; H, 7.79%.

*4.2.8. Preparation of the ketone **15**.* A mixture of the TBS ether **14** (1.1 g, 2.00 mmol), ethyl acetate (15 mL), and IBX (1.68 g,

6.00 mmol) was refluxed for 8 h. The reaction mixture was cooled to room temperature and passed through a bed of Celite. The bed of Celite was washed with ethyl acetate (2×50 mL), and the combined filtrate was evaporated under reduced pressure. The residue was purified by passing through a short column of silica gel (eluent: ethyl acetate/light petroleum, 1:9) to afford the racemic ketone **15** (1.05 g, 95%) as a gum. IR ($CHCl_3$): $\bar{\nu}$ 1737 (C=O) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.45–7.20 (m, 15H), 5.00–4.78 (m, 3H), 4.74 (s, 2H), 4.57 (d, J=11.7 Hz, 1H), 4.32–4.25 (m, 1H), 4.15–3.95 (m, 2H), 3.68 (dd, J=2.0 and 8.3 Hz, 1H), 2.55–2. 35 (m, 2H), 0.86 (s, 9H), 0.05 (s, 6H) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 203.7, 138.4, 138.1, 137.8, 128.3, 128.2, 128.05, 128.03, 127.64, 127.59, 127.5, 85.6, 82.1, 81.7, 75.7, 73.3, 72.9, 67.7, 45.0, 25.6, 18.0, −4.62, −5.16 ppm. Elemental Anal. $C_{33}H_{42}O_5Si$ (546.77): calcd C, 72.49; H, 7.74 found C, 72.15; H, 8.12%.

*4.2.9. Preparation of the racemic dichloromethyl derivative **16**.* To a cooled (dry ice-acetone, −78 °C) solution of LDA (1.17 mL, 2.0 M soln in THF/heptanes/ethyl benzene, 2.34 mmol) in THF (4.0 mL) was added dichloromethane (0.75 mL, 11.7 mmol) followed by (after 5 min) a solution of the ketone **15** (0.64 g, 1.17 mmol) in THF (4.0 mL). The reaction mixture was stirred at −78 °C for 2 h and then at 0 °C for 2 h. To the reaction mixture, a saturated solution of aq ammonium chloride (3.0 mL) was added, and concentrated under reduced pressure; the residue was worked up with ethyl acetate 'as usual'. The crude product was purified by flash column chromatography (eluent: ethyl acetate/light petroleum, 1:33) to afford racemic **16** (0.60 g, 82%) as a gum, which converted to a solid on storing in a refrigerator. Mp 59–60 °C (crystallized from pentane at rt); IR ($CHCl_3$): $\bar{\nu}$ 3500–3200 (OH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.45–7.15 (m, 15H), 5.94 (s, 1H), 5.08 (s, OH, 1H), 5.04 (d, J=11Hz, 1H), 4.97 (d, J=10.7 Hz, 1H), 4.86 (d, J=10.7 Hz, 1H), 4.83–4.62 (m, 3H), 4.44–4.36 (m, 1H), 4.21 (t, J=9.6 Hz, 1H), 3.84 (d, J=9.5 Hz, 1H), 3.42 (dd, J=9.6 and 2.8 Hz, 1H), 2.27 (dd, J=14.9 and 3.7 Hz, 1H), 1.79 (dd, J=14.9 and 2.4 Hz, 1H), 0.90 (s, 9H), 0.11 (s, 6H) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 138.3, 138.1, 138.0, 128.32, 128.27, 127.89, 127.86, 127.7, 127.63, 127.59, 127.56, 82.6, 81.9, 81.1, 79.5, 75.9, 75.7, 73.5, 70.1, 30.2, 25.7, 18.1, −4.5, −5.5 ppm. Mass calcd M (+Na) 653.23 found 653.26. Elemental Anal. calcd for $C_{34}H_{44}Cl_2O_5Si$ (630.23) C, 64.65; H, 7.02 found C, 64.59; H, 6.74%.

*4.2.10. Preparation of the racemic diol **17**.* To a solution of the dichloromethyl derivative **16** (0.23 g, 0.36 mmol) in DMSO (3 mL) was added *n*-tetrabutylammonium hydroxide (1.3 mL, 35% solution in H_2O, 1.82 mmol), at ambient temperature and stirred for 8 min. The reaction mixture was poured into a saturated solution of aq ammonium chloride (20 mL), diluted with ethyl acetate, and worked up with ethyl acetate 'as usual'. The residue obtained was taken in methanol (60 mL), cooled using ice bath and a solution of sodium borohydride (0.016 g, 0.44 mmol) in H_2O (12 mL) was added and stirred at 0–5 °C for 20 min. Acetone (2.0 mL) was added to the reaction mixture, stirred for 10 min and concentrated under reduced pressure. The residue was worked up with ethyl acetate 'as usual'. The crude product was purified by column chromatography (eluent: ethyl acetate/light petroleum, 4:1) to afford the racemic triol (0.09 g) as a thick gum.

A mixture of the triol (0.075 g, 0.16 mmol), dibutyltin oxide (0.046 g, 0.19 mmol), toluene (1 mL), methanol (1 mL) was refluxed for 24 h. The reaction mixture was cooled to ambient temperature, concentrated under reduced pressure and the residue co-evaporated with toluene (2×3 mL). To the residue, toluene (2.0 mL), benzyl bromide (0.038 mL, 0.32 mmol), and *n*-tetrabutylammonium bromide (0.01 g, 0.032 mmol) were added and refluxed for 5 h. The reaction mixture was cooled to ambient temperature, concentrated under reduced pressure and the residue was purified by column chromatography (100–200 mesh silica gel, eluent: ethyl acetate/light petroleum, 3:7) to afford the racemic tetrabenzyl ether **17**[16] (0.075 g, 43%) as a low melting solid. IR ($CHCl_3$): $\bar{\nu}$ 3650–3150 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.45–7.15 (m, 20H), 4.99 (d, J=10.6 Hz, 1H), 4.92 (d, J=11 Hz, 1H), 4.84 (d, J=10.6 Hz, 1H), 4.75 (s, 2H), 4.55 (d, J=11 Hz, 1H), 4.45 (d, J=11.9 Hz, 1H), 4.38 (d, J=11.9 Hz, 1H), 4.25–4.05 (m, 2H), 3.67 (d, J=9.6 Hz, 1H), 3.57–3.37 (m, 2×OH, 4H), 3.19 (d, J=8.6 Hz, 1H), 2.05 (dd, J=3.2 and 15.4 Hz, 1H), 1.85 (dd, J=2.8 and 15.4 Hz, 1H) ppm.

*4.2.11. Preparation of the racemic ketone **18**.* A mixture of the diol **17** (0.016 g, 0.029 mmol), IBX (0.024 g, 0.087 mmol) and ethyl acetate (3 mL) was refluxed for 7 h. The reaction mixture was cooled to ambient temperature and passed through a bed of Celite and washed with ethyl acetate (2×15 mL), concentrated under reduced pressure. The crude residue was purified by column chromatography (100–200 silica gel, eluent: ethyl acetate/light petroleum, 1:3) to afford the racemic ketone **18**[16] (0.01 g, 65%) as a solid. Mp 91–92 °C (crystals from Et_2O/light petroleum (1:2) at rt); IR ($CHCl_3$): $\bar{\nu}$ 3600–3250 (OH), 1738 (C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.50–7.27 (m, 18H), 7.23–7.13 (m, 2H), 5.05–4.90 (m, 3H), 4.74 (d, J=10.8 Hz, 1H), 4.61–4.52 (m, 2H), 4.47 (d, J=11.8 Hz, 1H), 4.41 (d, J=11.8 Hz, 1H), 4.19–4.10 (m, 1H), 4.09–3.97 (m, 2H), 3.53 (d, J=8.8 Hz, 1H), 3.15 (d, J=8.8 Hz, 1H), 2.84 (d, J=14.5 Hz, 1H), 2.47 (d, J=14.5 Hz, 1H), 2.40 (br s, D_2O exchangeable, OH, 1H) ppm.

*4.2.12. Preparation of the alkyne **21**.* To a cooled (dry ice-acetone, −78 °C) solution of LDA (2.88 mL, 2.0 M soln in THF/heptanes/ethyl benzene, 5.76 mmol) in THF (6.0 mL) was added dichloromethane (1.23 mL, 19.2 mmol) followed by (after 5 min) a solution of the ketone **15** (1.05 g, 1.92 mmol) in THF (6.0 mL). The reaction mixture was stirred at −78 °C for 4 h. To the reaction mixture a saturated solution of aq ammonium chloride (8.0 mL) was added and concentrated under reduced pressure, the residue was worked up with ethyl acetate 'as usual'. The crude product was purified by flash column chromatography (eluent: ethyl acetate/light petroleum, 1:33) to afford starting ketone **15** (0.63 g, 60%) and the racemic **21** (0.37 g, 29%) as a solid. Mp 93–95 °C (crystals from light petroleum at rt); IR (Nujol): $\bar{\nu}$ 3500–3250 (OH), 2229 (C≡C) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.50–7.27 (m, 15H), 4.92 (s, 2H), 4.89 (s, 2H), 4.84 (s, D_2O exchangeable, OH, 1H), 4.79 (d, J=11.6 Hz, 1H), 4.69 (d, J=11.6 Hz, 1H), 4.30–4.20 (m, 1H), 4.07 (t, J=9.6 Hz, 1H), 3.50 (d, J=9.5 Hz, 1H), 3.36 (dd, J=9.7 and 2.7 Hz, 1H), 2.32 (dd, J=15.0 and 3.6 Hz, 1H), 1.75 (dd, J=15.0 and 2.2 Hz, 1H), 0.88 (s, 9H), 0.08 (s, 6H) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 138.6, 138.1, 138.0, 128.5, 128.3, 128.2, 127.9, 127.7, 127.6, 127.53, 127.49, 86.2, 82.2, 79.6, 76.2, 75.9, 73.6, 71.6, 70.9, 70.6, 62.3, 39.7, 25.6, 18.0, −4.5, −5.5 ppm. Mass calcd M (+Na) 629.26; observed 629.25. Elemental Anal. $C_{35}H_{43}ClO_5Si$ (606.26): calcd C, 69.23; H, 7.14 found C, 69.15; H, 6.90%.

*4.2.13. Preparation of the racemic TBS ether **25**.* To a cooled (ice and salt mixture) mixture of the diol **12** (1.02 g, 2.35 mmol), dichloromethane (5 mL), and 2,6-lutidine (0.68 mL, 5.86 mmol) was added TBSOTf (0.8 mL, 3.52 mmol) and the reaction mixture was allowed to warm upto 10 °C over 1 h and then stirred at ambient temperature for 2 h. Ice was added to the reaction mixture, diluted with dichloromethane and worked up as usual. The crude product was purified by flash column chromatography (eluent: ethyl acetate/light petroleum, 1:4) to obtain the racemic TBS ether **25** (1.07 g, 83%) as a gum. IR (Neat): $\bar{\nu}$ 3300–3600 (OH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.40–7.20 (m, 15H), 4.90 (d, J=11.1 Hz, 1H), 4.81 (d, J=11.1 Hz, 1H), 4.82 (s, 2H), 4.73 (d, J=11.5 Hz, 1H), 4.65 (d, J=11.5 Hz, 1H), 4.16–4.00 (m, 2H), 3.79 (t, J=9.5 Hz, 1H), 3.46 (dd, J=9.5 and 3.1 Hz, 1H), 3.30 (t, J=9.2 Hz, 1H), 2.42 (br s, OH, 1H), 2.22–2.07 (m, 1H), 1.50–1.30 (m, 1H), 0.89 (s, 9H), 0.10 (s, 3H), 0.06 (s, 3H) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 139.1, 138.8, 138.0, 128.4,

128.2, 128.1, 127.89, 127.86, 127.7, 127.4, 127.1, 86.5, 82.9, 81.4, 75.9, 75.5, 72.8, 69.7, 66.1, 36.0, 25.8, 17.9, −4.5, −4.64 ppm. Elemental Anal. $C_{33}H_{44}O_5Si$ (548.78): calcd C, 72.22; H, 8.08 found C, 72.29; H, 7.92%.

*4.2.14. Preparation of the racemic ketone **26**.* The TBS ether **25** (1.0 g, 1.82 mmol), ethyl acetate (13 mL), and IBX (1.53 g, 5.46 mmol) were refluxed for 8 h. The reaction mixture was cooled to room temperature and passed through a bed of Celite. The bed of Celite was washed with ethyl acetate (2×40 mL), and the combined filtrate was evaporated under reduced pressure. The residue was purified by passing through a small column of silica gel (eluent: ethyl acetate/light petroleum, 1:6) to afford the racemic ketone **26** (0.85 g, 85%) as a colorless solid. Mp 53–55 °C; IR ($CHCl_3$): $\bar{\nu}$ 1732 (C=O) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.45–7.20 (m, 15H), 5.00–4.67 (m, 5H), 4.56 (d, J=11.5 Hz, 1H), 4.25 (d, J=9.5 Hz, 1H), 3.90–3.55 (m, 3H), 2.70–2.45 (m, 2H), 0.86 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 204.2, 138.3, 138.2, 137.5, 128.3, 128.2, 128.1, 127.9, 127.8, 127.6, 127.5, 85.06, 85.04, 81.8, 75.4, 74.9, 73.5, 69.5, 45.9, 25.7, 17.8, −4.7, −4.9 ppm. Elemental Anal. $C_{33}H_{42}O_5Si$ (546.77): calcd C, 72.49; H, 7.74 found C, 72.28; H, 7.82%.

*4.2.15. Preparation of chlorooxiranes **27** and **28**.* To a cooled (dry ice-acetone, −78 °C) solution of LDA (0.82 mL, 2.0 M soln in THF/heptanes/ethyl benzene, 1.64 mmol) in THF (1.0 mL), was added dichloromethane (0.35 mL, 5.49 mmol) followed by (after 5 min) the ketone **26** (0.30 g, 0.55 mmol). Resulting reaction mixture was stirred at −78 °C for 90 min, at 0 °C for 1 h and then at ambient temperature for 2 h. To the reaction mixture, a saturated solution of aq ammonium chloride (1.0 mL) was added and the volatiles were evaporated under reduced pressure, the residue was worked up with ethyl acetate 'as usual'. The crude product was purified by flash column chromatography (eluent: ethyl acetate/light petroleum 1:32) to afford racemic **27** (0.24 g, 70%) as a gum and racemic **28** (0.05 g, 15%) as a colorless solid. *Data for* **27**: ^1H NMR (400 MHz, $CDCl_3$): δ 7.35–7.17 (m, 15 H), 5.39 (s, 1H), 4.92 (d, J=11 Hz, 1H), 4.85 (d, J=11 Hz, 1H), 4.79 (s, 2H), 4.64 (d, J=10.5 Hz, 1H), 4.58 (d, J=10.5 Hz, 1H), 3.83–3.73 (m, 2H), 3.51–3.42 (m, 2H), 2.09 (dd, J=13.3 and 5.0 Hz, 1H), 1.99 (t, J=12.8 Hz, 1H), 0.9 (s, 9H), 0.11 (s, 3H), 0.07 (s, 3H) ppm; ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 138.6, 138.3, 137.7, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.6, 127.5, 127.4, 85.9, 83.1, 79.2, 76.1, 75.8, 75.4, 70.5, 70.0, 62.0, 34.1, 25.8, 17.9, −4.64, −4.74 ppm. Mass calcd M (+Na), 617.25; observed 617.30. Elemental anal. $C_{34}H_{43}ClO_5Si$ (594.26): calcd C, 68.60; H, 7.28 found C, 68.95; H, 7.38%.

Data for **28**: Mp 106–108 °C (Crystals obtained from acetonitrile at room temperature); ^1H NMR (200 MHz, $CDCl_3$): δ 7.40–7.15 (m, 15H), 5.17 (s, 1H), 5.00–4.70 (m, 5H), 4.54 (d, J=11.5 Hz, 1H), 4.01–3.86 (m, 1H), 3.77–3.61 (m, 2H), 3.54–3.42 (m, 1H), 2.01 (dd, J=14.1, 5.3 Hz, 1H), 1.81 (dd, J=14.0, 11.2 Hz, 1H), 0.89 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 138.7, 138.3, 137.2, 128.6, 128.3, 128.2, 128.1, 127.9, 127.6, 127.4, 127.3, 86.3, 83.1, 77.3, 76.0, 75.6, 75.1, 71.2, 70.5, 62.3, 33.8, 25.8, 17.9, −4.6, −4.7 ppm. Mass: calcd M (+Na), 617.25; observed 617.32. Elemental Anal. $C_{34}H_{43}ClO_5Si$ (594.26): calcd C, 68.60; H, 7.28 found C, 68.62; H, 7.65%.

*4.2.16. Preparation of racemic 1-deoxy 2,3,4,5 tetra-O-benzyl-myo-inositol (**29**).* To an ice cooled solution of the diol **12** (0.23 g, 0.53 mmol) in THF (3.0 mL) was added sodium hydride (0.023 g, 0.58 mmol) followed by a solution of benzyl bromide (0.07 mL, 0.58 mmol) in DMF (0.7 mL) and stirred at ambient temperature for 17 h. Ice was added to the reaction mixture, solvents were evaporated under reduced pressure and the residue worked up as usual with ethyl acetate. The crude product was purified by flash column chromatography to obtain the tetrabenzyl ether **29** (0.17 g, 60%) as a colorless solid [the starting diol **12** (0.05 g, 22%) was also recovered]. Mp 133–135 °C; IR (Nujol): $\bar{\nu}$ 3400–3100 (OH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.45–7.26 (m, 20H), 5.10–4.95 (m, 2H), 4.81 (d, J=10.7 Hz, 1H), 4.73–4.60 (m, 5H), 4.02 (t, J=9.5 Hz, 1H), 4.00–3.80 (m, 2H), 3.46 (dd, J=9.6 and 2.9 Hz, 1H), 3.29 (t, J=9.2 Hz, 1H), 2.40–2.18 (br s and dt, J=13.9 and 4.3 Hz, OH, 2H), 1.33–1.15 (m, 1H) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 138.8, 138.7, 138.4, 128.6, 128.29, 128.2, 128.0, 127.8, 127.6, 127.56, 127.52, 86.4, 83.4, 81.8, 75.6, 75.3, 72.5, 72.1, 71.5, 68.1, 31.9 ppm. Elemental Analysis calcd for $C_{34}H_{36}O_5$ (524.65); C, 77.84; H, 6.92; found C, 78.09; H, 7.16%.

*4.2.17. Preparation of **30**.* The TBS ether **25** (1.22 g, 2.22 mmol), ethyl acetate (15 mL), and IBX (1.87 g, 6.67 mmol) were refluxed for 8 h. The reaction mixture was cooled to room temperature and passed through a bed of Celite; the latter was washed with ethyl acetate, and the combined washings were evaporated under reduced pressure. Crude product obtained was purified by flash column chromatography (eluent: ethyl acetate/light petroleum, 1:9) to afford the α,β-unsaturated ketone **30** (0.85 g, 79%) as a colorless solid. The silica gel used was pre-eluted with triethylamine/light petroleum (1:49, 3–5 mL/g) mixture. Mp 72–74 °C; IR ($CHCl_3$): $\bar{\nu}$ 1697 (C=O) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.40–7.27 (m, 10H), 5.68 (d, J=3.3 Hz, 1H), 4.83 (q, J=12.4 Hz, 2H), 4.67 (q, J=11.9 Hz, 2H), 4.20–4.05 (m, 2H), 2.96–2.81 (m, 1H), 2.60–2.43 (m, 1H), 0.87 (s, 9H), 0.07 (s, 6H) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 191.8, 150.3, 137.9, 135.7, 128.5, 128.4, 128.0, 127.8, 127.7, 127.3, 115.0, 78.3, 72.6, 71.3, 69.7, 44.7, 25.6, 17.9, −4.8, −4.9 ppm. Elemental Anal. $C_{26}H_{34}O_4Si$ (438.63): calcd C, 71.19; H, 7.81, found C, 71.17; H, 7.98%.

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Supplementary data

X-ray data table and ORTEP diagram for **28** and copies of ^1H and ^{13}C NMR spectra for all the compounds appearing in schemes. Crystallographic data (excluding structure factors) for the compound **28** have been deposited with the Cambridge Crystallographic Data Centre as CCDC no. 823204. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.Uk). Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2011.08.027.

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13. This deoxygenation reaction required the use of fresh lithium triethyl borohydride solution. Use of old samples of super hydride solution (which were turbid) resulted in the formation of 2,4-di-benzyloxy phenol[7] exclusively. Hence we suspected that the basic impurities present in turbid samples of super hydride solution could be triggering the aromatization of the tosylate **11**. This suspicion was substantiated by the fact that treatment of **11** with sodium hydride (4.0 equiv) in THF, resulted in the formation of 2,4-di-benzyloxy phenol. However, consistent conversion of **11** to **12** could be realized by using fresh sample of super hydride.
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