# Concerning the reactivities of the C-1, C-2 and C-6 hydroxy groups of *myo*-inositol

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Regioselectivities in the reactions of the three contiguous free hydroxy groups at C-6, C-1, and C-2 of 3,4,5-tri-*O*-benzyl-D-*myo*-inositol have been examined. Stannylene activation permits selective alkylation and esterification at C-1; however, acyl migration back and forth between C-1 and C-2 leads to unpredictable ratios of the isolated regioisomers. With the stable C1-alkylated products, further alkylation is regioslective for the axial C-2–OH, whereas acylation is regioselective for the equatorial C-6–OH. In most cases the 'other' regioisomer is not observed, the by-products being those of dialkylation or diacylation.

## Introduction

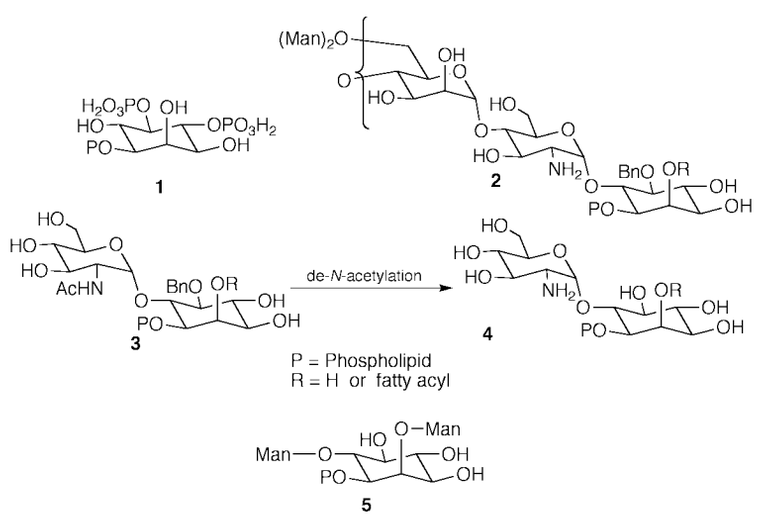
The discovery in 1983 of inositol 1,3,4-trisphosphate, **1**, as an intracellular second messenger which potentiates calcium release was of landmark biological significance.[1] Interest in phosphoinositides intensified with subsequent speculation that there is a connection between inositolphosphoglycans (IPGs) and insulin,[2,3] and with the identification of glycosylphosphatidylinositol (GPI) membrane anchors, summarized as **2**, in several pathogens.[4,5] The selective functionalization of the inositol moiety that is observed in **1** and **2** prompts speculation about the relative reactivities of *myo*-inositol's various hydroxy groups.[5] This speculation surfaces again in connection with the biosynthesis of GPI membrane anchors, where a phosphorylated inositol becomes glycosylated at the C-6–OH by *N*-acetylglucosamine to give the pseudo-disaccharide **3**. The latter is then de-N-acetylated to give a free amine, as in **4** (Scheme 1), which is then coupled to the first (of several) mannose residues, leading to **2**.[6]

The subsequent biosynthetic steps now depend on the organism concerned. Thus in mammalian systems and yeast, acylation of the inositols C-2–OH, as in **4** (R = acyl), is a necessary prelude to mannosylation.[7,8] This difference in biosynthesis is somewhat surprising in view of the fact that the GPI core itself is conserved throughout evolution,[4a] and a conserved biosynthetic pathway might therefore have been expected. However after mannosylation, the inositol's acyl group is lost in mammals, but is retained in (some) parasites, a circumstance which might provide an opening for parasite-specific therapeutic agents.[7]

Unusual differences in reactivity have also been observed in laboratory synthetic manipulations of *myo*-inositol. In their synthesis of a bis-mannosylated phosphoinositol from mycobacteria, van Boom and co-workers found that mannosylations leading to **5** must be done in the order C-2 then C-6.[9,10]

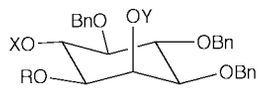
## Results and discussion

The foregoing summary therefore raises questions about the relative reactivities of the hydroxy groups of *myo*-inositol and its derivatives. Our interest in this matter[11] arose from recent observations in our laboratory[12] concerning the regioselective reactions of triol **6b**, prepared conveniently from acetate **6a** which was obtained by the elegant route of Bender and Budhu.[13] In keeping with David's precedent,[14] we anticipated that stannylene formation would occur preferentially at the *cis*-diol moiety, and that the intermediate[15] so formed, **7** (Scheme 2), would undergo alkylation at the equatorial site as is normally observed.[16] Monoalkylation of the diol obtained thereby, **8**,[12] was expected to favor the equatorial C-6–OH to give **9**; but this expectation was not fulfilled, since the regioisomer **10a** was




**Scheme 1**

**Table 1** C-2–OH *versus* C-6–OH: Regioselectivity in some partially protected *myo*-inositols



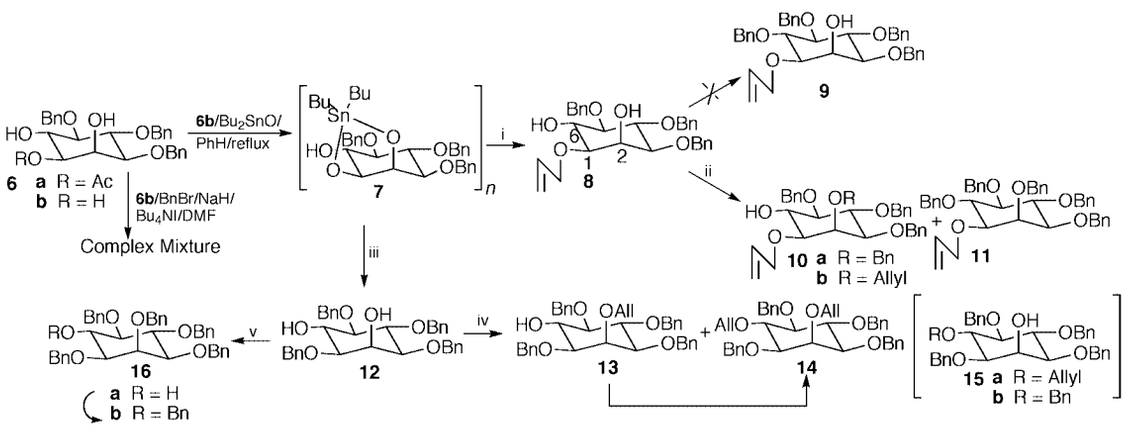
Starting Diols

**6a** R = Ac, X = Y = H
**8** R = All, X = Y = H
**12** R = Bn, X = Y = H

| Products | R | X | Y |
|---|---|---|---|
| **10a** | All | H | Bn |
| **10b** | All | H | All |
| **13** | Bn | H | All |
| **16a** | Bn | H | Bn |
| **17a** | Bn | Ac | H |
| **17b** | Bn | Palm[a] | H |
| **17c** | Bn | HCO | H |
| **19** | Ac | Palm[a] | H |

[a]-Palm = palmitoyl ($C_{15}H_{31}CO$)

| Entry | Substrate | Reaction conditions | Major product (%) |
|---|---|---|---|
| i | **8** | BnBr (1.2 equiv.), NaH, $Bu_4NI$, DMF, 0 °C, 1 h | **10a** (66) |
| ii | **8** | AllBr (1.2 equiv.), NaH, $Bu_4NI$, DMF, 0 °C, 1 h | **10b** (89) |
| iii | **12** | AllBr (1.2 equiv.), NaH, $Bu_4NI$, DMF, 0 °C, 1 h | **13** (76) |
| iv | **12** | BnBr (1.1 equiv.), NaH, $Bu_4NI$, DMF, 0 °C, 1 h | **16a** (78) |
| v | **12** | Benzyl trichloroacetimidate, TfOH, $CH_2Cl_2$, RT, 60 h | **16a** (80) |
| vi | **12** | $Ac_2O$ (3.5 equiv.), DMAP, Pyr, 0 °C, 30 min | **17a** (77) |
| vii | **12** | PalmCl (3 equiv.), DMAP, Pyr, 0 °C, 1 h | **17b** (73) |
| viii | **12** | PalmCl (3 equiv.), NaH, $Bu_4NI$, DMF, 0 °C–RT, 14 h | **17c** (71) |
| ix | **6a** | PalmCl (3 equiv.), DMAP, Pyr, RT, 60 h | **19** (75) |




**Scheme 2** *Reagents and conditions*: i, ref. 12; ii, RBr (1.2 equiv.), NaH, $Bu_4NI$, DMF, 0 °C, 1 h; iii, BnBr (3 equiv.), $Bu_4NI$, 70 °C, 2 h; iv, AllBr (1.2 equiv.), NaH, $Bu_4NI$, DMF, 0 °C, 1 h; v, BnBr (1.1 equiv.), NaH, $Bu_4NI$, DMF, 0 °C, 1 h.

obtained as the major product. Indeed, **9** was not observed at all, the by-product being the penta-O-benzylated material **11**. Similarly, treatment of the monoallyl compound **8** with one additional equivalent of allyl bromide gave the bis(allyl ether) **10b**.

The greater reactivity of the C-2–OH of diol **8** recalls the biosynthetic pathway **3** ⟶ **4** ⟶ **2** in Scheme 1, and invited speculation that the fatty acylation step was designed to 'block' the more reactive axial hydroxy group. In the hope of providing insight into this aspect, we have examined some alkylation and acylation experiments of related inositol diols and triols, and we report the results herein.

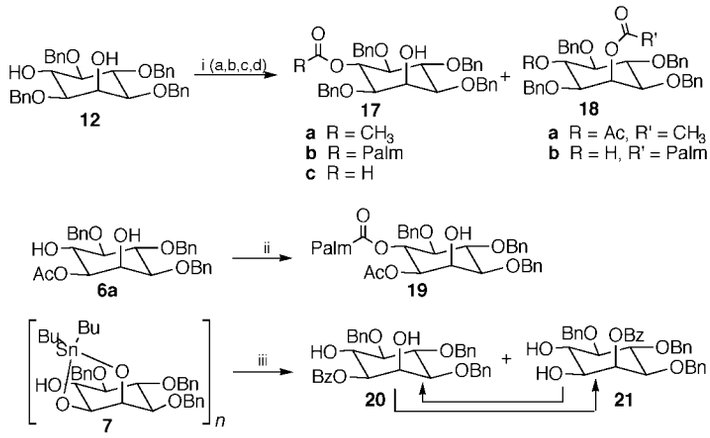
For a start, we established that benzylation of **6b**, without prior stannylene activation, led to a complex mixture. However, the stannylene intermediate **7** could also be trapped by benzylation to give the tetra-*O*-benzyl diol **12**, which underwent selective allylation at C-2 leading to **13**, the regioisomer of **10a**. Similarly, treatment of **12** with one equivalent of benzyl bromide gave the penta-O-benzylated material **16a** as the major product.The minor products in these reactions were not the regioisomers **15a** and **15b**, but the dialkylated analogues **14** and **16b**, identified by independant preparation from **13** and **16a**, respectively.

It was now of interest to see whether acylation followed a similar pattern as the above described alkylations. The tetra-*O*-benzyl diol **12** was therefore treated with 3.5 equivalents of acetic anhydride (Scheme 3). That the monoester obtained in 77% yield was the C-6 derivative, **17a**, was immediately apparent from the splittings of 10 and 10 Hz, for the proton which is shifted downfield to $\delta$ 5.53–5.48. Diacetate **18a** was obtained as the minor product. Notably, the C-2 monoacetate was not observed.

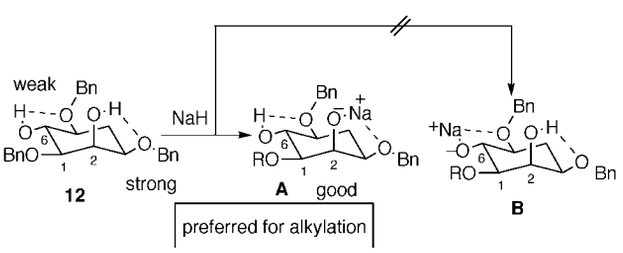
With palmitoyl chloride in pyridine and DMAP under standard conditions, the corresponding C-6 palmitate **17b** was obtained in 73% yield. However, in this case, the regioisomeric product, **18b**, was also observed (21%).

The regioselectivities observed for esterifications of **12** (Table 1, entries vi, vii) are seen to favor the C-6–OH, and therefore are clearly different from alkylations which seemed to favor C-2–OH. Are the above regioselectivities at C-2 and C-6 dependent on the nature of the C-1 functionality? This question is relevant since the starting material for the study is the C-1 acetate **6a**, the direct product of the Bender–Budhu process.[13] We wished to include the corresponding mono benzoyl analogue **20** in this study; but reaction of the stannylene intermediate **7** with benzoyl chloride was not selective for C-1. Thus, with 1.1 equivalents of the reagent, both esters **20** and **21** were obtained. In subsequent experiments it was shown, beginning with pure **20** or **21**, that benzoyl migration to give the other regioisomer occurred readily. Accordingly, the ratio of these benzoates varies widely from one experiment to another.

The ease of ester migration between **20** and **21** would clearly



**Scheme 3** *Reagents and conditions*: ia, $Ac_2O$ (3.5 equiv.), DMAP, Pyr, 0 °C, 30 min; ib, PalmCl (3 equiv.), DMAP, Pyr, 0 °C, 1 h; ic, BzCl (3 equiv.), DMAP, Pyr, 0 °C, 1 h; id, PalmCl (3 equiv.), NaH, $Bu_4NI$, DMF, 0 °C–RT, 14 h; ii, PalmCl (3 equiv.), DMAP, Pyr, RT, 60 h; iii, BzCl (1.1 equiv.), $Bu_4NI$, RT, 1 h.



**Scheme 4**

complicate any attempts at NaH-induced alkylation of C-1 esters such as **20** or **6a**. However, DMAP-induced palmitoylation of **6a** was as regioselective as for the C-1 benzyl analogue **12** (compare entries vii and ix).

The results in Table 1 show clearly that, for the 2,6-diols, alkylation is selective for the axial C-2–OH, and acylation for the equatorial C-6–OH. In an effort to rationalize these selectivities, we considered the H-bonding pattern shown for **12** in Scheme 4. It was possible that upon treatment with NaH, the chelate **A** would be preferred to **B**. The observed C-2-selective alkylation could therefore be chelation driven. In order to test this idea, we examined a mechanistically different benzylating reagent where chelation should not be a factor. Upon treatment of **12** with benzyl trichloromethylacetimidate[17] [entry (v)], the major product was also shown to be **16a**. This implies that chelation was not essential for the selectivity.

With regard to esterification, would chelation-driven acylation be shown to be C-2-selective? Palmitoylation of **12** was therefore examined under the standard alkylation conditions using NaH–$Bu_4NI$–DMF. However, instead of a palmitate, the formyl ester **17c** was obtained in 71% yield, with the formation of the equatorial palmitate **17b** in minor amounts. Although **17c** is the result of a Vilsmeier reaction,[18] its formation conforms to the trend of C-6-selectivity observed in esterification reactions.

We then turned to some early work of Angyal and Tate, on the vicinal *cis*-1,2-diol of the 3,4,5,6-tetra-*O*-benzylinositol. Reaction with one equivalent of benzyl chloride or methyl iodide led to overwhelming C-1 (equatorial) alkylation with ≈1% axial regioisomer. However, with benzyloxymethyl chloride and dihydropyran, the ratio of regioisomeric products was 1:1. Angyal and Tate suggested that reaction at the equatorial site is preferred in cases "which involve an intermediate or a transition state" — such as esterifications and $S_N2$ displacements. On the other hand, reactions which proceed through "carbonium ions, and the subsequent rapid reactions of the bond-deficient carbon atoms are not sensitive to steric hindrance".[19]

Our studies have shown that selective access can be had to each of the three contiguous hydroxy groups of compound **6b** which is readily obtained by the Bender–Budhu synthesis.[13] Stannylene mediated reactions allow excellent C-1–OH selectivities, affording products such as **8**, **12** and **20**. However, in the case of esterifications, the possibility of reversible acyl migration might cause complications. Further examination of these selectivities is underway and will be reported in due course.

## Experimental

### General methods

Solvents of commercial anhydrous grade have been used. All reactions were conducted under an inert argon atmosphere. TLC plates (Riedel-de Haen, coated with silica gel 60 F 254), were illuminated by UV light. Silica gel (Spectrum SIL 58, 230–400 mesh, grade 60) was used for column chromatography. All NMR spectra were recorded at 25 °C at 400 MHz ($^1$H) or 100 MHz ($^{13}$C), and chemical shifts are reported relative to internal TMS. *J*-values are given in Hz. Accurate mass measurements were made using FAB at 10 K resolution, and elemental analyses were conducted by Atlantic Microlab, Norcross, GA. 1-*O*-Allyl-3,4,5-tri-*O*-benzyl-D-*myo*-inositol **8** and 1-*O*-allyl-2,3,4,5-tetra-*O*-benzyl-D-*myo*-inositol **10a** were prepared as previously described.[12]

### 1,2-Di-*O*-allyl-3,4,5-tri-*O*-benzyl-D-*myo*-inositol 10b

A mixture of diol **8** (20 mg, 0.04 mmol), NaH (60% in mineral oil; 4 mg, 0.1 mmol) and tetrabutylammonium iodide (15 mg, 0.04 mmol) in anhydrous DMF (1 mL) under Ar was chilled in an ice-bath. To the stirred mixture was added allyl bromide (4.14 μL, 0.048 mmol). After 1 h the reaction mixture was quenched with drops of water and solvent was removed under reduced pressure. The residue was flash chromatographed (1:4 EtOAc–hexane) to afford **10b** (19 mg, 89%) as a colorless semi-solid, $R_f$ (1:2 EtOAc–hexane) 0.65; $^1$H NMR ($CDCl_3$) $\delta$ 7.38–7.22 (m, 15H), 5.98–5.86 (m, 2H, allyl), 5.31–5.29 (m, 1H, allyl), 5.27–5.25 (m, 1H, allyl), 5.21–5.14 (m, 2H, allyl), 4.92–4.80 (m, 4H, Bn), 4.70–4.69 (d, 2H, Bn), 4.31–4.27 (m, 2H), 4.16–4.10 (m, 1H), 4.08–3.99 (m, 4H), 3.96 (dd, *J* 2, 2.1, 1H), 3.38–3.33 (m, 2H), 3.09–3.06 (ddd, *J* 12, 2, 0.8, 1H), 2.46 (br s, 1H, OH); $^{13}$C NMR $\delta_C$ 139.16, 139.11, 135.89, 134.77, 128.70, 128.61, 128.34, 128.16, 127.98, 127.88, 127.82, 117.72, 117.13, 83.67, 81.70, 81.26, 80.00, 76.13, 75.63, 73.60, 73.33, 73.20, 72.94, 71.44; FABMS *m/z* (relative intensity) ($M^+ + 1$) 531 (60), 529 (100), 439 (72), 391 (66), 363 (51), 338 (45).

### 1,3,4,5-Tetra-*O*-benzyl-D-*myo*-inositol 12

A mixture of triol **6b** (990 mg, 2.2 mmol) and dibutyltin oxide

(660 mg, 2.65 mmol) in benzene (25 mL) was refluxed for 20 h with a Dean–Stark trap. The temperature was reduced to 70 °C, tetrabutylammonium iodide (815 mg, 2.2 mmol) and benzyl bromide (780 μL, 6.6 mmol) were added, and the mixture was stirred under Ar for 2 h. The solvent was evaporated off under reduced pressure and the residue, on flash chromatography (1 : 3 EtOAc–hexane), afforded **12** as a colorless solid (455 mg, 82%) [based on consumed triol **6b** (530 mg, 1.17 mmol recovered)], $R_f$ (1 : 2 EtOAc–hexane) 0.5; $^1$H NMR ($CDCl_3$) $\delta$ 7.34–7.24 (m, 20H, Bn), 4.90–4.87 (dd, *J* 10.8, 3.2, 2H, Bn), 4.83–4.79 (dd, *J* 10.8, 1.6, 2H, Bn), 4.69–4.61 (m, 4H, Bn). 4.18 (dd, *J* 2, 2.1, 1H), 4.09–4.04 (ddd, *J* 9.6, 9.6, 2, 1H) 3.98–3.93 (dd, *J* 9.6, 9.6, 1H), 3.38–3.35 (dd, *J* 10, 2.8, 1H), 3.34–3.30 (dd, *J* 9.2, 9.6, 1H), 3.21–3.17 (dd, *J* 9.6, 2.8, 1H), 2.65 (s, 1H, OH), 2.59 (s, 1H, OH); $^{13}$C NMR: $\delta_C$ 138.59, 137.77, 137.68, 128.40, 128.32, 128.28, 128.19, 127.82, 127.76, 127.73, 127.72, 127.49, 127.41, 82.76, 80.75, 79.78, 78.99, 75.65, 75.27, 72.47, 72.31, 72.14, 66.88. FABMS *m*/*z* (relative intensity) ($M^+$ + 1) 541 (100), 539 (68), 449 (30), 391 (15), 359 (15).

### 2-*O*-Allyl-1,3,4,5-tetra-*O*-benzyl-D-*myo*-inositol 13 and 2,6-di-*O*-allyl-1,3,4,5-tetra-*O*-benzyl-D-*myo*-inositol 14

A mixture of diol **12** (100 mg, 0.18 mmol), NaH (60% in mineral oil; 15 mg, 0.36 mmol) and tetrabutylammonium iodide (66 mg, 0.18 mmol) in anhydrous DMF (3 mL) under Ar was chilled in an ice-bath. To the stirred mixture was added allyl bromide (20 μL, 0.22 mmol). After 1 h the reaction mixture was quenched with drops of water and solvent was removed under reduced pressure. The residue was flash chromatographed (1 : 4 EtOAc–hexane) to afford **13** (80 mg, 76%) as a colorless semi-solid, $R_f$ (1 : 2-EtOAc–hexane) 0.7. The diallyl product **14** (10 mg, 9%) was obtained as the minor product.

**Data for 13.** $^1$H NMR ($CDCl_3$) $\delta$ 7.36–7.25 (m, 20H, Bn), 5.98–5.88 (m, 1H, allyl), 5.30–5.24 (ddd, *J* 17.2, 3.2, 1.6, 1H, allyl), 5.17–5.13 (ddd, *J* 10.4, 2.8, 1.2, 1H, allyl), 4.91–4.80 (m, 4H, Bn), 4.70–4.57 (m, 4H, Bn), 4.34–4.21 (m, 2H, allyl). 4.13–4.08 (dd, *J* 9.6, 9.6, 1H), 4.02–3.97 (dd, *J* 9.6, 9.6, 1H), 3.96–3.95 (dd, *J* 2.4, 2.4, 1H), 3.37–3.32 (m, 2H), 3.16–3.13 (dd, *J* 9.6, 2.4, 1H), 2.48 (s, 1H, OH); $^{13}$C NMR: $\delta_C$ 138.82, 138.79, 138.23, 137.90, 135.55, 128.47, 128.36, 128.34, 128.26, 127.97, 127.82, 127.70, 127.63, 127.53, 127.46, 116.69, 83.36, 81.36, 80.87, 79.98, 75.76, 75.30, 73.32, 73.28, 72.79, 72.30; FABMS *m*/*z* (relative intensity) ($M^+$ + 1) 581 (100), 579 (48), 531 (17), 489 (15), 391 (13) (Calc. for $C_{37}H_{40}O_6$: C, 76.53; H, 6.94. Found: C, 76.49; H, 6.97%).

**Data for 14.** $^1$H NMR ($CDCl_3$) $\delta$ 7.22–7.38 (m, 20H, Bn), 6.01–5.89 (m, 2H, allyl), 5.29–5.22 (m, 2H, allyl), 5.17–5.11 (m, 2H, allyl), 4.89–4.79 (m, 4H, Bn), 4.69–4.61 (m, 4H, Bn), 4.40–4.28 (m, 4H), 3.99–3.94 (dd, *J* 9.2, 9.6, 1H), 3.93–3.92 (dd, *J* 2.4, 2.4, 1H), 3.89–3.84 (dd, *J* 9.6, 9.6, 1H), 3.41–3.36 (dd, *J* 9.2, 9.2, 1H), 3.31–3.28 (dd, *J* 9.6, 1.6, 1H), 3.26–3.23 (dd, *J* 10, 2, 1H); $^{13}$C NMR $\delta_C$ 139.96, 139.89, 139.50, 139.38, 136.83, 136.47, 129.42, 129.38, 129.35, 129.07, 129.02, 128.69, 128.65, 128.60, 128.57, 128.53, 117.77, 117.59, 84.71, 82.65, 82.48, 81.77, 81.69, 77.01, 76.89, 75.61, 75.03, 74.40, 73.86, 73.81; FABMS *m*/*z* (relative intensity) ($M^+$ + 1) 621 (100), 619 (30), 529 (9), 460 (13), 391 (12).

### 1,2,3,4,5-Penta-*O*-benzyl-D-*myo*-inositol 16a

**Method A.** A mixture of diol **12** (50 mg, 0.09 mmol), NaH (60% in mineral oil; 7 mg, 0.18 mmol) and tetrabutylammonium iodide (33 mg, 0.09 mmol) in anhydrous DMF (2 mL) under Ar was chilled in an ice-bath. To the stirred mixture was added benzyl bromide (13 μL, 0.1 mmol). After 1 h the reaction mixture was quenched with drops of water and the solvent was evaporated off under reduced pressure. The residue was flash chromatographed (1 : 4 EtOAc–hexane) to afford **16a** (45 mg, 78%) as a colorless semi-solid. The hexabenzyl product **16b** was obtained as the minor product.

*Data for* ***16a***.—$^1$H NMR ($CDCl_3$) $\delta$ 7.38–7.24 (m, 25H, Bn), 4.92–4.77 (m, 6H, Bn), 4.68–4.51 (m, 4H, Bn), 4.19–4.15 (dd, *J* 9.6, 9.6, 1H), 4.08–4.02 (m, 2H), 3.39–3.35 (m, 2H), 3.20–3.17 (dd, *J* 9.6, 2, 1H), 2.55 (s, 1H, OH); $^{13}$C NMR $\delta_C$ 138.80, 138.78, 138.75, 138.27, 137.90, 128.43, 128.34, 128.32, 128.24, 128.10, 127.98, 127.78, 127.76, 127.67, 127.65, 127.58, 127.54, 127.50, 127.44, 127.31, 83.41, 81.35, 81.08, 81.05, 75.73, 75.29, 74.01, 73.63, 72.88, 72.79, 72.64; FABMS *m*/*z* (relative intensity) ($M^+$ + 1) 631 (100), 629 (89), 607 (36); HRFABMS [Calc. for $C_{41}H_{41}O_6$ ($M^+$ − H): *m*/*z* 629.2903. Found *m*/*z* 629.2901].

**Method B.** The diol **12** (50 mg, 0.09 mmol) dissolved in dry methylene dichloride (2 mL) was chilled in an ice-bath. Benzyl 2,2,2-trichloroacetimidate (66 μL, 0.36 mmol) and triflic acid (2 μL, 0.02 mmol) were added. The temperature was increased to room temp. and the mixture was stirred under Ar for 60 h. The solvents was evaporated off and the residue was flash chromatographed (1 : 4 EtOAc–hexane) to afford **16a** (40 mg, 80%) as the major product [the yield based on consumed diol **12** (7 mg, 0.013 mmol recovered)].

### 6-*O*-Acetyl-1,3,4,5-tetra-*O*-benzyl-D-*myo*-inositol 17a and 2,6-di-*O*-acetyl-1,3,4,5-tetra-*O*-benzyl-D-*myo*-inositol 18a

A mixture of diol **12** (20 mg, 0.04 mmol) and 4-(dimethylamino)pyridine (5 mg, 0.04 mmol) in anhydrous pyridine (1 mL) under Ar was chilled in an ice-bath. To the stirred mixture was added acetic anhydride (13 μL, 0.14 mmol). After 30 min the reaction mixture was quenched with drops of water and the solvent was evaporated off under reduced pressure. The residue was flash chromatographed (1 : 4 EtOAc–hexane) to afford **17a** (17 mg, 77%) as colorless semi-solid, $R_f$ (1 : 2 EtOAc–hexane) 0.52. The diacetyl product **18a** (5 mg, 20%) was obtained as the minor product.

**Data for 17a.** $^1$H NMR ($CDCl_3$) $\delta$ 7.36–7.22 (m, 20H, Bn), 5.53–5.48 (dd, *J* 10, 10, 1H), 4.92–4.48 (m, 8H, Bn), 4.22–4.21 (dd, *J* 2.8, 2.4, 1H), 4.10–4.05 (dd, *J* 9.6, 9.6, 1H), 3.42–3.36 (m, 2H), 3.30–3.27 (dd, *J* 9.6, 2.4, 1H), 2.51 (s, 1H, OH), 1.89 (s, 3H, Ac); $^{13}$C NMR $\delta_C$ 169.89, 138.54, 138.36, 137.84, 137.51, 128.47, 128.46, 128.34, 128.07, 127.94, 127.89, 127.86, 127.71, 127.61, 127.57, 80.99, 80.87, 79.37, 75.95, 75.32, 72.66, 72.62, 72.02, 66.97, 20.99; FABMS *m*/*z* (relative intensity) ($M^+$ + 1) 605 ($M^+$ + Na), 583 (100), 581 (32), 491 (21), 475 (16), 385 (13) (Calc. for $C_{36}H_{38}O_7$: C, 74.21, H, 6.57. Found: C, 74.41, H, 6.51%).

**Data for 18a.** $^1$H NMR ($CDCl_3$) $\delta$ 7.35–7.21 (m, 20H, Bn), 5.83–5.82 (dd, *J* 2.8, 2.8, 1H), 5.44–5.39 (dd, *J* 10, 10, 1H), 4.89–4.38 (m, 8H, Bn), 3.96–3.91 (dd, *J* 9.2, 9.6, 1H), 3.47–3.40 (m, 2H), 3.36–3.32 (dd, *J* 10, 2.8, 1H), 2.16 (s, 3H, Ac), 1.92 (s, 3H, Ac); FABMS *m*/*z* (relative intensity) ($M^+$ + 1) 625 (82), 623 (35), 517 (100), 475 (58), 439 (62), 427 (71), 391 (45), 383 (45).

### 1,3,4,5-Tetra-*O*-benzyl-6-*O*-palmitoyl-D-*myo*-inositol 17b and 1,3,4,5-tetra-*O*-benzyl-2-*O*-palmitoyl-D-*myo*-inositol 18b

A mixture of diol **12** (50 mg, 0.09 mmol) and 4-(dimethylamino)pyridine (11 mg, 0.09 mmol) in anhydrous pyridine (2 mL) was chilled in an ice-bath. To the stirred mixture was added freshly prepared palmitoyl chloride (92 μL, 0.27 mmol). After 1 h the reaction mixture was quenched with drops of water and the solvent was evaporated off under reduced pressure. The residue was flash chromatographed (1 : 4 EtOAc–hexane) to afford **17b** (52 mg, 73%) as colorless semi-solid, $R_f$ (1 : 2 EtOAc–hexane) 0.6. The axial palmitoyl ester **18b** (15 mg, 21%) was obtained as the minor product.

**Data for 17b.** $^1$H NMR ($CDCl_3$) $\delta$ 7.34–7.21 (m, 20H, Bn), 5.57–5.52 (dd, *J* 10, 10, 1H), 4.91–4.49 (m, 8H, Bn), 4.21–4.20 (dd, *J* 2.4, 2.4, 1H), 4.10–4.05 (dd, *J* 9.6, 9.2, 1H), 3.43–3.36 (m, 2H), 3.32–3.29 (dd, *J*10, 2.4, 1H), 2.50 (s, 1H, OH), 2.16–2.11 (m, 2H), 1.63–1.21 (m, 26H), 0.89–0.86 (t, 3H); $^{13}$C NMR $\delta_C$ 172.63, 138.53, 138.35, 137.84, 137.46, 128.42, 128.31, 128.24, 128.05, 127.88, 127.82, 127.58, 127.55, 127.51, 127.46, 80.96, 80.91, 79.33, 77.48, 75.91, 75.17, 72.59, 72.28, 71.99, 66.90, 34.39, 31.89, 29.66, 29.65, 29.62, 29.41, 29.33, 24.81, 24.68, 22.66, 14.09; FABMS *m*/*z* (relative intensity) ($M^+$ + 1) 779 (100), 777 (60), 685 (78), 671 (62), 595 (81), 581 (71), 533 (62) (Calc. for $C_{50}H_{66}O_7$: C, 77.09; H, 8.54. Found; C, 77.17; H, 8.58%).

**Data for 18b.** $^1$H NMR ($CDCl_3$) $\delta$ 7.36–7.22 (m, 20H, Bn) 5.89–5.88 (dd, *J* 2.8, 2.8, 1H), 4.90–4.46 (m, 8H, Bn), 4.00–3.95 (dd, *J* 9.2, 9.6, 1H), 3.87–3.82 (dd, *J* 9.6, 9.6, 1H), 3.52–3.48 (dd, *J* 9.6, 2.4, 1H), 3.43–3.38 (dd, *J* 9.2, 9.2, 1H), 3.32–3.29 (dd, *J* 10, 2.4, 1H), 2.36–1.22 (m, 29H), 0.90–0.86 (t, 3H, Palm); FABMS *m*/*z* (relative intensity) ($M^+$ + 1) 779 (50), 777 (80), 671 (75), 581 (100), 491 (40), 439 (45).

### 1,3,4,5-Tetra-*O*-benzyl-6-*O*-formyl-D-*myo*-inositol 17c

A mixture of diol **12** (50 mg, 0.09 mmol), NaH (60% in mineral oil; 7 mg, 0.18 mmol) and tetrabutylammonium iodide (33 mg, 0.09 mmol) in anhydrous DMF (2 mL) under Ar was chilled in an ice-bath. To the stirred mixture was added freshly prepared palmitoyl chloride (92 μL, 0.27 mmol). The temperature was slowly increased to room temperature and the mixture was stirred for 14 h. The reaction mixture was quenched with drops of water and the solvent was evaporated off. The residue was flash chromatographed (1 : 4 EtOAc–hexane) to afford **17c** (30 mg, 71%) as a colorless, viscous liquid, $R_f$ (1 : 2 EtOAc–hexane) 0.55 [yield based on consumed diol **12** (10 mg, 0.018 mmol recovery)]. The minor product obtained was **17b** (15 mg, 26%).

**Data for 17c.** $^1$H NMR ($CDCl_3$) $\delta$ 8.065 (s, 1H, formyl), 7.35–7.22 (m, 20H, Bn), 5.21–5.16 (dd, *J* 9.6, 10, 1H), 4.93–4.54 (m, 8H, Bn), 4.21–4.20 (dd, *J* 2.8, 2.4, 1H), 4.06–4.02 (dd, *J* 9.6, 9.6, 1H), 3.49–3.44 (dd, *J* 9.6, 9.6, 1H), 3.41–3.38 (dd, *J* 10, 2.8, 1H), 3.37–3.34 (dd, *J* 10, 2.8, 1H), 2.49 (s, 1H, OH); $^{13}$C NMR $\delta_C$ 161.34, 138.41, 137.82, 137.63, 137.10, 128.54, 128.50, 128.37, 128.11, 128.07, 127.96, 127.93, 127.90, 127.83, 127.82, 127.68, 80.86, 80.29, 79.31, 76.74, 75.94, 75.63, 72.75, 72.35, 66.94; FABMS *m*/*z* (relative intensity) ($M^+$ + 1) 569 (100), 567 (48), 477 (24), 391 (40).

### 1-*O*-Acetyl-3,4,5-tri-*O*-benzyl-6-*O*-palmitoyl-D-*myo*-inositol 19

A mixture of diol **6a** (50 mg, 0.1 mmol) and 4-(dimethylamino)pyridine (12 mg, 0.1 mmol) in anhydrous pyridine (2 mL) was chilled in an ice-bath. To the stirred mixture was added palmitoyl chloride (104 μL, 0.3 mmol). The temperature was increased to ambient and the mixture was stirred for 60 h before being quenched with drops of water and the solvent was evaporated off under reduced pressure. The residue was flash chromatographed (1 : 4 EtOAc–hexane) to afford **19** (20 mg, 75%) as colorless-semi solid [yield based on consumed diol **6a** (32 mg, 0.065 mmol recovered)], $^1$H NMR ($CDCl_3$) $\delta$ 7.36–7.22 (m, 15H, Bn), 5.64–5.59 (dd, *J* 10.4, 10, 1H), 4.95–4.47 (m, 7H), 4.26–4.25 (dd, *J* 2.4, 2.4, 1H), 4.05–4.00 (dd, *J* 9.2, 9.6, 1H), 3.56–3.48 (m, 2H), 2.16–2.12 (m, 2H), 2.07 (s, 3H, Ac), 1.64–1.21 (m, 26H), 0.89–0.86 (t, 3H); $^{13}$C NMR $\delta_C$ 172.49, 170.30, 138.13, 137.35, 128.55, 128.37, 128.32, 128.07, 128.01, 127.89, 127.69, 127.60, 80.97, 80.79, 79.59, 76.02, 75.46, 72.86, 71.37, 70.64, 67.79, 34.27, 31.90, 29.68, 29.58, 29.42, 29.34, 29.24, 29.06, 24.93, 24.71, 22.67, 14.10; FABMS *m*/*z* (relative intensity) ($M^+$ − 1) 729 (5), 713 (10), 623 (10), 533 (13), 443 (7), 368 (12), 334 (43), 316 (100).

### 1-*O*-Benzoyl-3,4,5-tri-*O*-benzyl-D-*myo*-inositol 20 and 2-*O*-benzoyl-3,4,5-tri-*O*-benzyl-D-*myo*-inositol 21

A mixture of the triol **6b** (80 mg, 0.18 mmol) and dibutyltin oxide (54 mg, 0.22 mmol) was refluxed for 20 h in benzene (3 mL) with a Dean–Stark trap. The temperature was reduced to ambient, tetrabutylammonium iodide (66 mg, 0.18 mmol) and benzoyl chloride (25 μL, 0.2 mmol) were added, and the mixture was stirred under Ar for 1 h. The solvent was evaporated off under reduced pressure and the residue on flash chromatography (1 : 3 EtOAc–hexane) afforded **20** (55 mg, 65%) as white semi-solid [$R_f$ (2 : 1 EtOAc–hexane) 0.75] and the regioisomer **21** (10 mg, 2%) [$R_f$ (2 : 1 EtOAc–hexane) 0.5] as colorless semi-solid [yield based on consumed triol **6b** (12 mg, 0.026 mmol recovery)].

**Data for 20.** $^1$H NMR ($CDCl_3$) $\delta$ 8.10–8.08 (m, 2H, ArH), 7.57–7.24 (m, 18H, ArH), 4.98–4.95 (dd, *J* 10.4, 2.8, 1H), 4.96–4.68 (m, 6H, Bn), 4.39–4.38 (dd, *J* 2.8, 2.8, 1H), 4.30–4.25 (ddd, *J* 10, 10, 2.8, 1H), 4.01–3.96 (dd, *J* 9.6, 9.2, 1H), 3.63–3.60 (dd, *J* 9.6, 2.4, 1H), 3.47–3.42 (dd, *J* 9.6, 9.2, 1H), 2.53 (s, 1H, OH), 2.34 (d, 1H, OH); $^{13}$C NMR $\delta_C$ 166.22, 138.47, 138.39, 137.38, 133.27, 129.85, 129.64, 128.53, 128.39, 128.38, 128.05, 127.91, 127.84, 127.65, 82.95, 80.88, 80.15, 75.80, 75.64, 73.60, 72.82, 70.54, 67.81; FABMS *m*/*z* (relative intensity) ($M^+$ + 1) 555 (100), 553 (86), 463 (65), 447 (20), 373 (26), 357 (30).

**Data for 21.** $^1$H NMR ($CDCl_3$) $\delta$ 8.02–8.00 (m, 2H, ArH), 7.50–7.22 (m, 18H, ArH), 6.89–6.87 (dd, *J* 2.8, 2.8, 1H), 4.95–4.50 (m, 6H, Bn), 3.95–3.89 (m, 2H), 3.58–3.55 (dd, *J* 9.6, 2.8, 1H), 3.54–3.50 (m, 1H), 3.37–3.32 (dd, *J* 9.2, 9.6, 1H), 3.21 (d, 1H, OH), 3.10 (d, 1H, OH); $^{13}$C NMR $\delta_C$ 166.16, 138.43, 138.30, 137.56, 133.12, 129.82, 129.73, 128.51, 128.36, 128.26, 128.11, 128.03, 127.93, 127.89, 127.64, 127.54, 82.58, 81.40, 78.54, 75.72, 75.68, 73.24, 71.92, 70.26, 70.21; FABMS *m*/*z* (relative intensity) ($M^+$ + 1) 555 (100), 553 (35), 463 (20), 447 (36), 357 (42).

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