# Inositol Derivatives. 10. Isopropylidenation of 1,2-*O*-Cyclohexylidene-*myo*-inositol Derivatives and Preparation of Unaccessible Blocked Inositols

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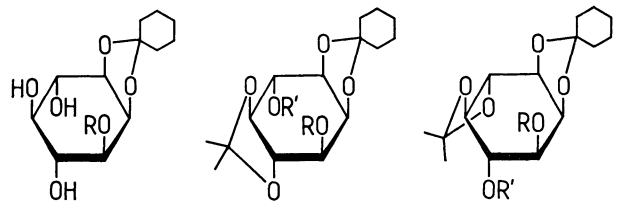
Isopropylidenation of 1,2-*O*-cyclohexylidene-*myo*-inositol and its 3-*O*-tosyl- and 3-*O*-benzoyl derivatives with 2,2-dimethoxypropane in *N,N*-dimethylformamide in the presence of acid catalyst gave the corresponding 4,5- and 5,6-*O*-isopropylidene derivatives. Selective benzoylation of 1,2-*O*-cyclohexylidene-4,5-*O*-isopropylidene-*myo*-inositol with benzoyl chloride in pyridine gave mainly the 3-*O*-benzoate, whereas with benzoic anhydride the 6-*O*-benzoate. Several unaccessible blocked inositols were prepared by displacement reaction of the protected sulfonyl derivatives with sodium benzoate.

Partially blocked *myo*-inositol is a potential intermediate for the synthesis of various kinds of inositol derivatives. In continuation to the previous paper,[1] isopropylidenation of 1,2-*O*-cyclohexylidene-*myo*-inositol (**1a**),[2] and its 3-*O*-tosyl- and 3-*O*-benzoyl derivatives (**1b**[2] and **1c**[1]) has been studied. Preparation of several unaccessible protected derivatives of *allo*-, *chiro*-, and *muco*-inositols starting from the sulfonates obtained in this studies has also been carried out.

*Isopropylidenation.* Treatment of **1a** with 2,2-dimethoxypropane in *N,N*-dimethylformamide in the presence of *p*-toluenesulfonic acid gave the 4,5-*O*-isopropylidene derivative (**2a**) as crystals in 22% yield, which was further characterized as the ditosylate and diacetate (**2b** and **2c**). The remaining syrupy product consisted mainly of the 5,6-*O*-isopropylidene derivative (**3a**) was directly tosylated or benzoylated to give the crystalline ditosylate (**3b**) or dibenzoate (**3c**) in an isolated yield of 26 or 62% based on **1a**. Positions of the isopropylidene groups in **2a** and **3a** were established by converting **2b** and **3b** into the known 1,4- and 1,6-di-*O*-tosyl-*myo*-inositol,[2] respectively.




| 1a~c | | 2a~j | | | 3a~j | |
|---|---|---|---|---|---|---|
| | | | R | R′ | | R | R′ |
| **a** | R=H | **a** | H | H | **a** | H | H |
| **b** | R=Ts | **b** | Ts | Ts | **b** | Ts | Ts |
| **c** | R=Bz | **c** | Ac | Ac | **c** | Bz | Bz |
| | | **d** | Ts | H | **d** | Ts | H |
| | | **e** | Ts | Ac | **e** | Ts | Ac |
| | | **f** | Bz | H | **f** | Bz | H |
| | | **g** | Bz | Ac | **g** | Bz | Ac |
| | | **h** | Bz | Me | **h** | Bz | Me |
| | | **i** | Bz | Bz | **i** | Me | Bz |
| | | **j** | H | Bz | **j** | Me | H |

Scheme 1.

Under the identical reaction conditions, 1,2-*O*-cyclohexylidene-3-*O*-tosyl-*myo*-inositol (**1b**) was acetonated to afford the crystalline 4,5- and 5,6-*O*-isopropylidene derivatives (**2d** and **3d**) in 18 and 19% yields, respectively. Their structures were determined by converting them into **2b** and **3b**, respectively.

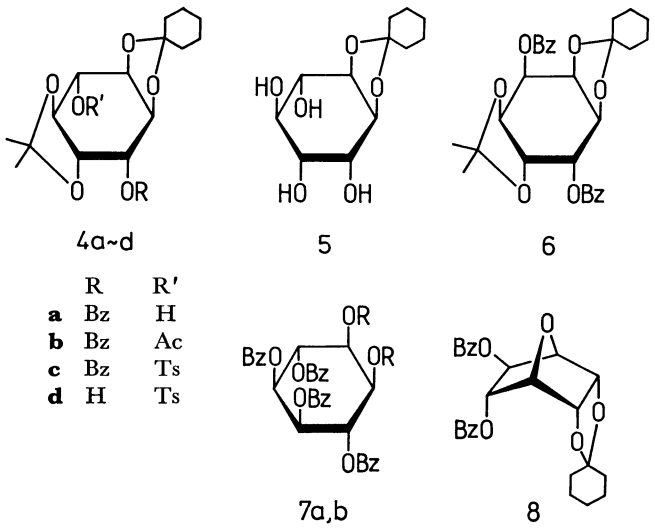
Similarly, isopropylidenation of 1-*O*-benzoyl-2,3-*O*-cyclohexylidene-*myo*-inositol (**1c**) gave, upon separation by silica gel chromatography, the 5,6-*O*-isopropylidene derivative (**2f**, 20%) as crystals, and the 4,5-*O*-isopropylidene derivative (**3f**, 43%) as a syrup. The assigned structures were confirmed on the basis of the following evidences. Acetylation of **2f** and **3f** afforded the corresponding acetates (**2g** and **3g**). In the NMR spectrum of **2g**, the signals due to two protons which attached to the carbon atoms bearing the acyloxy functions were shown not to be coupled with each other. Methylation of **3f** with methyl iodide and silver oxide in *N,N*-dimethylformamide gave two crystalline methyl ethers (**3h** and **3i**) in 75 and 4% yields, respectively.[3] While, the methyl ether (**2h**) derived from **2f** was different from either **3h** or **3i**. On removal of the blocking groups followed by acetylation, **3h** and **3i** were transformed into the known 4-[4] and 1-*O*-methyl-*myo*-inositol pentaacetate,[5] respectively.

*Selective Benzoylation and Tosylation.* Treatment of **2a** with 1.5 molar equiv of tosyl chloride in pyridine at 0—5 °C for 2 days yielded **2d** almost exclusively in 57% yield. When **2a** was treated with 1.3 molar equiv of benzoyl chloride in pyridine at −5 °C for 1.5 h, **2f** and the dibenzoate (**2i**) were obtained in 33 and 28% yields, respectively. These results indicated that the C-3 hydroxyl group being adjacent to *cis*-arranged cyclohexylidene oxygen atom is more reactive than the less hindered C-6 hydroxyl group.[6]

On the other hand, selective benzoylation of **2a** with 1.3 molar equiv of benzoic anhydride in pyridine at room temperature for 5 days gave rise to the 6-*O*-benzoate (**2j**) in 52% yield, together with **2i** (12%) and a trace of **2f**. Accordingly, in contrast to the case of acid halide, steric factor seemed to play a role in selectivity of *O*-acylation with acid anhydride.

*Preparation of Blocked Inositols.* Unaccessible partially protected *chiro*-inositol derivatives were obtained by nucleophilic displacement reaction of the tosylates of **2a** with a benzoate ion. Thus, **2d** was treated with an excess of sodium benzoate in boiling *N,N*-dimethylformamide for 120 h to give 1-*O*-benzoyl-5,6-*O*-cyclohexylidene-2,3-*O*-isopropylidene-*chiro*-inositol (**4a**) in 52% yield. On de-*O*-benzoylation followed by mild acid treatment, **4a** was converted into 1,2-*O*-cylohexylidene-*chiro*-inositol (**5**) in 95% yield, whose structure was ascertained by conversion to *chiro*-inositol.[7]

Treatment of **2b** with sodium benzoate under the




Scheme 2.

similar conditions for 50 h afforded 1-*O*-benzoyl-5,6-*O*-cyclohexylidene-2,3-*O*-isopropylidene-4-*O*-tosyl-*chiro*-inositol (**4c**) in 72% yield. When the reaction time was prolonged to 70 h, the tosyloxy group on C-6 was partially displaced with a benzoate ion giving 2,5-di-*O*-benzoyl-3,4-*O*-cyclohexylidene-1,6-*O*-isopropylidene-*allo*-inositol (**6**) in 10% yield, together with 31% yield of **4c**. The structure of **4c** was tentatively assigned by comparing the NMR spectrum with those of **4a** and its acetate (**4b**).

Additionally, the protected *muco*-inositol was prepared by the following reaction sequence. Reaction of **1b** with potassium carbonate in boiling 80% aqueous 2-methoxyethanol for 30 h followed by benzoylation gave 1,2,3,6-tetra-*O*-benzoyl-4,5-*O*-cyclohexylidene-*muco*-inositol (**7a**) in 51% yield, which was, upon de-*O*-cyclohexylidenation, converted into tetrabenzoyl-*muco*-inositol (**7b**) in 92% yield. The NMR spectrum of **7a** supported the assigned structure. Conversion of **7b** into *muco*-inositol[8] gave the final evidence.

A small amount of crystals (**8**, 1.3%) was isolated from the mother liquor from **7a** after a long storage. The elemental analysis and NMR spectrum suggested that **8** had an 1,4-anhydro ring. On lithium aluminum hydride reduction followed by benzoylation,[9] 1,4-anhydro-5,6-*O*-cyclohexylidene-3-*O*-tosyl-*chiro*-inositol[10] gave 1,4-anhydro-2,3-di-*O*-benzoyl-5,6-*O*-cyclohexylidene-*chiro*-inositol that was shown to be identical with **8**. Mechanistically, **7a** was formed by diaxial opening of the intemediate 3,4-epoxide with $OH^-$ and **8** was obtained by the rear-side attack of the 6-hydroxyl group on C-3.

## Experimental[11]

*Isopropylidenation of 1,2-*O*-Cyclohexylidene-*myo*-inositol (**1a**).* To a slurry of **1a** (20 g) in *N,N*-dimethylformamide (100 ml) was added 2,2-dimethoxypropane (30 ml) and *p*-toluenesulfonic acid (0.2 g), and the mixture was heated at 70—75 °C for 90 min. The cooled reaction mixture was treated with sodium hydrogencarbonate (5 g) and then evaporated to dryness. The crystalline residue was extracted with hot 2-butanone (3×50 ml) and the extracts were evaporated to give crystals that were recrystallized from 2-butanone–toluene to afford 1,2-*O*-cyclohexylidene-4,5-*O*-isopropylidene-*myo*-inositol (**2a**, 5.1 g, 22%) as needles: mp 180.5—181.5 °C.

Found: C, 60.12; H, 7.93%. Calcd for $C_{15}H_{24}O_6$: C, 59.98; H, 8.05%.

Compound **2a** (3 g) was treated with tosyl chloride (7.7 g) in pyridine (30 ml) at room temperature for 2 days. The reaction mixture was poured into ice–water and the resulting crystals were collected. Recrystallization from 2-butanone–toluene gave the ditosyl derivative (**2b**, 5.7 g, 93%): mp 192—195 °C; NMR ($CDCl_3$) $\delta$ 2.43 (s, 6, two tosyl $CH_3$), 3.35 (dd, 1, $J_{4,5}$=9 Hz, $J_{5,6}$=11 Hz, H-5), 4.01 (dd, 1, $J_{3,4}$=11 Hz, H-4), 4.12 (dd, 1, $J_{1,2}$=5 Hz, $J_{1,6}$=6.5 Hz, H-1), 4.41 (dd, 1, $J_{2,3}$=4 Hz, H-2), 4.80 (dd, 1, H-3), 5.38 (dd, 1, H-6).

Found: C, 57.37; H, 5.88; S, 10.47%. Calcd for $C_{29}H_{36}O_{10}S_2$: C, 57.22; H, 5.97; S, 10.53%.

Compound **2b** (0.1 g) was refluxed with 80% aqueous acetic acid (10 ml) for 2 h. After cooling, the resulting crystals were collected by filtration, washed with water, and dried to give 1,4-di-*O*-tosyl-*myo*-inositol (0.07 g, 89%): mp 199—200 °C. This compound was identified with an authentic sample[2] (mp 198—200 °C) by comparison with IR spectra.

Compound **2a** (0.2 g) was treated with acetic anhydride (5 ml) and pyridine (5 ml) at room temperature for 2 h. The mixture was poured into ice–water and the resulting crystals were collected by filtration. Recrystallization from ethanol gave the diacetyl derivative (**2c**, 0.24 g, 95%) as needles: mp 175.5—176.5 °C; NMR ($CDCl_3$)[12] $\delta$ 2.16 (s, 3) and 2.20 (s, 3) (OAc), 3.55 (dd, 1, $J_{4,5}$=11 Hz, $J_{5,6}$=9 Hz, H-5), 4.21 (dd, 1, $J_{2,3}$=5 Hz, $J_{3,4}$=6.5 Hz, H-3), 4.21 (dd, 1, $J_{1,6}$=11 Hz, H-6), 4.70 (t, 1, $J_{1,2}$=4.5 Hz, H-2), 5.20 (dd, 1, H-1), 5.38 (dd, 1, H-4).

Found: C, 59.60; H, 7.35%. Calcd for $C_{19}H_{28}O_8$: C, 59.36; H, 7.34%.

The mother liquor obtained from **2a** was concentrated and purified by passing through a short alumina column with 2-butanone as an eluent to give a syrupy product (*ca.* 16 g) consisting mainly of **3a**. A 6-g portion of the syrup was tosylated as described for **2a** to give 1,2-*O*-cyclohexylidene-5,6-*O*-isopropylidene-3,4-di-*O*-tosyl-*myo*-inositol (**3b**, 4.3 g, 25% yield based on **1a** used) as needles, after recrystallization from 2-butanone–toluene: mp 165—167 °C; NMR ($CDCl_3$) $\delta$ 2.47 (s, 6, two tosyl $CH_3$), 3.45 (dd, 1, $J_{4,5}$=8 Hz, $J_{5,6}$=10 Hz, H-5), 4.02 (dd, 1, $J_{1,6}$=7 Hz, H-6), 4.80 (t, 1, $J_{2,3}$=$J_{3,4}$=3 Hz, H-3), 4.99 (dd, 1, H-4).

Found: C, 57.12; H, 5.90; S, 10.92%. Calcd for $C_{29}H_{36}O_{10}S_2$: C, 57.22; H, 5.97; S, 10.53%.

Compound **3b** (50 mg) was treated with boiling 80% aqueous acetic acid followed by acetylation in the usual manner to give 1,6-di-*O*-tosyl-*myo*-inositol tetraacetate (40 mg, 84%) as crystals: mp 195—197 °C, which was identified with an authentic sample[2] (mp 196—197.5 °C) by comparison with IR spectra.

A 10-g portion of crude **3a** was treated with benzoyl chloride (30 ml) in pyridine (70 ml) at room temperature overnight. The reaction mixture was poured into ice–water and the resulting gum was extracted with chloroform (2×50 ml). The extracts were washed with aqueous sodium hydrogencarbonate and water, dried, and concentrated to leave a syrup, which was crystallized from toluene to give the dibenzoyl derivative (**3c**). Recrystallization from 2-butanone gave pure crystals (12.5 g, 62% yield besed on **1a** used): mp 199—202 °C.

Found: C, 68.43; H, 6.27%. Calcd for $C_{29}H_{32}O_8$: C, 68.49; H, 6.34%.

*Isopropylidenation of 1,2-O-Cyclohexylidene-3-O-tosyl-myo-inositol (**1b**).* To a solution of **1b**[2] (20 g) in *N,N*-dimethylformamide (100 ml) were added 2,2-dimethoxypropane (40 ml) and *p*-toluenesulfonic acid (0.2 g), and the mixture was heated at 90 °C for 15 min. After cooling, the reaction mixture was neutralized by treating with Amberlite IRA-410 ($OH^-$) and then concentrated to give a syrup that was crystallized from 2-butanone–toluene to give 1,2-*O*-cyclohexylidene-4,5-*O*-isopropylidene-3-*O*-tosyl-*myo*-inositol (**2d**, 4.3 g, 18%) as needles: mp 167—169 °C; NMR ($CDCl_3$) $\delta$ 2.46 (s, 3, tosyl $CH_3$), 3.31 (dd, 1, $J_{4,5}=10$ Hz, $J_{5,6}=10.5$ Hz, H-5), 4.45 (t, 1, $J_{1,2}=J_{2,3}=4.5$ Hz, H-2), 4.89 (dd, 1, $J_{3,4}=10$ Hz, H-3).

Found: C, 58.41; H, 6.65; S, 7.19%. Calcd for $C_{22}H_{30}O_8S$: C, 58.13; H, 6.65; S, 7.05%.

Compound **2d** (0.2 g) was acetylated in the usual manner and the crude product was recrystallized from 2-butanone–methanol to give the acetyl derivative (**2e**, 0.2 g, 91%): mp 215—216 °C; NMR ($CDCl_3$) $\delta$ 2.14 (s, 3, OAc), 2.48 (s, 3, tosyl $CH_3$), 3.40 (dd, 1, $J_{4,5}=9$ Hz, $J_{5,6}=11$ Hz, H-5), 4.12 (dd, 1, $J_{3,4}=10.5$ Hz, H-4), 4.13 (dd, 1, $J_{1,2}=4.5$ Hz, $J_{1,6}=7$ Hz, H-1), 4.46 (t, 1, $J_{2,3}=4.5$ Hz, H-2), 4.90 (dd, 1, H-3), 5.29 (dd, 1, H-6).

Found: C, 58.13; H, 6.46; S, 6.62%. Calcd for $C_{24}H_{32}O_9S$: C, 57.67; H, 6.46; S, 6.23%.

Treatment of **2d** (0.2 g) with tosyl chloride (0.25 g) in pyridine (2 ml) at room temperature for 2 days gave **2b** (0.21 g, 77%), mp 187—189 °C, after recrystallization from chloroform–ethanol, which was identified with the sample obtained before.

The mother liquor from **2d** was concentrated to leave a syrup that was crystallized from toluene giving 1,2-*O*-cyclohexylidene-5,6-*O*-isopropylidene-3-*O*-tosyl-*myo*-inositol (**3d**, 4.1 g, 19%) as crystals. It melted at 163—165 °C, solidified at 168—175 °C, and then remelted at 223—227 °C with decomposition; NMR ($CDCl_3$) $\delta$ 2.49 (s, 3, tosyl $CH_3$), 3.43 (dd, 1, $J_{4,5}=9$ Hz, $J_{5,6}=10$ Hz, H-5), 4.71 (t, 1, $J_{2,3}=J_{3,4}=ca.$ 4.5 Hz, H-3).

Found: C, 58.00; H, 6.61; S, 6.84%. Calcd for $C_{22}H_{30}O_8S$: C, 58.13; H, 6.65; S, 7.05%.

Compound **3d** (0.2 g) was acetylated to give, after crystallization from ethanol, the acetyl derivative (**3e**, 0.19 g, 91%) as crystals: mp 151—153 °C; NMR ($CDCl_3$) $\delta$ 2.04 (s, 3, OAc), 2.49 (s, 3, tosyl $CH_3$), 3.52 (dd, 1, $J_{4,5}=9$ Hz, $J_{5,6}$ 10.5 Hz, H-5), 3.99 (dd, 1, $J_{1,6}=7$ Hz, H-6), 4.86 (dd, 1, $J_{2,3}=4.5$ Hz, $J_{3,4}=5.5$ Hz, H-3), 5.41 (dd, 1, H-4).

Found: C, 58.04; H, 6.51; S, 6.46%. Calcd for $C_{24}H_{32}O_9S$: C, 57.67; H, 6.46; S, 6.23%.

Tosylation of **3d** (0.2 g) in the usual manner gave **3b** (0.16 g, 52%), mp 165—167 °C, which was identical with the compound obtained before.

*Isopropylidenation of 1-O-Benzoyl-2,3-O-cyclohexylidene-myo-inositol (**1c**).* To a solution of **1c** (6 g) in *N,N*-dimethylformamide (60 ml) were added 2,2-dimethoxypropane (12 ml) and *p*-toluenesulfonic acid (0.06 g), and the mixture was heated for 5 min at 90 °C. After cooling, the reaction mixture was neutralized with 5% aqueous potassium carbonate and then poured into ice–water(300 ml). The resulting white powder was collected by filtration and dried over phosphorus pentaoxide *in vacuo* giving a gum (*ca.* 6 g). A 4-g portion of this product was chromatographed on silica gel (135 g) with 2-butanone–toluene (1 : 6, v/v) as an eluent. Two fractions were separated according to the results of TLC. The first fractions gave 1-*O*-benzoyl-2,3-*O*-cyclohexylidene-4,5-*O*-isopropylidene-*myo*-inositol (**3f**, 1.9 g, 43%) as a homogeneous syrup. The second fractions gave a syrup (0.9 g) that was crystallized from ethanol to give 1-*O*-benzoyl-2,3-*O*-cyclohexylidene-5,6-*O*-isopropylidene-*myo*-inositol (**2f**, 0.6 g, 13%) as needles: mp 172.5—173 °C; NMR ($CDCl_3$), **2f**: $\delta$ 3.57 (dd, 1, $J_{4,5}=8.5$ Hz, $J_{5,6}=9.5$ Hz, H-5), 4.76 (t, 1, $J_{1,2}=J_{2,3}=4.5$ Hz, H-2), 5.41 (dd, 1, $J_{1,6}=10$ Hz, H-3); **3f**: $\delta$ 3.57 (dd, 1, $J_{4,5}=10$ Hz, $J_{5,6}=8.5$ Hz, H-5), 4.10 (dd, $J_{1,2}=4$ Hz, $J_{2,3}=7$ Hz, H-3), 5.31 (t, 1, $J_{1,6}=4$ Hz, H-1).

Found for **2f**: C, 65.58; H, 6.89%. Calcd for $C_{22}H_{28}O_7$: C, 65.32; H, 6.99%.

Compound **2f** (0.1 g) was acetylated in the usual manner to give, after crystallization from chloroform–ethanol, the acetyl derivative (**2g**, 0.09 g, 77%): mp 219 °C (sublimation); NMR ($CDCl_3$) $\delta$ 2.15 (s, 3, OAc), 3.59 (dd, 1, $J_{4,5}=11$ Hz, $J_{5,6}=9.5$ Hz, H-5), 4.23 (dd, 1, $J_{2,3}=4.5$ Hz, $J_{3,4}=7$ Hz, H-3), 4.34(dd, 1, $J_{1,6}=10$ Hz, H-6), 4.75 (t, 1, $J_{1,2}=4.5$ Hz, H-2), 5.38 (dd, 1, H-4), 5.43 (dd, 1, H-1).

Found: C, 64.40; H, 6.67%. Calcd for $C_{24}H_{30}O_8$: C, 64.55; H, 6.79%.

Compound **3f** (0.1 g) gave the acetyl derivative (**3g**, 0.1 g, 98%) as a homogeneous syrup; NMR ($CDCl_3$) $\delta$ 2.10 (s, 3, OAc), 3.71 (dd, 1, $J_{4,5}=10$ Hz, $J_{5,6}=8.5$ Hz, H-5), 4.07 (t, 1, $J_{2,3}=J_{3,4}=7$ Hz, H-3).

*Methylation of 3f.* To a solution of **3f** (1.9 g) in *N,N*-dimethylformamide (19 ml) were added silver oxide (2.8 g) and methyl iodide (2.8 ml), and the mixture was stirred at room temperature for 24 h under dark. An insoluble matter was filtered off and the filtrate was evaporated to dryness. The residue was extracted with hot ethyl acetate and the extract was passed through a short alumina column. The solution was evaporated and crystallized from ethanol to give the 6-*O*-methyl derivative (**3h**, 1.5 g, 75%) as prisms: mp 129—131 °C; NMR ($CDCl_3$) $\delta$ 3.58 (s, 3, $OCH_3$).

Found: C, 66.33; H, 7.10%. Calcd for $C_{23}H_{30}O_7$: C, 66.00; H, 7.24%.

The mother liquor from **3h** afforded, after long storage in a refrigerator, crystals that were recrystallized from ethanol to give 4-*O*-benzoyl-1,2-*O*-cyclohexylidene-5,6-*O*-isopropylidene-3-*O*-methyl-*myo*-inositol (**3i**, 0.07 g, 4%) as needles: mp 150.5—151.5 °C; NMR ($CDCl_3$) $\delta$ 3.58 (s, 3, $OCH_3$), 3.71 (dd, 1, $J_{4,5}=7.5$ Hz, $J_{5,6}=8.5$ Hz, H-5), 5.43 (dd, $J_{3,4}=2.5$ Hz, H-4).

Found: C, 66.16; H, 7.31%. Calcd for $C_{23}H_{30}O_7$: C, 66.00; H, 7.24%.

*1-O-Benzoyl-2,3-O-cyclohexylidene-5,6-O-isopropylidene-4-O-methyl-myo-inositol (**2h**).* Methylation of **2f** (0.45 g) with silver oxide (0.45 g) and methyl iodide (0.45 g) in *N,N*-dimethylformamide (5 ml) gave, after crystallization from ethanol, **2h** (0.33 g, 70%) as needles: mp 128—129.5 °C; NMR ($CDCl_3$) $\delta$ 3.61 (s, 3, $OCH_3$), 4.76 (t 1, $J_{1,2}=J_{2,3}=4.5$ Hz, H-2), 5.37 (dd, 1, $J_{1,6}=11$ Hz, H-1).

Found: C, 66.20; H, 7.33%. Calcd for $C_{23}H_{30}O_7$: C, 66.00; H, 7.24%.

*1,2-O-Cyclohexylidene-5,6-O-isopropylidene-3-O-methyl-myo-inositol (**3j**).* To a solution of **3i** (0.19 g) in methanol (5 ml) was added 0.1 M methanolic sodium methoxide (0.1 ml) and the mixture was allowed to stand at room temperature overnight. After having been neutralized with Amberlite IR-120 ($H^+$), the solution was evaporated and the crystalline residue was recrystallized from ethanol to give **3j** (0.12 g, 86%): mp 169—171 °C.

Found: C, 61.27; H, 8.14%. Calcd for $C_{16}H_{26}O_6$; C, 61.12; H, 8.35%.

Compound **3j** (0.21 g) was hydrolyzed with boiling 80% aqueous acetic acid (10 ml) for 2 h. The reaction mixture was evaporated and the product was crystallized from ethanol to give 1-*O*-methyl-*myo*-inositol (DL-bornesitol) (0.09 g, 71%)

as crystals: mp 197—198 °C (lit,[13] 198—200 °C). Acetylation gave the pentaacetyl derivative: mp 152—154 °C (lit,[4] 154—154.5 °C).

*1-O-Acetyl-2,3-O-cyclohexylidene-4,5-O-isopropylidene-6-O-methyl-myo-inositol (**3k**).* De-*O*-benzoylation of **3h** (5 g) with methanolic sodium methoxide in methanol (100 ml) gave a syrupy product, which was, without furhter purification, acetylated in the usual manner to give, after crystallization from ethanol, **3k** (3.7 g, 89%): mp 140.5—141.5 °C.

Found: C, 60.88; H, 7.75%. Calcd for $C_{18}H_{28}O_7$: C, 60.65; H, 7.93%.

Compound **3k** (0.2 g) was hydrolyzed with boiling 80% aqueous acetic acid (10 ml) and acetylated to give pentaacetyl-4-*O*-methyl-*myo*-inositol (-DL-ononitol) (0.21 g, 84%): mp 131—132 °C (lit,[5] 134—135 °C).

*Selective Tosylation of **2a**.* To a solution of **2a** (10 g) in dry pyridine (100 ml) was added tosyl chloride (9.5 g, 1.5 molar equiv) at −5 °C under stirring, and then the mixture was allowed to stand in a refrigerator for 2 days. The mixture was poured into ice–water and the precipitates were collected by filtration. The crude product (10.5 g) was recrystallized from toluene to give **2d** (8.6 g, 57%) as practically pure crystals: mp 154—155 °C.

*Selective Benzoylation of **2a**.* *a)* To a solution of **2a** (0.5 g) in dry pyridine (5 ml) was added benzoyl chloride (0.25 ml, 1.3 molar equiv) at −5 °C under stirring. After having been stood at room temperature for 1.5 h, the mixture was poured into ice–water to give 0.5 g of crude products. TLC indicated the presence of two components. Fractional crystallization from 2-butanone gave **2f** (0.22 g, 33%) and the dibenzoyl derivative (**2i**, 0.24 g, 28%): mp 230 °C; NMR ($CDCl_3$) $\delta$ 5.77 (dd, 1, $J_{4,5}$=11 Hz, $J_{5,6}$=9 Hz, H-5), 4.44 (dd, 1, $J_{2,3}$=4.5 Hz, $J_{3,4}$=6 Hz, H-3), 4.45 (dd, 1, $J_{1,6}$=10 Hz, H-6), 4.85 (t, 1, $J_{1,2}$=4.5 Hz, H-2), 5.51 (dd, 1, H-1), 5.69 (dd, 1, H-4).

Found: C, 68.56; H, 6.43%. Calcd for $C_{29}H_{32}O_8$; C, 68.49; H, 6.34%.

*b)* To a solution of **2a** (3 g) in dry pyridine (30 ml) was added benzoic anhydride (2.9 g, 1.3 molar equiv) and the mixture was allowed to stand at room temperature for 5 days. TLC indicated one major and one minor spots. The reaction mixture was poured into ice–water and the resulting crystals were recrystallized from 2-butanone to give **2i** (0.6 g, 12%). The mother liquor from **2i** was concentrated and crystallized from toluene to give 6-*O*-benzoyl-1,2-*O*-cyclohexylidene-4,5-*O*-isopropylidene-*myo*-inositol (**2j**, 2.1 g, 52%) as needles: mp 169—174 °C. Recrystallized sample melted at 177—178 °C: NMR ($CDCl_3$) $\delta$ 5.63 (dd, 1, $J_{1,6}$=6 Hz, $J_{5,6}$=11 Hz, H-6).

Found: C, 65.47; H, 7.00%. Calcd for $C_{22}H_{28}O_7$: C, 65.32; H, 6.99%.

The presence of a trace of **2f** was detected in crude **2j** by the NMR spectrum.

*1-O-Benzoyl-5,6-O-cyclohexylidene-2,3-O-isopropylidene-chiro-inositol (**4a**).* A mixture of **2d** (4 g) and sodium benzoate (3.8 g, 3 molar equiv) in *N,N*-dimethylformamide (100 ml) was refluxed for 120 h. After cooling, ethyl acetate (80 ml) was added to the reaction mixture and an insoluble matter was removed by filtration. The filtrate was evaporated to dryness and the residue was extracted with hot ethyl acetate (3×50 ml). The extracts were filtered through a short column of alumina and evaporated to give a syrup, which was crystallized from ethanol to give **4a** (1.8 g, 52%) as crystals: mp 176.5—177 °C.

Found: C, 65.46; H, 6.96%. Calcd for $C_{22}H_{28}O_7$: C, 65.32; H, 6.99%.

Compound **4a** (0.2 g) was acetylated in the usual manner to give, after crystallization from ethanol, the acetyl derivative (**4b**, 0.19 g, 86%) as needles: mp 166.5—167 °C; NMR ($CDCl_3$) $\delta$ 2.19 (s, 3, OAc), 5.42 (dd, 1, $J$=5.5 Hz, $J$=11 Hz, H-3), 6.07 (t, 1, $J$=1.5 Hz, H-6).

Found: C, 64.28; H, 6.67%. Calcd for $C_{24}H_{30}O_8$: C, 64.55; H, 6.79%.

*1,2-O-Cyclohexylidene-chiro-inositol (**5**).* Compound **4a** (3 g) was dissolved in a mixture of chloroform (60 ml) and ethanol (15 ml), and *p*-toluenesulfonic acid (0.3 g) was added at 0 °C. The mixture was allowed to stand in a refrigerator overnight. Then the mixture was diluted with methanol (60 ml) and 1 M methanolic sodium methoxide (12 ml) was added. After having been stood at room temperature, the resulting crystals were collected to give **5** (1.8 g, 95%): mp 181—183 °C. Recrystallization from ethanol–water gave pure prisms: mp 182—183 °C.

Found: C, 55.64; H, 7.73%. Calcd for $C_{12}H_{20}O_6$: C, 55.36; H, 7.76%.

Hydrolysis of **5** (0.05 g) with boiling 6 M hydrochloric acid (10 ml) for 1 h gave *chiro*-inositol (0.03 g, 81%) as crystals: mp 227—235 °C. Recrystallization from ethanol–water gave a pure sample: mp 245—247 °C (lit,[7] 253 °C).

*1-O-Benzoyl-5,6-O-cyclohexylidene-2,3-O-isopropylidene-4-O-tosyl-chiro-inositol (**4c**).* *a)* A mixture of **2b** (2.5 g) and sodium benzoate (2 g) in *N,N*-dimethylformamide (50 ml) was refluxed for 50 h. The reaction mixture was cooled to room temperature and diluted with 2-butanone (30 ml). An insoluble matter was removed by filtration and the filtrate was filtrated through a short alumina column. Evaporation gave a syrup that was crystallized from methanol to give **4c** (1.7 g, 72%): mp 141.5—144.5 °C. Recrystallization from 2-butanone–methanol gave pure product (1.4 g, 63%): mp 165.5—167 °C; NMR ($CDCl_3$) $\delta$ 2.43 (s, 3, tosyl $CH_3$), 4.70—5.00 (m, 1, H-4), 5.94 (broad d, 1, $J$=*ca.* 2 Hz, H-1).

Found: C, 62.57; H, 6.19; S, 5.92%. Calcd for $C_{29}H_{34}O_9S$: C, 62.34; H, 6.14; S, 5.74%.

*b)* A mixture of **2b** (2 g) and sodium benzoate (2 g) in *N,N*-dimethylformamide (70 ml) was refluxed for 70 h. The mixture was processed as described above to give crystalline mixtures. Fractional crystallization from ethanol–ethyl acetate gave **4c** (0.55 g, 31%): mp 162—165 °C, and 2,6-di-*O*-benzoyl-3,4-*O*-cyclohexylidene-1,6-*O*-isopropylidene-*allo*-inositol (**6**, 0.16 g, 10%): mp 210—212 °C; NMR ($CDCl_3$) $\delta$ 4.26 (dd, 1, $J$=10.5 Hz, $J$=2.5 Hz), 4.70 (dd, 1, $J$=3 Hz, $J$=10.5 Hz), 5.95—6.20 (m, 2, H-2 and H-5).

Found: C, 68.47; H, 6.44%. Calcd for $C_{29}H_{32}O_8$: C, 68.49; H, 6.34%.

*1,2-O-Cyclohexylidene-4,5-O-isopropylidene-3-O-tosyl-chiro-inositol (**4d**).* A solution of **4c** (2 g) in 2-butanone (20 ml) was treated with catalytic amount of methanolic sodium methoxide for 40 min at room temperature. The reaction mixture was neutralized with acetic acid and evaporated to give a white solid, which was chromatographed on silica gel (70 g) with 2-butanone–toluene (1 : 4, v/v). The major fractions were collected and crystallized from 2-butanone–toluene to give **4d** (0.5 g, 31%): mp 134—136 °C.

Found: C, 57.97; H, 6.58; S, 7.10%. Calcd for $C_{22}H_{30}O_8S$: C, 58.13; H, 6.65; S, 7.05%.

*1,2,3,6-Tetra-O-benzoyl-4,5-O-cyclohexylidene-muco-inositol (**7a**) and 1,4-Anhydro-2,3-di-O-benzoyl-5,6-O-cyclohexylidene-chiro-inositol (**8**).* A mixture of **1b** (10 g), anhydrous potassium carbonate (10 g) and 80% aqueous 2-methoxyethanol (200 ml) was refluxed for 3.5 h, and then evaporated to dryness. After the residue was dried by codistillation with dry toluene, it was treated with benzoyl chloride (23 ml) in pyridine (60 ml) under ice cooling. After overnight at room temperature, the reaction mixture was poured into ice–water (300 ml) and the resulting gum was extracted with chloro-

form (100 ml). The extract was washed successively with 1M hydrochloric acid, 5% aqueous sodium carbonate, and water, dried, and evaporated to give a syrup that was crystallized from chloroform–ethanol giving a mixture of **7a** and **8**. Fractional crystallization from the same solvents gave **7a** (8.3 g, 51%): mp 177—179 °C; NMR ($CDCl_3$) $\delta$ 4.58 (broad d, 2, $J$=4 Hz, H-4 and H-5), 5.86 (broad d, 2, $J$=6 Hz, H-1 and H-2), 6.14 (broad dd, 2, H-3 and H-6).

Found: C, 71.26; H, 5.39%. Calcd for $C_{40}H_{36}O_{10}$: C, 70.99; H, 5.36%.

From the mother liquor of **7a**, a small amount of **8** (0.14 g, 1.3%) was obtained as hair like needles: mp 155—157 °C; NMR ($CDCl_3$) $\delta$ 4.6—5.2 (m, 4, H-1, H-4, H-5, and H-6), 5.37 (broad t, 1, $J_{2,3}$=3.5 Hz, $J_{3,4}$=4.5 Hz, $J_{3,5}$=*ca.* 1 Hz, H-3), 6.05 (d, 1, H-2).

Found: C, 69.55; H, 5.90%. Calcd for $C_{26}H_{26}O_7$: C, 69.32; H, 5.82%.

*1,2,3,6-Tetra*-O-*benzoyl*-muco-*inositol (**7b**)*. A mixture of **7a** (6 g) and 80% aqueous acetic acid (50 ml) was refluxed for 1 h. After cooling, the resulting crystals were collected by filtration to give **7b** (4.9 g, 92%): mp 252—254 °C. An analytical sample melted at 256—257 °C after recrystallization from pyridine–ethanol.

Found: C, 68.24; H, 4.90%. Calcd for $C_{34}H_{28}O_{10}$: C, 68.47; H, 4.73%.

A solution of **7b** (0.5 g) in 2-methoxyethanol (10 ml) was treated with 1 M methanolic sodium methoxide (0.5 ml) at 90 °C for 10 min. The reaction mixture was diluted with water and treated with Amberlite IRA-120 ($H^+$) and then evaporated to give a crystalline residue that was pulverized with ethanol and collected to give crude *muco*-inositol (0.15 g, 98%): mp 190—220 °C. Recrystallization from water–ethanol gave a pure sample (0.13 g): mp 285—290 °C (lit,[8] 281—290 °C).

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11) Melting points were determined in a capillary in a liquid bath and are uncorrected. Solutions were evaporated under diminished pressure at 40—50 °C. NMR spectra were measured at 60 MHz on a Varian A-60D spectrometer in deuteriochloroform ($CDCl_3$) with reference to tetramethylsilane as an internal standard and the peak positions are give in $\delta$-values. Values given for coupling constants are of first-order. TLC was performed on silica gel (Wako gel B-10, Wako Pure Chemical Industries, Ltd.) using a mixture of 2-butanone and toluene as an eluent. Elemental analyses were performed by Mr. Saburo Nakada, to whom our thanks are due.

In this paper, all the compounds except for meso compounds are racemic. All the formulas depict one enantiomer of the respective racemates.

12) Compound **2c** is named 1,4-di-*O*-acetyl-2,3-*O*-cyclohexylidene-5,6-*O*-isopropylidene-*myo*-inositol.

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