Carbohydrate Research, 101 (1982) 209–219
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

THE PREPARATION OF CYCLOHEXANEPENTOLS FROM INOSITOLS BY DEOXYGENATION*

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(Received June 12th, 1981; accepted for publication, July 6th, 1981)

ABSTRACT

Several cyclohexanepentols have been synthesized from inositols by blocking all but one hydroxyl group, converting the free hydroxyl group into its *S*-methyl dithiocarbonate, and treating it with tributylstannane. Suitable blocking-groups are methyl, benzyl, and methylthiomethyl ethers, and acetals. One cyclohexanepentol was prepared by the reductive deamination of an aminodeoxyinositol.

INTRODUCTION

Of the sixteen possible cyclohexanepentols, only two have been found in Nature[2]. However, all of the four *meso* forms, and the racemate or at least one enantiomer of each of the optically active forms, have been synthesized; some of these syntheses are cumbersome, and the cyclohexanepentols can by no means be described as readily available.

For the study of their ^{13}C-n.m.r. spectra, we required some cyclohexanepentols which were not in our collection. We decided to synthesize them from inositols by the method of deoxygenation recently developed by Barton and McCombie[3]. In this method, the hydroxyl group to be eliminated is converted into its *S*-methyl dithiocarbonate which is then treated with tributylstannane. The other hydroxyl groups in the molecule have to be protected. Since the first reaction involves strongly basic conditions, ester groups are not suitable as protecting groups; however, acetals or ethers can be used. Many di-*O*-isopropylidene and di-*O*-cyclohexylidene derivatives of inositols are readily obtainable[4,5]; selective protection of the fifth hydroxyl group is usually not difficult.

A readily available starting-material of this type is D-1,2:5,6-di-*O*-cyclohexylidene-3-*O*-methyl-*chiro*-inositol[5] (**1**), obtainable from pinitol (D-3-*O*-methyl-*chiro*-inositol), a compound found in many species of pine trees[6]. It was easily converted into its *S*-methyl dithiocarbonate **2** which reacted with tributylstannane to give the

*Cyclitols, Part XXXVIII. For Part XXXVII, see ref. 1.
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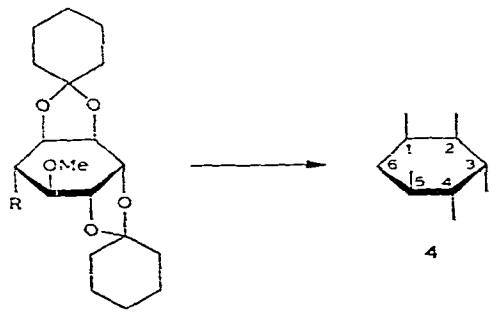
0008-6215/82/0000–0000/$ 02.75,

deoxy derivative **3**; both reactions proceeded in good yield, but column chromatography was required in order to separate the product from tin derivatives which have similar solubilities. Acid hydrolysis of the acetal groups and subsequent removal of the methyl group by hydriodic acid gave the previously unknown L-1,2,5/3,4-cyclohexanepentol (**4**).



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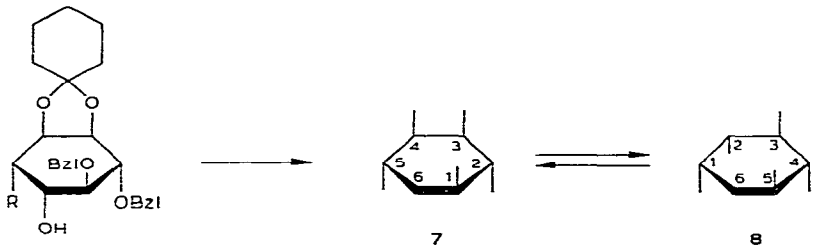
1 R = OH
2 R = OC(=S)SMe
3 R = H

Another recent method of deoxygenation involves the photolysis of esters[7]; this method was also tried starting with **1**. Acetylation gave the mono-acetate which, when irradiated with a u.v. lamp in hexamethylphosphoric triamide, yielded the deoxy compound **3**. Since this compound is not crystalline, we were unable to separate it fully from the high-boiling solvent, but acid hydrolysis, followed by treatment with hydriodic acid, gave the pentol **4**. Although the photolysis worked well in this instance, we were not successful with it in some other cases. In this method, benzyl ethers cannot be used as protecting groups, because they are also affected by u.v. radiation.

In order to synthesize the enantiomer[8] (**7**) of naturally occurring quercitol (L-1,3,4/2,5-cyclohexanepentol) by the same method from L-*chiro*-inositol, it is necessary to protect one pair of *cis*-hydroxyl groups but leave one hydroxyl group of the other pair unprotected. A suitable starting-material is L-3,4-di-*O*-benzyl-1,2-*O*-cyclohexylidene-*chiro*-inositol (**5**). Partial benzylation of this compound is not regioselective[9]; both tribenzyl compounds are formed, besides the di- and tetrabenzyl derivatives. The method recommended by Garegg *et al.*[10] for monobenzylation, using a phase-transfer catalyst, proved to be advantageous in this case. Although both tribenzyl derivatives were still formed, the reaction mixture was practically free of the di- and the tetra-benzyl compounds, and could be readily fractionated by chromatography on alumina. The desired L-1,3,4-tri-*O*-benzyl-5,6-*O*-cyclohexylidene-*chiro*-inositol (**6**) was thus obtained. Formation of the *S*-methyl dithiocarbonate and reaction with tributylstannane again proceeded smoothly, and the protecting groups were removed by hydriodic acid.

By regiospecific epimerization with sulfuric acid in 95% acetic acid[11], the



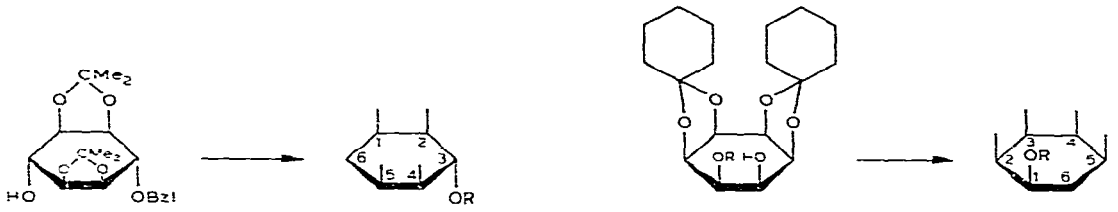
5 R = OH
6 R = OBzl

D-1,3,4/2,5-cyclohexanepentol (7) was partially converted into D-1,2,4/3,5-cyclohexanepentol (8), the enantiomer of naturally occurring viburnitol[2].

1,2:4,5-Di-*O*-isopropylidene-*muco*-inositol provides another suitable starting-material for the synthesis of a cyclohexanepentol. Its two hydroxyl groups are equivalent, and the monobenzyl derivative **9** was described by Espelie and Anderson[12]. In the hope of improving the yield of **9**, we tried monobenzylation with a phase-transfer catalyst, but the method yielded mainly the dibenzyl derivative. The deoxygenation of the monobenzyl ether was slower than in the foregoing preparations: after heating for 24 h with tributylstannane, and removal of the protecting groups, a mixture (~1:2) of *muco*-inositol and 1,2,4,5/3-cyclohexanepentol (**11**) was obtained. Barton and McCombie noted[3] that the reaction is sensitive to steric hindrance, and Copeland and Stick described an instance of a hindered compound[13] in which change of solvent (to Me_2SO) was required to obtain a good yield. However, prolonged reaction of the xanthate gave 3-*O*-benzyl-1,2,4,5/3-cyclohexanepentol (**10**) in good yield, and debenzylation then yielded the free pentol **11** containing only a small proportion of *muco*-inositol.

The all-*cis* (1,2,3,4,5/0) isomer of cyclohexanepentol is particularly inaccessible*. We synthesized it from 1,2:3,4-di-*O*-cyclohexylidene-*cis*-inositol[19] (**12**). This diol was converted into its monobenzyl derivative **13**. Here, again, the phase-transfer procedure[10] proved less successful than benzylation with a limited amount of benzyl bromide. The deoxygenation reaction was very slow, but prolonged heating gave,

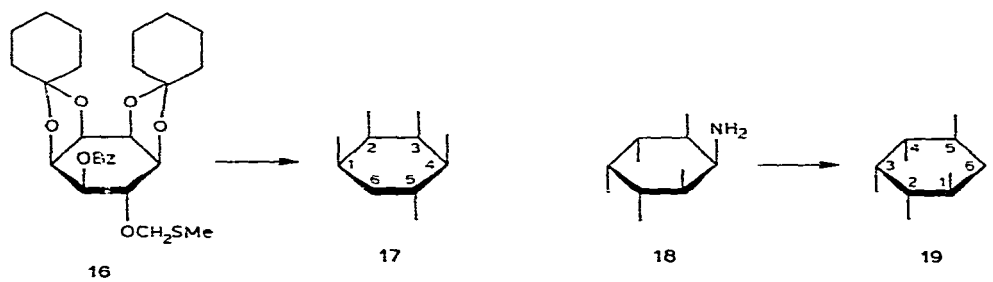
*McCasland and co-workers stated[14] that many attempts to produce cyclohexanepentols by the hydrogenation of benzenepentol had failed. We have succeeded in doing so, by using a large amount of a palladium oxide catalyst developed[15] for the synthesis of *cis*-inositol from benzenehexol. The product obtained by the hydrogenation of benzenepentol contained, as shown by g.l.c. of the acetates, most isomers of cyclohexanepentol and also some more-volatile products, presumably tetrols and triols. The products were separated on a cation-exchange resin in its calcium form[16]. Two of the cyclohexanepentols, the 1,2,3,4,5/0- and the 1,2,3,4/5-isomer, complex strongly with calcium ions[17]: the last fraction to be eluted from the column was shown, by its ^{13}C-n.m.r. spectrum[18], to consist of an ~3:1 mixture of the all-*cis*- and the 1,2,3,4/5-cyclohexanepentol. Two earlier fractions contained pure substances; one was a cyclohexanetriol, the other a cyclohexanetetrol. The n.m.r. spectrum of the acetate of the former identified it as the 1,4/2-isomer; the latter, based on n.m.r. evidence, is probably the 1,2,4/5- or the 1,2,4/3-isomer. This reaction has not been investigated in detail, nor were the reaction conditions optimized.



9 10 R = Bzl; 11 R = H 12 R = H; 13 R = Bzl 14 R = Bzl; 15 R = H

after acid hydrolysis, 1-*O*-benzyl-1,2,3,4,5/0-cyclohexanepentol (**14**) and then, by debenzylation, the free pentol **15**.

In another instance, we used a methylthiomethyl, rather than a benzyl, group to protect a free hydroxyl group. This substituent is readily introduced and readily removed under mild conditions[20], and is stable towards alkali. 1-*O*-Benzoyl-2,3:4,5-di-*O*-cyclohexylidene-6-*O*-methylthiomethyl-*epi*-inositol (**16**) was obtained previously as a by-product[19] in an oxidation, but was prepared here by methylthiomethylation of 1-*O*-benzoyl-2,3:4,5-di-*O*-cyclohexylidene-*epi*-inositol*. The benzoyl group was removed and the xanthate prepared in the usual way. Reaction with tributylstannane left the methylthiomethyl group intact, but completely eliminated the methyl dithiocarbonate group. However, when the protecting groups were removed, a mixture (~1:1) of *epi*-inositol and 1,2,3,4/5-cyclohexanepentol (**17**) was obtained.



16 17 18 19

Barton and McCombie[3] pointed out cases in which the reaction with tributylstannane produces an alcohol, rather than the deoxygenated compound, and Pozsgay and Neszmélyi have also reported the formation of 10–20% of the parent alcohol in the deoxygenation of some rhamnose derivatives[21]. In the present case, the reaction was hardly satisfactory, but it produced sufficient of the pentol for our purposes and was not pursued further.

1,5/2,3,4-Cyclohexanepentol was obtained by a reductive deamination procedure[22] using hydroxylamine-*O*-sulfonic acid which had been applied to amino sugars. 2-Amino-2-deoxy-*neo*-inositol (**18**), obtained by the hydrolysis[23] of hygromycin A,

*This reaction failed when applied to 1-*O*-benzoyl-2,3:4,5-di-*O*-cyclohexylidene-*cis*-inositol[19] and seems to be sensitive to steric hindrance.

reacted more slowly with the reagent than did the examples previously described[22] and the reaction was not complete, but removal of the unchanged aminocyclitol by an acidic ion-exchange resin left pure 1,5/2,3,4-cyclohexanepentol (**19**), which was characterised by its n.m.r. spectrum.

EXPERIMENTAL

Nomenclature. — The naming and numbering of all compounds follows the IUPAC-IUB 1973 recommendations for cyclitols[24].

General methods. — Evaporations were performed under diminished pressure below 45°. Optical rotations were measured with a Bendix automatic polarimeter. ^{1}H-N.m.r. spectra were recorded for solutions in deuteriochloroform with a JEOL JNM-4H-100S or a JEOL JNM-FX-100 spectrometer. Chemical shifts (δ) are reported with reference to internal Me_4Si or sodium 4,4-dimethyl-4-silapentane-1-sulfonate.

L-*1,2,5/3,4-Cyclohexanepentol.* — A mixture of D-1,2:5,6-di-*O*-cyclohexylidene-3-*O*-methyl-*chiro*-inositol[5] (2 g), sodium hydride dispersion (50%, 1 g), imidazole (20 mg), and dry tetrahydrofuran (50 mL) was boiled under reflux in an atmosphere of nitrogen for 3 h. Carbon disulfide (5 mL) was added and boiling was continued for 1 h. Iodomethane (3 mL) was added and boiling was maintained for 1 h. To the cooled mixture was slowly added acetic acid (4 mL), the solution was diluted with water and extracted with dichloromethane, and the extract was washed successively with water, aqueous sodium hydrogencarbonate and water, dried ($MgSO_4$), and concentrated. The oily residue was eluted from silica gel with light petroleum (b.p. 40–60°) containing increasing amounts of ether (5% increments), to give D-1,2:5,6-di-*O*-cyclohexylidene-3-*O*-methyl-*chiro*-inositol 4-(*S*-methyl dithiocarbonate) (**2**) as an oil (2.23 g, 90%). N.m.r. data ($CDCl_3$): δ 1–2 (20 H), 2.57 (s, SMe), 3.32 (dd, $J_{2,3}$ 7.1, $J_{3,4}$ 10.5 Hz, H-3), 3.45 (s, OMe), 3.7–4.4 (4 H), and 5.95 (dd, $J_{4,5}$ ~8 Hz, H-4).

A solution of **2** (2.1 g) in toluene (20 mL) was added dropwise, during 1 h, to a solution of tributylstannane (4 g) in toluene (30 mL) boiling under an atmosphere of nitrogen. Boiling under reflux was continued overnight. T.l.c. (silica gel, 2:1 light petroleum–ether) then showed that the reaction was complete. The solvent was removed under diminished pressure and the residue was chromatographed, as described above, to give, first, tin compounds, then an inositol derivative containing a tributyltin group, and finally L-1,2:3,4-di-*O*-cyclohexylidene-5-*O*-methyl-1,2,5/3,4-cyclohexanepentol (**3**; 1.32 g, 83%). N.m.r. data ($CDCl_3$): δ 1.3–1.8 (20 H), 2.10 (m, CH_2), 3.20 (ddd, $J_{4,5}$ 6.5, $J_{5,6}$ 3.3, $J_{5,6'}$ 11.7 Hz, H-5), 3.45 (s, OMe), and 4.1–4.4 (4 H).

A solution of **3** (1.0 g) in acetic acid (5 mL) and water (1 mL) was boiled for 4 h and then concentrated to give a syrup (0.485 g), the n.m.r. spectrum (D_2O) of which showed a singlet at δ 3.4 (OMe) and a multiplet at δ 2.2 (CH_2). An aliquot (0.4 g) was heated under reflux with 47% hydriodic acid for 2 h. The mixture was

diluted with water, extracted with chloroform (to remove iodine), and concentrated. Recrystallisation of the residue from water–ethanol gave L-1,2,5/3,4-cyclohexanepentol (0.335 g, 91%), m.p. 254–255°, $[\alpha]_D^{20}$ +50° (*c* 1.4, water); lit.[25] for the D isomer, m.p. 257–258°, $[\alpha]_D^{20}$ −48°.

Anal. Calc. for $C_6H_{12}O_5$: C, 43.9; H, 7.4. Found: C, 43.3; H, 7.7.

D-*3*-O-*Acetyl*-*1,2*:*5,6*-*di*-O-*cyclohexylidene*-*4*-O-*methyl*-chiro-*inositol*. — A mixture of D-1,2:5,6-di-*O*-cyclohexylidene-3-*O*-methyl-*chiro*-inositol (2 g), anhydrous pyridine (10 mL), and acetic anhydride (8 mL) was stirred at room temperature overnight and then concentrated. A solution of the residue in chloroform was washed with dilute sulfuric acid, aqueous sodium hydrogencarbonate, and water, dried (Na_2SO_4), and concentrated. The residue was crystallised from benzene, to give the title compound (1.99 g, 88%), m.p. 80–82°, $[\alpha]_D^{25}$ +78.5° (*c* 1.3, chloroform). N.m.r. data ($CDCl_3$): δ 1.4–1.8 (20 H), 2.10 (s, Ac), 3.17 (dd, $J_{3,4}$ 11.2, $J_{4,5}$ 7.2 Hz, H-4), 3.51 (s, OMe), 4.17 (m, H-1,6), 4.35 (m, H-2,5), and 4.96 (dd, $J_{2,3}$ 7.6 Hz, H-3).

Anal. Calc. for $C_{21}H_{32}O_7$: C, 63.6; H, 8.1. Found: C, 63.5; H, 8.4.

Irradiation. — A solution of the foregoing compound (0.9 g) in water–hexamethylphosphoric triamide (5:95) was irradiated in a quartz tube with u.v. light (λ 254 nm). After 24 h, t.l.c. showed the reaction to be incomplete, but after 48 h, no starting material remained. The solvent was removed under diminished pressure, and a solution of the residue in chloroform was washed with water, dried (Na_2SO_4), and concentrated. N.m.r. analysis showed that the product was **3**, contaminated with hexamethylphosphoric triamide.

L-*1,3,4*-*Tri*-O-*benzyl*-*5,6*-O-*cyclohexylidene*-chiro-*inositol* (**6**). — To a solution of L-3,4-di-*O*-benzyl-1,2-*O*-cyclohexylidene-*chiro*-inositol[9] (2 g), benzyl bromide (0.85 g), and tetrabutylammonium iodide (0.33 g) in dichloromethane was added aqueous 5% sodium hydroxide (8 mL), and the mixture was boiled under reflux for 48 h. T.l.c. then showed only a trace of the starting material and of the tetrabenzyl derivative. The organic layer was washed with water, dried (Na_2SO_4), and concentrated. The resulting oil (2.4 g) was eluted from a column of acid-washed alumina with benzene–chloroform (9:1), to yield two main fractions, namely, L-1,3,4-tri-*O*-benzyl-5,6-*O*-cyclohexylidene-*chiro*-inositol (1.07 g, 44%), m.p. 72–74° (from benzene) (lit.[9] m.p. 72–74°), and L-2,3,4-tri-*O*-benzyl-5,6-*O*-cyclohexylidene-*chiro*-inositol.

D-*1,3,4*/*2,5*-*Cyclohexanepentol* (**7**). — Compound **6** (3 g) was heated under reflux with a mixture of sodium hydride dispersion (50%, 2 g), imidazole (40 mg), and tetrahydrofuran (80 mL) under nitrogen for 4 h. Carbon disulfide (7 mL) was added, boiling under reflux was continued for 1 h, iodomethane (6 mL) was added, and boiling was maintained for 1 h. The mixture was cooled, treated with acetic acid (7.5 mL), and diluted with water and dichloromethane. The organic layer was washed with water, aqueous sodium hydrogencarbonate, and water, dried (Na_2SO_4), and concentrated. The residual oil was eluted from silica gel, with light petroleum (b.p. 40–60°) containing increasing amounts of ether. L-1,3,4-Tri-*O*-benzyl-5,6-*O*-cyclohexylidene-*chiro*-inositol 2-(*S*-methyl dithiocarbonate) (3.15 g,

89%) was obtained as an oil. N.m.r. data ($CDCl_3$): δ 1.2–1.9 (10 H), 2.50 (s, SMe), 3.8–4.8 (11 H), 6.09 (dd, $J_{1,2}$ 2.5, $J_{2,3}$ 5.5 Hz, H-2), and 7.3 (Bzl).

A solution of the foregoing compound (3 g) in toluene (20 mL) was added dropwise to a solution of tributylstannane (4 g) in toluene (40 mL) boiling under reflux under nitrogen. Next day, the reaction was found (t.l.c.) to be incomplete. More tributylstannane (2 g) in toluene (20 mL) was added and boiling under reflux was continued overnight. The mixture was then worked-up as described for **3**. The third fraction gave D-1,2,5-tri-*O*-benzyl-3,4-*O*-cyclohexylidene-1,3,4/2,5-cyclohexanepentol (1.98 g, 80%) as a yellow oil. N.m.r. data ($CDCl_3$): δ 2.2 (m, overlaps with the cyclohexylidene signals, CH_2), 4–5 (11 H), and 7.3 (Bzl).

A solution of the foregoing compound (1.5 g) in acetic acid (5 mL) and water (1 mL) was boiled for 4 h and then concentrated, to yield L-1,2,5-tri-*O*-benzyl-1,2,5/3,4-cyclohexanepentol (1.13 g, 90%) as an oil. An aliquot (1 g) was treated with boiling 47% hydriodic acid (4 mL) for 2 h. The solution was diluted with water, washed with chloroform, and concentrated. The residue was crystallised from water–ethanol, to give **7** (344 mg, 90%), m.p. 235–237°, $[\alpha]_D^{20}$ −29° (*c* 4.5, water); lit.[8] m.p. 238–239°, $[\alpha]_D^{25}$ −25°.

D-Penta-O-acetyl-1,2,4/3,5-cyclohexanepentol. — The quercitol **7** (263 mg) was treated with boiling 95% acetic acid (30 mL) containing 1.5% sulfuric acid for 15 h. The mixture was cooled and acetic anhydride (30 mL) was added. After 4 h, the solution was neutralised with sodium hydrogencarbonate. After a further 3 h, it was extracted with chloroform, and the extract was washed with water, dried, and concentrated. On addition of ethanol, D-penta-*O*-acetyl-1,2,4/3,5-cyclohexanepentol (180 mg, 30%) crystallised; m.p. 124–126°; lit.[26] m.p. 126°. The mother-liquor was concentrated and the residue was re-submitted to the same reaction, and gave another crop (60 mg, 10%).

*3-O-Benzyl-1,2:4,5-di-O-isopropylidene-*muco*-inositol 6-(S-methyl dithiocarbonate).* — 3-*O*-Benzyl-1,2:4,5-di-*O*-isopropylidene-*muco*-inositol[12] (**9**, 130 mg) was treated as described for **2**. The resulting oil was dissolved in light petroleum–benzene (1:1) and passed down a small column of silica gel. Concentration of the eluate and crystallisation of the residue from ethanol gave the dithiocarbonate (145 mg, 89%), m.p. 138°. N.m.r. data ($CDCl_3$): δ 1.32 and 1.48 (s, CMe_2), 2.57 (s, SMe), 4.0–4.4 (m, 5 H), 4.81 (s, $PhCH_2$), 6.15 (m, H-6), and 7.3 (m, Ph).

Anal. Calc. for $C_{21}H_{28}O_6S_2$: C, 57.3; H, 6.35. Found: C, 55.9; H, 6.7.

3-O-Benzyl-1,2,4,5/3-cyclohexanepentol (**10**). — A solution of the foregoing dithiocarbonate (120 mg) in toluene (6 mL) was added dropwise during 1 h to a solution of tributylstannane (0.5 g) in toluene (10 mL) boiling under nitrogen. After 48-h boiling, n.m.r. analysis showed the absence of the SMe signal at δ 2.57. The solution was concentrated and the residue was treated with boiling acetic acid (4 mL) and water (1 mL) for 4 h. The solution was concentrated, the residue was partitioned between water and ethyl acetate (to remove tin compounds), the aqueous layer was concentrated, and the residue was crystallised from ethanol, to give **10**

(60 mg, 86%), m.p. 146–148°. N.m.r. data (D_2O): δ 1.9–2.1 (m, CH_2), 3.5–4.2 (m, 5 H), 4.8 (s, PhCH_2), and 7.4 (5 H, Ph).

Anal. Calc. for $C_{13}H_{18}O_5$: C, 61.4; H, 7.1. Found: C, 59.1; H, 7.65.

1,2,4,5/3-Cyclohexanepentol (**11**). — The foregoing compound (45 mg) was heated under reflux with hydriodic acid (20%, 4 mL) for 2 h. The mixture was diluted with water and extracted with chloroform to remove iodine, treated twice with decolorising charcoal, and concentrated. Crystallisation of the residue from water–ethanol gave **11** (26.5 mg, 91%), m.p. 92–94°; lit.[27] m.p. 95°. N.m.r. data (D_2O): δ 1.75 (dt, $J_{1,6}$ 3, $J_{6,6'}$ −15 Hz, H-6), 2.06 (m, H-6'), 3.48 (dd, $J_{1,2}$ 2, $J_{2,3}$ 9 Hz, H-2,4), 3.85 (t, H-3), and 4.04 (m, H-1,5). The ^{13}C-n.m.r. spectrum[18] showed the presence of ~10% of *muco*-inositol.

1,2,3,4,5/0-Cyclohexanepentol (**15**). — Sodium hydride dispersion (50%, 250 mg) was washed with light petroleum and then stirred with Me_2SO (10 mL) under nitrogen for 30 min. 1,2:3,4-Di-*O*-cyclohexylidene-*cis*-inositol[19] (300 mg) and, after 30-min stirring, benzyl bromide (160 mg) were added, and the mixture was stirred overnight, poured into water (30 mL), and extracted with chloroform (5 × 10 mL). The combined extracts were washed with water (6 × 10 mL) and concentrated. The syrupy residue was eluted from a column of silica gel with chloroform. The first fraction contained the syrupy dibenzyl derivative, followed by DL-1-*O*-benzyl-2,3:4,5-di-*O*-cyclohexylidene-*cis*-inositol (**13**; 151 mg, 40%), which failed to crystallise.

Compound **13** (140 mg) was treated as described for **2**, to give DL-1-*O*-benzyl-2,3:4,5-di-*O*-cyclohexylidene-*cis*-inositol 6-(*S*-methyl dithiocarbonate) as an oil which was purified by elution from a column of silica gel with light petroleum–benzene (1:1). The n.m.r. spectrum ($CDCl_3$) contained singlets at δ 2.6 (SMe) and 4.9 (PhCH_2), and a triplet at 6.2 ($J_{1,6} = J_{5,6}$ ~3 Hz, H-6).

A solution of the dithiocarbonate (150 mg) in toluene (10 mL) was added dropwise, during 1 h, to a solution of tributylstannane (0.6 g) in toluene (10 mL) boiling under nitrogen. Boiling was maintained for 48 h. The solvent was then evaporated and the n.m.r. spectrum of the residue showed that the signals at δ 2.6 (SMe) and 6.2 (H-6) had disappeared. Acetic acid (4 mL) and water (2 mL) were added and the solution was boiled for 4 h. The solvents were removed, and the residue was dissolved in water and extracted repeatedly with ethyl acetate (to remove tin compounds). Concentration gave DL-1-*O*-benzyl-1,2,3,4,5/0-cyclohexanepentol (**14**) as a syrup (62 mg, 85%). N.m.r. data (D_2O): δ 2.2 (m, CH_2), 3.6–4.2 (m, 5 H), 4.70 (s, PhCH_2), and 7.6 (m, Ph).

A solution of **14** (62 mg) in hydriodic acid (20%, 4 mL) was boiled for 2 h, diluted with water, and extracted with chloroform. The aqueous layer was twice treated with decolorising charcoal and concentrated. The residue was crystallised from water–ethanol, to give **15** (36 mg, 90%), m.p. 233–237°; lit.[28] m.p. 235–240°. The n.m.r. spectrum was in accordance with the previous description[29].

DL-*1,2,3,4/5-Cyclohexanepentol* (**17**). — To a solution of 1-*O*-benzoyl-2,3:4,5-di-*O*-cyclohexylidene-*epi*-inositol[19] (250 mg) in Me_2SO (2 mL) was added a mixture

of acetic anhydride (1.4 mL) and acetic acid (0.25 mL). The mixture was stirred for 48 h, poured into saturated, aqueous sodium hydrogencarbonate (25 mL), stirred for 1 h, and extracted with chloroform (4 × 10 mL). The combined extracts were washed with aqueous sodium hydrogencarbonate and water, dried, and concentrated. The remaining Me_2SO was removed by co-distillation with xylene. The residual, syrupy DL-1-*O*-benzoyl-2,3:4,5-di-*O*-cyclohexylidene-6-*O*-methylthiomethyl-*epi*-inositol (**16**; 257 mg, 91%) showed only one spot in t.l.c., and the n.m.r. spectrum ($CDCl_3$) contained signals for an SMe group at δ 2.07 and a CH_2 group at 5.02.

To the solution of **16** (257 mg) in anhydrous methanol (10 mL) was added a small piece of sodium. The solution was boiled for 2 h, stored overnight at room temperature, and then concentrated. The residue was partitioned between water and chloroform, and the organic layer was washed with water, dried ($MgSO_4$), and concentrated, to give syrupy DL-1,2:3,4-di-*O*-cyclohexylidene-6-*O*-methylthiomethyl-*epi*-inositol (196 mg, 96%). T.l.c. and n.m.r. spectroscopy showed that the compound was homogeneous and it was used without purification. N.m.r. data ($CDCl_3$): δ 1.5 (m, 20 H), 2.20 (s, Me), 2.6 (broad s, OH?), 3.5 (m, H-5?), 4.2–4.5 (m, 5 H), and 4.90 (s, CH_2).

The foregoing compound (196 mg) was treated as described for **2**. The resulting syrup had an n.m.r. spectrum ($CDCl_3$) containing signals for methylthiomethyl (singlets at δ 2.15 and 4.80) and methyl dithiocarbonate (s, 2.70) groups. After the usual treatment with tributylstannane for 48 h, the latter signal disappeared, but the former were still present. The compound was hydrolysed with boiling, 60% acetic acid for 4 h. This treatment removed the acetal groups, but some methylthiomethyl ether was still present. It was then hydrolysed with boiling M hydrochloric acid for 2 h. The ^{13}C-n.m.r. spectrum (D_2O) of the product showed the signals of *epi*-inositol (δ 67.8, 71.1, 72.7, 75.5) and of 1,2,3,4/5-cyclohexanepentol[18] (δ 34.4, 67.2, 70.3, 71.4, 73.2, 74.6). From water–ethanol, star-shaped crystals of *epi*-inositol (30 mg), m.p. 295–300°, separated and were identified by its ^1H-n.m.r. spectrum[29]; the contents (50 mg) of the mother liquors were mainly 1,2,3,4/5-cyclohexanepentol (as shown by comparing its ^1H-n.m.r. spectrum with the published one[29]), but still contaminated by some *epi*-inositol.

Hydrogenation of benzenepentol. — The catalyst was prepared as follows[15]. Palladium metal (1.3 g) was dissolved by heating in a mixture of conc. hydrochloric acid (9 mL) and concentrated nitric acid (6 mL), and the solution was concentrated to dryness. A solution of the residue in concentrated hydrochloric acid (12 mL) was diluted with water to 1200 mL, and aqueous 40% sodium hydroxide (30 mL) was added. The resulting, clear yellow solution was heated to form a brown, gelatinous precipitate which gradually coagulated on boiling. The precipitate was washed by decantation with boiling water (6 × 600 mL); the supernatant liquid was then neutral. The catalyst is used in the moist state, since its activity is markedly diminished if it is dried.

A suspension of the catalyst in water was stirred in an atmosphere of hydrogen overnight; 250 mL of hydrogen was absorbed. Benzenepentol[30] (1.05 g) was added

and stirring was continued for 3 days. Filtration gave a colourless solution which was concentrated to an oil (580 mg). A sample was acetylated and analysed by g.l.c. on a column (0.45 × 115 cm) of 3% of SP 2401 (Supelco, Inc., Bellefonte, Pennsylvania) on Chromosorb W at 227°. Peaks coinciding with those of the acetates of 1,2,3,4,5/0-, 1,3,5/2,4-, 1,2,5/3,4-, 1,2,3/4,5-, and 1,2,4/3,5-cyclohexanepentols were found, besides 6 peaks of shorter retention times. The all-*cis* isomer represented ~33% of the cyclohexanepentols.

The reaction mixture was eluted[16] from a column (3 × 60 cm) of Dowex AG 50W-X2 (Ca^{2+}) resin with water. Most material emerged in the first two fractions (200–240 and 260–330 mL). The contents (60 mg) of the last fraction (980–1020 mL) showed only one spot (of the same mobility as that of *epi*-inositol) in paper electrophoresis in 0.2M calcium acetate[17]. The 1,2,3,4,5/0- and 1,2,3,4/5- cyclohexanepentols are not separated under these conditions. The ^{13}C-n.m.r. spectrum[18] showed signals at δ 74.2, 68.6, and 30.2 (all-*cis*), and at 74.6, 73.2, 71.4, 70.3, 67.2, and 34.4 (1,2,3,4/5).

The third fraction (370–410 mL) contained two compounds and was rechromatographed, using water–methanol (2:1). The fractions 350–380 mL contained a triol (55 mg). N.m.r. data ($CHCl_3$), after acetylation: δ 2.01, 2.05, and 2.10 (s, Ac), 1.40–2.20 (m, 6 H), 4.66–4.92 (m, 2 H), and 5.20 (quin, J 2.2 Hz, H-4). The quintet indicates the presence of an axial acetoxyl group flanked by two methylene groups. Since the compound is not symmetrical, it can only be 1,4/2-cyclohexanetriol.

The eluant 470–530 mL contained a tetrol (8 mg). N.m.r. data ($CDCl_3$), after acetylation: δ 2.00, 2.03, and 2.04 (s, equatorial OAc[31]), 2.12 (s, axial OAc[31]), 1.64–2.29 (m, 4 H), 4.70–5.14 (m, 2 H), and 5.33–5.56 (m, 2 H).

Reductive deamination of 2-amino-2-deoxy-neo-*inositol* (**18**). — The hydrochloride[23] of this base (136 mg) was dissolved in 2.5M sodium hydroxide (2 mL) with cooling. M Sodium hydroxide (5 mL) and then hydroxylamine-*O*-sulfonic acid (250 mg) were added, and the mixture was stirred under nitrogen in an ice-bath. After 1 h, more acid (125 mg) was added and stirring was continued for 3 h. The pH then was 7.5. After 3 days at 4°, the solution was freeze-dried, and the residue was dried and then treated with acetic anhydride and pyridine at 50° overnight.

The reaction mixture was freeze-dried, and a solution of the residue in chloroform was washed with aqueous sodium hydrogencarbonate and water, dried (Na_2SO_4), and concentrated. Crystallisation of the residue from ethanol gave crystals (80 mg), m.p. 276°, consisting mainly of 2-amino-2-deoxy-*neo*-inositol hexa-acetate (the ^1H-n.m.r. spectrum in $CDCl_3$ showed signals for one OAc at δ 2.18, four OAc at 2.04, and one NAc at 2.06, as described[31]).

The mother-liquor was concentrated and the syrupy residue (110 mg) was treated with boiling hydrochloric acid (10%, 5 mL) for 1 h. The solution was concentrated and a solution of the residue in water was passed down a small column of Amberlite IR-120 (H^+) resin in order to remove the unchanged amine. Concentration of the solution and crystallisation of the residue from ethanol gave 1,2,4,5/3-cyclohexanepentol (21 mg). N.m.r. data (D_2O): δ 1.37 (q, $J_{1,6ax}$ 11.8, $J_{6ax,6eq}$ −12.3 Hz, H-6*ax*), 2.21 (dt, $J_{1,6eq}$ 4.9 Hz, H-6*eq*), 3.50 (dd, $J_{1,2}$ 9.8, $J_{2,3}$ 2.9 Hz, H-2,4), 3.84

(ddd, H-1,5), and 4.08 (t, H-3). The penta-acetate had m.p. 180° (from ethanol); lit.[32] m.p. 182°.

The amine hexa-acetate, when deacetylated with boiling hydrochloric acid and deaminated as described above, gave more (21 mg) of the cyclohexanepentol (total yield, 44%).

ACKNOWLEDGMENTS

This work was supported, in part, by the Australian Research Grants Committee. The authors thank Professor Kazuhiko Yamamoto (Osaka) for his assistance in the preparation and hydrogenation of benzenepentol, and Dr. J. B. Patrick (American Cyanamid Co.) for a gift of 2-amino-2-deoxy-*neo*-inositol hydrochloride.

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