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727. *Cyclitols. Part VI.* The Hydrogenation of Hexahydroxybenzene.*

By S. J. Angyal and D. J. McHugh.

Catalytic hydrogenation of hexahydroxybenzene under various conditions gave complex mixtures of polyhydroxy*cyclo*hexanes which were separated by chromatography on cellulose powder. Seven inositols and four quercitols were obtained from various runs, including the previously unknown *cis*-inositol, *cis*quercitol, and *cis*inosose. At room temperature with a palladium catalyst *myo*inositol is the main product, whereas palladium-on-carbon yields mainly *cis*-inositol. High-temperature hydrogenation over Raney nickel shows little stereospecificity.

The first synthesis of an inositol was reported by Wieland and Wishart [1] who catalytically hydrogenated hexahydroxybenzene with a palladium catalyst at room temperature and atmospheric pressure. They obtained the biologically important *myo*inositol in a yield of over 50%. Such a high yield of one isomer—out of a possible eight—was tentatively explained by postulation of the all-*cis*-configuration for *myo*inositol; but since it is now known that *myo*inositol is the 1235/46-isomer, this reaction constitutes a remarkable instance of stereospecificity.

Two attempts to repeat this work, with platinum and palladium catalysts at various temperatures, failed.[2,3] Anderson and Wallis,[3] however, hydrogenated hexahydroxybenzene with Raney nickel at 125—150°/100 atm., the products ranging from *cyclo*hexanediols to inositols. Five cyclitols, including *myo*inositol, were isolated in small yield by tedious crystallisation and by fractional distillation of the acetates; the identity of these compounds will be discussed below.

In 1949, Kuhn, Quadbeck, and Röhm [4] confirmed Wieland and Wishart's original report by carrying out hydrogenations both at 50—55° and at 20°; though the reaction was slower at 20° the yield was better, being 35% of crude inositol from which pure *myo*-inositol was isolated in 13% yield. The authors recognised that the crude product represented a mixture of cyclitols but did not attempt to separate them. An improvement introduced by Kuhn *et al.* was the use of the stable and readily prepared tetrahydroxybenzoquinone as starting material instead of hexahydroxybenzene, which is difficult to purify owing to its rapid aerial oxidation. In the course of the hydrogenation the quinone is readily converted into hexahydroxybenzene.

The development of cellulose-powder chromatography as a convenient method for the separation of cyclitols [5] made it possible to investigate the products formed in the hydrogenation of hexahydroxybenzene under different conditions. A preliminary account of our results has been published.[6]

Under the conditions given by the German authors,[4] tetrahydroxybenzoquinone took up hydrogen, rapidly for the first mol., then very slowly; several additions of catalyst

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were needed to complete the reaction. Paper chromatography [7] (in acetone–water, 4 : 1 v/v) showed that a large number of compounds had been formed, some of which moved too rapidly to be inositols. By a combination of cellulose-powder chromatography and fractional crystallisation eleven products have been isolated and are listed in the first column of the Table.

Products isolated from the hydrogenation of hexahydroxybenzene.

Compound	Yield (%) Pd, 20°, 1 atm.	Ni, 120—140°, 150 atm.	10% Pd–C, 20°, 1 atm.
Inositols :			
myo- (1235/46)	17·2	1·9	7·5
cis- (123456/)	1·7 *	4·7	20·0
scyllo- (135/246)	1·2	0·1	1·0
epi- (12345/6)	0·2	1·8	0·3
(±)- (124/356)	2·9	—	0·05
neo- (123/456)	—	0·05	—
allo- (1234/56)	—	0·1	—
*cis*Inosose	2·0	—	—
Quercitols :			
cis- (12345/)	2·7	8·1	0·4
epi- (1235/4)	0·5	1·9	—
scyllo- (135/24)	0·05	0·1	0·05
*cyclo*Hexanetetrol (acetate, m. p. 124°)	1·2	—	—
all-*cis*-*cyclo*Hexane-1 : 2 : 3-triol	—	0·5	—
Reducing compound (m. p. 160—161°)	0·3	—	—

* A yield of 4·5% was obtained in a run in which PtO_2 was used to reduce any inososes remaining after the Pd-catalysed hydrogenation.

Considerable loss of oxygen by hydrogenolysis had occurred and the products ranged from *cyclo*hexanetriols to inositols, the latter accounting for only 25—30% of the yield. The triols and tetrols—of which there are many possible isomers—were not separated and the bulk of these fractions failed to crystallise. Several quercitols were obtained but, undoubtedly, others remained in mother-liquors. However, the chromatographic behaviour of the inositols is well known [7] and it was therefore possible to isolate all those which were formed in the reaction; it is estimated that *allo-*, *muco-*, and *neo*-inositol—which were not obtained—could not have been present in more than 0·1% yield. Thus fractions which should have contained *allo-* and *muco*-inositol failed to show the Scherer reaction characteristic for inositols; and *neo*inositol would have been separated by virtue of its very low solubility (as it has been in the high-pressure run, see below). In accordance with the earlier reports, *myo*inositol was the main product of the reaction though in a yield much below that claimed by Wieland and Wishart.

Some of the fractions, when examined by paper chromatography in acetone–water (4 : 1) and phenol–water (4 : 1), appeared to contain *epi*inositol, but the acetate obtained from them by acetylation was not identical with *epi*inositol acetate, or with the acetate of any other known inositol. Further examination by paper chromatography showed that the new compound could be separated from *epi*inositol in butan-1-ol–acetic acid–water (4 : 1 : 1) and in ethyl acetate–acetic acid–water (3 : 1 : 1). It gave the Scherer test, and analyses of this compound and its derivatives confirmed that it was an inositol. Since all the other isomers predicted by theory are known, the new compound must have the all-*cis*-configuration (I) * and has been named *cis*inositol. It completes the stereoisomeric group of inositols and is of interest as the only known compound which has, in its stable chair conformation, three axial hydroxyl groups on the same side of the ring. The energy of interaction between these hydroxyl groups has been estimated at 5·7 kcal./mole.[8]

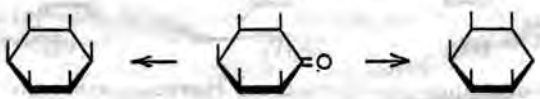
In its final stages the hydrogenation is very slow, and a paper chromatogram of the mixture, sprayed with a reagent which detects reducing compounds only,[9] showed a number of spots, indicating the presence of polyhydroxy-ketones. (The hydrogenation can be completed at this stage by the use of Adams catalyst.) One of these was isolated

* Hydroxyl groups are indicated but not shown in the formulæ.

during the chromatographic separation and was found to be a new inosose. On hydrogenation with platinum oxide in neutral solution it gave *cis*inositol, and reduction by sodium amalgam yielded *epi*inositol. The inosose therefore has the all-*cis*-configuration (II).

A new quercitol was isolated from the hydrogenation of tetrahydroxybenzoquinone; the same quercitol was also obtained by hydrogenation of *cis*inosose with a platinum catalyst in acid solution. This reaction, which is known [10] to remove the keto-group without affecting the hydroxyl groups, proves that the new quercitol has the all-*cis*-configuration (III) and hence it has been named *cis*quercitol.

Hydrogenation over Raney Nickel.—Successful separation of the cyclitols produced in the hydrogenation over palladium suggested that a re-investigation of the hydrogenation of tetrahydroxybenzoquinone over Raney nickel at high temperature and pressure, as described by Anderson and Wallis,[3] might establish the identity of their products. The reaction was carried out according to their description and the product was examined by paper chromatography. The pattern of the spots was different from that obtained on the hydrogenation over palladium, mainly in the region of the faster-running components; no reducing compounds were present. The mixture was again separated by cellulose-powder chromatography and by crystallisation of the cyclitols or their acetates; the ten products obtained are listed in the second column of the Table.



(I) (II) (III)

The total amount of inositols produced in this hydrogenation is much less (about 9%) than in the run with palladium and the yield of *myo*inositol is small. No pronounced stereospecificity is evident but the *cis*-isomer predominates amongst both the inositols and the quercitols.

Anderson and Wallis isolated five crystalline compounds considered to be inositols. Two were identified as *myo*- and *scyllo*-inositol, and another, m. p. 213—214°, was established as an inositol by analysis and Scherer test; its acetate was reported to melt at 205—206°. Since the acetate of *cis*inositol melts at 208°, it is probable that Anderson and Wallis had this compound in hand. *cis*Inositol itself melts at 377° (uncorr.) when placed on a preheated block but decomposes on slow heating; this decomposition may have been mistaken for melting by the American authors. No other compound isolated from the hydrogenation has an acetate melting near 205°.

The other two compounds, isolated as their acetates by Anderson and Wallis, were regarded as inositols although their analyses were closer to those of quercitol acetates and their behaviour in the Scherer test was not reported. One acetate, m. p. 189—190°, was tentatively identified as *epi*inositol acetate (m. p. 188°) and this identification was probably correct, although *scyllo*quercitol acetate (m. p. 193°) cannot be excluded. The second acetate, m. p. 139—140°, was—in view of the products obtained by us—probably not that of an inositol, but rather *epi*quercitol acetate (m. p. 140°); *allo*inositol acetate (m. p. 144°) appears less likely since it is present in such small amount in the hydrogenation mixture.

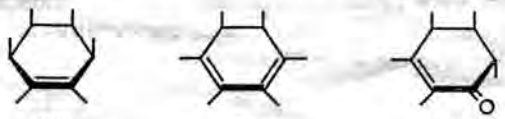
The Stereochemistry of the Hydrogenation.—Full knowledge of the products of the hydrogenation does not explain the surprising predominance of *myo*inositol. Even more surprising—in view of the large number of possible isomers—is the recent report [11] that hydrogenation of 1 : 4-diaminotetrahydroxybenzene and of triaminophloroglucinol produces mainly a single isomer in each case (in 43 and 60% yield, respectively); explanation of this stereospecificity will have to await the determination of the configuration of the products.

The formation of *cis*inositol and *cis*inosose is readily explained: if a molecule of hexahydroxybenzene takes up three molecules of hydrogen while adsorbed on the catalyst surface, *cis*inositol will result in view of the known *cis*-addition of hydrogen over metallic

catalysts. If only two mols. of hydrogen are taken up, the resulting enediol (IV) can isomerise to *cis*inosose (II) which gives *cis*inositol on further hydrogenation.

The formation of *myo*inositol, on the other hand, is not readily explained. It is not formed from *cis*inositol by the epimerisation which is known to occur [12] with some *cyclo*hexanols in the presence of metallic catalysts: prolonged shaking of *cis*inositol with palladium does not cause detectable isomerisation. The *trans*-arrangement of some hydroxyl groups in *myo*inositol must be the result of isomerisation at intermediate stages of the hydrogenation.

Desorption from the catalyst surface after the uptake of only one mol. of hydrogen gives a dihydrobenzene derivative (V) which can react in several ways: (i) It can aromatise by the loss of water to give pentahydroxybenzene. This explains the formation of quercitols and, by repetition of the process, *cyclo*hexanetetrols, etc. (ii) It can be re-adsorbed on the catalyst and further hydrogenated. (iii) It can rearrange to an unsaturated ketone (VI) with formation of a new asymmetric centre. Further hydrogenation will yield an enediol which can also ketonise. It is possible that, as the result of



(IV) (V) (VI)

these reversible keto–enol interconversions, the thermodynamically most stable inosose, the all-equatorial *scyllo*inosose, could emerge as the main product. The hydrogenation of *scyllo*inosose is known [10] to yield *myo*inositol accompanied by small amounts of *scyllo*inositol. *scyllo*Inosose has not been isolated from the hydrogenation mixture but a compound of its R_F value has been detected on paper chromatograms. *cis*Inosose, once formed, is not isomerised when shaken with the catalyst.

It was found that, in accordance with the report by Anderson and Wallis, neither hexaacetoxybenzene nor hexamethoxybenzene could be reduced over the palladium catalyst at atmospheric pressure. This may indicate that hexahydroxybenzene is hydrogenated *via* a tautomeric form; mechanisms based on this assumption, however, fail to explain the formation of *myo*inositol.

It appears therefore that complete hydrogenation of hexahydroxybenzene while adsorbed on the catalyst yields *cis*inositol, whereas desorption after the uptake of one mol. of hydrogen will result in hydrogenolysis and also in the formation of *myo*inositol. It is concluded that prolongation of the contact with the catalyst, by augmenting its surface, would increase the yield of *cis*inositol. The palladium catalyst prepared according to Kuhn *et al.* appears to have a small surface: it coagulates readily and does not yield a fine suspension. A catalyst of presumably larger surface was prepared by precipitating palladium, according to the method of Kuhn *et al.*, but in the presence of activated charcoal. Hydrogenation with this palladium–carbon catalyst, at room temperature and atmospheric pressure, did not proceed faster than with palladium alone but the proportion of the products, listed in the third column of the Table, was different. The yield of inositols was somewhat higher and *cis*-, not *myo*-, inositol was the main product. The use of high pressure in the hydrogenation over palladium–carbon did not further increase the yield of *cis*inositol.

By use of the palladium–carbon catalyst, the interesting *cis*inositol can be produced in reasonable yield but its separation from other cyclitols by chromatography is tedious. Its strong ability to form a complex with boric acid [13] suggested another method of separation: it was found that *cis*inositol was completely removed from aqueous solution by the borate form of a strongly basic anion-exchange resin.[14] Some other cyclitols, however, also reacted with the resin and were only slowly removed from it by water; complete separation of *cis*inositol by this method alone was not achieved. A new quercitol of unknown configuration was separated in small amounts from the resin.

Experimental

M. p.s are corrected. Paper chromatography was carried out as previously described;[7] R_F values refer to acetone–water (4 : 1 v/v) unless otherwise stated. Cyclitols were identified by mixed m. p.s and by paper chromatography in at least two solvent systems. Acetyl derivatives were prepared by 30 minutes' heating, on the steam-bath, with acetic anhydride and sulphuric acid (19 : 1 v/v); the mixture was poured into water, any solid which separated after 1—2 hr. was filtered off, and the rest of the acetate was recovered by extraction with chloroform.

Chromatography on Cellulose Powder.—Acetone–water (4 : 1 v/v) was used as the mobile phase unless otherwise stated. Compounds emerged from the cellulose-powder column[5] generally in order of decreasing R_F values, but one exception was noted. (±)-Inositol (R_F 0·27) was not eluted ahead of *cis*- and *epi*-inositol (R_F of both 0·22); in every case *cis*- and *epi*-inositol appeared first, and the (±)-isomer emerged around the middle of the (*cis* + *epi*)-fraction but disappeared before that fraction was completely eluted. This phenomenon is explained by the difference between the properties of powdered cellulose and cellulose filter paper.[15] It was also found that *cis*inositol was eluted from the column somewhat ahead of the *epi*-isomer (though they have the same R_F value) so that *cis*inositol crystallised from earlier fractions and *epi*inositol from the later ones. The separation was not complete, however, and a mixture of the two inositols was left in the mother-liquors.

Palladium Catalyst.—A solution of palladium chloride (1·7 g.) in water (400 ml.) and 10N-hydrochloric acid (10 ml.) was neutralised at 80° with 25% sodium hydroxide, and then formic acid (0·5 ml.) was added. The evolution of carbon dioxide, as described by Kuhn *et al.*,[4] could not be seen at this point, so additional 25% sodium hydroxide (7·5 ml.) and formic acid (1·0 ml.) were added as soon as a brown cloudiness developed in the solution. The precipitated catalyst was washed with hot water until the washings were no longer alkaline, and dried over sulphuric acid.

The 10% palladium–carbon catalyst was prepared in the same way except that unwashed activated charcoal (10 g.) was suspended in the solution with vigorous stirring. Additional sodium hydroxide and formic acid were added one minute after the first addition of formic acid. The use of acid-washed charcoal seems to lower the activity of the catalyst.

It has been reported, both by Wieland and Wishart[1] and by Kuhn *et al.*,[4] that traces of hydrogen chloride inactivated their palladium catalyst. Since the catalyst is prepared under alkaline conditions this may be taken as an indication that traces of absorbed alkali are responsible for the activity of the catalyst. It was found, however, that addition of small amounts of hydrochloric acid to the hydrogenation mixture made no difference to the rate of the hydrogenation with either the palladium or the palladium–carbon catalyst; it even caused a slight increase with the former. The 10% palladised charcoal catalyst prepared, in a solution of sodium acetate, according to Mozingo[16] also produced inositols, as shown by paper chromatography, though hydrogenation was very slow.

Hydrogenation of Tetrahydroxybenzoquinone with Palladium Catalyst.—Hexahydroxybenzene is only slightly soluble in water and is precipitated during the hydrogenation, covering the catalyst. It was therefore advisable to carry out this first stage of the hydrogenation by the use of a small amount of palladised charcoal[16] (which is more effective in this step) and add the palladium catalyst subsequently.

A suspension of tetrahydroxybenzoquinone[17] (4 g.) and 10% palladised charcoal[16] (0·2 g.) in water (250 ml.) was hydrogenated at room temperature and pressure. The initial reduction to hexahydroxybenzene was complete in 7 hr., whereupon palladium catalyst (1·0 g.) was added and the hydrogenation continued. More catalyst (total, 3 g.) was added whenever the uptake of hydrogen became slow; after the last addition, only 30 ml. of hydrogen were absorbed. The reduction took 82 hr. and 2280 ml. of hydrogen (calc. 2210 ml.) were taken up. The catalyst was removed and washed with hot water, and the filtrate was evaporated under reduced pressure and dried over sulphuric acid.

scyllo*Inositol.* The partly crystalline residue (3·14 g.) was warmed with water (6 ml.) and filtered; the solid, recrystallised from water–ethanol, had m. p. 330—340° (47 mg.). Acetylation and recrystallisation from ethanol gave hexa-acetyl*scyllo*inositol, m. p. 292—293°, mixed m. p. 293—295°.

The filtrate after isolation of *scyllo*inositol was seeded with *neo*inositol and left at 0° overnight but no further crystallisation took place. The solution was diluted with acetone and run through a column of cellulose powder (12 × 1¾" containing about 150 g. of cellulose): 250

fractions of 10 ml. were collected and examined by paper chromatography. Fractions 44—75 contained a mixture of inositols, and fractions 76—250 contained *myo*inositol; their isolation is described further below.

cis*Inosose*. Fractions 20—36 contained a reducing compound, as shown by paper chromatography and development with ferricyanide–ferric chloride.[9] They were combined, concentrated to 5 ml., and treated with phenylhydrazine according to the method of Carter *et al.*;[18] cooling and scratching gave red crystals which were recrystallised from methanol–water, to yield cis*inosose phenylhydrazone* (120 mg.); a further crystallisation gave colourless crystals, decomp. 150—160° (Found: N, 10·35. $C_{12}H_{16}O_5N_2$ requires N, 10·45%).

The phenylhydrazone (90 mg.) was reconverted into the inosose by the method of Carter *et al.*;[18] recrystallisation from water–ethanol gave cis*inosose* (44 mg.), m. p. 179—180° (decomp.) (Found: C, 40·15; H, 5·65. $C_6H_{10}O_6$ requires C, 40·45; H, 5·65%).

The mother-liquors from the separation of the phenylhydrazone were freed from phenylhydrazine by warming with benzaldehyde and extraction with ether; they were then evaporated and the residue chromatographed through the cellulose column. Fractions 1—20 and 37—43 of the original separation were combined in such a way that each combination gave only two or three spots on paper chromatograms; these combinations were then also run separately through the column. In this manner the components of each mixture were separated; corresponding fractions of each chromatogram were combined with each other to give seven fractions (A—G), each showing a single black spot on a silver nitrate-developed paper chromatogram. Each fraction was evaporated to a small volume, treated with charcoal, dissolved in the minimum amount of ethanol or aqueous ethanol, and stored at 0°. If no crystallisation occurred after several weeks, the solution was evaporated, the residue being acetylated and stored under the minimum amount of ethanol.

Fraction A, R_F 0·85 (the R_F values of the fractions are only approximate) (73 mg.). After acetylation, crystals of a cyclo*hexanetetrol tetra-acetate* (40 mg.) slowly separated. Recrystallised from ethyl acetate–light petroleum (b. p. 40—60°) they had m. p. 124° (Found: C, 53·45; H, 6·5. $C_{14}H_{20}O_8$ requires C, 53·15; H, 6·35%). Deacetylation with boiling ethanol containing 5% of hydrochloric acid gave crystals which darkened at 195—200° and melted at 205—210°. The residue from the mother-liquors of the acetate was distilled under reduced pressure to give a mixture of *cyclo*hexanetetrol tetra-acetates which did not crystallise (Found: C, 53·7; H, 6·4%).

Fraction B, R_F 0·70 (60 mg.). No crystalline material could be isolated. In another run (from 10 g. of tetrahydroxybenzoquinone) this fraction showed strong reducing properties and, after further chromatography, crystals (44 mg.) were obtained. Recrystallisation from ethanol gave a product (26 mg.), m. p. 160—161°, which reduced Fehling's solution in the cold and so probably contained a keto-group. It was acetylated but then failed to crystallise.

Fractions C, D, and E [R_F 0·62 (75 mg.), 0·53 (115 mg.), *and* 0·45 (135 mg.), *respectively*]. No crystalline product could be obtained. After acetylation, each fraction was distilled under reduced pressure and analysed: the first two proved to be mixtures of tetra-acetoxy*cyclo*hexanes and the last a mixture of penta-*O*-acetylquercitols (Found: Fraction C: C, 52·55; H, 6·4. Fraction D: C, 52·9; H, 6·4. Calc. for $C_{14}H_{20}O_8$: C, 53·15; H, 6·35%. Fraction E: Found: C, 51·55; H, 5·85. Calc. for $C_{16}H_{22}O_{10}$: C, 51·35; H, 5·9%).

cis- *and* epi-*Quercitol*. From Fraction F (R_F 0·39, 200 mg.) crystals (105 mg.) separated. Acetylation and crystallisation from ethanol–water gave *penta*-O-*acetyl*cis*quercitol*, m. p. 162·5° (Found: C, 51·6; H, 5·95. $C_{16}H_{22}O_{10}$ requires C, 51·35; H, 5·9%). A sublimed sample had m. p. 165·5°. Hydrolysis of the acetate, followed by sublimation *in vacuo*, gave crystals of cis*quercitol*, m. p. 235—240° (decomp.) (Found: C, 44·05; H, 7·5. $C_6H_{12}O_5$ requires C, 43·9; H, 7·35%).

The mother-liquors of the *cis*quercitol fraction, after several weeks, yielded a further crop of crystals (18 mg.). Recrystallisation from water–ethanol gave *epi*quercitol, m. p. 206—209° (decomp.), mixed m. p. 207—209° (decomp.). Acetylation yielded penta-*O*-acetyl*epi*quercitol, m. p. and mixed m. p. 141—142°.

scyllo*Quercitol*. From Fraction G (R_F 0·31, 165 mg.) a few crystals separated. Acetylation, followed by sublimation *in vacuo*, gave *scyllo*quercitol acetate, m. p. and mixed m. p. 193—194°. The acetate was hydrolysed to the quercitol, m. p. 235°, mixed m. p. 236°. The mother-liquors of this fraction gave no Scherer test, indicating the absence of *allo*inositol (R_F 0·30).

(±)-, epi-, *and* cis-*Inositol*. Fractions 44—75 of the preliminary separation were found, by paper chromatography, to contain *cis*-, *epi*-, and (±)-inositol. Since the first two have the

same R_F value in acetone–water, another solvent system was used for separation. The content of these fractions (390 mg.) was dissolved in butan-1-ol–acetic acid–water (4 : 1 : 1 v/v, 30 ml.); after 2 days, (±)-inositol (120 mg.) had separated. After two crystallisations from water–ethanol the product was acetylated, to yield the hexa-acetate, m. p. and mixed m. p. 110°.

The mother-liquors from the isolation of (±)-inositol were run through a cellulose-powder column (9 × 1¼ in.) in butan-1-ol–acetic acid–water (4 : 1 : 1); separation of *cis*- and *epi*-inositol was not complete but from the appropriate fractions *cis*-inositol (70 mg.) was obtained by crystallisation from water–ethanol. Acetylation and crystallisation from ethanol–water gave cis*inositol hexa-acetate*, m. p. 208° (Found: C, 49·95; H, 5·45. $C_{18}H_{24}O_{12}$ requires C, 50·0; H, 5·6%). Hydrolysis with boiling ethanol containing 5% of hydrogen chloride gave cis*inositol* which was crystallised from water–ethanol (Found: C, 40·3; H, 6·9. $C_6H_{12}O_6$ requires C, 40·0; H, 6·7%). *cis*Inositol decomposes on slow heating but its uncorrected m. p. was found to be 377° (decomp.) by placing samples on a preheated aluminium block; the corrected m. p. would be approx. 390°. The *hexabenzoate*, prepared by the method described for (±)-inositol by Fletcher and Findlay,[19] crystallised from anhydrous ethanol and melted at 252° (Found: C, 71·85; H, 4·55. $C_{48}H_{36}O_{12}$ requires C, 71·65; H, 4·5%).

The fractions containing mainly *epi*inositol were combined and evaporated, and the residue was acetylated. From a solution in aqueous ethanol, *epi*inositol acetate (11 mg.) slowly crystallised; after sublimation *in vacuo* it melted at 187° (mixed m. p. 187—188°).

myo*Inositol*. Fractions 76—250 of the preliminary separation were evaporated to give *myo*inositol (712 mg.); after one crystallisation from aqueous ethanol its m. p. was 222—224°.

Hydrogenation of cis*Inosose*.—*cis*Inosose (18 mg.) was hydrogenated for 3 hr. in N-hydrochloric acid with Adams catalyst (5 mg.). After removal of the platinum, the solution was evaporated in a desiccator over sodium hydroxide, and the residue was separated by chromatography on a small cellulose-powder column. The inositol fraction (3 mg.) was acetylated, and the product, recrystallised from ethanol–water, had m. p. 207—208°, undepressed by admixture of *cis*inositol acetate. The quercitol fraction was acetylated to give *cis*-quercitol penta-acetate (5 mg.), m. p. 162—163°, undepressed by a sample obtained from the hydrogenation of tetrahydroxybenzoquinone.

After a small-scale hydrogenation in water with Adams catalyst paper chromatography in butan-1-ol–acetic acid–water showed the formation of *cis*inositol accompanied by a trace of *epi*inositol.

Reduction of cis*Inosose with Sodium Amalgam*.—To a solution of *cis*inosose (50 mg.) in water (3 ml.), kept slightly acid by additions of N-sulphuric acid as required, sodium amalgam (1 g.) was added in several portions with shaking. When the solution no longer reduced Fehling solution, it was evaporated; acetylation of the residue gave penta-*O*-acetyl*epi*inositol which, after crystallisation from ethanol–water, had m. p. and mixed m. p. 188°.

Hydrogenation of Tetrahydroxybenzoquinone with Raney Nickel.—A mixture of tetrahydroxybenzoquinone (10 g.), Raney nickel W-2 [20] (2 teaspoons; *ca.* 6 g.), ethanol (100 ml.), and water (70 ml.) was hydrogenated in a steel autoclave at 120°/150 atm. for 40 min. and then at 140° for 30 min. The solution was filtered, concentrated under reduced pressure, and dried over sulphuric acid.

scyllo- *and* neo-*Inositol*. The syrupy residue (7·4 g.) was diluted with methanol and crystals (65 mg.) gradually separated. Crystallisation from water–ethanol gave a product (37 mg.), m. p. >280°; on addition of more ethanol, the mother-liquor deposited further crystals (11 mg.), m. p. 218—220°, identified as *myo*inositol. The former product was acetylated and the resulting mixture of acetates was separated by extraction with hot ethanol. The ethanol solution deposited *neo*inositol hexa-acetate (8 mg.), m. p. 254°, mixed m. p. with a pure sample (m. p. 257°) 256°. The ethanol-insoluble residue (32 mg.) was sublimed *in vacuo* to give *scyllo*inositol hexa-acetate, m. p. 295—297°, mixed m. p. with an authentic sample (m. p. 292—294°) 293—295°.

The filtrate from the *scyllo*- and *neo*-inositol was worked up by cellulose-powder chromatography as described above. After preliminary separation all the fractions—except those containing *epi*-, *cis*-, and *myo*-inositol—were rechromatographed and the products grouped into Fractions A—F (not necessarily identical with the fractions carrying the same designations in the previous run). There was some overlapping of fractions: only those which appeared to show a single spot on the chromatogram were worked up.

Fraction A (R_F 0·77, 700 mg.) deposited crystals (125 mg.) contaminated by oil, when stored in ethanol–ethyl acetate at 0°. Recrystallisation to constant m. p. from ethanol–ethyl acetate gave all-*cis*-*cyclo*hexane-1:2:3-triol [21] (39 mg.), m. p. and mixed m. p. 146—147° (Found: C, 54·6; H, 9·1. Calc. for $C_6H_{12}O_3$: C, 54·55; H, 9·15%). The hexabenzoate had m.p. and mixed m. p. 145°.