804. *Cyclitols. Part IX.*[1] *Cyclohexylidene Derivatives of Myoinositol.*

By S. J. Angyal, M. E. Tate, and (in part) S. D. Gero.

Condensation of myoinositol with cyclohexanone yields 1,2-*O*-cyclohexylidenemyoinositol and three diketals—1,2:3,4-, 1,2:4,5-, and 1,2:5,6-di-*O*-cyclohexylidenemyoinositol. The preparation of 1,4,5,6-tetra-*O*-acetylmyoinositol in good yield is described. 1,2-*O*-Cyclopentylidenemyoinositol has also been synthesised.

In Part I of this Series [2] the conversion of cyclitols into their ketals with acetone was described. These compounds proved to be key intermediates for much subsequent work and,

[1] Part VIII, Angyal and Gilham, *J.*, 1958, 375.
[2] Angyal and Macdonald, *J.*, 1952, 686.

in particular, isopropylidenemyoinositol has been in constant demand in our laboratories. Unfortunately the preparation of this compound—in contrast to that of the ketals of other cyclitols—is satisfactory only on a very small scale [3] and, despite a later modification,[4] the yield remains poor and inconsistent.

In order to combat an unfavourable position of the equilibrium water has to be removed from the reaction mixture. Unfortunately acetone, as a solvent, does not lend itself well to azeotropic separation of water. Moreover, acetone is not stable to strong dehydrating agents and self-condensation actually produces water, which may reverse the reaction if it is prolonged. Mićović and Stojilković [5] recently recommended the preparation of cyclohexylidene derivatives of sugars and polyols because of the ease with which they crystallise, and encouraged by Salmi's earlier use [6] of azeotropic dehydration in the condensation of glycols with several ketones, including cyclohexanone, we now report the reaction of cyclohexanone with myoinositol.

Myoinositol gradually dissolved in a boiling mixture of cyclohexanone and benzene, containing some toluene-*p*-sulphonic acid. Considerably more than one mol. of water, however, separated, and a monocyclohexylidene derivative, which was obtained by extraction of the reaction mixture with water, was only a minor product (2%). Most of the inositol was converted into three diketals which were separated by chromatography on alumina, and by crystallisation. They were identified as 1,2:3,4-, 1,2:4,5-, and 1,2:5,6-di-*O*-cyclohexylidenemyoinositol and were characterised as their diacetates and dibenzoates. A triketal of myoinositol appears to be present in the mother-liquors but could not be isolated.

Since the monocyclohexylidene compound gave 1,4,5,6-tetra-*O*-acetylmyoinositol after acetylation and subsequent acid hydrolysis, it is the 1,2-ketal (I), and, as in the monoisopropylidene derivative of myoinositol,[2] the ketal ring was preferentially formed by reaction with *cis*-hydroxyl groups. Each of the three diketals was hydrolysed under mild conditions (ethylene glycol and acid) to give the 1,2-cyclohexylidene derivative; consequently each has one cyclohexylidene group in the 1,2-position.

Each of the diketals was treated with sodium periodate, and also was methylated and the mixture of methyl ethers was examined by paper chromatography and ionophoresis. Only one diketal (m. p. 174°) was found to be resistant to the action of periodate: this compound, obtained in 16% yield, must therefore have the 1,2:4,5-dicyclohexylidene structure. Methylation gave a dimethyl ether and 4-*O*-methylmyoinositol, together with a small amount of 1-*O*-methylmyoinositol.

The diketal, m. p. 158°, isolated in 5% yield, reacted rapidly with periodate, whilst methylation yielded 5-*O*-methylmyoinositol, a dimethyl ether, and 4-*O*-methylmyoinositol. This ketal is therefore 1,2:3,4-di-*O*-cyclohexylidenemyoinositol.

The third diketal, m. p. 133°, isolated in 15% yield, reacted slowly with periodate,* and methylation yielded 4-*O*-methylmyoinositol, together with a small amount of the 1-isomer, and a dimethyl ether. This compound is therefore the 1,2:5,6-diketal (II). This structure was confirmed by partial benzoylation, from which two monobenzoates were isolated. The major product was identified as the 3-benzoate (III) by toluenesulphonylation, followed by hydrolysis, which gave † 4-*O*-tosylmyoinositol, identical with a sample prepared by Mr. J. S. Murdoch in this laboratory from 1,2,3,4,5-penta-*O*-acetylmyoinositol. The minor product of the benzoylation was the 4-benzoate, as shown

* An inspection of Dreiding models shows that the deformation of the cyclohexane ring, owing to the attachment of the five-membered ketal rings, brings the hydroxyl groups nearer to each other in the 1,2 : 3,4-diketal than in the 1,2 : 5,6-compound.

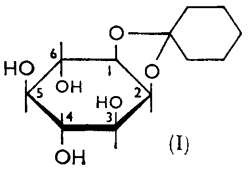
† A considerable amount of epi-inositol is also formed by solvolysis of 4-*O*-tosylmyoinositol. In the other cases studied by us,[7] solvolysis of tosylinositols was much slower.

[3] Charalampous, *J. Biol. Chem.*, 1957, **225**, 585.
[4] Angyal, Gilham, and Macdonald, *J.*, 1957, 1417.
[5] Mićović and Stojilković, *Tetrahedron*, 1958, **4**, 186.
[6] Salmi, *Ber.*, 1938, **71**, 1803.
[7] Angyal and Anderson, *Adv. Carbohydrate Chem.*, 1959, **14**, 155.

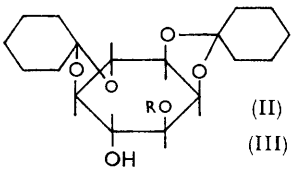
by its conversion into 1-*O*-tosylmyoinositol.[8] Preferential benzoylation of the diketal (II) on the 3-hydroxyl group which has an oxygen atom in an adjacent *cis*-position, is now recognised as being in accordance with the recently observed facilitation of acylation by neighbouring oxygen atoms.[9] Other instances of this effect are the preferential toluenesulphonylation [10] of 1,2:3,4-di-*O*-isopropylidene-epi-inositol in the 5-position, and the enhanced rate of esterification of *cis*-1,3-*O*-benzylideneglycerol.[11]

The two monobenzoates derived from 1,2:5,6-di-*O*-cyclohexylidenemyoinositol are the first examples of myoinositol derivatives unsubstituted only on the 1- and the 4-hydroxyl group, respectively. They are valuable intermediates for the synthesis of substituted myoinositols (see Part X).

In Part I it was concluded [2] that, on reaction of a cyclitol with acetone in the presence of zinc chloride, normally only *cis*-hydroxyl groups react; ketal formation across *trans*-hydroxyl groups occurs only with cyclitol derivatives which already contain *two cis*-ketal



(I)



(II) R = H

(III) R = Bz

[The compounds isolated were racemic.]

groups. This unusual reaction was explained as being due to the distortion of the chair form of the cyclohexane ring by the attachment of two five-membered rings. One case which does not conform to this conclusion is that of a di-*O*-isopropylidene-(—)-bornesitol,[12] which is, however, produced only in very small yield. The present work shows that, under the more stringent conditions now employed, a *trans*-ketal can be introduced into a cyclitol containing only one *cis*-ketal group. In a forthcoming paper it will be shown that the same is true of isopropylidene ketals when formed by the reaction of cyclitols with acetone diethyl ketal.

Although satisfactory conditions could not be found for the preparation of the monoketal (I) by the condensation of myoinositol with cyclohexanone, this compound was obtained in good yield by partial hydrolysis of the diketals. The hydrolysis could not be stopped satisfactorily at the monoketal stage merely by reliance on the different rates of reaction of the *cis*- and *trans*-ketal groups; but the *cis*-monoketal was separated, in excellent yield, from the reaction mixture by the use of hydrocarbon solvents in which it has a very low solubility. By this method, the monoketal was obtained in 90% yield from the crude reaction mixture of inositol with cyclohexanone. By acetylation and hydrolysis 1,4,5,6-tetra-*O*-acetylmyoinositol, an important intermediate for the preparation of cyclitol derivatives, readily resulted.

Myoinositol was also condensed with cyclopentanone, which is less reactive than its six-membered analogue, and 1,2-*O*-cyclopentylidenemyoinositol was obtained in 29% yield. Higher ketals were also formed, but have not been isolated.

Experimental

M. p.s are corrected. All the compounds described in this paper are racemic.

Reaction of Myoinositol with Cyclohexanone.—(a) 1,2-O-*Cyclohexylidenemyoinositol.* Powdered myoinositol (50 g.) was heated with cyclohexanone (500 ml.) and benzene (130 ml.) under a Dean and Stark separator until no more water separated (5 ml.). Toluene-*p*-sulphonic

[8] P. T. Gilham, Ph.D. Thesis, University of New South Wales, 1956.
[9] Kupchan, Slade, and Young, unpublished work; personal communication by Dr. R. J. Young.
[10] Angyal and Gilham, *J.*, 1957, 3691.
[11] Baggett, Brimacombe, Foster, Stacey, and Whiffen, *J.*, 1960, 2577.
[12] Bien and Ginsburg, *J.*, 1958, 3189.

acid (1 g.) was then added and heating continued with vigorous stirring for 3½ hr. during which 23 ml. of water collected. The hot mixture was filtered to remove unchanged myoinositol (5 g.), and the filtrate was washed while still hot (to avoid the formation of emulsions) with 1·5N-ammonia (4 × 100 ml.). After addition of sodium carbonate (0·5 g.), the mixture was steam-distilled to remove benzene and cyclohexanone. The resulting organic layer was set aside for the isolation of the diketals. The aqueous layer was combined with the ammoniacal washings and was evaporated to dryness. The residue was extracted with hot ethanol, and the extract was filtered to remove some myoinositol and concentrated to a small volume. On addition of chloroform and cooling 1,2-O-*cyclohexylidenemyoinositol* (1·45 g., 2%), m. p. 174—177°, crystallised in needles. Recrystallisation from ethanol raised the m. p. to 179° (Found: C, 55·9; H, 7·8. $C_{12}H_{20}O_6$ requires C, 55·4; H, 7·75%).

(b) 1,2:4,5-*Di*-O-*cyclohexylidenemyoinositol*. The organic layer remaining after the steam-distillation was diluted to 450 ml. with benzene and azeotropically distilled to remove all water. The solution was then made up to 500 ml. with n-hexane and was poured on a column (27″ × 2″) of alumina packed in n-hexane. The column was eluted with benzene–n-hexane (1 : 1; 3 l.), then with chloroform (3 l.), and finally with ethanol (4 l.).

The first fraction gave inositol on hydrolysis and probably contained tricyclohexylidene-inositol besides condensation products of cyclohexanone. No crystalline compound was obtained from this fraction.

The chloroform eluates were concentrated *in vacuo* to a brown oil which, after dissolution in benzene (40 ml.), gradually deposited 1,2:4,5-*di*-O-*cyclohexylidenemyoinositol* (13·5 g., 16%) as hexagonal plates which changed to needles at 158—159° and melted at 174° (Found: C, 63·15; H, 8·0. $C_{18}H_{28}O_6$ requires C, 63·5; H, 8·3%). The *diacetate*, m. p. 179°, formed needles from ethanol (Found: C, 62·0; H, 7·45. $C_{22}H_{32}O_8$ requires C, 62·25; H, 7·6%). Benzoylation with benzoyl chloride and pyridine gave the *dibenzoate*, needles (from benzene), m. p. 262° (Found: C, 70·5; H, 6·75. $C_{32}H_{36}O_8$ requires C, 70·05; H, 6·6%).

(c) 1,2:5,6-*Di*-O-*cyclohexylidenemyoinositol*. The ethanolic eluates were concentrated *in vacuo*; the oily residue was dissolved in a mixture of benzene (60 ml.) and n-hexane (90 ml.) which, after inoculation with crystals from a previous run, deposited crystals (19 g.), m. p. 95—100°. This material was extracted with boiling light petroleum (b. p. 60—90°) which left the *diketal* (13·0 g., 15%), m. p. 126—128°, undissolved. Recrystallisation from benzene–light petroleum raised the m. p. to 133° (Found: C, 63·25; H, 8·3. $C_{18}H_{28}O_6$ requires C, 63·5; H, 8·3%). The *diacetate*, needles from ethanol, melted at 120° (Found: C, 62·7; H, 7·7. $C_{22}H_{32}O_8$ requires C, 62·25; H, 7·6%). The *dibenzoate* crystallised from ethanol in two allotropic forms, m. p. 136—137° and 158° (Found: C, 70·2; H, 6·5. $C_{32}H_{36}O_8$ requires C, 70·05; H, 6·6%).

(d) 1,2:3,4-*Di*-O-*cyclohexylidenemyoinositol*. The combined benzene–light petroleum liquors and extracts from the isolation of the 1,2:5,6-diketal were kept at 0° for 3 weeks whereupon a creamy solid was deposited (9·8 g.; m. p. 94—100°). After a further nine weeks at 0°, formation of small rosettes of well-defined rods (4·1 g., 5%), m. p. 155—157°, was observed. This *diketal* crystallised from benzene–n-hexane as needles, m. p. 158° (Found: C, 63·7; H, 8·4. $C_{18}H_{28}O_6$ requires C, 63·5; H, 8·3%). The diacetate did not crystallise. The *dibenzoate*, needles from ethanol, melted at 205° (Found: C, 69·9; H, 6·45. $C_{32}H_{36}O_8$ requires C, 70·05; H, 6·6%).

Periodate Oxidation of the Isomeric Diketals.—Each diketal (10 mg.) was dissolved in ethanol (2 ml.) and a 2% aqueous solution (3 ml.) of sodium metaperiodate was added. After 2 hr. the excess of periodate was destroyed by addition of ethylene glycol. After 15 min. the solution was heated on the water bath with 5N-hydrochloric acid (4 ml.) for 30 min., then evaporated to dryness, and the residue was dissolved in water (1 ml.) and examined by paper chromatography in acetone–water (4 : 1). The 2,3:4,5-diketal had been partially oxidised to reducing material visible at R_F 0·90 and 0·99; myoinositol was also present (R_F 0·14). The 1,2:3,4-diketal had been completely oxidised, only one (reducing) material showing (at R_F 0·99). The 1,2:4,5-diketal gave only a myoinositol spot. Myoinositol used in a control experiment was completely oxidised and gave no reducing material.

Partial Methylation of the Isomeric Diketals.—Each diketal (340 mg.) was heated with stirring for 1 hr. on the water bath with 30% sodium hydroxide solution (0·8 ml.) and dimethyl sulphate (0·4 ml.). The mixture was extracted with chloroform (3 × 5 ml.), and the combined organic layers were washed with water (3 × 5 ml.) and evaporated to dryness. The residue was heated with 80% acetic acid for 30 min. at 100° to remove the cyclohexylidene groups.

After evaporation to dryness, the residue (42 mg. from the 1,2:4,5-, 105 mg. from the 1,2:5,6-, and 131 mg. from the 1,2:3,4-diketal) was examined by paper chromatography in butan-1-ol–pyridine–water (3 : 2 : 1 v/v).[13] In this system, after descending chromatography for 18 hr., the following displacements are observed: myoinositol, 4·1 cm.; 1-methyl ether, 7·6; 2-methyl ether, 10·0; 4-methyl ether, 9·5; 5-methyl ether, 9·5 cm.; the dimethyl ether from the 1,2:5,6-diketal appears at 16·5, those from the other diketals at 18·1 cm. The products from the 1,2:4,5- and the 1,2:5,6-diketal contained 1-*O*-methylmyoinositol as a minor product. Each of the mixtures gave a strong spot in the overlapping 4- and 5-methyl ether region. Examination of this spot by paper ionophoresis[14] in 0·012M-sodium tetraborate (for 3 hr. at 550 v) indicated the presence of 4-*O*-methylmyoinositol in all the three reaction mixtures. The presence of the 5-methyl ether in the product obtained from the 1,2:3,4-diketal was shown by subjecting the dried ionophoretogram to descending chromatography in butan-1-ol–pyridine–water (3 : 2 : 1) (from the " positive " to the " negative " side). 5-*O*-Methylmyoinositol, which was not separated from the dimethyl ether by ionophoresis, is clearly separated from it by the subsequent chromatography.

Partial Hydrolysis of the Diketals.—Each of the dicyclohexylidene derivatives (36 mg.) was heated in chloroform (2 ml.) under reflux for 15 min. with a solution (0·9 ml.) of ethylene glycol (6·7 mg./ml.) and toluene-*p*-sulphonic acid (1 mg./ml.) in chloroform. Separation of crystals commenced almost immediately. Next day the 1,2-*O*-cyclohexylidenemyoinositol (25 mg., 95%), m. p. 177—178°, was collected; it contained a trace of myoinositol (paper chromatography) but did not depress the m. p. (179°) of an authentic sample.

Benzoylation of 1,2:5,6-*Di*-O-*cyclohexylidenemyoinositol* (II).—The diketal (20·4 g.) was dissolved in dry pyridine (140 ml.), and benzoyl chloride (9 ml.) was added. After 18 hr. the mixture was poured on ice, and the semi-solid precipitate was taken up in benzene (4 × 400 ml.). Evaporation of the solvent left an oil (30·5 g.) which was chromatographed in benzene (30 ml.) on alumina (1200 g.), packed in benzene. The column was eluted with benzene–chloroform (9 : 1), 500 ml. fractions being collected. Fraction 1—14 on evaporation gave crystals (5·62 g., 17%), m. p. 154—158°, of 3,4-di-*O*-benzoyl-1,2:5,6-di-*O*-cyclohexylidenemyoinositol.

Fractions 20—24 contained the 4-benzoate (0·93 g.). The eluting solvent was changed to benzene–chloroform (2 : 1) and a further amount (0·9 g.) of 4-benzoate was collected in fractions 25—30. Recrystallisation of the combined material from ethanol gave 4-O-*benzoyl*-1,2:5,6-*di*-O-*cyclohexylidenemyoinositol* (1·05 g., 4%), m. p. 185° (Found: C, 67·5; H, 7·1. $C_{25}H_{32}O_7$ requires C, 67·55; H, 7·25%).

The eluting solvent was changed to chloroform, and the 3-benzoate (14·4 g.), m. p. 160—165°, was collected in fractions 31—42. Recrystallisation from ethanol gave 3-O-*benzoyl*-1,2:5,6-*di*-O-*cyclohexylidenemyoinositol* (III) (8·9 g., 33%), m. p. 173° (Found: C, 67·25; H, 7·05%).

3-O-*Benzoyl*-1,2:5,6-*di*-O-*cyclohexylidene*-4-O-*tosylmyoinositol.*—3-*O*-Benzoyl-1,2:5,6-di-*O*-cyclohexylidenemyoinositol (444 mg.) was heated in dry pyridine (0·4 ml.) with toluene-*p*-sulphonyl chloride (200 mg.) for 2 hr. on a steam bath. The mixture solidified overnight; it was dissolved in hot pyridine (2 ml.) and poured on ice. The precipitate was collected and then dissolved in boiling methanol (25 ml.); the solution was filtered, concentrated to 15 ml., and cooled to 0°, whereupon needles of the *tosyl compound* (271 mg., 45%), m. p. 140—143°, separated. Recrystallisation from ethanol raised the m. p. to 146—147° (Found: C, 64·0; H, 6·4. $C_{32}H_{38}O_9S$ requires C, 64·2; H, 6·4%).

4-O-*Tosylmyoinositol.*—The preceding compound (271 mg.) was heated under reflux with ethanol (8 ml.) and 10N-hydrochloric acid (2 ml.) for 13 hr. (Paper chromatography after 8 hr. showed that the benzoyl group was not yet completely removed.) The mixture was evaporated to dryness and redissolved in water (0·4 ml.); cellulose powder (0·1 g.) and then acetone (4 ml.) were added, and the resulting slurry was poured on a cellulose powder (11 g.) column and eluted with acetone–water (9 : 1). Fractions 3—5 (6·5 ml. each) contained a solid (77 mg.), which was crystallised twice from ethanol to give needles of 4-O-*tosylmyoinositol* (12 mg., 8%), m. p. 173—174° (decomp. in a capillary), 181—182° (decomp. on a Kofler block) (Found: C, 46·9; H, 5·6. $C_{13}H_{18}O_8S$ requires C, 46·7; H, 5·4%). An authentic sample was prepared by acid hydrolysis of 1,2,3,4,5-penta-*O*-acetyl-6-*O*-tosylmyoinositol, kindly supplied by Mr. J. S. Murdoch. The m. p. was not depressed.

[13] Chargaff, Levine, and Green, *J. Biol. Chem.*, 1948, **175**, 67.
[14] Angyal and McHugh, *J.*, 1957, 1423.

Further elution of the column with acetone–water (4 : 1) gave fractions containing (paper chromatography) epi-inositol. The content of these fractions (14·5 mg.) was crystallised from aqueous ethanol and yielded needles (3·5 mg., 4%) of epi-inositol, m. p. 270—280° (Kofler block). The crystals and the contents of the mother liquors were treated with acetic anhydride and sulphuric acid, and the crude hexa-acetate was crystallised from methanol and then sublimed at 160—180°/3 mm. The m. p., 187—188°, was undepressed by admixture with hexa-*O*-acetylepi-inositol, m. p. 188°.

4-O-*Benzoyl*-1,2:5,6-*di*-O-*cyclohexylidene*-3-O-*tosylmyoinositol*.—4-*O*-Benzoyl-1,2:5,6-di-*O*-cyclohexylidenemyoinositol (222 mg.) was heated in dry pyridine (0·2 ml.) with toluene-*p*-sulphonyl chloride (100 mg.) for 1½ hr. on a steam bath. The mixture, that solidified overnight, was dissolved in boiling methanol (25 ml.). The solution was filtered and concentrated to 5 ml.: on cooling it deposited rosettes (87 mg., 28%), m. p. 204—206° (decomp.). A further quantity (85 mg., 28%) of less pure material was obtained by the addition of water to the mother liquors. Recrystallisation from ethanol gave the *tosyl compound* as needles, m. p. 207° (decomp.) (Found: C, 64·65; H, 6·5. $C_{32}H_{38}O_9S$ requires C, 64·2; H, 6·4%).

1-O-*Tosylmyoinositol*.—The preceding compound (75 mg.) was heated under reflux with methanol (10 ml.) and 4N-hydrochloric acid (10 ml.) for 16 hr. After extraction with ether, the solution was evaporated to dryness and the residue was crystallised from water (7 ml.) to give 1-*O*-tosylmyoinositol (19·5 mg., 46%), m. p. 223—224° (decomp.). With acetic anhydride and pyridine it gave 1,2,4,5,6-penta-*O*-acetyl-3-*O*-tosylmyoinositol, needles (from ethanol), m. p. 149—150°; the m. p. was not depressed by admixture with an authentic sample,[8] m. p. 150°.

Preparation of 1,2-O-*Cyclohexylidenemyoinositol and of* 1,4,5,6-*Tetra*-O-*acetylmyoinositol*.—In a flask fitted with a Hirschberg stirrer and a Dean and Stark separator powdered myoinositol (50 g.) was heated under reflux with cyclohexanone (technical, 500 ml.) and benzene (130 ml.) until no more water distilled. Toluene-*p*-sulphonic acid (1 g.) was then added and heating continued with vigorous stirring for 6 hr.; by that time nearly all the inositol had dissolved and 24 ml. of water had collected in the separator. Benzene (250 ml.), light petroleum (b. p. 60—80°; 250 ml.), and ethanol (50 ml.) were added to the cooled solution which was then inoculated with 1,2-*O*-cyclohexylidenemyoinositol (0·5 g.) and left overnight. The resulting slurry was filtered and the solid was well washed with benzene. Paper chromatography indicated that the product contained some myoinositol; it was therefore extracted three times with anhydrous ethanol (3 × 200 ml.). Evaporation of the extracts gave 1,2-*O*-cyclohexylidenemyoinositol (67·8 g., 90%), m. p. 178°, which was sufficiently pure for the preparation of the tetra-acetate.

The monoketal (48 g.) was heated on the steam bath for 2 hr. with anhydrous pyridine (280 ml.) and acetic anhydride (320 ml.). The cooled mixture was poured on ice, and 1,4,5,6-*tetra*-O-*acetyl*-2,3-O-*cyclohexylidenemyoinositol* (78 g., 98%), m. p. 116°, was collected. The crude material was sufficiently pure for the next reaction but a pure sample, m. p. 118°, was obtained as needles by crystallisation from ethanol (Found: C, 55·85; H, 6·5. $C_{20}H_{28}O_{10}$ requires C, 56·05; H, 6·6%).

The tetra-acetate (51 g.) was heated for 2 hr. on the steam bath with glacial acetic acid (80 ml.) and water (20 ml.). The solution was evaporated *in vacuo*, the residue redissolved in water, and again evaporated. The residue was then dissolved in boiling water (50 ml.), and the solution was filtered and set aside at 0°: it deposited 1,4,5,6-tetra-*O*-acetylmyoinositol monohydrate (33 g., 77%) as needles, m. p. 100° after shrinking at 94—97° (Found: C, 46·25; H. 6·0. Calc. for $C_{14}H_{20}O_{10},H_2O$: C, 45·9; H, 6·05%). Complete removal of water from this compound requires long and careful heating; crystallisation from anhydrous ethanol, however, yields a hemihydrate, m. p. 138—140°, which loses the water readily, even during the determination of the m. p. (Found: C, 47·15; H, 5·75. Calc. for $C_{14}H_{20}O_{10},\frac{1}{2}H_2O$: C, 47·05; H, 5·9%).

The over-all yield of tetra-acetate from myoinositol was 68%.

1,2-O-*Cyclopentylidenemyoinositol*.—Powdered myoinositol (20 g.) was heated under reflux with cyclopentanone (300 ml.), benzene (50 ml.), and toluene-*p*-sulphonic acid (0·5 g.) for 6 hr., with vigorous stirring, under a Dean and Stark separator: 2·7 ml. of water collected. The hot reaction mixture was filtered to remove unchanged myoinositol (7·7 g.), and the filtrate was extracted, while still warm, with 2N-ammonia (6 × 75 ml.). The organic layer was steam-distilled to remove the cyclopentanone; the resulting aqueous layer was combined with the

ammoniacal washings and evaporated to dryness *in vacuo*. The residue (8·9 g.) was crystallised from anhydrous methanol, with the addition of chloroform, to give plates of 1,2-O-*cyclopentylidenemyoinositol* (5·33 g., 29%), m. p. 164—166°. The pure substance melts at 166° (Found: C, 53·75; H, 7·5. $C_{11}H_{18}O_6$ requires C, 53·65; H, 7·4%). With acetic anhydride and pyridine it gave an 82% yield of 1,4,5,6-*tetra*-O-*acetyl*-2,3-O-*cyclopentylidenemyoinositol*, needles (from ethanol), m. p. 132° (Found: C, 55·1; H, 6·2. $C_{19}H_{26}O_{10}$ requires C, 55·05; H, 6·3%). Hydrolysis of this compound by the method described for the cyclohexylidene analogue gave 1,4,5,6-tetra-*O*-acetylmyoinositol, m. p. 139°, in 73% yield.

SCHOOL OF CHEMISTRY, UNIVERSITY OF NEW SOUTH WALES,
SYDNEY.

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