Tetrahedron, 1958, Vol. 4, pp. 186–196. Pergamon Press Ltd., London

THE CONDENSATIONS OF POLYHYDRIC ALCOHOLS AND MONOSACCHARIDES WITH *CYCLO*PENTANONE AND *CYCLO*HEXANONE

V. M. Mićović and Miss A. Stojiljković
Institute of Chemistry, Faculty of Science, University of Belgrade, Yugoslavia

(*Received* 14 *February* 1958)

Abstract—*cyclo*Pentanone and *cyclo*hexanone have been shown to condense with polyhydric alcohols and monosaccharides to yield di- and tri-*cyclo*pentylidene and *cyclo*hexylidene derivatives. Series of new compounds with glycerol, pentaerythritol, *meso*erythritol, arabitol, mannitol, sorbitol, xylose, arabinose, glucose, mannose and fructose have been prepared and characterised. In some instances attempts have been made to prove the structures of the products obtained or to give some experimental evidence for the already proposed structures.

In 1895 Fischer[1] and Speier[2] discovered a new class of sugar derivatives by condensing polyhydroxy compounds with acetone. Since then, these compounds have been employed for purification, isolation and characterisation of polyhydric alcohols and monosaccharides and also as intermediates in the syntheses of partially substituted compounds. Recently, the importance of cyclic ketals and acetals has increased especially in connexion with constitution and configuration of these compounds, i.e. with the size, position and stability of the ketal and acetal rings formed in the course of these condensations.

We have attempted to condense *cyclo*pentanone and *cyclo*hexanone with polyhydroxy compounds with the intention of finding out the possibility of correlating these compounds with already known and well defined acetone derivatives, and in order to see if these compounds would be more convenient than acetone derivatives either for the identification or for the syntheses of polyhydroxy compounds.

The condensations of ketones with polyhydroxy compounds are usually carried out in acid media and in the presence of some dehydrating agent.[3] First, the hemiketal is formed, followed by subsequent ring closure with elimination of 1 molecule of water. The course of the reaction depends to a large extent upon the configuration of the compounds involved in the condensations. The optimum conditions are found when the hydroxy groups are in *cis* positions in Fischer's projection formulae, i.e. when the distance between two oxygen atoms is 2·51 Å. With increasing distance the tendency for cyclic acetal and ketal formation decreases. It seems likely that there exists a parallel between the formation of cyclic ketals and glycolic complexes with boric acid.[4]

---

[1] E. Fischer, *Ber. Dtsch. Chem. Ges.* **28**, 1167 (1895).

[2] A. Speier, *Ber. Dtsch. Chem. Ges.* **28**, 2531 (1895).

[3] E. Fischer and E. Pfühler, *Ber. Dtsch. Chem. Ges.* **53**, 1606 (1920); R. Dworzak and K. Hermann, *Mh. Chem.* **52**, 83 (1929); H. O. L. Fischer and C. Trabue, *Ber. Dtsch. Chem. Ges.* **60**, 485 (1927); H. Baer and H. O. L. Fischer, *Ber. Dtsch. Chem. Ges.* **63**, 1749 (1930); L. Smith and J. Lindberg, *Ber. Dtsch. Chem. Ges.* **64**, 505 (1931); M. M. Maglio and C. A. Beirger, *J. Amer. Chem. Soc.* **68**, 529 (1946); H. Hibbert and J. Morazain, *Canad. J. Res.* **2**, 35 (1930); *Chem. Abstr.* **24**, 2108 (1930); E. Salmi, *Ber. Dtsch. Chem. Ges.* **71B**, 1803 (1938); A. Dupire, *C. R. Acad. Sci., Paris* **214**, 359 (1942).

[4] J. Boeseken, *Rec. Trav. Chim. Pays-Bas* **40**, 553 (1921); J. Boeseken, *Ber. Dtsch. Chem. Ges.* **56**, 2411 (1923); Chr. Maan, *Rec. Trav. Chim. Pays-Bas* **48**, 332 (1929).

The direct condensation of polyhydroxy compounds with ketones affords five-membered cyclic ketals, substituted dioxolane rings; in the condensations with aldehydes, six-membered acetal rings are formed. The formation of rings of different size has been explained with the help of the Ingold–Thorpe theory.[5] Later, Hann and Hudson[6] and Barker and Bourne[7] presented rules enabling the prediction of the course of condensation of polyhydric alcohols with aldehydes. These rules, based exclusively upon experimental evidence, have been explained on the assumption that polyhydric alcohols have a planar zigzag conformation,[8] with hydroxy groups having positions considerably different from the apparent positions in Fischer's projection formulae. From these rules it could be concluded that the formation of those rings requiring the least deformation of the planar conformations would be mostly favoured. From the point of view of conformational analyses of the (six-membered) cyclic compounds formed, those rules are in full agreement with the general principles of conformational stabilities. However, they cannot be applied to cyclic ketals. That was one of the reasons why we began to study the condensations of polyhydroxy compounds with cyclic ketones.

Many facts indicate the size of the ring to be an important factor in the chemical behaviour of cyclic compounds. According to the I-strain theory[9] and the proposed generalisation for the *exo* and *endo* double bonds[10] in five-and six-membered ring systems, one might expect *cyclo*hexanone to be more reactive than *cyclo*pentanone. Some evidence that this is the case can be found in published papers and is also offered in the present work. However, the size of the ketal rings formed is not in accordance with the theory mentioned above; this fact can be explained only by assuming that the I-strain is not the dominating factor in these condensations.

Condensations of polyhydric alcohols with cyclo*pentanone and* cyclo*hexanone*

Almost all open-chain polyhydric alcohols have been condensed with acetone, but the structures of the products obtained have only been determined in the case of glycerol,[11] xylitol,[12] sorbitol,[13], iditol,[14] mannitol[15] and dulcitol[16] (the information available for xylitol is contradictory). All these condensations afforded five-membered ketal rings, whereas six-membered ketal rings were obtained only in a few cases by condensing derivatives of polyhydric alcohols; no seven-membered ring formation has been reported so far.

---

[5] H. S. Hills and H. Hibbert, *J. Amer. Chem. Soc.* **45**, 3122 (1923).

[6] R. M. Hann and C. S. Hudson, *J. Amer. Chem. Soc.* **66**, 1909 (1944); A. T. Hess, R. M. Hann and C. S. Hudson, *J. Amer. Chem. Soc.* **70**, 765 (1948).

[7] S. A. Barker and E. J. Bourne, *J. Chem. Soc.* 905 (1952).

[8] S. A. Barker, E. J. Bourne and D. H. Whiffen, *J. Chem. Soc.* 3865 (1952).

[9] H. C. Brown, R. S. Fletcher and J. Johansen, *J. Amer. Chem. Soc.* **73**, 212 (1951); H. C. Brown and M. Borkowski, *J. Amer. Chem. Soc.* **74**, 1894 (1952).

[10] H. C. Brown, J. H. Browster and H. Schlecher, *J. Amer. Chem. Soc.* **76**, 467 (1954).

[11] J. C. Irvine, J. L. A. Macdonald and Ch. W. Soutar, *J. Chem. Soc.* **107**, 337 (1915); H. Hibbert and J. Morazain, *Canad. J. Res.* **2**, 214 (1930); *Chem. Abstr.* **24**, 2988 (1930); N. M. Carter, *Ber. Dtsch. Chem. Ges.* **63B**, 2399 (1930); E. Baer and H. O. L. Fischer, *J. Amer. Chem. Soc.* **67**, 944 (1945).

[12] R. B. Tripson and L. H. Cretcher, *J. Org. Chem.* **8**, 95 (1943); R. Hann, A. T. Ness and C. S. Hudson, *J. Amer. Chem. Soc.* **66**, 73 (1944); E. Valentin and D. Tomkuljak, *Chem. Zvesti* **3**, 146 (1949), *Chem. Abstr.* **44**, 7234 (1950).

[13] H. H. Strain, *J. Amer. Chem. Soc.* **56**, 1756 (1954); B. C. Pressman, L. Andersen and H. A. Lardy, *J. Amer. Chem. Soc.* **72**, 2404 (1950); E. J. Bourne, G. P. McSweeney and M. Stacey, *J. Chem. Soc.* 1408 (1952).

[14] E. J. Bourne, G. P. McSweeney and L. F. Wiggins, *J. Chem. Soc.* 2542 (1952).

[15] E. Fischer and Ch. Rund, *Ber. Dtsch. Chem. Ges.* **49**, 88 (1916); L. F. Wiggins, *J. Chem. Soc.* 13 (1946).

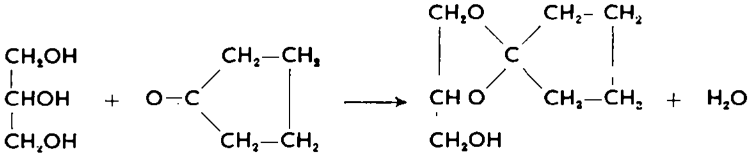
[16] E. Fischer, *Ber. Dtsch. Chem. Ges.* **48**, 266 (1915); A. Pizzarello and W. Freudenberg, *J. Amer. Chem. Soc.* **61**, 611 (1939); R. Hann, W. Maclay and C. S. Hudson, *J. Amer. Chem. Soc.* **61**, 2432 (1939).

Ketones other than acetone have rarely been used. *cyclo*Hexanone is the only cyclic ketone which has been condensed, the other reactant being mannitol.[17]

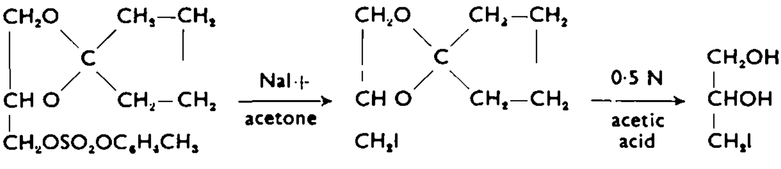
In the present work the condensations of *cyclo*pentanone with glycol, glycerol, pentaerythritol, *meso*erythritol, arabitol, mannitol and sorbitol, as well as of *cyclo*hexanone with pentaerythritol and *meso*erythritol, are described. Condensations were carried out in the presence of gaseous hydrochloric acid, concentrated sulphuric acid and phosphorus pentoxide. Owing to the fact that polyhydroxy compounds are very sparingly soluble in cyclic ketones, 3–5 moles per mole of polyhydroxy compound were used and in some cases even a much greater excess.

Glycol has been condensed with *cyclo*pentanone under the experimental conditions given by Dworzak[3] for the condensation of glycol with acetone, i.e. in the presence of 40% suphuric acid and at elevated temperatures. Boeseken and Tellegan[18] have reported that they were unable to carry out the condensation of *cyclo*pentanone with glycol in the presence of either gaseous hydrochloric or concentrated sulphuric acid; but Salmi[3] by azeotropic elimination of the water formed in the course of the reaction, succeeded in obtaining the condensation product. The *cyclo*pentylideneglycol prepared in the present work was identical with that obtained by Salmi; the yield of the reaction was very small, probably owing to the self-condensation of *cyclo*pentanone.

The condensation of glycerol with *cyclo*pentanone was carried out in the presence of gaseous hydrochloric acid and sodium sulphate as well as in the presence of concentrated sulphuric acid. The condensation product (I) was obtained in yields ranging from 41 to 51 per cent. The presence of one free hydroxy group in compound (I) was demonstrated by preparing the crystalline toluene-*p*-sulphonate (tosylate) (II) and mono-3:5-dinitrobenzoate. In order to establish whether compound (I) could be considered as a 1:2- or 1:3-glycerol derivative, the *p*-tosylate (II) was heated with sodium iodide in acetone at 100°. It has long been known, from the works of Oldham and Rutherford,[19] that the toluenesulphonate group could be displaced by iodine when attached to a primary carbon atom, whereas the same group on a secondary carbon atom is displaced only with difficulty. On heating the compound (II) with sodium iodide at 100°, either in a sealed tube or at atmospheric pressure, *cyclo*pentylidenemonoiodohydrin (III) was obtained. Hydrolysis of compound (III) with



(I)



(IIa) (III) (IV)

---

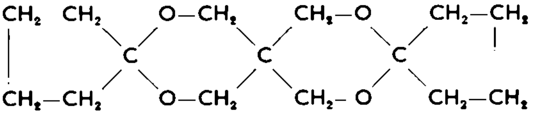
[17] E. J. Bourne, W. M. Corbett and D. Erilinne, *J. Chem. Soc.* 786 (1950).

[18] J. Boeseken and F. Tellegan, *Rec. Trav. Chim. Pays-Bas* 57, 133 (1938).

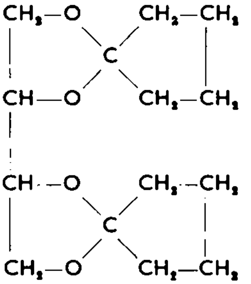
[19] J. W. H. Oldham and J. K. Rutherford, *J. Amer. Chem. Soc.* **54**, 366 (1932).

0·5 N acetic acid afforded glyceroliodohydrin, identical with an authentic specimen prepared according to the method of Glattfeld and Klaas.[20]

The tetritols, pentaerythritol and *meso*erythritol were condensed with *cyclo*pentanone. The analyses of the products obtained have shown that in both cases all four hydroxy groups had reacted and that di*cyclo*pentylidene derivatives (V) and (VI) were obtained. It has been assumed that in the case of *meso*erythritol the adjacent hydroxy groups had been involved in the ketal formation and that the condensation product was 1:2–3:4-di*cyclo*pentylidene*meso*erythritol. (This assumption has been made in connexion with the determined structure of *cyclo*pentylideneglycerol.)



(V)



(VI)

The condensation of *cyclo*pentanone with L-arabitol yielded a syrupy product, which was identified by preparation of a crystalline toluene-*p*-sulphonate. According to the analysis of this derivative, di*cyclo*pentylidenearabitol was obtained.

The condensation with hexitols (D-mannitol and D-sorbitol) proceeded with the formation of the corresponding tri*cyclo*pentylidene derivatives, thus showing that all six hydroxy groups were involved in the reaction.

By condensing *cyclo*hexanone with pentaerythritol and *meso*erythritol, the corresponding di*cyclo*hexylidene derivatives were obtained.

All the condensation products were found to be crystalline solids (except those of glycol, glycerol and L-arabitol), soluble in common organic solvents but insoluble in water. The specific rotations of the compounds in question, owing to their cyclic structures, were much greater than those of the corresponding alcohols.

Condensations of monosaccharides with cyclo*pentanone and* cyclo*hexanone*

The published literature concerning the acetonisation of monosaccharides is rather complex, since most of the monosaccharides have been condensed with acetone. The most important references concern arabinose,[21] xylose,[22] mannose,[23] glucose,[24]

---

[20] J. W. E. Glattfeld and R. Klaas, *J. Amer. Chem. Soc.* **55**, 1117 (1933).

[21] E. Fischer, *Ber. Dtsch. Chem. Ges.* **28**, 1145 (1895); H. Ohle and G. Berend, *Dtsch. Ber. Chem. Ges.* **60**, 810 (1927).

[22] O. Svanberg, *Ber. Dtsch. Chem. Ges.* **56**, 863 (1923); K. Freudenberg and O. Svanberg, *Ber. Dtsch. Chem. Ges.* **55**, 3239 (1922); W. N. Haworth and Ch. R. Porter, *J. Chem. Soc.* 611 (1928).

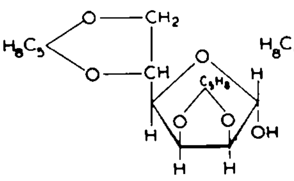
[23] K. Freudenberg and R. Hixon, *Ber. Dtsch. Chem. Ges.* **56**, 2119 (1923); *Ibid.* **58**, 300 (1925); H. Ohle and G. Berend, *Ber. Dtsch. Chem. Ges.* **58**, 2590 (1925); J. Irvine and A. F. Skinner, *J. Chem. Soc.* 1089 (1926).

[24] J. Irvine and J. Patterson, *J. Chem. Soc.* **121**, 2146 (1922); J. Macdonald, *J. Chem. Soc.* **103**, 1896 (1913); J. Irvine and T. Hogg, *J. Chem. Soc.* **105**, 1386 (1914); K. Freudenberg and E. Doser, *Ber. Dtsch. Chem. Ges.* **56**, 1243 (1923); P. Karrer and O. Hurwitz, *Helv. Chim. Acta.* **4**, 728 (1921); C. G. Anderson, W. Charlton and W. N. Haworth, *J. Chem. Soc.* 1329 (1929).

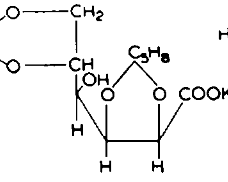
galactose,[25] altrose,[26] gulose,[27] talose,[28] idose,[29] fructose,[30] sorbose,[31] tagatose[32] and psycose.[33] The structures of the condensation products have been determined beyond question only in a few cases; usually, among many possible structures the most probable were suggested as being correct.

Among cyclic ketones only *cyclo*hexanone has been condensed with glucose.[34] By condensing the pentoses D-xylose and L-arabinose with *cyclo*pentanone and *cyclo*hexanone in the presence of concentrated sulphuric acid the corresponding di-derivatives have been obtained. The condensation products were shown to be optically active crystalline solids (contrary to diacetonexylose, which is a liquid) that do not reduce Fehling's solution and are insoluble in water but soluble in most organic solvents. *cyclo*Hexanone was found to condense much more readily than *cyclo*pentanone.

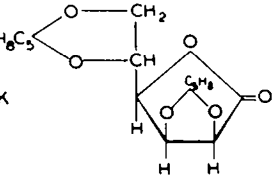
The condensations of D-glucose and D-mannose with *cyclo*pentanone and *cyclo*hexanone resulted in the formation of the corresponding di-derivatives. The condensation product of *cyclo*pentanone with D-glucose was obtained after a long series of experiments, the yield being very poor (0·25 per cent). The condensation of the same ketone with D-mannose proceeded much more readily, the yields being quite satisfactory (44 per cent). The products obtained were likewise solids having no reducing properties. According to published data, mannose reacts with acetone in the furanoside form. In order to find out whether in the condensations with *cyclo*pentanone and *cyclo*hexanone mannose reacted in the same furanoside form, di*cyclo*pentylidenemannose (VII) was subjected to oxidation with potassium permanganate in alkaline solution to yield the potassium salt of the corresponding mannonic acid (VIII). By addition of one equivalent of 0·5 N sulphuric acid the lactone of di*cyclo*pentylidenemannonic acid (IX) was obtained. This oxidation confirms the presence of a free aldehyde group in compound (VII), whereas the easy formation of the



VII



VIII



IX

---

[25] H. Ohle and G. Berend, *Ber. Dtsch. Chem. Ges.* **58**, 2585 (1925).

[26] M. Steibner and T. Reichstein, *Helv. Chim. Acta* **19**, 1011 (1936); F. H. Newth and L. F. Wiggins, *J. Chem. Soc.* 1734 (1950).

[27] K. Iwadare, *Bull. Chem. Soc. Japan* **18**, 226 (1943).

[28] W. Bossard, *Helv. Chim. Acta* **18**, 482 (1935).

[29] K. Iwadare, *Bull. Chem. Soc. Japan.* **19**, 27 (1944).

[30] J. Irvine and A. Hydn, *J. Chem. Soc.* **95**, 1220 (1909); J. Irvine and J. P. Scott, *J. Chem. Soc.* **103**, 564 (1913); W. N. Haworth, E. L. Hirst and A. Learner, *J. Chem. Soc.* 1040 (1927); C. G. Anderson, W. Charlton and W. N. Haworth, *J. Chem. Soc.* 1337 (1929); H. Ohle and G. Berend, *Ber. Dtsch. Chem. Ges.* **60**, 1159 (1927); W. L. Wolfrom, W. L. Shiling and W. W. Binkley, *J. Amer. Chem. Soc.* **72**, 4544 (1950).

[31] T. Reichstein and O. Grüssner, *Helv. Chim. Acta* **17**, 311 (1934); H. Ohle, *Ber. Dtsch. Chem. Ges.* **71B**, 762 (1938).

[32] L. D. Bruyn and W. A. van Ekenstein, *Rec. Trav. Chim. Pays-Bas* **16**, 265 (1897); T. Reichstein and J. Bossard, *Helv. Chim. Acta* **17**, 753 (1934).

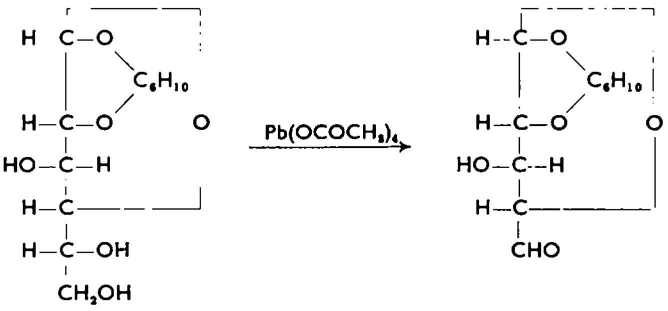
[33] M. Steigner and T. Reichstein, *Helv. Chim. Acta* **18**, 790 (1935).

lactone ring speaks in favour of the furanoside structure of the mannose being involved in the reaction.

Di*cyclo*pentylidene-D-mannose is *dextro*rotatory, the potassium salt of the di*cyclo*pentylidene-D-mannonic acid (VIII) is *laevo*rotatory and the lactone (IX), in accordance with Hudson's lactone rule, is again *dextro*rotatory.

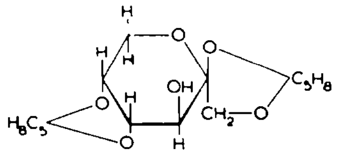
The condensation of D-mannose with *cyclo*hexanone resulted in the formation of a crystalline di-derivative.

The structure of di*cyclo*hexylidene-D-glucose has been determined by Hockett *et al.*[34] According to their work, the condensation product was found to be the 1:2-5:6-derivative of the glucofuranose. In an attempt to prove directly the size of the lactol ring, mono*cyclo*hexylidene-D-glucose, obtained by hydrolysis of the di-derivative, was oxidised with lead tetra-acetate. The crystalline derivative obtained was 1:2-mono*cyclo*hexylidene-trihydroxyglutar-dialdehyde (XI), which was identified by conversion to its monosemicarbazone (the second aldehyde group being blocked by the *cyclo*hexylidene). The formation of this product is only possible if the starting substance has a furanoside structure.

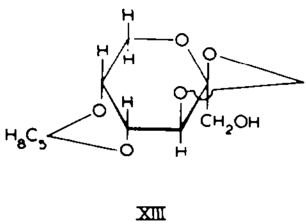


(X) (XI)

The condensation of D-fructose with *cyclo*pentanone produced a syrupy product, which was characterised by preparation of its toluene-*p*-sulphonate. The condensation of the same ketose with *cyclo*hexanone gave likewise a di-derivative, but in crystalline form. Since the analyses of the products obtained corresponded to the di-derivatives and attempts to oxidise the product with potassium permanganate failed, it has been assumed that the most probable structure of the derivative concerned is (XII). In the case of the alternative structure (XIII), upon oxidation the potassium salt of *cyclo*pentylidene-2-oxogluconic acid would have been obtained.



XII



XIII

---

[34] R. C. Hockett, R. E. Miller and A. Scattergood, *J. Amer. Chem. Soc.* 71, 3072 (1949).

EXPERIMENTAL

cyclo*Pentylideneglycol.* In a round-bottomed flask fitted with a mechanical stirrer and a reflux condenser there were placed glycerol (31 g), *cyclo*pentanone (42 g) and 4 drops of 40% sulphuric acid. The reaction mixture was stirred and heated on a water bath for 10 hr, cooled and extracted with ether, and the ethereal solution was dried and distilled. The fraction boiling from 136 to 155° was collected and treated with twice its volume of saturated bisulphite solution to remove the unchanged *cyclo*pentanone. The filtrate was extracted with ether and the ethereal solution was dried and distilled. The fraction boiling at 153° was collected (4 g, 6·2 per cent), $n_D^{20·5°}$ 1·4537, $d_4^{20·5°}$ 1·024 (M.R. found: 33·82; $C_7H_{12}O_2$ requires: 33·47).

cyclo*Pentylideneglycerol* (I). A mixture of glycerol (20 g), gaseous hydrochloric acid (0·4 g) and anhydrous sodium sulphate (8 g) was stirred for 24 hr at room temperature. After neutralisation, the inorganic salts were removed by filtration and, after addition of a small amount of silver oxide, the filtrate was distilled under diminished pressure. The unchanged *cyclo*pentanone having been removed, the fraction distilling at 127–129°/10 mm was collected (14 g, 41 per cent).

Glycerol (10 g), *cyclo*pentanone (20 g) and 95% sulphuric acid (3 g) were kept at room temperature for 24 hr and occasionally shaken. The reaction mixture was made neutral with lead carbonate, filtered and distilled; b.p. 122–123°/16 mm (9·3 g, 54 per cent), n_D^{20} 1·4793, d_4^{18} 1·073 (M.R. found 39·30. $C_8H_{14}O_3$ requires: 39·63. Found: C, 60·50; H, 8·84. $C_8H_{14}O_6$ requires C, 60·75; H, 8·86 per cent).

cyclo*Pentylideneglycerol 3:5-dinitrobenzoate.* 3:5-Dinitrobenzoyl chloride (1·2 g) and *cyclo*pentylideneglycerol (1 g) were dissolved in anhydrous benzene. To the clear solution pyridine (2 ml, dried and distilled over potassium hydroxide) was added. After standing for 1 hr the reaction mixture was diluted with dry ether; pyridine hydrochloride separated and was collected, and the ethereal solution was washed successively with 2% sodium hydroxide, 2% hydrochloric acid and water and then dried and the ether was finally evaporated. The yield was 1·5 g (68 per cent), m.p. 79° after recrystallisation from ethanol (Found:C, 51·18; H, 4·72; N, 8·40. $C_{15}H_{16}O_8N_2$ requires: C, 51·13; H, 4·54; N, 7·95 per cent).

cyclo*Pentylideneglycerol toluene-*p*-sulphonate* (II). Toluene-*p*-sulphonyl chloride (15 g), dissolved in anhydrous pyridine (30 ml), was added to a solution of *cyclo*pentylideneglycerol (10 g) in dry pyridine (10 ml). The reaction mixture was kept in an ice-bath for some time and then at room temperature for 36 hr. The pyridine hydrochloride that separated was dissolved by adding a small quantity of water, and the mixture was poured with stirring into ice-water (150 g). The heavy oil was extracted with chloroform and the chloroform solution was separated, washed, dried and evaporated to a thick syrup, which was triturated with light petroleum. The solid so obtained (7 g, 35 per cent) was collected and crystallised from light petroleum and ethanol, m.p. 38° (Found: S, 10·08; $C_{16}H_{20}O_5S$ requires: S, 10·25 per cent).

cyclo*Pentylideneglycerolmonoiodohydrin* (III). A mixture of compound (II) (3 g) and sodium iodide (3·7 g) was dissolved in anhydrous acetone and heated in a sealed tube at 100° for 12 hr. The sodium toluene-*p*-sulphonate was collected and the acetone was evaporated to leave a reddish brown syrup, which decomposed when subjected to a distillation under diminished pressure.

Compound (II) (9 g) and sodium iodide (11 g) were dissolved in dry acetone and heated on an oil-bath for 20 hr. The yield of sodium toluene-*p*-sulphonate was 4 g

(73 per cent). After evaporation of the acetone, the syrupy residue was treated first with light petroleum to remove compound (II) and then with ether to remove the unchanged sodium iodide. The filtrate yielded on evaporation a syrupy product (6 g, 78 per cent) that contained iodine and did not solidify at temperatures as low as −21°.

Glycerolmonoiodohydrin (IV). An emulsion of compound (III) (6 g) in water (18 ml) and 5 N hydrochloric acid (2 drops) was heated under reflux until a clear solution was obtained. The cold solution was made neutral to litmus and extracted with ether. After evaporation of the ether, an oily product was obtained, which, when triturated with light petroleum, gave a crystalline solid. After recrystallisation from chloroform–light petroleum it had m.p. 48°.[20]

*Di*cyclo*pentylidenepentaerythritol* (V). A mixture of pentaerythritol (3 g), *cyclo*pentanone (11·6 g) and concentrated sulphuric acid (5 drops) was stirred for 3 days. Then potassium hydroxide was added until the reaction mixture was alkaline and the separated product was collected and washed thoroughly with water. The yield was 2·3 g (24 per cent), having after recrystallisation from ethanol m.p. 152° (Found: C, 67·08; H, 9·17. $C_{15}H_{24}O_4$ requires: C, 67·16; H, 8·95 per cent).

*Di*cyclo*hexylidenepentaerythritol.* A mixture of pentaerythritol (6 g) *cyclo*hexanone (25 g) and concentrated sulphuric acid (5 drops) was stirred for 1 day. When all the pentaerythritol had dissolved, the mixture was neutralised and poured into a large volume of water. The solid that separated (10 g, 87 per cent) was collected and recrystallised from ethanol, m.p. 135° (Found: C, 68·96; H, 9·54. $C_{17}H_{28}O_4$ requires: C, 68·91; H, 9·45 per cent).

*Di*cyclo*pentylidene*meso*erythritol*(VI). This was prepared in the same way as the pentaerythritol derivative (V). After being recrystallised from 60% ethanol it had m.p. 64°; yield was 40 per cent (Found: C, 66·16; H, 8·84. $C_{14}H_{22}O_4$ requires: C, 66·14; H, 8·66 per cent).

*Di*cyclo*hexylidene*meso*erythritol.* This was prepared in the same way as the *cyclo*pentylidene derivative (VI). The yield was 87 per cent. After being recrystallised from ethanol m.p. 95 °(Found: 67·86; 9·35. $C_{16}H_{26}O_4$ requires: C, 68·08; H, 9·21 per cent).

*Di*cyclo*pentylidene-*L*-arabitol.* A mixture of arabitol (1·5 g, obtained by the reduction of L-arabinose with Raney nickel[35]), *cyclo*pentanone (7 g) and concentrated sulphuric acid (0·25 ml) was stirred for 1 day at room temperature. The reaction mixture was made neutral and extracted with ether. The etheral solution was washed with water and after evaporation of the ether yielded a syrupy product (0·8 g, 28 per cent), insoluble in water.

cyclo*Pentylidene-*L*-arabitol toluene-*p*-sulphonate.* This was prepared in the same way as compound (II). Yield 32 per cent. Recrystallised from light petroleum, it had m.p. 68° (Found: S, 7·30; $C_{22}H_{33}O_7S$ requires S, 7·30 per cent).

*Tri*cyclo*pentylidene-*D*-mannitol.* Phosphorus pentoxide (5 g) was added to a stirred mixture of mannitol (9 g) and *cyclo*pentanone (50 ml). The reaction mixture was stirred for some hours, and then made neutral and poured into water. The oily product that separated turned into a crystalline mass on standing. The yield was 4·5 g (25 per cent). Recrystallised from ethanol, it had m.p. 70°, $[\alpha]_D^{18}$ +11·27° (*c*, 1·35 in

---

[35] K. Gätzi and T. Reichstein, *Helv. Chim. Acta* **21**, 195 (1938).

chloroform) (Found: C, 66·23; H, 8·35. $C_{21}H_{32}O_6$ requires: C, 66·31; H, 8·42 per cent).

*Tri*cyclo*pentylidene*-D-*sorbitol*. This was prepared in the same way as the mannitol derivative from D-sorbitol (2 g), *cyclo*pentanone (8 ml) and concentrated sulphuric acid. After being recrystallised from ethanol, it had m.p. 75° $[\alpha]_D^{18}$ +7·3° (*c*, 1·09 in ethanol) (Found: C, 66·51; H, 8·67. $C_{21}H_{32}O_6$ requires: C, 66·31; H, 8·42 per cent).

*Di*cyclo*pentylidene*-L-*arabinose*. L-Arabinose (2 g), *cyclo*pentanone (20 g) and concentrated sulphuric acid (15 drops) were stirred for 24 hr. Since only a small amount of the sugar was dissolved, the reaction mixture was filtered (when 1·5 g of arabinose was recovered), and the filtrate was made neutral, and then diluted with water and extracted with ether. After evaporation of the ether a solid product was obtained (0·5 g), 53 per cent. After being recrystallised from 60% ethanol, it had m.p. 62° (Found: C, 64·60; H, 8·12. $C_{15}H_{22}O_5$ requires: C, 63·82; H, 7.80 per cent).

*Di*cyclo*hexylidene*-L-*arabinose*. This was prepared in the same way as the *cyclo*pentylidene derivative from L-arabinose (4 g), *cyclo*hexanone (25 g) and concentrated sulphuric acid (0·7 ml). The yield was 73 per cent; after being recrystallised from 70% ethanol, it had m.p. 86° (Found: C, 65·78; H, 8·35. $C_{17}H_{26}O_5$ requires: C, 65·80; H, 8·38 per cent).

*Di*cyclo*pentylidene*-D-*xylose*. A suspension of D-xylose (1 g), *cyclo*pentanone (20 g) and concentrated sulphuric acid was stirred for 48 hr and then neutralised. The oil thus obtained was dissolved in ethanol and, on adding water, a crystalline solid was precipitated (0·6 g, 31 per cent). Recrystallised from 50% ethanol, it had m.p. 89° (Found: C, 63·45; H, 7·70. $C_{15}H_{22}O_5$ requires: C, 63·82; H, 7·80 per cent).

*Di*cyclo*hexylidene*-D-*xylose*. This was prepared from D-xylose (2 g), *cyclo*hexanone (20 g) and concentrated sulphuric acid (15 drops). The yield was 3 g (72 per cent). After recrystallisation from 80% ethanol it had m.p. 104° (Found: C, 65·88; H, 8·49. $C_{17}H_{26}O_5$ requires: C, 65·80; H, 8·38 per cent).

*Di*cyclo*pentylidene*-D-*mannose* (VII). This was obtained by condensing D-mannose (2 g) with *cyclo*pentanone in the presence of concentrated sulphuric acid. The yield was 1·5 g (44 per cent). After being recrystallised from 40% ethanol, it had m.p. 116°, $[\alpha]_D^{18}$ +8·7° (*c*, 1·04 in alchol) (Found: C, 61·81; H, 7·90. $C_{16}H_{24}O_6$ requires: C, 61·53; H, 7·69 per cent).

*Di*cyclo*hexylidene*-D-*mannose*. This was prepared in the same way as the *cyclo*pentylidene derivative. The yield was 52 per cent, m.p. 122° (Found: C, 63·72; H, 8·00. $C_{18}H_{28}O_6$ requires: C, 63·52; H, 8·23 per cent).

Potassium salt of cyclo*pentylidene*-D-*mannonic acid* (VIII). Potassium permanganate (0·33 g) was added to a suspension of compound (VII) (1 g) in aqueous potassium hydroxide (0·18 g in 10 ml of water). The reaction mixture was stirred and heated for 6 hr, and then filtered, and the filtrate was evaporated under diminished pressure. The potassium salt was treated with acetone to remove the starting material; the product had m.p. 235° (dec.), $[\alpha]_D^{18}$ −23·9° (*c*, 2·55 in water).

*Lactone of di*cyclo*pentylidene*-D-*mannonic acid* (IX). To a solution of compound (VIII) in a small amount of water the equivalent amount of 0·5 N sulphuric acid was added and the resulting solution was extracted with ether. From the ethereal solution, on evaporation, a crystalline solid was obtained, m.p. 129°, $[\alpha]_D^{18}$ +35·98° (*c*, 1·32 in chloroform) (Found: C, 62·03; H, 7·17. $C_{16}H_{22}O_6$ requires: C, 61·93; H, 7·09 per cent).

*Di*cyclo*pentylidene*-D-*glucose*. A mixture of zinc chloride (6 g), phosphorus pentoxide (1 g) and 85% phosphoric acid (2 g) was added to a stirred suspension of D-glucose (5 g) in *cyclo*pentanone (100 ml). The reaction mixture was stirred for 24 hr, and then neutralised with potassium carbonate. The inorganic salts and the unchanged glucose were removed by filtration and washed with ether; the dark brown filtrate was made neutral with some more potassium carbonate. The excess of *cyclo*pentanone was removed by distillation under diminished pressure and the oil thus obtained, when treated with ethanol and light petroleum, turned on standing into a crystalline mass (0·2 g, 2·5 per cent). After being recrystallised from light petroleum and ethanol, it had m.p. 104° (Found: C, 61·72; H, 7·78. $C_{16}H_{24}O_6$ requires: C, 61·53; H, 7·69 per cent).

*Di*cyclo*hexylidene- and mon*cyclo*hexylidene*-D-*glucose* (X). These were prepared according to the procedures given by Hockett *et al.*[34]

1:2-*Mono*cyclo*hexylidene*-xylo*trioxyglutarialdehyde* (XI). To a stirred solution of lead tetra-acetate (13·4 g) in dry benzene, heated under reflux, there was added dropwise mono*cyclo*hexylidene-D-glucose (8 g), dissolved in dry benzene (200 ml). After the addition, the reaction mixture was heated on a water bath for ½ hr, lead acetate being thereby precipitated. The mixture was then filtered and the filtrate was evaporated. The oily residue was triturated with water and the solid so obtained (5 g, 71 per cent) was recrystallised from 50% ethanol, m.p. 178° (Found: C, 58·06; H, 7·23. $C_{11}H_{16}O_5$ requires: C, 57·89; H, 7·01 per cent).

Semicarbazone of compound (XI). Compound (IX) (1 g), dissolved in ethanol (20 ml) was added to a solution of sodium acetate (3 g) and semicarbazide hydrochloride (2 g) in water (16 ml). The reaction mixture was heated under reflux for ½ hr; on cooling, crystals of the semicarbazone separated (1 g, 80 per cent), m.p. 215° (dec.) (Found: C, 50·63; H, 6·92; N, 14·55. $C_{12}H_{19}O_5N_3$ requires: C, 50·52; H, 6·68; N, 14·37 per cent).

*Di*cyclo*pentylidene*-D-*fructose* (XII). A mixture of D-fructose (2 g), *cyclo*pentanone (25 g) and concentrated sulphuric acid (1 ml) was stirred at room temperature for 40 hr. The reaction mixture was neutralised and then poured into water and extracted with ether. On evaporation of the ethereal solution, a syrupy residue was obtained (2 g, 58 per cent).

*Di*cyclo*pentylidene*-D-*fructose toluene*-p-*sulphonate*. This was prepared in the same way as compound (II) from compound (XII) (2 g) and toluene-*p*-sulphonyl chloride (1·5 g). The yield was 1·5 g (50 per cent). After being recrystallised from 50% ethanol, it had m.p. 116° (Found: S, 6·77. $C_{23}H_{30}O_8S$ requires: S, 6·88 per cent).

*Di*cyclo*hexylidene*-D-*fructose*. A mixture of D-fructose (2 g), *cyclo*hexanone (10 g) and concentrated sulphuric acid was stirred at room temperature. After a short period all the starting material had dissolved and the condensation product was separated. The reaction mixture was then made alkaline and poured into water; an oily product separated, and when treated with light petroleum, it formed a crystalline mass (2·3 g, 62 per cent); after recrystallisation from 50% ethanol it had m.p. 142° (Found: C, 63·78; H, 8·27. $C_{18}H_{28}O_6$ requires: C, 63·52; H, 8·23 per cent).

SUMMARY

Polyhydroxy compounds and monosaccharides were found to react with *cyclo*pentanone and *cyclo*hexanone to yield mono-, di- and tri-*cyclo*pentylidene and -*cyclo*hexylidene derivatives, respectively.

1. By condensing *cyclo*pentanone and *cyclo*hexanone with polyhydric alcohols, the following condensation products were obtained: *cyclo*pentylideneglycerol, di*cyclo*pentylidene-pentaerythtritol, -*meso*erythritol and -L-arabitol, tri*cyclo*pentylidene-D-sorbitol and -D-mannitol, as well as di*cyclo*hexylidene-pentaerythritol and -*meso*erythritol.

2. By condensing *cyclo*pentanone and *cyclo*hexanone with monosaccharides, the following compounds were obtained: di*cyclo*pentylidene-D-xylose, -L-arabinose, -D-glucose, -D-mannose and -D-fructose, as well as di*cyclo*hexylidene-D-xylose, -L-arabinose, -D-mannose and -D-fructose.

3. The structure of *cyclo*pentylideneglycerol has been established by conversion into its toluene-*p*-sulphonyl derivative, which, on treatment with sodium iodide in acetone at 100°C yielded the known glycerolmonoiodohydrin.

4. The structure of di*cyclo*pentylidene-D-mannose has been established by converting it into the lactone of di*cyclo*pentylidene-D-mannonic acid.

5. The furanoside structure of di*cyclo*hexylidene-D-glucose has been confirmed by oxidation with lead terra-acetate; the resulting mono*cyclo*hexylidene-D-*xylo*-trihydroxygutardialdehyde was characterised by conversion into its semicarbazone.

6. In the condensation reactions with polyhydroxy compounds *cyclo*pentanone and *cyclo*hexanone behave similarly to acetone—the resulting condensation products having five-membered ring structures.

7. In the course of the condensations *cyclo*hexanone reacted much more readily than *cyclo*pentanone, this fact being consistent with the proposed I-strain hypothesis.

8. Unlike diacetonexylose, *cyclo*pentylidene- and *cyclo*hexylidene-xylose are crystalline solids that can be easily isolated and purified.