363. *Carbohydrate Carbonates. Part II.* Their Preparation by Ester-exchange Methods.*

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1,2:3,4:5,6-Tricarbonates of D-glucitol, galactitol, and D-mannitol have been prepared by the reaction of diphenyl carbonate with the respective hexitols. D-Mannitol 3,4-carbonate was similarly obtained from the 1,2:5,6-di-*O*-isopropylidene derivative by transesterification and subsequent hydrolysis of the acetal groups.

Application of the reaction to methyl 4,6-*O*-benzylidene-α-D-mannopyranoside gave the 2,3-carbonate, whereas methyl α-D-glucopyranoside and methyl α-D-mannopyranoside afforded a polycarbonate derivative and a di(methyl α-D-mannopyranoside) tricarbonate, respectively.

Few examples are known[1] of transesterification between carbohydrates and simple organic carbonates such as diethyl or diphenyl carbonate. Scheuble and Hochstetter[2] in 1911, and several later workers,[3,4] have applied this type of reaction to glycerol, and the crystalline product has been recently identified[5] as di(glycerol 1,2-carbonate) 3,3′-carbonate. Hochstetter also prepared,[6] but did not characterise, carbonates from D-glucose, D-mannitol (I), sucrose, and starch by heating the carbohydrates with diphenyl carbonate in molten pyrocatechol or resorcinol. The product from sucrose has since been shown by Theobald[7] to be a poly(sucrose carbonate), contrasting with the *O*-ethoxycarbonylsucroses formed when diethyl carbonate was employed in the ester-exchange. Use of ethylene carbonate as a carbonate source is complicated by its tendency to function as a hydroxyethylating agent[8] or, as in the case of glycerol,[4] to produce an epoxide; however, the preparation of a starch carbonate by means of this reagent has been claimed by Opie.[9]

The present study has confirmed the value of diphenyl carbonate in synthesising carbonic esters of polyalcohols and of certain carbohydrates, in particular those having no free reducing groups, such as glycosides. A trace of an alkaline catalyst, for example, sodium hydrogen carbonate, is advantageous in all cases and essential in most, whilst the molten dihydric phenols employed as solvents by Hochstetter may be conveniently replaced by *NN*-dimethylformamide or dimethyl sulphoxide.

In addition to the known D-mannitol ester,[6] crystalline, fully substituted carbonates have now been obtained from D-glucitol (sorbitol) and galactitol (dulcitol). These derivatives ($C_9H_8O_9$) were shown by molecular-weight determination to be monomeric and hence were considered to be the symmetrical 1,2:3,4:5,6-tricarbonates each having three five-membered cyclic carbonate groups. It is well known[5,10] that five-membered organic cyclic carbonates show a C=O vibration near 1800 cm.$^{-1}$, whereas acrylic and six-membered cyclic carbonates absorb near 1760 cm.$^{-1}$. The infrared spectra of the D-glucitol

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* Part I, *J.*, 1961, 3178.

[1] Hough, Priddle, and Theobald, *Adv. Carbohydrate Chem.*, 1960, **15**, 91.

[2] Scheuble and Hochstetter, B.P. 19,924/1911; *Chem. Zentr.*, 1912, **83**, II, 1756.

[3] Soc. industrielle Vator, F.P. 779,342/1935; *Chem. Abs.*, 1935, **29**, 5460; Contardi and Ercoli, *Gazzetta*, 1934, **64**, 522.

[4] Bruson and Riener, *J. Amer. Chem. Soc.*, 1952, **74**, 2100.

[5] Hough and Priddle, *J.*, 1961, 581.

[6] Hochstetter, G.P. 268,452/1912; *Friedländer*, 1913, **11**, 1211.

[7] Theobald, *J.*, 1961, 5370.

[8] Monson and Dickson, U.S.P. 2,819,260/1958; *Chem. Abs.*, 1958, **52**, 10166; Carlson, U.S.P. 2,448,767/1948; *Chem. Abs.*, 1949, **43**, 673.

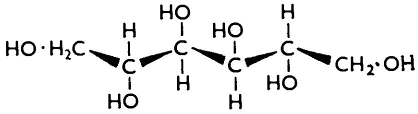
[9] Opie, U.S.P. 2,767,171/1956; *Chem. Abs.*, 1957, **51**, 2237.

[10] Hough, Priddle, Theobald, Barker, Douglas, and Spoors, *Chem. and Ind.*, 1960, 148; Angell, *Trans. Faraday Soc.*, 1956, **52**, 1178; Hales, Jones, and Kynaston, *J.*, 1957, 618; Gatehouse, Livingstone, and Nyholm, *J.*, 1958, 3137; Sarel, Pohoryles, and Ben-Shoshan, *J. Org. Chem.*, 1959, **24**, 1873.

and D-galactitol esters each include maxima at 1810 cm.$^{-1}$, and hence these derivatives are 1,2:3,4:5,6-tricarbonates (II and III). The D-galactitol derivative is optically inactive, as required by the internally compensated structure (III).

In contrast to the above carbonates, D-mannitol tricarbonate showed two C=O maxima, at 1795 and 1830 cm.$^{-1}$, and it was thus necessary to establish its structure chemically. 1,2:5,6-Di-*O*-isopropylidene-D-mannitol (IV) was esterified by the diphenyl carbonate method, and the product (V) was selectively hydrolysed by dilute acid to D-mannitol 3,4-carbonate (VI). Upon treatment with carbonyl chloride in pyridine, the monocarbonate (VI) afforded a tricarbonate, which on steric grounds must be D-mannitol 1,2:3,4:5,6-tricarbonate (VII). The latter was identical with that resulting from the action of diphenyl carbonate upon D-mannitol (I).

It is noteworthy that D-glucitol and D-mannitol (I) can react in their preferred, staggered, zigzag conformations to give tricarbonates (II; VII) with the carbon chain in the *trans*-conformation around C-3 and C-4, whereas D-galactitol must undergo a conformational change to bring the 3- and 4-hydroxyl groups closer together, leading to a strained structure (III).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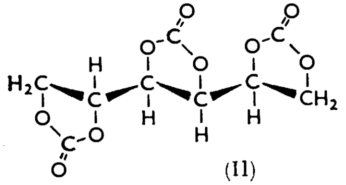
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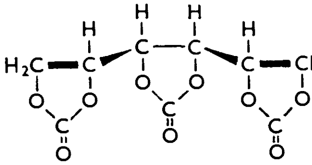
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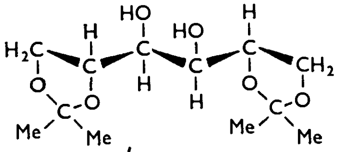
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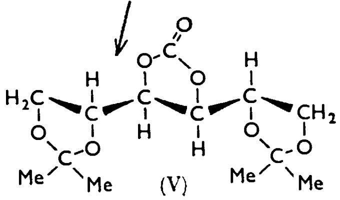
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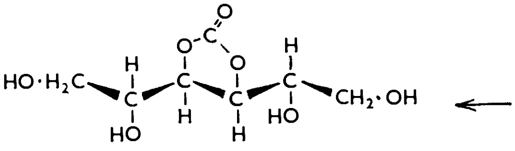
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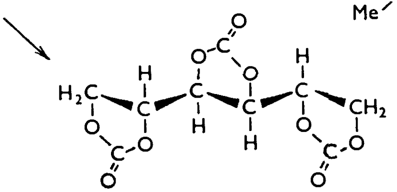
(VII)

Application of the diphenyl carbonate method to methyl 4,6-*O*-benzylidene-α-D-mannopyranoside introduced a 2,3-cyclic carbonate group, the product being identical with that obtained by reaction with carbonyl chloride.[11] However, where no possibility of normal cyclic carbonate formation exists, owing to the absence of *cis*-adjacent hydroxyl groups,[1] an intermolecular or polymeric carbonate may result. Thus methyl α-D-glucopyranoside, like sucrose,[7] yielded a polycarbonate bearing some *O*-phenoxycarbonyl substituents. On the other hand, infrared examination of a crystalline carbonate obtained from methyl α-D-mannopyranoside revealed absorption maxima at both 1820 and 1755

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[11] Hough and Priddle, *Chem. and Ind.*, 1959, 1600; and Part I.

cm.$^{-1}$, the former being the more intense. This derivative must be regarded as a di(methyl α-D-mannopyranoside) tricarbonate, containing two cyclic groups and one intermolecular (probably 6,6′) group, and structurally analogous to di(glycerol 1,2-carbonate) 3,3′-carbonate.[5] Cyclic carbonate formation, where possible, appears to take precedence over the synthesis of further intermolecular linkages.

The transesterification process using diphenyl carbonate probably occurs in two stages, involving an *O*-phenoxycarbonyl derivative as intermediate.[7] Thus a sample of authentic *O*-phenoxycarbonylsucrose (average degree of substitution, 3·4), prepared by the action of phenyl chloroformate upon sucrose in pyridine, gelled to a poly(sucrose carbonate) when heated in dimethyl sulphoxide containing a trace of an alkaline catalyst.

The application of the diphenyl carbonate method to reducing sugars is now being studied.

EXPERIMENTAL

M. p.s of the carbonates were determined in sealed Pyrex capillaries to minimise the variation of m. p. with rate of heating.

D-*Glucitol* 1,2:3,4:5,6-*Tricarbonate* (II).—D-Glucitol (7 g.) and diphenyl carbonate (26 g.) were stirred in *NN*-dimethylformamide (20 ml.; dried over $CaSO_4$) containing sodium hydrogen carbonate (0·02 g.) for 40 min. at 110°. The dark syrup precipitated by pouring the mixture into ether (500 ml.) was washed with more ether by decantation, and was then scratched under water (250 ml.) until granular. The light brown solid was collected and washed successively with water, ethanol, and ether, yielding 7·2 g. of crude ester. After two recrystallisations from glacial acetic acid (*ca.* 400 ml.) D-*glucitol* 1,2:3,4:5,6-*tricarbonate* (5·4 g., 54%) melted at 207—208° (decomp.). The pure compound separated from acetic acid in needles, m. p. 208—209° (decomp.), $[\alpha]_D^{20}$ +82·0° (*c* 2·0 in $COMe_2$), $\nu_{max.}$ (C=O stretching) 1810 cm.$^{-1}$ [Found: C, 41·7; H, 2·9%; *M*, 257 (v. p. in $COMe_2$). $C_9H_8O_9$ requires C, 41·5; H, 3·1%; *M*, 260].

Galactitol 1,2:3,4:5,6-*Tricarbonate* (III).—Galactitol (7 g.), diphenyl carbonate (26 g.), sodium hydrogen carbonate (0·02 g.), and *NN*-dimethylformamide (40 ml.) were heated together at 135° for ½ hr. The crude ester (6 g.), isolated similarly to D-glucitol tricarbonate, was recrystallised from aqueous acetone, yielding *galactitol* 1,2:3,4:5,6-*tricarbonate* (3·4 g., 34%), m. p. 234—236° (decomp.). Further crystallisations afforded cubes, m. p. 238—239° (decomp.), $[\alpha]_D^{20}$ 0° (*c* 5·0 in $H{\cdot}CO{\cdot}NMe_2$), $\nu_{max.}$ (C=O stretching) 1810 cm.$^{-1}$ [Found: C, 41·7; H, 2·9%; *M*, 263 (v. p. in $COMe_2$)].

1,2:5,6-*Di-O-isopropylidene-*D-*mannitol* 3,4-*Carbonate* (V).—1,2:5,6-Di-*O*-isopropylidene-D-mannitol[12] (IV) (5 g.) in *NN*-dimethylformamide (20 ml.) was heated at 125° for 45 min. with diphenyl carbonate (6·15 g.) and sodium hydrogen carbonate (0·04 g.). The mixture was poured into water (250 ml.), and the precipitate filtered off and extracted with light petroleum (b. p. 60—80°) (200 ml.). Recrystallised from aqueous acetone, 1,2:5,6-*di-*O*-isopropylidene-*D-*mannitol* 3,4-*carbonate* (5 g.) had m. p. 146·5—147°, $[\alpha]_D^{20}$ +14·9° (*c* 1·8 in $COMe_2$) and $\nu_{max.}$ (C=O stretching) 1790 cm.$^{-1}$ (Found: C, 54·4; H, 7·15. $C_{13}H_{20}O_7$ requires C, 54·1; H, 6·95%).

D-*Mannitol* 3,4-*Carbonate* (VI).—The preceding 3,4-carbonate (5·8 g.) was dissolved in acetone (40 ml.), and N-hydrochloric acid (10 ml.) was added. The mixture was left overnight at room temperature and then neutralized with silver carbonate. After filtration and evaporation the residue was extracted with ether (2 × 25 ml.) to remove unchanged 1,2:5,6-di-*O*-isopropylidene-D-mannitol 3,4-carbonate. The product (2·5 g.), D-*mannitol* 3,4-*carbonate*, was dissolved in ethanol (charcoal) and recrystallised from ethanol–light petroleum. It had m. p. 138—139°, $[\alpha]_D^{20}$ +26·9° (*c* 1·6 in $COMe_2$) and $\nu_{max.}$ (C=O stretching) 1790 cm.$^{-1}$ (Found: C, 40·6; H, 5·7. $C_7H_{12}O_7$ requires C, 40·4; H, 5·8%).

D-*Mannitol* 1,2:3,4:5,6-*Tricarbonate* (VII).—(*a*) A solution of D-mannitol 3,4-carbonate (1 g.) in dry pyridine (50 ml.) was treated at 0° (stirring) with dry gaseous carbonyl chloride until an almost solid white mass was obtained. This was left for 1 hr. at 0°, then decomposed with ice (*ca.* 500 g.) to give a clear yellowish solution. An excess of powdered barium carbonate was added, and the mixture was extracted with ethyl acetate (2 × 500 ml.). Evaporation of the dried ($CaSO_4$) extract afforded a crystalline residue, which was treated with ethanol (50 ml.), collected, and washed successively with ether and water. The dried product (0·99 g.) recrystallised from glacial acetic acid (100 ml.) in needles, m. p. 222—223° (0·84 g.), and the

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[12] Baer and Fischer, *J. Amer. Chem. Soc.*, 1939, **61**, 761.

purified D-*mannitol* 1,2:3,4:5,6-*tricarbonate* had m. p. 233—234° (decomp.) alone and mixed with the product from D-mannitol (below), $[\alpha]_D^{25}$ +31·9° (*c* 2·1 in $COMe_2$), and $\nu_{max.}$ (C=O) 1795 and 1830 cm.$^{-1}$ (Found: C, 41·3; H, 2·9. $C_9H_8O_9$ requires C, 41·5; H, 3·1%).

(*b*) D-Mannitol (7 g.), diphenyl carbonate (26 g.), and sodium hydrogen carbonate (0·02 g.) were stirred together in *NN*-dimethylformamide (20 ml.) at 130—140°. Crystalline material separated from the hot mixture, and after ½ hr. the product was isolated and purified similarly to D-glucitol 1,2:3,4:5,6-tricarbonate. The *tricarbonate* (6·8 g., 68%) had m. p. 235—236° (decomp.), $[\alpha]_D^{25}$ +32·4° (*c* 2·25 in $COMe_2$) and $\nu_{max.}$ (C=O) 1795 and 1830 cm.$^{-1}$ [Found: C, 41·5; H, 3·35%; *M*, 255 (v. p. in $COMe_2$)].

Poly(*methyl* α-D-*Glucopyranoside Carbonate*).—A solution of methyl α-D-glucopyranoside (7 g.) in *NN*-dimethylformamide (20 ml.) was stirred at 135° with diphenyl carbonate (11·6 g., 1·5 mol.) and sodium hydrogen carbonate (0·02 g.). After 17 min. the mixture suddenly gelled. The cooled product was macerated with ether (250 ml.), collected, and washed with more ether. The air-dried solid was triturated with water, collected, washed with ethanol and ether, and then continuously extracted (Soxhlet) over boiling aqueous dioxan (1 : 1 v/v) for 6 hr. The *polymer* was dried *in vacuo* at 80° [yield 7·49 g.; $\nu_{max.}$ (C=O stretching) 1765 cm.$^{-1}$] (Found: C, 44·7; H, 5·3; OMe, 16·3; phenol, estimated as 2,4,6-tribromophenol after alkaline hydrolysis,[7] 1·4%, equiv. to *ca.* 0·03 *O*-phenoxycarbonyl group per glucoside unit).

Methyl 4,6-O-*Benzylidene*-α-D-*mannopyranoside* 2,3-*Carbonate*.—Methyl 4,6-*O*-benzylidene-α-D-mannopyranoside[13] (1 g.) was dissolved in *NN*-dimethylformamide (5 ml.), and a mixture of diphenyl carbonate (1 g.) and sodium hydrogen carbonate (0·01 g.) was added. The solution was kept at 110—115° for 45 min., then poured into water (250 ml.). The crystalline precipitate was dried and then extracted with light petroleum (b. p. 60—80°) to remove the excess of diphenyl carbonate. Recrystallised from aqueous acetone methyl 4,6-*O*-benzylidene-α-D-mannopyranoside 2,3-carbonate[11] (0·8 g.) had m. p. 125·5—126°, $[\alpha]_D$ −20·9° (*c* 1·3 in $CHCl_3$) and $\nu_{max.}$ (C=O stretching) 1800 cm.$^{-1}$ (Found: C, 58·6; H, 5·1; OMe, 10·4. Calc. for $C_{15}H_{16}O_7$: C, 58·4; H, 5·2; OMe, 10·1%).

Di(*methyl* α-D-*Mannopyranoside*) *Tricarbonate*.—Methyl α-D-mannopyranoside (7 g.) and sodium hydrogen carbonate (0·02 g.) were dissolved in *NN*-dimethylformamide (20 ml.) at 125°. Diphenyl carbonate (15·5 g.) was added and the mixture kept at 125—135° for 2 hr., then poured into ether (250 ml.). The precipitate was filtered off and washed successively with water, ethanol, and ether (yield 5·7 g.). Recrystallised from acetone–ethanol it afforded *di*(*methyl* α-D-*mannopyranoside*) *tricarbonate*, m. p. 153—155°, $[\alpha]_D$ +36·4° (*c* 1·28 in $COMe_2$), $\nu_{max.}$ (OH) 3550, (C=O) 1755 and 1820 cm.$^{-1}$ (Found: C, 44·0; H, 4·8; OMe, 12·1. $C_{17}H_{22}O_{15}$ requires C, 43·8; H, 4·7; OMe, 13·3%).

Phenyl Chloroformate.—Crosby and Niemann's method[14] gave a product contaminated with phenol, which was not wholly removed by fractional distillation. The ester, b. p. 71—73°/12 mm., was conveniently prepared in 62% yield by the general technique for aryl chloroformates described by Raiford and Inman.[15] The colourless mobile liquid possessed a pungent odour and showed no tendency to crystallise (cf. Crosby and Niemann[14]).

O-*Phenoxycarbonylsucrose*.—A stirred solution of sucrose (5 g.) in warm, dry pyridine (100 ml.) was cooled in ice and treated dropwise (in 15 min.) with phenyl chloroformate (11·5 g., 5 mol.). Stirring was continued at room temperature for 4 hr., the whitish solid initially present slowly dispersing and a small amount of crystalline matter separating. The mixture was left overnight, most of the pyridine was removed *in vacuo* below 40°, and the resulting thick crystalline suspension was treated with water (250 ml.). Extraction of the sticky solid with chloroform (250 ml.), followed by washing of the extract with 0·5N-hydrochloric acid (2 × 200 ml.) and water (4 × 200 ml.), drying ($CaSO_4$), and evaporation, gave 14·5 g. of colourless syrup, $\nu_{max.}$ (C=O) 1765 cm.$^{-1}$ (Found: C, 59·45; H, 4·45; phenol, by estimation as above,[7] 42·2%, equiv. to *ca.* 3·4 *O*-phenoxycarbonyl groups per sucrose unit).

Poly(*sucrose Carbonate*) *from* O-*Phenoxycarbonylsucrose*.—The *O*-phenoxycarbonyl derivative (2·0 g.) was stirred in dimethyl sulphoxide (20 ml.) containing sodium hydrogen carbonate (0·02 g.) at 100°. The solution suddenly gelled after 20 min., a period comparable to that required (17 min.) for the gelling of a mixture of sucrose and diphenyl carbonate (4 mol.) in catalysed dimethyl sulphoxide.[7] The polymer was isolated and purified as previously described

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[13] Schwarz, unpublished method.

[14] Crosby and Niemann, *J. Amer. Chem. Soc.*, 1954, **76**, 4458.

[15] Raiford and Inman, *J. Amer. Chem. Soc.*, 1934, **56**, 1586.

(yield, 0·95 g). It was identical in its infrared spectrum with that obtained by the diphenyl carbonate method [7] (Found: C, 44·0; H, 4·25; phenol 9·7%, equiv. to *ca.* 0·3 *O*-phenoxycarbonyl group per sucrose unit).

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