1056. *Carbonic Esters of Sucrose. Part I. The Preparation of*
O-Alkyloxycarbonylsucroses.

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Sucrose reacts with alkyl chloroformates at 0° in the presence of aqueous alkali, yielding incompletely substituted O-alkyloxycarbonyl derivatives. Partial separation of the mixed esters is achieved by chromatography on papers impregnated with dimethyl sulphoxide as the stationary phase. Crystalline octa-O-ethoxycarbonylsucrose has been prepared by further acylation in pyridine. The more highly substituted O-alkyloxycarbonyl-sucroses show unusual stability to acid. An approximately trisubstituted O-ethoxycarbonylsucrose polymerises when heated.

THE " bridging " of the two hexose residues of sucrose (I), an acid-labile disaccharide, with bivalent atoms or small radicals, as for example methylenedioxy and carbonate, was attempted in order to retain the two monosaccharides in combination with one another after hydrolysis of the hemiacetal linkage. By this means it was hoped to prepare new long-chain polyhydric alcohols bearing two reducing groups. Only one example of a bridged sucrose derivative is known, the 1′,2:3,6:3′,6′-trianhydro-compound obtained by Lemieux and Barrette.[1]

The use of methylene sulphate to prepare cyclic methylene ethers of *ortho*-dihydric phenols and glycols has been reported,[2] but under the alkaline reaction conditions required for sucrose this reagent was without effect upon the carbohydrate. With molecular models, strainless carbonate bridges may be constructed between, for example, positions

[1] Lemieux and Barrette, *Canad. J. Chem.*, 1959, **37**, 1964.
[2] Baker, *J.*, 1931, 1765.

6,6'; 6,1'; 2,6'; and 2,1' of sucrose. Whilst no evidence of such bridging has been obtained experimentally, the properties of the carbonic esters prepared in the investigation have proved of interest.
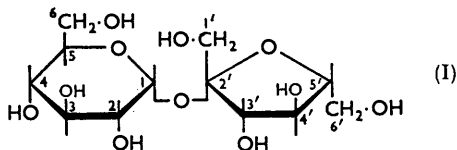
Hochstetter[3] in 1912 obtained an amorphous uncharacterised " carbonate " by the action of diphenyl carbonate on sucrose in molten resorcinol at 130°. Allpress and Haworth,[4] treating sucrose in pyridine at 0° with methyl chloroformate, synthesised a " hepta- or octa- " O-methoxycarbonyl derivative in low yield. Their glassy product corresponds more closely in analysis to a hexasubstituted ester, but was probably not homogeneous. The addition-polymerisation of octa-O-allyloxycarbonylsucrose was examined by Zief[5] in 1950.

Although Allpress and Haworth[4] appear to have originated the use of aqueous alkali as an acid-acceptor in chloroformate reactions upon carbohydrates, they did not apply this method to sucrose. It has now been found that high yields of O-alkyloxycarbonyl-sucroses result from the slow addition of 2N-sodium hydroxide to a well-stirred mixture of concentrated aqueous sucrose with an alkyl chloroformate at 0°. The precipitated syrups comprise esters at various stages of substitution and also isomers of the same degree of substitution (D.S.). An indication of the complexity of the mixtures was afforded by paper chromatography with an organic two-phase solvent system, a technique employed by Wickberg[6] for the separation of sugar acetates: the choice of a polar solvent for the stationary phase may be critical for a particular ester mixture; an O-methoxycarbonyl-sucrose (D.S. 6·8) appeared to consist of only three components when subjected to chromatography on a dimethyl sulphoxide-treated paper, but was separated into at least eight components when formamide was used. Whilst the preparative separation of individual O-alkyloxycarbonylsucroses has not yet been attempted, a partial solvent-fractionation is possible in some cases, and such fractions are suitable for many purposes (see below).

The introduction of five-membered cyclic carbonate groups into sucrose is theoretically impossible owing to the lack of *cis*-adjacent hydroxyl groups,[7] and their absence in these esters was confirmed by the single C=O stretching maximum, in the range 1754—1760 cm.$^{-1}$, observed in the infrared absorption spectra.[8] Comparison of the methoxyl value (micro-Zeisel) of an O-methoxycarbonylsucrose with the total carbonate content, estimated after alkaline hydrolysis, indicated that only O-methoxycarbonyl groups were present. The average degrees of substitution of various O-alkyloxycarbonylsucroses, prepared by using 10 mol. each of alkyl chloroformate and sodium hydroxide per mol. of sucrose, are listed in the Table. A difunctional chloroformic ester can lead to polymer formation. Thus, from sucrose, ethylene dichloroformate, and sodium hydroxide was obtained about 30% of an amorphous insoluble polycarbonate.

Except in the case of benzyl chloroformate, complete (octa)substitution of sucrose was not achieved by the chloroformic ester–aqueous alkali method, even with a large molar excess of reagents: 50 mol. each of methyl chloroformate and sodium hydroxide introduced only an average of 6·8 ester groups. This resistance is probably connected with

[3] Hochstetter, G.P. 268,452/1912 (*Friedländer*, 1913, **11**, 1211).
[4] Allpress and Haworth, *J.*, 1924, **125**, 1223.
[5] Zief, *J. Amer. Chem. Soc.*, 1950, **72**, 1137.
[6] Wickberg, *Acta Chem. Scand.*, 1958, **12**, 615.
[7] Hough, Priddle, and Theobald, *Adv. Carbohydrate Chem.*, 1960, **15**, 101.
[8] Hough, Priddle, Theobald, Barker, Douglas, and Spoors, *Chem. and Ind.*, 1960, 148.

the alkali-lability of the O-alkyloxycarbonyl group.[4] A crystalline octa-O-ethoxycarbonyl-sucrose was, however, readily prepared by treating the partly esterified derivative (D.S. 5·7) with an excess of ethyl chloroformate in pyridine, further evidence that no carbonate bridges were present in the starting material.

O-Alkyloxycarbonylsucroses, $C_{12}H_{22-n}O_{11}(CO\cdot OR)_n$.

R	Yield (%) (based on sucrose)	Found (%)			n (calc. from % OR) [c]	$[\alpha]_D^{25}$ (c in EtOH)	$\nu_{max.}$ (cm.$^{-1}$) (C=O stretching) [b]
		C	H	OR			
Me	76	41·5	5·4	24·1	4·9	+50·6° (4·34)	1760
Et	86	45·9	6·3	31·9	4·9	+43·6 (5·55)	1760
Pr	87	49·4	7·0	38·1	5·0	+37·3 (3·84)	1755
Pr^i	90	50·2	7·0	39·5	6·0	+37·5 (1·68)	1754
Bu	92	53·2	7·5	43·3	5·0	+33·3 (6·04)	1760
Bu^i	89	53·7	7·4	45·1	5·5	+29·5 (5·51)	—
Bu^s	70	53·9	7·0	46·5	6·0	+31·5 (4·52)	1754
CH$_2$Ph	79	64·9	4·7	—	8·0 [a]	+21·2 (2·04 [d])	1760

[a] Calc. from C,H values.   [b] Determined on Unicam S.P. 100 double-beam infrared spectrometer with a rock-salt prism; evaporated film, (CHCl$_3$).   [c] Variation of C,H with n is small, especially for lower members.   [d] In CHCl$_3$.

The O-alkyloxycarbonylsucroses listed in the Table were colourless syrups at room temperature, increasing slightly in mobility with increasing size of the alkyl group.   Although only sparingly soluble in water, they dissolved in most common organic solvents except light petroleum.   As with organic carbonates in general, alkaline hydrolysis
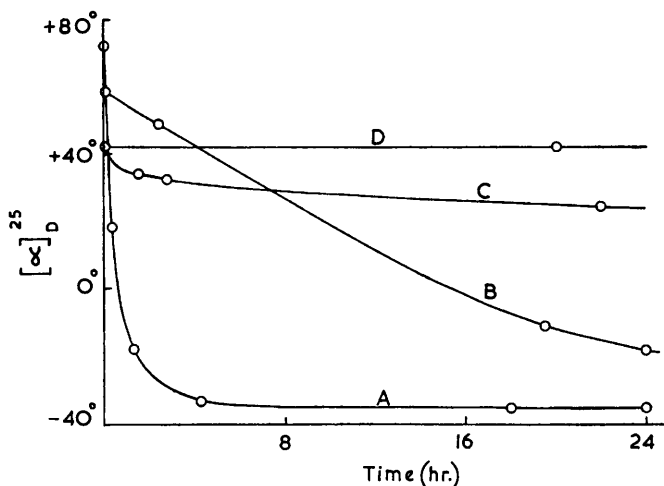
Hydrolysis of sucrose and its esters in N-aqueous-alcoholic hydrochloric acid.

(A) Sucrose.   (B) Sucrose octa-acetate.   (C) O-Ethoxycarbonylsucrose (D.S. 3·1).
(D) O-Ethoxycarbonylsucrose (D.S. 4·9).

occurred easily.   Aqueous-alcoholic barium hydroxide rapidly yielded a precipitate of barium carbonate, and sucrose was detected in the solution.

On the other hand, like the simple dialkyl carbonates, which undergo no measurable hydrolysis in 0·2N-acid at 35°,[9] the O-alkyloxycarbonyl derivatives of carbohydrates are more stable to acid than are many other carbohydrate esters and acetals.[10]   Further, in the case of sucrose, the extreme acid-sensitivity of the glycoside link itself is considerably modified by even a low degree of substitution with O-alkyloxycarbonyl groups, presumably by steric inhibition.[11]   A tri-O-ethoxycarbonylsucrose, being only slowly de-esterified

[9] Palomaa, Salmi, and Suoja, *Ber.*, 1939, **72**, 313.
[10] Ref. 7, p. 146.
[11] Shafizadeh, *Adv. Carbohydrate Chem.*, 1958, **13**, 24.

by acid, possesses higher glycosidic stability than sucrose octa-acetate (see Figure). The use of optical rotatory power to measure the extent of glycosidic hydrolysis is not completely valid in view of the possibility that the fructofuranose ⟶ fructopyranose conversion, which is mainly responsible for the large optical change (" inversion ") attending the hydrolysis of sucrose, may be blocked in some isomeric components by substitution at position 6'. However, the very slow development of reducing power during the acid hydrolysis of more highly substituted derivatives (average D.S. 5—8) supports the view that slight glycosidic fission rather than inhibited configurational change is responsible for the polarimetric observations. The O-methoxycarbonyl derivative prepared by Allpress and Haworth " displayed unexpected stability towards 1 per cent hydrochloric acid at 100° " and caused only slight reduction of Fehling's solution after 1 hour's boiling in 5% hydrochloric acid.[4] Octa-O-ethoxycarbonylsucrose was not immediately hydrolysed by concentrated sulphuric acid.

When a reaction mixture containing O-ethoxycarbonylsucroses for which only 5 mol. of reagents had been used was shaken with ether, not all the syrupy ester dissolved and three layers were obtained. The ether-insoluble derivative (average D.S. 3·3) polymerised at 150° *in vacuo*; it frothed vigorously and set rapidly to a horny mass, insoluble in all common organic solvents. The choice of this sample for a pyrolysis study was fortunate, since it later emerged that owing to its method of isolation it contained a trace of alkaline impurity which catalysed polymerisation and it was of such a degree of substitution as to possess a very short setting-time. These factors will be discussed in greater detail in Part II.[12]

EXPERIMENTAL

Analyses are by the Scandinavian Microanalytical Laboratory, Copenhagen, and by University of Bristol analysts.

General Method for the Preparation of O-Alkyloxycarbonylsucroses.—The chloroformic ester (10 mol. per mol. of sucrose) and water (100 ml.) were stirred vigorously together, and any slight acidity of the aqueous phase was neutralised with solid sodium hydrogen carbonate. Sucrose (50 g.) was added and allowed to dissolve before the reaction flask was cooled to about −5°. Dropwise addition of 2N-sodium hydroxide (730 ml.) was then begun, the internal temperature being kept at 0° ± 2°. The syrupy derivatives were precipitated almost immediately, and after the alkali addition was complete (3 hr.) stirring was continued overnight, the mixture being left gradually to attain room temperature.

The esters were extracted with ether (2 × 500 ml.), except that for the O-methoxycarbonyl derivative chloroform was used, and the extracts were washed with water (2 × 500 ml.) and dried (CaSO₄). After being recovered by evaporation, the syrups were freed from traces of chloroformic esters by heating *in vacuo* at temperatures appropriate to the volatility of the reagent (*e.g.*, methyl, 80°/12 mm.; benzyl, 135°/5 × 10⁻⁴ mm.). The O-alkyloxycarbonyl-sucroses thus prepared were sparingly soluble in water or light petroleum, but dissolved readily in acetone, chloroform, and ethyl acetate. All except the O-benzyloxycarbonyl derivative were also soluble in methanol and ethanol, whilst all except the O-methoxycarbonyl esters dissolved in ether and benzene. The viscosity of the products decreased from the O-methoxy-carbonylsucroses, a brittle glass at room temperature, to the O-butyloxycarbonyl esters, fairly mobile syrups. None reduced Fehling's solution.

Paper Chromatography of O-Alkyloxycarbonylsucroses.—Owing to their high mobility on untreated paper, the O-alkyloxycarbonylsucroses could not be separated by normal chromatographic techniques. Paper chromatography of the O-ethoxycarbonyl derivatives was carried out on Whatman No. 1 paper impregnated [6] with dimethyl sulphoxide, with a mobile phase of benzene–light petroleum (b. p. 60—80°; 4 : 1 v/v). Migration with light petroleum alone was negligible. After development for 3—4 hr. the papers were dried at 100° and sprayed with 2% w/v of potassium hydroxide in methanol, followed, after 5 min., by *p*-anisidine hydrochloride reagent [13] containing 5% v/v of concentrated hydrochloric acid. Careful heating revealed at least 5 components as brown spots. An O-methoxycarbonylsucrose (D.S. 6·8)

[12] Part II, following paper.
[13] Hough, Jones, and Wadman, *J.*, 1950, 1702.

provided only 3 spots by this technique, but showed at least 8 components when formamide was used as the stationary phase.[6] Separation of the O-ethoxycarbonyl derivatives was inferior when formamide or NN-dimethylformamide was used. The O-benzyloxycarbonyl ester (D.S. 8·0) appeared to be homogeneous. Owing to the difficulty of achieving reproducible impregnation of the paper with stationary phase, R_F values are not recorded.

The Reaction of Ethylene Dichloroformate with Sucrose.—The dichloroformate [14] (27·4 g.), chloroform (100 ml.), and water (20 ml.) were stirred together vigorously and treated with a small amount of sodium hydrogen carbonate to neutralise slight acidity. Sucrose (10 g.) was added, and the chilled (ice–salt) stirred mixture treated dropwise during 2 hr. with 2N-aqueous sodium hydroxide (146 ml.), the temperature being kept at $0° \pm 2°$. A white flocculent polymer began to separate after 1 hr., increasing in amount during overnight stirring. Centrifugation of the thick suspension caused the polymer to accumulate between the chloroform and the aqueous phase. The liquids were decanted and the white product was freed from inorganic chloride by repeated centrifugation with water. Finally it was centrifuged twice with absolute ethanol, washed with ether, and collected by filtration. After drying *in vacuo* at 60°, the polymer (4·2 g., 31·2%) was insoluble in all common organic solvents including pyridine, NN-dimethylformamide and dimethyl sulphoxide. It shrunk slightly at about 270°, darkened, and decomposed without melting at 290—300°. Hydrolysis of the suspended polymer with 0·2N-barium hydroxide at room temperature, followed by neutralisation with carbon dioxide, filtration, and paper chromatography revealed sucrose as the sole carbohydrate constituent [Found: C, 41·6; H, 4·9; Ash, 0. $(C_{16}H_{24}O_{15})_n$ requires C, 42·1; H, 5·3%. $(C_{20}H_{27}O_{19})_n$ requires C, 42·1; H, 4·7%].

Estimation of Total Hydrolysable Carbonate Group in O-Methoxycarbonylsucrose.—An aliquot portion (10 ml.) of an approximately 2% w/v (accurately known) methanolic solution of vacuum-dried O-methoxycarbonylsucrose (OMe, 25·9%; D.S. 5·7) was transferred carefully to 0·125N-sodium hydroxide (50 ml.) in a covered beaker and heated for 5 min. on a boiling water-bath to complete the hydrolysis of ester groups. The solution was diluted with distilled water (50 ml.), gently stirred, and cooled to below 5°. It was then titrated slowly against 0·1N-sulphuric acid, with mixed Thymol Blue–Cresol Red as indicator [15] (4 drops), the tip of the burette being just covered by liquid. The end-point was taken as the first appearance of orange after the disappearance of blue, and the titration was repeated with a further aliquot part of the methanolic solution.

A blank titration was carried out similarly on the above sodium hydroxide solution (50 ml.), diluted with water (50 ml.) and methanol (10 ml.), and cooled to below 5°. Calculation of the inorganic carbonate formed by hydrolysis followed in the usual way [16] from the difference between the blank and the ester titres. The whole determination was repeated with fresh solutions of alkali and sucrose derivative (Found : CO_2, 37·45%; CO_2 : OMe, 1·44. Calc. for CO_2Me group: CO_2 : OMe, 1·42).

Octa-O-ethoxycarbonylsucrose.—The partly esterified derivative (12·9 g.; D.S. 5·7), obtained by the aqueous alkali method, was dissolved in pyridine (50 ml.; KOH-dried) and the solution was cooled in ice–salt and treated cautiously (shaking) with ethyl chloroformate (32 ml.). Much fuming occurred but the temperature was easily kept below 0°. The mixture was then refrigerated, with occasional shaking, for 40 hr., then poured into water (2 l.), and the precipitated syrup was extracted with ether (1 l.). The extract was shaken repeatedly with N-hydrochloric acid until no further colour was removed, washed with water, dried ($CaSO_4$), decolorised with charcoal, and evaporated. The resulting syrup was further decolorised by shaking its solution in acetone with activated alumina. Final evaporation yielded 15·3 g. (97%) of very pale yellow syrup (Found: OEt, 38·8%; average D.S. 7·9). The product showed no OH absorption at 3530 cm.$^{-1}$, and crystallised, during several months, to colourless rosettes, m. p. 70—73°. Recrystallisation from ether–light petroleum (b. p. 40—60°) afforded *octa-O-ethoxycarbonylsucrose* in needles, m. p. 79—80°, $\nu_{max.}$ (C=O stretching) 1760 cm.$^{-1}$, $[\alpha]_D^{25}$ +43·8° (*c* 0·913 in EtOH) (Found: C, 47·0; H, 5·9; OEt, 39·9. $C_{36}H_{54}O_{27}$ requires C, 47·1; H, 5·9; OEt, 39·2%). In methanol solution at 20° the derivative gave an almost instantaneous precipitate with an excess of aqueous-methanolic barium hydroxide. Neutralisation of the

[14] Strain, U.S.P. 2,397,630 (*Chem. Abs.*, 1946, **40**, 3769).
[15] Simpson, *Ind. Eng. Chem.*, 1924, **16**, 709.
[16] Vogel, " A Textbook of Quantitative Inorganic Analysis," Longmans Green, London, 2nd edn., 1951, p. 242.

excess of alkali with carbon dioxide, followed by filtration and paper chromatography (butan-1-ol–pyridine–water, 10 : 3 : 3 v/v), indicated the presence of sucrose.

Acid Hydrolysis of Sucrose Esters.—The optical rotations of solutions of (*a*) sucrose (0·5% w/v in methanol), (*b*) sucrose octa-acetate (1% w/v in methanol), (*c*) *O*-ethoxycarbonylsucrose (D.S. 3·1; 9·05% w/v in ethanol) and (*d*) *O*-ethoxycarbonylsucrose (D.S. 4·9; 1·11% w/v in ethanol) were determined at 25°. Aliquot portions (9 ml.) were then mixed with concentrated hydrochloric acid (1 ml.), the solutions kept at 25°, and their optical rotations measured at intervals.

The hydrolysis of (*c*) was also followed chromatographically [Solvent: butan-1-ol–pyridine–water (10 : 3 : 3 v/v). Sprays: as above]. Components were attacked in the order of increasing R_F value. Sucrose disappeared in 1—2 hr., esters with R_F 0·34 (? mono-*O*-ethoxycarbonyl derivatives) in 24 hr. Ester(s) with R_F 0·63 (? di-*O*-ethoxycarbonyl derivatives) were hydrolysed in 24 hr. to substances with R_F 0·56 (pink with spray; ? mono-*O*-ethoxycarbonylglucoses) and R_F 0·62 (yellow with spray; ? mono-*O*-ethoxycarbonylfructoses). No further change was then detected on paper chromatograms.

After 24 hr. the acid solutions of sucrose and its octa-acetate reduced Fehling's solution strongly. Treatment of solution (*b*) with barium hydroxide, followed by paper chromatography in the usual way showed that glycosidic hydrolysis was complete. Only very slight reduction of Fehling's solution was exhibited by (*c*) after 24 hr., and the more highly substituted ester (*d*) was non-reducing. All the esters in the Table were non-reducing after 3 hr. at 20° in 5N-aqueous-alcoholic hydrochloric acid and showed unchanged optical rotations after 48 hr. in N-acid.

Powdered octa-*O*-ethoxycarbonylsucrose (0·85 g.) was dissolved in concentrated sulphuric acid (10 ml.) at room temperature by stirring, and after 5 min. the colourless solution was poured into cold water (200 ml.). The resulting oily suspension was saturated with sodium chloride and extracted with chloroform (2 × 250 ml.), and the extract was washed with saturated sodium hydrogen carbonate and dried (CaSO₄). Evaporation gave 0·52 g. of pale yellow syrup (Found: OEt, 35·5%, equiv. to D.S. 6·2). Although the syrup strongly reduced Benedict's reagent, alkaline hydrolysis, followed by paper chromatography, showed sucrose esters to be present.

Partial Solvent Fractionation of O-Ethoxycarbonylsucrose.—Sucrose (50 g.) was caused to react with ethyl chloroformate (70 ml., 5 mol. per mol. of sucrose) and 2N-sodium hydroxide (365 ml., 5 mol.) at 0° ± 2° by the general method described above. A product began to separate early in the addition. After being stirred overnight, the total mixture was shaken vigorously with ether (500 ml.) and allowed to separate into three layers.

The syrupy lowest layer was run off and dried by repeated evaporation with benzene under reduced pressure, the final benzene solution being filtered. The clear colourless gum (40 g.) was dried at 60° *in vacuo* (Found: C, 46·1; H, 6·1; OEt, 25·3%, equiv. to D.S. 3·3; sulphated ash, 0·6%). The pH of 4% solution in 50% aqueous t-butyl alcohol was 8·2.

The ether layer was dried (CaSO₄) and concentrated (finally *in vacuo*) to 31 g. of colourless syrup (Found: OEt, 30·6%, equiv. to D.S. 4·6).

Paper chromatography of the aqueous layer (butan-1-ol–pyridine–water; 10 : 3 : 3 v/v) revealed traces of sucrose and some water-soluble esters, R_F 0·34 and 0·63, which were not investigated.

Polymerisation of O-Ethoxycarbonylsucrose.—The ether-insoluble ester obtained by fractionation (D.S. 3·3; *ca.* 2 g.) was heated at 150°/12 mm. (oil-bath temperature). The initially mobile syrup bubbled vigorously, thickened, and set in 15 min. to a slightly discoloured horny mass with entrapped bubbles. Some further darkening occurred on prolonged heating (4 hr.). The powdered *polymer* was insoluble in water, alcohols, chloroform, acetone, and pyridine. It swelled but did not dissolve in dimethyl sulphoxide or *NN*-dimethylformamide (Found: C, 43·6; H, 5·7; OEt, 13·5%), $\nu_{max.}$ (C=O stretching) 1760 cm.⁻¹ (broad-based peak). On being heated, the polymer darkened slightly at 210° and decomposed without melting at 250—260°. Alkaline hydrolysis and paper chromatography indicated the presence of sucrose.

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