

CHEMISTRY AND NEW USES OF SUCROSE: HOW IMPORTANT?

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Abstract - Some recent work on selective reactions of sucrose is described. These reactions reveal a profile of chemical reactivity which has been exploited to produce a number of products of commercial significance. The potential of sucrose as a raw material for chemicals and energy is also indicated.

INTRODUCTION

The world economy is critically dependent upon oil which is a non-regenerable material. In order to maintain an economic order in the world it is therefore imperative that the future energy and chemical needs are secured. In the short-term we must curb on wasteful consumption of oil and in the long-term dependence on oil must be reduced. Alternative resources such as coal, tarsands, shale oil, natural gas and lignite, agricultural and aquatic materials must be considered as sources of energy and chemicals. The potential of carbohydrates as feedstocks for chemicals has been demonstrated, but not yet significantly commercially realised except in a few instances. Although cellulose is the most abundant carbohydrate, several technical difficulties in its processing makes it economically unattractive as a raw material for energy and chemicals. In contrast sucrose and starch are readily amenable to chemical and biochemical modifications giving a range of compounds presently derived through petrochemical routes, as well as new derivatives of potential commercial significance.

Sucrose is obtained from two sources, in the tropics from sugar cane and in the temperate zone from sugar beet. The production in all forms exceeds ninety six million tonnes per year. Considering the current low raw sugar prices, £160 per tonne on the world market, and the fact that production exceeds consumption by over five million tonnes, it is logical that other uses of sucrose are found.

With a view to exploiting sucrose as a synthetic industrial raw material, the fundamental chemistry of sucrose has been investigated and has led to the development of a number of products of commercial importance. Several reviews on the chemistry of sucrose have appeared and therefore in this review only some current work on selective reactions of sucrose will be discussed. Some industrial applications of sucrose will also be reviewed.

STRUCTURE

The configuration and conformation of sucrose has been determined by X-ray crystallography (Ref. 1), neutron diffraction (Ref. 2), ^1H - (Refs. 3, 4) and ^{13}C -n.m.r. (Refs. 4, 5) spectroscopy. The positions of the hydrogen atoms in the crystal lattice of sucrose were determined by neutron diffraction technique. It was found that the D-glucopyranosyl moiety adopts the $^4\text{C}_1$ conformation while the D-fructofuranosyl unit has the $^3\text{T}^4$ conformation. All hydroxyl groups except O-4 are involved in hydrogen bonding, two of them intramolecular, O-6'---O-5 and O-1'---O-2 (Fig. 1).

Based on Laser-Raman (Refs. 6, 7) and X-ray diffraction (Ref. 8) studies of sucrose in aqueous solution it has been suggested that in dilute solution, sucrose lacks intramolecular hydrogen bonds but, as the concentration increased, the bridging together of the molecules is accompanied by a twisting around the glycosidic linkage that leads to the form of sucrose molecule found in crystal. This contention has, however, been criticised by Bock and Lemieux (Ref. 4). A detailed analysis of ^1H - and ^{13}C -n.m.r. spectra of sucrose, both in DMSO and D_2O , and hard-sphere calculation revealed a strong conformational preference about the glycosidic linkage that is near to that for sucrose in the crystalline state.

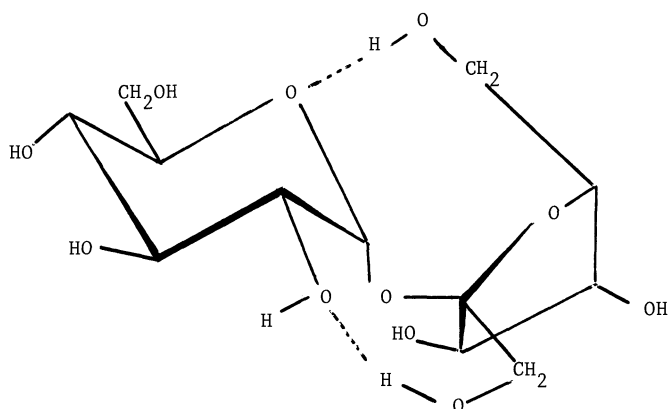
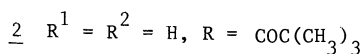
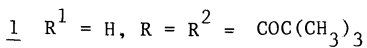
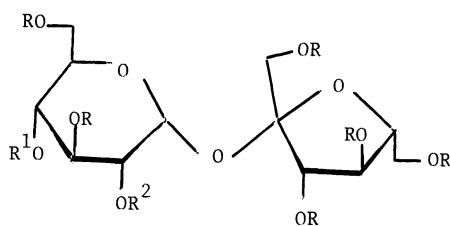


Fig. 1

SELECTIVE ACYLATION REACTIONS

Selective acetylation of sucrose using 1.6 molar equivalents of acetic anhydride in pyridine has been claimed to give a mono-*O*-acetylsucrose in 95% yield (Ref. 9). However, the product was not characterised, and in the light of recent results it is almost certainly not a homogenous material. Treatment of sucrose with 1.1 molar equivalents of acetic anhydride in pyridine at -40° gave, after chromatographic separation, 6-*O*-acetylsucrose in 40% yield. Its structure has been supported by ^{13}C -n.m.r. and by chemical transformation (Ref. 10).

Sterically hindered pivaloyl chloride has been used to selectively block hydroxyl groups in sucrose. Reaction of sucrose with 20 molar equivalents of pivaloyl chloride in pyridine at -40° for 6 h and then at ambient temperature for 24 h gave crystalline 1',2,3,3',4',6,6'-hepta-*O*-pivaloylsucrose (1) in 50% yield. Under slightly modified conditions the reaction yielded, in addition to the 4-hydroxy compound 1, the 2,4-dihydroxy 2 (33%), the 3,3'-dihydroxy (10%), the 3',4'-dihydroxy, and two pentapivalates as the 2,4,4'-trihydroxy, and the 3,3',4'-trihydroxy compound (10%). Crystalline 1',3,3',4',6,6'-hexa-*O*-pivaloylsucrose (2) has been obtained directly in ca. 45% yield. The trimolar pivaloylation of sucrose afforded 6,1',6'-tri-*O*- and 6,6'-di-*O*-pivaloylsucroses in 42 and 22% yield, respectively (Ref. 11).

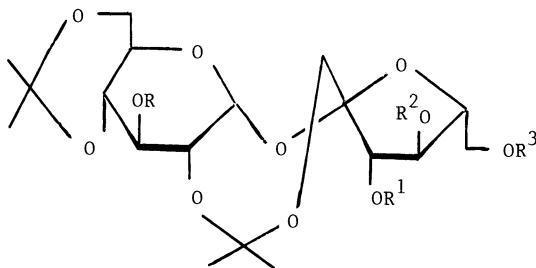


These results indicate that the pattern of reactivity of sucrose towards pivaloyl chloride is different from that of the selective acylation with other acid chlorides. For example, the tetramolar tosylation reaction of sucrose revealed a reactivity order of $0-6 \approx 0-6' > 0-1' > 0-2$, but the tetramolar pivaloylation gave mainly the 1',4',6,6'-tetrapivalate with the 1',3',6,6'-tetrapivalate as a minor product. The expected 1',2,6,6'-isomer was not detected in the mixture. Two principle, but divergent, reaction pathways have been suggested to exist between sucrose and its octapivalate in which the order of reactivity of the hydroxyl groups towards acylation are (a) $6,6'-OH > 1'-OH > 4'-OH > 2-OH > 4-OH > 3'-OH > 3-OH$; (b) $6,6'-OH > 1'-OH > 3'-OH > 3-OH > 4'-OH > 2-OH$ and $4-OH$ (Ref. 11).

The regioselective enhancement of the nucleophilicity of the hydroxyl groups in sucrose has been achieved by the use of trialkylstannyl oxide. Treatment of sucrose with 3 equivalents of bis (tributylstannyl) oxide and 6 molar equivalents of benzoyl chloride in toluene afforded 1',2,3,6,6'-penta-0-benzoylsucrose in 87% yield (Ref. 12).

Selective esterification of sucrose via metal chelates has been reported to give predominantly monoesters. Treatment of the cobalt (II) chelate, formed from sucrose, sodium hydride and cobalt (II) chloride in DMF in the molar ratio of 2:7:1, with 1.3 molar equivalents of acetic anhydride gave sucrose monoacetates in 98% yield. The product was shown by mass spectrometry and gas chromatography to be a mixture containing a major and two minor products (Ref. 13).

Selective benzylation of 4,6:1',2-di-0-isopropylidenesucrose (3) with 3.78 molar equivalents of benzoyl chloride in pyridine and chloroform at 0° for 1 h gave the 3',6'-dibenzoate 4, the 3',4',6'-tribenzoate 5 and the 3,3',6'-tribenzoate 6 in yields of 36, 9 and 8% respectively. These results indicated the reactivity order of $HO-3' \approx HO-6' > HO-4' > HO-3$. The greater reactivity of the hydroxyl group at C-3' can be explained on the basis of the cis- arrangement of the HO-3' and the glycosidic oxygen O-2 (Ref. 14).



<u>3</u>	$R = R^1 = R^2 = R^3 = H$
<u>4</u>	$R = R^2 = H, R^1 = R^3 = Bz$
<u>5</u>	$R = H, R^1 = R^2 = R^3 = Bz$
<u>6</u>	$R = R^1 = R^3 = Bz, R^2 = H$
<u>7</u>	$R = R^1 = R^2 = R^3 = Ac$

SELECTIVE DEESTERIFICATION REACTIONS

Selective deesterification of sucrose octaacetate has been achieved on a column of alumina. The treatment gave a complex mixture from which 2,3,6,1',3',4',6'-, 2,3,4,6,1',3',6'-, and 2,3,4,6,1',3',4'-hepta-0- acetylsucroses were isolated in yields of 2.7, 6 and 9%, respectively (Ref. 15).

Reaction of 4,6:1',2-di-0-isopropylidenesucrose tetraacetate (7) with methanolic ammonia at -10° for 15 min. gave, in addition to the starting material (24%), an inseparable mixture of the 3'- and 4'- monohydroxy compounds (32%), and the 3',4'-dihydroxy compound (30%). When the deesterification reaction was performed at -10° for 0.5h and then at 5° for 3.5 h it gave the 3',4'-dihydroxy, the 3',4',6'-trihydroxy, and the free diacetal (3), in yields of 35, 44.5 and 5.2%, respectively. On the basis of these results it is suggested that the rate of hydrolysis of the acetyl groups in 7 is in the order of $0-3' \approx 0-4' > 0-6' > 0-3$. The low reactivity of AcO-3 has been attributed to steric hindrance by the 4,6- and 1',2- acetal groups (Ref. 16).

SULPHONYLATION REACTIONS

Di- (Ref. 17), tri- (Refs. 18-21) and tetra- (Ref. 22) molar tosylation reactions of sucrose revealed a reactivity order of $\text{HO-6} \approx \text{HO-6}' > \text{HO-1}' > \text{HO-2}$.

Trimolar tosylation of sucrose afforded, after high pressure liquid chromatography, 6,1',6'-tri-O-tosylsucrose and 2,6,6'-tri-O-tosylsucrose in yields of 26 and 7% respectively (Ref. 21). Tetramolar tosylation of sucrose in pyridine at 0° has been reported to afford 6,1',6'-tri-O-tosylsucrose (40%) and 2,6,1',6'-tetra-O-tosylsucrose (32%) (Ref. 22).

In order to achieve greater selectivity "bulky" sulphonyl chlorides, mesitylenesulphonyl and 2,4,6-triisopropylbenzenesulphonyl chlorides, have been employed. Trimolar mesitylenesulphonylation of sucrose in pyridine afforded the 6,1',6'-trimesitylenesulphonate in ~50% yield (Refs. 21, 22). Treatment of sucrose with 5 molar equivalents of tripsyl chloride in pyridine at ambient temperature gave crystalline 6,1',6'-tri-O-tripsylsucrose in 54% yield (Ref. 23). Attempts to synthesise mono- or di- tripsylsucroses using low temperature and long reaction time surprisingly led to a complicated mixture.

Trimolar tosylation of 6,6'-di-O-tritylsucrose in pyridine at 0° for 48 h gave, after chromatographic separation, 1',2'-di-O-tosyl-6,6'-di-O-trityl-sucrose and 1'-O-tosyl-6,6'-di-O-tritylsucrose in 21 and 24% yield, respectively. When the reaction was carried out with a slight excess of methanesulphonyl chloride the 1'-O-mesylate was obtained in 45% yield (Ref. 24).

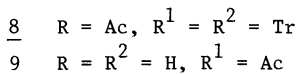
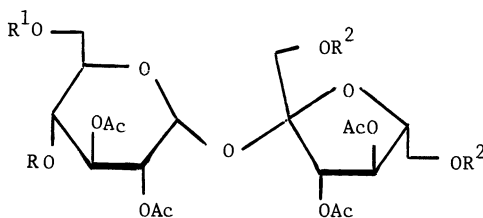
Treatment of 3,6'-di-O-acetyl-4,6:1',2-di-O-isopropylidenesucrose with 1.3 molar equivalents of tosyl chloride in pyridine afforded the 3',4'-ditosylate, the 4'-tosylate and the 3'-tosylate in yields of 3.7, 3.1 and 31%, respectively. Thus indicating that the hydroxyl group at C-3 is more reactive towards tosylation than at C-4' group (Ref. 16).

SELECTIVE ETHERIFICATION REACTIONS

TRITYLATION

Reaction of sucrose with 1.2 molar equivalents of trityl chloride in pyridine at ambient temperature for 96h yielded 6- and 6'-O-tritylsucroses in yields of 18.6 and 19.1%, respectively. The absence of 1'-O-trityl sucrose in the mixture indicated that the reactivity of the primary hydroxyl groups in sucrose was in the order of $\text{C-6} \approx \text{C-6}' > \text{C-1}'$ (Ref. 25).

Dimolar tritylation of sucrose yielded 6,6'-, 6,1'- and 1',6'-di-O-trityl sucroses in yields of 27.4, 4.4 and 5.2%, respectively (Ref. 26). Tetramolar tritylation of sucrose in pyridine at room temperature for 48h gave the 6,6'-di-(30%) and 6,1',6'-tri-(58%) trityl ethers (Ref. 27). Detritylation of 6,1',6'-tri-O-tritylsucrose pentaacetate (8) with boiling aqueous acetic acid occurred with the 0-4 \rightarrow 0-6 migration of the acetyl group to give crystalline 2,3,3',4',6-penta-O-acetylsucrose (9) in 43% yield (Ref. 28). Little or no ester groups migration was observed when 6,1',6'-tri-O-tritylsucrose pentabenzate was detritylated, using either hydrobromic acid in glacial acetic acid or boiling aqueous acetic acid (Ref. 29).



SILYLATION

The reaction of sucrose with 0.65 molar equivalent of tert-butyldimethyl silyl chloride in pyridine has been described to give 6'-,6,6'-di-, and 6,1',6'-tri-tert-butyldimethylsilylsucroses in yields of 10.5, 36.4 and 33.5%, respectively. Monosubstitution at C-6 and C-1' under the reaction conditions was not observed. These results indicated that HO-6' in sucrose is the most reactive site towards the silylation reaction (Ref. 30).

The tert-butyldiphenylsilyl group is much more stable towards acid and hydrogenolysis than the related silyl and trityl ethers. The reaction of sucrose with 1.1 molar equivalents of tert-butyldiphenylsilyl chloride in pyridine in the presence of a catalytic amount of 4-dimethylamino- pyridine at room temperature for 4 h gave crystalline 6'-tert-butyldi- phenylsilylsucrose in 49% yield. When the silylation reaction of sucrose was performed with 3 molar equivalents of the reagent, chromatography gave the crystalline 6,6'-di- and 6,1',6'-tri-tert-butyldiphenyl- sucroses in yields of 78 and 18.7%, respectively. The latter compound was obtained as the major product when sucrose was treated with 4.6 molar equivalents of the silylating reagent. Removal of the silyl protecting group in 6,6'-di-tert-butyldiphenylsilylsucrose hexabenzoate using tetrabutylammonium fluoride has been described to proceed smoothly, but with 4→6 migration of the benzoate group (Ref. 31).

METHYLATION

Selective methylation of sucrose can be expected to occur preferentially at O-1', O-2, and O-3' (the most acidic hydroxyl groups) followed by O-6 and O-6' (the least hindered hydroxyl groups). Partial methylation of sucrose using sodium hydroxide and dimethyl sulphate has been described to give 3'-O-methylsucrose and 4'-O-methylsucrose. The presence of the latter compound as the preponderant mono-O-methyl derivative has been explained on the basis that it is less liable to further methylation than some of the other mono-O-methyl sucroses (Ref. 32).

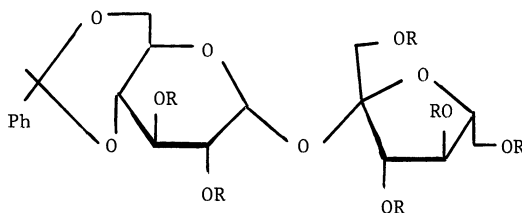
ALLYLATION AND CARBOXYMETHYLATION

Avela and coworkers have reviewed their work on selective etherification reactions of sucrose via metal chelates (Ref. 13). Reaction of sucrose with sodium hydride, cobalt (II) chloride, and allyl chloride in DMF in the molar ratio of 2:4:1:4 gave 69% of mono-O-allylsucroses and 2% of di-O- allylsucroses. Synthesis of mono-O-carboxymethylsucroses (41-48%) via metal chelates has been achieved.

ACETALATION REACTIONS

Acetalation reactions of sucrose and its derivatives revealed a reactivity order of 4,6 > 1',2 > 2,3 > 3,4.

4,6-O-Benzylidene sucrose has been synthesised in 35% yield, using α,α -dibromotoluene (Ref. 33) or benzaldehyde dimethyl acetal (Ref. 34) as acetalating reagents. The acetonation of sucrose with 2,2-dimethoxy- propane in DMF in the presence of a catalytic amount of toluene-p- sulphonic acid afforded after acetylation the 4,6-mono-(10) and the 4,6:1',2-di-(7)-acetals in yields of 15 and 55%, respectively (Ref. 35).



10 R = Ac

High yields of kinetic acetal products have been achieved by use of 2-methoxypropene. Treatment of sucrose with 5 molar equivalents of 2-methoxypropene in dry DMF in the presence of a strictly catalytic amount of toluene-*p*-sulphonic acid at 70° for 40 min. gave after acetylation the diacetal 7 in 70% yield. When the reaction was performed with 1.5 molar excess of the reagent the 4,6-acetal 10 was obtained in 60% yield (Ref. 36).

The formation of 10 and 7 from sucrose under kinetic control conditions has been rationalised. Initial attack by the reagent at O-6, the most sterically unhindered of the three hydroxyl groups, to yield a transitory ion of the type C(6)H₂O-CMe₂⁺ or an acyclic acetal C(6)H₂OCMe₂OMe, would proceed rapidly because of unhindered access to O-4 to generate the 1,3-dioxalane ring. A greater excess of the reagent would then predictably initiate attack at one of the other primary hydroxyl groups (O-1' and O-6'). Reaction at O-1' would allow direct bridging to O-2 to generate the observed diacetal 7 with minimal displacement from the favoured geometry of sucrose.

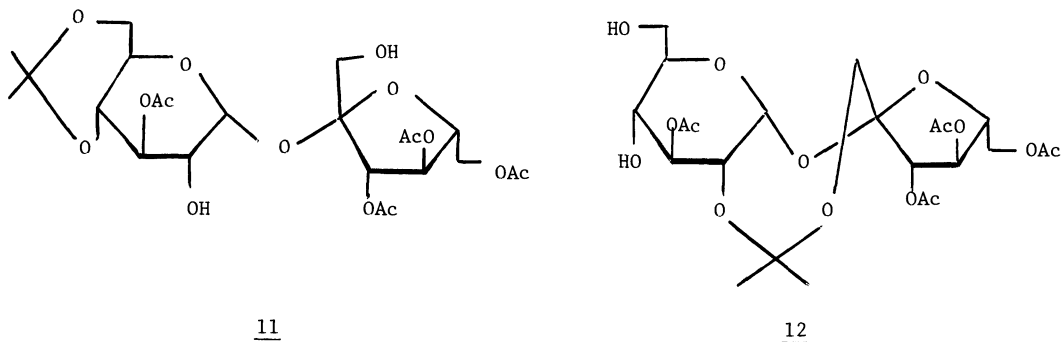
The crystal structure of 7 has been studied which reveals that the hexopyranosyl residue is in ⁴C₁ conformation. The conformation of the six-membered cyclic acetal ring is equivalent, the rings having parallel chair conformations. The conformation of the 8-membered ring, involving the two monosaccharide units through the 1',2-linkage is a boat-chair. The conformation of the fructofuranosyl ring is unexpected (P=277.1°) with O-2' *exo* to C-6' furthest from the ring, and can be called E₀ with a slight distortion towards O¹T² (Ref. 37).

In order to study the formation of acetals at other positions in the sucrose molecule, the acetalation reaction using 2,2-dimethoxypropane--DMF--toluene-*p*-sulphonic acid was performed with 6,6'-dichloro-6,6'-dideoxysucrose and 6,1',6'-tri-O-tritylsucrose. The dichloride gave, after acetylation, the corresponding 3,4:1',2-diacetal and the 1',2-monoacetal in 40 and 37% yields, respectively; while the tritryl derivative afforded the corresponding 2,3- and 3,4-monoacetals in 24 and 20% yields, respectively.

Dimethoxydiphenylsilane--DMF--toluene-*p*-sulphonic acid as a novel acetalating reagent for sucrose has been reported (Ref. 38). Treatment of sucrose with this reagent initially at 0° and then at ambient temperature gave, after acetylation, crystalline 1',2-O-(diphenylsilylene)sucrose hexaacetate (46%) and 1',2:6,6'-di-O-(diphenylsilylene)sucrose tetraacetate (4%). The expected 4,6-silylene acetal was not detected in the mixture, which was probably due to the larger atomic radius of the silicon atom compared to that of a carbon atom.

SELECTIVE DEACETALATION REACTIONS

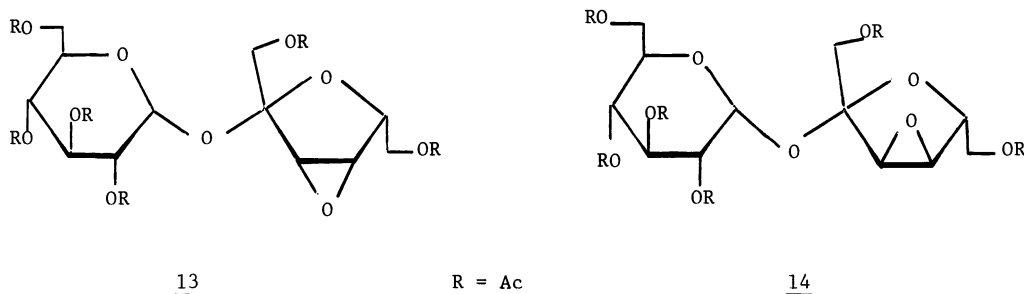
Selective deacetalation of 4,6:1',2-di-O-isopropylidenesucrose tetraacetate (7) has been achieved by use of aqueous acetic acid, methanolic hydrogen chloride, and cation-exchange resins. All three reagents were equally effective, however, from a practical point of view, the first reagent is preferred. Treatment of 7 with aqueous acetic acid at room temperature for 4h gave 7, the 4,6-acetal 11, the 1',2-acetal 12, and 3,3',4',6'-tetra-O-acetylsucrose in yields of 11, 4.7, 23 and 28%, respectively (Ref. 39).



On the basis of the yields of 11 and 12, it was concluded that the 8-membered (1,3,6-trioxane) cyclic acetal group in 7 is more stable to acid hydrolysis than the 6-membered (1,3-dioxane) cyclic acetal group. The greater stability of the 1',2-acetal ring is probably due to its being sterically more hindered than the 4,6-ring, and/or the boat-chair conformation adopted by the 1',2-ring is probably energetically a more stable conformation than the chair conformation of the 4,6-ring.

EPOXIDATION REACTIONS

Reaction of 3',4'-di-O-tosylsucrose hexaacetate with M-methanolic sodium methoxide at 70° for 2 min has been reported to give, after acetylation, the 3',4'-lyxo-epoxide 13 and the 3',4'-ribo-epoxide 14 in yields of 61 and 22% respectively. The fact that 13 was isolated in a higher yield than 14 indicates that the 3'-tosyl group is more readily attacked by methoxide ion than the 4'-tosyl group, affecting 3'-sulphonate group cleavage by O-S fission (Ref. 16). Treatment of 2,4-di-O-mesylysucrose hexapivalate with sodium methoxide for 48 h has been described to give, after acetylation, 6-O-acetyl-3,4-anhydro-2-O-mesyl- α -D-galactopyranosyl 1,3,4,6-tetra-O-acetyl- β -D-fructofuranoside in 25% yield (Ref. 11). These results are consistent with the fact that the sulphonate group at C-4 in sucrose is more prone to nucleophilic substitution reaction than the sulphonate group at C-2.

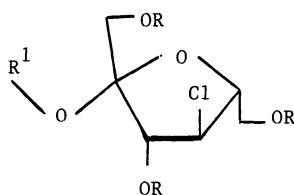
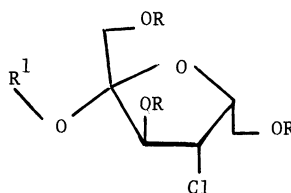


A facile synthesis of the 3',4'-lyxo-epoxide 13 using triphenylphosphine (TPP) and diethylazodicarboxylate (DEAD) has been described. Treatment of sucrose in DMF with acetic acid (2.2 mol. equiv.), TPP (4.5 mol. equiv.), and DEAD (4.5 mol. equiv.) at ambient temperature for 16 h afforded, after conventional acetylation, 13 in 42% yield (Ref. 40). Similarly, when 6,1',6'-tri-O-tritylsucrose and 4,6:1',2-di-O-isopropylidenesucrose were treated with TPP and DEAD they gave the corresponding 3',4'-lyxo-epoxides in \sim 80% yields (Ref. 41).

RING OPENING REACTIONS

Ring opening reactions of the 3',4'-lyxo-epoxide 13 and the 3',4'-ribo-epoxide 14 with azide and chloride nucleophiles have been described. Treatment of 13 and 14 with sodium azide in aqueous ethanol in the presence of ammonium chloride at 80° for 72 h gave, after acetylation, 4'-azido-4'-deoxysucrose heptaacetate and 2,3,4,6-tetra-O-acetyl- α -D-glucopyranosyl 1,3,6-tri-O-acetyl-4-azido-4-deoxy- β -D-sorbofuranoside in 63 and 82% yields, respectively. It is of interest to note that the nucleophilic attack occurred exclusively at C-4' position. The regiospecific attack by the nucleophile has been explained on the basis of steric and polar interactions (Ref. 42). The ring opening reactions of 13 and 14 with lithium chloride in DMF have been investigated; in both cases the nucleophilic attack occurred, as expected, at C-4' position affording, after acetylation, peracetates of 4'-chloro-4'-deoxysucrose (15) and α -D-glucopyranosyl 4-chloro-4-deoxy- β -D-sorbofuranoside (16), respectively. It was observed that the ring opening of the lyxo epoxide 13 was complete within 2 h, while in the case of the ribo-epoxide 14, the reaction after 2h showed little or no formation of the desired product. This difference in the reactivity of 13 and 14 towards S_N2 reaction has been explained on the basis of polar and steric factors (Ref. 43).

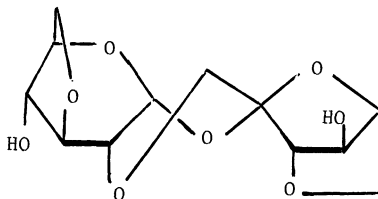
Ring opening reaction of 4-O-acetyl-2,3-anhydro-6-O-trityl- α -D-mannopyranosyl 3,4-di-O-acetyl-1,6-di-O-trityl- β -D-fructofuranoside with sodium azide has been reported to give, after conventional acetylation, 2,4-di-O-acetyl-3-azido-3-deoxy-6-O-trityl- α -D-altropyranosyl 3,4-di-O-acetyl-1,6-di-O-trityl- β -D-fructofuranoside in 92% yield (Ref. 44).

1516

R = Ac, R¹ = α -D-Glcp-tetraacetate

ANHYDRIDE FORMING REACTIONS

Synthesis of 3,6- (Ref.45), 3',6'- (Ref.46), 1',2- (Ref.47), 3,6:3',6'- di- (Ref.17), 1',4':3',6'-di- (Ref.46), 3,6:1',4':3',6'-tri- (Refs. 21, 29, 48), and 3,6:1',2:3',6'-tri- (17, Ref. 24) anhydrosucroses has been described.

17

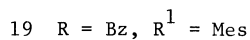
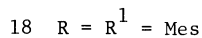
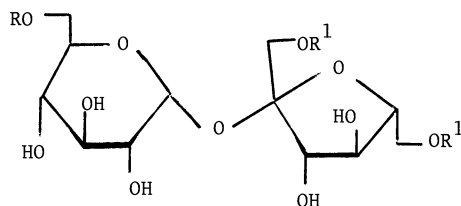
Compound 17 was claimed to be derived from alkaline alcoholysis of 6,1',6'-tri-0-tosylsucrose (Ref. 20). However, a subsequent report (Ref. 21) revealed that its structure was incorrectly assigned and in fact it was 3,6:1',4':3',6'-trianhydrosucrose. An unequivocal synthesis of 3,6:1',2:3',6'-trianhydrosucrose has been achieved by the following sequence of reactions: 1'-0-mesyl-6,6'-di-0-tritylsucrose \rightarrow 1',2- anhydro-6, 6'-di-0-tritylsucrose tetrabenzoate \rightarrow 1',2-anhydro-3, 3',4,4'-tetra-0- benzoylsucrose \rightarrow 1',2-anhydro-6,6'-di-0-mesylsucrose tetrabenzoate \rightarrow 17 (Ref. 24).

S_N2 REACTIONS OF SUCROSE SULPHONATES

The order of reactivity of the sulphonate groups in sucrose towards S_N2 reaction is 6 > 6' > 4 > 1'.

Selective displacement reactions of mesyl (Ref. 49), tosyl (Ref. 17, 50), mesitylenesulphonyl (Ref. 44), and tripsyl (Refs. 23, 24) derivatives of sucrose with various nucleophiles have been extensively investigated.

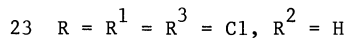
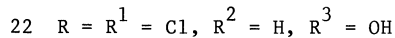
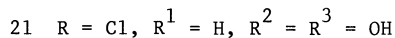
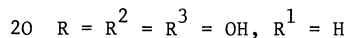
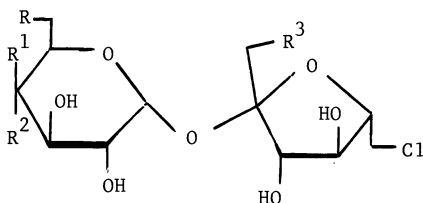
The reaction of 6,1',6'-tri-0-mesitylenesulphonylsucrose (18) with sodium benzoate in DMF at 85° for 30 h gave, after conventional benzylation, 1',6'-di-0-mesitylenesulphonylsucrose hexabenzoate (19) in 70% yields (Ref. 44). Similarly, when 6,1',6'-tri-0-tripsylsucrose was treated with nucleophiles such as azide (Ref. 23), benzoate, thioacetate, and thiocyanate (Ref. 24) in an aprotic solvent, the corresponding 6-substituted derivatives were obtained in high yields.



SULPHURYL CHLORIDE REACTIONS OF SUCROSE

Reaction of sucrose with sulphuryl chloride in pyridine has been reviewed (Ref. 51). The reaction involves the initial formation of a chlorosulphate ester group which under goes an intramolecular nucleophilic substitution reaction with insertion of chloride, with inversion of configuration.

Under controlled reaction conditions, sucrose reacts with sulphuryl chloride in pyridine in a highly specific manner to give 6'-chloro-6'-deoxy- (20, 43%, Ref. 52), 6,6'-dichloro-6,6'-dideoxy- (21, 29%, Ref. 52) sucroses, 4,6,6'-trichloro-4,6,6'-trideoxy- (22, 50%, Ref. 53, 54) or 4,6,1',6'-tetrachloro-4,6,1',6'-tetraideoxy- (23, 40%, Ref. 55) galacto-sucroses. These results suggest a reactivity order of $\text{HO-6}' \cong \text{HO-6} > \text{HO-4} > \text{HO-1}'$.



MESYL HALIDE -- N, N-DIMETHYLFORMAMIDE REACTION

The selective replacement of 6- and 6'- primary hydroxyl groups in sucrose has been achieved by the use of mesyl chloride--DMF or mesyl bromide -- DMF reagent to give the 6,6'-dichloride (51%) or 6,6'-dibromide (24%) derivatives (Ref. 56). Under forcing conditions the chlorination also occurred at C-4 and C-1' positions in sucrose (Ref. 57). The reactivity order of the hydroxyl groups in sucrose was similar to that observed with the sulphuryl chloride reagent. The formation of formic esters during the reaction of sucrose with mesyl halide and DMF by way of hydrolysis of the $(\text{Me}_2\text{N}^+=\text{CHOR})\text{X}$ complex has been observed.

The formylation reaction was particularly pronounced at secondary and hindered primary (HO-1') positions (Ref. 45).

TRIALKYL (OR ARYL) PHOSPHINE -- CARBON TETRAHALIDE OR HALOSUCCINIMIDE

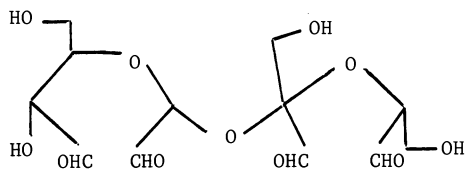
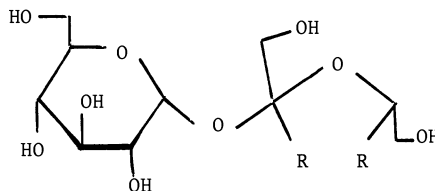
Reaction of tris (dimethylamino) phosphine, carbon tetrachloride and potassium hexafluorophosphine with sucrose in water has been reported to afford a mixture of alkoxytris (dimethylamino) phosphonium salts, which on treatment with sodium chloride in DMF gave, after acetylation and chromatographic separation, the peracetates of 6-chloro-6-deoxy- and 6,6'-dichloro-6,6'-dideoxy-(21)sucroses in yields of 46 and 15%, respectively (Ref. 58).

The selective replacement of 6- and 6'-primary hydroxyl groups in sucrose by halogens (chloro and bromo) has been achieved, albeit in low yields, by the use of triphenylphosphine--N-halosuccinimide in DMF (Ref. 56).

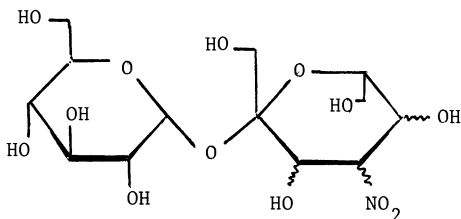
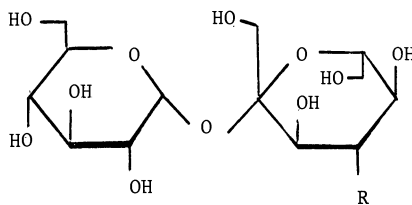
Triphenylphosphine and carbon tetrachloride has been shown to be an efficient chlorinating reagent for sucrose. Treatment of sucrose with the reagent in pyridine at 70° for 2 h gave 6,6'-dichloro-6,6'-dideoxy-sucrose (21) in 92% yield (Ref. 59). A similar treatment of sucrose in pyridine with triphenylphosphine--carbontetrabromide gave the expected 6,6'-dibromo derivative in 72% yield (Ref. 60). The greater selectivity for primary hydroxyl group has been associated with a bulky halogenating complex formed from triphenylphosphine dihalide ($\text{Ph}_3\text{PC} = \text{X}_2$) and pyridine (Ref. 59).

SELECTIVE OXIDATION REACTIONS

Lead tetraacetate oxidation of sucrose in dry acetic acid has been shown to proceed without appreciable cleavage of the glycosidic linkage (Ref. 61). The oxidation reaction in pyridine afforded the tetraaldehyde 24 in high yield. When sucrose was treated with a limited proportion of lead tetraacetate in acetic acid the 3,4-glycal group in the D-fructofuranosyl ring was cleaved preferentially to give 25 (Ref. 62). However, periodate attacked the D-glucopyranosyl unit more readily. These characteristics have been related to the nature of oxidant themselves. The dialdehyde 25 was reduced by catalytic hydrogenation or sodium borohydride to give the syrupy polyol 26.

2425 R = CHO26 R = CH₂OH

The dialdehyde 25 has been cyclised with nitromethane to afford a stereoisomeric mixture of nitro derivatives 27 which on catalytic hydrogenation gave α -D-glucopyranosyl 4-amino-4-deoxy- β -D-glucopyranoside hydrochloride (28, 23%, based on sucrose, Ref. 63).

2728 R = NH₂, HCl

Microbial oxidation of sucrose by *Agrobacterium tumefaciens* has been reported to give β -D-fructofuranosyl α -D-ribo-hexosid-3-ulose, which on reduction afforded α -D-allopyranosyl β -D-fructofuranoside (Ref. 64).

SUCROSE AS A CHEMICAL FEEDSTOCK

Conversion of sucrose to ethanol by a process of fermentation is a well known technology. In a batch fermentation process sucrose is diluted to 12 to 15 per cent, treated with nitrogen and phosphate nutrient and then inoculated with yeast. The fermentation is complete within 36 h. Theoretical yield of anhydrous ethanol from one tonne of sucrose is 640 L⁻¹. In practice, however, due to some side reactions, the yield is 80-90% of the theoretical yield (Ref. 65, 66). The total cost of ethanol production depends on the raw material cost, capital, labour and energy. It is economical for a sugar factory to have a distillery, because it comes with its own factory fuel (bagasse). The total cost of the fermentation alcohol varies from around £0.16 per litre in the Philippines to £0.21 per litre in Brazil and £0.24 in the United States.

Ethanol is the most widely used solvent, apart from water, in the chemical industry. Its applications include for example, pharmaceutical and cosmetic uses, in production of paints and resins, and as extender for petrol. Ethanol can be dehydrated by catalytic dehydration to give ethylene, one of the most important chemical feedstocks. Ethanol can also be transformed into acetaldehyde and from it a host of industrial chemicals and solvents such as acetic acid, acetic anhydride and vinyl acetate can be produced.

Most important organic acids used in food, detergent, pharmaceutical, and polymer industries can be obtained from sucrose by chemical or fermentation processes. These include citric acid, lactic acid, oxalic acid, gluconic acid, and glucuronic acid.

Long-chain fatty acid esters of sucrose are produced commercially. They possess surface active properties and are non-ionic, non-toxic and biodegradable. Their value as dispersing and emulsifying agents in various food formulations has been recognised. Sucrose esters being compatible with skin and totally non-irritant should find application in cosmetics (Ref. 67). Their use as plasticiser and as antistatic agent in plastics has also been considered. Sucrose esters exhibit excellent fruit preservative property.

Sucrose octaacetate is extremely bitter and finds application as a denaturant. Sucrose octabenzoate (Ref. 68) and sucrose diacetate hexaisobutyrate (Ref. 68a) are commercially used as plasticisers for cellulose acetate films and are compatible with a wide variety of polymers, resins, plasticisers, oils and waxes. In many countries sucrose diacetate hexaisobutyrate is used as a soft drink modifier for flavouring, oil suspension and clouding purposes (Ref. 68a).

Largest chemical use of sucrose is in rigid polyurethane foams, a market which is increasing at the rate of nearly 12% a year. Suitably modified sucrose derivatives could impart fire-retardancy properties to the polymer (Ref. 68b).

A crystalline halogenated sucrose derivative, 1,6-dichloro-1,6-dideoxy-β-D-fructofuranosyl 4-chloro-4-deoxy-α-D-galactopyranoside, has been shown to be 650 times sweeter than sucrose. Its sweetness profile is similar to that of sucrose. It is resistant to enzymic hydrolysis and considerably more stable to acid than sucrose (Ref. 69).

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