LONG-CHAIN DERIVATIVES OF MONOSACCHARIDES AND OLIGOSACCHARIDES

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CONTENTS

I. INTRODUCTION

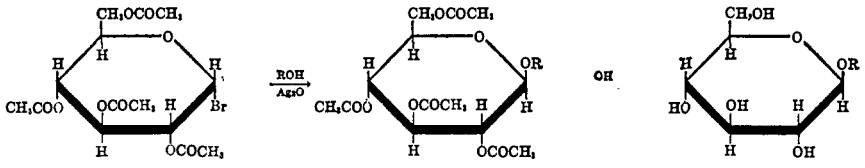
The first preparation of long-chain alkyl derivatives of carbohydrates was in 1855, when Berthelot (9, 10) obtained mixtures of esters by heating glucose and sucrose with fatty acids. Little attention was paid to this field for many years, but interest has grown steadily in the last twenty or thirty years on account of the commercial importance of hexitan esters and the potential surface activity of fatty derivatives of sugars.

This review covers the preparation and properties of compounds containing a mono- or oligosaccharide group and an alkyl chain of more than six carbon atoms. The compounds described include glycosides, esters, glycosylamines, glycosamines, urethans, and amides derived from sugar acids. Since all of the reactions described in this review have usually involved the use of the most accessible isomers of the carbohydrates concerned, it is convenient not to specify the ring size of the compounds but to refer, for instance, to "glucopyranosides" as "glucosides."

II. PREPARATION OF GLYCOSIDES

The conventional method of preparation of lower glycosides—namely, by causing a solution of a reducing sugar in the appropriate alcohol to react in the presence of an acid catalyst (64)—has been used to prepare the hexyl, octyl, and decyl glucosides (159). However, this method cannot be extended to the glycosides of higher alcohols.

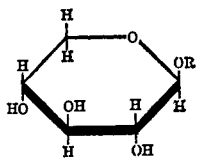
The Koenigs–Knorr reaction (36), in which a hydroxylic compound is condensed with an acetylglycosyl halide (61), can conveniently be used for the synthesis of higher glycosides. The reaction is carried out in an inert solvent in the presence of a condensing agent such as silver oxide, and the resulting acetylglycoside is deacetylated with dilute alkali (36). Most acetylglycosyl halides have the α-configuration (77); as the reaction occurs with inversion, β-glycosides are normally obtained (36):



This reaction was used by Fischer and Helferich (42) and by Salway (125) to prepare cetyl β-D-glucoside (II: R = $C_{16}H_{33}$). The latter worker also prepared the glucosides of the so-called "melissyl" and "ceryl" alcohols (these substances are invariably mixtures of several homologs (68)).

Subsequently heptyl (116) and hexyl, octyl, nonyl, decyl, and dodecyl β-D-glucosides (103) were also synthesized from tetraacetyl-α-D-glucosyl bromide. More recently, the reaction has been extended to the

preparation of alkyl β-D-xylosides (III) (72) and β-cellobiosides (IV) (73); in each case the glycosides of the even-numbered fatty alcohols from C_6 to C_{18} were obtained.



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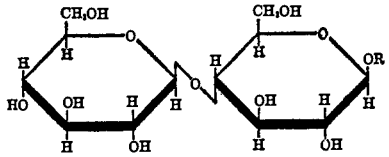
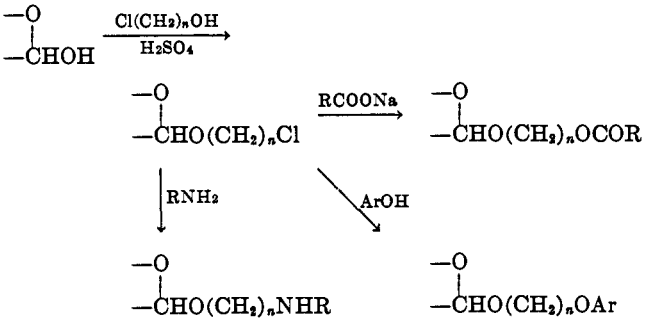


IV

A simpler synthesis of glucosides consists of the zinc chloride-catalyzed reaction of fatty alcohols with pentaacetylglucose, followed by alkaline hydrolysis of the initial product (11).

β-D-Glucosides of lower alcohols are produced by the action of emulsin on aqueous alcoholic solutions of glucose (14, 15). After a careful study of the composition of the substrate, it was found possible to prepare hexyl β-D-glucoside in this way (152).

A wide range of compounds can be prepared (25) by the reaction of reducing sugars with halogeno-alcohols such as ethylene chlorohydrin or 3-chloro-propanol. The resulting chloroalkyl glycosides can be condensed with the sodium salts of carboxylic acids, with phenols, or with primary amines:



Related to the glycosides are the acetyl esters (I: R = acyl), which are obtained when an acetyl-glycosyl halide reacts with the silver salt of a fatty acid. In this way Hess and Messmer (65) prepared 1-β-stearoyl-2,3,4,6-tetraacetyl-D-glucose (I: R = $COC_{17}H_{35}$). This compound, and also the lauroyl analog (I: R = $COC_{11}H_{23}$), were subsequently synthesized by Staudinger and Werner (142), using this method.

III. PREPARATION OF ESTERS

There have been two reports of the isolation of carbohydrate esters (other than sulfuric esters) from natural sources. Acetone extracts of ustilaginoidin, a dye obtained from fermented rice, yielded a small quantity of a fatty substance which is claimed (158) to be arabityl margarate. However, since "margaric" acid had previously been shown to be a mixture of palmitic and stearic acids (69), this claim needs to be reëxamined.

More recently, it has been reported (1) that ether and benzene extracts of diphtheria microörganisms contain fatty acid esters of trehalose and mannose; the sugars were identified chromatographically.

A. Preparation of esters by heating with fatty acids

The simplest procedure for the preparation of esters is to heat together a mixture of the appropriate alcohol and acid. In this way, Berthelot (9, 10) obtained fatty esters from glucose and sucrose by heating with the desired acid in a sealed tube at 120°C. for 50–60 hr. Trehalose esters were obtained by reaction at 180°C. This method, however, suffers from the disadvantages that the products are mixtures which are difficult to separate and also that the sugars decompose at the temperatures involved.

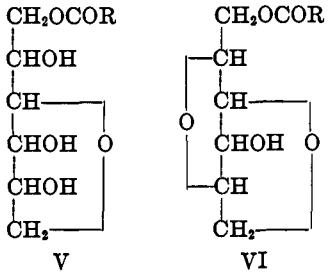
Decomposition of the carbohydrates may be avoided by the alternative use of glycosides, which are generally more heat-resistant than the sugars. Thus a wide range of glycosides, including methyl and ethyl α- and β-D-glucosides, allyl α-D-glucoside, methyl α-D-galactoside, and methyl β-L-arabinoside may be esterified by heating with fatty acids at temperatures between 160° and 300°C. (46, 47, 49); it is claimed that di-, tri-, or tetraesters may be obtained according to the initial proportion of the reactants. Again, drying oils are obtained when methyl α-D-glucoside is heated with the fatty acids of linseed oil (48).

The direct reaction of glycosides and fatty acids may conveniently be carried out by azeotropic esterification in xylene. In this way, Jedlinski (83, 84) has prepared the dihexanoyl, tetrahexanoyl, tetraoctanoyl, dilauroyl, and tetralauroyl esters of methyl α-D-glucoside, as well as the tetraoctanoate, monolaurate, and tetralaurate of the β-isomer. It has been shown (49) that when methyl α-D-glucoside is treated with up to two moles of a fatty acid in xylene in the presence of litharge or sodium hydroxide, only the diester is produced, even when equimolecular proportions of the reactants are used. However, when stannous oleate is used as a catalyst, high yields of the monoöleate are obtained.

Drying oils are produced when the monoglucosides of ethylene glycol or glycerol are heated with the fatty acids of linseed oil or soybean oil (146).

Work published before 1943 on the direct esterification of hexitols has been reviewed in detail by Goldsmith (51). Shortly after this review appeared, it was shown (17, 18) that when a hexitol and a fatty acid were heated together in the presence of sodium methoxide, esterification occurred and one additional molecule of water was lost by internal condensation of

water to give a "hexitan" ester (formula V represents one of the many possible structures). On the other hand, when sulfuric or phosphoric acid was used as catalyst, two additional molecules of water were lost with the formation of a "hexide" ester (17, 18) such as VI.



V VI

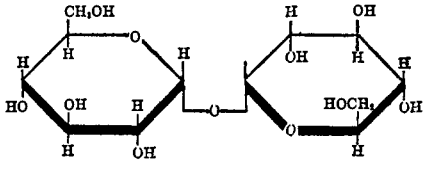
Other hexitol esters have been prepared by heating sorbitol hexahydroxyethyl ether with fatty acids (127) and sorbitol or mannitol with α-hydroxy acids (28).

B. Preparation of esters by reaction with acid chlorides

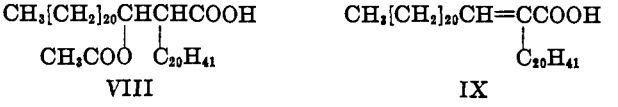
A more convenient, although more expensive, method for the synthesis of fatty esters of carbohydrates consists in the reaction of a solution of the sugar in pyridine or quinoline with an acid chloride in a solvent such as chloroform (51). When an excess of the acid chloride is used, fully esterified products are obtained. Thus, treatment of α- and β-glucose with lauroyl, palmitoyl, or stearoyl chloride yielded the α- and β-forms of the pentaesters (160). The method has also been applied to the preparation of tetrapalmitoylarabinose (106), hendecapalmitoylraffinose and hendecastearoylraffinose (65, 105), and octastearoyltrehalose (156). The following octaacyl derivatives of sucrose have also been obtained in this way: hexanoyl, octanoyl, decanoyl, lauroyl, myristoyl, palmitoyl, stearoyl, and undecenoyl (65, 161, 162).

Partial esterification of carbohydrates leads, as may be expected, to mixtures of compounds of closely similar physical properties, which may therefore be difficult to separate. For example, treatment of lactose with the chlorides of the even-numbered fatty acids from C_6 to C_{18} yields products containing between 6.5 and 7.2 acyl groups per molecule, and mixtures containing 4.7 octanoyl and 4.8 decanoyl groups per molecule were obtained from glucose (132). Sucrose reacts with lauroyl chloride to give mixtures of the mono-, di-, and trilaurates (101) and tri- and tetrastearates are formed from methyl α-D-glucoside (104).

Chromatographic separation enabled Asselineau (6) to identify the products of the reaction of palmitoyl chloride with glucose and methyl α-D-glucoside. Glucose afforded the 6-monopalmitoyl, the 2,6-dipalmitoyl, and an unidentified tripalmitoyl ester, while from methyl α-D-glucoside the 6-monoester, two isomeric diesters, and the 2,3,4,6-tetraester were obtained. Trehalose (VII) reacts with the chlorides of 2-eicosyl-3-acetoxytetracosanoic acid (VIII) and 2-eicosyltetracos-2-enoic acid (IX) to give mixtures of the 6-monoester, the 6,6′-diester, and the 2,6,6′-triester (118).



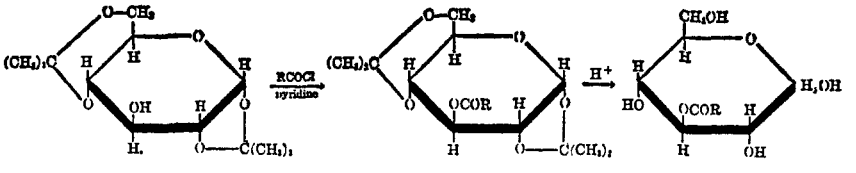
VII



VIII IX

In the patent literature there are many reports of the preparation of fatty esters of glucose and sucrose using acid chlorides (22, 57, 58, 78, 123, 124, 126, 144). The preparation of esters by the action of palmitic anhydride on sucrose in molten chloroacetic acid has also been described (92).

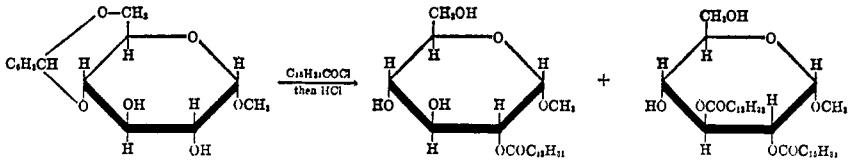
Carbohydrate esters of known structure may be produced unambiguously by protecting all except one of the hydroxyl groups of the carbohydrate, treating the protected molecule with the acid chloride, and finally removing the protecting groups. Thus, 1,2,4,6-diisopropylidene-D-glucose reacts with an acyl chloride to give the diisopropylidene ester, which, on mild acid hydrolysis, affords the 3-acylglucose (X) (6, 75, 111):



X

6-Monoesters of galactose were also prepared (74) in this way from 1,2,3,4-diisopropylidenegalactose. On the other hand, methyl 4,6-benzylidene-α-D-glucoside, which contains two free hydroxyl groups, was converted into methyl 2-palmitoyl- and 2,3-dipalmitoyl-

α-D-glucoside on treatment with palmitoyl chloride followed by acid hydrolysis (6):



Trehalose (VII) reacts with tosyl chloride to give, on acetylation, the 6,6′-di(*p*-tosyl)-2,2′,3,3′,4,4′-hexaacetyltrehalose. When this compound is treated with the potassium salt of the acid (VIII: H for $COCH_3$) in dimethylformamide, the tosyl groups are displaced; mild hydrolysis then yields the trehalose 6,6′-diester of the acid (VIII: H for $COCH_3$) (118). Similarly, reaction of triphenylmethyl chloride with trehalose affords the 6,6′-bistriphenylmethyl ether, which is converted by treatment with stearoyl chloride followed by hydrolysis into 2,2′,3,3′,4,4′-hexastearoyltrehalose (156).

The polyhydric alcohols derived from monosaccharides react with acid chlorides in the same way as carbohydrates. Xylitol, on treatment with six moles of lauroyl, myristoyl, palmitoyl, or stearoyl chloride, affords the corresponding pentaesters (24). Reaction of mannitol with six moles of lauroyl chloride yields only the pentalaurate; a large excess of the acid chloride is required for the formation of the hexalaurate (102, 112).

N-Methyl-2-pyrrolidone and 2-pyrrolidone have recently been reported (154) to be suitable solvents for many reactions of sugars. Sucrose tetra- and octastearates have been obtained by the reaction of sucrose with stearoyl chloride in these solvents.

Recently there has been described the reaction of pentasodium sucrate, obtained from sucrose and sodium in liquid ammonia, with lauroyl and stearoyl chlorides (12); uncharacterized products were obtained.

C. Preparation of esters by exchange reactions

When a hydroxylic compound and an ester are heated together in the presence of an alkaline catalyst, exchange of the acyl group occurs. The reaction is reversible, but if the ester of a volatile alcohol is used and the alcohol is allowed to escape from the reaction, then the exchange reaction is favored. When pure esters of a single fatty acid are not required, it is frequently convenient to use the natural glycerides. For instance, Irvine and Gilchrist (80) found that the reaction of methyl α-D-glucoside with olive oil in the presence of sodium methoxide afforded a crude monooleate as a sirup; it was considered that dehydration had occurred and therefore that the product was an anhydroglucoside derivative.

This reaction was subsequently repeated by Wolff and Hill (157), who again obtained a monoester (even when an excess of olive oil was used), but who found no evidence of dehydration and, in consequence, disagreed with the earlier formulation. A monoester was also obtained when methyl α-D-glucoside was treated with soybean oil in the presence of sodium methoxide at 225°C. and 2–3 mm. pressure. However, when methyl oleate was used instead of olive oil, mono-, di-, or trioleates were produced according to the initial proportions of the reactants. It was also found that in these compounds the glucosidic alcohol residue could not be removed by hydrolysis to give the glucose esters, because on treatment with 0.1 *N* hydrochloric acid, preferential hydrolysis of the ester linkage took place.

Pentitol and hexitol esters may be prepared by exchange reactions with glycerides, using sodium methoxide or sulfonic acids as catalysts (52). When mannitol is heated with olive oil and sodium methoxide, mannitan dioleate is formed (81, 90).

In the last five years much attention has been given to the preparation of mono- and diesters of carbohydrates, especially sucrose, by means of exchange reactions. For this purpose, it is necessary to use a solvent in which both the reactants are soluble. It was found (60, 107, 108) that dimethylformamide and dimethyl sulfoxide were suitable solvents for the reaction of sucrose with lower alkyl esters of fatty acids. Potassium carbonate was recommended as the catalyst, and the reaction was conveniently carried out by heating at 90–95°C. and 80–100 mm. pressure for 9 to 12 hr. When three moles of sucrose and one mole of fatty ester were used, sucrose monoesters were obtained. The use of two moles of ester per mole of sucrose led to diesters. In this way the sucrose mono- and diesters have been prepared from lauric, myristic, palmitic, stearic, oleic (107), ricinoleic, and 12-oxoöctadec-9-enoic acids (98).

A series of patents issued to the Procter and Gamble Company describes conditions for the preparation of fatty esters of nonreducing sugars in which sodium methoxide is the preferred catalyst and dialkyl sulfoxides (76), *N*,*N*-dialkylamides (62), pyridine (94), *N*-acylpiperidines, or *N*-acylmorpholines (149, 150) are recommended as the solvent. The reaction can be effected by using either glycerides or carbohydrate esters as the ester moiety. In dimethyl sulfoxide the reaction of sucrose with a methyl ester of

a fatty acid, using sodium methoxide as the catalyst, is extremely rapid, and equilibrium is reached within 5 min. at 100°C. (76). The use of reduced pressures may be advantageous (76).

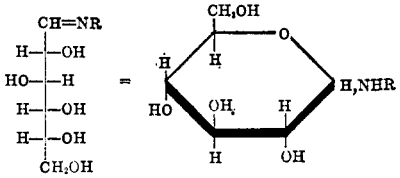
A recent patent (44) described the preparation of biscarbohydrate esters of substituted dicarboxylic acids. These compounds appear to have higher surface activities than the monoacyl carbohydrates. Various dicarboxylic acids were considered, but substituted succinic acids were preferred to derivatives of malonic, glutaric, adipic, sebacic, or pimelic acid. The most useful product is apparently the disucrose ester of the acid produced by the sulfuric acid-catalyzed addition of triisobutylene to maleic anhydride.

Before the exchange reaction described above had been developed, a number of sugar oleates, including fructose dioleate, sorbose pentaoleate, arabinose mono- and dioleates, sucrose tetraoleate, and glucose pentaoleate, were described in the patent literature (26). The method by which these compounds were prepared was not given.

IV. NITROGEN-CONTAINING DERIVATIVES

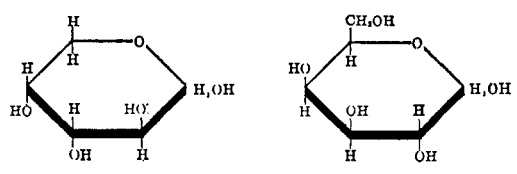
A. Glycosylamines

The reaction of reducing sugars with primary aromatic (139) and aliphatic (82) amines affords *N*-substituted glycosylamines such as XI. The preparation of these compounds has been reviewed by Ellis and Honeyman (32). Although their structures are uncertain, the glycosylamines probably possess the pyranose configuration, as shown in formula XIb (32).

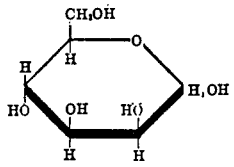


XIa XIb

Long-chain alkylglycosylamines were first prepared by Votoček and Valentin (153) by reaction in aqueous alcoholic solution. In this way the hexyl- and heptylglycosylamines were synthesized from arabinose (XII), xylose (III: H for R), glucose, galactose (XIII), mannose (XIV), rhamnose (6-desoxy-L-mannose), and fucose (6-desoxy-L-galactose).

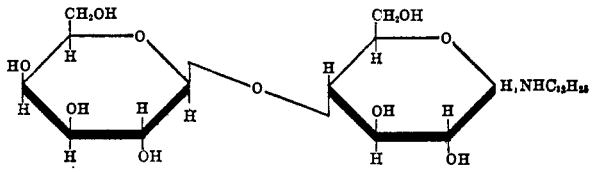


XII XIII



XIV

N-Heptyl-, *N*-hexadecyl-, and *N*-octadecylglucosylamines were prepared by refluxing ethanolic solutions of the reactants (99) and later, in improved yield, by the use of hot methanol as the solvent (113). *N*-Octyl-, *N*-decyl-, and *N*-dodecylglucosylamines, *N*-dodecyllactosylamine (XV), *N*-dodecyl- and *N*-octadecylmaltosylamines (XVI) (113), and *N*-hexylsorbosylamine (XVII) (67) have also been prepared. The maltosylamines (XVI: R = $C_{16}H_{33}$; XVI: R = ($C_{18}H_{37}$) have been described in the patent literature (155).



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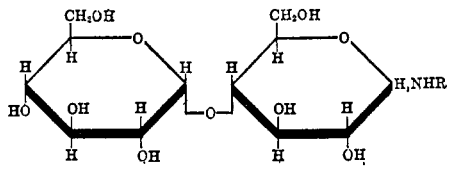

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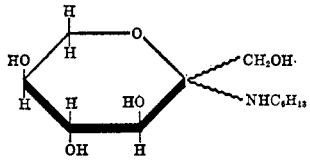


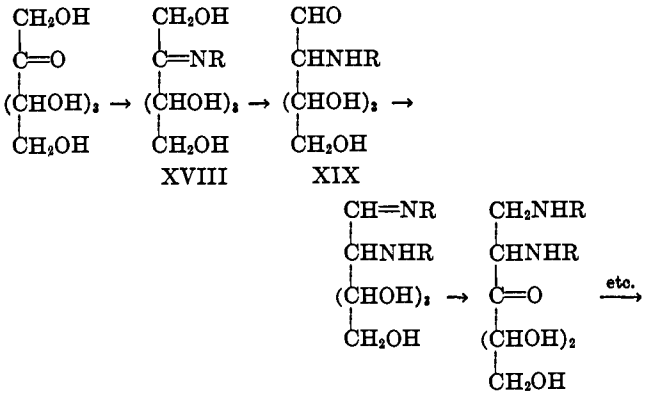
XVII

Erikson (33, 34) has made a more thorough study of the reaction of reducing sugars with long-chain amines. Whereas previous preparations had yielded colored materials, Erikson obtained good yields of "white or nearly white" glycosylamines by carrying out the reaction in a small volume of aqueous ethanol at room temperature. Furthermore, it was shown that the reaction can proceed beyond the glycosylamine stage and that it is possible for at least five molecules of an amine to react with a single molecule of a hexose. At room temperature glucose, maltose, and lactose are converted only to the glycosylamine, even when an excess of the amine is present. When glucose is treated with six moles of octadecylamine at 60–70°C., the product is "glucose quateroctadecylamine." Galactose similarly yields "galactose trisoctadecyl-

amine," while lactose and maltose each form compounds with two moles of the amine.

Ketoses were found to be more reactive than aldoses. Thus at room temperature fructose gave a mixture of *N*-octadecylfructosylamine (XVIII: R = $C_{18}H_{37}$) (or an Amadori rearrangement product such as XIX) and a bisoctadecylamine derivative. L-Sorbose, at room temperature, yields a mixture of bis- and trisoctadecylamine compounds, while at 60°C. reaction occurs with five molecules of amine.

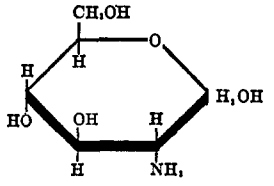
The structures of the polycondensation products have not been determined, but Erikson (34) has suggested that a series of osazone-type reactions occur, as in the following scheme:



It was considered that this type of mechanism was supported by the fact that in the reaction with amines, as in osazone formation (5, 40), ketoses are more reactive than aldoses. However, if the above mechanism operates, it remains to be explained why only two phenylhydrazine residues are incorporated in the sugar molecule in osazone formation (38), compared with up to five molecules of an amine.

B. Amides derived from D-*glucosamine*

D-Glucosamine, 2-desoxy-2-amino-D-glucose (XX), occurs as a polysaccharide in chitin (114) and may conveniently be prepared by the acid hydrolysis of lobster or crab shells (121).

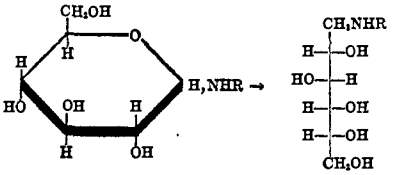


XX

Four papers have appeared in which *N*-acyl or *ON*-acyl derivatives of D-glucosamine are described. The *N*-acylamides are obtained by reaction with an acid anhydride in anhydrous methanol (79) or with an acid chloride in aqueous alkaline solution (39, 79). The amide, or D-glucosamine itself, reacts with an excess of an acid chloride in pyridine to give the *ON*-pentaacyl derivative (79, 87). The amides and ester-amides of the even-numbered carboxylic acids from hexanoic to stearic acid have been prepared.

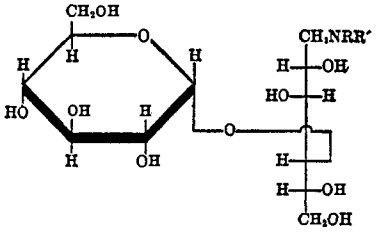
C. Glycamine derivatives

Glycamines, sugar alcohols in which a —CH_2OH group is replaced by —CH_2NH_2 or —CH_2NHR, are produced by the catalytic hydrogenation of glycosylamines (115). For example:



XXI

This reaction has been applied to long-chain compounds by Mitts and Hixon (99), who reduced *N*-heptyl-, *N*-hexadecyl-, and *N*-octadecylglucosylamines to the corresponding glucamines (XXI); however, poor yields were obtained in the case of XXI (R = $C_{16}H_{33}$ and $C_{18}H_{37}$). The *N*-dodecyl- and *N*-hexadecylglycamines of maltose (presumably XXII: R′ = H) have been prepared by hydrogenation of a mixture of maltose and the appropriate amine in the presence of a nickel catalyst (155). The amine XXII (R = CH_3; R′ = $C_{18}H_{37}$) was prepared by the alkylation of XXII (R = CH_3; R′ = H) with octadecyl bromide (155).



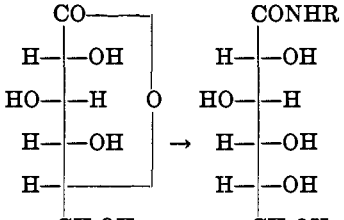
XXII

Substituted glycamines have been prepared by the hydrogenation of mixtures of glucose and *N*-lauroyl- or *N*-stearoyl-*p*-phenylenediamine (138).

Amides such as *N*-lauroyl-*N*-methylglucamine have been obtained (130) by heating an *N*-alkylglucamine with the methyl ester of a fatty acid; these amides can be sulfated by, for example, chlorosulfonic acid (131). When an alkylglycamine is heated at 180–200°C. with a fatty acid, esterification occurs, accompanied by the loss of at least two moles of water, to give "hexityl amines" (143); this reaction can be applied, for instance, to methyl- or hexadecylglucamine or methylfructosamine.

D. Amides derived from sugar acids

Treatment of a sugar lactone with a long-chain amine results in the opening of the lactone ring with the formation of an *N*-alkylamide. Thus, D-gluconolactone (XXIII) reacts with fatty amines to give amides (XXIV: R = C_7H_{15}, C_8H_{17}, C_9H_{19}, $C_{10}H_{21}$, $C_{12}H_{25}$, $C_{14}H_{29}$, $C_{16}H_{33}$, $C_{18}H_{37}$, and octadecadienyl) (39, 95, 97, 151). These amides can be converted to sulfonates by the action of chlorosulfonic acid (95, 96).



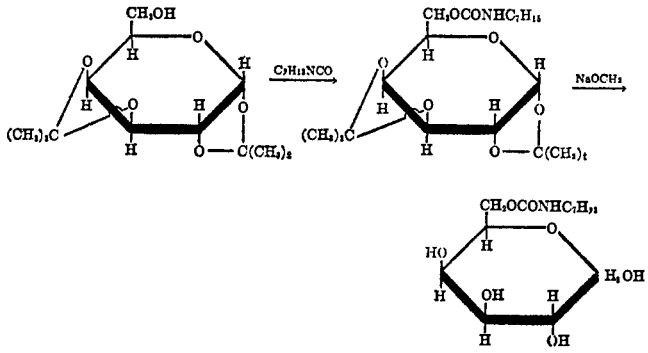
XXIII XXIV

N-Octadecylglucoheptonamide has been prepared in this way from glucoheptonolactone (39). Similar products can also be obtained by the reaction of a fatty amine with the methyl ester of an aldonic acid; this procedure has been used (39) to prepare the *N*-decyl-, *N*-dodecyl-, *N*-tetradecyl-, *N*-hexadecyl-, and *N*-octadecyl-L-arabonamides.

In order to prepare *N*-alkylglucuronamides from glucuronolactone it is necessary to protect the acetal group. On treatment with long-chain amines, β-methylglucofururonoside γ-lactone (XXV) and 1,2-isopropylideneglucofururonolactone (XXVIII) afforded the corresponding glucuronamides (XXVI and XXIX) (39). XXVI and XXIX were hydrolyzed to the *N*-alkylglucuronamides, which probably possess the pyranose structure (XXVII). Oxidation of XXVII with bromine water gave the corresponding *N*-alkyl glucosaccharonamides (XXX).

E. Urethan, urea, and hydrazide derivatives

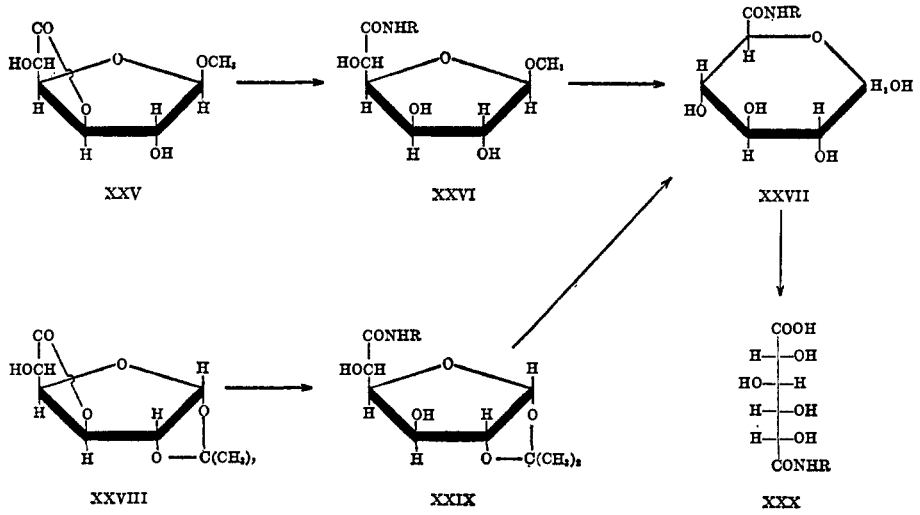
Since sugars are polyhydric alcohols, they are capable of reacting with several molecules of alkyl isocyanates to give polyurethans. In order that a specific known product may be obtained it is necessary to protect all the remaining hydroxyl groups. For instance, 1,2,3,4-diisopropylidenegalactose reacts with heptyl isocyanate to give the *N*-heptyl-6-urethan, which may be hydrolyzed to *N*-heptylgalactose-6-urethan (151).



1,2,3,4-Tetraacetyl-β-D-glucose can be converted into *N*-heptylglucose-6-urethan in the same way (151).

A number of *N*-alkyl sucrose monourethans have recently been prepared by the action of alkyl isocyanates on sucrose (60a, 89). It was shown that primary alcohols are much more reactive towards isocyanates than are secondary alcohols, and it was therefore considered that the products were 6- or 6′-derivatives (89).

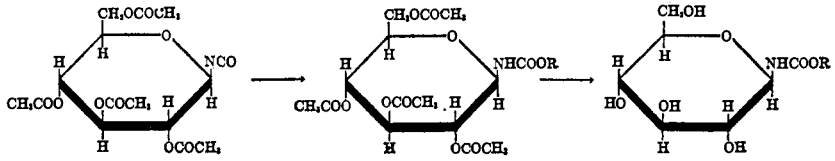
Tetraacetyl-β-D-glucopyranosyl isocyanate (XXXI) can be prepared from the corresponding bromide and silver cyanate (41, 85). On reaction with octyl, nonyl, decyl, undecyl, or dodecyl alcohol, XXXI is converted into the corresponding tetraacetylglucoseurethan,



XXV XXVI XXVII

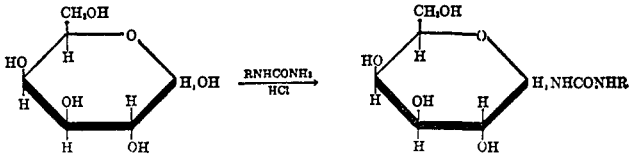
XXVIII XXIX XXX

which affords the glucoseurethan on hydrolysis with sodium methoxide (151):



XXXI

Erikson and Keps (35) have shown that *N*-dodecyl- and *N*-octadecylurea *N'*-galactosides are produced by the acid-catalyzed reaction of galactose with the alkylurea. This reaction is analogous to the formation of *N*-alkylglycosylamines.



The preparation of monoesters of *N*-glucosylurea (129) and of *N,N'*-diglucosyl urea (8) has recently been described (109, 110). Reaction of the glucosylurea with the methyl ester of a fatty acid and sodium methoxide in dimethyl sulfoxide affords the 6-acyl derivative, the structure of which was proved by periodate oxidation.

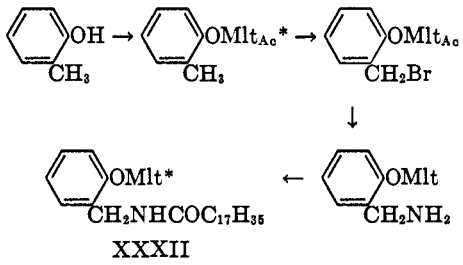
The products of the condensation of reducing sugars with fatty acid hydrazides have been described in the patent literature (56, 135, 136, 137).

V. ALKYL DERIVATIVES OF ARYL GLYCOSIDES

A number of carbohydrate derivatives containing a long-chain alkyl or acyl group as well as an aromatic ring have been described. For example, Odén (104) has prepared the tetralaurate, myristate, palmitate, and stearate of 2,4,6-tribromophenyl glucoside.

Nitration of 3-pentadecylphenol affords a mixture of the 4- and 6-nitro compounds, which react with tetraacetylglucosyl bromide to give the corresponding tetraacetylglucosides (91). The latter can be hydrogenated to the amines and the acetyl groups removed by hydrolysis.

Helferich and Petersen (63) prepared heptaacetyl-*o*-cresol α-maltoside by the reaction of octaacetyl-maltose with *o*-cresol in the presence of zinc chloride. Bromination converted the maltoside into the bromomethyl derivative, which with methanolic ammonia gave *o*-aminomethylphenyl α-maltoside. Successive treatment with stearoyl chloride–pyridine and methanolic ammonia then yielded the stearoyl amide (XXXII).

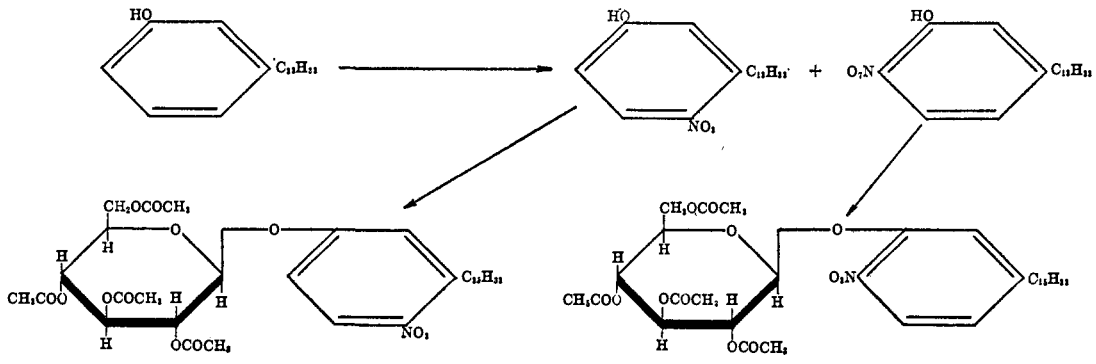


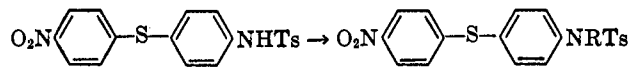
XXXII

*Mlt = α-maltosyl; Mlt_{Ac} = heptaacetyl α-maltoside.

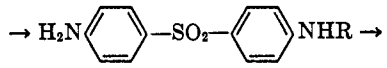
The preparation of some chaulmoogryl derivatives of galactosylaminodiphenyl sulfone has been investigated with a view to obtaining compounds having the pharmacological properties of the two groups. *p*-Nitro-*p'*-tosylaminodiphenyl sulfide (XXXIII) was alkylated with hexyl, octyl, dodecyl, chaulmoogryl, and hydnocarpyl iodides. Oxidation with hydrogen peroxide then gave the corresponding sulfones, which were treated with sulfuric acid to remove the tosyl group and with stannous chloride to reduce the nitro group. Reaction of the resultant amines with galactose gave the galactosylamines (XXIV: R = C_6H_{13}, C_8H_{17}, and $C_{12}H_{25}$), but the chaulmoogryl and hydnocarpyl analogs could not be prepared (2).

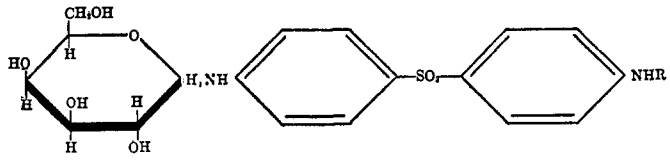
The chaulmoogroyl analog (XXXV) of XXXIV has been prepared from *p*-amino-*p'*-nitrodiphenyl-





XXXIII





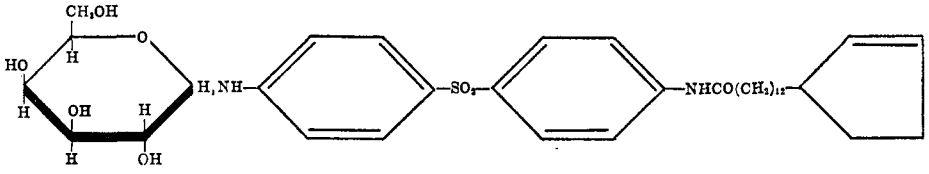
XXXIV

sulfone (XXXVI) by successive treatment with chaulmoogroyl chloride, stannous chloride, and finally galactose (100).

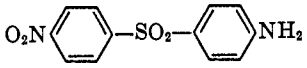
decylamine gluconate (43) is produced. Finally, it has been reported (133) that antioxidant compositions are produced by the interaction of fructose, betaine, and lauric acid.

VII. PROPERTIES AND USES

The majority of the compounds described above were synthesized in attempts to prepare materials with surface-active properties—detergents, dispersing or emulsifying agents, etc. By far the most important group of compounds are the mannitan and sorbitan esters (Spans) and their ethylene oxide condensation products (Tweens). The literature concerning the uses of these compounds is so extensive that only a few of the applications may be mentioned as examples. Hexitan esters are of value as detergents



XXXV

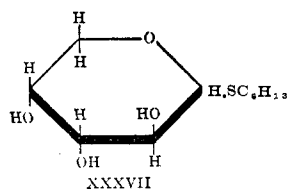


XXXVI

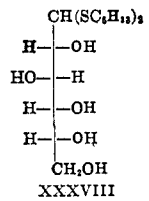
Finally, there has been a report of a substituted tolylurethan of glucose and sucrose (13). Alkylation of toluene with nonylene or dodecylene (from the polymerization of propylene) afforded an alkyltoluene, which was nitrated and then reduced to the alkyltoluidine. Reaction with phosgene then gave the isocyanate which, with glucose or sucrose, yielded the nonyl- or dodecyltolylurethan.

VI. MISCELLANEOUS COMPOUNDS

It has recently been reported (66) that carbohydrates may be characterized by the crystalline derivatives formed on reaction with hexyl mercaptan. Arabinose gives the thiohexylglycoside (XXXVII), while xylose, mannose, galactose, glucose, maltose, and lactose give bishexyl mercaptals, e.g., XXXVIII.



XXXVII



XXXVIII

1-Thiosorbitol, produced by the hydrogenation of a mixture of glucose, sulfur, and cobalt sulfide, can be alkylated with dodecyl bromide to give 1-dodecylthiosorbitol (37). When an aqueous solution of gluconic acid is shaken with heptadecylamine in ether, hepta-

(120), dispersing agents for insecticides (19, 20, 21), and plasticizers for vinyl resins (50); they may also be used in rust preventatives (30, 140) and for deicing aircraft (29). Triricinoleates of mannitol and sorbitol have been suggested (55) as deëmulsifiers for breaking petroleum emulsions.

However, the special value of these compounds lies in their lipophilic nature, compared with the hydrophilic properties of their ethylene oxide condensation products. Mixtures of the two types of compounds are of particular value as emulsifying and dispersing agents (53, 54).

The polyoxyethylene derivatives of hexitan esters can be used alone or mixed with the hexitan ester as dispersing agents for essential oils (147), for insecticides (90), and in pharmaceutical preparations; for example, those containing penicillin (141), progesterone (71), cortisone acetate (93), or DDT (70). Since these compounds are nontoxic, they may conveniently be used in foodstuffs (86), for example, as bread-softeners (31); it was estimated in 1952 that the average diet in the United States contained 0.5 g. of these polymers per person per day (119). Polyoxyethylene derivatives of hexitan esters have also been used to solubilize carotene (145), as ingredients of extinguishers for oil fires (27), as plasticizers for acrylonitrile–dichloroethylene copolymers (128), and in the prevention of fogging of transparent wrappers

(23). The condensation product of mannitan monopalmitate and the chloromethyl ether of nonaethylene glycol is of value as a detergent (45), and the use of a mixture of a polyoxyethylene sorbitan ester and the condensation product of *N*-methylglucamine with lauric acid as an emulsifier has recently been described (7).

The monoester and, to a lesser extent, the diesters of sucrose are of potential value as surfactants (59, 117, 122). However, the applicability of these compounds is restricted by their low solubility in water. It is claimed (44) that the sucrose ester of triisobutenylsuccinic acid and related compounds show greater water-solubility and can be used as detergents. The use of 3-stearoylglucose (111) and sucrose stearate (13b) as bread-softening agents has been reported, and the esters obtained from glucose or sucrose and stearoyl chloride showed emulsifying properties (57, 58). A number of esters, such as sucrose tetraoleate and glucose pentaoleate, can be used as lubricants (26). Esters of sorbitol hexahydroxyethyl ether show emulsifying and wetting properties (127), and the reaction products from hexitols and α-hydroxy acids may be used in linoleum cements (28).

Octakis(2-hydroxypropyl)sucrose, obtained by the action of propylene oxide on sucrose (3), reacts with methyl esters of fatty acids in the presence of sodium methoxide to give esters which may be used as emulsifying agents (4).

The linseed oil fatty acid esters of sucrose (13a), sorbitol (16), xylitol (148), and methyl α-D-glucoside (48), and the monoglucosides of ethylene glycol or glycerol (146) have been suggested as drying oils. The hexitol esters of the fatty acids of sardine oil can also be used in this way.

The *N*-alkylgluconamides (XXIV) have been reported (97) to be wetting agents and useful in the mercerization of cotton. On the other hand, these compounds were considered (39) insufficiently water-soluble to be useful emulsifying agents. Contrary to expectation, *N*-octadecylglucoheptonamide was even less soluble than the corresponding hexose derivative (39).

The products obtained from *N*-alkylglucamines by heating with a fatty acid (143) or by an exchange reaction with a methyl ester (130) can be used as detergents, as may sulfated *N*-acylglucamines (131). It has been claimed (109, 110) that the 6-acyl derivatives of *N*-mono- and *N,N'*-diglucosylurea have excellent detergent properties. Finally, the products of the reaction of fatty acid hydrazides with sugars are of value as textile assistants, showing wetting, foaming, dispersing, and levelling properties (56, 135, 136, 137).

In order that a fatty derivative of a carbohydrate shall be sufficiently water-soluble to be an effective surface-active agent in aqueous media, it appears to be necessary, either for at least two separate carbohydrate groups to be present (as, for example, in the disucrose ester of triisobutenylsuccinic acid or in the diglucosylurea esters) or to increase the solubility of a compound which contains only a single carbohydrate moiety by the introduction of solubilizing groups (such as the ethyleneoxy groups in the Tweens).

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