Polymers and Copolymers of Unsaturated Derivatives of Di-O-isopropylidene-D-galactopyranose

by

Joseph Adams Colquhoun B.Sc.

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SUMMARY

The purpose of this study was the synthesis of new derivatives of galactose of possible industrial potential. It is believed that the preparation of synthetic polymers and copolymers based on galactose monomers is a promising method of introducing galactose to the chemical industry.

In order to ensure the formation of linear polymers, only monofunctional monomers of galactose have been considered. For this reason, 1,2:3,4-di-O-isopropylidene-α-D-galactopyranose was used as starting material.

Crystalline 6-O-acryloyl-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (diisopropylidenegalactose acrylate, DGA) was prepared by transesterification with ethyl acrylate in the presence of titanium isopropoxide as catalyst.

The crystalline methacryloyl ester, 1,2:3,4-di-O-isopropylidene-6-O-methacryloyl-α-D-galactopyranose (diisopropylidenegalactose methacrylate, DGM) was prepared in a similar manner using methyl methacrylate as the transesterifying agent.

6-O-Allyl/

6-O-Allyl-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (allyl diisopropylidenegalactose, ADG) was prepared by a modification of the standard allylation procedure. Distillation under high vacuum gave the pure compound as a colourless oil which failed to crystallise.

2,3-O-Isopropylidene-1-O-methacryloyl-DL-glyceritol (isopropylideneglyceryl methacrylate, IGLM) was prepared for comparison purposes.

Deacetonation of diisopropylidenegalactose methacrylate yielded the crystalline, water-soluble monomer, 6-O-methacryloyl-α-D-galactopyranose (α-GM). This monomer was prepared for polymerisation in theoretical yield as an aqueous syrup (GM).

The molecular structures of all five monomers were confirmed by proton magnetic resonance spectroscopy.

Diisopropylidenegalactose methacrylate and diisopropylidenegalactose acrylate were polymerised in benzene solution, under nitrogen with azobisisobutyronitrile as initiator, to give polymers (P-DGM and P-DGA) of high molecular weight.

Removal/

Removal of the isopropylidene residues from these polymers was achieved by hydrolysis at 20° with aqueous formic acid to give the novel, water-soluble, synthetic "polysaccharides", poly-(6-O-methacryloyl-D-galactose) [poly-(galactose methacrylate) (P-GM)] and poly-(6-O-acryloyl-D-galactose) [poly-(galactose acrylate) (P-GA)].

The deacetonated polymers were characterised by standard carbohydrate reactions and the products of acetylation, benzoylation, phenylcarbamoylation, nitration, phenylhydrazone formation, phenylosazone formation, oxidation and reduction are described.

Three deacetonation procedures for the conversion of poly-(isopropylideneglyceryl methacrylate) (P-IGLM) into linear, water-soluble poly-(glyceryl methacrylate) (P-GLM) were worked out and the extent of reaction determined by the formaldehyde released on quantitative periodate oxidation.

By comparing the properties (e.g. glass transition temperature, hydrolysis of isopropylidene residues, and cross-linking reactions) of galactose and glycerol polymers, it was possible to assess the influence of the heterocyclic ring/

ring and glycosidic hydroxyl group of the galactose moiety in synthetic polymer systems.

Some solution properties of poly-(galactose methacrylate) are described.

The reactivity ratios for the free radical copolymerisation, methyl methacrylate (MM)- diisopropylidene-galactose methacrylate (DGM), were determined and were:

$$r_1 = 0.93 \pm 0.03 \text{ (MM)}$$
$$r_2 = 1.30 \pm 0.19 \text{ (DGM)}$$

This agreed with the general principle that increase in size of the alkyl group in an ester of an α.β-unsaturated acid does not greatly influence the reactivity ratios of such esters with many vinyl monomers. These values also showed that DGM could be copolymerised in any proportion with MM to give a final copolymer containing these units in approximately the initial monomer ratio. This was found in practice.

A series of galactose methacrylate-methyl methacrylate random copolymers, containing different proportions/

proportions of sugar residues, was prepared and it was shown that the hydrophilic properties could be accurately controlled by the amount of galactose methacrylate in the copolymer. The industrial significance of this reaction is discussed.

Successful copolymerisations of diisopropylidenegalactose acrylate and methyl acrylate, diisopropylidenegalactose methacrylate and styrene, diisopropylidenegalactose acrylate and acrylonitrile, diisopropylidenegalactose methacrylate and vinyl acetate, and allyl diisopropylidenegalactose and maleic anhydride, are described, and in most cases, the copolymers were readily deacetonated and characterised by phenylhydrazone formation.

Evidence is presented to show that, in general, the introduction of reducing sugar units is a convenient method of increasing the reactivity and hydrophilicity of synthetic polymers and copolymers.

Possible industrial applications of galactose polymers and copolymers are discussed.

CONTENTS

1. INTRODUCTION

Naturally occurring polymeric materials have fed, clothed and given shelter to mankind from Creation. However, lack of understanding of the structures of these important materials thwarted classical organic chemists for many years. In the last fifty years, however, after the pioneering researches of those such as Staudinger, Carothers and Flory, a vast world-wide synthetic polymer industry has been formed and continues to grow. The synthetic polymer production in the U.K. alone nears two million tons annually.

Synthetic polymers have many economic and physical advantages over naturally occurring materials. A variety of monomeric building units at man's disposal can be homopolymerised or copolymerised to give products with specific properties, determined by the chemical structure of the monomer or monomers. The principal products are fibres, synthetic rubbers, thermosetting resins (adhesives, surface coatings, composites, etc.) and thermoplastics (mouldings, transparent sheet, surgical implants, packaging etc.).

The heavy organic chemical industry is now committed to existing monomers for the production of cheap materials and it is unlikely that any new monomer with only marginally better properties will emerge because of the enormous capital investment required. Therefore any new polymer system must necessarily have novel properties and/

and as such be used as a high-cost, specialised product. Current research in polymer science is directed towards the preparation of polymer systems which maintain their shape and strength up to about 500°C and to systems which maintain elastomeric properties at extremely low temperatures. As these systems would be used in supersonic aircraft or spacecraft, cost would be of secondary importance.

There are, however, certain fields at the present time where synthetic polymers cannot compete with natural materials such as the polysaccharides. Cellulose is the most important of these. The comfortable, moisture absorbing properties of cotton fabrics and the huge consumption of cellulose in paper manufacture will always ensure that this cheap, readily available material will be used by the chemical industry. The novel, thermally-reversible gelling properties of the water-soluble, algal polysaccharides, agar, and kappa-carrageenan have not yet been equalled by synthetic systems, although the limited availability, both actual and political, of the parent seaweeds is causing concern to the food industry at the present time.

Several attempts have been made to combine the properties of synthetic polymers with those of the polysaccharides by the preparation and polymerisation of vinyl monomers containing carbohydrate residues. These will be reviewed later. The first successful preparation of linear polymers combining these properties, natural with synthetic, hydrophilic with hydrophobic, resulted/

resulted from the study of Black, Dewar and Rutherford[1] on unsaturated derivatives of 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose. The 3-O-methacryloyl derivative of this compound yielded linear, organic soluble, methacrylate polymer containing the bulky diisopropylideneglucofuranose residue on every second carbon atom of the polymer chain. Removal of the protecting isopropylidene groups yielded the novel, water-soluble, synthetic "polysaccharide", poly-(glucose methacrylate), which was characterised by standard carbohydrate reactions. This polymer differed from natural polysaccharides in that every polymer unit contained the reactive glycosidic hydroxyl group at C-1. Oxidation gave poly-(gluconic acid methacrylate) which had properties comparable with those of natural polyuronides. The research described in this thesis is a consequence of this work and is concerned with polymers and copolymers of unsaturated derivatives of 1,2:3,4-di-O-isopropylidene-α-D-galactopyranose.

Although D-galactose occurs widely in nature as a constituent of polysaccharides, the only economic source for its production is 4-O-β-D-galactopyranosyl-D-glucopyranose (lactose) from which it is easily prepared by acidic hydrolysis and fractional crystallisation from the concentrated, neutralised hydrolysate. Lactose is produced commercially as the crystalline α-monohydrate in about 3% yield from whey, a by-product of cheese production. According to Harding[2], the total annual production of whey in the U.K. is about 200 million gallons. Of this total only 40 million gallons are currently utilised in lactose production,/

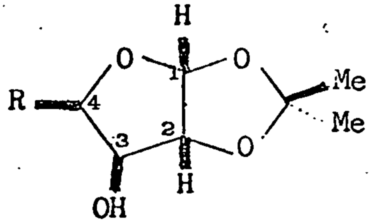
production, but if all available whey were used for lactose production and this material hydrolysed to galactose, the maximum production of galactose, based on a 25% yield (theory 50%) from lactose, would be approximately 7,000 tons annually in the U.K. The current price of galactose is about £1,750/ton. Obviously galactose can never compete with glucose (£76/ton) on grounds of cost or availability, and if it is ever to be introduced to the chemical industry, it could conceivably be in the form of pure galactose monomers, for the plastics and polymer industry frequently uses expensive monomers for the production of materials with unique chemical and physical properties or for modifying the properties of cheap polymers by copolymerisation. A typical example of an expensive polymer with unique, heat-resistant properties is poly(tetrafluoroethylene). It is possible that "blocked" galactose monomers could give rise to polymers and copolymers with special properties.

Acetone condenses with neighbouring cis hydroxyl groups of the cyclic aldoses to form isopropylidene derivatives. These compounds have been reviewed by Mills[3] and de Belder[4]. Under the reversible conditions of reaction, the composition of the products is quite independent of the mechanism of reaction, and is determined solely by the relative thermodynamic stabilities of the constituents, even though the rate of the individual reactions may be very different.

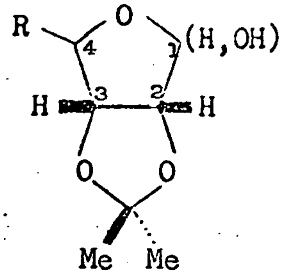
The commonest structure formed has the 1,3-dioxolane

ring/

ring fused *cis* to a furanose ring either on the 1,2 or 2,3 positions of the aldofuranose. The other isopropylidene group (5,6, or 3,5 as in xylofuranose) is extremely acid labile and may be removed by partial acid hydrolysis to give the stable structure (I) or (II)



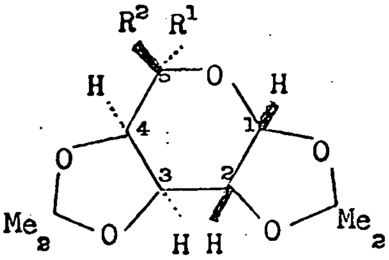
(I)



(II)

The ring junction is *cis* and the two rings are in the shape of a V- into the plane of the paper. Heavy lines are *exo*-substituents (outside the V) and dotted lines are *endo*-substituents (inside the V). Hence a structure with the least number of *endo* substituents is preferred. This is shown by the preferential formation of 2,3-*O*-isopropylidene-β-D-ribofuranose in which all substituents other than one Me group are *exo*. Similar arguments can explain the observed formation of 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose and the 2,3:5,6-derivatives of gulose and talose.

The only examples where the aldose reacts in its pyranose form with acetone under equilibrium conditions are the 1,2:3,4-di-*O*-isopropylidene derivatives of arabinose, galactose and altrose.



$R^1 = R^2 = H$, L-arabinose

$R^1 = H, R^2 = CH_2OH$, D-galactose

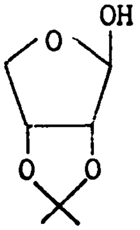
$R^1 = CH_2OH, R^2 = H$, L-altrose

(III)

The steric arrangement is cis-anti-cis (III). This involves much smaller repulsions between substituents than the isomeric cis-syn-cis arrangement as evidenced by the failure of ribose to form a 1,2:3,4-di-*O*-isopropylidene derivative.

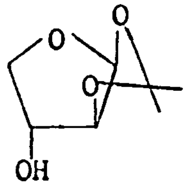
The major products formed on condensation of acetone with the aldoses are given below.

Tetroses



β-D-Erythrofuranose

2,3-*O*-

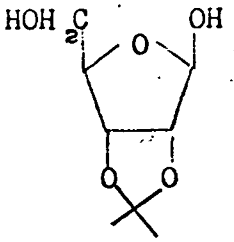


β-D-threofuranose

1,2-*O*-

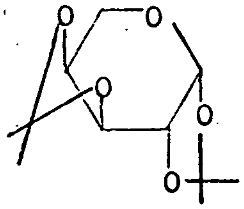
Pentoses/

Pentoses



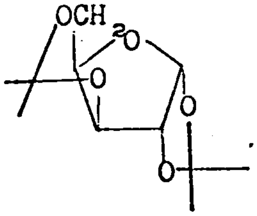
β-D-Ribofuranose

2,3-*O*-



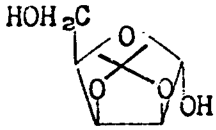
β-L-Arabinopyranose

1,2:3,4-di-*O*-



α-D-Xylofuranose

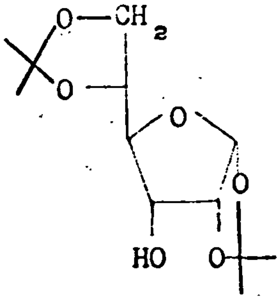
1,2:3,5-di-*O*-



α-D-Lyxofuranose

2,3-*O*-

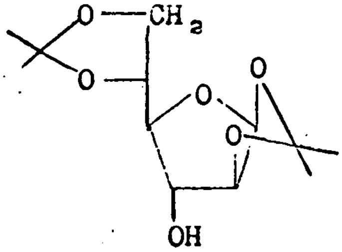
Hexoses



α-D-Allofuranose

1,2:5,6-di-*O*-

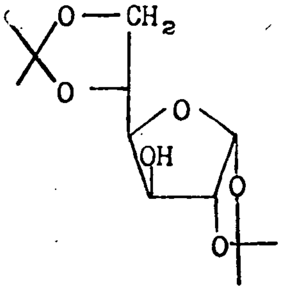
2,3:5,6-predicted (a)



β-D-Altrofuranose

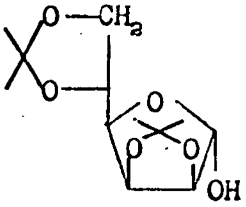
1,2:5,6-di-*O*-

and 1,2:3,4-pyranose



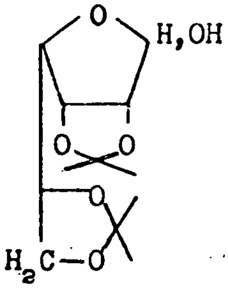
α-D-Glucofuranose

1,2:5,6-di-*O*-

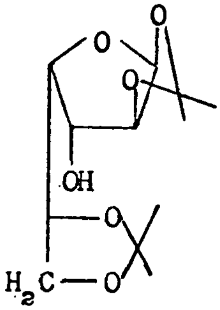


α-D-Mannofuranose

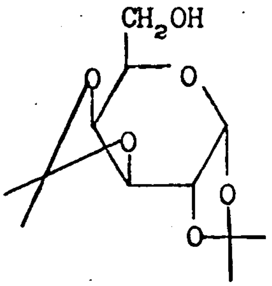
2,3:5,6-di-*O*-



D-Gulofuranose
2,3:5,6-di-*O*-
and 1,2:5,6-di-*O*-



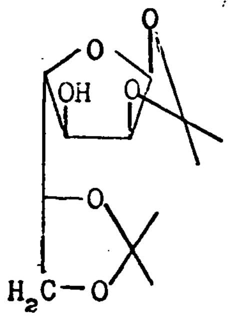
β-D-Idofuranose
1,2:5,6-di-*O*-



α-D-Galactopyranose

1,2:3,4-di-*O*-

and 1,2:5,6-furanose



β-D-Talofuranose

1,2:5,6-di-*O*-

and 2,3:5,6-di-*O*-

(a) 1,2:5,6-Di-*O*-isopropylidene-α-D-allofuranose was prepared by inversion at C-3 of the corresponding glucose derivative. The 2,3:5,6- compound has not been prepared.

Cyclic acetals of the aldoses are also formed by condensation with other aldehydes and ketones e.g. with formaldehyde (methylene derivatives), acetaldehyde (ethylidene derivatives) and benzaldehyde (benzylidene derivatives). The rates of acid hydrolysis of these acetals are benzylidene > isopropylidene > ethylidene > methylene and this should be taken into account when preparing blocked, monofunctional monomers for the ultimate production of water-soluble polymers. It can be seen that only the tetroses and the hexoses will give monofuctional monomers and of these only altrose and galactose will exist in the pyranose form. This may be an important factor in view of subsequent polymerisation reactions. The extra carbon linkage at C-6may decrease steric overcrowding between the bulky carbohydrate residue and the polymerisable vinyl group. Galactose is a readily crystallisable sugar as are many of its derivatives. This is an important factor when purifying monomers for polymerisation as it is well known that purity of the monomer is perhaps the most important factor in determining high molecular weight.

2. MONOMERS

2.1 Literature Survey

Many examples of unsaturated derivatives of carbohydrates have appeared in the literature but only those derivatives which are polymerisable will be reviewed here.. Acryloyl and methacroyloyl derivatives have had most attention in this respect due to their ease of polymerisation with free radical initiators or by heat alone. Earlier work in this field was mainly concerned with making insoluble cross-linked polymers for use in surface coatings and resins, rather than with well-defined linear polymers; consequently, no special care was taken to control the degree of substitution. In certain cases complete substitution of all the free hydroxyl groups in the sugar unit was achieved in an effort to gain the highest degree of cross-linking in the final polymer.

Treadway and Yanovsky[5] prepared methacrylic esters of several carbohydrates. Glucose, for example, when heated at 65° with methacrylic anhydride in pyridine, formed a pentamethacrylate which gelled in the presence of benzoyl peroxide or copper naphthenate in solution in organic solvents. The derivative became insoluble in organic solvents when it was heated in air at 100° for two hours. Other derivatives reported, all with the/

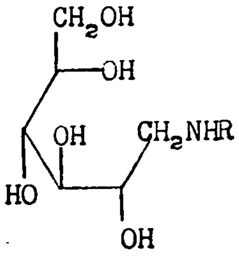
the same tendency to polymerise, were the fully methacrylated derivatives of maltose, dextrin and starch.

Haworth *et al*[6] formed dimethacrylate and diacrylate esters from derivatives of D-mannitol and D-glucitol, including the 1,4:3,6-dianhydrides and 2,4:3,5-di-*O*-methylene acetals of both hexitols, by treatment in sodium hydroxide solution with methacryloyl or acryloyl chloride. The outstanding feature of these di-esters was their ready polymerisation to form hard, transparent, insoluble resins.

Interest in nitrated polymers led Wolfrom *et al*[7] to synthesise the 3-*O*-acryloyl and 3-*O*-methacryloyl derivatives of D-mannitol pentanitrate. Reaction with acryloyl chloride in acetonitrile containing *N*,*N*-dimethylaniline gave in 72% yield the crystalline 3-*O*-acryloyl derivative, which polymerised with benzoyl peroxide, but only low molecular weight, gumming polymers were obtained. The syrupy 3-*O*-methacryloyl derivative, similarly prepared in 40% yield, polymerised to a hard polymer on exposure to light and air.

Whistler, Panzer and Roberts[8] discussed the advantages of polymers containing sugar units attached to every second carbon atom in a hydrocarbon chain and emphasised the commercial importance of synthetic polymers of a hydrophilic nature. Preferring a straight chain sugar to a ring form for this purpose, they synthesised *N*-acryloyl and *N*-methacryloyl derivatives/

derivatives of 1-amino-1-deoxy-D-glucitol by N-acylation with the appropriate acid anhydrides in methanol at temperatures below 0°:-



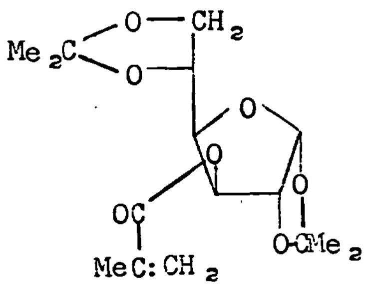
where R = CH_2:CHCO

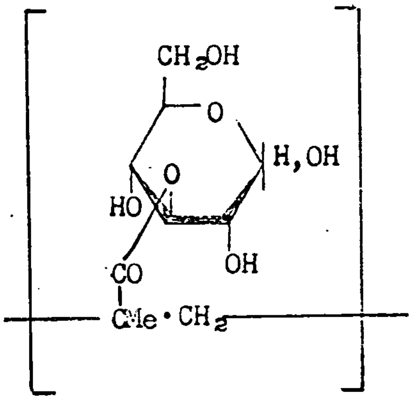
or

CH_2:CMeCO

These authors found that saturated aqueous solutions of the unsaturated amides were polymerised to viscous solutions by ultraviolet and gamma irradiation and to insoluble gels with ammonium persulphate; treatment of the monomers in dimethylformamide solution with azobisisobutyronitrile or benzoyl peroxide initiators at 60-100° gave high yields of water-soluble, but low molecular weight, polymers.

In a preliminary note Bird et al[9] described the preparation, polymerisation and deacetonation to water-soluble polymer of the monomer, 1,2:5,6-di-O-isopropylidene-3-O-methacryloyl-α-D-glucofuranose.

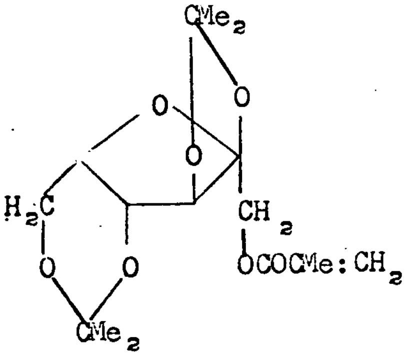




These/

These authors described, in a later publication[10], the characterisation of the deacetonated homopolymer, poly-(3-O-methacryloyl-D-glucose) by standard carbohydrate reactions. Complete substitution of all four free hydroxyl groups was difficult and acetylation, methylation and phenylcarbamoylation yielded approximately trisubstituted derivatives. Oxidation with chlorous acid yielded the polymeric aldonic acid which had certain similarities to the naturally occurring polyuronic acids such as alginic acid. Reactions of the reducing group in the polymer led to partly substituted derivatives, complete substitution being prevented by precipitation of the polymer derivative before the reaction had gone to completion. Thus a partially substituted polymer phenylhydrazone, diphenylformazan and dithioacetal were described.

Kimura et al[11] prepared 2,3:4,6-di-O-isopropylidene-1-O-methacryloyl-α-L-sorbofuranose from the sorbose diacetal and methacryloyl chloride.

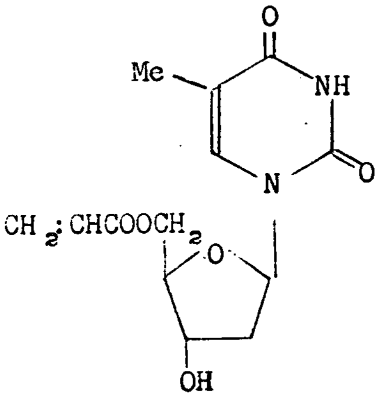


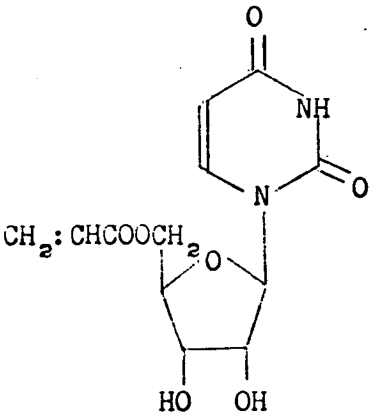
A/

A later publication[12] showed that they had difficulty in the preparation of the fully deacetonated polymer as reducing power and periodate oxidation gave low results. This was explained by acid reversion.

Anikeeva and Danilov[13] prepared monomethacryloyl esters from xylitol derivatives. These were the 2,4:3,5-dimethylene, 2,4:3,5-dibenzylidene, 2,3:4,5-diisopropylidene, 1,4-anhydro-3,5-methylene, 1,4-anhydro-3,5-benzylidene and 1,4-anhydro-3,5-isopropylidene acetals. The mono-esters were prepared from the corresponding acetal in pyridine with methacrylic anhydride or with methacryloyl chloride in the presence of 20% aqueous alkali at 0°. The polymerisation of these monomers was not reported.

DNA type macromolecules have been prepared by Cassidy and Jones[14] from 5′-*O*-acryloylthymidine and 5′-*O*-acryloyluridine.

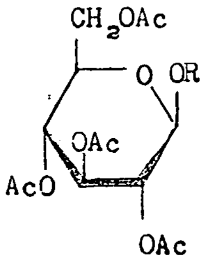




Treatment of thymidine with one molecular proportion of acrylic anhydride gave the 5′-*O*-acryloyl derivative as the major product. The/

The 5′-O-acryloyl-uridine derivative was prepared from 2′,3′-O-isopropylidene-uridine followed by deacetonation with dilute acid. These monomers were copolymerised with acrylamide to give a series of water-soluble copolymers. A fraction of the copolymer of 5′-O-acryloyluridine and acrylamide formed a hybrid with denatured DNA.

Commercial interest in monomeric sugar derivatives is shown by a recent U.S. Patent[15]. A number of vinyl monomers were prepared by a Koenigs-Knorr reaction of 2,3,4,6-tetra-O-acetylglucopyranosyl halide with methacrylic and acrylic acid, and their hydroxyethyl and hydroxypropyl esters.



$R = CH_2{:}CMeCO,\ CH_2{:}CHCO,$

$CH_2{:}CMeCOO(CH_2)_2,\ CH_2{:}CHCOO(CH_2)_2$

$CH_2{:}CMeCOO(CH_2)_3,\ CH_2{:}CHCOO(CH_2)_3$

The crystalline β-glycosides were polymerised in benzene solution with azobisisobutyronitrile to give organic soluble polymers. Poly-(tetra-O-acetylglucosyloxyethyl methacrylate) was deacetylated with sodium methoxide in chloroform to yield water-soluble polymer, poly-(glucosyloxyethyl methacrylate) which was not characterised.

Three new sugar monomers have been reported[16] recently from Japan. Tetra-O-acetyl-1-O-methacryloyl-D-glucose- described above -, and tetra-O-acetyl-1-O-methacryloyl-D-galactose were prepared/

prepared by glycosidation of the corresponding glycosyl bromide. 1,2,3,4-Tetra-*O*-acetyl-6-*O*-methacryloyl-*D*-glucose was prepared from glucose tetraacetate with methacryloyl chloride, using triethylamine as hydrogen chloride acceptor. The polymethacrylates obtained were converted into water-soluble polymers on deacetylation with sodium methoxide. 1,2:3,4-Di-*O*-isopropylidene-6-*O*-methacryloyl-α-*D*-galactopyranose was prepared by esterification of diisopropylidenegalactose with methacryloyl chloride. *N*-Methacryloyl-*D*-glucosamine was prepared by esterification of 2-amino-2-deoxy-*D*-glucose with methacrylic anhydride.

Alkyl vinyl ethers, $CH_2{:}CH\ O\ R$, are generally polymerised with cationic catalysts such as boron trifluoride and modified Ziegler-Natta catalysts. Vinyl carbohydrate ethers have been reviewed by Rutherford[16] and several examples of polymerisation quoted. However, Whistler and Seib[17] have shown that isopropylidene derivatives of *D*-glucofuranose, particularly the 1,2-*O*-isopropylidene derivative, eliminated acetone with boron trifluoride to form a highly branched, water-soluble glucan.

The polymerisation of mono allyl ethers of carbohydrates to polymers of high molecular weight has not been reported.

Helferich and Höffman[18] synthesised *p*-hydroxystyrene β-*D*-glucoside from *p*-ethylphenyl tetra-*O*-acetyl-α-*D*-glucoside. Details of polymerisation were reported.

Synthetic/

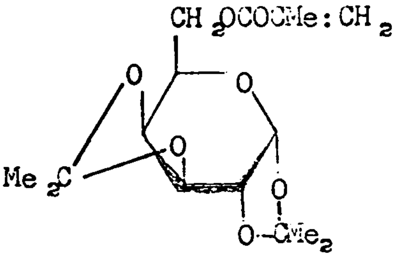
Synthetic carbohydrate polymers may also be prepared from carbohydrate derivatives other than vinyl-type derivatives. Previous work[19] in this Institute has demonstrated that a range of high molecular weight nylon-type linear carbohydrate polyamides can be synthesised from substituted carbohydrate diamines and diacid chlorides by interfacial polycondensation. The hydroxyl groups in the sugar monomers were protected by methylene, benzylidene, and isopropylidene residues, and in some cases it was possible to remove the blocking groups from the polymers to yield hydroxypolyamides.

Mention may also be given to the synthetic polysaccharides prepared from monosaccharide units. Examples of these are the acid catalysed polymerisation of 1,6-anhydro-α-D-galactopyranose[20], the basic polymerisation of 5,6-anhydro-3-O-methyl-1,2-O-isopropylidene-α-D-glucofuranose[21] and the polycondensation of free sugars when heated above their melting point under vacuum[22].

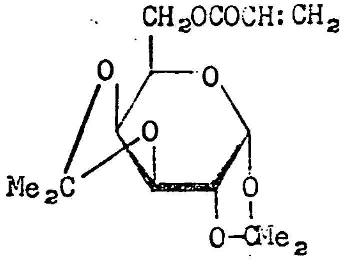
An interesting development has been the first chemical synthesis of a stereoregular polysaccharide. Ruckel and Schuerch[23] prepared poly-α-(1→6)-anhydro-D-glucopyranose (dextran) by the phosphorus pentafluoride-catalysed polymerisation of 1,6-anhydro-2,3,4-tri-O-benzyl-β-D-glucopyranose and subsequent debenzylation. The chemical synthesis of polysaccharides has been reviewed by Goldstein and Hullar[24].

2.2 Results and Discussion

Di-*O*-isopropylidene-*D*-galactose has been shown by mass spectrometry to be a mixture[25], the major component (>97%) under normal conditions of preparation being the syrupy isomer, 1,2:3,4-di-*O*-isopropylidene-α-*D*-galactopyranose, and the minor being crystalline 1,2:5,6-di-*O*-isopropylidene-α-*D*-galactofuranose. Mr. Tom Bird and Dr. David Rutherford in this laboratory first prepared the 6-*O*-methacryloyl and 6-*O*-acryloyl derivatives of the galactopyranose acetal[26,27]. Treatment of crude diisopropylidenegalactose in pyridine with methacrylic anhydride at 65° yielded the crystalline monomer, 1,2:3,4-di-*O*-isopropylidene-6-*O*-methacryloyl-α-*D*-galactopyranose (diisopropylidenegalactose methacrylate, DGM,IV) in 47.5% yield.



(IV)



(V)

The 6-*O*-acryloyl derivative could not be prepared directly from/

from acrylic anhydride. Hickmott[28] showed that acryloyl chloride reacts with alcohols (ROH) in the presence of pyridine or other tertiary amines in a different way from methacryloyl chloride. The main product of the reaction is the water-soluble 1-2′-alkoxycarbonylethylpyridinium chloride which breaks down with cold sodium hydroxide to give the acrylate ester by elimination of pyridine hydrochloride.

$$\mathrm{ROH + CH_2{:}CH{\cdot}COCl + C_5H_5N \longrightarrow RO_2C{\cdot}CH_2{\cdot}CH_2{\cdot}\overset{+}{N}C_5H_5Cl^-}$$

$$\xrightarrow{\mathrm{OH}'} \mathrm{RO_2C{\cdot}CH{:}CH_2 + H\overset{+}{N}C_5H_5Cl^-}$$

Diisopropylidenegalactose reacted with acrylic anhydride in a similar manner to give a water-soluble adduct which was broken down with sodium hydroxide to give the crystalline ester (V) in low (14%) yield.

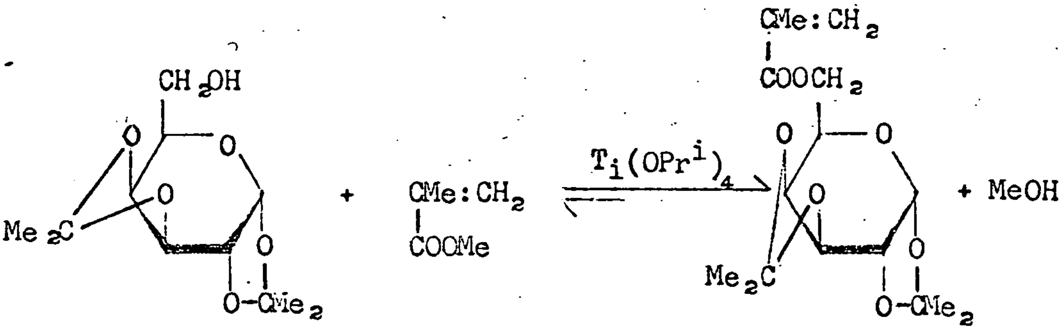
6-*O*-Acryloyl-1,2:3,4-di-*O*-isopropylidene-α-*D*-galactopyranose (diisopropylidenegalactose acrylate, DGA, V) was best prepared (52.6%) by a transesterification reaction between ethyl acrylate and diisopropylidenegalactose in the presence of titanium isopropoxide as catalyst and *p*-methoxyphenol as polymerisation inhibitor.

All other monomer syntheses and modifications of known syntheses were carried out for the first time by the author.

As methacrylic anhydride is such an expensive chemical, an alternative method for the preparation of DGM was sought.

It/

It was found that the transesterification reaction for the preparation of DGA could be successfully applied to the preparation of DGM using methyl methacrylate as the transesterifying agent. The first report of this method[29] described the use of p-methoxyphenol as polymerisation inhibitor. This procedure, however, had the disadvantage of requiring a charcoal decolorisation step. By using tetrachloroquinol as polymerisation inhibitor, this step was not required and it is recommended that this inhibitor be used in transesterification reactions of the above type owing to its low volatility and efficiency.



(IV)

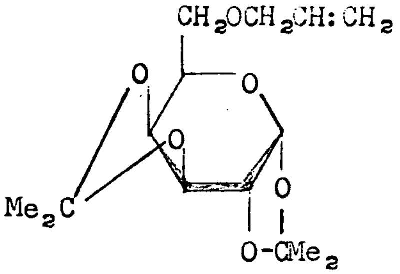
Continuous removal of methanol by distillation drove the equilibrium to the right and reaction was essentially complete after 1 hr. at 110°. Pure DGM was isolated in 75.2% yield by a recrystallisation procedure using ethanol/water. The high yield of the pure crystalline monomer, together with the cheapness and availability of methyl methacrylate, indicates that/

that this method of preparation could be used on an industrial scale.

Allyl ethers of carbohydrates are readily synthesised by direct allylation with allyl bromide in the presence of excess sodium hydroxide.

$$ROH + CH_2{:}CHCH_2Br \xrightarrow{NaOH} ROCH_2CH{:}CH_2 + HBr$$

Although allyl compounds do not readily homopolymerise, they copolymerise with compounds such as maleic anhydride and vinyl acetate where the reactivity ratios are favourable. With this objective in mind, the 6-O-allyl ether of diisopropylidenegalactose, 6-O-allyl-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (ADG, VI) was prepared[29].



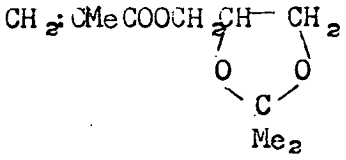
(VI)

Two treatments of diisopropylidenegalactose in p-dioxane with allyl bromide, in the presence of an excess of powdered sodium hydroxide, were necessary for complete reaction.

The/

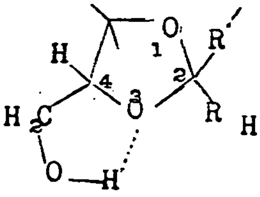
The pure compound was isolated in 91.8% yield as a colourless oil after distillation.

In order to evaluate the effect of heterocyclic structure and the glycosidic hydroxyl group on the physical and chemical properties of galactose polymers, the monomer, 2,3-*O*-isopropylidene-1-*O*-methacryloyl-DL-glyceritol (isopropylideneglyceryl methacrylate, IGLM, VII) was prepared for comparison.

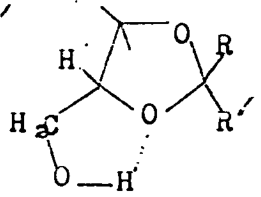


(VII)

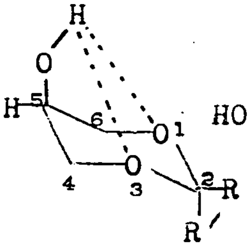
When a ketone ($RR'CO$) condenses with glycerol, two possible products may result, either the 2,2-disubstituted-1,3-dioxolane-4-methanol (VIII, IX) or the 2,2-disubstituted-*m*-dioxan-5-ol (X, XI)[30].



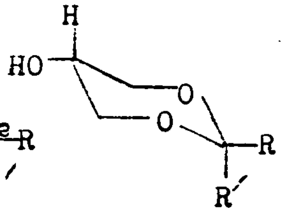
(VIII)



(IX)



(X)



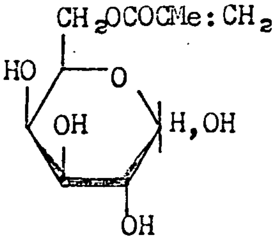
(XI)

In (X) the hydroxyl group is axial and stabilised by hydrogen bonding while in (XI) it is stabilised by being in an equatorial position, but in both geometrical isomers and both conformations one of the substituent groups on the 2-position is always axial. Thus the whole structure is sterically unfavoured relative to the dioxolane structures (VIII) and (IX) in which all groups occupy similar conformational positions and are relatively more stable, so that when ketones condense with glycerol, only the 2,2-disubstituted-1,3-dioxolane-4-methanols are obtained.

When R = R', these compounds exist as optical isomers and D-(-)-2,2-dimethyl-1,3-dioxolane-4-methanol has been synthesised[31] from 1,2:5,6-di-O-isopropylidene-D-mannitol. When R and R' are dissimilar, there are four isomers, each geometrical isomer (VIII) and (IX) possessing D and L forms[30].

IGLM (VII) was first described by Fegley and Rowland[32] and was prepared under identical conditions to that of DGM. IGLM is a colourless liquid and, as it is a racemic mixture, is optically inactive.

The water-soluble monomer, 6-O-methacryloyl-D-galactose (GM, XII) was also prepared[33].



(XII)

DGM (10%) was deacetonated in 80% formic acid, containing p-methoxyphenol as polymerisation inhibitor, the hydrolysis at 20° being followed polarimetrically in a 2 dm tube. The molecular rotation, defined as

$$M_D = \frac{[\alpha]_D \times M}{100} = \frac{\alpha}{C \times l}$$

where C is the concentration in g-mol/100ml solution, α is the rotation in circular degrees and l the length of the tube in dm, was used:

t(hr.)	0.25	0.5	1.0	1.5	2.5	3.5	4.5	6.0	24.0
M_D	-100	-66.7	-13.9	27.2	82.3	120.8	144.6	167.2	202.0

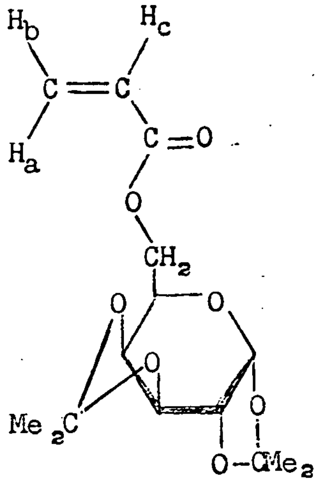
The extrapolated value at zero time for DGM was -133. After 24 hr..formic acid was removed by repeated evaporation at 35° and addition of water. D-Galactose 6-methacrylate (GM) was isolated in 48.0% yield as a white crystalline compound

(m.p./

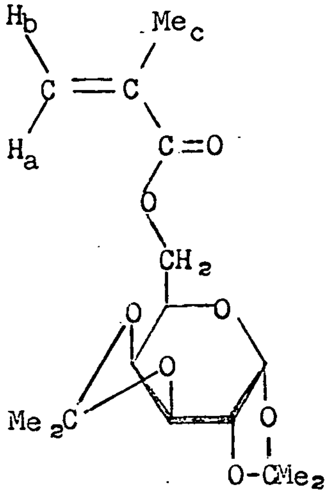
(m.p. 108-118°) from ethanol solution. This compound was mainly the α-anomer of (XII) as it mutarotated from $[\alpha]_D$ + 91.5° ⟶ + 53.8° in water. GM was further purified by recrystallisation from 90% ethanol to give the pure monomer, 6-O-methacryloyl-α-D-galactopyranose (α-GM), m.p. 142-145°, in 22.0% yield.

The infrared spectrum of α-GM showed hydroxyl absorption as a broad band between 3500 and 3100 cm^{-1} and as a sharp peak at 3560 cm^{-1}, ester carbonyl at 1710 cm^{-1}, and double bond unsaturation at 1638 cm^{-1}. The α-anomer was indicated[34] by anomeric C-H equatorial deformation at 844 cm^{-1}, and non-anomeric equatorial deformation was present at 880 cm^{-1}.

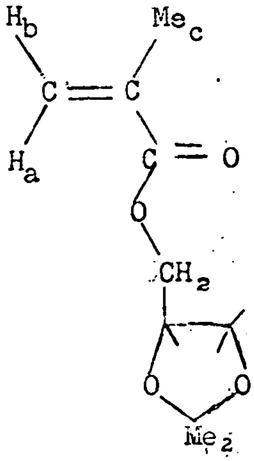
Proton magnetic resonance spectroscopy (p.m.r.) was used to confirm the molecular structures of DGM(IV)[29], DGA(V), ADG(VI)[29], IGLM(VII) and α-GM(XII)[33]. Cone and Hough[35] have analysed the p.m.r. spectra of a series of derivatives of 1,2:3,4-di-O-isopropylidene-α-D-galactopyranose at 60 MHz. It was claimed that the pyranose ring adopts a non-chair conformation in these derivatives. However, an X-ray analysis of the molecular structure of 1,2-O-aminoisopropylidene-α-D-glucopyranose hydroiodide[89] showed that the non-chair conformation assigned to 1,2-O-alkylidene-α-D-glucopyranose derivatives[90] from p.m.r. evidence was incorrect. Assignments for the above monomers were made by comparison with these spectra and with those of methyl acrylate[36], methyl methacrylate[37] and allyl alcohol[38].



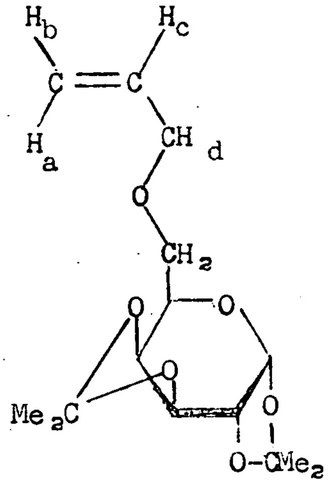
DGA, $C_{15}H_{22}O_7$



DGM, $C_{16}H_{24}O_7$



IGLM, $C_{10}H_{16}O_4$



ADG, $C_{15}H_{24}O_6$

Spectra were recorded in carbon tetrachloride solution on a Perkin-Elmer R10 (60MHz) NMR Spectrophotometer and chemical shifts (τ) were measured relative to tetramethylsilane (TMS). Integration/

Integration of all peaks in the p.m.r. spectrum of DGA (Plate I) showed the expected twenty-two protons. The pattern of peaks between 3.3 - 4.4τ corresponded to three protons and was identical to that of the three olefinic protons in the p.m.r. spectrum of methyl acrylate.

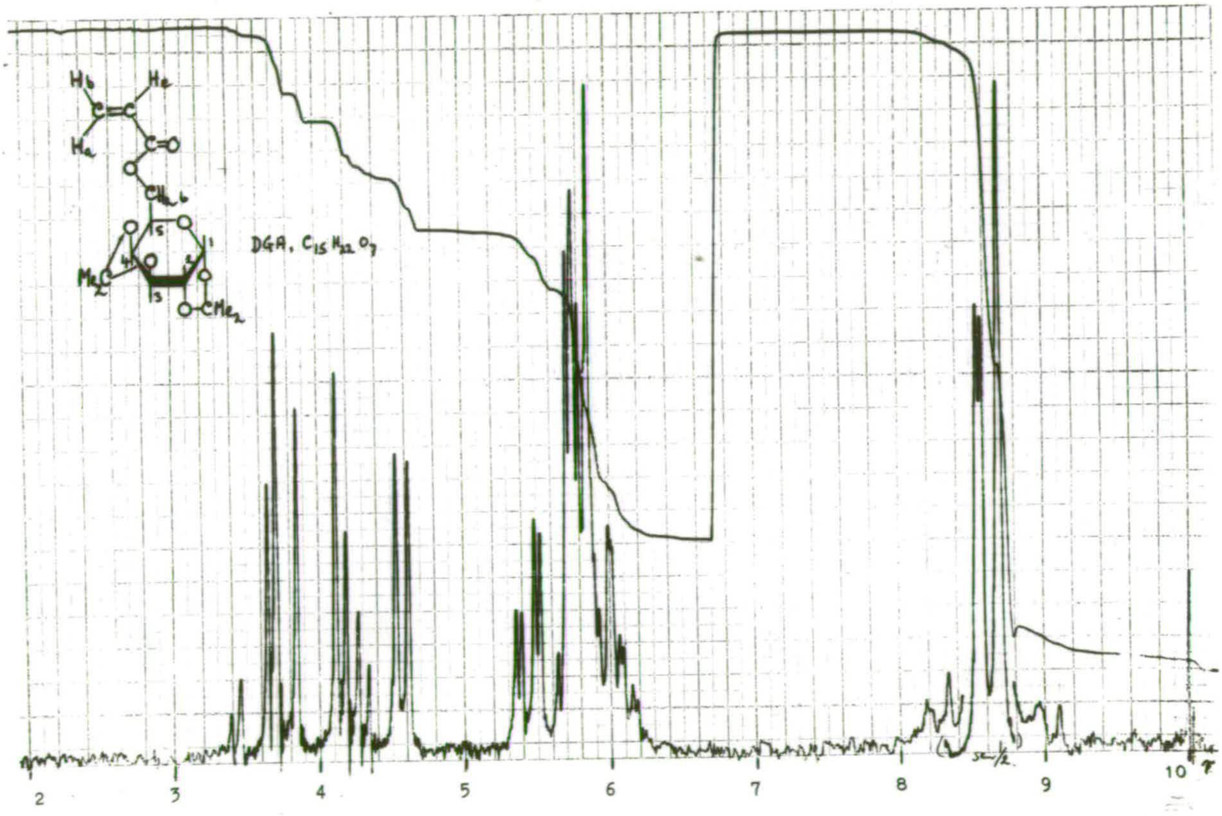


Plate I. The p.m.r. spectrum of 6-O-acryloyl-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (V)

The/

The one proton doublet at 4.57τ was readily assigned to H-1 and the spacing gave the coupling constant $J_{1,2}$ = 5.0 Hz. The one proton quartet at 5.43τ was assigned to H-3, $J_{3,2}$ = 2.4 Hz and $J_{3,4}$ = 7.8 Hz. The remaining protons could not be assigned as the two H-6 protons had been shifted downfield by the deshielding effect of the ester carbonyl to give the complex multiplet between 5.6 - 6.2 τ which corresponded to five protons. The downfield shift of H-6 proved that the acryloyl residue was attached to C-6. The twelve isopropylidene C-Me protons appeared as three peaks at 8.55, 8.57 and 8.71τ, the last being twice the intensity of the other two peaks.

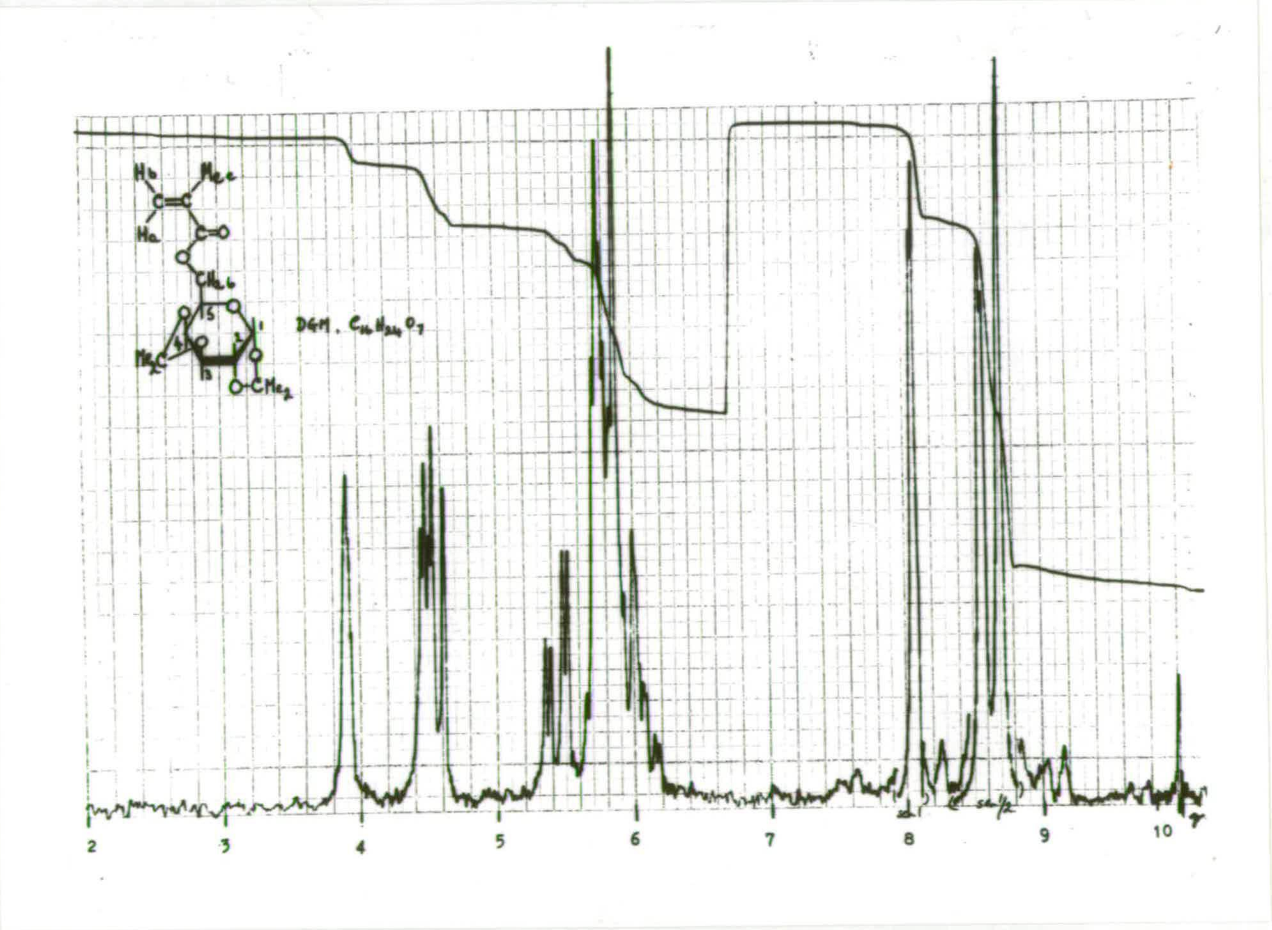


Plate II. The p.m.r. spectrum of 1,2:3,4-di-O-isopropylidene-6-O-methacryloyl-α-D-galactopyranose (IV)

Integration of all peaks in the p.m.r. spectrum of DGM showed the expected twenty-four protons. It was possible to distinguish the H-1 doublet ($J_{1,2}$ = 5.0 Hz) in the pattern of peaks corresponding to two protons at 4.5τ. The other proton was assigned to H_b. The one proton peak at 3.91τ was identical to that of methyl methacrylate and was assigned H_a. The α-methyl group (H_c) was readily detected at 8.07τ. The remainder of the spectrum was identical to DGA:- H-3, 5.44τ was a quartet ($J_{3,2}$ = 2.4 Hz, $J_{3,4}$ = 7.8 Hz) and H-6_1 and H-6_2 were again moved downfield by the ester carbonyl.

IGLM showed the three charactistic methacrylate signals at 3.91, 4.43 and 8.10τ. The two non-equivalent isopropylidene C-Me groups gave equal signals at 8.63 and 8.69τ. The two primary methylene protons (H-1) were contained in the complex five proton multiplet 5.5 - 6.4τ. The deshielding effect of the ester carbonyl had moved this signal downfield from 6.35τ (deuterated isopropylideneglycerol) to a superimposed position assigned tentatively as 5.85τ. These values are of the order expected for a methylene group adjacent to a hydroxyl and ester group respectively and prove that the methacryloyl group is exclusively at position 1 of the isopropylideneglycerol residue.

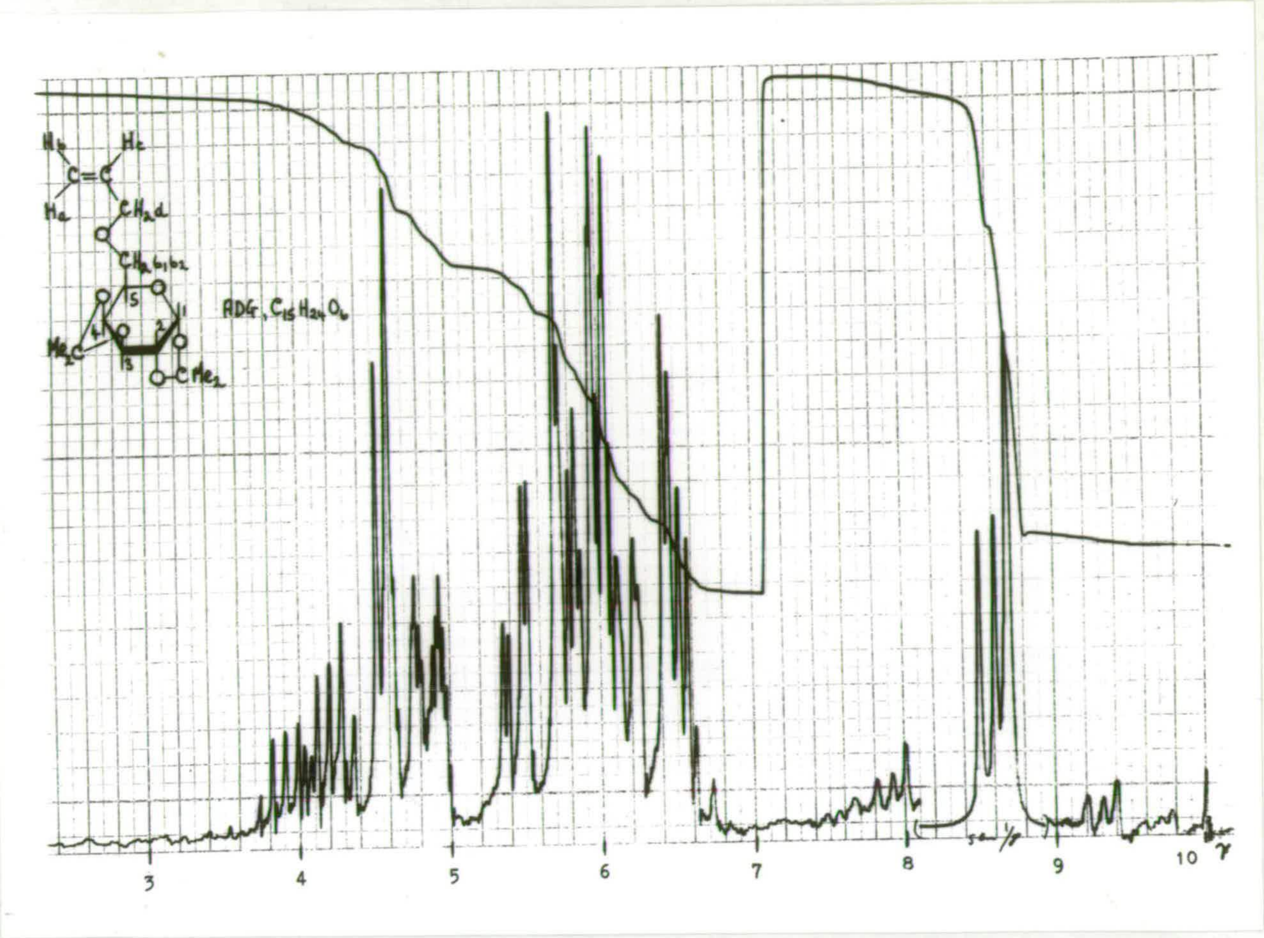


Plate III. The p.m.r. spectrum of 6-O-allyl-1,2:3.4-di-O-isopropylidene-α-D-galactopyranose (VI)

Integration of all peaks in the p.m.r. spectrum of ADG showed the expected twenty-four protons. The pattern of peaks centred at 4.0, 4.75 and 4.87τ corresponded to three protons which were identical in shape and position to that of allyl alcohol and were assigned H_c, H_a and H_b respectively. The H-1 doublet at 4.55τ was distorted by a part of the signal from H_a. H-3, 5.44τ was a quartet ($J_{3,2}$ = 2.4 Hz and $J_{3,4}$ = 7.8 Hz). H-6_1/

H-6_1 and H-6_2 were assigned 6.44 and 6.55$^\tau$ by comparison with other diisopropylidenegalactose derivatives. The complex multiplet, 5.6 - 6.3$^\tau$, contained the two allylic protons H_d and H-2, H-4 and H-5.

Assignments are shown in Table I and they are in good agreement with the results of Cone and Hough[35] who found H-1, 4.40$^\tau$ ($J_{1,2}$ = 5.0 Hz) and H-3, 5.34$^\tau$ ($J_{3,2}$ = 2.4 Hz and $J_{3,4}$ = 8.0 Hz) for diisopropylidenegalactose in $CDCl_3$.

In deuterium oxide solution, protons attached to oxygen form an exchanging pool with residual water in deuterium oxide and have a single sharp resonance at 5.25$^\tau$ in the p.m.r. spectrum. The p.m.r. spectrum of α-GM (XII) in deuterium oxide was complicated however by two variables; (i) mutarotation and (ii) gradual polymerisation. This is represented in Fig. I, where OD groups have been omitted for convenience.

TABLE I. Chemical Shifts (τ-values)

Compound	H_a	H_b	H_c	H_d	H-1	H-2	H-3	H-4	H-5	H-6	Isopropylidene C-Me
DGA	3.55	4.23	3.85	-	4.57	i	5.43	i	i	i	8.55, 8.58, 8.71 x 2
DGM	3.91	ca. 4.5	8.07	-	4.50	i	5.44	i	i	i	8.57, 8.59, 8.71 x 2
IGLM	3.91	4.43	8.10	-	ii	ii	ii	-	-	-	8.63, 8.69
ADG	4.75	4.87	ca. 4.0	iii	4.55	iii	5.44	iii	iii	6.44, 6.55	8.51, 8.61, 8.71 x 2

i Complex five proton multiplet 5.6 - 6.2τ

ii Complex five proton multiplet 5.5 - 6.4τ

iii Complex five proton multiplet 5.6 - 6.3τ

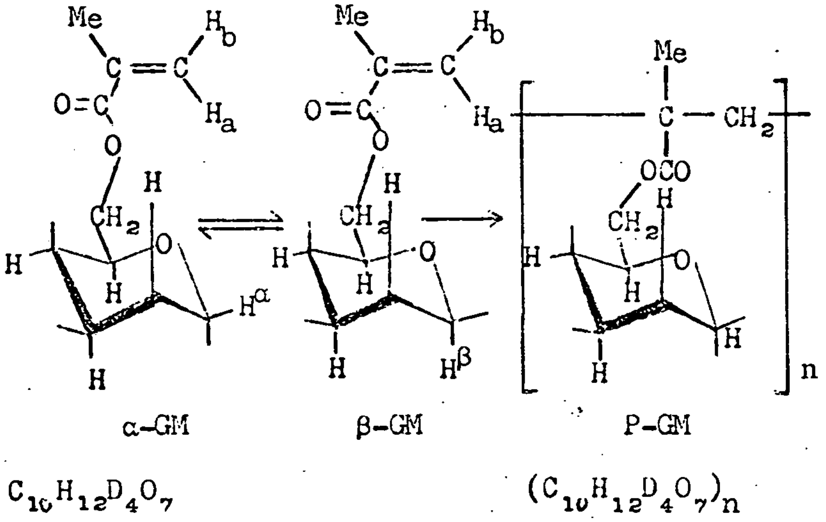


Fig. I. Mutarotation and polymerisation of α-GM in deuterium oxide

An axially oriented hydrogen (H^{β}) is more shielded than an equatorially oriented hydrogen (H^{α}) and resonated at a higher applied magnetic field[39]. Van der Veen[40] has studied the mutarotation of D-galactose in deuterium oxide by p.m.r. and found the following τ-values and coupling constants between H_1-H_2: H^{α}, 4.77τ ($J_{1,2}$ 2.7 Hz) and H^{β}, 5.43τ ($J_{1,2}$ 6.7 Hz). The difference in coupling constants is a measure of the dihedral angle between H-1 and H-2 and is a consequence of the more effective coupling of two axially oriented hydrogens (H^{β}-H_2) than axial-equatorial/

equatorial coupling $(H^{\alpha}-H_2)^{39}$.

Table II shows τ-values and the change in the number of protons contributing to these values with time, thus confirming the reaction scheme of Fig. I. τ-values were measured relative to the single resonance due to water at 5.25τ. The first spectrum was recorded immediately after α-GM had dissolved in deuterium oxide.

TABLE II

τ-values and number of protons in the mutarotation and polymerisation of α-GM in deuterium oxide.

	Ha	Hb	H^{α}	H^{β}, H_2-H_6	αMe	$-(CMe.CH_2)n$
τ-values	3.80	4.20	4.66	5.4 -6.6	8.00	8.5 - 9.5
No. of protons α-GM	1	1	1	0 , 6	3	0
No. of protons P-GM	0	0	7		0	5
No. of protons t = 0	0.71	0.71	0.85	6.07	2.25	1.41
No. of protons t = 24 hr.	0.22	0.22	0.60	6.56	0.83	3.54
No. of protons t = 96 hr.	0	0	0.64	6.65	0	4.71

At/

At t = 0, a distinct doublet at 4.64τ ($J_{1,2}$ 3.0 Hz) indicated H^{α}. The integral showed that 85% of the compound was in the α-form at this time and after mutarotation had taken place, approximately 60% was still in this anomeric state. The gradual decrease in the number of vinyl protons (Ha, Hb and α-Me) with the concomitant appearance of these protons at higher field proved that polymerisation was taking place and after 96 hr. there was 94% conversion into polymer. The gradual decrease in resolution of the spectra was also a consequence of polymerisation.

As the inhibitor-free monomer polymerised so readily in aqueous solution and the yield of crystalline material was only 48%, the monomer was best prepared for polymerisation as an aqueous solution containing p-methoxyphenol as inhibitor.

2.3 Experimental

Materials

Allyl Bromide	B.D.H. reagent, redistilled.
Anhydrous Acetone	Analar B.D.H. reagent was dried over calcium chloride and filtered immediately before use.
Anhydrous Copper Sulphate	Copper sulphate pentahydrate was crushed, heated in an oven at 105° for three days, and finally heated cautiously with a bunsen until it was a white and free-flowing powder.
Anhydrous p-Dioxan	B.D.H. reagent, dried over sodium hydroxide and sodium wire, refluxed and distilled over sodium wire.
Ethyl Acrylate	B.D.H. reagent.
Formic Acid	Analar B.D.H. reagent.
D-Galactose	B.D.H. reagent.
Glycerol	Analar B.D.H. reagent.
p-Methoxyphenol	B.D.H. reagent.
Methyl Methacrylate	B.D.H. reagent.
Tetrachloroquinol	Eastman Organic Chemical.
Tetraisopropyl Titanate (Titanium isopropoxide)	Eastman Organic Chemical.

General/

General Methods

Elementary Analyses were carried out by A. Bernhardt, Mülheim, Germany.

Infrared Spectra were measured with a Perkin-Elmer "Infracord" 137 and a Perkin-Elmer 257 Grating Infrared Spectrophotometer in potassium chloride discs.

Specific Rotations were measured in a 2 dm. tube.

Melting Points were determined with a hot stage microscope.

Refractive Index was measured with an Abbé refractometer.

Thin Layer Chromatrography, T.L.C. was performed on Silica Gel G with chloroform-ethanol (99:1); spray reagent, 90% sulphuric acid (10 min. at 140°).

All evaporations were carried out under reduced pressure below 40° and all crystalline materials dried to constant weight *in vac.* over phosphoric oxide at 20°.

1,2:3,4-Di-O-isopropylidene-α-D-galactopyranose[41]

D-Galactose (82.3g), anhydrous copper sulphate (200g) anhydrous acetone (2 litres), and concentrated sulphuric acid (10 ml) were shaken together for 24 hr. The copper sulphate was filtered, washed with acetone (200 ml), and the combined filtrate and washings neutralised by shaking with powdered calcium hydroxide (100 g) for 24 hr., when the solution was shown to be neutral to an aqueous solution of Congo Red. Solids were filtered and washed with acetone, and the filtrate and washings concentrated and distilled (b.p. 100°/0.04 mm) to give a greenish yellow, viscous syrup (83.58 g, 70.3%) which had $[\alpha]_D$ -57.4° (c 2.0 in chloroform). Lit $[\alpha]_D$ -55° (c 3.5 in chloroform).

6-O-Acryloyl-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (DGA, V)

Diisopropylidenegalactose (21.72 g), ethyl acrylate (180 ml), p-methoxyphenol (4 g) and titanium isopropoxide (4 ml), were heated at 110° for 2 hr. with stirring in an atmosphere of nitrogen. During the course of the transesterification, the ethyl acrylate-ethanol azeotrope (15 ml) was collected; this had a b.p. of *ca.* 72° at the distilling head, and when the temperature dropped to 30° it was assumed that all of the azeotrope had been removed. The condenser was then fitted vertically, water (16 ml) and light petroleum (b.p. 60-80°, 80 ml) added and the mixture cooled to 20°. The gelatinous titanium dioxide was centrifuged, washed with/

with light petroleum, and the supernatant and washings concentrated to a sticky yellow solid (19.46 g). This was dissolved in methanol (100 ml), water (40 ml) added and left to crystallise at 0° for 18 hr. This crystalline product was dissolved in methanol (50 ml), water (20 ml) and tetrachloroquinol (2 mg) added, and the solution heated under reflux for 5 min with charcoal (5 g). The mixture was filtered through celite, washed with methanol (10 ml), water (30 ml) added and the solution left at 0° for 18 hr. to give the acrylate as needles (8.93 g) m.p. 56.5-57°, $[\alpha]_D$ -50.2° (c 1.0 in chloroform). Infrared analyses showed ester C:O, 1737 cm^{-1}, C:C, 1640 cm^{-1}, and gem-dimethyl, 1380 cm^{-1}. (Found: C, 57.5; H, 7.0. $C_{15}H_{22}O_7$ requires C, 57.3; H, 7.05%). Mother liquors were worked up to give a second crop (5.82 g, m.p. 55-56.5°) thus giving a total yield of 14.75 g (56.2%). For polymerisations, the monomer was recrystallised three times from methanol-water.

1,2:3,4-Di-O-isopropylidene-6-O-methacryloyl-α-D-galactopyranose (DGM, IV)

Diisopropylidenegalactose (80 g) was dissolved in methyl methacrylate (480 ml) containing tetrachloroquinol (4 g). Titanium isopropoxide (16 ml) was added, the flask flushed with nitrogen for 10 min, and the temperature raised to 110°. A methanol-methyl methacrylate azeotrope distilled at 82-85°. After 1 hr., water (16 ml) and light petroleum (b.p. 60-80°, 80 ml)/

80 ml) were added and the mixture allowed to come to 20°. After 2 hr., titanium compounds were filtered, washed with light petroleum, the filtrate and washings washed with water (3 x 20 ml), and the solution evaporated to a syrup. This was dissolved in ethanol (400 ml) and recrystallised with water (400 ml) at 0°. The pure methacrylate was a white, crystalline compound (75.87 g, 75.2%), m.p. 62.5-63°, $[\alpha]_D$ -49.3° (c 1.12 in chloroform), and infrared analysis showed ester C:O, 1730 cm^{-1}, C:C, 1640 cm^{-1} and gem-dimethyl, 1380 cm^{-1}. (Found: C, 58.1; H, 7.21. $C_{16}H_{24}O_7$ requires C, 58.5; H, 7.36%). The monomer was purified further for polymerisation by recrystallisation from 50% ethanol:- yield, 90.3%.

6-O-Allyl-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (ADG, VI)

Diisopropylidenegalactose (19.9 g) was dissolved in anhydrous p-dioxane (100 ml) and powdered sodium hydroxide (8 g) added. Allyl bromide (80 ml) was added over 20 min to the stirred mixture at 45°. Heating was increased to 50° for 30 min, and finally to 60° for 2 hr. Water (100 ml) was added, and the mixture was extracted with chloroform (3 x 100 ml). The chloroform extract was washed with water (3 x 250 ml), dried over anhydrous sodium sulphate, and evaporated to a yellow oil (22.1 g). This material was re-allylated as before to give the crude allyl ether (22.08 g) which was distilled to give a colourless/

colourless oil (21.08 g, 91.8%), b.p. 86°/0.03 mm. T.l.c. showed one component (R_F 0.89), and infrared analysis showed absorptions at 3080 (=CH) and 1645 cm^{-1} (C:C); OH absorption was absent. The allyl ether had $[\alpha]_D$ -71.8° (c 1.0 in chloroform) and n_D^{25} 1.4595. (Found: C, 60.2; H, 8.13. $C_{15}H_{24}O_6$ requires C, 60.0; H, 8.06%).

1,2-O-Isopropylidene-DL-glyceritol[42]

Dry hydrogen chloride was passed through a mixture of glycerol (104 g) and acetone (200 ml) until a homogeneous solution was obtained (30 min). The solution was neutralised with anhydrous sodium carbonate, filtered and evaporated to a syrup which was dissolved in water (100 ml) and extracted with chloroform (3 x 100 ml). Chloroform was removed by evaporation and the syrup distilled (b.p. 81°/12 mm) in the presence of silver oxide to give a colourless oil (81.68 g., 54.6%) which had n_D^{25} 1.4330 (lit.,[43] n_D^{25} 1.4326). Infrared analysis showed sharp hydroxyl absorption at 3500 cm^{-1} and the *gem*-dimethyl doublet at 1380-1360 cm^{-1}.

2,3-O-Isopropylidene-1-O-methacryloyl-DL-glyceritol (IGLM, VII)

Isopropylideneglycerol (20.2 g) was transesterified with methyl methacrylate (120 ml) in the presence of tetrachloroquinol/

tetrachloroquinol (1 g), with titanium isopropoxide (4 ml), as catalyst, under identical conditions to those described above for the preparation of DGM. The monomer oil was distilled (b.p. 65°/0.01 mm); approximately the first gram of distillate was discarded. The methacrylate (21.54 g) was further purified by a second distillation in the presence of tetrachloroquinol to give the pure monomer as a colourless oil (20.65 g., 67.5%) which had n_D^{25} 1.4435 (lit.,[32] n_D^{20} 1.442) and was optically inactive; infrared analysis showed ester C:O at 1730 cm^{-1} and C:C, 1645 cm^{-1} (OH absent). (Found: C, 60.4; H, 8.51. Calc. for $C_{10}H_{16}O_4$: C, 60.0; H, 8.06%).

6-O-Methacryloyl-α-D-galactopyranose (α-GM, XII)

Diisopropylidenegalactose methacrylate (DGM, 10.02 g, 0.0305 mol) and p-methoxyphenol (0.5 g) were dissolved in formic acid (80 ml) and the solution made up to 100 ml with water. The deacetonation was followed polarimetrically (2-dm tube) at 20°, and after 24 hr., the solution was diluted to 50% with water and formic acid removed by repeated evaporation at 35° and addition of water. The thick syrup was dissolved in ethanol (100 ml) and polymeric material (403 mg) filtered off. The clear ethanol solution was evaporated at 20° to ca. 20 ml and left at 0° for three days. The white crystalline material was filtered, washed with ethanol (2 x 2 ml), and dried to give the methacrylate as plates (m.p. 108-118°, 3.63 g, 48.0%) which mutarotated/

mutarotated from $[\alpha]_D$ + 91.5° ⟶ + 53.8° (c 1.516 in water). This material (2.50 g) was dissolved in water (10 ml) and ethanol (90 ml) added and the solution left at 0° for three days to give the α-anomer as white plates (m.p. 142-145°, 551 mg, 22.0%). (Found: C, 48.1; H, 6.39. $C_{10}H_{16}O_7$ requires C, 48.4; H, 6.50%).

6-O-Methacryloyl-D-Galactose (GM) 25 w/w% Aqueous Solution

DGM (41 g) with p-methoxyphenol (1.5 g) was deacetonated in 80% formic acid (400 ml) and after 24 hr. at 20°, formic acid removed as before. A weighed amount of water was added to the monomer syrup to give a solution which was 25 w/w% with respect to GM and 1.21% with respect to inhibitor.

3. POLYMERS

3.1 Free-Radical Polymerisation: General Introduction

Flory[44] showed that a free-radical polymerisation reaction, like other radical processes, is a typical chain reaction requiring three distinct steps:

(1) initiation, which is dissociation of the initiator and addition of the initiator fragment to the first monomer molecule,

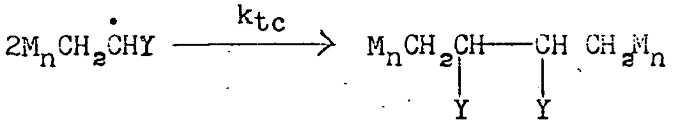
$$I_2 \xrightarrow{k_d} 2I\cdot \qquad I\cdot + M \xrightarrow{k_i} IM\cdot \qquad (1)$$

$$\text{where } M = H_2C = CHY$$

(2) propagation, which is the addition of a free-radical to a double bond, and is the mechanism of polymer chain-growth,

$$M_xCH_2\dot{C}HY + CH_2 = CHY \xrightarrow{k_p} M_{x+1}CH_2\dot{C}HY \qquad (2)$$

(3) and termination, which is the coreaction of two polymer chain radicals by combination,



$$2M_nCH_2\dot{C}HY \xrightarrow{k_{tc}} M_nCH_2\underset{\displaystyle Y}{\underset{|}{CH}}-\underset{\displaystyle Y}{\underset{|}{CH}}\,CH_2M_n \qquad (3)$$

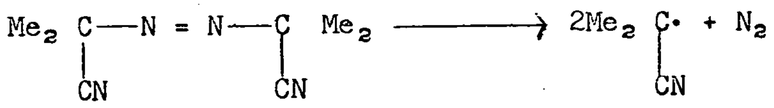
or/

or disproportionation

$$2M_nCH_2\dot{C}HY \xrightarrow{k_{td}} M_nCH = CHY + M_nCH_2CH_2Y \qquad (3)$$

In general, there are three limiting conditions for the polymerisation of olefin monomers by a free-radical process. As the propagation step requires a "head to tail" monomer to radical addition, only those monomers containing the $=CH_2$, $=CHF$, or $=CF_2$ group are suitable on steric grounds. Secondly, the substituent Y must be electron-withdrawing to facilitate the formation of a free radical. These substituents include Cl, Ph, OCOR, COR, COOR, CN. Finally, the free-radical must be resonance stabilised. For these reasons monomers such as 1,2-dichloroethylene, $ClHC = CHCl$, propylene, $H_2C = CHMe$, and vinyl ethers, $H_2C = CHOR$, show no tendency to polymerise under free-radical conditions.

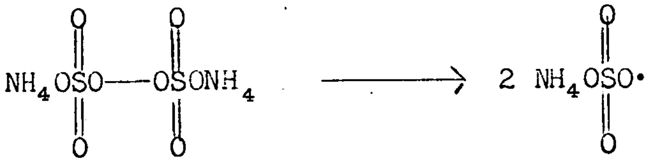
The usual free-radical initiators are benzoyl peroxide and azobisisobutyronitrile (AIBN), but as the latter dissociates in the lower temperature range (40 - 60°), AIBN was used exclusively in this work for polymerisations in bulk or benzene solution.



$$Me_2\underset{\displaystyle CN}{\overset{}{C}}{-}N = N{-}\underset{\displaystyle CN}{C}Me_2 \longrightarrow 2Me_2\underset{\displaystyle CN}{C}\cdot + N_2$$

Bulk/

Bulk polymerisation is the simplest technique for converting monomer into polymer. In this method initiator is added to undiluted monomer and polymerisation is carried out in a sealed tube in an atmosphere of nitrogen. Crystalline monomers are best polymerised in solution in benzene or water-solvents which show small tendency to enter into transfer reactions with the growing polymer chain. Where polymerisation is violently exothermic, the reaction is best carried out in aqueous emulsion using a water-soluble initiator such as ammonium persulphate.

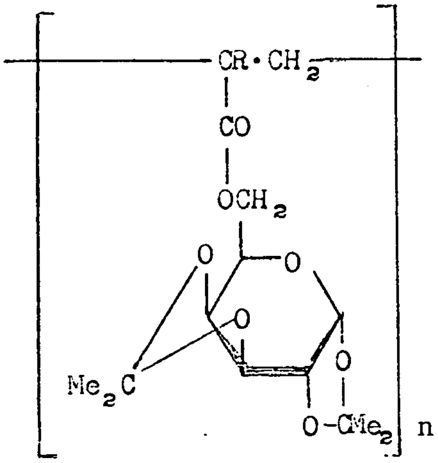


$$\mathrm{NH_4O\overset{O}{\underset{O}{S}}O{-}O\overset{O}{\underset{O}{S}}ONH_4} \longrightarrow 2\ \mathrm{NH_4O\overset{O}{\underset{O}{S}}O\cdot}$$

These three techniques were used for the polymerisation and copolymerisation of galactose monomers.

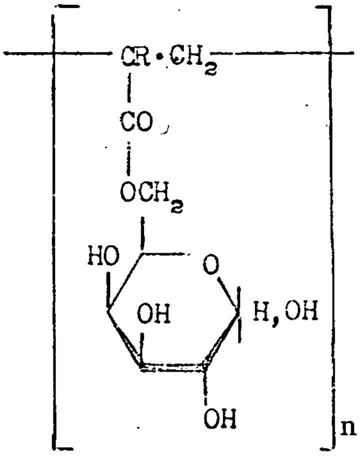
3.2 Results and Discussion

The optimum conditions for the polymerisation of diisopropylidenegalactose methacrylate (DGM) and diisopropylidenegalactose acrylate (DGA) to the acetonated polymers, P-DGM (XIII) and P-DGA (XIV), were worked out by Mr. Tom Bird[27]. He also successfully deacetonated these polymers by hydrolysis in aqueous formic acid at 20° to give the water-soluble, synthetic "polysaccharides", poly-(6-*O*-methacryloyl-*D*-galactose) (P-GM, XV) and poly-(6-*O*-acryloyl-*D*-galactose) (P-GA, XVI) which had the reducing, glycosidic hydroxyl group free on every polymer unit.



(XIII: R = Me)

(XIV: R = H)



(XV: R = Me)

(XVI: R = H)

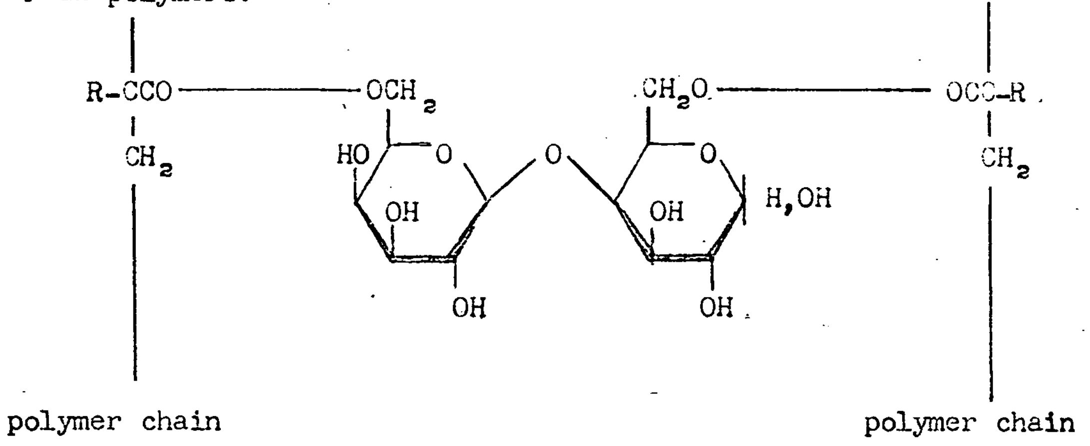
DGM and DGA were polymerised in benzene solution (22.5% of monomer) under nitrogen with AIBN (0.1 - 0.2%) at 50°. The clear polymer glass was dissolved in chloroform and reprecipitated with methanol to give high yields of polymer with inherent viscosity comparable with that of commercial poly-(methyl methacrylate).

Unlike poly-(diisopropylideneglucofuranose)[10], these acetonated polymers were resistant to hydrolysis with N-hydrochloric acid at 100°. The significance of this will be discussed later. However, dissolution of the polymer in anhydrous formic acid, followed by the controlled addition of water to 66.7% formic acid, brought about the smooth hydrolysis of the isopropylidene residues to give the fully unsubstituted, water-soluble polymers which were isolated by freeze-drying, after the removal of formic acid by dialysis.

All further work on galactose polymers and copolymers was carried out by the author.

It was observed that these deacetonated polymers became water-insoluble, i.e. and, therefore, presumably cross-linked, after periods of 1 - 2 years at 20°. The same effect could be observed after heating at 60° <u>in vac.</u> over phosphoric oxide. It was thought that traces of formic acid in the freeze-dried polymer, detected at 1600 cm^{-1} in the infrared spectrum, catalysed condensation between a glycosidic hydroxyl group and another secondary hydroxyl group/

group of a neighbouring polymer chain. This process is of course made more probable under the forcing conditions at 60°. In order to eliminate this acid catalysed condensation, a sample of acid-free poly-(galactose methacrylate) was prepared from P-DGM by the formic acid method, by introducing a bicarbonate neutralisation step. P-GM was isolated from neutral aqueous solution by precipitation with isopropanol and further purified by a second reprecipitation. The infrared spectrum of the polymer did not show absorption at 1600cm^{-1}, but cross-linking still occurred at 60° <u>in vac.</u> over phosphoric oxide although it is predicted that the "shelf-life" water-solubility of the polymer will be greatly increased. Crystalline D-galactose is stable indefinitely at 20° but polymerises by a poly-condensation reaction when heated under vacuum above its melting point. In a similar manner it can be visualised that in amorphous, i.e. non-crystalline, P-GM and P-GA, galactose units of neighbouring polymer chains come into intimate contact at 60° and only a small amount of condensation would be required to bring about insolubility. Polycondensation of reducing sugars has been reviewed by Mora[22] and one possibility, a β-1⟶4 linkage, is represented as follows for the P-GM and P-GA polymers:



Confirmation of this type of mechanism was shown by the fact that poly-(glyceryl methacrylate), described later, remained water-soluble after identical treatment at 60°.

Water-soluble monomers, such as glyceryl methacrylate, hydroxyethyl methacrylate and the N-acryloyl and N-methacryloyl derivatives of 1-amino-1-deoxy-D-glucitol, give three-dimensional cross-linked hydrogels when polymerised in concentrated aqueous solution. The 25 w/w% aqueous solution of 6-O-methacryloyl-D-galactose (GM, XII) also polymerised with ammonium persulphate to a cross-linked hydrogel[33]. However, the mechanism of this cross-linking reaction is not known and is probably different from that outlined above.

Poly-(galactose methacrylate) and poly-(galactose acrylate) have been characterised by standard carbohydrate reactions. Esterification reactions were carried out in dimethylformamide solution[27].

P-GM was acetylated in dimethylformamide solution by two treatments with acetic anhydride-pyridine for 24 hr at 20° to give the white acetate derivative (XVII) in 82.6% yield. The specific rotation was + 47° and the polymer had an inherent viscosity $\eta_{inh.}$ of 5.2 dl/g in tetrachloroethane. The acetyl content was 39.1% and this corresponded to a degree of substitution (D.S.) of 3.65.

P-GA/

P-GA was acetylated under identical conditions to give the polymer acetate (XX) in 84.2% yield. The acetyl content of 40.1% corresponded to a D.S. of 3.6 and infrared analysis showed negligible hydroxyl content; the spectrum was almost identical to that of the methacrylate polymer. The acrylate polymer had a similar specific rotation of +52° but did not show the high inherent viscosity of the methacrylate polymer in tetrachloroethane.

Benzoylation of P-GM in dimethylformamide solution with benzoyl chloride-pyridine for 7 days at 20° yielded essentially the tribenzoate derivative (XVIII). The degree of substitution was calculated from carbon analysis as follows:

Let the degree of substitution = n

The repeating unit is $C_{10}H_{16-n}O_7.(C_6H_5CO)_n$

$= C_{7n+10}H_{4n+16}O_{n+7}$

$\therefore$ Weight of unit = 104n + 248

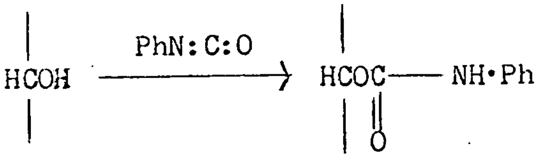
and $$\%C = \frac{(7n + 10) \times 12 \times 100}{104n + 248}$$

The degree of substitution was 2.7 and the benzoate had $[\alpha]_D$ + 100° in tetrachloroethane and a high inherent viscosity, 9.3 dl/g.

In marked contrast to the methacrylate polymer, the benzoate derivative of the acrylate polymer (XXII) had a degree of substitution of 3.7. The acrylate had a similar specific rotation/

rotation, $[\alpha]_D$ + 94°, but, as with the acetate derivative, did not show a large increase in inherent viscosity.

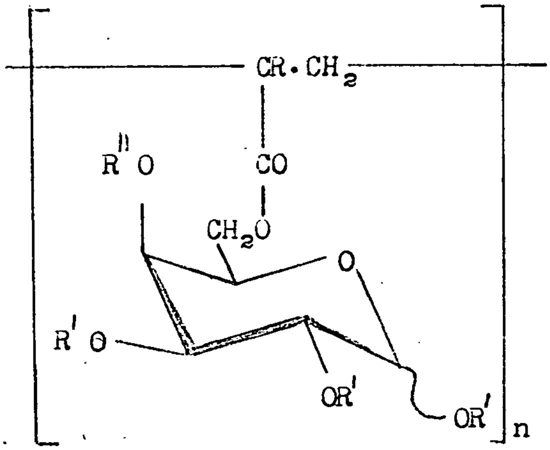
Reaction of carbohydrates with phenylisocyanate in pyridine solution gives the phenylcarbamate derivative:



$$\text{HCOH} \xrightarrow{\text{PhN:C:O}} \text{HCO}\underset{\overset{\|}{\text{O}}}{\text{C}}\text{—NH·Ph}$$

The phenylcarbamate derivative of P-GM (XIX) was prepared by two treatments of the polymer in dimethylformamide solution with phenylisocyanate, at 100° for 3 hr. The D.S., 3.2, was determined by nitrogen analysis.

The phenylcarbamate of P-GA was prepared essentially as described for the methacrylate polymer. However, the polymer derivative (XXII) did not precipitate from dimethylformamide solution with ethanol but it precipitated with isopropanol. The D.S. was 3.6. The acrylate polymer showed a remarkable difference in solubility from the methacrylate polymer in that it gave an insoluble gel in chloroform and tetrachloroethane. It was, however, extremely soluble in dimethylformamide and acetone.



(XVII: R = Me, R′ = R″ = Ac)
(XVIII: R = Me, R′ = Bz, R″ = H)
(XIX: R = Me, R′ = PhNH·CO, R″ = H)
(XX: R = H, R′ = R″ = Ac)
(XXI: R = H, R′ = R″ = Bz)
(XXII: R = H, R″ = R′ = PhNH·CO)

These results indicated that, in general, acetylation of P-GM and P-GA tended to give the fully acetylated derivative (XVII, XX). However, benzoylation and phenylcarbamoylation tended to give the fully substituted derivatives (XXI) and (XXII), with P-GA only, while the methacrylate polymers (XVIII) and (XIX) were trisubstituted. The galactose residue exists in the/...

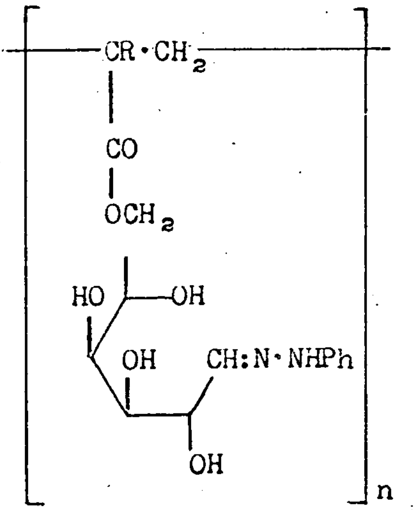
the stable C1 conformation in which the 4-hydroxyl group is axial and substituents on C-2 and C-3 are equatorial. It is well-known that axial hydroxyl groups are generally less rapidly acylated than equatorial hydroxyl groups. Richardson and Williams[45] have shown that reaction of methyl α-D-galactopyranoside, in which the 4-hydroxyl group is axial, with 4.1 moles of benzoyl chloride in pyridine at -40° gives methyl 2,3,6-tri-O-benzoyl-α-D-galactopyranoside in 56% yield. The generalisation, however, did not apply to the axial 2-hydroxyl group of methyl α-D-mannopyranoside. It would appear that the additional C-methyl group of P-GM introduces a steric factor. It is, therefore, suggested that, in the benzoylation and phenylcarbamoylation of the acrylate polymer, the difficulty in obtaining a tetrasubstituted derivative is governed by the lower reactivity of the axial 4-hydroxyl group, whereas with the methacrylate polymer, the combined effects of steric hindrance and the lower reactivity of the 4-hydroxyl group result in trisubstitution. However, in the acetylation reaction, the smaller size of the attacking acetyl radical would render steric hindrance of less importance and the D.S. would be governed largely by the reactivity of the 4-hydroxyl group. Rutherford[1,10] showed that poly-(3-O-methacryloyl-D-glucose) gives trisubstituted products on acetylation, methylation and phenylcarbamoylation. In this polymer, however, the glucose residue is one carbon-bond length nearer the polymer chain with the result that one of the hydroxyl/

hydroxyl groups may be completely shielded.

Caesar and Goldfrank[46] prepared fully substituted starch nitrates, soluble in ethyl acetate, with no depolymerisation, using nitrogen pentoxide in chloroform in the presence of sodium fluoride. P-GM gave essentially the tri-nitrate with this system but as it was insoluble in organic liquids, it was not characterised further.

All the above substitution reactions can be applied to natural polysaccharides. Hence, reactions specific to the reducing group at C-1 of the galactose residues were carried out. As these reactions are impossible for normal polysaccharides, except at the reducing end of each polymer, a number of novel polymers resulted.

Rutherford[1,10] prepared a phenylhydrazone of poly-(glucose methacrylate) in which two out of three units in the polymer chain were substituted. As addition of phenylhydrazine to an aqueous solution of P-GM or P-GA caused immediate precipitation, dimethylformamide was used as solvent in an effort to drive the reaction to completion. This was achieved, and treatment of P-GM and P-GA in dimethylformamide, with phenylhydrazine in the presence of glacial acetic acid, gave high yields of the fully substituted, polymeric phenylhydrazones (XXIII) and (XXIV):

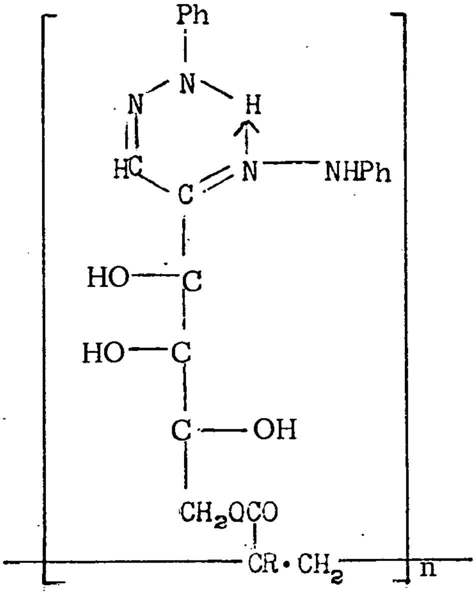


(XXIII: R = Me)
(XXIV: R = H)

Elemental analysis showed the reaction to be complete and strong infrared absorption at $1610cm^{-1}$ indicated C:N·NHPh. Although originally soluble in the reaction mixture, the polymer phenylhydrazones failed to redissolve in dimethylformamide after isolation. This reaction has proved valuable for the chemical characterisation of copolymers of galactose monomers with various industrial monomers.

Water proved to be the only successful medium for preparing the phenylosazone derivatives. Treatment of aqueous solutions of P-GM and P-GA at 90° with excess of phenylhydrazine and glacial acetic acid gave phenylosazone derivatives but reaction was incomplete owing to precipitation of/

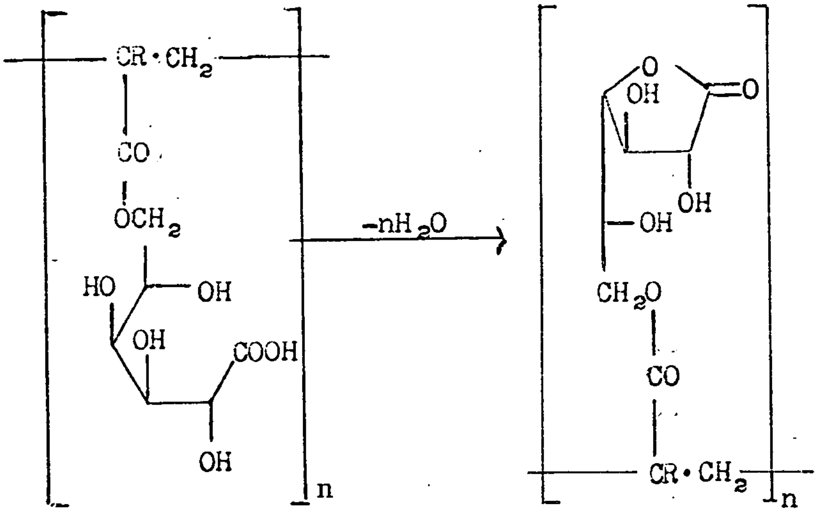
of the polymer from solution. Analysis was consistent with substitution of one in three galactose units as D-*lyxo*-hexose phenylosazone (XXV, XXVI), the other two remaining as the phenylhydrazone (XXIII, XXIV). The infrared spectrum showed four bands at 1610, 1570, 1530 and 1500cm^{-1} which are believed to be characteristic of a phenylosazone structure[47].



(XXV: R = Me)
(XXVI: R = H)

Chlorous acid at pH3 oxidised P-GM and P-GA to soluble poly-(6-O-methacryloyl-D-galactonic acid) (XXVII) and poly-(6-O-acryloyl-D-galactonic acid) (XXVIII) respectively. Freshly prepared solutions of these poly-acids showed no measurable/

measurable optical rotation but a negative value was obtained on standing. During isolation and drying, a molecule of water was lost from each repeating unit to yield the water-insoluble polymer lactones (XXIX, XXX) with characteristic infrared absorption at 1780cm^{-1} due to the 1,4-lactone carbonyl group.



(XXVII: R = Me) (XXIX: R = Me)

(XXVIII: R = H) (XXX: R = H)

The course of oxidation was followed polarimetrically.

P-GM (1%) in 0.4 M-sodium chlorite and 2 M-acetic acid gave:

Time (hr)	0.25	0.50	0.75	1.17	2.17	5.0	24.0
$[\alpha]_D$	+42°	27°	22°	17°	15°	14°	12°

c 1.15, calculated as poly-(sodium 6-O-methacryloyl-D-galactonate)

P-GA/

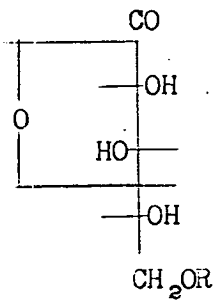
P-GA (1%) in 0.4 M-sodium chlorite and 2 M-acetic acid gave:

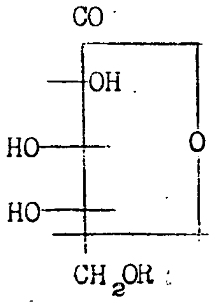
Time (hr)	0.13	0.27	0.50	0.70	1.10	2.0	24.0
$[\alpha]_D$	+38°	31°	19°	15°	10°	8°	7°

c 1.172, calculated as poly-(sodium 6-O-acryloyl-D-galactonate)

Inorganic material was removed by dialysis and the free-acid liberated by Amberlite IR-120 (H^+) resin.

Hudson's lactone rule[48] states that a lactone, in which the oxide ring, as represented in the conventional Fischer projection formula with the CO_2H group at the top, lies to the left, is more laevorotatory than the parent acid, while with the oxide ring to the right the lactone is more dextrorotatory.





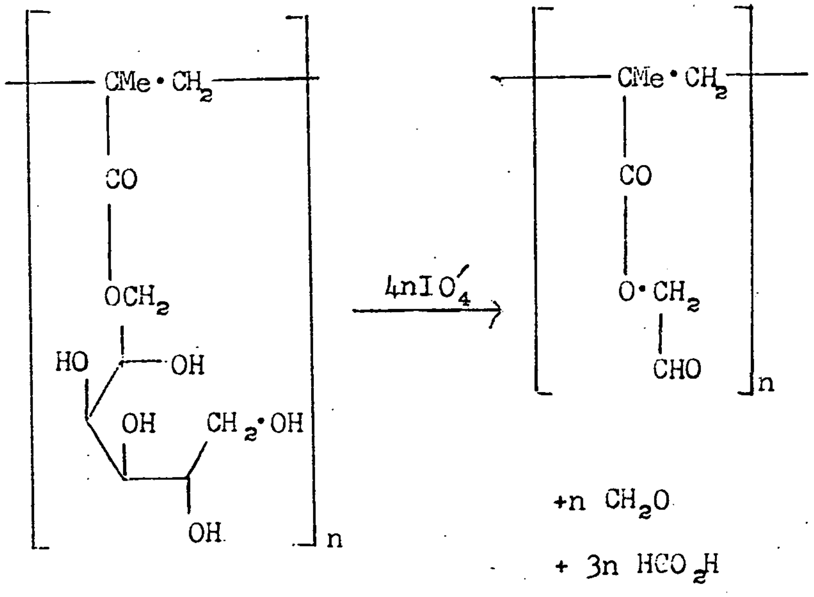
The negative rotations of the water-soluble partial lactones point exclusively to the 1,4-lactone structure. This reaction parallels the ready conversion of D- or L-galactonic acid into its 1,4-lactone[49] and agrees with the fact that a carbonyl group in a five-membered ring represents a highly stable arrangement, whereas a similar arrangement in a pyranose (1,5-lactone) introduces/

introduces an element of instability[50].

The sodium salts of these polyacids behaved as typical polyelectrolytes. They exhibited high inherent viscosities in water which were drastically lowered on the addition of sodium chloride - a characteristic of all water-soluble polyanions such as carrageenan[51] etc. Addition of Ag^+, Ba^{++}, Ca^{++}, Co^{++}, Cu^{++}, Pb^{++}, Al^{+++} and Fe^{+++} caused immediate precipitation of the polymer.

An unsuccessful attempt was made to prepare an amide[52] from the polymeric lactone (XXX) by treatment with liquid ammonia at 20°. However, ammonolysis resulted, and the ester linkage joining the galactose residues to the poly-(acrylic acid) backbone was cleaved.

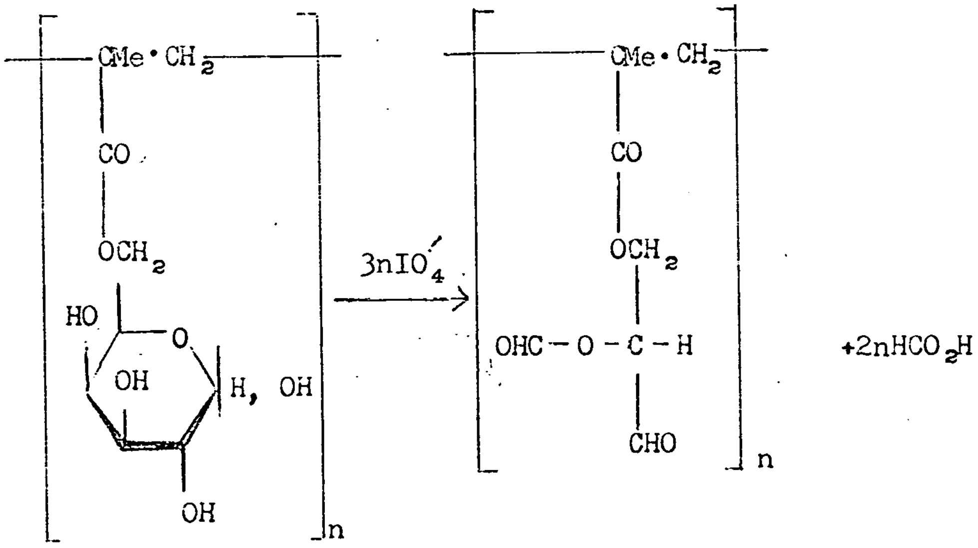
The reducing group of P-GM was readily reduced with sodium borohydride in aqueous solution, to give poly-(6-O-methacryloyl-D-galactitol) (XXXI) in high yield; the course of the reaction was followed by oxidising the isolated products with periodate. The fully reduced polymer, on oxidation with 100% excess of 0.05 M-sodium periodate for 2 hours at 20°, consumed 3.7 mol. of periodate and released 0.89 mol. of formaldehyde, compared with the theoretical values of 4 and 1, respectively, for each galactitol 6-methacrylate unit: This suggests the presence of either 10% w/w sodium methacrylate units or 10% water.



(XXXI)

P-GM liberated no formaldehyde on oxidation with periodate and 2.92 mol. of periodate was consumed after 24 hr.

Oxidation time for P-GM (hr.)	0.3	1.0	2.0	24.0
Periodate consumed (mol.)	1.34	1.87	2.22	2.92



Poly-(galactitol methacrylate)/

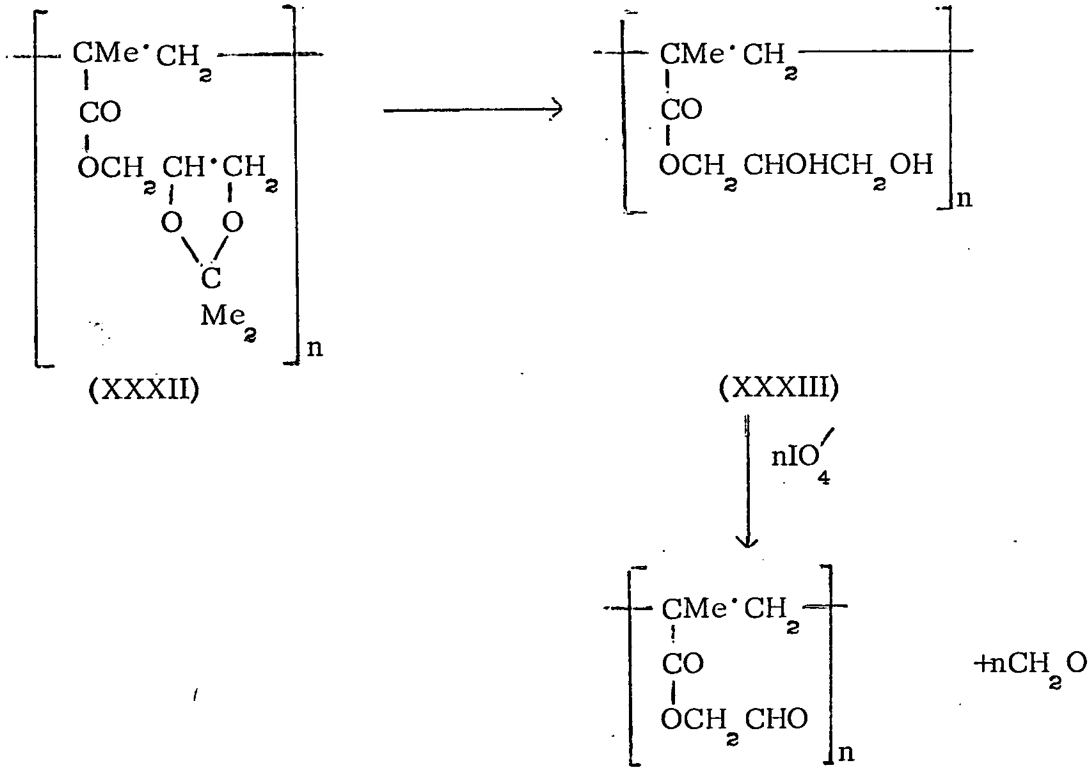
Poly-(galactitol methacrylate) was nitrated[46] with nitrogen pentoxide in chloroform in the presence of sodium fluoride, to give essentially the tetranitrate in 93.5% yield.

In order to evaluate the effect of ring structure and the glycosidic hydroxyl group on the physical and chemical properties of galactose polymers, methacrylate polymers containing glyceryl residue were made for comparison.

Isopropylideneglyceryl methacrylate (IGLM, VII) polymerises readily with free-radical initiators to form a linear thermoplastic polymer (P-IGLM, XXXII) which has high optical clarity and can be cross-linked by the action of heat or by a catalyst such as boron trifluoride. The cross-linked polymer has the properties of a thermoset resin and it has been claimed that cross-linking occurs by opening of the 1,3-dioxolane ring[32,53].

The removal of the protecting isopropylidene group from organic-soluble P-IGLM to form linear, water-soluble poly-(glyceryl methacrylate) (P-GLM, XXXIII) does not appear to have been previously described. However, the water-soluble monomer, 1-O-methacryloyl-DL-glyceritol, has been prepared by deacetonation of IGLM with dilute mineral acid. It can also be prepared by the acid hydrolysis of the commercially available glycidyl methacrylate. Refojo[54] found that glyceryl methacrylate, polymerised/

polymerised in bulk or concentrated aqueous solutions, yielded water-insoluble polymers with variable swelling power (70-90%), indicating the formation of cross-links. He pointed out that these hydrogels would be particularly useful in the field of ophthalmology because of their softness, transparency and ability to be cast in any shape.



(XXXII)

(XXXIII)

It/

It has been found that the isopropylidene group of P-IGLM is more resistant to formic acid hydrolysis than the isopropylidene groups of P-DGM and P-DGA as the formic acid hydrolysis conditions worked out for the acetonated galactose polymers did not produce a water-soluble glycerol polymer when applied to P-IGLM.

Table III. Deacetonation of poly-(isopropylideneglyceryl methacrylate) to poly-(glyceryl methacrylate)

Method	P-IGLM inh (dl/g, c 0.5 in chloroform)	P-GLM inh (dl/g, c 0.1 in water)	Molar Consumption of periodate (mol./mol.)	Molar Release of Formaldehyde (mol./mol.)
50.0% Formic acid at 100° for 8 hr.	1.8	1.4	0.70	0.70
N-Hydrochloric acid at 100° for 30 min.	3.66	8.25	0.86	0.88
2-Methoxyethanol/hydrochloric acid at 100° for 2 hr.	1.8	1.0*	0.96	1.04

* c 0.5 in water.

It/

It can be seen from Table III that formic acid is not a good medium for deacetonation of this polymer as these vigorous conditions, although producing a water-soluble polymer, gave only 70% reaction.

The glass transition temperature (T_G) of a polymer represents the boundary between its glassy and rubbery state. All linear polymers will undergo this transition unless thermal degradation occurs first. Polymers having crystalline regions show both T_G and a crystalline melting point (T_m) which is much higher than T_G, whereas amorphous polymers show only T_G. A complex theoretical treatment of T_G has been given by Gibbs and DiMarzio[55], but in simple terms, second order transitions in properties such as specific volume and specific heat occur at this temperature and this is a result of the breaking down of the secondary valence forces holding the polymer chains together in the glassy state. Above T_G the polymer chains have free movement and solution properties are shown. A correlation between T_G and chemical structure has been found in terms of polar and steric factors. Polar polymers have relatively high values of T_G, but a more important factor is the steric effect of the chain substituent groups. Stiff and bulky side groups, which inhibit free rotation of the chain segments, increase T_G, whereas flexible side groups, which serve to hold the chains apart, free their motions and decrease T_G[56]. The effect of flexible side groups on/

on T_G has been shown by Wiley and Brauer[57] for a series of poly-(n-alkylacrylates): T_G becomes progressively lower as the length of the n-alkyl side chain is increased; e.g., they reported T_G values for poly-(methyl acrylate) and poly-(ethyl acrylate) as 0° and -23° respectively.

The T_Gs of P-DGM and P-DGA were measured at the Royal Aircraft Establishment, Farnborough, with an automated dilatometric apparatus and were found to be 126° and 98° respectively[58].

T_Gs were also determined by the author using differential thermal analysis (DTA). This technique measures the heat energy change occurring in a substance as a function of temperature. Experimentally, the sample is heated side by side with an inert reference material at a uniform rate and the temperature difference between them (Δ T) measured as a function of temperature (T). The resulting curve, which is a plot of T against Δ T, is called a thermogram and the T_G is detected as a base-line shift, caused by the sudden changes of specific heat, free volume and thermal conduction of the polymer at this temperature[59]. The acetonated polymers showed well-defined, repeatable base-line shifts at 130° for P-DGM, 104° for P-DGA and 61.5° for P-IGLM. Base-line shifts were not detected for the deacetonated polymers.

The/

The T_G values for P-DGM and P-DGA are the highest yet recorded for a methacrylate or acrylate polymer[60], and this fact must be attributed to the presence of the bulky, tricyclic diisopropylidenegalactose groups attached to otherwise flexible carbon-carbon main chains. The higher T_G of the methacrylate may be attributed to the α-methyl groups which give rise to an increased barrier to rotation about the polymer main chain. These differences in T_G can be correlated with differences in two of the chemical properties of the acetonated polymers:

(1) Unlike P-DGM, which is resistant to heterogeneous acid hydrolysis and can be recovered almost unchanged after prolonged heating in hydrochloric acid at 100°, P-IGLM is readily deacetonated to P-GLM on heating at 100° with N-hydrochloric acid alone. Obviously this effect is not due to a difference in the acid stability of the respective isopropylidene rings as it was found (Table III) that the 1,3-dioxolan ring of P-IGLM was more resistant to acid hydrolysis in solution than those of P-DGM and P-DGA. However, if the physical state of the two polymers in this heterogeneous reaction at 100° is considered, it will be seen that P-IGLM (T_G, 61.5°) will exhibit solution properties whereas P-DGM (T_G, 126°) will still be in its glassy, rigid state in which the secondary valence forces holding the chains together inhibit the deacetonation reaction. Illustrating this, P-DGA (T_G, 98°)/

(T_G, 98°) yielded water-soluble polymer after heating at 100° in N-hydrochloric acid for 2 hr, and IGLM:DGM copolymers[61] could only be deacetonated heterogeneously with ease below 15 mol.% of DGM.

(2) Secondly, it was found that P-IGLM cross-linked (became chloroform-insoluble) on heating at 105° in air. P-DGA cross-linked after 3 days at 105° whereas P-DGM was completely chloroform-soluble after this treatment. It would appear, therefore, that cross-linking by heating polymers containing the isopropylidene group will occur only at temperatures above their T_G.

Some solution properties of poly-(galactose methacrylate) were studied. The reducing power of P-GM, determined with alkaline iodine[62], was 96.6%. This value was used to convert all weights in subsequent measurements into the anhydrous values by multiplication by 0.966. The specific rotation of the polymer in water was +64°.

The intrinsic viscosity $[\eta]$ is defined as the limit of/

of the inherent viscosity η_{inh} at zero concentration:-

$$[\eta] = \lim_{c \to 0} 1/c \ln(t/t_0)$$

where c = concentration of polymer in g/100 ml solution

t_0 = solvent flow time

and t = solution flow time.

A plot of the change of inherent viscosity with concentration gives the intrinsic viscosity at zero concentration. A convenient method of following this change is by using an Ubbelohde dilution or suspended-level viscometer. Results for P-GM in water, 0.1M-sodium chloride and dimethyl sulphoxide in viscometers of different bore are given in Table IV.

It can be seen from the graph that below c 0.06 the change of η_{inh} with c increases more rapidly in every case except in 0.1M sodium-chloride. Consequently, the intrinsic viscosity was extrapolated from the linear part of the curve between c 0.2 - 0.1. The extrapolated values were:- No. 3 viscometer, dimethyl sulphoxide, $[\eta]$ = 3.73 dl/g; No. 2 viscometer, water, $[\eta]$ = 2.81 dl/g; No. 3 viscometer, water, $[\eta]$ = 2.54 dl/g; and No. 2 viscometer 0.1M sodium chloride, $[\eta]$ = 2.43 dl/g. These results show the importance/

TABLE IV. The intrinsic viscosity of poly-(galactose methacrylate)

Dimethyl Sulphoxide - No. 3 BS/IP/SL(S)5573 Viscometer

c(g/100 ml)	0.1936	0.1291	0.0968	0.0484
η_{inh}(dl/g)	3.348	3.485	3.533	3.702

Water - No. 2 BS/IP/SL(S)336 Viscometer

c	0.1830	0.1307	0.0915	0.0458	0.0229	0.0057
η_{inh}	2.483	2.580	2.647	2.838	3.037	3.251

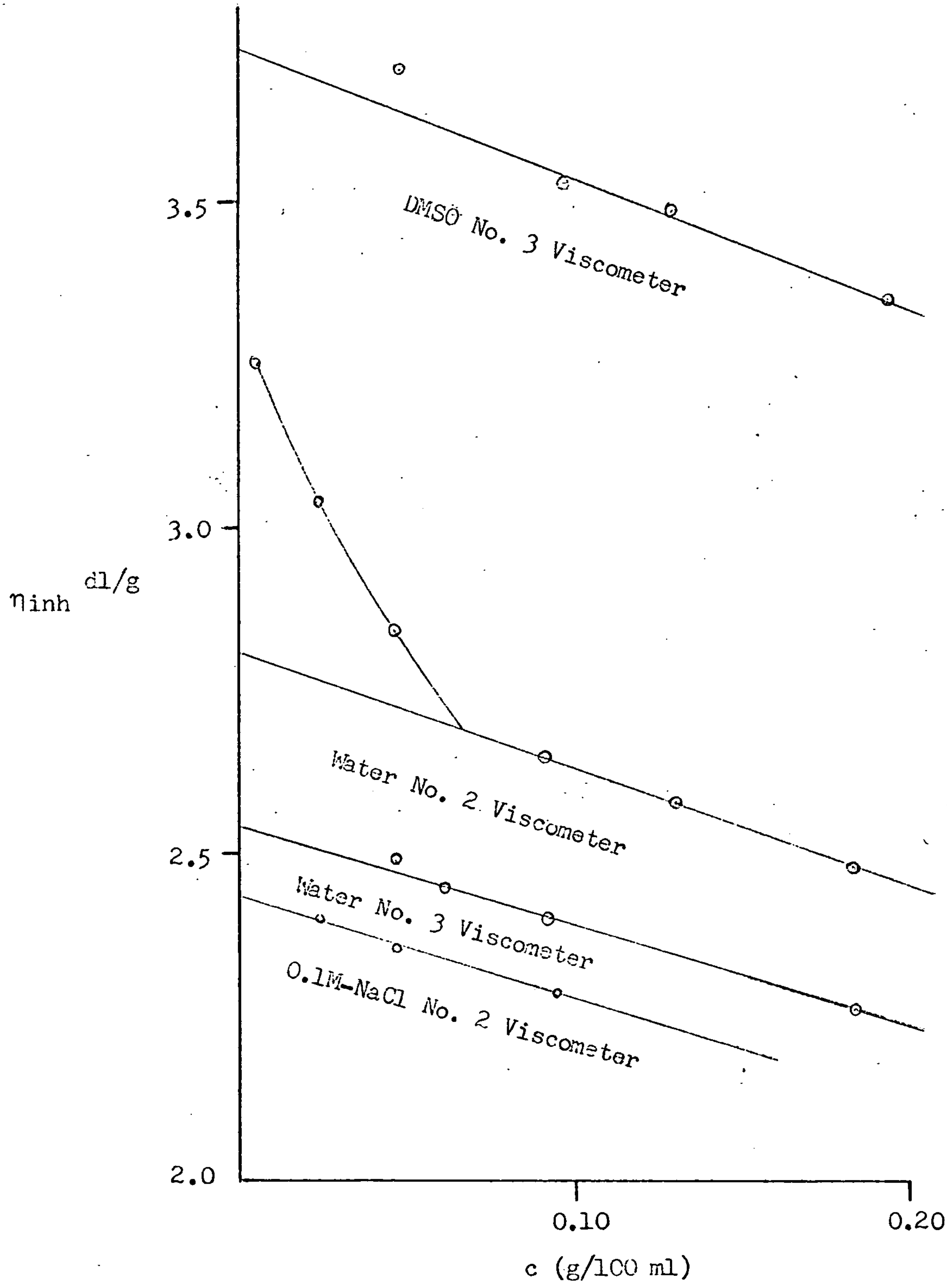
Water - No. 3 BS/IP/SL(S)5573 Viscometer

c	0.1830	0.0915	0.0605	0.0458
η_{inh}	2.262	2.403	2.448	2.493

0.1M-Sodium Chloride - No. 2 BS/IP/SL(S)336 Viscometer

c	0.0940	0.0470	0.0235
η_{inh}	2.279	2.351	2.400

FIG. II Intrinsic viscosity of poly-(galactose methacrylate) in water, 0.1M-sodium chloride and dimethyl sulphoxide (DMSO)



importance of using the same viscometer for all viscosity measurements and the validity, for general purposes, of using inherent viscosity values between c 0.1 - 0.2 as these values are not far removed from the extrapolated intrinsic viscosity.

A correlation of intrinsic viscosity with molecular weight for linear polymers can be achieved through the empirical equation proposed by Mark and Houwink[63], based on earlier work by Staudinger[64].

$$[\eta] = KM^a$$

where M is molecular weight, and K and a are constants for the particular polymer-solvent system. The value of a for most polymers has been found to be around 0.7.

The determination of molecular weight in polymeric materials yields a value which is always an average of the molecular weights of the molecules present. What kind of average is obtained depends on the method of measurement. One of the most common average molecular weights is the average, M_w. It is defined as:-

$$M_w = \Sigma NM^2 / \Sigma NM$$

where/

where N = number of molecules of molecular weight M. The M_w of P-GM was determined in aqueous solution by the light scattering technique of Zimm[91]. The SOFICA Photo Gonio Diffusometer was used and M_w calculated from the equation[92]

$$\frac{Hc}{\tau} = \frac{1}{M_w} + \frac{2Bc}{RT} \qquad \ldots\ldots\ldots(1)$$

where τ = turbidity due to polymer,

c = concentration of polymer in g/ml water,

H = a constant $= \frac{32\pi^3 n^2}{3\lambda^4 N_o} \cdot \left(\frac{dn}{dc}\right)^2$,

n = refractive index of water = 1.340,

λ = wavelength of incident light = 4.358×10^{-5} cm,

N_o = Avogadros number = 6.023×10^{23},

and dn/dc = refractive index increment due to increase in concentration of polymer. The dn/dc of P-GM in water was measured by a differential refractometer at 4.358×10^{-5} cm and found to be 0.1430.

The SOFICA was first calibrated with aqueous silica sol[93]. The turbidity of the sol was determined at 4.358×10^{-5} cm on a visible spectrophotometer, according/

according to the equation:

$$I = I_o e^{-\tau c}$$

This value was related to the intensity of scatter of the sol at 90° (I_{90}) by the ratio $\tau/I_{90} = 0.0013$. Hence the scale deflections obtained with polymer solution could be related to polymer turbidity.

Subtraction of the observed scale deflections for water from those of polymer solution at the corresponding angle gave a measure of the intensity of scatter due to polymer. This value was multiplied by the coefficient $\sin\theta/(1 + \cos^2\theta)$ to give the corrected intensity of scatter I_c.

Equation (1) can now be re-written as

$$\frac{c}{I_c} \cdot \frac{H}{0.0013} = \frac{1}{M_w} + \frac{2Bc}{RT}$$

I_c was measured at several angles for each concentration of the polymer and the results were plotted as a mesh of points using as axis c/I_c and $\sin^2\theta/2 + Kc$ --- K is a constant (10^3) arbitrarily chosen to give an open display/

display of the experimental data, and to enable the two extrapolations to $c = 0$ and $\theta = 0$ to be carried out with comparable accuracy.

Experimental data are shown in Fig. III.

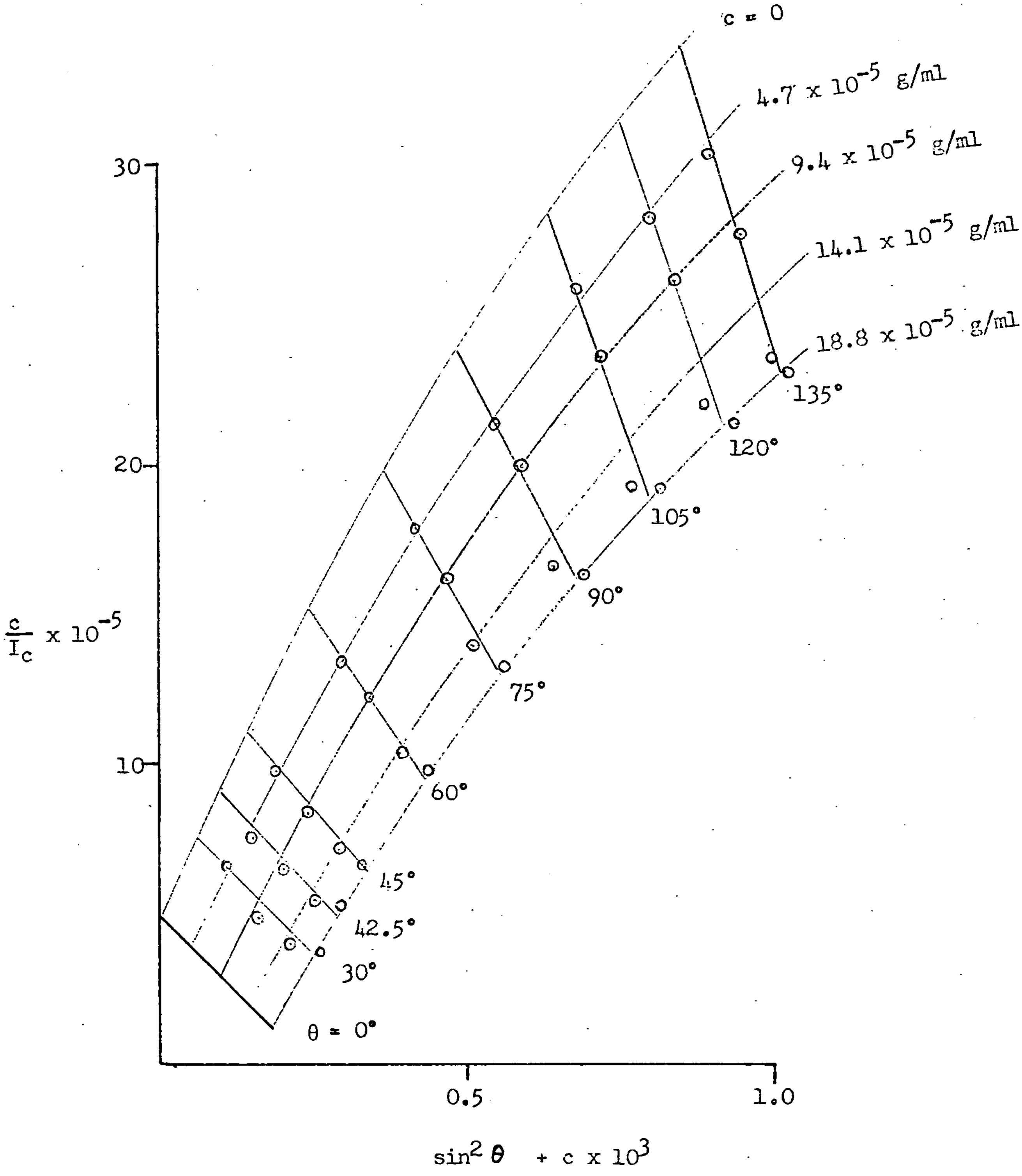
The common intercept $c/I_c = 5.0 \times 10^{-5}$

and $H/0.0013 = 4.29 \times 10^{-3}$

$\therefore \underline{M_w} = \underline{4.66 \times 10^6}$

The Zimm-plot obtained is not normal. At higher concentrations the plot tended to fold back on itself, however, it was felt that further investigation into the cause of this behaviour was beyond the scope of this thesis.

FIG. III Zimm-plot of poly-(galactose methacrylate) in water



3.3 Experimental

Materials

Azobisisobutyronitrile (AIBN)	Polymer Consultants Ltd.
Acetic Anhydride	M & B Laboratory Chemicals
Ammonium Persulphate	Analar B.D.H. reagent
Anhydrous Dimethylformamide	B.D.H. reagent, distilled over barium oxide
Anhydrous Pyridine	Analar B.D.H. reagent, distilled over phosphoric oxide
Benzene	Analar B.D.H. reagent, washed with concentrated sulphuric acid and water to remove thiophene, dried over sodium sulphate and sodium wire, and distilled over phosphoric oxide
Benzoyl Chloride	B.D.H. reagent
2-Methoxyethanol	B.D.H. reagent
Phenylhydrazine	B.D.H. reagent, distilled immediately before use
Phenylisocyanate	B.D.H. reagent
Sodium Borohydride	B.D.H. reagent
Sodium Chlorite	B.D.H. technical reagent recrystallised from 50% aqueous solution

Methods/

Methods

Acetyl Content was determined by the method of Whistler and Jeanes[65].

Periodate Consumption was measured by Aspinall and Ferrier's spectrophotometric method[66].

Formaldehyde Release was determined by the direct colorimetric method of Frisell *et al*[67] with chromotropic acid.

Differential Thermal Analysis (DTA). Polymer samples (10 mg) were heated under vacuum (0.1 mm) relative to glass beads in a DuPont 900 Differential Thermal Analyser at T = 20°/min and ΔT = 0.2 and 0.5°/in from -40° until the removal of solvent. The removal of solvent showed as a large endothermic peak at about T_G. On second and subsequent heating, T_G was shown as a well-defined, repeatable base-line shift.

Inherent viscosity (or logarithmic viscosity number) was measured in a BSU-tube viscometer (size 1) at 25°.

$$\eta_{inh} = c^{-1} \ln (t_{soln.}/t_{solv.})$$

where η_{inh} = inherent viscosity in dl/g

c = concentration of polymer in g/100ml

$t_{soln.}$ = time of flow for the polymer solution

$t_{solv.}$ = time of flow for the solvent

Other materials and methods were described previously.

Poly-(1,2:3,4-di-O-isopropylidene-6-O-methacryloyl-α-D-galactopyranose) (P-DGM, XIII)

DGM (20g) and AIBN (20 mg) were dissolved in thiophene-free benzene (4.5 g) and the solution frozen at -80°. The tube was evacuated, filled with nitrogen and then allowed to come to 20°. This degassing procedure was repeated three times after which the tube was sealed and heated at 50° for 4 hr. The polymer plug was dissolved in chloroform (400 ml) and the polymer reprecipitated with methanol (4 litres), washed with methanol and dried to a white powder (18.90 g, 94.5%), $[\alpha]_D$ -60° (c 0.5 in chloroform), η_{inh} 3.7 (c 0.1 in chloroform). [Found: C, 59.1; H, 7.4. $(C_{16}H_{24}O_7)_n$ requires C, 58.5; H, 7.4%].

Poly-(6-O-methacryloyl-D-galactose) (P-GM, XV)

P-DGM (14 g) was dissolved in formic acid (1400 ml) and water (70 ml) added, and the solution stirred at 20° for 18 hr, when more water (630 ml) was added and the solution stirred a further 6 hr; the rotation was now constant ($[\alpha]_D$ +76°, calculated on P-GM). The bulk of the formic acid was removed by dialysis against running water for 3 days, and the solution concentrated under reduced pressure to 500 ml. Sodium bicarbonate (5 g) was added and the solution stirred at 20° for 18 hr, dialysed against running water and insoluble/

insoluble carbonates removed at the centrifuge. The solution was taken to pH7 with hydrochloric acid and the polymer precipitated with isopropanol (2.5litres), washed with isopropanol, ether and dried. The polymer was reprecipitated from water solution (250 ml) with isopropanol (1.25 litres) to give a white powder (9.80 g, 92.6%) which had a reducing power of 96.6% and $[\alpha]_D$ +64° (c 0.459 in water). Infrared analysis showed strong hydroxyl absorption at 3400cm^{-1}, ester carbonyl at 1730cm^{-1} (gem-dimethyl absent). [Found: C, 48.75; H, 6.6. $(C_{10}H_{16}O_7)_n$ requires C, 48.4; H, 6.5%]

Poly-(6-O-acryloyl-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose) (P-DGA, XIV)

DGA (10 g) and AIBN (20 mg) in benzene (2.25 g) were heated under nitrogen at 50° for 24 hr. The polymer was reprecipitated from chloroform solution as before with methanol to give a white powder (9.10 g, 91%) which had $[\alpha]_D$ -50° (c 0.5 in tetrachloroethane), η_{inh} 0.9 (in tetrachloroethane). [Found: C, 57.6; H, 7.05. $(C_{15}H_{22}O_7)_n$ requires C, 57.3; H, 7.05%].

Poly-(6-O-acryloyl-D-galactose) (P-GA, XVI)

P-DGA (8.8 g) was dissolved in formic acid (1160 ml) and/

and water (70 ml) added. To this solution during 2.5 hr, water (530 ml) was added gradually, and the solution stirred for 3 days at 20°, when the specific rotation was constant ($[\alpha]_D$ +71°). The solution was dialysed, concentrated and freeze-dried to a white powder (6.90 g, 105%) which had a reducing power of 90.9% and $[\alpha]_D$ +56° (c 0.5 in water), η_{inh} 0.6 (c 0.5 in water). [Found: C, 45.3; H, 6.05. $(C_9H_{14}O_7)_n$ requires C, 46.15; H, 6.0%].

Polymerisation of 6-O-Methacryloyl-D-galactose (GM) 25 w/w % Aqueous solution

GM 25 w/w % aqueous solution (19.1 g) was washed with chloroform (4 x 5 ml). The chloroform washings were optically inactive and consisted mainly of p-methoxyphenol. The inhibitor-free solution was evaporated at 20° under reduced pressure until free from chloroform and water added to 25 w/w % solution.

Ammonium persulphate (50 mg) was added and the solution heated at 100° under reflux for 4 hr. The thick polymer gel was broken down with isopropanol (100 ml), filtered, washed with isopropanol and ether and dried to a white powder (4.39 g, 91.8%) which was swellable but not soluble in water although it had identical infrared absorption to authentic, water-soluble P-GM described above.

Acetylation/

Acetylation of Poly-(6-O-methacryloyl-D-galactose) (XVII)

A solution of P-GM (1 g) in anhydrous dimethylformamide (100 ml) was treated with dry pyridine (12 ml) and acetic anhydride (24 ml) at 20° for 24 hr. On careful addition to water, a white precipitate formed, which was washed with water and dried. The product was acetylated again with pyridine (25 ml) - acetic anhydride (50 ml), isolated by pouring into water, and purified by reprecipitation of a dimethylformamide solution (100 ml) with water (400 ml). Washing with water gave the polymer acetate as a white powder (1.335 g, 82.6%), $[\alpha]_D$ +47° (c 0.5 in tetrachloroethane), η_{inh} 5.2 (c 0.1 in tetrachloroethane). [Found: C, 51.6; H, 5.85; Ac, 39.1. $(C_{10}H_{12.4}Ac_{3.6}O_7)_n$ requires C, 51.7; H, 5.85; Ac, 39.1%].

Acetylation of Poly-(6-O-acryloyl-D-galactose) (XX)

P-GA (303 mg) was converted into its acetate in the manner described above for the polymethacrylate. It was purified by dissolution in chloroform and reprecipitation with light petroleum (b.p. 40-60°) (5 vol). The polymeric acetate (420 mg, 84.2%) had $[\alpha]_D$ +52° (c 0.5 in tetrachloroethane), η_{inh} 0.9 (in tetrachloroethane). [Found: C, 50.8; H, 5.4; Ac, 40.1. $(C_9H_{10.4}Ac_{3.6}O_7)_n$ requires C, 50.5; H, 5.55; Ac, 40.2%].

Benzoylation of Poly-(6-O-methacryloyl-D-galactose) (XVIII)

P-GM (252 mg) was dissolved in anhydrous dimethylformamide (25 ml) and dry pyridine (5 ml) was added. The solution was cooled to 0°, benzoyl chloride (2.5 ml) added dropwise, and after 7 days at 20° the red solution was added slowly with stirring to ice-water. The resulting sticky precipitate was washed with water, hardened with methanol, dissolved as far as possible in acetone (50 ml), and an insoluble gel removed at the centrifuge. The viscous supernatant was added dropwise with stirring to water, and the white precipitate washed and dried. The polymer benzoate (422 mg, 78.6%) had $[\alpha]_D$ +100° ± 5° (c 0.1 in tetrachloroethane), η_{inh} 9.3 (c 0.1 in tetrachloroethane) [Found: C, 65.5; H, 4.85; $(C_{10}H_{13.3}Bz_{2.7}O_7)_n$ requires C, 65.6; H, 5.1%].

Benzoylation of Poly-(6-O-acryloyl-D-galactose) (XXI)

P-GA (207 mg) was benzoylated in the manner described above for the polymethacrylate. The polymeric benzoate (368 mg, 67.3%), which was purified by dissolution in chloroform and reprecipitation with light petroleum (b.p. 40-60°) (5 vol), had $[\alpha]_D$ +94° (c 0.5 in tetrachloroethane), η_{inh} 1.5 (in tetrachloroethane)

[Found:/

[Found: C, 67.7; H, 5.25, $(C_9H_{10.3}Bz_{3.7}O_7)_n$ requires C, 67.7; H, 4.7%].

Phenylcarbamoylation of Poly-(6-O-methacryloyl-D-galactose) (XIX)

A solution of P-GM (0.4 g) in dimethylformamide (20 ml) was heated with phenyl isocyanate (2 ml) at 100° for 3 hr and poured into ethanol. The precipitate was treated again in the same way and purified by solution in acetone (100 ml) and reprecipitation with light petroleum (b.p. 40-60°) (400 ml). The light brown triphenylcarbamate (845 mg; 82.8%) had $[\alpha]_D$ +20° (c 0.1 in tetrachloroethane), η_{inh} 1.3 (c 0.1 in tetrachloroethane) [Found: C, 61.9; H, 5.1; N, 7.2. $(C_{31}H_{31}N_3O_{10})_n$ requires C, 61.5; H, 5.2; N, 6.9%].

Phenylcarbamoylation of Poly-(6-O-acryloyl-D-galactose) (XXII)

P-GA (0.2 g) was converted into its phenylcarbamate in the manner described above for the polymethacrylate, using propan-2-ol-ether (5:1) instead of ethanol to precipitate the product from the reaction solution. The polymeric phenylcarbamate (352 mg, 62.2%), after being purified by dissolution in dimethylformamide and reprecipitation with water/

water (10 vol), had $[\alpha]_D$ +30° (c 0.52 in dimethylformamide), η_{inh} 1.0 (in dimethylformamide), ν_{max} 3400 (NH), 1750-1720 (C═O), 1610 cm^{-1} (conjugated C═C) {Found: C, 61.9; H, 5.1; N, 7.6. $[C_9H_{14}O_7(PhNCO)_{3.6}]_n$ requires C, 61.9; H, 4.85; N, 7.6%}. This derivative was insoluble in tetrachloroethane.

Nitration of Poly-(6-O-methacryloyl-D-galactose)

Sodium fluoride (0.2 g) was added to a solution of nitrogen pentoxide (1.32 g) in chloroform (10 ml), prepared as described by Caesar and Goldfrank[46], the mixture cooled to 0°, and polymer(XIII) (211 mg) added. The mixture was stirred for 45 min; the final temperature was 10°. The product was washed with chloroform and hot water, dialysed against running water for 3 days, and the insoluble trinitrate isolated as a white powder (285 mg, 87.4%), ν_{max} 1660 cm^{-1} (ester $O\cdot NO_2$) [Found: C, 30.0; H, 3.2; N, 10.5. $(C_{10}H_{13}N_3O_{13})_n$ requires C, 31.3; H, 3.4; N, 11.0%].

Phenylhydrazone of Poly-(6-O-methacryloyl-D-galactose) (XXIII)

A solution of P-GM (306 mg) in dimethylformamide (27 ml) was treated with glacial acetic acid (3 ml) and freshly/

freshly distilled phenylhydrazine (3 ml), and after 24 hr at 20° the yellow solution was poured into water. The *polymer phenylhydrazone* was washed thoroughly with water and ethanol, and dried to a yellow powder (357 mg, 85.6%), which was now completely insoluble in organic liquids including dimethylformamide and dimethyl sulphoxide [Found: C, 55.4; H, 6.6; N, 8.2. $(C_{16}H_{22}N_2O_6)_n$ requires C, 56.8; H, 6.55; N, 8.3%] ν_{max} 1610 cm^{-1} (PhNH·N:).

Phenylhydrazone of Poly-(6-O-acryloyl-D-galactose) (XXIV)

P-GA (102 mg) was converted into its *phenylhydrazone* (120 mg, 85%) in the manner described for the polymethacrylate; ν_{max} 3500-3300 (OH), 1730 (ester C=O), and 1610 cm^{-1} (PhNH·N:) [Found: C, 54.0; H, 6.35; N, 8.0. $(C_{15}H_{20}N_2O_6)_n$ requires C, 55.6; H, 6.6; N, 8.6%]. The hydrazone was insoluble.

Phenylosazone Formation of Poly-(6-O-methacryloyl-D-galactose) (XXV)

A solution of P-GM (204 mg) in water (20 ml) at 90° was treated with glacial acetic acid (0.2 ml) and phenylhydrazine (0.35 ml) with vigorous stirring; a precipitate separated almost/

almost immediately. The mixture was stirred at 90° for 2 hr, and the orange product (248 mg) washed with ethanol and ether {Found: C, 58.7; H, 6.55; N, 10.3. Substitution of two units as phenylhydrazone and one unit as phenylosazone, i.e. $[(C_{16}H_{22}N_2O_6)_2C_{22}H_{26}N_4O_5]_n$ requires C, 58.5; H, 6.4; N, 10.2%}.

Phenylosazone Formation of Poly-(6-O-acryloyl-D-galactose) (XXVI)

P-GA (0.1 g) was converted into a mixed phenylhydrazone-phenylosazone (2:1)(136 mg) in the manner described for the polymethacrylate {Found: C, 58.9; H, 6.15; N, 10.4. Substitution of two units as phenylhydrazone and one unit as phenylosazone, $[(C_{15}H_{20}N_2O_6)_2C_{21}H_{24}N_4O_5]_n$, requires C, 57.6; H, 6.25; N, 10.5%}.

Oxidation of Poly-(6-O-methacryloyl-D-galactose)

M-Sodium chlorite (40 ml) was added to a solution of P-GM (991 mg) in 4 M-acetic acid (50 ml), the solution diluted to 100 ml with water, and the oxidation allowed to proceed at 20° for 24 hr. Acetic acid and inorganic ions were removed by dialysis, first against tap-water and then against distilled/

distilled water, and cations were removed by passage through an Amberlite resin IR-120-H column (20 ml). The eluate (170 ml) contained poly-(6-*O*-methacryloyl-*D*-galactonic acid) and showed no measurable optical rotation in a 2-dm tube. One half of this solution was freeze-dried to a white powder (330 mg, 67.1%), which was partly converted into the polymeric 1,4-lactone on drying at 20°/0.1 mm over phosphoric oxide for 18 hr. It had $[\alpha]_D$ -36° (c 0.5 in H_2O after 5 days), η_{inh} 7.4 (c 0.11 in H_2O). Complete conversion into the water-insoluble *poly-(6-O-methacryloyl-D-galactono-1,4-lactone)*, ν_{max} 1780 (γ-lactone C═O) and 1730 cm^{-1} (ester C═O), was effected by drying at 60° [Found: C, 48.9; H, 5.95. $(C_{10}H_{14}O_7)_n$ requires C, 48.8; H, 5.75%].

The other half of the polyacid solution was titrated to pH 9 with 0.1 N-sodium hydroxide (20 ml), and the solution dialysed, concentrated, and freeze-dried, to give the *polymeric sodium salt* as a monohydrate (350 mg, 61.2%), $[\alpha]_D$ +17° (c 0.5 in H_2O), η_{inh} 14.9 (c 0.1 in H_2O) and 2.2 (c 0.1 in 0.1 M-NaCl), ν_{max} 1730 (ester C═O) and 1600 cm^{-1} (CO_2^-) [Found: C, 39.0; H, 6.0; Na, 7.6. $(C_{10}H_{15}NaO_8,H_2O)_n$ requires C, 39.5; H, 5.65; Na, 7.6%].

Oxidation/

Oxidation of Poly-(6-O-acryloyl-D-galactose)

P-GA (504 mg) was oxidised with chlorous acid at pH 3 in the manner described for the polymethacrylate, to give a white powder (402 mg), which was partly lactonised even by freeze-drying. Drying at 60°/0.1 mm gave poly-(6-O-acryloyl-D-galactono-1,4-lactone), ν_{max} 1780 (γ-lactone C═O) and 1740 cm^{-1} (ester C═O), which was insoluble in water [Found: C, 45.9; H, 5.35. $(C_9H_{12}O_7)_n$ requires C, 46.6; H, 5.2%]. Poly(sodium 6-O-acryloyl-D-galactonate) had $[\alpha]_D$ +10° (c 0.5 in H_2O), η_{inh} 12.2 (c 0.1 in H_2O) and 1.4 (c 0.1 in 0.1 M-NaCl).

Attempted Preparation of Poly-(6-O-acryloyl-D-galactonamide)

The above polymeric lactone (105 mg) was shaken with liquid ammonia (10 ml) in a sealed tube at 20° for 3 days. The lactone partly dissolved to give a mobile supernatant and an insoluble gel which adhered to the sides of the tube. The supernatant was decanted, the ammonia removed, and the solid recrystallised from ethanol, to give D-galactonamide (50 mg), m.p. 171-173°, $[\alpha]_D$ +26° (c 3.2 in H_2O) (lit,[18] m.p. 176°, $[\alpha]_D$ +31.8°) (Found: C, 36.9; H, 6.8; N, 7.0. Calc. for $C_6H_{13}NO_6$: C, 36.9; H, 6.7; N, 7.2%). The insoluble residue (35 mg) was presumably chiefly polyacrylamide.

Poly/

Poly-(6-O-methacryloyl-D-galactitol) (XXXI)

P-GM (0.5 g, 2.01 mmoles of $C_{10}H_{16}O_7$) in water (45 ml) was cooled to 0°, sodium borohydride (152 mg, 4.02 mmoles) in water (5 ml) added dropwise with stirring, and the solution left at 20° for 24 hr. After acidification with acetic acid, the solution was dialysed, concentrated, and freeze-dried, to give a white, non-reducing *poly-(6-O-methacryloyl-D-galactitol)* (419 mg, 83.1%), $[\alpha]_D$ +15° (c 0,5 in H_2O), η_{inh} 2.7 (in H_2O) [Found: C, 47.9; H, 7.2. $(C_{10}H_{18}O_7)_n$ requires C, 48.0; H, 7.25%].

Nitration of Poly-(6-O-methacryloyl-D-galactitol)

The above reduced polymer (152 mg) was nitrated with nitrogen pentoxide in chloroform as described above for poly-(6-O-methacryloyl-D-galactose), to give a *tetranitrate* (244 mg, 93.5%), which was only partly soluble (40%) in boiling ethyl acetate [Found: C, 26.9; H, 3.25; N, 13.4. $(C_{10}H_{14}N_4O_{15})_n$ requires C, 27.9; H, 3.3; N, 13.0%].

Poly-(2,3-O-isopropylidene-1-O-methacryloyl-DL-glyceritol) (P-IGLM) (XXXII)

IGLM (5 g) was polymerised in bulk under nitrogen

at/

at 50° for 24 hr with azobisisobutyronitrile (25 mg) as initiator. The polymeric glass was broken down with some mechanical loss and this material (4.23 g) dissolved in chloroform (100 ml), filtered and reprecipitated with methanol (1 litre). The polymer was a white powder (4.07 g, 96.2%) which was optically inactive and had η_{inh} 3.66 (c 0.509 in chloroform). [Found: C, 59.7; H, 8.01, Calc. for $(C_{10}H_{16}O_4)_n$ C, 60.0; H, 8.0%].

Poly-(1-O-methacryloyl-DL-glyceritol) (P-GLM) (XXXIII)

Hydrolysis with (a) 50% Formic Acid

P-IGLM (992 mg) was dissolved in formic acid (50 ml) and water (50 ml) added to give a 50% aqueous formic acid solution. This solution was stirred at 100° under reflux for 8 hr and the solution dialysed against running water for 3 days, concentrated, and freeze-dried to give a white powder (810 mg, 102.0%) which had η_{inh} 1.4 (c 0.1 in water).

Hydrolysis with (b) N-Hydrochloric Acid

P-IGLM (1 g) was stirred vigorously with N-hydrochloric acid (20 ml) at 100°. The polymer dissolved quickly/

quickly with the evolution of acetone. After 30 min, the solution was neutralised with N-sodium hydroxide, filtered, and the deacetonated polymer precipitated with ethanol (400 ml), centrifuged, washed with ethanol and ether and dried in vac over phosphoric oxide to give a white powder (670 mg, 83.8%) which had η_{inh} 8.25 (c 0.103 in water). [Found: C, 51.4; H, 7.72. Calc. for $(C_7H_{12}O_4)_n$ C, 52.5; H, 7.53%].

Hydrolysis with (c) 2-Methoxyethanol/Hydrochloric Acid

P-IGLM (1.02 g) was dissolved in 2-methoxyethanol (45 ml) and the solution heated to 100° on a water bath. The solution was stirred vigorously and 5 N-hydrochloric acid (5 ml) added dropwise over 30 min to ensure that precipitation of the polymer did not occur. Water (50 ml) was then added dropwise over a further 30 min when the solution was heated for another hour. 2-Methoxyethanol and hydrochloric acid were removed by dialysis against running water for 3 days when the solution was concentrated under reduced pressure and freeze-dried to give a white powder (800 mg, 98.0%) which had η_{inh} 1.0 (c 0.5 in water). Polymers from methods (a), (b), and (c) had identical infrared spectra and showed strong hydroxyl absorption at 3400 cm^{-1}, and ester C:O at 1730 cm^{-1} (gem-dimethyl at 1380 cm^{-1} absent).

4. COPOLYMERS

4.1 Free-Radical Copolymerisation: General Introduction

Copolymers have great industrial importance. The simultaneous polymerisation of two or more monomers in the same reaction mixture leads to products with significantly different properties from those possessed by the individual homopolymers or their mixtures. Free-radical copolymerisation reactions are very closely related to radical-initiated polymerisation reactions of single olefin monomers in that both proceed by a typical chain reaction with discrete initiation, propagation and termination steps. However, the rate of copolymerisation may vary considerably from that of the homopolymerisation reactions of either monomer alone. These rate differences are a consequence of the differences in rates of addition of a monomer to itself or to a comonomer (reactivity ratios) and are responsible for the final chemical composition of the copolymer. Hence the usual industrial practice is to copolymerise monomers which are not widely different in rate characteristics. For this reason, it is difficult to copolymerise hydrophobic with hydrophilic monomers. Apart from differences in their solubility, their reactivities are generally very different with the result that a wide spectrum of copolymer compositions/

compositions is obtained in the final copolymer.

The object of this work was the preparation of hydrophilic copolymers of industrial, hydrophobic monomers and galactose monomers. It was thought that the acetonated galactose monomers would copolymerise with monomers such as methyl methacrylate, styrene, acrylonitrile etc. to give copolymers with a narrow spectrum of copolymer compositions and that deacetonation of these copolymers would give reactive, hydrophilic copolymers of potential commercial value.

Several examples of the copolymerisation of carbohydrate monomers with industrial monomers have appeared in the literature. Whistler and Goatley[68] described the copolymerisation of 1-acrylamido-1-deoxy-D-glucitol (A) and 1-deoxy-1-methacrylamido-D-glucitol (B) with vinyl acetate, methyl methacrylate and styrene. Copolymerisations with vinyl acetate were performed in water with ammonium persulphate initiator, while copolymerisations with methyl methacrylate and styrene were done in aqueous methanol solvent and benzoyl peroxide initiator. The reaction temperature was 50°. The following reactivity ratios were found:

(A)/

M_1	M_2	r_1	r_2
(A)	vinyl acetate	2.41	0.18
	styrene	0.056	2.72
	methyl methacrylate	0.206	4.22
(B)	vinyl acetate	0.56	0.16
	styrene	0.005	2.09
	methyl methacrylate	0.036	4.20

It can be seen that both of these water-soluble, carbohydrate monomers are much less reactive in copolymerisation than their parent monomers, acrylamide and methacrylamide - the reactivity ratios[69] in the copolymerisation of methacrylamide (M_1) and methyl methacrylate (M_2) are $r_1 = 0.47$ and $r_2 = 1.5$. Whistler also pointed out that the different solubility properties of the very water-soluble amides and the other water-insoluble monomers greatly limited the choice of solvent for the polymerisation.

Kimura and Imoto[70] copolymerised 1,2:5,6-di-*O*-isopropylidene-3-*O*-methacryloyl-α-*D*-glucofuranose with varying proportions of acrylonitrile. The copolymers were deacetonated in acidic zinc chloride solution to give hydrophilic copolymers which had better dyeing properties than poly/

poly-(acrylonitrile). They also quoted reactivity ratios for the copolymerisation of the glucose monomer (M_1) and acrylonitrile (M_2) as $r_1 = 0$ and $r_2 = 0.25$. These values were calculated on three copolymerisations only. In view of subsequent work in this thesis it seemed strange that the glucose monomer should show no tendency to homopolymerise in the presence of acrylonitrile. The results of Kimura and Imoto were, therefore, recalculated on the five copolymerisations quoted - Table 2 of their paper[70]. It was found that r_1 was then considerably negative and, as this is impossible, it is suggested that the above values are rather optimistic.

Copolymers of 3-O-allyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose and acrylonitrile have been prepared in this laboratory[71]. The maximum content of the allyl monomer in the copolymer was 2 mole - %, which represented 10.35% on a weight basis. The copolymers were deacetonated in sulpholane solution with hydrochloric acid at 30°, the specific rotation changing from a negative to a positive value in agreement with the formation of deacetonated glucopyranose residues in the copolymers.

Recent industrial interest in hydrophilic copolymers lies in the production of semi-permeable membranes for/

for the desalination of salt and brackish waters by reverse osmosis and for haemodialysis in artificial kidney machines, although the permeability of the membranes for the two processes is quite different. Membranes of low salt permeation are required for reverse osmosis desalination, while high salt permeability is desired for haemodialysis membranes.

4.2 Results and Discussion

It is will known[72] that increase in size of the alkyl group in an ester of an α,β-unsaturated acid does not greatly influence the reactivity ratios of such esters with many vinyl monomers, although a few exceptions to this general rule have been noted[73]. It has also been shown[74] that the relative reactivity of these esters to reference radicals is influenced by a steric effect if the alkyl group in the α-position is varied. Bevington and Malpass[75] have determined the monomer reactivity ratios for the radical copolymerisation of various esters of methacrylic acid with methyl methacrylate using tracer techniques. It was found that these reactivity ratios were approximately unity and their products not far from unity and, with one exception, the higher esters had a higher reactivity than the methyl ester.

The copolymerisation of two monomers M_1 and M_2 may be described schematically as follows, where $M_1\cdot$ and $M_2\cdot$ represent their respective radicals:

$$M_1\cdot + M_1 \xrightarrow{k_{11}} M_1\cdot$$
$$M_1\cdot + M_2 \xrightarrow{k_{12}} M_2\cdot$$
$$M_2\cdot + M_2 \xrightarrow{k_{22}} M_2\cdot$$
$$M_2\cdot + M_1 \xrightarrow{k_{21}} M_1\cdot$$

The/

The monomer reactivity ratios are given by $r_1 = k_{11}/k_{12}$ and $r_2 = k_{22}/k_{21}$, and the copolymer composition equation which relates the polymer composition to the monomer composition is given by:

$$\frac{dM_1}{dM_2} = \frac{M_1}{M_2} \cdot \frac{r_1M_1 + M_2}{r_2M_2 + M_1} = \frac{m_1}{m_2} \quad \text{for low conversion} \quad (1)$$

where M_1 and M_2 refer to monomer composition and m_1 and m_2 to the polymer composition[76].

This equation can be rearranged to a straight line form[77]. If $f = (m_1/m_2)$ and $F = (M_1/M_2)$, then equation (1) can be rewritten as:

$$f = F \cdot \frac{r_1F + 1}{r_2 + F}$$

or $fr_2 + fF = r_1F^2 + F$

or $fF - F = r_1F^2 - fr_2$ Dividing each side of this equation by f one obtains:

$$\frac{F}{f}(f - 1) = r_1\frac{F^2}{f} - r_2 \qquad (2)$$

A plot of $(F/f)(f-1)$ as ordinate and (F^2/f) as abscissa is a straight line whose slope is r_1 and whose intercept is $-r_2$. This plot was used to determine the reactivity ratios[78] r_1 and r_2 of methyl methacrylate (M_1) and diisopropylidene-galactose/

galactose methacrylate (M_2) in their copolymerisation to low conversion, in bulk, at 50° with AIBN as initiator. Experimental conditions are shown in Table V the copolymerisation being stopped after the time indicated by precipitation of the copolymer with methanol.

TABLE V. Copolymerisation of MM with DGM to Low Conversion

MM (mg.)	DGM (mg.)	MM:DGM Mole Ratio	AIBN (mg.)	Time (min.)	Yield of Copolymer (mg.)
1027.0	-	-	2.0	120	84.1
546.0	202.6	8.843	1.6	60	50.2
604.4	246.9	8.031	1.5	60	71.6
467.0	255.5	5.996	1.5	60	57.7
458.8	299.6	5.024	1.6	60	59.2
381.0	403.0	3.102	1.5	45	43.9
318.0	521.0	2.003	1.6	45	92.3

The composition of the copolymers was determined from methoxyl content as follows:-

If the copolymer is represented by the average unit, $C_{16}H_{24}O_7\cdot(C_5H_8O_2)_n$, where n is the ratio MM:DGM, then the weight of each repeating unit is 328.4 + 100.1n and the percentage methoxyl is:

$$\% \text{ OMe} = \frac{3103n}{328.4 + 100.1n}$$

Hence/

TABLE VI. Analysis of Copolymers

F (M_1/M_2) molar ratio	OMe Content of monomer mixture, %	OMe$^+$ Content of copolymers %	f (m_1/m_2) molar ratio	(F/f)(f-1) (Y_i)	F^2/f (X_i)	$X_i Y_i$	X_i^2
8.843	22.60	22.13	8.183	7.764	9.556	74.19	91.32
8.031	22.01	21.17	7.065	6.896	9.130	62.96	83.36
5.996	20.04	19.47	5.541	4.913	6.488	31.88	42.09
5.024	18.75	18.06	4.580	3.927	5.511	21.64	30.37
3.102	15.07	13.71	2.601	1.910	3.699	7.07	13.68
2.003	11.75	10.89	1.776	0.875	2.259	1.98	5.10
				$\sum$ 26.285	$\sum$ 36.643	$\sum$ 199.72	$\sum$ 265.92

+ corrected value

Hence n can be calculated from the methoxyl contents determined experimentally and corresponds to the values of F and f in Table VI. Methoxyl estimations were carried out in duplicate and corrected with the value determined for poly-(methyl methacrylate) prepared under the same conditions. This value was 30.71% and as poly-(methyl methacrylate) requires OMe, 31.00%, the observed copolymer methoxyl contents were increased by division of the observed value by 0.991.

The data (Table VI), in the Fineman-Ross form, were treated by the method of least squares to get the best fit to the experimental values as follows:

Let $Y = (F/f)(f-1)$ and $X = F^2/f$, then the coefficients m and c of the equation $Y = mX + c$ are found from the simultaneous equations:

$$\sum Y_i = nc + m \sum X_i \text{ ....(3)}$$

and

$$\sum X_i Y_i = c \sum X_i + m \sum X_i^2 \text{.....(4)}$$

where n is the number of points and $i = 1 \text{ ....} n$.

Substitution of these values (Table VI) in the above equations gives:

$$26.285 = 6c + 36.643m \text{ ....}(5)$$

$$199.72 = 36.643c + 265.92m\text{..........}(6)$$

Multiplying (5) x 36.643 and (6) x 6 and subtraction gives $\underline{m = 0.93}$

Substitution of this value in (5) gives $\underline{c = -1.30}$

The straight line with gradient 0.93 and intercept -1.30 is shown drawn through the experimental values (Table VI) in Fig. III.

The deviation from the fitted line is given by

$$d_i = Y_i - (mX_i + c)$$

and S_y, the standard error of estimate, equals the root mean square of the y deviations about the fitted line, i.e.

$$S_y = \sqrt{\sum d_i^2 / n}$$

The deviation from the fitted gradient m is given by

$$d_j = m - Y_j/X_j \text{ (where } Y_j = Y_i - c \text{ and } X_j = X_i\text{)}$$

and the standard error of estimate S_m, equals the root mean square deviation, i.e.

$$S_m = \sqrt{\sum d_j^2 / n}$$

These errors were calculated from Table VII.

Fig. III. Fineman-Ross plot in the copolymerisation
$F = [MM]/[DGM]$, $f = d[MM]/d[DGM]$

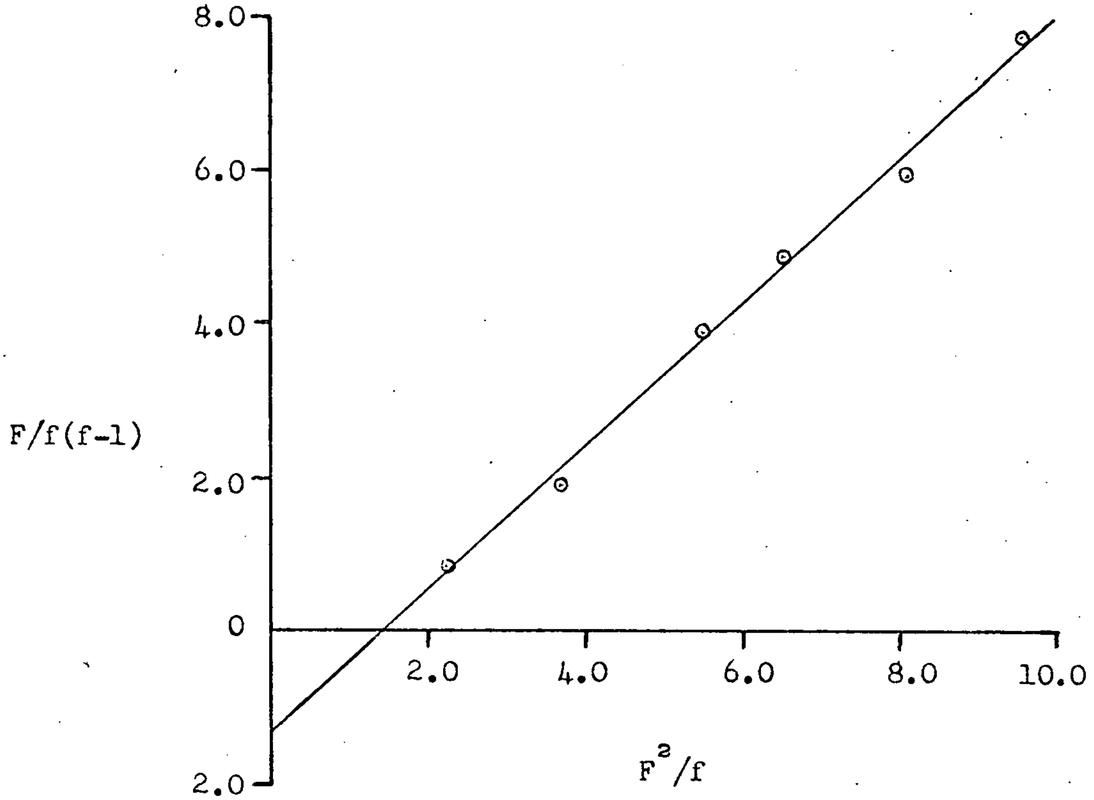


TABLE VII

Y_i	X_i	d_i	d_i^2	d_j	d_j^2
7.764	9.556	0.157	0.025	0.020	0.0004
6.896	9.130	-0.295	0.087	-0.032	0.0010
4.913	6.488	0.179	0.032	0.028	0.0008
3.927	5.511	0.102	0.010	0.019	0.0004
1.910	3.699	-0.230	0.053	-0.062	0.0038
0.875	2.259	0.074	0.005	0.033	0.0011
			$\sum$ 0.212		$\sum$ 0.0075

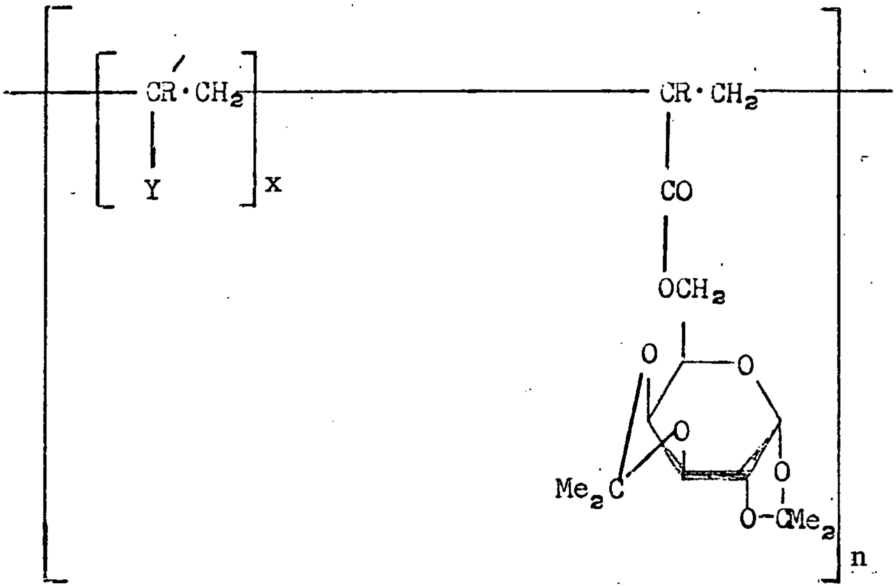
$$\therefore \quad S_y = \pm 0.19 \text{ and } S_m = \pm 0.03$$

Hence the copolymerisation reactivity ratios of methyl methacrylate, r_1, and diisopropylidenegalactose methacrylate, r_2, are 0.93 ± 0.03 and 1.30 ± 0.19 respectively.

These results prove that diisopropylidenegalactose methacrylate can be copolymerised to completion with any proportion of methyl methacrylate to give a copolymer, in which the units are arranged in a random manner and in the same molar ratio to that of the initial monomers, as their reactivity ratios and the product[79] of these ratios is approximately unity. This has been found in practice[80].

DGM was copolymerised in bulk at 50° with five different molar ratios (x) of MM to give a series of DGM:MMx random copolymers (XXXIV) in high yield and with high/

high inherent viscosities. The protecting isopropylidene groups were removed from XXXIV by hydrolysis in aqueous formic acid at 20° to give the series of water-insoluble, hydrophilic GM:MMx random copolymers (XXXV).



XXXIV: $R = R' = Me$, $Y = CO_2Me$

XXXVII: $R = R' = H$, $Y = CO_2Me$

XXXIX: $R = Me$, $R' = H$, $Y = Ph$

XLII: $R = R' = H$, $Y = CN$, $x = 6$

XLV: $R = Me$, $R' = H$, $Y = OAc$, $x = 0.46$

$$\mathrm{HCO_2H}\ \Big\downarrow\ \mathrm{H_2O}$$

XXXIV: $R = R' = Me$, $Y = CO_2Me$

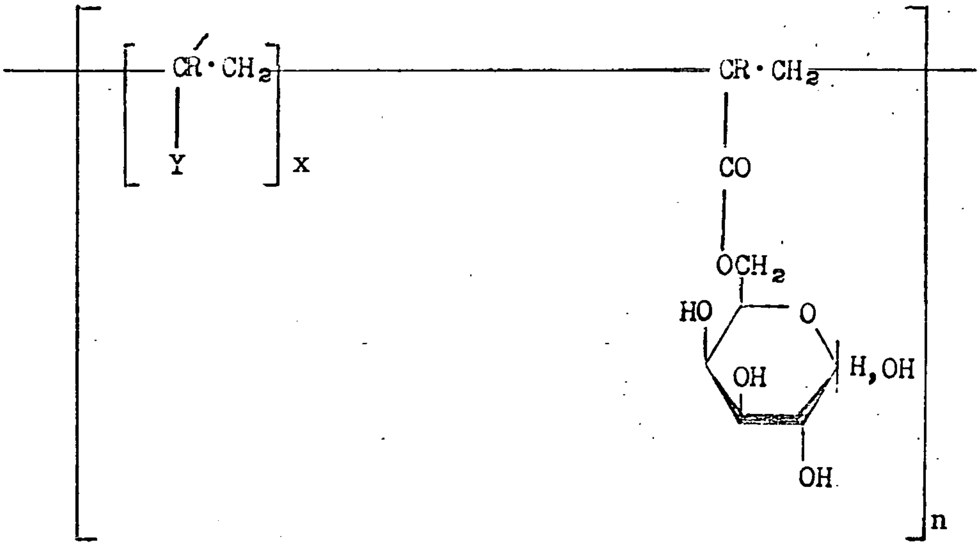
XXXVII: $R = R' = H$, $Y = CO_2Me$

XXXIX: $R = Me$, $R' = H$, $Y = Ph$

XLII: $R = R' = H$, $Y = CN$, $x = 6$

XLV: $R = Me$, $R' = H$, $Y = OAc$, $x = 0.46$

$\downarrow$ HCO_2H H_2O



XXXV: $R = R' = Me$, $Y = CO_2Me$

XXXVIII: $R = R' = H$, $Y = CO_2Me$

XL: $R = Me$, $R' = H$, $Y = Ph$, $x = 1$

XLIII: $R = R' = H$, $Y = CN$, $x = 6$

XLVI: $R = Me$, $R' = H$, $Y = OAc$, $x = 1$

$\downarrow$ $PhNH.NH_2$ $HOAc$

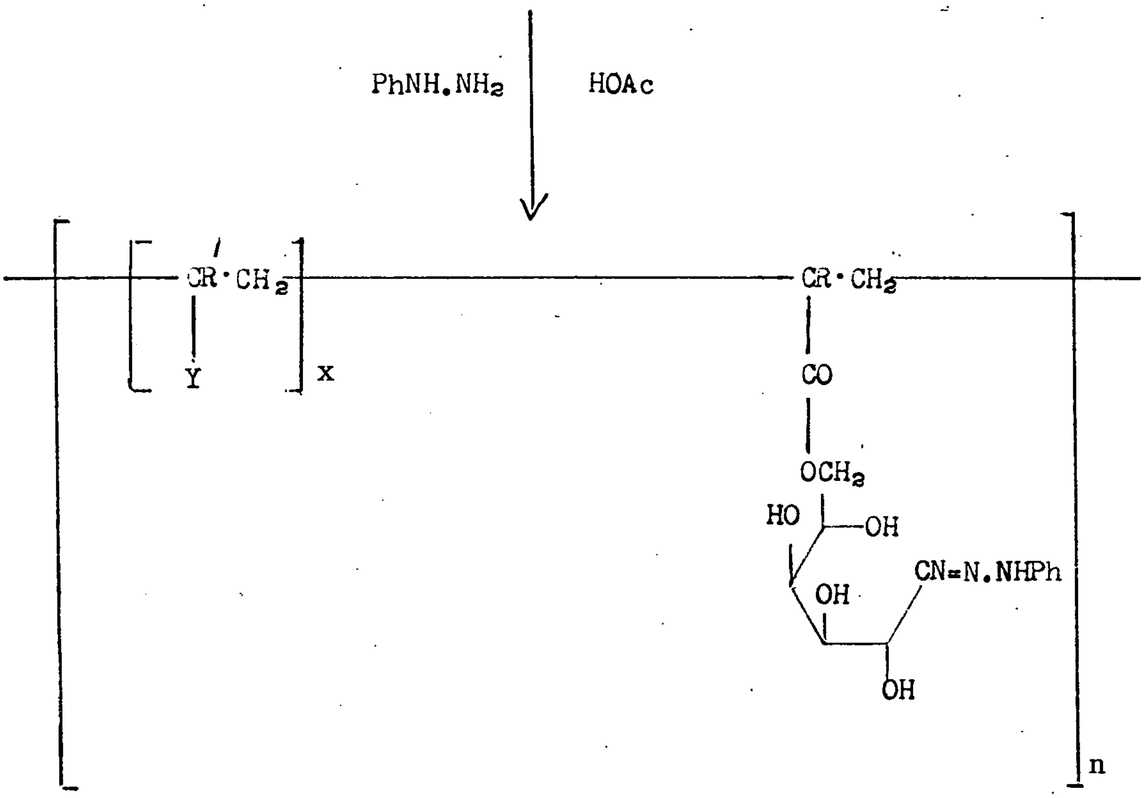
XXXV: $R = R' = Me$, $Y = CO_2Me$

XXXVIII: $R = R' = H$, $Y = CO_2Me$

XL: $R = Me$, $R' = H$, $Y = Ph$, $x = 1$

XLIII: $R = R' = H$, $Y = CN$, $x = 6$

XLVI: $R = Me$, $R' = H$, $Y = OAc$, $x = 1$



XXXVI: $R = R' = Me$, $Y = CO_2Me$

XLI: $R = Me$, $R' = H$, $Y = Ph$, $x = 1$

XLIV: $R = R' = H$, $Y = CN$, $x = 6$

XLVII: $R = Me$, $R' = H$, $Y = OAc$, $x = 1$

Yields/

Yields, analysis and physical properties of DGM:MMx and GM:MMx random copolymer series are shown in Tables VIII and IX. Chemical analysis of all copolymers showed that approximately initial DGM:MM monomer ratio had been maintained in the final copolymer. The high yields of water-insoluble GM:MMx copolymers showed that none of the water-soluble GM units had been lost in the preparation and they were, therefore, chemically bound to MM units. Water-soluble P-GM was not detected at any stage in the deacetonation procedure. GM:MMx copolymers were insoluble in methyl n-propyl ketone and no P-MM was extracted with this solvent. The deacetonated copolymers were, however, readily soluble in chloroform-ethanol and acetone-water mixtures although they were insoluble in each single component of these systems. They were also soluble in dimethylformamide.

It has been found that the MM units in DGM:MMx and GM:MMx copolymers did not influence the optical activity of the DGM and GM units in the copolymers but acted merely as a diluent of optical activity. Specific rotations were calculated by multiplying the specific rotation of the homopolymer in the appropriate solvent by the weight fraction of the sugar units in the copolymer. The uncertainty in $[\alpha]_D$ was ± 1°.

The/

TABLE VIII. Diisopropylidenegalactose methacrylate - methyl methacrylate system of copolymers

DGM:MMx Monomer Molar Ratio x	DGM:MMx Copolymer [$C_{16}H_{24}O_7.(C_5H_8O_2)_x$]$_n$ (XXXIV)									
	Yield %	η_{inh} in $CHCl_3$	[α]$_D$ Calcd.	[α]$_D$ Found c,0.5 in $CHCl_3$	Analysis Calcd.			Analysis Found		
					C,	H,	OMe%	C,	H,	OMe%
0	95.1			-60°	58.5	7.4	0	59.1	7.4	0
3.07	80.1	4.1	-31.0°	-31	59.2	7.7	15.0	58.9	7.95	14.8
4.0	89.3	2.3	-27.0	-27	59.3	7.75	17.0	58.6	7.28	16.8
6.2	92.7	2.6	-20.8	-20	59.5	7.82	20.3	59.5	7.83	19.3
9.0	96.9	2.2	-16.0	-18	59.6	7.87	22.7	58.6	7.52	23.7
12.0	93.0		-12.9	-12						

TABLE IX. Galactose methacrylate - methyl methacrylate system of copolymers

DGM:MMx Monomer Molar Ratio x	GM:MMx Copolymer $[C_{10}H_{16}O_7(C_5H_8O_2)_x]_n$ (XXXV)										
	Yield %	η_{inh} in DMF	$[\alpha]_D$ Calcd.	$[\alpha]_D$ Found c,0.5 in DMF	Analysis Calcd.			Analysis Found			Water Uptake %
					C,	H,	OMe%	C,	H,	OMe%	
0	96.8			+45°	48.4	6.5	0	48.75	6.6	0	Soluble
3.07	83.1	4.4	+20.1°	+21	54.8	7.36	17.1	53.5	7.55	16.1	
4.0	89.1	2.2	+17.2°	+15	55.5	7.46	19.1	55.6	7.64	17.3	19.1
6.2	99.1	2.0	+12.9	+15	56.7	7.61	22.1	56.6	7.71	20.4	14.0
9.0	95.4	2.3	+ 9.7	+ 8	57.5	7.72	24.3	56.6	7.87	23.4	10.0
12.0	94.0		+ 7.7	+ 8							7.7

The percentage water uptake of GM:MMx random copolymers in the form of thin, transparent films (Table IX) could be expressed linearly as a function of the mol. % GM units in the copolymer[81]. Above 20 mol. % GM, however, this value increased rapidly and it is predicted that at a certain critical GM:MM ratio a water-soluble copolymer will be produced. It is, therefore, possible to prepare GM:MMx random copolymer films with any desired water uptake between 0 - 20% by copolymerising DGM with MM in the appropriate molar ratio and removing the isopropylidene groups.

GM:MMx random copolymer films are successful membranes for the desalination of brine by the process of reverse osmosis[82]. Values for desalination of up to 98% have been obtained with water-throughput comparable with that of cellulose acetate. A GLM:MM_4 copolymer membrane was unsuccessful owing to compaction of the membrane under the high pressure necessary for reverse osmosis. It is thought that the heterocyclic galactose residues impart rigidity to the system, whereas acyclic, flexible glycerol residues may in fact reduce the resistance of the methacrylic backbone to compaction.

GM:MMx random copolymers (x = 3.07 and 6.2) were characterised by phenylhydrazone (XXXVI) formation (Table X). Elemental/

Elemental analysis agreed with the expected copolymer ratios. The copolymer phenylhydrazones became isoluble after isolation (phenylhydrazones of P-GM and P-GA are also insoluble) and showed strong infrared absorption at 1610 (CH:N.NHPh), 1730 (ester C:O) and 3400 cm^{-1} (CH).

<u>TABLE X.</u> Phenylhydrazones of the galactose methacrylate-methyl methacrylate system of copolymers (XXXVI)

Copolymer	Yield (%)	Analysis
GM:$MM_{3.07}$ copolymer	97.0	Found: C, 57.4; H, 7.55; N, 4.1 $[C_{16}H_{22}N_2O_6.(C_5H_8O_2)_{3.07}]_n$ requires C, 58.3; H, 7.27; N, 4.3
GM:$MM_{6.2}$ copolymer	92.0	Found: C, 57.9; H, 7.47; N, 3.2 $[C_{16}H_{22}N_2O_6.(C_5H_8O_2)_{6.2}]_n$ requires C, 58.9; H, 7.53; N, 2.9

The bulk copolymerisation of DGA (V) with methyl acrylate (MA) under free-radical conditions is a violent exothermic reaction. Hence DGA was copolymerised with MA in aqueous emulsion under reflux conditions. (Plate IV). DGA:MAx copolymers (XXXVII) are described in Table XI. The deacetonation procedure for these copolymers had to be modified as they were insoluble in formic acid. However, addition of formic acid (9 vol.) to a solution of the copolymer in acetone (10% w/v) followed by the addition of water/

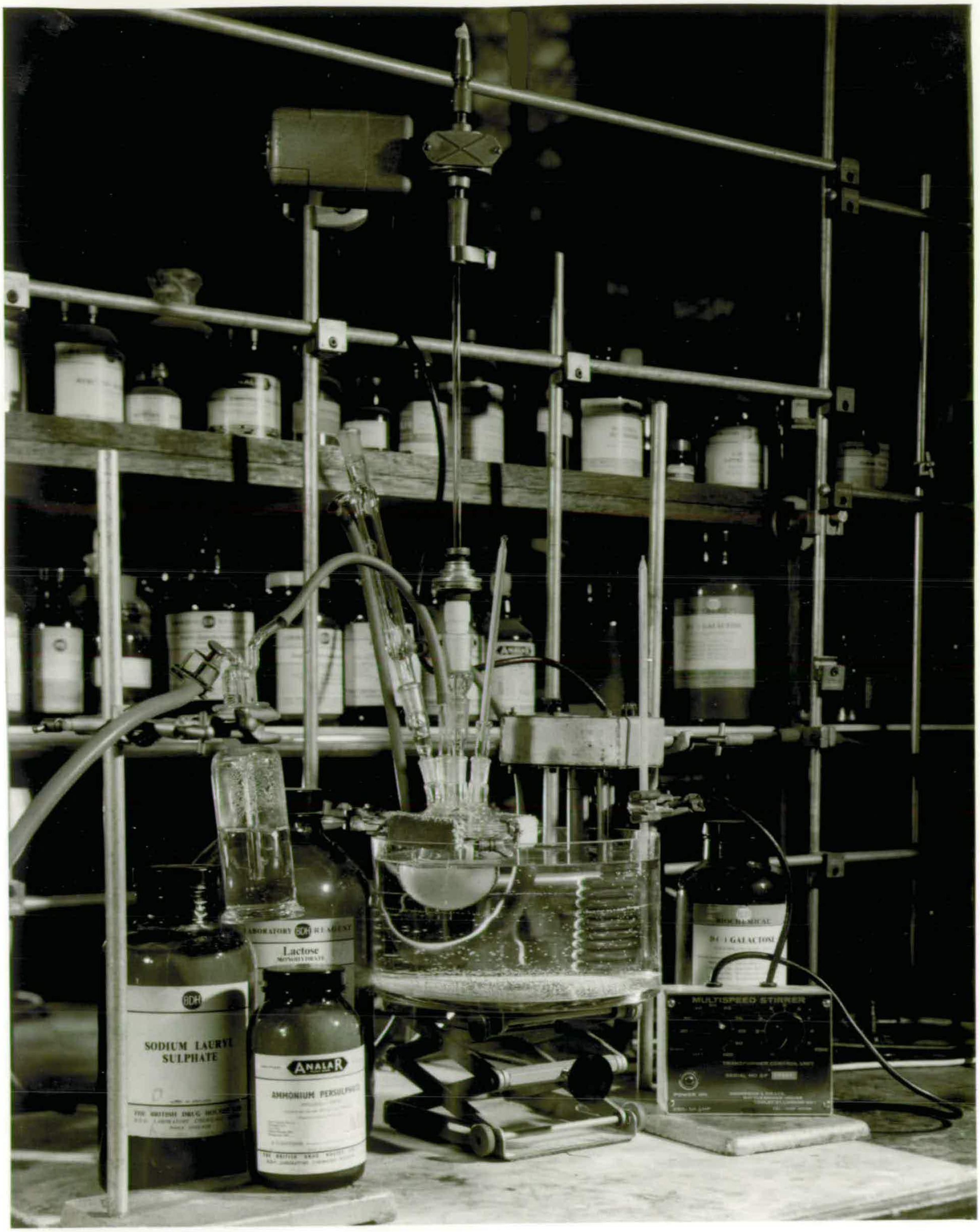


PLATE IV. Emulsion copolymerisation of diisopropylidenegalactose acrylate with methyl acrylate

TABLE XI. Diisopropylidenegalactose acrylate-methyl acrylate system of copolymers

DGA:MAx Monomer Molar Ratio x	DGA:MAx Copolymer $[C_{15}H_{22}O_7.(C_4H_6O_2)_x]_n$ (XXXV11)									
	Yield %	η_{inh} in $CHCl_3$	$[\alpha]_D$ Calcd.	$[\alpha]_D$ Found c 0.5 $CHCl_3$	Analysis Calcd C,	H,	OMe%	Analysis Found C,	H,	OMe%
0	91.0	..		-56°	57.3	7.05	0	57.6	7.05	0
9	89.7	2.7	-16°	-15	56.2	7.03	25.6	56.2	7.20	22.9
20	92.6	3.6	-9	-8	56.2	7.03	30.5	56.0	7.05	29.8

TABLE XII. Galactose acrylate-methyl acrylate system of copolymers

DGA:MAx Monomer Molar Ratio x	GA:MAx Copolymer $[C_9H_{14}O_7.(C_4H_6O_2)_x]_n$ (XXXV111)									
	Yield %	η_{inh} in DMF	$[\alpha]_D$ Calcd.	$[\alpha]_D$ Found c 0.5 DMF	Analysis Calcd C,	H,	OMe%	Analysis Found C,	H,	OMe%
0	105.0	.		+43°	46.15	6.0	0	45.3	6.05	0
9	101.1	2.3	+10°	+17	53.6	6.79	27.7	54.0	7.26	24.4
20	90.5	3.7	+5	+9	54.6	6.91	31.7	54.75	7.11	31.7

water (1 vol.) did not cause precipitation and deacetonation was taken to be complete after three days at 20°. GA:MAx copolymers (XXXVIII) are described in Table XII. They were insoluble in chloroform-ethanol and acetone-water (unlike GM:MMx random copolymers) but were soluble in dimethylformamide. Analysis showed that approximately the initial monomer ratios had been maintained in the final copolymer. The optical activity of DGA:MAx copolymers was near to the calculated value if it was assumed that MA units acted as a diluent of optical activity. This relationship, however, did not hold for the deacetonated copolymers.

The T_Gs of copolymers show a number of interesting features. Block and graft copolymers may have two transition temperatures, one close to the T_G for each homopolymer. Ordinary random vinyl copolymers show only a single T_G which is between the T_G of the corresponding homopolymers[56]. DGA:MAx and GA:MAx copolymers showed a single T_G on DTA (Table XIII).

TABLE XIII. Glass transition temperature in the DGA:MAx and GA:MAx system of copolymers

Copolymer	T_G °C
DGA:MA_{20}	25
GA:MA_{20}	29
DGA:MA_9	34
GA:MA_9	39

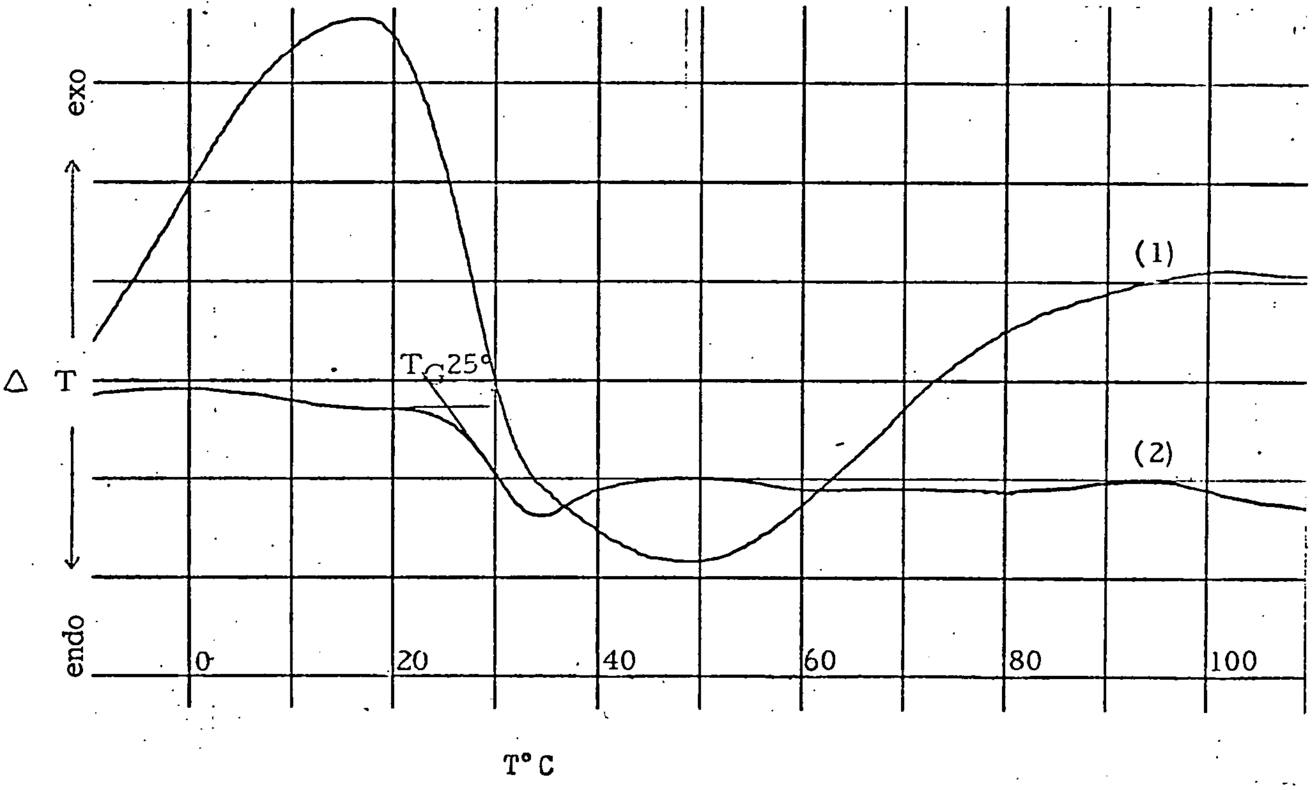


Fig. IV. Thermogram of DGA:MA_{20} Copolymer

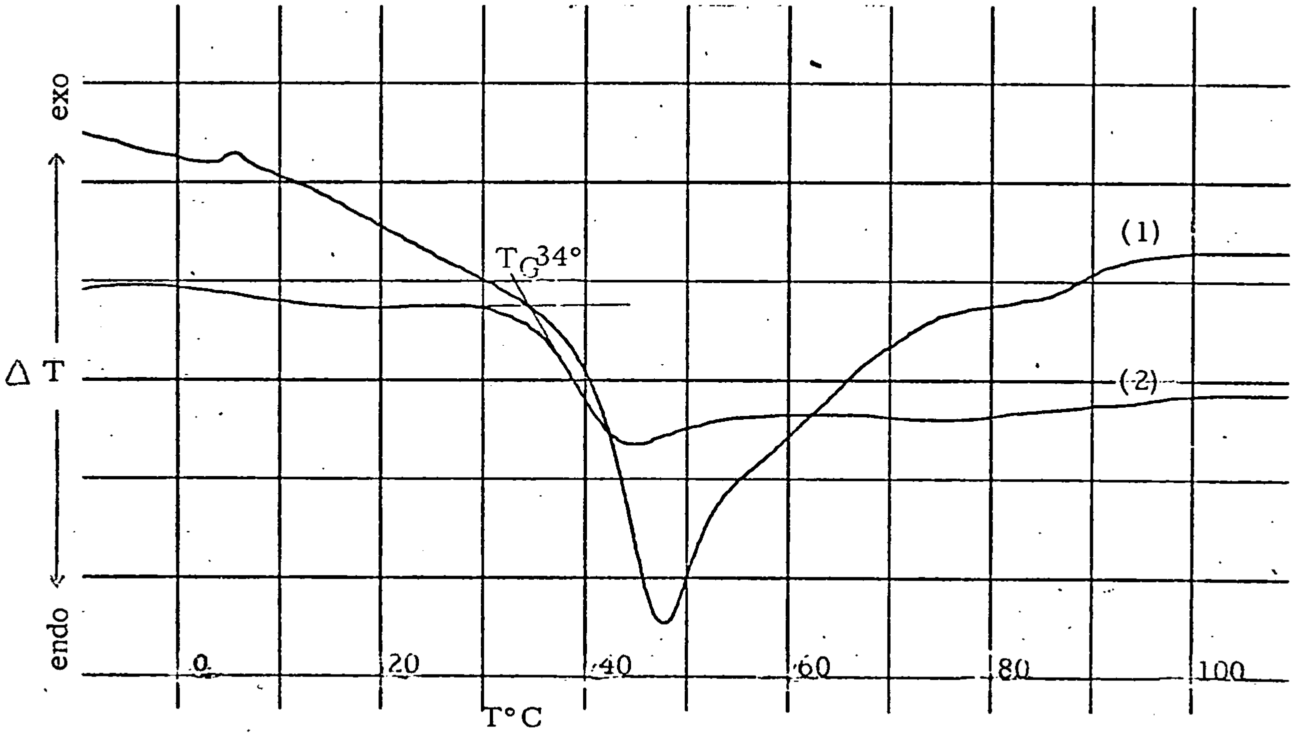


Fig. V. Thermogram of DGA:MA_9 Copolymer

Thermograms for DGA:MAx copolymers are shown in Figs IV and V. The T_G for P-MA prepared under identical conditions, was 14°. The usually reported value is $T_G = 0°$.

The similarity of DGM and DGA to MM and MA respectively has also been shown by copolymerisation with other vinyl monomers. The reactivity ratios for MM and styrene (S) are 0.46 and 0.52 respectively[83]. The azeotropic or constant copolymer composition from initial monomer ratios MM:S is about 1:1. DGM was copolymerised with S to give a series of DGM:Sx copolymers (XXXIX, Table XIV). Only the initial monomer ratios of DGM:S, x = 1 gave a constant copolymer composition. The ratio DGM:S in these copolymers was calculated from oxygen analysis as follows:-

> If an average repeating unit in the copolymer be represented as $C_{16}H_{24}O_7$, $(C_8H_8)_x$ where x is the molar ratio of S to DGM, then the weight of each unit is 328 + 104x and $O\% = \frac{7 \times 16 \times 100}{328 + 104x}$

It can be seen from Table XIV that the optical rotation of these copolymers is not that expected if the styrene units act merely as a diluent.

TABLE XIV. The Diisopropylidenegalactose methacrylate-styrene system of copolymers (XXXIX)

DGM:Sx Monomer Molar Ratio x	Copolymerisation Time (hr)	Yield %	η_{inh} in toluene	Oxygen content (%)	Copolymer composition (S:DGM)	$[\alpha]_D$ [a] Calcd.	$[\alpha]_D$ Found c 0.5 toluene
5.74	18	67.1	1.3	14.1	4.48	-24.8°	-32°
3.03	72	89.1	1.8	17.7	2.93	-31.1	-40°
1.01	72[b]	89.7	0.6	26.1	0.97	-45.9	-56°

(a) P-DGM has $[\alpha]_D$ -60° in toluene. (b) Copolymerised in 31.3% benzene solution.

The deacetonation of DGM:$S_{4.48}$ and DGM:$S_{2.93}$ copolymers was unsuccessful as both were insoluble in formic acid. Attempts at deacetonation in other organic solvents were also unsuccessful as addition of water caused immediate precipitation. However, DGM:S_1 copolymer was soluble in formic acid owing to the high concentration of DGM (75.8 w/w %) and deacetonation proceeded normally to give water-insoluble, benzene-insoluble GM:S_1 copolymer (XL, Table XV), which was characterised by phenylhydrazone (XLI) formation.

TABLE XV. Galactose methacrylate-styrene-1:1-copolymer (XL) and phenylhydrazone (XLI)

GM:S Copolymer Ratio	Yield %	η_{inh} in DMF	Oxygen Content Calcd.	Oxygen Content Found	$[\alpha]_D$ Calcd.	$[\alpha]_D$ Found c 0.5 DMF
1.0	82.2	0.9	31.7	31.5	+32°	+24°

GM:S_1 copolymer phenylhydrazone was isolated at 91.7% yield [Found: C, 65.3; H, 6.97; N, 6.2 $(C_{16}H_{22}N_2O_6.C_8H_8)_n$. requires C, 65.1; H, 6.84; N, 6.3%].

The optical rotation of GM:S_1 copolymer was not the calculated value.

The reactivity ratios for the system methyl acrylate-acrylonitrile (MA - AN) are 0.95 and 1.4 respectively[84]. DGA was copolymerised with AN in bulk at 50° with AIBN as initiator in the molar ratio AN:DGA, x = 6 to give a white powder which was partially (63%) soluble in dimethylformamide. Elemental analysis (Table XVI showed that the initial monomer ratio had been maintained in the soluble copolymer fraction) (XLII). The insoluble fraction 18.6% showed identical infrared absorption to (XLII) and had the same nitrogen content. The insolubility of this fraction suggested that cross-linking/

cross-linking had occurred probably at "hot spots" in the exothermic polymerisation. Soluble DGA:AN_6 copolymer was deacetonated in formic acid to give water-insoluble GA:AN_6 copolymer (XLIII). Infrared analysis showed strong hydroxyl absorption at 3400, nitrile absorption at 2260 and ester C:O at 1730 cm^{-1}. Elemental analysis showed that the initial monomer ratio had been approximately maintained. The optical rotation of both copolymers was near to the calculated values. GA:AN_6 copolymer was characterised by phenylhydrazone (XLIV) formation which showed the characteristic absorption at 1610 cm^{-1}.

TABLE XVI. Diisopropylidenegalactose acrylate-acrylonitrile-1:6-copolymer (DGA:AN_6 copolymer, XLII) Galactose Acrylate-acrylonitrile-1:6-copolymer (GA:AN_6 copolymer, XLIII) and Phenylhydrazone (XLIV)

Copolymer	Yield (%)	η_{inh} in DMF	$[\alpha]_D^a$ Calcd	$[\alpha]_D$ Found c 0.5 DMF	Analysis
DGA:AN_6	63.0	2.0	-24°	-24°	Found C, 62.5; H, 6.57; N, 12.8. $[C_{15}H_{22}O_7.(C_3H_3N)_6]_n$ requires C, 62.6; H, 6.37; N, 13.8%.
GA:AN_6	95.4	2.6	+18°	+21	Found C, 57.5; H, 6.19; N, 14.3. $[C_9H_{14}O_7.(C_3H_3N)_6]_n$ requires C, 58.7; H, 5.84; N, 15.2%.
GA:AN_6 Phenyl-hydrazone	96.4				Found C, 61.5; H, 6.58; N, 16.1. $[C_{15}H_{20}N_2O_6(C_3H_3N)_6]_n$ requires C, 61.7; H, 5.96; N, 17.4%.

a P-DGA has $[\alpha]_D$ -49° in dimethylformamide

The reluctance of vinyl acetate (VA) to copolymerise with esters of α,β-unsaturated acids is evidenced by the reactivity ratios for the system MM-VA which are 20 and 0.015 respectively[85]. MM is used up quickly in bulk copolymerisation leaving the system rich in VA towards the end of reaction. DGM was copolymerised with VA in 18 w/w % benzene solution with the initial molar ratio VA:DGM = 3:1. The resulting sticky copolymer plug was dissolved in benzene and reprecipitated with methanol to remove vinyl acetate homopolymer. The acetyl content (Table XVII) of the precipitated copolymer was 5.4% which corresponds to an DGM:VA ratio of 1:0.46 (DGM:$VA_{0.46}$ copolymer XLV) showing that only 15% of original vinyl acetate had reacted to form copolymer.

TABLE XVII. Copolymerisation of diisopropylidenegalactose methacrylate with vinyl acetate (XLV), copolymer deacetonation (XLVI) and phenylhydrazone formation (XLVII)

Copolymer	Yield %	η_{inh}	$[\alpha]_D$ Calcd	$[\alpha]_D$ Found	Analysis
$DGM_{2.19}$:VA	97.0	2.9 in $CHCl_3$	-54°	-52° c 0.5 $CHCl_3$	Found C, 58.0; H, 7.29; Ac, 5.4. $[C_{16}H_{24}O_7.(C_2H_3OAc)_{0.46}]_n$ requires C, 58.2; H, 7.33, Ac, 5.4%.
GM:$VA_{1.0}$		7.1 c 0.1 DMF	+33°	+31 c 0.5 DMF	Found C, 49.2; H, 6.77, Ac, 12.8. $(C_{10}H_{16}O_7.C_2H_3OAc)_n$ requires C, 50.3; H, 6.63; Ac 12.9%.
GM:$VA_{1.0}$ Phenylhydrazone	93.0				Found C, 55.4; H, 6.56; N, 6.7. $(C_{16}H_{22}N_2O_6.C_2H_3OAc)_n$ requires C, 56.6; H, 6.65; N, 6.6%.

Deacetonation of DGM:$VA_{0.46}$ copolymer with 66.7% formic acid yielded a gel fraction (77%) which analysed as GM:$VA_{1.0}$ copolymer (XLVI), and was soluble in dimethylformamide. The remainder of the copolymer was water-soluble and elemental analysis and optical rotation showed a high proportion of P-GM as expected. GM:$VA_{1.0}$ copolymer was characterised by phenylhydrazone (XLVII) formation. (Table XVII).

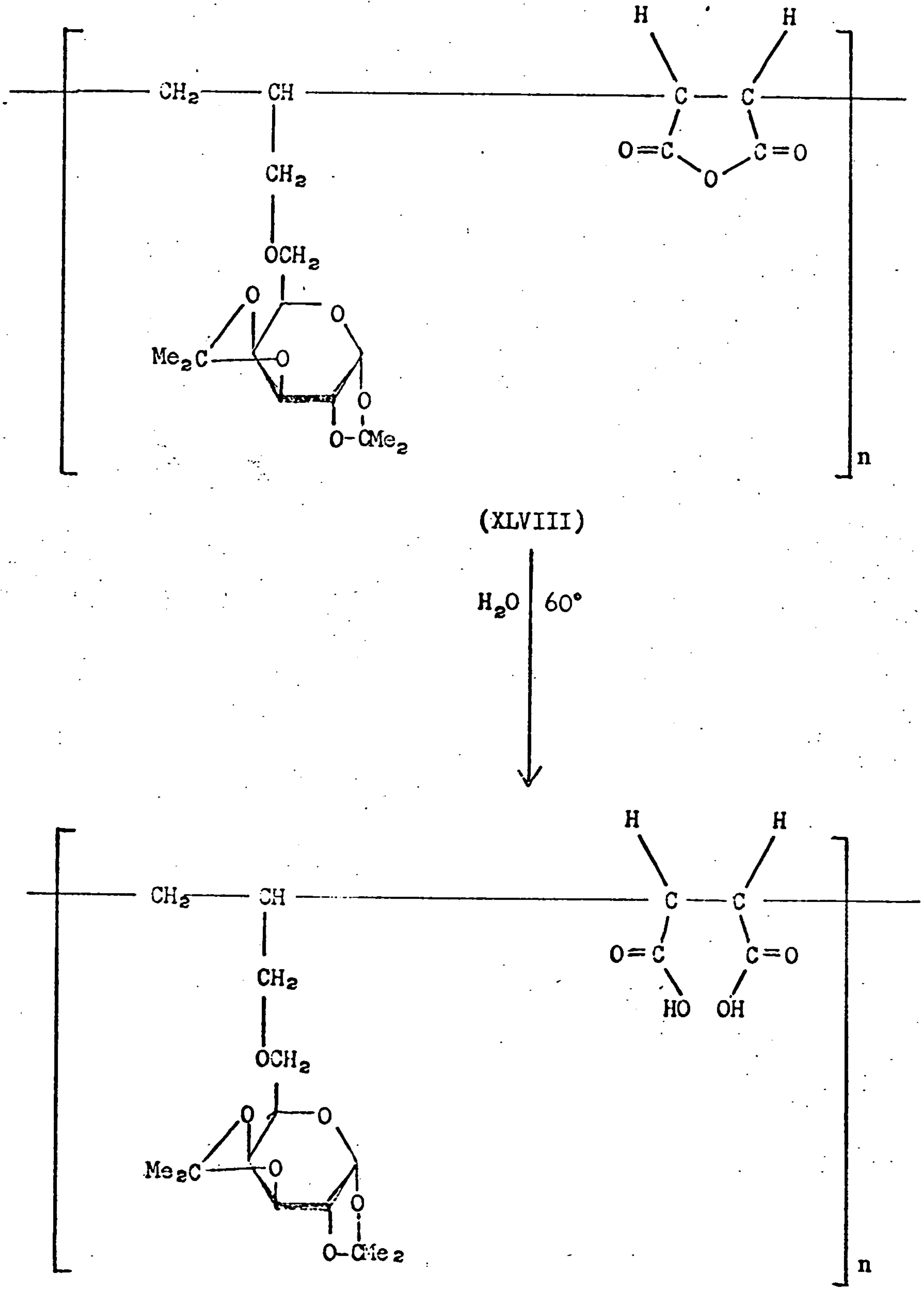
The failure of monomers possessing allylic hydrogens to form high molecular weight homopolymers through a free-radical process is due to chain transfer with monomer. The growing polymer chain is terminated early in its existence by abstraction of a labile allylic hydrogen from the monomer, giving a new radical which is too stable to initiate a new chain[86]:

Where copolymerisation occurs, e.g. the alternating copolymers of maleic anhydride which will not homopolymerise, the cross-propagation step is able to compete very effectively with such allylic terminations, as high molecular weight copolymers are produced. Walling[87] explained alternation in terms of transition state stabilisation resulting from electron transfer between radical and olefin in the styrene-maleic anhydride system. However, Martin and/

and Jensen[86] have claimed that this view is not consistent with the alternation of 3-phenylprop-1-ene, 4-phenylbut-1-ene and 5-phenylpent-1-ene with maleic anhydride, as the transition state postulated by Walling, would be insufficiently stabilised. Price[88] explained alternation in terms of monomer and radical polarity, stating that substituents attached to the double bond or radical centre lead to electron-rich and electron-poor centres, the interaction of which increases or decreases the energy required for the two species to react. Martin and Jensen[86] favour this explanation. Maleic anhydride has a very strong dipole with the postive end towards the double bond. The radical is also electron-poor, i.e., it will be the positive end of a dipole. A simple olefin has a weak dipole with the negative end towards the double bond. An alkyl radical is more polar in character, the radical carbon being the negative end of a dipole. Alternation then is explained simply as dipolar attraction.

It has already been shown that the diisopropylidenegalactose residue behaves as an alkyl group in polymerisation reactions. It was of interest, therefore, to determine whether the 6-<u>O</u>-allyl ether of diisopropylidenegalactose (VI) formed an alternating 1:1-copolymer with maleic anhydride, regardless of the initial monomer ratio. ADG and/

and maleic anhydride, in the molar ratio ADG: maleic anhydride = 2:1, were copolymerised under nitrogen in bulk with AIBN at 60 for three d days. The copolymer was isolated by reprecipitation with methanol from dioxan solution. Anhydride in the copolymer was detected by infrared analysis as a strong doublet at 1860 and 1780 cm^{-}, and the amount of anhydride was determined by hydrolysis in dioxan/water (2:1) to the diacid (XLIX) which was neutralised with 0.1 N-sodium hydroxide. The acid equivalent showed the presence of 50.6 mol. % of maleic anhydride units in the copolymer and elemental analysis also indicated an approximately 1:1-copolymer structure (XLVIII).



(XLVIII)

(XLIX)

4.3 Experimental

Materials and Methods

Methyl Acrylate, Styrene, Acrylonitrile, and Vinyl Acetate were all B.D.H. reagents and were distilled immediately before use to remove inhibitor.

Maleic Anhydride (B.D.H, 54 g) was dissolved as far as possible in refluxing chloroform-carbon tetrachloride (1:1, 100 ml), filtered and the filtrate left to crystallise at 0° for 18 hr. The pure anhydride was filtered, washed with carbon tetrachloride and dried to yield 38.2 g of pure material which was used in copolymerisation.

Other materials and methods have been described previously.

Copolymerisation of Methyl Methacrylate with 1,2:3,4-di-O-isopropylidene-6-O-methacryloyl-α-D-galactopyranose to Low Conversion (Table V)

DGM was dissolved in MM in a 75 x 10 mm test tube, and the solution, containing approximately 0.2 wt.-% AIBN, frozen and the tube sealed. The tube was heated at 50°, and after the time indicated (Table V), opened and the contents poured into methanol (50 ml). The white precipitate was washed/

washed thoroughly with methanol, dissolved in chloroform (5 ml) and reprecipitated with methanol (50 ml). This precipitate was washed thoroughly with methanol, dried, ground to a white powder, and finally dried in vac. over phosphoric oxide at 60° for 8 hr, to remove traces of methanol.

1,2:3,4-Di-O-isopropylidene-6-O-methacryloyl-α-D-galactopyranose - Methyl Methacrylate Random Copolymers (DGM:MMx Random Copolymers. XXXIV)

In a typical experiment, DGM (1 g) and AIBN (8 mg) were dissolved in MM (1.89 g) (molar ratio MM:DGM, $x = 6.2:1$) and the solution frozen at -80°. The tube was evacuated, then filled with nitrogen, and allowed to warm to 20°. This degassing process was repeated three times, after which the tube was sealed and heated at 50° for 18 hr. The clear copolymer plug was broken down, the product (2.75 g) dissolved in chloroform (250 ml) and the copolymer reprecipitated with methanol (2.5 litres), filtered, washed with methanol and dried to a white powder (2.55 g, 92.7%). Infrared analysis showed ester C:O at 1730 and gem-dimethyl absorption at 1380 cm^{-1}.

6-O-Methacryloyl-D-galactose-Methyl Methacrylate Random Copolymers (GM:MMx Random Copolymers. XXXV)

In a typical experiment, the above DGM:MM$_{6.2}$ random copolymer/

copolymer (2.32 g) was dissolved in formic acid (230 ml) and stirred at 20° for 18 hr. Water (115 ml) was added dropwise and the solution stirred at 20° for a further 24 hr. to constant rotation, $[\alpha]_D$ +26° c 0.614, calculated on the theoretical yield (2.12 g) of deacetonated copolymer XXXV, x = 6.2; P-GM has $[\alpha]_D$ +76° in 66.7% formic acid . Formic acid was removed by dialysis against running water for three days during which the deacetonated copolymer precipitated. This was filtered, washed thoroughly with water, and dried to a white powder (2.1 g, 99.1%). Infrared analysis showed strong hydroxyl absorption at 3400 cm^{-1}, and ester C:O at 1730 cm^{-1} (*gem*-dimethyl absent). Copolymers with $x > 9$ were deacetonated in 80% formic acid.

Copolymer Phenylhydrazones (XXXVI, XLI, XLIV, XLVII)

In a typical experiment, $GM:MM_{6.2}$ random copolymer (0.2 g) was dissolved in dimethylformamide (18 ml), glacial acetic acid (1 ml) and phenylhydrazine (1 ml) added, and the solution left in the dark at 20° for 24 hr. The solution was added dropwise to water, the yellow precipitate washed thoroughly with ethanol, and the copolymer phenylhydrazone (XXXVI, x = 6.2) dried to a yellow powder (202 mg. 92.0%). It was insoluble in dimethylformamide. All copolymer phenylhydrazones were prepared under the same conditions.

2,3-O-Isopropylidene-1-O-methacryloyl-DL-glyceritol-Methyl Methacrylate-1:4-Copolymer (IGLM:MM$_4$ Copolymer)

IGLM (2.057 g) was copolymerised with MM (4.184 g) with AIBN (31 mg) at 60° under air for 24 hr. The copolymer plug was broken down with some mechanical loss, and this material (6.24 g) dissolved in chloroform.(120 ml), reprecipitated with methanol, and dried to a white powder (6.1 g, 97.8%) which had η_{inh} of 1.0 (in chloroform). {Found: C, 60.1; H, 8.00; $[C_{10}H_{16}O_4\ (C_5H_8O_2)_4]_n$ requires C, 60.0; H, 8.00%}.

1-O-Methacryloyl-DL-glyceritol-Methyl Methacrylate Copolymer (GLM:MM$_4$ Copolymer)

IGLM:MM$_4$ Copolymer (5.01 g) was dissolved in 2-methoxyethanol (225 ml) and the solution heated to 100° and stirred vigorously. 5N-Hydrochloric acid (25 ml) was added dropwise over a period of 30 min to ensure that precipitation of the copolymer did not occur. The solution was stirred at 100° for a further 90 min and 2-methoxyethanol and hydrochloric acid removed by dialysis. The water-insoluble, hydrophilic copolymer (4.47 g, 95.5%) had η_{inh} 0.9 (in dimethylformamide). Infrared analysis showed strong hydroxyl absorption at 3500 and ester C:O at 1730 cm^{-1}. Methoxyl could not be accurately determined owing to interference/

interference from the glyceryl residues. {Found: C, 58.0; H, 8.38; $[C_7H_{12}O_4(C_5H_8O_2)_4]_n$ requires C, 57.8; H, 7.91%}.

Emulsion Copolymerisation of 6-O-Acryloyl-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose with Methyl Acrylate (DGA:MAx Copolymers. XXXVII)

In a typical experiment, a five-necked, 100 ml reaction vessel, fitted with stirrer, condenser, nitrogen inlet tube, thermometer and stopper, was charged with distilled water (20 g), containing sodium lauryl sulphate (250 mg) and ammonium persulphate (10 mg), DGA (1.63g) and MA (8.99 g) (molar ratio MA:DGA, x = 20:1). The mixture was stirred slowly and the apparatus flushed for 30 min with a flow of nitrogen. A water bath was placed under the reaction vessel and heated to 70°. When the emulsion attained this temperature, refluxing began and the temperature rose rapidly to 80°. This temperature was maintained for 2 min when refluxing stopped and the temperature began to fall. The bath temperature was then raised to 100° for 30 min and the hot polymer emulsion added dropwise to hot 5% w/v sodium chloride solution. The sticky white polymer was washed free of sodium chloride with hot water and air dried. This material was reprecipitated from acetone solution (400 ml) with water (2 litres), filtered, and dried to give the white, rubbery copolymer (9.87 g, 92.2%).

6-O-Acryloyl-D-galactose-Methyl Acrylate Copolymers (GA:MAx Copolymers. XXXVIII)

In a typical experiment DGA:MA$_{20}$ copolymer (1.0 g) was dissolved in acetone (10 ml) and formic acid (90 ml) added dropwise. Water (10 ml) was added slowly and the solution stirred at 20° for 3 days, filtered, and dialysed against running water for 24 hr. The precipitated copolymer (XXXVIII, x = 20) was filtered, washed with water, and dried to give a hard, white polymer (0.87 g, 90.5%). A film of this material was cast from dimethylformamide, washed with water and dried. Infrared analysis showed sharp hydroxyl absorption at 3500 and ester C:O at 1730 cm^{-1}.

1,2:3,4-Di-O-isopropylidene-6-O-methacryloyl-α-D-galactopyranose - Styrene Copolymers (DGM:Sx Copolymers. XXXIX)

DGM:Sx monomer ratios x = 5.74 and 3.03 were copolymerised in bulk with AIBN at 50° for 18 hr and 72 hr respectively. DGM:S$_1$ copolymer was prepared as follows. DGM (499 mg) was copolymerised with S (160 mg) in benzene (0.3 g, 31.3 w/w%) with AIBN (3 mg) at 50° for 3 days. The copolymer plug was dissolved in benzene (10 ml) and reprecipitated with methanol (100 ml). The copolymer was a white powder (591 mg, 89.7%).

6-O-Methacryloyl-D-galactose-Styrene-1:1-Copolymer (GM:S_1 Copolymer. XL)

DGM:S_1 copolymer (0.2 g) was shaken with formic acid (20 ml) for 18 hr at 20°. The copolymer dissolved and had $[\alpha]_D$ +50° (c 0.815 calculated on the theoretical yield of GM:S copolymer, XL). Water (10 ml) was added dropwise, and the solution stirred a further 24 hr at 20° when $[\alpha]_D$ was +46° (c 0.543). Formic acid was removed by dialysis against running water for 3 days during which the copolymer precipitated. This was filtered, washed with water, and dried to give a white powder (134 mg, 82.2%) which was insoluble in benzene. Infrared analysis showed strong hydroxyl absorption (3400 cm^{-1}) and benzenoid absorption at 1600, 760 and 700 cm^{-1}.

6-O-Acryloyl-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose - Acrylonitrile-1:6-Copolymer (DGA:AN_6 Copolymer. XLII)

DGA (506 mg) was copolymerised in bulk with AN (513 mg) with AIBN (2.3 mg) at 50° for 5 hr. The copolymer powder (1.015 g) was dissolved as far as possible in dimethylformamide (50 ml) and methanol (20 ml) added to harden the insoluble gel for ease of filtration. The insoluble gel was filtered off, washed with methanol, and dried to a white powder (189 mg, 18.6%), which had a nitrogen content of 13.3% and identical infrared/

infrared absorption to that of the soluble fraction below. The filtrate was added dropwise to methanol (500 ml) to give a white precipitate which was filtered, washed with methanol, and dried to a white powder (639 mg, 63.0%). Infrared analysis showed nitrile at 2260 cm^{-1} and ester C:O at 1730 cm^{-1}.

6-O-Acryloyl-D-galactose-Acrylonitrile-1:6-Copolymer (GA:AN$_6$ Copolymer. XLIII)

DGA:AN$_6$ Copolymer (250 mg) was shaken with formic acid (25 ml) at 20° for 18 hr and water (12.5 ml) added dropwise to the clear solution which was stirred a further 24 hr at 20° when the final rotation was $[\alpha]_D$ +29° [c 0.581 calculated on the theoretical yield (218 mg) of GA:AN$_6$ copolymer, XLIII.]. Formic acid was removed by dialysis as before and the water-insoluble copolymer was isolated as a white powder (208 mg, 95.4%).

Copolymerisation of 1,2:3,4-Di-O-isopropylidene-6-O-methacryloyl-α-D-galactopyranose with Vinyl Acetate. (DGM:VA$_{0.46}$ Copolymer. XLV)

DGM (3.08 g) was copolymerised with VA (2.43 g) in benzene (1.25 g) with AIBN (12 mg) under nitrogen at 50° for 18 hr (initial monomer ratio VA:DGM = 3:1). The resulting/

resulting sticky copolymer plug was dissolved in benzene (100 ml) and the solution added dropwise to methanol to give a white precipitate, which was filtered, washed with methanol, and dried to a white powder (3.35 g, 97.1%; calculated on the theoretical yield of DGM:$VA_{0.46}$ copolymer, XLV).

Deacetonation of DGM:$VA_{0.46}$ Copolymer with Formic Acid

DGM:$VA_{0.46}$ copolymer (1 g) was dissolved in formic acid (100 ml), and after 18 hr at 20° water (50 ml) was added and the solution stirred a further 24 hr at 20° when the final rotation was $[\alpha]_D$ +48° [c 0.538, calculated on the theoretical yield (807 mg) of GM:$VA_{0.46}$ copolymer]. Formic acid was removed by dialysis to give a cloudy solution, which was concentrated to 100 ml and centrifuged to give a gel and a clear supernatant. The gel was dried in vac. over calcium chloride to give a white powder (526 mg) which analysed as GM:$VA_{1.0}$ copolymer XLVI. The water soluble fraction was freeze dried (154 mg) and had $[\alpha]_D$ +47° (c 0.5 water), η_{inh} 0.6 (c 0.5 water). [Found: C, 48.6; H, 6.60; $(C_{10}H_{16}O_7)_n$ (P-GM) requires C, 48.4; H, 6.50%].

6-O-Allyl-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose Maleic Anhydride-1:1-copolymer. (XLVIII)

Maleic anhydride (0.204 g, 2.08 mmol) and AIBN (1 mg, 0.1 mol%) were dissolved in ADG (1.237 g, 4.12 mmol) in a tube which was evacuated to 0.1 mm at 20° and filled with nitrogen to atmospheric pressure. Polymerisation was carried out at 60° for 3 days to give a clear glass, which was dissolved in dioxan (2 ml), precipitated with methanol (50 ml), centrifuged and dried to a white powder (560 mg). This material was redissolved in dioxan (2 ml) and reprecipitated with methanol (50 ml) to give a white powder (502 mg, 60.5%) which had $[\alpha]_D$ -51° (c 0.5 in chloroform) and η_{inh} 0.1 in chloroform. Infrared analysis showed anhydride ($C_4H_2O_3$) as a strong doublet at 1860 and 1780 cm^{-1} with no evidence of unsaturation. [Found: C, 57.95; H, 6.93; $C_4H_2O_3$, 25.1. $(C_{15}H_{34}O_6.C_4H_2O_3)_n$ requires C, 57.3; H, 6.58; $C_4H_2O_3$, 24.6%].

Determination of Anhydride in ADG-Maleic Anhydride-1:1-Copolymer

The copolymer (120.5 mg) was dissolved in dioxan (10 ml) when addition of water (5 ml) caused precipitation. The mixture was heated at 60° for 8 hr to give a cloudy solution which was titrated with 0.1 N-sodium hydroxide (6.68 ml)/

(6.68 ml) to a phenolphthalein end point. This value was corrected for a blank titration (0.52 ml 0.1 N-NaOH) of dioxan (10 ml) and water (5 ml) to give an actual titre of 6.16 ml 0.1 N-NaOH which was equivalent to 0.308 m equiv. diacid or 25.1 wt % $C_4H_2O_3$ in copolymer (XLVIII).

5. POSSIBLE INDUSTRIAL APPLICATIONS

From the outset, the purpose of this study was the synthesis of new derivatives of galactose of possible industrial potential and the characterisation of these derivatives by physical and chemical methods. The physical and chemical evidence presented, suggest the following possible industrial applications of galactose polymers and copolymers.

1. Use as hydrophilic plastics in medicine and surgery; e.g. in the form of dressings, contact lenses, external prostheses, and surgical implants.

2. Use as hydrophilic coatings on various plastics and photosensitive films to improve sensitivity towards such things as printing ink and dyes.

3. Use in fibres to improve moisture absorbing properties and dyeability.

4. Use as cross-linking agents in emulsion polymers employed in the textile and paper industries.

5. Use as new gelling agents. Water-soluble galactose polymers and copolymers can be oxidised to form linear/

linear, water-soluble viscous solutions which give strong gels on the addition of multivalent cations.

6. Use as semi-permeable membranes for the desalination of sea or brackish water by the process of reverse osmosis and for haemodialysis in artificial kidney machines.

7. Use as transparent plastics of high softening-point.

6. CONCLUSION

Suitable unsaturated derivatives of di-O-isopropylidene-D-galactopyranose can be polymerised by a free-radical mechanism to polymers of high molecular weight which contain the bulky, tricyclic sugar derivative on every second carbon atom of the polymer chain. The diisopropylidenegalactose residue does not inhibit the polymerisation reaction by a steric effect but behaves as an alkyl substituent in radical polymerisation. However, use of this carbohydrate substituent has several advantages over simple alkyl vinyl monomers in that polymers with exceptionally high glass transition temperatures are produced which can then be cross-linked as an after-treatment if desired.

A significant feature of these polymers is that they can be modified i.e. "deblocked", to produce water-soluble, synthetic "polysaccharides" which differ from all other natural polysaccharides, such as cellulose and starch, in being much more reactive. For example, they are readily oxidised without degradation and the resulting polyacids resemble alginic acid, pectic acid and poly-(methacrylic acid). In general, these synthetic polysaccharides will undergo most of the reactions of galactose while at the same time/

time they possess the physical properties of a typical macromolecule.

The alkyl-type properties of the diisopropylidenegalactose residue are retained on copolymerisation. Diisopropylidenegalactose methacrylate and diisopropylidenegalactose acrylate copolymerise with methyl methacrylate and methyl acrylate respectively to form random copolymers which contain these units in the same proportion to that of the initial monomer mixture. Evidence is given that monomers containing the diisopropylidenegalactose residue will copolymerise in a similar monomer with any other monomer which will copolymerise with the parent monomer, i.e. methyl methacrylate, etc..

Deacetonation of these copolymers yields reactive, hydrophilic copolymers with novel and useful properties. This modification shows that these materials are true copolymers and not mixtures of homopolymers as their properties combine those of each homopolymer, hydrophilic with hydrophobic, and homopolymer is not detected at any stage of the deacetonation procedure.

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Arthur D. Little Research Institute,
Inveresk Gate,
Musselburgh,
Midlothian.

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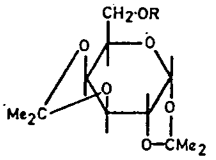
Synthetic Polymers Containing Galactose Residues

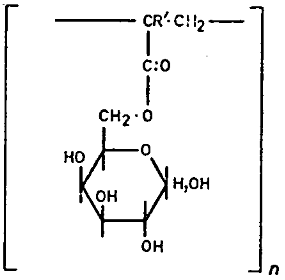
*By T. P. Bird, W. A. P. Black, J. A. Colquhoun, E. T. Dewar and D. Rutherford**

Arthur D. Little Research Institute, Inveresk Gate, Musselburgh, Midlothian

The synthesis and polymerisation of several unsaturated derivatives of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose have been described recently.[1] We report now the preparation of two crystalline monomers from galactose and their polymerisation to polymers of high molecular weight.[2]



(I, R=H)
(II, R=CO·CMe:CH₂)
(V, R=CO·CH:CH₂)



(IV, R′=Me)
(VII, R′=H)

1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranose (I) was esterified with methacrylic anhydride in pyridine solution to give the crystalline 6-methacrylate (II) in 47·5% yield, m.p. 62·5-63°, $[\alpha]_D$ –49·2°($CHCl_3$). Monomer (II) was polymerised in oxygen-free benzene solution with azobisisobutyronitrile as catalyst, and the product purified by solution in chloroform and reprecipitation with methanol to give the polymethacrylate (III) in near quantitative yield with an inherent viscosity $[\eta_{inh.} = c^{-1}\ln(\eta_{rel.})]$ of 2·8 dl./g. in *sym.*-tetrachloroethane (*c.*, 0·5 g. 100 ml.⁻¹; 25°). The isopropylidene blocking groups in polymer (III) were removed by solution in formic acid and gradual addition of water, and the water-soluble poly(6-*O*-methacryloyl-D-galactose)(IV) was isolated after dialysis. It had $[\alpha]_D + 62°$ (H_2O) and $\eta_{inh.}$ 1·9 dl./g. (*c.*, 0·5 in H_2O, 25°), and a quantitative determination of reducing power with sodium hypoiodite[3] gave a value of 91·2% calculated on the basis of structure IV.

The crystalline acrylate (V) (m.p. 57·5°, $[\alpha]_D$ –50·2° in $CHCl_3$) was synthesised in 54% yield by transesterification between ethyl acrylate and diisopropylidene-galactose (I) in the presence of tetraisopropyl titanate as catalyst.[4] Free-radical polymerisation in benzene solution readily furnished polyacrylate (VI) with inherent viscosity of 1·5 dl./g. in tetrachloroethane. Deacetonation of polymer (VI) was effected as described for the polymethacrylate and the resulting poly(6-*O*-acryloyl-D-galactose)(VII) had $[\alpha]_D + 56°$ (H_2O) and $\eta_{inh.}$ 0·6 dl./g. in water.

Satisfactory analyses were obtained for all compounds. Derivatives of the hydroxylated polymers (IV) and (VII) are being prepared and will be described elsewhere.

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* Present address of T.P.B., Imperial Chemical Industries Ltd, Nobel Division, Stevenston, Ayrshire and of D.R., Department of Organic Chemistry, University of New South Wales, Kensington, New South Wales, Australia

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Preparation and Derivatives of Poly-(6-*O*-methacryloyl-D-galactose) and Poly-(6-*O*-acryloyl-D-galactose)

By T. P. Bird, W. A. P. Black, J. A. Colquhoun, E. T. Dewar, and D. Rutherford

The 6-methacryloyl and 6-acryloyl esters of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose have been synthesised and polymerised to polymers of high molecular weight. The isopropylidene blocking groups have been removed by treatment with formic acid–water at 20°, to give poly-(6-*O*-methacryloyl-D-galactose) and poly-(6-*O*-acryloyl-D-galactose), which are linear, water-soluble, and reducing polymers with novel properties not possessed by natural polysaccharides. Various derivatives of these polymers are described. Chlorous acid at pH 3 oxidises the reducing group at C-1 of these polymers to give poly-(6-*O*-methacryloyl-D-galactonic acid) and poly-(6-*O*-acryloyl-D-galactonic acid), which exist in solution only; isolation and drying leads to loss of water from each galactonic acid residue with formation of the poly-1,4-lactones. The sodium salts of these polyacids are viscous polyelectrolytes which precipitate in the presence of many metal ions.

THE synthesis and polymerisation of several unsaturated derivatives of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose [1-5] and 2,3:4,6-di-*O*-isopropylidene-α-L-sorbofuranose [4] have been described recently. The main interest in these polymers lies in the fact that acidic hydrolysis removes the isopropylidene protecting groups and liberates water-soluble, linear, and reducing polymers with novel properties not possessed by natural polysaccharides. For example, poly-(1,2:5,6-di-*O*-isopropylidene-3-*O*-methacryloyl-α-D-glucofuranose) was converted into poly-(3-*O*-methacryloyl-D-glucopyranose) with its reducing hemiacetal group at C-1 free, and various derivatives of this polymer were described.[1] We now report the preparation of two crystalline monomers of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (I) and their polymerisation to polymers of high molecular weight. A preliminary note on part of this work has been published.[6]

Di-*O*-isopropylidene-D-galactose has recently been shown [7] by gas chromatography to be a mixture, the major component (>97%) under normal conditions of preparation [8] being syrupy isomer (I), and the minor being crystalline 1,2:5,6-di-*O*-isopropylidene-α-D-galactofuranose (II).

The 6-methacrylate (III) was prepared in 47·5% yield by esterifying crude di-*O*-isopropylidene-D-galactose [8] with methacrylic anhydride and pyridine by essentially the same method used to synthesise the 3-*O*-methacryloyl ester of di-isopropylideneglucose,[1] with the modification that high-vacuum distillation was dispensed with. The galactose monomer readily crystallised and was obtained in very pure form by repeated recrystallisations from ethanol–water mixtures. The monomer polymerised readily, both in bulk and in the presence of benzene, with a free-radical catalyst, such as azobisisobutyronitrile, and the effect of varying the amount of benzene on yield and inherent viscosity is shown in the Table. Polymerisations were carried out at 70° with 0·2% of catalyst. A compromise between yield and viscosity was reached by using 22·5% of oxygen-free benzene, and polymerisations were carried out at 50° rather than 70°. Poly(1,2:3,4-di-*O*-isopropylidene-6-*O*-methacryloyl-α-D-galactopyranose) (IV) was soluble in a

Benzene (wt. % of monomer)	90	60	30	0
Yield (%)	96·7	97·4	86·9	43·8
Inherent viscosity (dl./g.)	0·90	1·62	2·07	3·28

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[1] W. A. P. Black, E. T. Dewar, and D. Rutherford, *J. Chem. Soc.*, 1963, 4433.

[2] W. A. P. Black, E. T. Dewar, and D. Rutherford, *Makromol. Chem.*, 1964, **71**, 189.

[3] S. Kimura and M. Imoto, *Makromol. Chem.*, 1961, **50**, 155; 1962, **53**, 210.

[4] S. Kimura, K. Hirai, and M. Imoto, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, 1962, **65**, 688; S. Kimura and K. Hirai, *Makromol. Chem.*, 1962, **58**, 232.

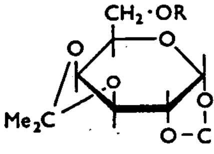
[5] E. E. Fisher and J. L. Harper, U.S.P. 3,103,508/1963.

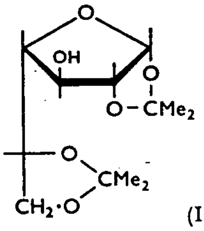
[6] T. P. Bird, W. A. P. Black, J. A. Colquhoun, E. T. Dewar, and D. Rutherford, *Chem. and Ind.*, 1965, 1073.

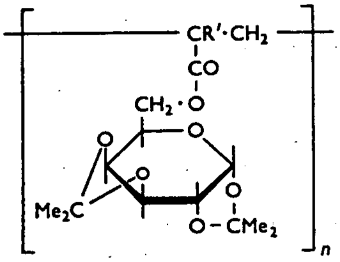
[7] D. C. De Jongh and K. Biemann, *J. Amer. Chem. Soc.*, 1964, **86**, 67.

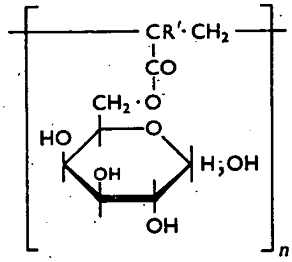
[8] O. T. Schmidt, *Methods Carbohydrate Chem.*, 1963, **2**, 324.

range of organic solvents but insoluble in water and simple alcohols. The specific rotation (—54° in tetrachloroethane) was independent of viscosity and general polymerisation conditions, such as concentration of benzene and catalyst. The viscosity (2·8 dl./g.) of polymer (IV) was much higher than that (0·5 dl./g.) of poly-(1,2:5,6-di-*O*-isopropylidene-3-*O*-methacryloyl-α-D-glucofuranose)[1] because the galactose monomer (III) is crystalline (m. p. 63°) and can be obtained purer than the glucose monomer.


(I: R = H)
(III: R = CO·CMe:CH₂)
(IX: R = CO·CH:CH₂)


(II)

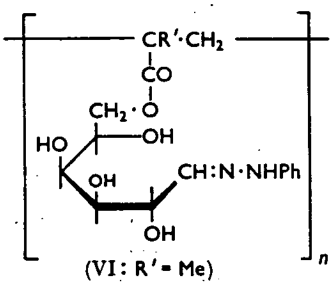

(IV: R′ = Me)
(XI: R′ = H)

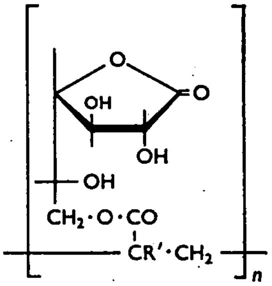

(V: R′ = Me)
(XII: R′ = H)

The removal of the isopropylidene residues from polymer (IV) to give poly-(6-*O*-methacryloyl-D-galactose) (V) was more difficult than in the case of the glucose polymer.[1] Heating with N-hydrochloric acid at 100° for several hours failed to dissolve the polymer, and the acetone–sulphuric acid procedure[3] was also unsuccessful. The blocking groups, however, were hydrolysed by dissolution in anhydrous formic acid and careful addition of water to give an acid concentration of 94%, the hydrolysis at 20° being followed polarimetrically when the specific rotation changed from a negative to a positive value. With polymers of very high viscosity, it was necessary to add further water to reduce the concentration of acid to 66% and allow the deacetonation to proceed for a further 3 hour. The solution was finally dialysed, and polymer (V) isolated by freeze-drying or by precipitation with ethanol.

Deacetonated polymer (V) was a white powder with a positive rotation ($[\alpha]_D$ +62° in water) and a high viscosity ($\eta_{inh.}$ 1·9 dl./g. in water). It was readily soluble in water and dimethyl sulphoxide but less soluble in dimethylformamide. It strongly reduced Fehling's solution, and quantitative determination of reducing power with hypoiodite[9] gave a value of 91·2% calculated on structure (V). Treatment with cold 1% methanolic hydrogen chloride gave a derivative that had the analysis required for a poly(methyl 6-*O*-methacryloyl-D-galactoside), but its insolubility in water suggested that some cross-linking had occurred. Polymer (V) was readily acetylated, benzoylated, and phenylcarbamoylated by standard procedures, the degree of substitution being 3·6, 2·7, and 3·0, respectively; in no case was complete substitution of all four hydroxyl groups effected. The polymeric acetate and benzoate showed greatly increased viscosities compared with the acetonated and hydroxylated polymers. Nitration with nitrogen pentoxide in chloroform[10] gave a trinitrate derivative which was insoluble in organic solvents.

Reactions at the reducing group of these synthetic polymers are important because they are not possible with natural polysaccharides except at the reducing unit at the ends of polymer chains. Thus, the fully substituted poly-(6-*O*-methacryloyl-D-galactose phenylhydrazone) (VI) was prepared by treating polymer (V) in solution in dimethylformamide with phenylhydrazine in the presence of acetic acid. Although originally soluble in the reaction medium, the isolated phenylhydrazone failed to redissolve in dimethylformamide.


(VI: R′ = Me)
(XIII: R′ = H)


(VII: R′ = Me)
(XIV: R′ = H)

A phenylosazone derivative was prepared by treating polymer (V) in aqueous solution at 90° with an excess of phenylhydrazine and acetic acid, but reaction was incomplete owing to precipitation of the polymer from solution. Analysis was consistent with substitution of one in three galactose units as the phenylosazone, the other two remaining as the phenylhydrazone. The infrared spectrum showed four bands at 1610, 1570, 1530, and 1500 cm.$^{-1}$ which are believed to be characteristic of a phenylosazone structure.[11]

Chlorous acid at pH 3 oxidised polymer (V) to soluble poly-(6-*O*-methacryloyl-D-galactonic acid), which, on isolation and drying, lost a molecule of water from each repeating unit to yield the water-insoluble polymeric lactone (VII) with its characteristic absorption at 1780 cm.$^{-1}$ in the infrared due to the γ-lactone carbonyl group. The extent of lactonisation was determined by the drying conditions; for example, the product immediately after freeze-drying was essentially the polyacid, while drying at 60°/0·1 mm. over phosphoric oxide gave the lactone (VII). This reaction parallels

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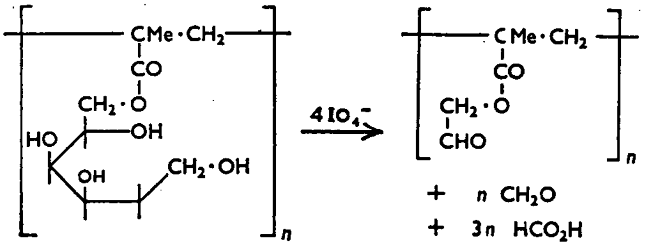
[9] E. L. Hirst, L. Hough, and J. K. N. Jones, *J. Chem. Soc.*, 1949, 928.

[10] G. V. Caesar and M. Goldfrank, *J. Amer. Chem. Soc.*, 1946, **68**, 372.

[11] L. Mester, *Angew. Chem., Internat. Edn.*, 1965, **4**, 574.

the ready conversion of D- or L-galactonic acid into its 1,4-lactone.[12] The sodium salt of the polyacid, which was isolated as a monohydrate, behaved as a typical polyelectrolyte, giving extremely viscous solutions in water ($\eta_{\text{inh.}}$ 14·9 dl./g.) but becoming less viscous in the presence of an electrolyte ($\eta_{\text{inh.}}$ 2·2 in 0·1M-sodium chloride). Replacement of the sodium with silver and many multivalent cations caused precipitation.

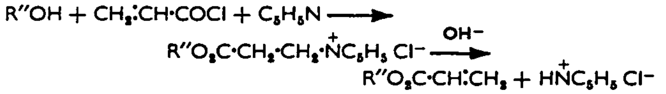
The reducing group of polymer (V) was readily reduced with sodium borohydride in aqueous solution, to give poly-(6-*O*-methacryloyl-D-galactitol) (VIII) in high yield; the course of the reaction was followed by oxidising the isolated products with periodate. The fully reduced polymer (VIII), on oxidation with 100% excess of 0·05M-sodium periodate for 2 hours at 20°, consumed 3·7 mol. of periodate and released 0·89 mol. of formaldehyde, compared with the theoretical values of 4 and 1, respectively, for each galactitol 6-methacrylate unit.



(VIII)

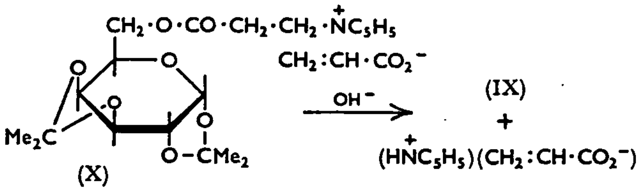
The reducing polymer (V) liberated no formaldehyde on oxidation with periodate. On treatment with nitrogen pentoxide in chloroform,[10] polymer (VIII) gave a tetranitrate, which, however, was only partly soluble in ethyl acetate, thus indicating that nitration has caused some cross-linking.

An unsuccessful attempt was made to synthesise 6-*O*-acryloyl-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (IX) by reaction of di-*O*-isopropylidenegalactose with acrylic anhydride in pyridine solution using the method developed for the methacrylate (III). A crystalline solid was isolated in low yield, but infrared and elemental analyses showed clearly that it was not the correct compound. Hickmott[13] recently showed that acryloyl chloride reacts with alcohols (R″OH) in the presence of pyridine or other tertiary amines in a different way from methacryloyl chloride. The main product of the reaction is the water-soluble 1-2′-alkoxycarbonylethylpyridinium chloride, which breaks down with cold sodium hydroxide to give the acrylate ester by elimination of pyridine hydrochloride. It is suggested



$$\mathrm{R''OH + CH_2{:}CH{\cdot}COCl + C_5H_5N \longrightarrow R''O_2C{\cdot}CH_2{\cdot}CH_2{\cdot}\overset{+}{N}C_5H_5\ Cl^- \xrightarrow{OH^-} R''O_2C{\cdot}CH{:}CH_2 + H\overset{+}{N}C_5H_5\ Cl^-}$$

that a similar alkoxycarbonylethylpyridinium acrylate adduct (X) is formed from di-*O*-isopropylidenegalactose and acrylic anhydride. Evidence for this hypothesis was obtained by decomposing the water-soluble adduct (X) by careful addition of cold N-sodium hydroxide to raise the pH of the acylation solution to 9·5, when subsequent extraction with light petroleum gave the crystalline ester (IX) in 14% yield.



The 6-acrylate (IX), however, was more readily synthesised (52·6%) by a transesterification reaction between ethyl acrylate and di-*O*-isopropylidenegalactose in the presence of tetraisopropyl titanate as catalyst and *p*-methoxyphenol as polymerisation inhibitor.[5] Like the methacrylate, monomer (IX) is a solid (m. p. 57·5°) that can be readily purified by repeated recrystallisations. It polymerised with azobisisobutyronitrile in the presence of benzene (22·5%) to poly-(6-*O*-acryloyl-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose) (XI), although the viscosity was generally lower than that of the methacrylate polymer (IV). Despite the precautions taken to remove oxygen from the system, viscosities were dependent on the scale of the experiment; for example, there was a gradual decrease in viscosity with increase in the amount of monomer being polymerised. Polymer (XI), with an inherent viscosity of 0·91 (in tetrachloroethane), was converted into water-soluble poly-(6-*O*-acryloyl-D-galactose) (XII), with a viscosity of 0·58 (in water), by treatment with formic acid–water at 20°, as described for the polymethacrylate. Polymer (XII) readily yielded an acetate, benzoate, and phenylcarbamate, and the degree of substitution (3·6—3·7) was higher than in the case of the polymethacrylate, although complete substitution was not achieved. The fully substituted poly-(6-*O*-acryloyl-D-galactose phenylhydrazone) (XIII) and a partly substituted phenylosazone derivative were also prepared.

The behaviour of poly-(6-*O*-acryloyl-D-galactose) (XII) towards chlorous acid at pH 3 was similar to that of the polymethacrylate (V). Poly-(6-*O*-acryloyl-D-galactonic acid) existed in solution only; isolation and drying gave the water-insoluble poly-1,4-lactone (XIV). The sodium salt of the polyacid was a viscous polyelectrolyte, and replacement of the sodium with many cations caused immediate precipitation. An unsuccessful attempt was made to prepare an amide from the polymeric lactone (XIV) by treatment with liquid amonia at 20°. However, ammonolysis resulted, and the ester linkage joining the galactose residues to the poly(acrylic acid) backbone was cleaved.

EXPERIMENTAL

General Methods and Materials.—Concentrations were carried out under reduced pressure. M. ps. and polymer melt temperatures were recorded on a Kofler hot-stage.

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[12] N. K. Richtmyer, R. M. Hann, and C. S. Hudson, *J. Amer. Chem. Soc.*, 1939, **61**, 340.

[13] P. W. Hickmott, *J. Chem. Soc.*, 1964, 883.

Compounds and polymers were dried at 20°/0·1 mm. over phosphoric oxide. Specific rotations were measured at 20° in a 2-dm. tube. Infrared spectra were determined as potassium chloride discs. Inherent viscosity $[\eta_{\text{inh.}} = \ln(\eta_{\text{soln.}}/\eta_{\text{solv.}})/c]$ was measured at 25° at a concentration (c) of 0·5 g. of polymer per 100 ml.; results are expressed in dl./g. Acetyl content was determined by the method of Whistler and Jeanes.[14] Consumption of periodate was measured by Aspinall and Ferrier's spectrophotometric method,[15] and formaldehyde was estimated colorimetrically with chromotropic acid.[16]

Acrylic and methacrylic anhydrides (Monomer-Polymer Laboratories, Borden Chemical Co., Philadelphia, U.S.A.), ethyl acrylate (British Drug Houses Ltd.), and tetraisopropyl titanate (Eastman Organic Chemicals) were used as received. Benzene used as solvent in polymerisations was freed from oxygen with " white spot " nitrogen in a Hersch deæration apparatus as described by Gilroy and Mayne.[17]

*1,2:3,4-Di-*O*-isopropylidene-6-*O*-methacryloyl-α-*D*-galactopyranose* (III).—A solution of di-*O*-isopropylidene-D-galactose [8] (26·8 g.) in anhydrous pyridine (135 ml.) was heated at 65° for 3·5 hr. with methacrylic anhydride (27 ml.), water (135 ml.) added, the solution heated at 65° for 1 hr. and at 30° for 17 hr., and the mixture extracted with light petroleum (b. p. 30—40°) (3 × 50 ml.). The extracts were washed with water (3 × 140 ml.) and 5% sodium hydrogen carbonate solution (3 × 140 ml.), dried (Na_2SO_4), tetrachloroquinol (28 mg.) was added, and the solvent removed. The solid residue was recrystallised from ethanol (140 ml.)–water (100 ml.), to give the *methacrylate* as needles (16·1 g., 47·5%), m. p. 62·5—63°, $[\alpha]_D$ −49·2° (c 1·13 in $CHCl_3$), $\nu_{max.}$ 1730 (unsat. ester C=O) and 1640 cm.$^{-1}$ (C=C) (OH absorption absent) (Found: C, 58·4; H, 7·4. $C_{16}H_{24}O_7$ requires C, 58·5; H, 7·4%). For polymerisations, the crystalline monomer (35·4 g.) was further purified by a second recrystallisation from ethanol–water, to give needles (27·6 g., 78·1%).

Poly-(*1,2:3,4-di-*O*-isopropylidene-*6-O*-methacryloyl-α-*D*-galactopyranose*) (IV).—The above crystalline monomer (10·13 g.), azobisisobutyronitrile (20 mg.), and deoxygenated benzene (2·5 ml.; 22·5 wt. % of monomer) were heated at 50° for 24 hr. in a glass-stoppered flask, the polymer dissolved in chloroform (400 ml.), and the solution added slowly with stirring to methanol (4 l.). The supernatant was decanted, and the white precipitate washed thoroughly by decantation with methanol, to yield pure *polymer* (9·60 g., 95·1%), $[\alpha]_D$ −54° (c 0·5 in tetrachloroethane), $\eta_{\text{inh.}}$ 2·82 (in tetrachloroethane), polymer melt temperature 162—165°. There was no evidence of unsaturation at 1640 cm.$^{-1}$ in the infrared spectrum [Found: C, 59·1; H, 7·4. $(C_{16}H_{24}O_7)_n$ requires C, 58·5; H, 7·4%].

Poly-(6-O*-methacryloyl-*D*-galactose*) (V).—The above polymer (3·3 g.) was dissolved at 20° in formic acid (396 ml.), water (24 ml.) added, and the solution stirred at 20° for 22 hr. ($[\alpha]_D$ +59°). Further water (180 ml.) was then added, and the solution stirred for 3 hr., when the rotation was constant ($[\alpha]_D$ +58°). The solution was dialysed against running water until free from acid, concentrated to small volume, and *poly-*(6-O*-methacryloyl-*D*-galactose*) isolated after freeze-drying as a white powder (2·42 g., 96·8%), $[\alpha]_D$ +62·4° (c 0·5 in H_2O), $\eta_{\text{inh.}}$ 1·91 (in H_2O) [Found: C, 48·75; H, 6·6. $(C_{10}H_{16}O_7)_n$ requires C, 48·4; H, 6·5%]. The product strongly reduced Fehling's solution; quantitative determination of reducing power with sodium hypoiodite [9] gave a value of 91·2%. The polymer was soluble in water and dimethyl sulphoxide.

Methyl Glycoside Formation.—The above polymer (V) (1·05 g.) was shaken for 4 days at 20° with 1% methanolic hydrogen chloride (100 ml.); there was no evidence of solution. The acid was neutralised with 0·1N-sodium hydroxide, the mixture dialysed against running water, and the insoluble *poly*(*methyl galactoside*) centrifuged and isolated as a non-reducing, white powder (802 mg., 72·3%) [Found: C, 49·0; H, 7·05; OMe, 11·0. $(C_{11}H_{18}O_7)_n$ requires C, 50·4; H, 6·9; OMe, 11·8%].

Acetylation of Poly-(6-O*-methacryloyl-*D*-galactose*).—A solution of the above polymer (V) (1 g.) in anhydrous dimethylformamide (100 ml.) was treated with dry pyridine (12 ml.) and acetic anhydride (24 ml.) at 20° for 24 hr. On careful addition to water, a white precipitate formed, which was washed with water and dried. The product was acetylated again with pyridine (25 ml.)–acetic anhydride (50 ml.), isolated by pouring into water, and purified by reprecipitation of a dimethylformamide solution (100 ml.) with water (400 ml.). Washing with water gave the *polymer acetate* as a white powder (1·335 g., 82·6%), $[\alpha]_D$ +47° (c 0·5 in tetrachloroethane), $\eta_{\text{inh.}}$ 5·2 (c 0·1 in tetrachloroethane) [Found: C, 51·6; H, 5·85; Ac, 39·1. $(C_{10}H_{12\cdot4}Ac_{3\cdot6}O_7)_n$ requires C, 51·7; H, 5·85; Ac, 39·1%].

Benzoylation of Poly-(6-O*-methacryloyl-*D*-galactose*).—Polymer (V) (252 mg.) was dissolved in anhydrous dimethylformamide (25 ml.), and dry pyridine (5 ml.) was added. The solution was cooled to 0°, benzoyl chloride (2·5 ml.) added dropwise, and after 7 days at 20° the red solution was added slowly with stirring to ice–water. The resulting sticky precipitate was washed with water, hardened with methanol, dissolved as far as possible in acetone (50 ml.), and an insoluble gel removed at the centrifuge. The viscous supernatant was added dropwise with stirring to water, and the white precipitate washed and dried. The *polymer benzoate* (422 mg., 78·6%) had $[\alpha]_D$ +100° ± 5° (c 0·1 in tetrachloroethane), $\eta_{\text{inh.}}$ 9·3 (c 0·1 in tetrachloroethane) [Found: C, 65·5; H, 4·85. $(C_{10}H_{13\cdot3}Bz_{2\cdot7}O_7)_n$ requires C, 65·6; H, 5·1%].

Phenylcarbamoylation of Poly-(6-O*-methacryloyl-*D*-galactose*).—A solution of polymer (V) (0·4 g.) in dimethylformamide (20 ml.) was heated with phenyl isocyanate (2 ml.) at 100° for 3 hr. and poured into ethanol. The precipitate was treated again in the same way and purified by solution in acetone (100 ml.) and reprecipitation with light petroleum (b. p. 40—60°) (400 ml.). The light brown *triphenylcarbamate* (845 mg.; 82·8%) had $[\alpha]_D$ +20° (c 0·1 in tetrachloroethane), $\eta_{\text{inh.}}$ 1·3 (c 0·1 in tetrachloroethane) [Found: C, 61·9; H, 5·1; N, 7·2. $(C_{31}H_{31}N_3O_{10})_n$ requires C, 61·5; H, 5·2; N, 6·9%].

Nitration of Poly-(6-O*-methacryloyl-*D*-galactose*).—Sodium fluoride (0·2 g.) was added to a solution of nitrogen pentoxide (1·32 g.) in chloroform (10 ml.), prepared as described by Caesar and Goldfrank,[10] the mixture cooled to 0°, and polymer (V) (211 mg.) added. The mixture was stirred for 45 min.; the final temperature was 10°. The product was washed with chloroform and hot water, dialysed against running water for 3 days, and the insoluble *trinitrate*

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[14] R. L. Whistler and A. Jeanes, *Ind. Eng. Chem., Analyt.*, 1943, **15**, 317.

[15] G. O. Aspinall and R. J. Ferrier, *Chem. and Ind.*, 1957, 1216.

[16] W. R. Frisell, L. A. Meech, and C. G. Mackenzie, *J. Biol. Chem.*, 1954, **207**, 709.

[17] D. Gilroy and J. E. O. Mayne, *J. Appl. Chem.*, 1962, **12**, 382.

isolated as a white powder (285 mg., 87·4%), $\nu_{max.}$ 1660 cm.$^{-1}$ (ester $O{\cdot}NO_2$) [Found: C, 30·0; H, 3·2; N, 10·5. $(C_{10}H_{13}N_3O_{13})_n$ requires C, 31·3; H, 3·4; N, 11·0%].

Phenylhydrazone Formation.—Poly-(6-*O*-methacryloyl-D-galactose) (306 mg.) in dimethylformamide (27 ml.) was treated with glacial acetic acid (3 ml.) and freshly distilled phenylhydrazine (3 ml.), and after 24 hr. at 20° the yellow solution was poured into water. The *polymer phenylhydrazone* was washed thoroughly with water and ethanol, and dried to a yellow powder (357 mg., 85·6%), which was now completely insoluble in organic liquids including dimethylformamide and dimethyl sulphoxide [Found: C, 55·4; H, 6·6; N, 8·2. $(C_{16}H_{22}N_2O_6)_n$ requires C, 56·8; H, 6·55; N, 8·3%], $\nu_{max.}$ 1610 cm.$^{-1}$ (PhNH·N:).

Phenylosazone Formation.—Poly-(6-*O*-methacryloyl-D-galactose) (204 mg.) in water (20 ml.) at 90° was treated with glacial acetic acid (0·2 ml.) and phenylhydrazine (0·35 ml.) with vigorous stirring; a precipitate separated almost immediately. The mixture was stirred at 90° for 2 hr., and the orange *product* (248 mg.) washed with ethanol and ether {Found: C, 58·7; H, 6·55; N, 10·3. Substitution of two units as phenylhydrazone and one unit as phenylosazone, *i.e.*, $[(C_{16}H_{22}N_2O_6)_2C_{22}H_{26}N_4O_5]_n$ requires C, 58·5; H, 6·4; N, 10·2%}.

Oxidation of Poly-(6-O-*methacryloyl-*D-*galactose*).—M-Sodium chlorite (40 ml.) was added to a solution of polymer (V) (991 mg.) in 4M-acetic acid (50 ml.), the solution diluted to 100 ml. with water, and the oxidation allowed to proceed at 20° for 24 hr. Acetic acid and inorganic ions were removed by dialysis, first against tap-water and then against distilled water, and cations were removed by passage through an Amberlite resin IR-120-H column (20 ml.). The eluate (170 ml.) contained poly-(6-*O*-methacryloyl-D-galactonic acid) and showed no measurable optical rotation in a 2-dm. tube. One half of this solution was freeze-dried to a white powder (330 mg., 67·1%), which was partly converted into the polymeric 1,4-lactone on drying at 20°/0·1 mm. over phosphoric oxide for 18 hr. It had $[\alpha]_D$ −36° (*c* 0·5 in H_2O after 5 days), $\eta_{inh.}$ 7·4 (*c* 0·11 in H_2O). Complete conversion into the water-insoluble *poly-*(6-O-*methacryloyl-*D-*galactono-*1,4-*lactone*), $\nu_{max.}$ 1780 (γ-lactone C=O) and 1730 cm.$^{-1}$ (ester C=O), was effected by drying at 60° [Found: C, 48·9; H, 5·95. $(C_{10}H_{14}O_7)_n$ requires C, 48·8; H, 5·75%].

The other half of the polyacid solution was titrated to pH 9 with 0·1N-sodium hydroxide (20 ml.), and the solution dialysed, concentrated, and freeze-dried, to give the *polymeric sodium salt* as a monohydrate (350 mg., 61·2%), $[\alpha]_D$ +17° (*c* 0·5 in H_2O), $\eta_{inh.}$ 14·9 (*c* 0·1 in H_2O) and 2·2 (*c* 0·1 in 0·1M-NaCl), $\nu_{max.}$ 1730 (ester C=O) and 1600 cm.$^{-1}$ (CO_2^-) [Found: C, 39·0; H, 6·0; Na, 7·6. $(C_{10}H_{15}NaO_8,H_2O)_n$ requires C, 39·5; H, 5·65; Na, 7·6%].

Poly-(6-O-*methacryloyl-*D-*galactitol*) (VIII).—Polymer (V) (0·5 g., 2·01 mmoles of $C_{10}H_{16}O_7$) in water (45 ml.) was cooled to 0°, sodium borohydride (152 mg., 4·02 mmoles) in water (5 ml.) added dropwise with stirring, and the solution left at 20° for 24 hr. After acidification with acetic acid, the solution was dialysed, concentrated, and freeze-dried, to give a white, non-reducing *poly-*(6-O-*methacryloyl-*D-*galactitol*) (419 mg., 83·1%), $[\alpha]_D$ +15° (*c* 0·5 in H_2O), $\eta_{inh.}$ 2·7 (in H_2O) [Found: C, 47·9; H, 7·2. $(C_{10}H_{18}O_7)_n$ requires C, 48·0; H, 7·25%].

Nitration of Poly-(6-O-*methacryloyl-*D-*galactitol*).—The above reduced polymer (152 mg.) was nitrated with nitrogen pentoxide in chloroform as described above for poly-(6-*O*-methacryloyl-D-galactose), to give a *tetranitrate* (244 mg., 93·5%), which was only partly soluble (40%) in boiling ethyl acetate [Found: C, 26·9; H, 3·25; N, 13·4. $(C_{10}H_{14}N_4O_{15})_n$ requires C, 27·9; H, 3·3; N, 13·0%].

Preparation of 6-O-*Acryloyl-*1,2:3,4-*di-*O-*isopropylidene-*α-D-*galactopyranose* (IX).—(a) *With acrylic anhydride and pyridine.* A solution of di-*O*-isopropylidene-D-galactose (2·81 g.) in dry pyridine (15 ml.) was heated at 65° for 3·5 hr. with acrylic anhydride (3 ml.), water (25 ml.) was added, and the solution heated at 65° for 1 hr. and at 30° for 17 hr. The pyridinium acrylate adduct (X) was decomposed by adding cold N-sodium hydroxide (15 ml.) to pH 9·5, and the solution immediately extracted with light petroleum (b. p. 30—40°) (3 × 25 ml.). The extracts were washed with 5% sodium hydroxide (25 ml.) and water (3 × 25 ml.), dried (Na_2SO_4), tetrachloroquinol (5 mg.) added, and the solvent removed, to give a yellow syrup (2·32 g.). Distillation (bath temp. 130—135°/0·015 mm.) yielded a colourless syrup (1·38 g.), which crystallised from ethanol–water (1 : 1; 18 ml.), to give the *acrylate ester* as long needles (487 mg., 14·3%), m. p. 57—57·5°, $[\alpha]_D$ −50·8° (*c* 1 in $CHCl_3$) $\nu_{max.}$ 1725 (unsat. ester C=O), 1635—1615 cm.$^{-1}$ (C=C) (OH absorption absent) (Found: C, 57·8; H, 7·1. $C_{15}H_{22}O_7$ requires C, 57·3; H, 7·05%).

(b) *By transesterification with ethyl acrylate.* Di-isopropylidenegalactose [8] (5·5 g.), ethyl acrylate (33 ml.), *p*-methoxyphenol (1·1 g.), and tetraisopropyl titanate (1·1 ml.) were heated at 110° for 2 hr. with stirring in an atmosphere of nitrogen. During the course of the transesterification, the ethyl acrylate–ethanol azeotrope (15 ml.) was collected; this had a b. p. of *ca.* 72° at the distilling head, and when the temperature dropped to 30° it was assumed that all of the azeotrope had been removed. The condenser was then fitted vertically, water (4 ml.) and light petroleum (b. p. 60—80°) (20 ml.) were added to the refluxing mixture, and the mixture was cooled to 20°. The gelatinous titanium dioxide was centrifuged, washed with light petroleum, and the supernatant liquid and washings were washed with water (3 × 50 ml.), 0·5N-potassium hydroxide (3 × 50 ml.), and water (3 × 50 ml.). Removal of the solvent gave a syrup (6·05 g.), which was dissolved in methanol (20 ml.); water (10 ml.) was added to a slight turbidity, and the solution kept at 0° overnight, when an orange-red oil had separated. On decantation, the supernatant crystallised to give needles (2·69 g., 40·6%), m. p. 57·5°, $[\alpha]_D$ −50·2° (*c* 1 in $CHCl_3$), identical with those described in (a) (Found: C, 57·5; H, 7·0%). The mother-liquor was worked up to give a second crop (0·80 g., 12%), making a total yield of 52·6%. For polymerisations, the monomer was recrystallised three times from methanol–water.

Poly-(6-O-*acryloyl-*1,2:3,4-*di-*O-*isopropylidene-*α-D-*galactopyranose*) (XI).—The above monomer (10 g.) azobisisobutyronitrile (20 mg.), and oxygen-free benzene (2·5 ml.; 22·5 wt. % of monomer) were heated at 50° for 24 hr. in a glass-stoppered flask, and the polymerised product was isolated as described for the polymethacrylate, to yield the *polymer* (9·10 g., 91%), $[\alpha]_D$ −50·1° (*c* 0·5 in tetrachloroethane), $\eta_{inh.}$ 0·91 (in tetrachloroethane) [Found: C, 57·6; H, 7·05. $(C_{15}H_{22}O_7)_n$ requires C, 57·3; H, 7·05%].

Poly-(6-O-*acryloyl-*D-*galactose*) (XII).—The above polymer (8·8 g.) was dissolved in formic acid (1160 ml.), and water (70 ml.) added to give an acid concentration of 94%. To this solution, during 2·5 hr., water (530 ml.) was added gradually, and the solution stirred for 3 days at 20°, when the specific rotation was constant (+53°). The solution was dialysed, concentrated, and freeze-dried, to give *poly-*(6-O-*acryloyl-*D-*galactose*) as a white powder (6·90 g., 105%), $[\alpha]_D$ +56·3° (*c* 0·5 in H_2O), $\eta_{\text{inh.}}$ 0·58 (in H_2O) [Found: C, 45·3; H, 6·05. $(C_9H_{14}O_7)_n$ requires C, 46·15; H, 6·0%. Reducing power (with sodium hypoiodite[9]), 90·9%]. The polymer was soluble in water, dimethyl sulphoxide, and *N*-methyl-2-pyrrolidone.

Acetylation of Poly-(6-O-*acryloyl-*D-*galactose*).—Polymer (XII) (303 mg.) was converted into its acetate in the manner described above for the polymethacrylate. It was purified by dissolution in chloroform and reprecipitation with light petroleum (b. p. 40—60°) (5 vol.). The *polymeric acetate* (420 mg., 84·2%) had $[\alpha]_D$ +52° (*c* 0·5 in tetrachloroethane), $\eta_{\text{inh.}}$ 0·9 (in tetrachloroethane) [Found: C, 50·8; H, 5·4; Ac, 40·1. $(C_9H_{10\cdot4}Ac_{3\cdot6}O_7)_n$ requires C, 50·5; H, 5·55; Ac, 40·2%].

Benzoylation of Poly-(6-O-*acryloyl-*D-*galactose*).—Polymer (XII) (207 mg.) was benzoylated in the manner described above for the polymethacrylate. The *polymeric benzoate* (368 mg., 67·3%), which was purified by dissolution in chloroform and reprecipitation with light petroleum (b. p. 40—60°) (5 vol.), had $[\alpha]_D$ +94° (*c* 0·5 in tetrachloroethane), $\eta_{\text{inh.}}$ 1·5 (in tetrachloroethane) [Found: C, 67·7; H, 5·25. $(C_9H_{10\cdot3}Bz_{3\cdot7}O_7)_n$ requires C, 67·7; H, 4·7%].

Phenylcarbamoylation of Poly-(6-O-*acryloyl-*D-*galactose*).—Polymer (XII) (0·2 g.) was converted into its phenylcarbamate in the manner described above for the polymethacrylate, using propan-2-ol–ether (5 : 1) instead of ethanol to precipitate the product from the reaction solution. The *polymeric phenylcarbamate* (352 mg., 62·2%), after being purified by dissolution in dimethylformamide and reprecipitation with water (10 vol.), had $[\alpha]_D$ +30° (*c* 0·52 in dimethylformamide), $\eta_{\text{inh.}}$ 1·0 (in dimethylformamide), $\nu_{\text{max.}}$ 3400 (NH), 1750—1720 (C=O), 1610 cm.$^{-1}$ (conjugated C=C) {Found: C, 61·9; H, 5·1; N, 7·6. $[C_9H_{14}O_7(PhNCO)_{3\cdot6}]_n$ requires C, 61·9; H, 4·85; N, 7·6%}. This derivative was insoluble in tetrachloroethane.

Phenylhydrazone Formation.— Poly-(6-*O*-acryloyl-D-galactose) (102 mg.) was converted into its *phenylhydrazone* (120 mg., 85%) in the manner described for the polymethacrylate; $\nu_{\text{max.}}$ 3500—3300 (OH), 1730 (ester C=O), and 1610 cm.$^{-1}$ (PhNH·N:) [Found: C, 54·0; H, 6·35; N, 8·0. $(C_{15}H_{20}N_2O_6)_n$ requires C, 55·6; H, 6·6; N, 8·6%]. The hydrazone was insoluble.

Phenylosazone Formation.— Poly-(6-*O*-acryloyl-D-galactose) (0·1 g.) was converted into a mixed *phenylhydrazone–phenylosazone* (2 : 1) (136 mg.) in the manner described for the polymethacrylate {Found: C, 58·9; H, 6·15; N, 10·4. Substitution of two units as phenylhydrazone and one unit as phenylosazone, $[(C_{15}H_{20}N_2O_6)_2C_{21}H_{24}N_4O_5]_n$, requires C, 57·6; H, 6·25; N, 10·5%}.

Oxidation of Poly-(6-O-*acryloyl-*D-*galactose*).—Polymer (XII) (504 mg.) was oxidised with chlorous acid at pH 3 in the manner described for the polymethacrylate, to give a white powder (402 mg.), which was partly lactonised even by freeze-drying. Drying at 60°/0·1 mm. gave *poly-*(6-O-*acryloyl-*D-*galactono-*1,4-*lactone*), $\nu_{\text{max.}}$ 1780 (γ-lactone C=O) and 1740 cm.$^{-1}$ (ester C=O), which was insoluble in water [Found: C, 45·9; H, 5·35. $(C_9H_{12}O_7)_n$ requires C, 46·6; H, 5·2%]. Poly(sodium 6-*O*-acryloyl-D-galactonate) had $[\alpha]_D$ +10° (*c* 0·5 in H_2O), $\eta_{\text{inh.}}$ 12·2 (*c* 0·1 in H_2O) and 1·4 (*c* 0·1 in 0·1M-NaCl).

Attempted Preparation of Poly-(6-O-*acryloyl-*D-*galactonamide*).—The above polymeric lactone (105 mg.) was shaken with liquid ammonia (10 ml.) in a sealed tube at 20° for 3 days. The lactone partly dissolved to give a mobile supernatant and an insoluble gel which adhered to the sides of the tube. The supernatant was decanted, the ammonia removed, and the solid recrystallised from ethanol, to give D-galactonamide (50 mg.), m. p. 171—173°, $[\alpha]_D$ +26° (*c* 3·2 in H_2O) (lit.,[18] m. p. 176°, $[\alpha]_D$ +31·8°) (Found: C, 36·9; H, 6·8; N, 7·0. Calc. for $C_6H_{13}NO_6$: C, 36·9; H, 6·7; N, 7·2%). The insoluble residue (35 mg.) was presumably chiefly polyacrylamide.

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ARTHUR D. LITTLE RESEARCH INSTITUTE,
INVERESK GATE, MUSSELBURGH,
MIDLOTHIAN.

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Kurzmitteilung

Monomer Reactivity Ratios in the Copolymerisation of 1.2:3.4-Di-O-isopropylidene-6-O-methacryloyl-α-D-galactopyranose with Methyl Methacrylate

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From the Arthur D. Little Research Institute, Inveresk, Musselburgh, Midlothian, Scotland

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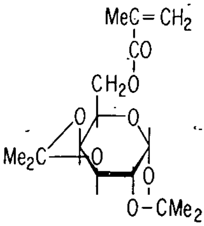
(Eingegangen am 9. Dezember 1966)

It is well known[1–3] that increase in size of the alkyl group in an ester of an α.β-unsaturated acid does not greatly influence the reactivity ratios of such esters with many vinyl monomers, although a few exceptions to this general rule have been noted[4,5]. It has also been shown[6] that the relative reactivity of these esters to reference radicals is influenced by a steric effect if the alkyl group in the α-position is varied. Bevington and Malpass[7] have determined the monomer reactivity ratios for the radical copolymerisation of various esters of methacrylic acid with methyl methacrylate using tracer techniques. It was found that these reactivity ratios were approximately unity and their product not far from unity and, with one exception, the higher esters had a higher reactivity than the methyl ester. The preparation and free-radical polymerisation to polymer of high molecular weight of the crystalline monomer, 1.2:3.4-di-O-isopropylidene-6-O-methacryloyl-α-D-galactopyranose (diisopropylidenegalactose methacrylate, (I)), have been described recently[8]. A study of the copolymerisation of this monomer with industrial monomers, such as methyl methacrylate, acrylonitrile, styrene, *etc.*, is currently in progress in this laboratory. It was of importance, therefore, to determine whether this complex, carbohydrate monomer, which is essentially a rigid, tricyclic alkyl ester of methacrylic acid, was comparable in reactivity with methyl methacrylate.



$C_{16}H_{24}O_7$ (328.4)

(I)

The copolymerisation of two monomers can be adequately described by four propagation steps which constitute the basis for the development of the well known copolymer composition equation[9]. The Fineman and Ross[10] modification, Eq. (1), was used to evaluate all of the copolymerisation data obtained in this investigation (Table 1).

$$(F/f)(f-1) = r_1F^2/f - r_2 \qquad (1)$$

Table 1. Bulk copolymerisation of MM with DGM at 50°C to low conversions

MM M_1 (mg)	DGM M_2 (mg)	F (M_1/M_2) molar ratio in monomer mixture	AIBN (mg)	Time (min)	Yield of co-polymer (mg)	OMe content of copolymers (%)	f (m_1/m_2) molar ratio in copolymer
1027.0	–	–	2.0	120	84.1	31.00	–
546.0	202.6	8.843	1.6	60	50.2	22.13	8.183
604.4	246.9	8.031	1.5	60	71.6	21.17	7.065
467.0	255.5	5.996	1.5	60	57.7	19.47	5.541
458.8	299.6	5.024	1.6	60	59.2	18.06	4.580
381.0	403.0	3.102	1.5	45	43.9	13.71	2.601
318.0	521.0	2.003	1.6	45	92.3	10.89	1.776

A plot of $(F/f)(f-1)$ as ordinate and (F^2/f) as abscissa is a straight line whose slope is r_1 and whose intercept is $-r_2$. This plot was used to determine the reactivity ratios r_1 and r_2 of methyl methacrylate (MM, M_1) and diisopropylidenegalactose methacrylate (DGM, M_2) in their bulk copolymerisation at 50 °C to low conversions with azobisisobutyronitrile (AIBN) as catalyst. The results are given in Table 1.

The composition of the copolymers was determined from methoxyl content as follows. If the copolymer is represented by the average repeating unit, $C_{16}H_{24}O_7 \cdot (C_5H_8O_2)_n$, where n is the molar ratio of MM to DGM, then the weight of each repeating unit is $(328.4 + 100.1\ n)$ and the percentage methoxyl is given by $31.03 \cdot n \cdot 100/(328.4 + 100.1\ n)$. DGM contains no methoxyl. Hence n can be calculated from the methoxyl

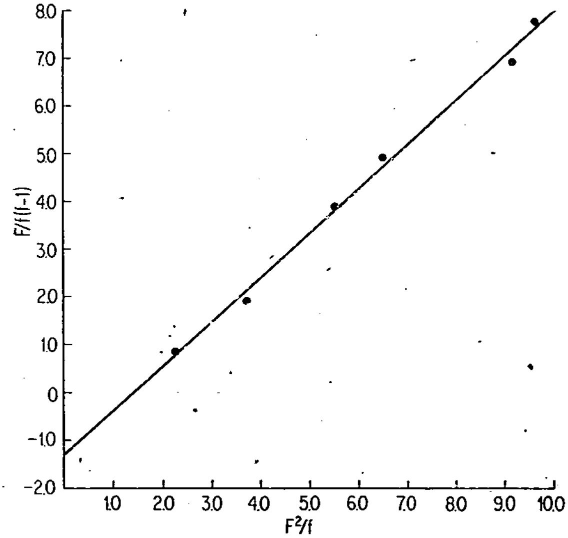


Fig. 1. FINEMAN-ROSS plot in the copolymerisation
$F = [MM]/[DGM]$,
$f = d[MM]/d[DGM]$

contents determined experimentally and corresponds to the values of f in Table 1.

The reactivity ratios were determined from Fig. 1 and were

$$r_1 = 0.93 \pm 0.03 \text{ (MM)}$$
$$r_2 = 1.30 \pm 0.19 \text{ (DGM)}$$

These figures show that diisopropylidenegalactose methacrylate behaves as an alkyl methacrylate in radical polymerisation and agrees with the fact[11] that it can be copolymerised in any proportion with methyl methacrylate to give a final copolymer containing these units in approximately the initial monomer ratio.

Experimental

Materials and methods

Methyl methacrylate (MM) was purified by distillation at 30°C under reduced pressure immediately before use. 1.2:3.4-Di-O-isopropylidene-6-O-methacryloyl-α-D-galactopyranose (DGM) (I) was prepared and purified as previously described[8]. Methoxyl estimations were determined by the ZEISEL method in duplicate.

Copolymerisation of MM with DGM to low conversion

DGM was dissolved in MM in a 75×10 mm test tube, and the solution, containing approximately 0.2 wt.-% AIBN, frozen and the tube sealed. The tube was heated at 50°C and, after the time indicated (Table 1), opened and the contents poured into methanol (50 ml). The white precipitate was filtered, washed thoroughly with methanol, dissolved in chloroform (5 ml), and reprecipitated with methanol (50 ml). This precipitate was washed thoroughly with methanol, dried *i.vac.* over phosphoric oxide, ground to a white powder, and finally dried *i.vac.* over phosphoric oxide at 60°C for 8 hrs, to remove traces of methanol.

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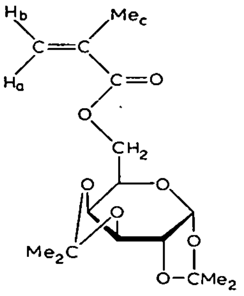
Polymerisable monomers of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose

The preparation and free-radical polymerisation of the crystalline monomer, 1,2:3,4-di-*O*-isopropylidene-6-*O*-methacryloyl-α-D-galactopyranose (**1**) have been described recently[1]. Deacetonation of the homopolymer with aqueous formic acid yielded the novel, water-soluble, synthetic "polysaccharide", poly(6-*O*-methacryloyl-D-galactose)[1]. Determination of the reactivity ratios[2] in the radical copolymerisation of acetal **1** with methyl methacrylate showed that this complex, carbohydrate monomer behaves as a simple alkyl methacrylate in radical polymerisation, and subsequent work[3] has shown it to be a valuable intermediate for the introduction of hydrophilic properties into hydrophobic polymers. We now report an improved and much cheaper synthesis of acetal **1**, together with the synthesis of a new monomer, 6-*O*-allyl-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**2**).



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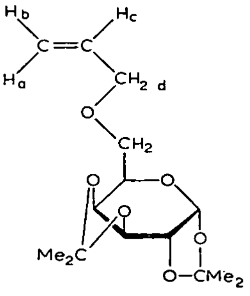

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Acetal **1** was prepared previously[1] by treatment of 1,2:3,4-di-*O*-isopropylidene-α-D-galactose (**3**) in pyridine with the expensive chemical, methacrylic anhydride. It has now been prepared in better yield (65.5%) by a simple transesterification between compound **3** and the readily available methyl methacrylate, in the presence of tetraisopropyl titanate as catalyst and *p*-methoxyphenol as polymerisation inhibitor[4]. Continuous removal by distillation of methanol formed in the reaction drove the equilibrium to the right, and reaction was essentially complete after 1 h.

6-*O*-Allyl-1,2:3,4-di-*O*-isopropylidene-α-D-galactose (**2**) was prepared by a modification of the allylation procedure of Bladon and Owen[5]. Two treatments of compound **3** in *p*-dioxane with allyl bromide, in the presence of an excess of powdered sodium hydroxide, were necessary for complete reaction. The pure compound was obtained in 91.8% yield as a colourless oil.

The molecular structures of compounds **1** and **2** were confirmed by p.m.r. spectroscopy. Cone and Hough[6] have analysed the p.m.r. spectra of a series of derivatives of 1,2:3,4-di-*O*-isopropylidene-α-D-galactose, and assignments for compounds **1** and **2** (Table I) were made by comparison with these spectra and with those of methyl methacrylate[7] and allyl alcohol[8].

Integration of all peaks in the p.m.r. spectrum of acetal **1** showed the expected 24 protons. The one-proton peak at τ 3.91 was identical to that of methyl methacrylate and was assigned to H_a. It was possible to distinguish the H-1 doublet ($J_{1,2}$ 5.0 Hz) in the pattern of peaks corresponding to two protons at τ *ca.* 4.5. The other proton was assigned to H_b. The α-methyl group (H_c) was readily detected at τ 8.07. The signal for H-3 at τ 5.44 was a quartet ($J_{3,2}$ 2.4 and $J_{3,4}$ 7.8 Hz). The remaining ring protons could not be detected, as the two H-6 protons had been moved downfield by the deshielding effect of the ester carbonyl group.

TABLE I

CHEMICAL SHIFTS (τ-VALUES)

Compound[a]	H_a	H_b	H_c	H_d	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*Isopropylidene C-Me*		
1	3.91	*ca.* 4.5	8.07	—	4.50	[b]	5.44	[b]	[b]	[b]	8.57	8.59	8.71×2
2	4.75	4.87	*ca.* 4.0	[c]	4.55	[c]	5.44	[c]	[c]	6.44, 6.55	8.51	8.61	8.71×2

[a] **1**, 1,2:3,4-Di-*O*-isopropylidene-6-*O*-methacryloyl-α-D-galactopyranose; **2**, 6-*O*-allyl-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose. [b] Complex multiplet, 5.6–6.2. [c] Complex multiplet, 5.6–6.3.

The pattern of peaks in the p.m.r. spectrum of compound **2** centred at τ 4.0, 4.75, and 4.87 corresponded to three protons which were identical in shape and position to the olefinic protons of allyl alcohol and were assigned to H_c, H_a, and H_b, respectively. The H-1 doublet at τ 4.55 was distorted by a part of the signal from H_a. The signal for H-3, at τ 5.44, was a quartet ($J_{3,2}$ 2.4 and $J_{3,4}$ 7.8 Hz). The two H-6 protons were assigned to the signals at τ 6.44 and 6.55, by comparison with other derivatives of 1,2:3,4-di-*O*-isopropylidene-α-D-galactose. The complex multiplet at τ 5.6–6.3, corresponding to five protons, contained the two allylic protons H_d, and H-2, H-4, and H-5. The total integral showed 24 protons.

EXPERIMENTAL

P.m.r. spectra were recorded in carbon tetrachloride solution on a Perkin-Elmer R10 (60 MHz) n.m.r. spectrophotometer, and chemical shifts (τ) were measured relative to tetramethylsilane. T.l.c. was performed on Silica Gel G with chloroform–ethanol (99:1); spray reagent, 90% sulphuric acid (10 min at 140°).

1,2:3,4-Di-O-isopropylidene-6-O-methacryloyl-α-D-galactopyranose (**1**).—1,2:3,4-Di-*O*-isopropylidene-α-D-galactose[9] (6.45 g) and *p*-methoxyphenol (1.3 g) were dissolved in methyl methacrylate (39 ml), and tetraisopropyl titanate (1.3 ml) was added. The flask was flushed with nitrogen for 10 min, and the temperature was raised to 110°. A methanol–methyl methacrylate azeotrope distilled at 82–85° and ceased after *ca.* 30 min (final volume, 4 ml). The bath temperature was maintained at 110° for a further 30 min, the condenser was then fitted vertically, water (4 ml) and light petroleum (20 ml, b.p. 60–80°) were added, and the temperature was allowed to fall to 20° (18 h). The resulting orange precipitate was centrifuged, and washed with light petroleum, and the yellow supernatant and washings were evaporated under reduced pressure at 30°. A solution of the thin, syrupy residue in 50% aqueous ethanol (40 ml) deposited the crude methacrylate (6.20 g) as yellow crystals after 18 h at 0°. This material was purified with charcoal in the presence of tetrachloroquinol (60 mg) in ethanol (30 ml) and water (3 ml) for 15 min at 70°. The colourless filtrate was made up to 50% ethanol with water, and the pure methacrylate then crystallised, as before, as needles (5.33 g, 65.5%), m.p. 62.5–63°, $[\alpha]_D$ −49.3° (*c* 1.12, chloroform), and showed the same i.r. spectrum as the authentic material[1] (Found: C, 58.1; H, 7.21. $C_{16}H_{24}O_7$ calc.: C, 58.5; H, 7.36%). Polymerisation of the monomer in benzene solution, with azobisisobutyronitrile as catalyst, as previously described[1], gave polymer having an inherent viscosity of 3.2 dl/g (*c* 0.5, chloroform, 25°).

6-O-Allyl-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (**2**). — 1,2:3,4-Di-*O*-isopropylidene-α-D-galactose[9] (19.9 g) was dissolved in anhydrous *p*-dioxane (100 ml), and powdered sodium hydroxide (8 g) was added. Allyl bromide (80 ml) was added over 20 min to the stirred mixture at 45°. Heating was increased to 50° for 30 min, and finally to 60° for 2 h. Water (100 ml) was added, and the mixture was extracted with chloroform (3 × 100 ml). The chloroform extract was washed with water (3 × 250 ml), dried over anhydrous sodium sulphate, and evaporated to a yellow oil (22.1 g). This material was re-allylated as before to give the crude allyl ether (22.08 g) which was distilled to give a colourless oil (21.08 g, 91.8%), b.p. 86°/0.03 mm. T.l.c. showed one component (R_F 0.89), and infrared analyses showed absorptions at 3080 (=CH.) and 1645 cm^{-1} (C=C); OH absorption was absent. The allyl ether had $[\alpha]_D$ −71.8° (*c* 1, chloroform) and n_D^{25} 1.4595 (Found: C, 60.2; H, 8.13. $C_{15}H_{24}O_6$ calc.: C, 60.0; H, 8.06%).

ACKNOWLEDGMENTS

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Arthur D. Little Research Institute,
Inveresk,
Midlothian (Scotland)

W. A. P. BLACK
J. A. COLQUHOUN
E. T. DEWAR

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6-*O*-Methacryloyl-D-galactose: A Reactive, Water-soluble Monomer

by

W. A. P. Black, J. A. Colquhoun, and E. T. Dewar

HÜTHIG & WEPF VERLAG · BASEL

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From the Arthur D. Little Research Institute, Inveresk, Musselburgh, Midlothian, Scotland

6-*O*-Methacryloyl-D-galactose: A Reactive, Water-soluble Monomer

By W. A. P. Black, J. A. Colquhoun, and E. T. Dewar

(Eingegangen am 28. Mai 1968)

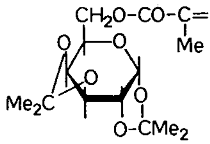
SUMMARY:

Deacetonation of the crystalline monomer, 1.2 : 3.4-di-*O*-isopropylidene-6-*O*-methacryloyl-α-D-galactopyranose (DGM, I) in 80% formic acid solution at 20°C gave the syrupy, water-soluble monomer 6-*O*-methacryloyl-D-galactose (GM, II) in quantitative yield. The α-anomer of GM, 6-*O*-methacryloyl-α-D-galactopyranose (α-GM) was a white crystalline compound which showed characteristic infrared absorption. The NMR spectrum of α-GM in deuterium oxide was complicated by two variables: (i) mutarotation and (ii) gradual polymerisation. Syrupy GM was polymerised with ammonium persulphate to a water-insoluble, cross-linked hydrogel.

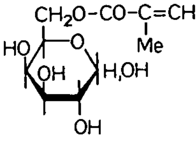
ZUSAMMENFASSUNG:

Die bei 20°C in 80-proz. Ameisensäurelösung vorgenommene Acetonabspaltung vom kristallinen Monomeren, der 1.2;3.4-Di-*O*-isopropyliden-6-*O*-methacryloyl-α-D-galactopyranose (DGM, I) ergab in quantitativer Ausbeute das sirupartige, wasserlösliche Monomere, die 6-*O*-Methacryloyl-D-galactose (GM, II). Das α-Anomere von GM, die 6-*O*-Methacryloyl-α-D-galactopyranose (α-GM), ist eine weiße, kristalline Verbindung, die eine charakteristische IR-Absorption zeigt. Das NMR-Spektrum von α-GM in Deuteriumoxid wird durch zwei Variable beeinflußt, 1. durch die Mutarotation und 2. durch die langsam fortschreitende Polymerisation. Das sirupartige Monomere GM wurde mit Ammoniumpersulfat zu einem wasserunlöslichen, vernetzten Hydrogel polymerisiert.

The preparation[1,2], and free-radical polymerisation[2] of the crystalline monomer, 1.2 : 3.4-di-*O*-isopropylidene-6-*O*-methacryloyl-α-D-galactopyranose (DGM, I) have been described previously. Deacetonation of the homopolymer with aqueous formic acid yielded the novel, water-soluble, synthetic "polysaccharide", poly-(6-*O*-methacryloyl-D-galactose) (P-GM)[2]. Determination of the reactivity ratios[3] in the radical copolymerisation of DGM with methyl methacrylate showed that this complex, carbohydrate monomer behaves as a simple alkyl methacrylate in radical polymerisation and subsequent work[4] has shown DGM to be a valuable intermediate for the introduction of hydrophilic properties into hydrophobic polymers. We now report the synthesis and polymerisation to a cross-linked hydrogel of the reactive, water-soluble monomer, 6-*O*-methacryloyl-D-galactose (GM, II).



(I)



(II)

DGM[1] was deactonated in 80 % formic acid, containing *p*-methoxyphenol, the hydrolysis at 20 °C being followed polarimetrically when the molecular rotation changed from a negative (M_D − 133) to a positive (M_D + 202) value after 24 hrs. Formic acid was removed by repeated evaporations at 35 °C under reduced pressure and additions of water. GM was isolated in 48 % yield as a white crystalline compound (mp 108 to 118 °C) from ethanol solution and was mainly the α-anomer as it mutarotated from $[\alpha]_D + 91.5° \rightarrow + 53.8°$ in water. The compound was further purified by recrystallisation from 90 % ethanol to give the pure monomer, 6-*O*-methacryloyl-α-D-galactopyranose (α-GM), mp 142–145 °C.

The infrared spectrum of α-GM showed hydroxyl absorption as a broad band between 3500 and 3100 cm^{-1}, ester carbonyl at 1710 cm^{-1} and double bond unsaturation at 1638 cm^{-1}. The α-anomer was indicated[5] by anomeric C–H equatorial deformation at 844 cm^{-1} and non-anomeric equatorial C–H deformation was present at 880 cm^{-1}.

In deuterium oxide solution, the protons attached to oxygen form an exchanging pool with residual water in deuterium oxide and have a single sharp resonance at 5.25 τ in the NMR spectrum. The NMR spectrum of α-GM in deuterium oxide was complicated however by two variables: (i) mutarotation and (ii) gradual polymerisation. This is represent in Fig. 1, where OD groups have been omitted for convenience.

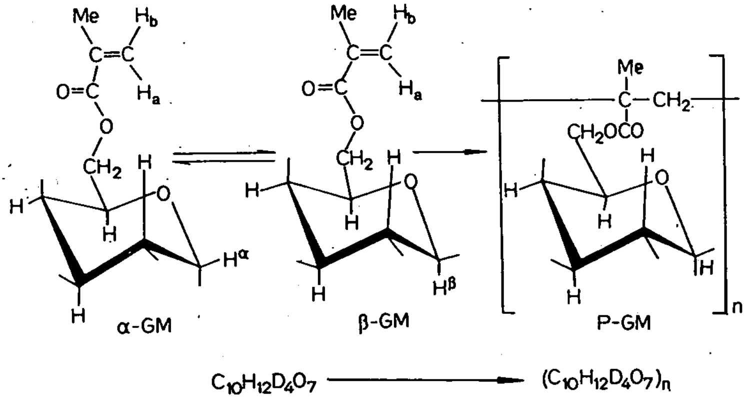


Fig. 1. Mutarotation and polymerisation of α-GM in deuterium oxide

An axially oriented hydrogen (H^β) is more shielded than an equatorially oriented hydrogen (H^α) and resonates at a higher applied magnetic field[6]. Van der Veen[7] has studied the mutarotation of D-galactose in deuterium oxide by NMR and found the following τ-values and coupling constants between H_1–H_2: H^α, 4.77 τ ($J_{1,2}$ 2.7 Hz) and H^β, 5.43 τ ($J_{1,2}$ 6.7 Hz). The difference in coupling constants is a measure of the dihedral angle between H_1 and H_2 and is a consequence of the more effective coupling of two axially oriented hydrogens (H^β–H_2) compared with axial-equatorial coupling (H^α–H_2)[6]. Table 1 shows τ-values and the change in the number of protons contributing to these values with time, thus confirming the reaction scheme of Fig. 1. τ-values were measured relative to the single resonance signal due to water at 5.25 τ.

Table 1. τ-Values[a] and number of protons in the mutarotation and polymerisation of α-GM in deuterium oxide

	H_a	H_b	H^α	H^β, H_2–H_6	α-Me	–(CMe·CH$_2$)–$_n$
τ-Values	3.80	4.20	4.66	5.4–6.6	8.00	8.5–9.5
No. of protons α-GM	1	1	1	0, 6	3	0
No. of protons P-GM	0	0		7	0	5
No. of protons t = 0	0.71	0.71	0.85	6.07	2.25	1.41
No. of protons t = 24 hr	0.22	0.22	0.60	6.56	0.83	3.54
No. of protons t = 96 hr	0	0	0.64	6.65	0	4.71

[a] See ref. [1].

The first spectrum was recorded immediately after α-GM had dissolved in deuterium oxide. At t = 0, a distinct doublet at 4.64 τ ($J_{1,2}$ 3.0 Hz) indicated H^α. The integral showed that 85 % of the compound was in the α-form at this time and after mutarotation had taken place approximately 60 % was still in this anomeric state. The gradual decrease in the number of vinyl protons (H^a,H^b and α-Me) with the concomitant appearance of these protons at higher field proved that polymerisation was taking place and after 96 hrs there was 94 % conversion into polymer. The gradual decrease in resolution of the spectra was also a consequence of polymerisation.

As the inhibitor-free monomer polymerised so readily in aqueous solution and as the yield of crystalline material was only 48 %, the monomer was prepared for polymerisation in theoretical yield as an aqueous syrup (25 wt.-% GM) containing *p*-methoxyphenol (1.21 %) as inhibitor. Inhibitor was removed with chloroform and residual chloroform removed from the syrup by evaporation. The syrup was polymerised with ammonium persulphate to give a 91.8 % yield of cross-linked, hydrophilic but water-insoluble polymer, which showed identical infrared absorption to authentic, water-soluble P-GM[2]).

It is known that water-soluble monomers such as glyceryl methacrylate[8]), hydroxyethyl methacrylate and the N-acryloyl and N-methacryloyl derivatives[9]) of 1-amino-1-deoxy-D-glucitol give cross-linked hydrogels when polymerised in concentrated aqueous solution and water-soluble polymers in dilute solution. Water-soluble P-GM[2]) may be cross-linked simply by heating at 60 °C *i. vac.* over phosphoric oxide. It is considered that this cross-linking is analogous to the polycondensation of reducing sugars when they are heated above their melting point under *vac.*[10]). Hence for P-GM, condensation is believed to occur *via* the anomeric hydroxyl group and a secondary hydroxyl group on a neighbouring polymer chain. The exact mechanism of cross-linking when GM is polymerised is not known but it is thought that this monomer may be a valuable cross-linking agent for many polymer systems.

Experimental

Materials and methods

1.2:3.4-Di-O-isopropylidene-6-O-methacryloyl-α-D-galactopyranose (DGM, I) was prepared and purified as previously described[1]). Formic acid was Analar B.D.H. reagent. IR spectra were recorded in potassium chloride discs on a Perkin-Elmer 257 Grating Infrared Spectrophotometer and NMR spectra on a Perkin-Elmer R10 (60 MHz) NMR Spectrophotometer. All products were dried *i. vac.* over phosphoric oxide at 20 °C.

6-O-Methacryloyl-α-D-galactopyranose (α-GM)

DGM (10.02 g) and *p*-methoxyphenol (0.5 g) were dissolved in formic acid (80 ml) and the solution made up to 100 ml with water. The deacetonation was followed polarimetrically (2-dm tube) at 20 °C, and after 24 hrs the solution was diluted to 50 % with water and formic acid removed by repeated evaporation at 35 °C and addition of water. The thick syrup was dissolved in ethanol (100 ml) and polymeric material (0.4 g) filtered off. The clear ethanol solution was evaporated at 20 °C to *ca.* 20 ml and left at 0 °C for 3 days. The white crystalline material was filtered and washed with ethanol (2×2 ml) to give the methacrylate as plates (mp, 108–118 °C, 3.63 g, 48.0 %) which mutarotated from $[\alpha]_D + 91.5^\circ \rightarrow +53.8^\circ$ (c 1.5 in water). This material (2.50 g) was dissolved in water (10 ml) and ethanol (90 ml) added and the solution left at 0 °C for 3 days to give the α-anomer of II as white plates (mp, 142–145 °C, 0.55 g, 22.0 %).

$C_{10}H_{16}O_7$ (248.2, II)	Calcd.	C 48.4	H 6.50
	Found	C 48.1	H 6.39

6-O-Methacryloyl-D-galactose (GM) 25 wt.-% aqueous solution

DGM (41 g) with *p*-methoxyphenol (1.5 g) as inhibitor was deacetonated in 80% formic acid (400 ml) and after 24 hrs at 20 °C, formic acid removed as before. A weighed amount of water was added to the monomer syrup to give a solution which was 25 wt.-% with respect to GM and 1.21% with respect to inhibitor.

Polymerisation of GM 25 wt.-% aqueous solution

The above monomer syrup (19.1 g) was extracted with chloroform (4 × 5 ml) to remove inhibitor. The inhibitor-free aqueous solution was evaporated at 20 °C under reduced pressure until free from chloroform and water added to 25 wt.-% solution. Ammonium persulphate (50 mg) was added and the solution heated at 100 °C under reflux for 4 hrs. The thick polymer gel was broken down with isopropanol (100 ml), and washed with isopropanol and ether to give a white powder (4.39 g, 91.8%) which was swellable but insoluble in water although it had identical IR absorption to authentic, water-soluble P-GM[2].

This research on the utilisation of whey products is supported by the Milk Marketing Board of England and Wales to whom we are indebted for permission to publish. We thank Dr. D. A. Rees for advice, and Miss Madeline Methven, Chemistry Department, University of Edinburgh, for recording the NMR spectra.

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PATENT SPECIFICATION

NO DRAWINGS

Inventors: ERIC THOMAS DEWAR and JOSEPH ADAMS COLQUHOUN

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THE PATENT OFFICE LONDON

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Int. Cl.:—C 08 f 19/00

COMPLETE SPECIFICATION

Improvements relating to Carbohydrate-Derived Polymers

We MILK MARKETING BOARD, a British Body Corporate established by statute, of Thames Ditton, Surrey, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to new synthetic copolymers containing carbohydrate residues, and a method of preparing same.

According to the present invention there is provided a method of preparing a synthetic copolymer containing a carbohydrate residue, comprising polymerising together in the presence of a catalyst a vinylidene or a vinyl monomer and a polymerisable ester of galactose formed by reaction of an α,β-olefinically unsaturated mono- or di-carboxylic acid with the hydroxyl group in the 6-position of galactose.

Preferably the polymerisable ester of galactose is formed by reacting a 1,2:3,4-diketal or galactose with an α,β-olefinically unsaturated polymerisable mono- or dicarboxylic acid.

Preferably the ketal residues are removed from the galactose units in the copolymer by controlled hydrolysis.

Our pending British Patent Application No. 9065/65 (Final Number 1,099,372), proposes the synthesis of high-molecular weight homopolymers containing carbohydrate residues by treating suitably substituted carbohydrate methacrylates and acrylates with free-radical catalysts. Examples of such sugar monomers are 1,2:3,4 - di-*O*-isopropylidene-6-*O*-methacryloyl-α-*D*-galactopyranose and 6-*O*-acryloyl-1,2:3,4 - di - *O* - isopropylidene - α - *D*-galactopyranose, hereafter described as diisopropylidene-galactose methacrylate (II) and acrylate respectively, the synthesis and polymerisation of which are disclosed in the above application.

It is further proposed in our pending British Patent Application No. 9065/65 (Final Number 1,099,372) to remove the protecting isopropylidene residues from the above polymerised products by dissolving the poly(diisopropylidenegalactose methacrylate) and poly (diisopropylidenegalactose acrylate) in an organic acid preferably formic acid, and diluting the solutions gradually with water. In this way novel water-soluble, high-molecular-weight polymers are formed, i.e. poly(galactose methacrylate) and poly(galactose acrylate), and these can be reacted with well-known reagents to give useful derivatives.

By virtue of the present invention reactive copolymers are provided having exceptional commercial promise.

Preferably the synthetic copolymers of the present invention contain substituted or unsubstituted *D*-galactose residues. Kimura and Imoto (Makromol. Chem., 1961, 50, 155) showed that the copolymer of acrylonitrile and glucose 3-methacrylate had better dyeing properties than the polyacrylonitrile homopolymer itself, and this effect can be attributed to the presence of the hydroxyl groups in the glucose residues of the copolymer. Similarly, Black, Dewar, and Rutherford (Makromol. Chem., 1964, 71, 189) modified the properties of polyacrylonitrile by forming high-mole-

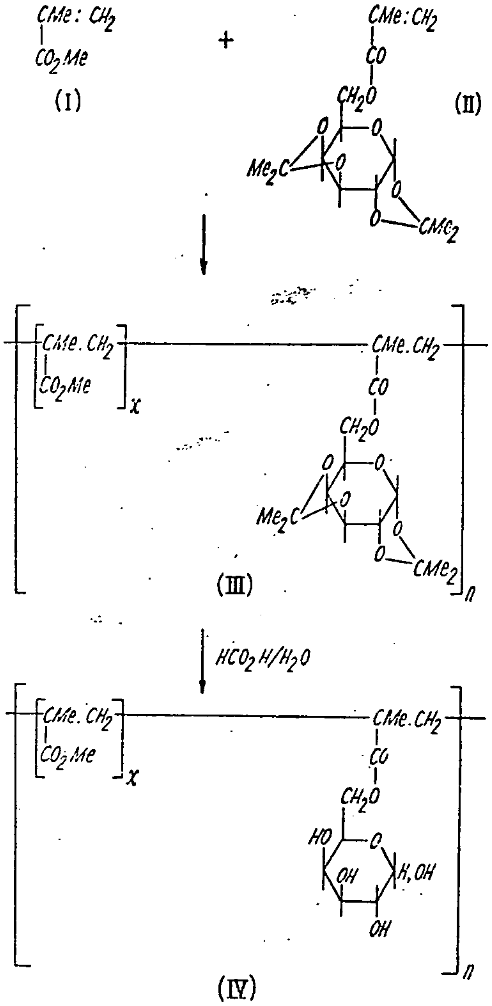
[*Price* 4*s*. 6*d*.]

cular-weight copolymers of acrylonitrile and 3-*O*-allyl-*D*-glucose.

The method of the present invention provides for an increase in the usefulness of synthetic polymers by altering their chemical and physical properties. It is well-known that many industrial synthetic fibres and plastics are chemically inert owing to the absence of reactive groups in their polymer chains, but their reactivity can be increased by incorporating galactose units that contain a reactive aldehydic group and several hydroxyl groups. The hydrophilicity, i.e. affinity for water, of many synthetic fibres can also be increased by copolymerisation with galactose. Therefore the present invention enables the preparation of synthetic copolymers which are capable of taking up water in much the same way as cellulose and its derivatives.

We have discovered that copolymers containing galactose residues possess higher molecular weights than those containing other sugar units, such as glucose. This is attributed to the fact that the galactose monomers used in this invention are well-defined, crystalline compounds that can be obtained in an exceptionally pure state by repeated recrystallisation.

A typical copolymerisation within the scope of this invention is represented structurally in the following scheme. The monomers depicted in this scheme are methyl methacrylate (I) and diisopropylidenegalactose methacrylate (II), although it must be emphasised that the invention is not restricted to these monomers. (I) may be any vinylidene or vinyl monomer, such as styrene, acrylonitrile, vinyl chloride, or vinyl acetate, while (II) may be any galactose ester monomer disclosed in pending British Patent Application No. 9065/65 (Final Number 1,099,372). (III) represents the methyl methacrylate/diisopropylidene - galactose methacrylate random copolymer before the removal of the diisopropylidene (diketal) residues, while (IV) is the methyl methacrylate/galactose methacrylate random copolymer after the removal of the diisopropylidene residues.



The extent of polymerisation of the random copolymers may be indicated from the inherent viscosity (ηinh.), which is measured at 25° in an Ostwald viscometer and is defined by the equation:

$$\eta\text{inh.} = \frac{1}{c} \ln (\eta\text{rel.})$$

wherein c represents the grams of copolymer in 100 millilitres of solution and ηrel. represents the relative viscosity of the solution. When the above equation is used to define the inherent viscosity, the term may be conveniently expressed in units such as decilitres per gram (dl./g.).

The random copolymers are conveniently characterised by their specific rotation ((α)$_D$), which is measured at 20° C in a suitable solvent and is defined by:

$$[\alpha]_D = \frac{100 \times \alpha}{c \times 1}$$

wherein c represents the grams of copolymer in 100 millilitres of solution, α is the observed optical rotation of the co-polymer solution in circular degrees, and 1 represents the length of the polarimeter tube in decimetres. The copolymers are also characterised by chemical analysis and by characteristic bands in their infrared absorption spectra.

The following examples are included to illustrate the practice of the present invention.

EXAMPLE 1

Preparation of 6:1 Methyl Methacrylate/Diisopropylidenegalactose Methacrylate Random Copolymer (III, x=6.2).

Diisopropylidenegalactose methacrylate (1 g.), prepared as described in pending British Patent Application No. 9065/65 (Final Number 1,099,372) and azobisisobutyronitrile (8 mg.) were dissolved in inhibitor-free methyl methacrylate (1.89 g.) (molar ratio 6.2:1), and the solution frozen at −80° C. The tube was evacuated, then filled with nitrogen, and allowed to warm to 20° C. This de-gassing process was repeated three times, after which the tube was sealed and heated at 50° C for 18 hr. The clear copolymer plug was broken down, the product (2.75 g.) dissolved in benzene (250 ml.), and the copolymer reprecipitated with methanol (2.51). After being washed with methanol and dried *in vacuo*, the copolymer was isolated as a white powder (2.55 g.; 92.7% yield), which had $[\alpha]_D - 18°$ (c 0.5 in tetrachloroethane) and η_{inh} 2.6 dl./g. (c 0.1 in tetrachloroethane). Anal.: C, 59.5; H, 7.83; OMe, 19.3 Calc. for $[(C_5H_8O_2)_{6.2}.C_{16}H_{24}O_7]_n$: C, 59.5; H, 7.82; OMe, 20.3%.

Preparation of 6:1-Methyl Methacrylate/Galactose Methacrylate Random Copolymer (IV, x=6.2).

The above acetonated copolymer (III) (2.32 g.) was shaken with formic acid (232 ml.) at 20° C for 18 hr. to give a clear solution, water (115 ml.) was added dropwise with stirring, and the solution was stirred at 20° C for a further 24 hr. to constant rotation, $[\alpha]_D + 26°$ [c0.614, calculated on the theoretical yield (2.12g.) of deacetonated copolymer (IV)]. Formic acid was removed by dialysis against running water for 3 days during which the deacetonated copolymer (IV) precipitated. This was filtered and dried *in vacuo* to give a white powder (2.1 g.; 99.1% yield). The copolymer was completely insoluble in water, which is a solvent for poly(galactose methacrylate) homopolymer, and in methyl n-propyl ketone, which is a solvent for poly(methyl methacrylate) homopolymer. It had $[\alpha]_D + 16°$ (c 0.5 in dimethylformamide) and η_{inh} 2.0 dl./g (c. 0.5 in dimethylformamide). Anal.: C, 56.6; H, 7.71; OMe, 20.4. Calc. for $[(C_5H_8O_2)_{6.2}.C_{10}H_{16}O_7]_n$: C, 56.7; H, 7.61; OMe, 22.1%. The copolymer showed an absorption band at 3500 cm^{-1} in its infrared spectrum due to the presence of hydroxyl groups in the galactose methacrylate residues of copolymer (IV).

This copolymer material is capable of taking up water without dissolving, and films cast from this copolymer formed useful membranes for desalting brackish and sea water by the process of reverse osmosis. At the present time cellulose acetate is the only polymer which is capable of giving commercially suitable membranes for reverse osmosis.

Preparation of Phenylhydrazone of 6:1 Methyl Methacrylate / Galactose Methacrylate Random Copolymer

The above deacetonated copolymer can be characterised further by treatment with phenylhydrazine, which reacts specifically with the C—1 reducing group in the galactose methacrylate residues.

The above copolymer (IV) (0.2 g.) was dissolved in dimethylformamide (18 ml.), glacial acetic acid (1 ml.) and phenylhydrazine (1 ml.) added, and the solution left at 20° C in the dark for 24 hr. The solution was added dropwise to water the yellow precipitate washed thoroughly with ethanol and water, and the copolymer phenylhydrazone dried to a yellow powder weighing 202 mg. (92% yield). It was insoluble in dimethylformamide. Anal.: C, 57.9; H, 7.47; N, 3.2. Calc. for $[(C_5H_8O_2)_{6.2}.C_{16}H_{22}N_2O_6]_n$: C, 58.9; H, 7.53; N, 2.9%. Its infrared spectrum showed $\nu_{max.}$ at 1610 cm^{-1} (CH:N.NHph).

EXAMPLE 2

Preparation of 3:1 Methyl Methacrylate/Diisopropylidenegalactose Methacrylate Random Copolymer (III, x=3.1).

Diisopropylidenegalactose methacrylate (501 mg.) was copolymerised in bulk with methyl methacrylate (469 mg.) with azobisisobutyronitrile (3 mg.) as catalyst as described in Example 1. After purification by solution in benzene and reprecipitation with methanol, the white powder, recovered in 80% yield, had $[\alpha]_D - 31°$ (c 0.5 in chloroform) and $\eta_{inh.}$ 4.1 dl./g. (c 0.5 in chloroform). Anal.: C, 58.9; H, 7.95; OMe, 14.8. Calc. for $[(C_5H_8O_2)_{3.1}.C_{16}H_{24}O_7]_n$: C, 59.2; H, 7.70; OMe, 15.0%.

Preparation of 3:1 Methyl Methacrylate/Galactose Methacrylate Random Copolymer (IV, x=3.1).

The above acetonated copolymer (III) (0.5 g) was dissolved in formic acid (50 ml) and the solution stirred at 20° C for 24 hr. Water (25 ml) was added dropwise with stirring and the solution stirred for a further 24 hr., when the specific rotation was +31° (c 0.583, calculated on the theoretical yield (437 mg.) of deacetonated copolymer (IV)). The solution was worked up as described in Example 1 to give copolymer (IV) as a white powder weighing 363 mg. (83.1% yield), and exhibiting $[\alpha]_D+21°$ (c 0.5 in dimethylformamide) and $\eta_{inh.}$ 4.4 dl./g. (c 0.1 in dimethylformamide). The infrared spectrum showed strong hydroxyl absorption at 3500—3400 cm^{-1}. The copolymer was insoluble in water and methyl n-propyl ketone. Anal.: C, 53.5; H, 7.55; OMe, 16.1. Calc. for $[(C_5H_8O_2)_{3.1}\,.\,C_{10}H_{16}O_7]_n$: C, 54.8; H, 7.36; OMe, 17.1%.

The specific rotation (+21°) was significantly higher than that of the 6:1 copolymer described in Example 1 owing to the increased content of galactose methacrylate.

Films cast from this copolymer formed suitable membranes for desalination by the process of reverse osmosis.

Preparation of Phenylhydrazone of 3:1 Methyl Methacrylate/Galactose Methacrylate Random Copolymer.

The above copolymer (IV) was characterised by conversion into its phenylhydrazone as described in Example 1. The copolymer phenylhydrazone was isolated in 97% yield and its infrared spectrum showed $\nu_{max.}$ at 1610 cm^{-1}. Anal.: C, 57.4: H, 7.55; N, 4.1. Calc. for $[(C_5H_8O_2)_{3.1}\,.\,C_{16}H_{22}N_2O_6]_n$: C, 58.3; H, 7.27; N, 4.3%.

EXAMPLE 3

Preparation of 9:1 Methyl Methacrylate/Diisopropylidenegalactose Methacrylate Random Copolymer (III, x=9).

Diisopropylidenegalactose methacrylate (2.34 g.) was copolymerised in bulk with methyl methacrylate (6.4 g.) with azobisisobutyronitrile (18 mg.) as catalyst as described in Example 1. After purification by solution in benzene and reprecipitation with methanol the white copolymer powder, isolated in 97% yield, had $[\alpha]_D-18°$ (c 0.5 in chloroform) and $\eta_{inh.}$ 2.2 dl./g. (c 0.5 in chloroform). Anal.: C, 58.6; H, 7.52; OMe, 23.7. Calc. for $[(C_5H_8O_2)_9\,.\,C_6H_{24}O_7]_n$: C, 59.6; H, 7.87; OMe, 22.7%.

Preparation of 9:1 Methyl Methacrylate/Galactose Methacrylate Random Copolymer (IV, x=9).

The above acetonated copolymer (III) (6.7 g.) was dissolved in formic acid (670 ml) and the solution stirred at 20° C for 24 hr. Water (335 ml.) was added dropwise with stirring and the solution stirred for a further 24 hr., when the specific rotation was +15° (c 0.0623, calculated on the theoretical yield (6.26 g.) of deacetonated copolymer (IV)). The solution was worked up as described in Example 1 to give copolymer (IV) as a white powder weighing 5.97 g. (95.4%), and exhibiting $[\alpha]_D+8°$ (c 0.5 in dimethylformamide) and $\eta_{inh.}$ 2.3 dl./g. (c. 0.1 in dimethylformamide); $\nu_{max.}$ 3500—3400 cm.$^{-1}$. The copolymer was insoluble in water and methyl n-propyl ketone. Anal.: C, 56.6; H, 7.87; OMe, 23.4. Calc. for $[(C_5H_8O_2)_9\,.\,C_{10}H_{16}O_7]_n$: C, 57.5; H, 7.72; OMe, 24.3%.

Films cast from this product formed suitable membranes for desalination by the process of reverse osmosis.

EXAMPLE 4.

Preparation of 4:1 Methyl Methacrylate/Diisopropylidenegalactose Methacrylate Random Copolymer (III, x=4).

Diisopropylidenegalactose methacrylate (3.28 g.) and methyl methacrylate (4 g.) were copolymerised in bulk with azobisisobutyronitrile (14 mg.) as catalyst as described in Example 1. After purification by solution in benzene and reprecipitation in methanol, the white copolymer, isolated 89% yield, had $[\alpha]-27°$ (c 0.5 in chloroform) and $\eta_{inh.}$ 2.3 dl./g. (c 0.5 in chloroform). Anal.: C, 58.6; H, 7.28; OMe, 16.8. Calc. for $[(C_5H_8O_2)_4\,.\,C_{16}H_{24}O_7]_n$: C, 59.3; H, 7.75; OMe, 17.0%.

Preparation of 4:1 Methyl Methacrylate/Galactose Methacrylate Random Copolymer (IV, x=4).

The above acetonated copolymer (III) (4.87 g) was dissolved in formic acid (500 ml.), and after 24 hr. water (250 ml.) was added dropwise with stirring. The solution was stirred for a further 24 hr., when the specific rotation was +26° (c 0.577, calculated on the theoretical yield (4.33 g.) of deacetonated copolymer (IV)). The solution was worked up as described in Example 1 to give copolymer (IV) as a white powder weighing 3.86 g. (89.1% yield), and exhibiting $[\alpha]_D+15°$ (c 0.5 in dimethylformamide) and $\eta_{inh.}$ 2.2 dl./g. (c 0.5 in dimethylformamide). The copolymer was insoluble in water and methyl n-propyl ketone. Anal.: C, 55.6; H, 7.64; OMe, 17.3. Calc. for $[(C_5H_8O_2)_4\,.\,C_{10}H_{16}O_7]_n$: C, 55.5; H, 7.46; OMe, 19.1%.

Films cast from this product formed suitable membranes for desalination by the process of reverse osmosis.

We have determined experimentally the reactivity ratios of the monomers in the copolymerisation of methyl methacrylate with diisopropylidenegalactose methacrylate and found them to be very similar:

$r_1=0.93\pm0.03$ (methyl methacrylate).

$r_2 = 1.30 \pm 0.19$ (diisopropylidenegalactose methacrylate).

This means that diisopropylidenegalactose methacrylate behaves as an alkyl methacrylate in radical copolymerisations and can thus be copolymerised in any proportion with methyl methacrylate to give a final copolymer containing these units in approximately their initial monomer ratio. Examples 1—4 confirm that this in fact occurs in practice at high conversions.

It is thus possible to prepare by the practice of this invention a series of methyl methacrylate/galactose methacrylate random copolymers containing any desired ratio of monomers. The water-uptake, i.e. hydrophilicity, of the copolymers increases as the amount of galactose methacrylate in the copolymer increases. When the molar ratio of methyl methacrylate to galactose methacrylate is greater than 3 : 1, the copolymers are insoluble in water although they are capable of taking up considerable amounts of water in much the same was as cellulose and cellulose acetate can absorb water without dissolving. However, when the molar ratio of methyl methacrylate to galactose methacrylate falls much below 3 : 1, the copolymers become water-soluble. It is thus possible by the practice of this invention to prepare random copolymers containing any desired level of water-swell. It is also possible to control the reactivity of the copolymers by increasing or decreasing the proportion of galactose methacrylate.

EXAMPLE 5

Preparation of 20 : 1 Methyl Acrylate/Diisopropylidenegalactose Acrylate Random Copolymer.

A five-necked, 100 ml. reaction vessel, fitted with a stirrer, condenser, nitrogen-inlet and thermometer, was charged with water (20 ml.), sodium lauryl sulphate (0.25 g.), ammonium persulphate (0.01 g.), freshly-distilled methyl acrylate (8.99 g.), and diisopropylidenegalactose acrylate (1.63 g.), prepared as described in pending British Patent Application No. 9065/65 (Final Number 1,099,372). The mixture was slowly stirred to give an emulsion and the reaction flask was flushed with a stream of nitrogen. After 30 min. the emulsion was heated to 70° C, when refluxing began and the temperature rose rapidly to 80° C. Refluxing stopped after about 2 min. and the temperature began to fall. The polymer emulsion was finally heated to 100° C for 30 min. and added dropwise to hot 5% sodium chloride solution (100 ml.). The white rubbery copolymer was washed with hot water, air-dried, dissolved in acetone (400 ml.), and reprecipitated with water (2l.). Washing with water and drying *in vacuo* gave a stiff, white rubber weighing 9.83 g. (92.6% yield), and exhibiting $[\alpha]_D - 8°$ (c 0.5 in chloroform) and $\eta_{inh.}$ 3.6 dl./g. (c 0.5 in chloroform). Anal.: C, 56.0; H, 7.05; OMe, 29.8. Calc. for $[(C_4H_6O_2)_{20} . C_{15}H_{22}O_7]_n$; C, 56.0; H, 7.03; OMe, 30.5%.

Preparation of 20 : 1 Methyl Acrylate/Galactose Acrylate Random Copolymer.

The above acetonated copolymer (1 g.) was dissolved in acetone (10 ml.) and formic acid (90 ml.) was added gradually with stirring to the solution so that precipitation was prevented. Water (10 ml.) was then added dropwise and the solution stirred at 20° C for 3 days to effect deacetonation, after which the solution was filtered and dialysed against running water for 24 hr. The precipitated copolymer was filtered, washed with water, and dried *in vacuo* to yield a hard, white product, which weighed 0.87 g. (90.5% yield) and exhibited $[\alpha]_D + 9°$ (c 0.5 in dimethylformamide) and $\eta_{inh.}$ 3.7 dl./g. (c 0.1 in dimethylformamide). The infrared spectrum of a film of this material, cast from dimethylformamide solution, showed a sharp hydroxyl peak at 3550 cm.$^{-1}$. Anal.: C, 54.7; H, 7.11; OMe, 31.7. Calc. for $[(C_4H_6O_2)_{20} . C_9H_{14}O_7]_n$: C, 54.6; H, 6.91; OMe, 31.7%.

The analysis shows that the initial monomer ratio (20 : 1) has been maintained in the copolymer.

EXAMPLE 6

Preparation of 9 : 1 Methyl Acrylate/Diisopropylidenegalactose Acrylate Random Copolymer.

Diisopropylidenegalactose acrylate (2.89 g.) and methyl acrylate (7.11 g.) were emulsified in water (20 ml.) with sodium lauryl sulphate (250 mg.), and copolymerisation initiated with ammonium persulphate (10 mg.) as described in Example 5. The copolymer was isolated as before by coagulation with 5% sodium chloride solution and purified by solution in acetone and reprecipitation with water. The white rubbery product weighed 8.97 g. (89.7% yield) and showed $[\alpha]_D - 15°$ (c 0.5 chloroform) and $\eta_{inh.}$ 2.7 dl./g. (c 0.5 in chloroform). Anal.: C, 56.2; H, 7.20; OMe, 22.9. Calc. for $[(C_4H_6O_2)_9 . C_{15}H_{22}O_7]_n$: C, 56.2; H, 7.03; OMe, 25.6%.

Preparation of 9 : 1 Methyl Acrylate/Galactose Acrylate Random Copolymer.

The above acetonated copolymer (2.01 g.) was dissolved in acetone (20 ml.), and to the solution were added gradually with stirring first formic acid (180 ml.) and then water (20 ml.). The solution was worked up as described in Example 5 to give a white product weighing 1.88 g., and exhibiting $[\alpha]_D + 17°$ (c 1 in dimethylformamide) and $\eta_{inh.}$ 2.3 dl./g. (c 0.2 in dimethylformamide). Anal.: C, 54.0; H, 7.26; OMe, 24.4. Calc. for $[(C_4H_6O_2)_9 . C_9H_{14}O_7]_n$: C, 53.6; H, 6.79; OMe, 27.7%.

Fractional precipitation of this product in dimethylformamide solution with water proved the absence of methyl acrylate homopolymer, thus confirming that the material is a true random copolymer.

Example 7

Preparation of 6:1 Acrylonitrile/Diisopropylidenegalactose Acrylate Random Copolymer.

Acrylonitrile (513 mg.) and diisopropylidenegalactose acrylate (506 mg.) were copolymerised in bulk with azobisisobutyronitrile (2.3 mg.) as catalyst at 50° C for 5 hr. in a sealed tube in the usual manner. The product (0.015 g.) was taken up in dimethylformamide (50 ml.), methanol (20 ml.) was added, and the insoluble gel removed by filtration. The filtrate was added slowly with stirring to methanol (500 ml.), and the precipitate was filtered, washed with methanol, and dried *in vacuo* to yield a white powder weighing 639 mg. (63% yield), and exhibiting $[\alpha]_D -24°$ (c 0.5 in dimethylformamide) and $\eta_{inh.}$ 2.0 dl./g. (c 0.5 in dimethylformamide). The infrared spectrum showed $\nu_{max.}$ 2260 cm.$^{-1}$ (CN). Anal.: C, 62.5; H, 6.57; N, 12.8. Calc. for $[(C_3H_3N)_6 . C_{15}H_{22}O_7]_n$: C, 62.6; H, 6.37; N, 13.8%.

Preparation of 6:1 Acrylonitrile/Galactose Acrylate Random Copolymer.

The above acetonated copolymer (0.25 g.) was dissolved in formic acid (25 ml.) by shaking for 18 hr. at 20°, water (12.5 ml.) was added dropwise with stirring, and the solution was stirred for a further 24 hr. at 20° C when the final specific rotation was +29° (c 0.581, calculated on the theoretical yield (218 mg.) of deacetonated copolymer). Formic acid was removed by dialysis against running water for 3 days, during which time the deactonated copolymer precipitated. It was filtered, washed with water, and dried *in vacuo* to a white powder, which weighed 208 mg. (95.4% yield) and showed $[\alpha]_D +21°$ (c 0.5 in dimethylformamide) and $\eta_{inh.}$ 2.6 dl./g. (c 0.1 in dimethylformamide). The infrared spectrum showed $\nu_{max.}$ at 3400 (OH) and 2260 cm.$^{-1}$ (CN). Anal.: C, 57.5; H, 6.19; N, 14.3. Calc. for $[(C_3H_3N)_6 . C_9H_{14}O_7]_n$: C, 58.7; H, 5.84; N, 15.2%.

It is thus possible to increase the reactivity of poly(acrylonitrile) by introducing hydroxyl groups in the manner described. The capacity of the polymerised product to take up water is also increased by this copolymerisation.

Preparation of Phenylhydrazone of 6:1 Acrylonitrile/Galactose Acrylate Random Copolymer.

The above deacetonated copolymer (50 mg.) was dissolved in dimethylformamide (4.5 ml.), glacial acetic acid (0.5 ml.) and phenylhydrazine (0.25 ml.) were added, and the yellow solution was kept in the dark at 20° C for 24 hr. The copolymer phenylhydrazone was precipitated in water, washed thoroughly with water and ethanol, and dried to a pale yellow powder weighing 56.4 mg. (96.4% yield), which showed $\nu_{max.}$ at 1610 cm.$^{-1}$ (CH:N.NHPh). Anal.: C, 61.5; H, 6.58; N, 16.1. Calc. for $[(C_3H_3N)_6 . C_{15}H_{20}N_2O_6]_n$: C, 61.7; H, 5.96; N, 17.4%.

Example 8

Copolymerisation of Diisopropylidenegalactose Methacrylate with Vinyl Acetate.

It is well known that vinyl acetate does not readily copolymerise with esters of α,β-unsaturated acids; for example, for the system methyl methacrylate/vinyl acetate, the reactivity ratios have been reported (Mayo, Walling, Lewis and Hulse, J. Amer. chem. Soc., 1948, 70, 1523) as 20±3 and 0.015 ±0.015 respectively. Despite the unfavourable reactivity ratios, it is possible to copolymerise diisopropylidenegalactose methacrylate and vinyl acetate, as described in the following example.

Vinyl acetate (2.43 g.) and diisopropylidenegalactose methacrylate (3.08 g.) (initial monomer molar ratio 3:1) were copolymerised in benzene (1.25 g.) with azobisisobutyronitrile (12 mg.) as catalyst at 50° C for 18 hr. under nitrogen. The sticky polymer plug was dissolved in benzene (100 ml.), the solution added dropwise with stirring to methanol (1 l.) and the white precipitate filtered, washed thoroughly with methanol to remove vinyl acetate homopolymer, and dried *in vacuo*. The white copolymer weighed 3.35 g., which corresponds to a yield of 97% based on the weight of diisopropylidenegalactose methacrylate and on a 2.17:1 diisopropylidenegalactose methacrylate/vinyl acetate copolymer composition, which was determined from the analysis given below. The copolymer had $[\alpha]_D -52°$ (c 0.5 in chloroform) and $\eta_{inh.}$ 2.9 dl./g. (c 0.5 in chloroform). Anal.: C, 58.0, H. 7.29; Ac, 5.4. Calc. for $[(C_{16}H_{24}O_7)_{2.17} . C_2H_3OAc]_n$: C, 58.2; H, 7.33; Ac, 5.4%.

Preparation of Vinyl Acetate/Galactose Methacrylate Copolymer.

The above acetonated copolymer (1 g.) was dissolved in formic acid (100 ml.), and after 18 hr. at 20° C water (50 ml.) was added dropwise and the solution stirred for 24 hr. at 20° C, when the specific rotation was +48° (c 0.538, calculated on the theoretical yield (807 mg.) of 2.17:1 galactose methacrylate/vinyl acetate copolymer). Formic acid was removed by dialysis against running water for 3 days, the cloudy solution concentrated to 100 ml. and centrifuged, and the insoluble gel was dried *in vacuo*. The resulting white powder weighed 526 mg., and had $[\alpha]_D +31°$ (c 0.5 in dimethylformamide) and $\eta_{inh.}$ 7.1

dl./g. (c 0.1 in dimethylformamide). Analysis showed this was a 1:1 galactose methacrylate/vinyl acetate copolymer. Anal.: C, 49.2; H, 6.77; Ac, 12.8. Calc for $[C_{10}H_{16}O_7 . C_2H_3OA_c]_n$: C, 50.3; H, 6.63; Ac, 12.9%.

The water-soluble fraction was essentially galactose methacrylate homopolymer.

Preparation of Phenylhydrazone of 1:1 Vinyl Acetate/Galactose Methacrylate Copolymer.

The above deacetonated copolymer (52 mg.) was dissolved in dimethylformamide (4.5 ml.), glacial acid (0.5 ml.) and phenylhydrazine (0.5 ml.) added, and the yellow solution kept in the dark at 20° C. for 24 hr. The copolymer phenylhydrazone was precipitated in water, washed with water and ethanol, and dried to a pale yellow powder weighing 62 mg. (93% yield). Anal.: C, 55.4; H, 6.56; N, 6.7. Calc. for $[C_{16}H_{22}N_2O_6 . C_2H_3OA_c]_n$: C, 56.6; H, 6.65; N, 6.6%.

EXAMPLE 9

Preparation of 6:1 Styrene/Diisopropylidenegalactose Methacrylate Random Copolymer.

Inhibitor-free styrene (914 mg.) and diisopropylidenegalactose methacrylate (502 mg.) (i.e. molar ratio of monomers 5.7:1) were copolymerised in bulk with azobisisobutyronitrile (4 mg.) as catalyst by heating 50° C for 18 hr. in a sealed tube under nitrogen. The polymerised plug was dissolved in benzene (150 ml.), reprecipitated with methanol (1.51), and the precipitate washed with methanol and dried to a white powder weighing 950 mg. (67.1% yield), which showed $[\alpha]_D-32°$ (c 0.5 in toluene) and $\eta_{inh.}$ 1.3 dl./g. (c 0.5 in toluene). Anal.: O, 14.1. Calc. for $[(C_8H_8)_{5.7} . C_{16}H_{24}O_7]_n$: O, 12.1%.

EXAMPLE 10

Preparation of 3:1 Styrene/Diisopropylidenegalactose Methacrylate Random Compolymer.

Styrene (482 mg.) and diisopropylidenegalactose methacrylate (501 mg.) were copolymerised in bulk at 50° C for 3 days with azobisisobutyronitrile (4 mg.) as catalyst. The hard glass was broken down with some mechanical loss, and the product (940 mg.) was dissolved in benzene (50 ml.) and reprecipitated with methanol (500 ml.). The dry copolymer weighed 838 mg. (89.1% yield), and gave $[\alpha]_D-40°$ (c 0.5 in toluene) and $\eta_{inh.}$ 1.8 dl./g. (c 0.5 in toluene). Anal.: O, 17.7. Calc. for $[(C_8H_8)_3 . C_{16}H_{24}O_7]_n$: O, 17.4%.

EXAMPLE 11

Preparation of 1:1 Styrene/Diisopropylidenegalactose Methacrylate Random Copolymer.

Styrene (160 mg.) and diisopropylidenegalactose methacrylate (499 mg.) were copolymerised in benzene (0.3 g.) at 50° C for 3 days with azobisisobutyronitrile (3 mg.) as catalyst. The copolymer plug was dissolved in benzene (10 ml.), reprecipitated with methanol (100 ml.), and dried to give 591 mg. (89.7% yield) of white powder, which showed $[\alpha]_D-56°$ (c 0.5 in toluene) and $\eta_{inh.}$ 0.6 dl./g. (c 0.5 in toluene). Anal.: O, 26.1. Calc. for $(C_8H_8 . C_{16}H_{24}O_7)_n$: O, 25.8%.

Preparation of 1:1 Styrene/Galactose Methacrylate Random Copolymer.

The above acetonated copolymer (0.2 g.) was dissolved in formic acid (20 ml.) and after 18 hr. at 20° C water (10 ml.) was added dropwise and the solution stirred for 24 hr. at 20° C, when the specific rotation was +46° (c 0.543, calculated on the theoretical yield (163 mg.) of deacetonated copolymer). Formic acid was removed by dialysis against running water for 3 days, during which the copolymer precipitated. It was filtered, washed with water, and dried to give a white powder weighing 134 mg. (82.2% yield), which was insoluble in benzene and had $[\alpha]_D+24°$ (c 0.5 in dimethylformamide) and $\eta_{inh.}$ 0.9 dl./g. (c 0.5 in dimethylformamide). The infrared spectrum showed strong hydroxyl absorption at 3400 cm.$^{-1}$ and benzenoid absorption at 1600, 760, and 700 cm.$^{-1}$. Anal.: 31.5. Calc. for $(C_8H_8 . C_{10}H_{16}O_7)_n$: O, 31.7%.

Preparation of Phenylhydrazone of 1:1 Styrene/Galactose Methacrylate Copolymer.

The above deacetonated copolymer (50 mg.) was dissolved in dimethylformamide (4.5 ml.), glacial acetic acid (0.5 ml.) and phenylhydrazine (0.5 ml.) added, and the solution kept in the dark at 20° C for 24 hr. The copolymer phenylhydrazone was precipitated in water, washed with water and ethanol, and dried to a pale yellow powder weighing 58 mg. (92% yield). Anal.: C, 65.3; H, 6.97; N, 6.2 Calc. for $(C_8H_8 . C_{16}H_{22}N_2O_6)_n$: C, 65.1; H, 6.84; N, 6.2%.

WHAT WE CLAIM IS:—

1. A method of preparing a synthetic copolymer containing a carbohydrate residue, comprising polymerising together in the presence of a catalyst a vinylidene or a vinyl monomer and a polymerisable ester of galactose formed by reaction of an α,β-olefinically unsaturated mono- or di-carboxylic acid with the the hydroxyl group in the 6-position of galactose.

2. A method as claimed in claim 1, wherein the catalyst is a free-radical catalyst.

3. A method as claimed in claim 1 or claim 2 wherein the polymerisable ester of galactose is formed by reacting a 1,2:3,4-diketal of galactose with an α,β-olefinically unsaturated polymerisable acid.

4. A method as claimed in claim 3 wherein the ketal residues are removed from the galactose units in the copolymer by controlled hydrolysis.

5. A method as claimed in any one of the preceding claims, wherein the vinylidene or

vinyl monomer is an alkyl methacrylate or an alkyl acrylate or acrylonitrile or vinyl acetate or styrene.

6. A method as claimed in any one of the preceding claims, wherein the vinylidene or vinyl monomer is methyl methacrylate or methyl acrylate.

7. A method as claimed in any one of the preceding claims, wherein the polymerisable ester of galactose is any one of those disclosed in pending British Patent Application No. 9065/65 (Final Number 1,099,372).

8. A method as claimed in any one of the preceding claims wherein the controlled hydrolysis is effected by dissolving the polymerised product in an organic acid and diluting the solution gradually with water.

9. A method as claimed in claim 8 wherein the organic acid is formic acid.

10. A method as claimed in any one of the preceding claims wherein a free-radical catalyst comprising azobisisobutyronitrile is used to catalyse the polymerisation.

11. A copolymer containing a vinylidene or vinyl monomer and an ester between the hydroxy group in the 6-position of galactose and an α,β-olefinically unsaturated mono- or di-carboxylic acid.

12. A copolymer containing a vinylidene or vinyl monomer and an ester between the hydroxy group in the 6-position of galactose and an α,β-olefinically unsaturated mono- or di-carboxylic acid, positions one, two, three, and four of the galactose molecule containing hydroxyl groups.

13. A methyl methacrylate/diisopropylidenegalactose 6-methacrylate random copolymer.

14. A methyl methacrylate/galactose 6-methacrylate random copolymer.

15. A phenylhydrazone of a methyl methacrylate/galactose 6-methacrylate random copolymer.

16. A methyl acrylate/diisopropylidenegalactose 6-acrylate random copolymer.

17. A methyl acrylate/galactose 6-acrylate random copolymer.

18. An acrylonitrile/diisopropylidenegalactose 6-acrylate random copolymer.

19. An acrylonitrile/galactose 6-acrylate random copolymer.

20. A phenylhydrazone of an acrylonitrile/galactose 6-acrylate random copolymer.

21. A vinyl acetate/diisopropylidenegalactose 6-methacrylate copolymer.

22. A vinyl acetate/galactose 6-methacrylate copolymer.

23. A phenylhydrazone of a vinyl acetate/galactose 6-methacrylate copolymer.

24. A styrene/diisopropylidenegalactose 6-methacrylate random copolymer.

25. A styrene/galactose 6-methacrylate random copolymer.

26. A phenylhydrazone of a styrene/galactose 6-methacrylate random copolymer.

27. A method of preparing a new synthetic copolymer containing a carbohydrate residue, according to any one of the Examples.

28. A new synthetic copolymer containing a carbohydrate residue, whenever prepared by the method of any one of claims 1 to 10 or 27.

29. A phenylhydrazone of the copolymer claimed in claim 28.

H. D. FITZPATRICK & CO.,
Chartered Patent Agents
5 Park Gardens, Glasgow C.3.
and
27 Chancery Lane, London W.C.2.

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Synthetic Sugar Polymers

J. A. Colquhoun* B.Sc., **and E. T. Dewar†** Ph.D.

The synthesis of carbohydrate polymers from sugar monomers might lead to the production of films and membranes. This article discusses the polymerisation of sugar monomers to polyamides, polyesters, polyacrylates giving products with better hydrophilic properties for potential use as membranes, contact lenses, etc.

THE idea of synthesising carbohydrate polymers using sugar monomers is not new. In 1939, Walter Reppe, working in the laboratories of I. G. Farbenindustrie in Germany, was granted a patent[1] for the production and polymerisation of vinyl ethers derived from glucose and fructose, and many attempts were made during the 1940s and 1950s by the late Sir Norman Haworth and his colleagues at Birmingham University and elsewhere to prepare nylon-type polyamides and polyacrylics from sugar monomers. These attempts, however, were mainly unsuccessful owing to the inadequate polymerisation techniques existing at the time. For example, the high temperature (nearly 300°C) necessary in the conventional melt-polymerisation used for the production of nylon from hexamethylenediamine and adipic acid is quite unsuitable for the preparation of carbohydrate polyamides.

Sugar nylons

The new technique of interfacial polycondensation,[2] in which the dibasic acid (e.g. adipic acid) is replaced by its acid dichloride, is well suited to carbohydrate monomers because of the low temperatures required for polymerisation, and we have used it to prepare carbohydrate polyamides with viscosities comparable to those of commercial nylons. Two series of high-viscosity methylenedioxy-nylons have been prepared: (*i*) from a 1,6-diamino-1,6-dideoxy-di-*O*-methylenehexitol, e.g. diamines (I) to (IV), and sebacoyl or adipoyl dichloride, and (*ii*) from hexamethylenediamine or decamethylenediamine and a di-*O*-methylenehexaroyl dichloride, e.g. (V) to (VII). The synthesis of substituted sugar diamines and diacid chlorides from readily available hexose sugars, e.g. glucose, mannose and galactose, has been extensively investigated in this institute,[3] and a range of methylene-, benzylidene-, and isopropylidene-blocked monomers is now available for polycondensation. It is necessary to protect the hydroxyl groups of the sugar monomer before polycondensation to prevent cross-linking, which would lead to insoluble, infusible and intractable polymers.

As a typical example, the di-*O*-methylene hexitol diamines, (I) to (IV), were synthesised from galactitol (dulcitol), *D*-mannitol, *D*-glucitol (sorbitol), and *L*-iditol respectively. These four stereoisomeric diamines all have the same molecular formula ($C_8H_{16}N_2O_4$) and differ only in the configuration of the oxygen atoms and in the linking of the methylene bridges. These dimethylenedioxy-diamines were condensed with sebacoyl dichloride, and it was observed that the polymer melt temperature (pmt) and solubility of the resulting dimethylenedioxy-6, 10-nylons were markedly dependent on the structure and conformation of the sugar diamine. The polyamides containing the *D-gluco* (III) and *L-ido* (IV) structures had high pmts ($>270°$), which can be attributed to the ridigity imposed by the fused, bicylic, 2,4:3,5-dimethylenedioxy ring system.

Pmt and solubility also depended on the size of the blocking group; e.g. when 1,6-diamino-1,6-dideoxy-2,3:4,5-di-*O*-isopropylidenegalactitol (I, R=Me) was condensed with sebacoyl dichloride, the polymer melted at a lower temperature than the corresponding dimethylenedioxy-nylon prepared from (I, R=H), and was more soluble in organic solvents. The protecting isopropylidene residues were readily removed from this polymer by treatment with acid to give the tetrahydroxy-nylon 6, 10, which, however, failed to dissolve in water, due presumably to hydrogen bonding interaction between the polymer chains (see below).

The sugar nylon systems offer the polymer chemist and technologist a unique opportunity to study property-structure relationships, and it is suggested that such a study could lead to the production of hydrophilic or soluble polyamides, which could be used in films, membranes, and many other fields from which the present industrial nylons are excluded because of their inability to take up water and their general lack of reactivity.

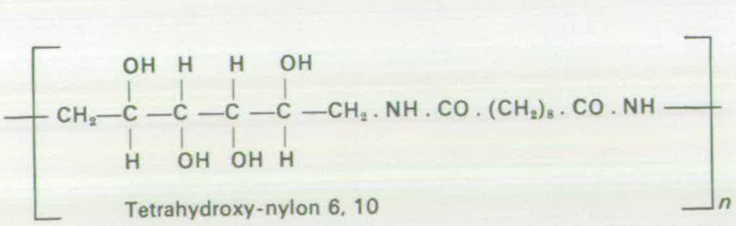
Polyesters

Interfacial polycondensation cannot be used for the preparation of linear polyesters of the *Terylene* type by reaction of aliphatic glycols with acid dichlorides, because the condensation is too slow, relative to competing hydrolysis of the acid chloride, for the formation of high polymers. However, polyphenyl esters of high molecular weight can be prepared by mixing an aqueous solution of the sodium salt of a bisphenol,[4] e.g. 4,4′-isopropylidenediphenol *(Bisphenol A)*, with a solution of a diacid chloride, e.g. terephthaloyl dichloride, in a water-immiscible organic solvent. Sugar polyphenyl esters were prepared by condensation of *Bisphenol A* with 2,3:4,5-di-*O*-methylenegalactaroyl (V), and 2,4:3,5-di-*O*-methylene-*D*-glucaroyl (VI) and-*L*-idaroyl dichloride (VII).[5]

In general, viscosities were higher than those for polyesters prepared from simple acyl chlorides (adipoyl and sebacoyl dichloride), but lower than those of polymers from terephthaloyl and isophthaloyl dichloride. As in the case of the polyamides, pmt and solubility varied over a wide range depending on the structure of the sugar acid chloride.

Addition polymers

One of the most successful synthetic plastics is poly (methyl methacrylate), known as *Perspex* or *Plexiglas*. It is made by polymerising the unsaturated liquid, methyl methacrylate, $H_2C{:}CMe\,.\,CO_2Me$, with a free-radical initiator. Work in this institute[6] and in Japan[7] has resulted in the synthesis of a number of substituted sugar acrylates and methacrylates, which can be polymerised to polymers of high molecular weight. In order to prepare a useful monomer from a sugar such as glucose,



$$\left[-CH_2-\underset{H}{\overset{OH}{C}}-\underset{OH}{\overset{H}{C}}-\underset{OH}{\overset{H}{C}}-\underset{H}{\overset{OH}{C}}-CH_2\,.\,NH\,.\,CO\,.\,(CH_2)_8\,.\,CO\,.\,NH- \right]_n$$

Tetrahydroxy-nylon 6, 10

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[*] J. A. Colquhoun graduated in chemistry from Edinburgh in 1962, and has since been employed by the Arthur D. Little Research Institute. He is particularly interested in natural and synthetic carbohydrate polymers.

[†] E. T. Dewar, before joining ADL in 1956 was research chemist for the Institute of Seaweed Research. He is now Head of the carbohydrate section in the chemical sciences division of ADL.

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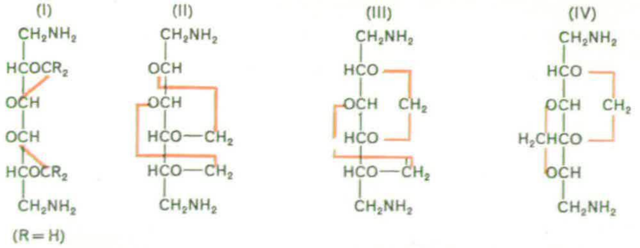
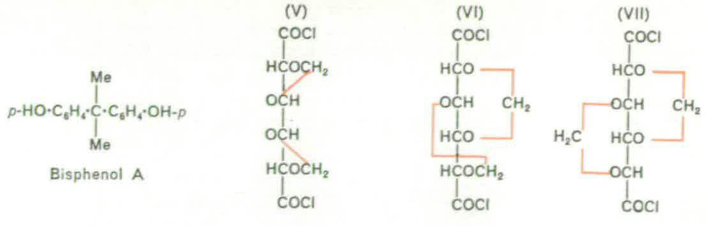
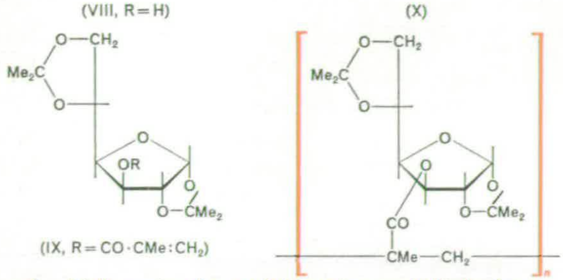


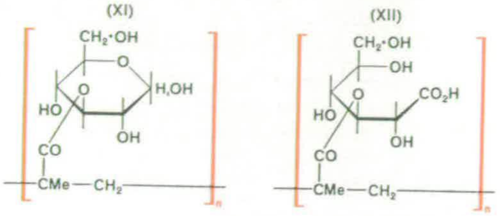
di-O-methylene hexitol-diamines ($C_8H_{16}N_2O_4$)



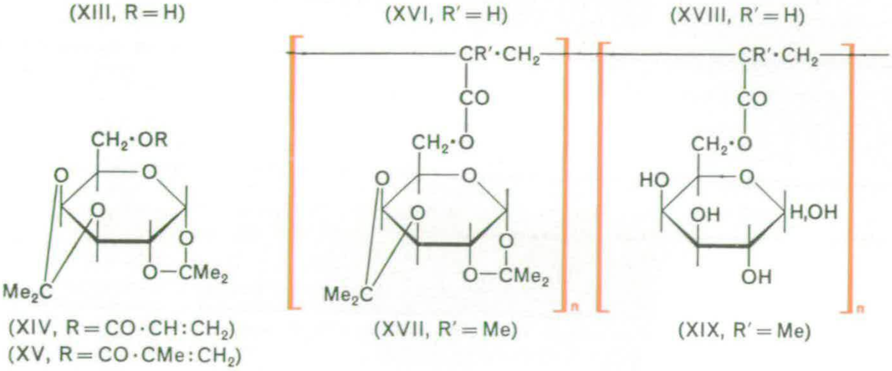
Preparation of sugar polyphenyl esters



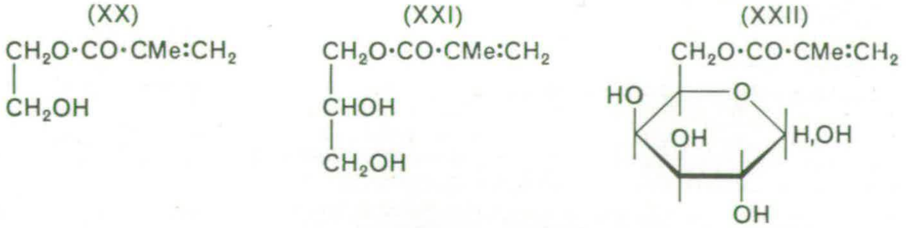
Preparation of a high molecular weight polymer, initially from glucose and acetone to give compound VIII which is esterfied



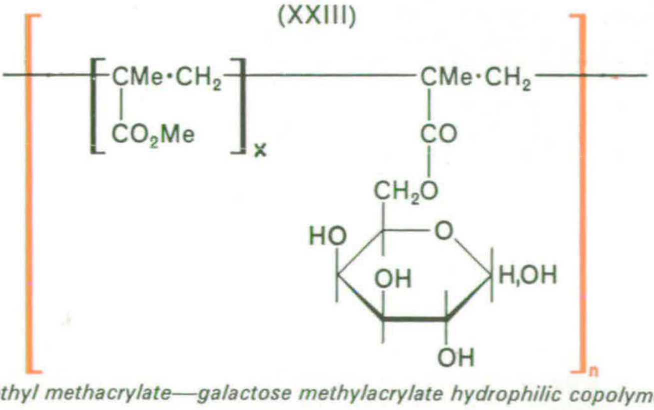
Preparation of a high molecular weight polyacid by acid hydrolysis of X and subsequent oxidation of XI



Preparation of water-soluble galactose polymers



Water-soluble methacrylate monomers which, on polymerisation, give insoluble hydrogels



Methyl methacrylate—galactose methylacrylate hydrophilic copolymers it is necessary to block four of the five hydroxyl groups to convert the glucose into a monohydric alcohol. An ideal starting compound is 1,2:5,6-di-*O*-isopropylidene-α-*D*-glucofuranose (VIII), a beautifully crystalline compound that is easily prepared from glucose and acetone. The hydroxyl group on C-3 was then esterified and the methacrylate monomer (IX) polymerised in benzene solution to the high-molecular-weight polymer (X).

An interesting feature of this polymethacrylate (X) is that on treatment with acid the protecting isopropylidene groups are removed, and the water-soluble poly (glucose 3-methacrylate) (XI) is obtained. The reaction is accompanied by a change in optical rotation and by a furanose → pyranose ring conversion. This is a completely new type of glucose polymer for it has a free reducing group at C-1 on every glucose unit, while in all natural glucose polysaccharides, such as starch, cellulose, dextran, etc., the hemi-acetal hydroxyl group is combined in the glycosidic linkage (except in the one reducing unit at the end of each polysaccharide molecule).

Reactions at the reducing group of these synthetic polymers are thus important because they are not possible with natural polysaccharides. For example, oxidation of poly(glucose methacrylate) (XI) gave poly-(3-*O*-methacryloyl-*D*-gluconic acid) (XII), the sodium salt of which behaved as a typical polyelectrolyte, yielding extremely viscous solutions in water but becoming less viscous in the presence of an electrolyte. These polyacids in some respects resemble the natural polyuronides, alginic and pectic acid, which are widely used in industry. Other reactions at the reducing group are also possible, such as reduction, phenylhydrazone and phenylosazone formation, but in some cases reaction was incomplete owing to precipitation of the polymer from solution. Similarly, galactose reacted with acetone to give 1,2:3,4-di-*O*-isopropylidene-α-*D*-galactopyranose (XIII), which was easily converted into its crystalline 6-acrylate (XIV) and 6-methacrylate (XV). Polymerisation of these monomers produced the acetonated polyacrylate (XVI) and polymethacrylate (XVII), and these polymers were then deacetonated with acid as in the case of the glucose polymer to yield the viscous, water-soluble poly (galactose 6-acrylate) (XVIII) and poly (galactose 6-methacrylate) (XIX). These water-soluble galactose polymers undergo all the reactions described previously for the glucose polymer (XI). The fact that these synthetic sugar polymers are water-soluble is interesting and important, because polymerisation of water-soluble methacrylate monomers, such as hydroxyethyl methacrylate (XX), glyceryl methacrylate (XXI) and 6-*O*-methacryloyl-*D*-galactose (XXII), invariably leads to cross-linked, insoluble hydrogels.

Copolymers

The successful utilisation of these carbohydrate monomers will undoubtedly be found in their copolymerisation with cheap industrial monomers, such as styrene, methyl methacrylate, acrylonitrile, etc., as a means of upgrading the chemical and physical properties of many industrial plastics, films, and fibres. For example, the properties of the hydrophilic galactose 6-methacrylate have been studied in copolymers of methyl methacrylate with the specific object of producing membranes suitable for desalting sea-water by the process of reverse osmosis—now seriously challenging distillation as a method of desalination. This work on the synthesis of new membranes is being carried out in this institute by Dr. Allan Sharples under a contract from the US Office of Saline Water. Cellulose acetate is the only polymer used for reverse osmosis at the present time, and suitable membranes were developed only after many years of research.

Briefly, reverse osmosis involves forcing a salt solution through a hydrophilic membrane by means of high pressure (100 atm), when pure water is 'squeezed' out of the solution. The membrane operates by selectively dissolving the water and rejecting the salt because of its lower affinity for the membrane. The reactivity ratios of methyl methacrylate and diisopropylidenegalactose methacrylate (XV) have been shown to be quite similar, and a series of random copolymers with different monomer ratios has been prepared. The acetone blocking groups on the sugar units are then removed as before by acid treatment to give the methyl methacrylate-galactose methacrylate hydrophilic copolymers (XXIII). The hydrophilic-hydrophobic balance can be accurately controlled from the monomer ratios in the original feedstock. It is too early to say whether membranes made from these copolymers will be competitive in performance and cost with those prepared from cellulose acetate, but the advantages of an entirely synthetic system from an industrial point of view are obvious.

The medical and surgical applications of synthetic plastics and polymers have greatly increased in recent years, although the question of compatibility of the plastic with the living tissue has only rarely been considered. Incompatibility and impermeability to water and metabolites frequently lead to local irritation or a tumourous growth.[8] Hydrogels prepared from polymers of hydroxyethyl methacrylate (XX) and glyceryl methacrylate (XXI) may soon replace poly(methyl methacrylate) in the manufacture of soft contact lenses,[9] and this trend to synthesise plastics with specific chemical and physical properties will continue in the future. It is suggested that there is an outlet for synthetic sugar polymers and copolymers as hydrophilic plastics in medicine and surgery, e.g. in the form of dressings, orthopaedic appliances, contact lenses, external prostheses, and surgical implants. It seems reasonable that a sugar-containing material will represent less of a foreign body to living tissues than *Perspex, Terylene, Teflon,* and the other commercial plastics presently being used.

Successful copolymerisations of sugar monomers with styrene, acrylonitrile, vinyl acetate, methyl acrylate, maleic anhydride, etc., have also been effected, and the physical and chemical properties of these new products are being studied. The introduction of hydroxyl-containing sugar units into cheap, readily available plastics and polymers is an excellent method of increasing chemical reactivity (e.g. dyeing) and water-uptake, and the potential of this technique is being actively assessed in a number of industrial fields.

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