

Chemical Modification of Carbohydrates through Reaction with Organometallic Agents¹⁾

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Abstract

Intimate, homogeneous modification of two polyhydroxylic polysaccharides derived from both of cotton (1) and dextran (2) has been studied through reaction with a wide variety of organometallic reactants. Cotton (1), a water insoluble, cellulosic polysaccharide, was treated with a variety of organotin halides in the presence of bis(ethylenediamine)copper(II) hydroxide as both solvent and added base using an interfacial condensation system. Dextran (2), a water soluble polysaccharide, was modified through condensation with both organotin and organotitanium halides employing sodium hydroxide and/or triethylamine as the added base. Analysis of both condensation products indicated the presence of tin or titanium in the crosslinked lattice of the polysaccharide. The product is a combination of a number of modified structure units linked to each other or to unmodified saccharide units. In addition, sucrose (3), which is a naturally occurring disaccharide, was successfully polymerized through reaction with a number of organotin dihalides employing the aqueous interfacial condensation technique to form crosslinked networks.

Introduction

Currently, when the ready sources of feedstocks, such as mineral, coal and petroleum based products, are being consumed at a faster rate than they are being discovered, there exists a need for both conservation of our resources and the development of readily available, renewable natural products. Polysaccharides are

one such family of renewable natural resource available in the world.

Recently, we have synthesized a number of organometallic polymers through reaction with a wide variety of diols including ethylene glycol and hydroquinone.²⁻⁴⁾ Further polyvinyl alcohol was successfully modified through condensation with a wide variety of organometallic halides.^{5, 6)} An extension of this work is the chemical modification of natural products including polysaccharides through reaction of the reactive groups contained on these products.^{7, 8)}

Carbohydrates are the most abundant group of naturally occurring organic compounds, constituting three-fourths of the dry weight of the plant world. They are produced through natural photosynthesis by plants for their own nutritional and physiological needs, and represent a great storehouse of energy as food and fuel for man and animals. Polysaccharides are typically polymeric organic substances (molecular weight ca 25,000 to 15,000,000) composed of monosaccharide units. The chemical and physical modification of polysaccharides is one of man's oldest technologies typically focusing on cotton since 1850's. Most of these modifications are topochemical in nature, occurring through reactions involving cellulosic reactive groups, which are available in the amorphous regions and on the surfaces of crystalline areas.

Here we report more thorough, homogeneous modifications of a cellulosic material derived from cotton (1) and of dextran (2) using an interfacial condensation system,⁹⁾ in the belief that such modification will provide products having enhanced thermal, solvent and biological properties. Also the synthesis of cross-linked polymers is described derived from sucrose (3) and organotin dihalides.

Experimental

Reactions were conducted at about 25°C using a one pint Kinex emulsifying jar placed on a Waring Blendor (Model 1120) with no load stirring rate of 18,500 rpm. In a typical procedure, an aqueous solution (25 ml) of cotton (0.62 mmol) dissolved in bis(ethylenediamine)copper(II) hydroxide was added to rapidly stirred solution of the organotin halide in carbon tetrachloride (25 ml) for 30 seconds stirring time. Stirring was stopped and the reaction mixture filtered using a Buchner filter with suction. Repeated washings with a typical organic solvent as carbon tetrachloride and water assisted in the purification of the product. Solubility studies were carried out by placing about 20 mg of sample in three milliliters of liquid. Elemental analysis was effected for copper and tin utilizing a Varian

Techtron AA6 atomic absorption spectrophotometer. Copper content was found to be less than $10^{-2}\%$. Elemental analyses for titanium were conducted by heating known weight of samples until a white product, titanium dioxide, was formed. Infrared spectra were obtained using KBr pellets on Perkin-Elmer 457 and 1330 or Hitachi 260-10 infrared spectrophotometers and a Digilab FTS-20 C/D FT-IR. Mass spectral analysis was performed employing direct insertion probe in JEOL JMS-D300 or Kratos MS-50 mass spectrometers, operating in the electron impact ionization mode, 70 eV ionization voltage, 300 μ A ionization current, and 3 or 8 KV accelerating voltage. Biological analysis was conducted using *Aspergillus flavus*, *niger* and *fumigatus* as the test organisms. Spores of each organism were suspended in sterile water and inoculated (1000 cells) onto Sabouraud's dextrose agar plates. Solid, ground, and modified saccharides (0.1 g), added to paper discs were placed at separate locations onto the inoculated medium. Inhibition of growth about the added saccharide was an indication of the antifungal potential of the particular compound after incubation at room temperature for 24 hr.

Results and Discussion

1. Modification of Cotton

Cellulose is a naturally occurring polymeric carbohydrates making up about one-third of all vegetable matter. Cotton (1) is a relatively pure natural cellulose containing only about 3-15% noncellulosic materials. The modification of cotton has occurred for years being one of the earliest executed chemical processes in man's history.

Bis(ethylenediamine)copper(II) hydroxide solution was used to effect solution of cotton, which is a water insoluble polysaccharide. Organotin halides would be utilized for the first study, since they have successfully been condensed with a

Table 1. Result as a Functional of Tin Monomer

Organotin Halide	Amount Tin Reactant (m mole)	Yield (g)	Yield ^a (%)	Tin Found (%)	Tin ^a Calculated (%)	Sample Designation
(C ₃ H ₇) ₂ SnCl ₂	0.93	0.19	38	21	27	1
(C ₆ H ₅) ₃ SnCl	1.86	0.50	65	19	29	2
(C ₈ H ₁₇) ₂ SnCl ₂	0.93	0.31	40	18	29	3
(C ₈ H ₁₇) ₂ SnCl ₂	2.79	0.66	86	18	29	4
(C ₄ H ₉) ₂ SnCl ₂	4.65	0.58	103	37	40	5

^a Assuming complete inclusion.

wide variety of diols to form tin containing polyethers and with polyvinyl alcohol. Results are shown in Table 1.

Analysis of the infrared spectra of the products was consistent with the tin-modified product being formed through reaction with hydroxyl groups contained on the polysaccharide. For products from the dibutyltin dichloride bands characteristic of methylene deformation appeared at 1470 and 1150 cm^{-1} ; bands characteristic of methyl groups were present at 1420 and 1380 cm^{-1} . Formation of the ether linkage was indicated by the presence of bands about 660 to 690 cm^{-1} characteristic of the Sn-O asymmetric stretch from Sn-O-R and a doublet about 550 - 600 cm^{-1} attributed to the Sn-O-R symmetric stretch for tin ethers.¹⁰ Both bands were present in the modified cellulose. Mass spectral data were also consistent with the products containing moieties derived from cotton and organotin halides.

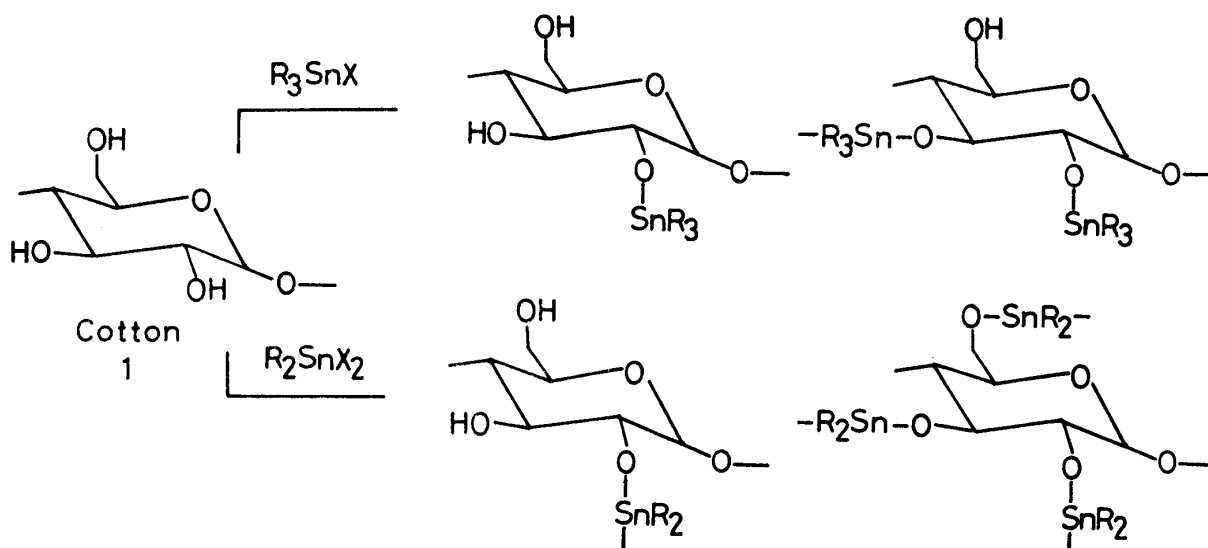


Fig. 1. Probable Structures of the Product Derived from Cotton.

The modified polysaccharides were insoluble in all attempted solvents including DMSO, HMPA, and DMF typical of crosslinked products. The products were hydro-

Table 2. Result of Biological Assays for Several Tin Modified Compound

Compound ^a	A. Flavus	Growth Inhibition		
		A. Niger	A. Fumigatus	
1	E	E	S +	
2	E	S +	S +	
3	S +	U	U	
4	U	U	U	
5	E	E	S +	
$(C_4H_9)_2SnCl_2$	E	E	E	

^a Designation from Table 1.

E=100%, S+=75%, S=50%, S-=25%, U=0%

phobic and resistant to hydrolysis giving them utility as insulation materials and rainware. They were solid, generally exhibiting flexibility, and had typically lower heats of combustion than unmodified cellulose. All but the products from dioctyltin dichloride showed good fungi inhibition rendering them suitable for use as topical bandages (Table 2). The fungi tested are typical and widespread and the results obtained are therefore indicative of applicability of such modified polysaccharides for retardation of bacteria related to rot and mildew.

2. Modification of Dextran

Dextran (**2**) was the second polysaccharide chosen for preliminary study, since it is water soluble, permitting the evaluation of aqueous reaction systems. An underlying assumption is that dextran is a representative polysaccharides source with results derived from studying its modification directly applicable to other appropriate polysaccharides.

(1). Reaction with Organotin Halides

Dextran modification with organotin halides was carried out employing both the aqueous and nonaqueous interfacial condensation techniques. Thus, dextran

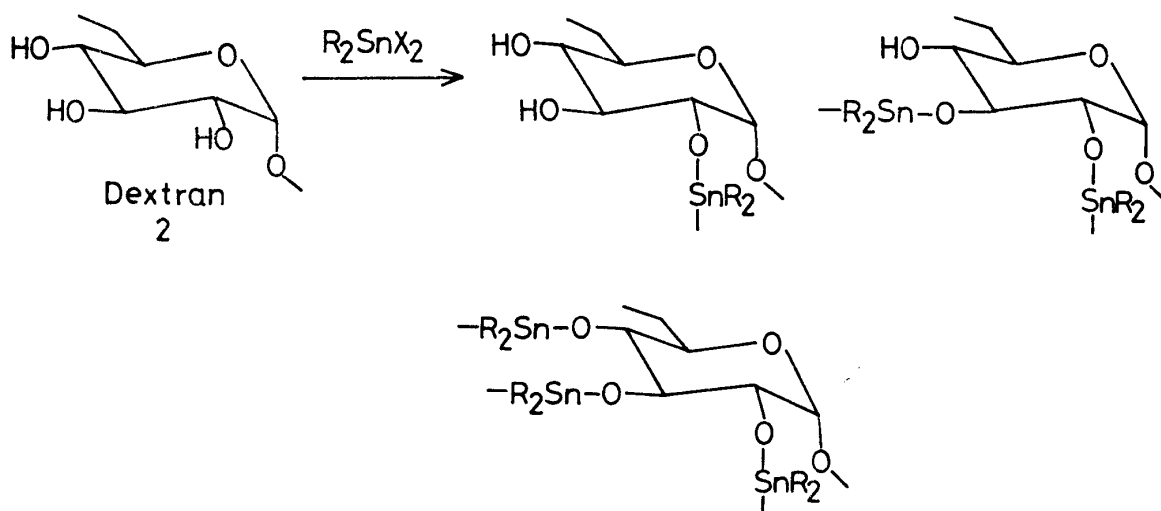


Fig. 2. Probable Structures of the Tin Containing Product Derived from Dextran.

and base (NaOH etc.) were dissolved in water and organotin halide was dissolved in carbon tetrachloride. The nonaqueous technique was conducted in an aqueous manner except that two immisible organic solvents were used. The solution condensation system was also carried out using a single organic solvent. In some cases salts were added to effect the solubility of dextean in the solvent. Modification was general for the classical aqueous interfacial (I) and bis(ethylenediamine)cop-

per(II) hydroxide interfacial (II) systems, less general for two nonclassical interfacial systems (III and IV) and largely unsuccessful for solution systems (V) (Table 3). The diversity of systems that lead to the modification of dextran should permit

Table 3. Summary of Systems Evaluated

System	Description	Evaluation
I. Aqueous Interfacial	Organic/H ₂ O	Good
II. Bis (ethylenediamine) Copper Interfacial	Organic/H ₂ O, BEDC	Good
III. Layered Liquid Organotin Interfacial	Liquid Tin/H ₂ O	Satisfactory
IV. Nonaqueous Interfacial	like Decane/DMSO	Satisfactory
V. Solution	like DMSO	Largely Unsatisfactory

the modification of polysaccharide derived from many other sources. The dextran modified with dimethyltin dichloride exhibited good against the two test species, *Pseudomonas aeruginosa* and *E. coli*. Further biological testing of the modified dextran is underway.

(2). *Reaction with Bis(cyclopentadienyl)titanium Dichloride*

Dextran (2) was further condensed with bis(cyclopentadienyl)titanium dichloride employing the aqueous interfacial system (Table 4).^{11, 12} Product analysis

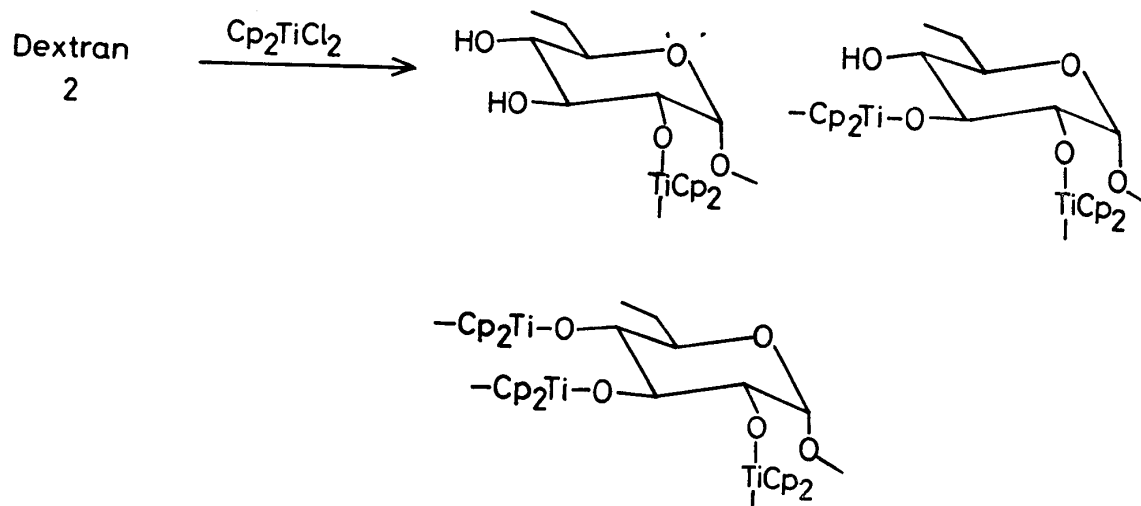


Fig. 3. Probable Structures of the Titanium Containing Product Derived from Dextran.

was made utilizing infrared spectroscopy, elemental analysis, solubility, and mass spectroscopy.

Analysis of the infrared spectra of the products was consistent with the dextran being modified by formation of Ti-O-R ether linkages through condensation at the

Table 4. Result as a Function of Molar Ratio of Reactants

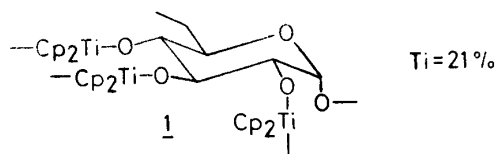
Cp ₂ TiCl ₂ (mmole)	Dextran (mmole)	Molar Ratio (Cp ₂ TiCl ₂ / Dextran)	Yield ^b (%)	Yield (g)	Ti (%)	Ti ^d (%)
0.5	3.0	0.17	24	0.03	8	7
1.0	3.0	0.33	56	0.14	9	9
2.0	3.0	0.67	67	0.33	16	12
3.0	3.0	1.0	46	0.34	29 ^c	21
4.0	3.0	1.3	1	0.01	19	18
6.0	3.0	2.0	0	0	—	—
3.0	0.5	6.0	65	0.24	23 ^c	21
3.0	1.0	3.0	40	0.30	25 ^c	15
3.0	4.0	0.75	46	0.34	19	17

^a Reaction conditions - Dextran and TEA (9.0 mmole) dissolved in 50 ml water added to stirred solutions of Cp₂TiCl₂ in 50 ml CHCl₃ with 30 secs stirring time at 25°C.

^b Based on structure **1** with OH end groups.

^c Incomplete oxidation to TiO₂.

^d By use of HClO₄.



hydroxyl sites. Bands characteristic of the Cp₂Ti moiety were present at 1405, 1030 and 855 cm⁻¹. Mass spectra showed fragmentation patterns characteristic of cyclopentadiene and dextran. The John Wiley reference spectrum of cyclopentadiene is compared in Table 5, in which the ion intensities have been adjusted so

Table 5. Ion Fragment Patterns of Cyclopentadiene

Cyclopentadiene Ion Fragment (m/z)	66	65	39	40	38	63	67	62	31	61
John Wiley ^{a, b}	100	47	32	27	8	8	7	6	5	5
Product ^a	100	52	73	22	13	8	8	6	3	3

^a Normalized to most abundant ion fragment.

^b "Atlas of Mass Spectral Data," ed. by E. Stenhagen, S. Abrahamsson, and F.W. McLafferty, John Wiley & Sons, Inc., New York, N.Y., 1969.

that m/z 66=100%. From the data it is possible that cyclopentadiene is being evolved. The products were insoluble in all solvents tested including acetone, chloroform, DMF, DMSO, and water consistent with the products being crosslinked.

3. Modification of Sucrose

Organotin dihalides have successfully been condensed, through the hydroxyl groups, with polyhydroxylic polysaccharides derived from cotton (**1**) and dextran (**2**). Here we report an extension of this work with synthesis of crosslinked networks derived from sucrose (**3**), a naturally occurring disaccharide, and organotin dihalides.

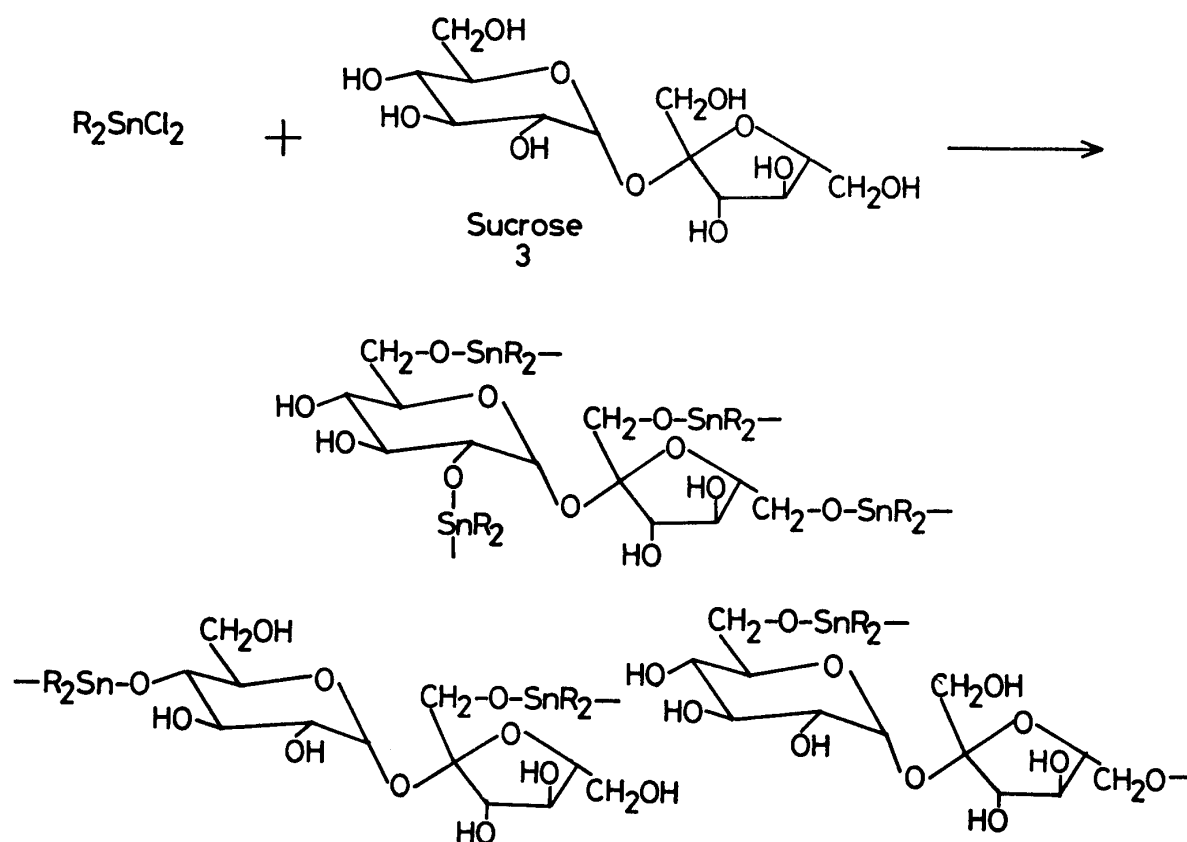


Fig. 4. Probable Structures of the Product Derived from Sucrose.

Reaction was carried out using the aqueous interfacial system. The condensation products between sucrose and organotin dihalides consisted of a crosslinked network containing organotin moieties chemically bound to sucrose in varying proportions. Analysis of the infrared and mass spectra was consistent with a product containing units with formation of the Sn-O-R ether linkage with hydroxyl groups contained on the sucrose. Crosslinking was indicated by the general insolubility of the products. The products swelled in HMPA and small amounts dissolved in HMPA after several days. The tin containing products all exhibited inhibition to at least some bacteria consistent with previous results.

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