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Syntheses of some sulfur- and phosphorus-containing carbohydrate polymer derivatives

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Tetraphosphorus decasulfide treatment of various carbohydrate polymers has been performed in the absence or presence of dimethyl formamide, affording materials with sulfur contents of about 2–22%, phosphorus contents of about 1–10%, and sulfur-to-phosphorus ratios of 0·2–5·6. These modifications are applied to cellulose, β-cyclodextrin and starch. The highest sulfur incorporations and S/P ratios are obtained when no solvent is employed. Conversely, maximum phosphorus incorporations and low S/P ratios are achieved when the reactions are conducted in dimethyl formamide. High sulfur contents appear to be correlated to derivatives with sulfide and thiophosphate substitutions, whereas high phosphorus contents are likely based on the predominance of phosphate residues.

In a more conventional approach, sodium pyrophosphate has been employed for the phosphorylation of xanthan, chitin and chitosan, resulting in phosphorus incorporation levels of 4–7%.

INTRODUCTION

The synthesis of anionic, heteroatom-containing carbohydrate polymers is of interest for a variety of reasons, including the preparation of anticoagulants, metal-chelating agents and fire-retardant materials. For these and other commercial uses, inexpensive methods are desirable to facilitate the incorporation of sulfur- and phosphorus-containing residues into polysaccharides. Highly effective metal chelating agents, as well as heparin-like materials have, for instance, been obtained by phosphorylation, sulfation or xanthation of glycans, such as cellulose (Langley *et al.*, 1980; Batura *et al.*, 1981), chitin and chitosan (Nishi *et al.*, 1987), and starch (Wing & Doane, 1976). One generally finds a relatively limited range of well-established methods for phosphorus and sulfur modifications. Thus, phosphorylations are most commonly effected by reagents, such as phosphorus oxyhalides, orthophosphoric acid and sodium tripolyphosphate (Sakaguchi *et al.*, 1981; Rutenberg & Solarek, 1984), and exceptionally by acyl phosphites or similar organic reagents (Inant'ev, 1968). The levels of phosphorus incorporation attainable by these methods are typically in the range of 1–6% (Inant'ev, 1968; Bauman, 1969; Clermont, 1971). The preparation of glycan sulfate esters or xanthates, relies on the use of sulfur trioxide-trimethylamine or chlorosulfonic acid (Wolfram & Shen Han, 1959; Whistler & Spencer, 1961; Schweiger, 1972) and, of course, on carbon disulfide, respectively.

A cursory review of recent literature reveals surprisingly that the inexpensive, industrial reagent tetraphosphorus decasulfide (Hoffman & Becke-Goehring, 1976) has not been widely used for the preparation of phosphorus or sulfur derivatives of carbohydrates or other alcohols (Sandler & Karo, 1983). The exiguous applications of this reagent include the synthesis of aromatic thiophosphonic acids (Tajber *et al.*, 1989), acetylene derivatives (Toda & Tokunaga, 1967), dithioesters (Davy & Metzner 1985), phosphorylated adamantane (Yurchenko *et al.*, 1989) and poly-β-pinene derivatives (Martinez & Retuert, 1982), the transformation of ketones into thiones (Scheeren *et al.*, 1973; Stahly, 1990), and the deoxygenation of aldosuloses (Köll *et al.*, 1976). More recent studies have demonstrated (Yalpani & Madgzinski, 1990) that modification of lignocellulosic and lignin-derived polymers with this reagent produces materials with sulfur and phosphorus contents of up to 17–19% and 5–9%, respectively. The

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sulfur-to-phosphorus ratios of the modified materials ranged from about 2:1 to 3:1 in the lignin-derived products to 4:1 in lignocellulosic substrates, indicating, together with other evidence, the predominant incorporation of thiophosphate residues. The modified products were found to be highly effective metal-chelating agents and potential flame-retardants.

Prompted by these observations, the application of this method to carbohydrate polymers was explored. The present article reports on a new method for the incorporation of phosphorus and sulfur residues by tetraphosphorus decasulfide treatment of carbohydrate polymers. Using this technique, the sulfur-to-phosphorus ratio of the modified polymers are found to be variable over a wide range by appropriate control of the reaction parameters. The phosphorylation of several glycans via more conventional pyrophosphate modifications has also been examined.

RESULTS

Two approaches were investigated for the preparation of sulfur- and phosphorus-modified polysaccharides. In the first method, the reactions were conducted at elevated temperatures in the absence of solvents. Thus, treatment of a mixture of solid cellulose powder and tetraphosphorus decasulfide at temperatures of about 110°C for a relatively brief (2-h) period yielded a product with a sulfur content of about 4% and a sulfur/phosphorus ratio of 5·6 (see Table 1). When the same modifications were conducted in the presence of an organic solvent, lower sulfur contents and substantially lower S/P ratios were obtained. For instance, a similar 2-h reaction was performed as above, by suspending cellulose in *N*,*N*-dimethyl formamide (DMF). This treatment afforded a modified product with a sulfur incorporation of about 1·8% and an S/P ratio of 0·2. A 4-h reaction in DMF suspension yielded a cellulose derivative with a somewhat higher sulfur content (2·9%) and an S/P ratio of 0·3. It is noteworthy that, while the maximum attained levels of sulfur incorporation for cellulose were not exceedingly high, the corresponding phosphorus incorporations ranged from about 1% (no solvent) to over 10% (in DMF). There appear to be no previous reports of such high P-contents in cellulose derivatives.

Similar observations were made for other carbohydrate polymers. For the case of starch, a 2-h tetraphosphorus decasulfide treatment in the absence of solvents afforded a derivative with a sulfur content of about 19% and an S/P ratio of 3·9, while 2- and 4-h reactions conducted in DMF yielded derivatives with S-contents of about 4% and 5%, and S/P ratios of 0·4 and 0·6, respectively. The corresponding phosphorus incorporations ranged from 4·8 to 10·6%, with the lowest P-contents being again achieved in the absence of solvents (see Table 1).

The condensation of β-cyclodextrin with tetraphosphorus decasulfide for 2 h yielded a modified derivative with an S-content of close to 22% and an S/P ratio of 4·3. Similar treatments were conducted in DMF solution for periods of either 30 min or 2 h, and afforded materials with sulfur incorporations of 6% and 3·7%, and S/P ratios of 0·6 and 0·4, respectively. As in the case of starch, the P-contents of the β-cyclodextrin derivatives ranged from about 5–10%, with the highest incorporations being attained when the reactions were performed in DMF (see Table 1).

One noteworthy feature of the P_4S_{10} reagent is the convenient removal of unreacted reagent from the modified products. In view of the hydrolytic lability of the reagent, either hot aqueous or aqueous alkaline workup conditions can be employed to avoid product contamination.

The modified carbohydrate polymers were generally amorphous materials that were characterized by IR spectroscopy. The IR spectra displayed weak P-S adsorptions at 640–660 cm^{-1}, P = S adsorptions at 740–770 cm^{-1}, C-S adsorptions at 840–870 cm^{-1}, strong

Table 1. Phosphorus- and sulfur-modified glycans

Glycan	Reaction conditions[a]		Percent[b]		S/P ratio
	Time (h)	Solvent	Sulfur	Phosphorus	
Cellulose	2	None	3·95	0·71	5·6
	2	DMF	1·79	10·27	0·2
	4	DMF	2·92	8·69	0·3
Starch	2	None	18·79	4·80	3·9
	2	DMF	4·05	10·61	0·4
	4	DMF	5·33	8·60	0·6
β-Cyclodextrin	2	None	21·81	5·03	4·3
	0·5	DMF	6·09	10·19	0·6
	2	DMF	3·69	10·31	0·4

[a] All reactions were conducted at 110°C.
[b] On a weight basis.

P-O-C adsorptions in the region 980–1100 cm^{-1} and weak P-S-H adsorptions at 2300–2350 cm^{-1}.

An alternative, more conventional phosphorylation method was also evaluated. Treatment of solid mixtures of xanthan, chitin or chitosan and sodium pyrophosphate at 60°C for 2 h afforded materials with phosphorus levels of 4–7%. This method constitutes, therefore, a viable extension to some of the more established procedures for the phosphorylation of carbohydrate polymers.

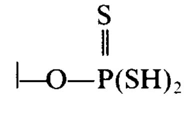
DISCUSSION

The above results demonstrate that tetraphosphorus decasulfide treatment of carbohydrate polymers in the absence of solvents affords materials with the highest sulfur incorporation levels. Thus, for cellulose, starch and β-cyclodextrin, sulfur contents of about 4%, 19% and 22% were respectively achieved with corresponding phosphorus contents of about 1%, 5% and 5%, respectively. Conversely, when the tetraphosphorus decasulfide modifications were performed in DMF for two hours, maximum phosphorus incorporations were observed. For cellulose, starch as well as β-cyclodextrin, phosphorus contents of about 10% were attained, while the sulfur contents declined substantially to about 2–4%. The levels of sulfur and phosphorus incorporation into glycans can hence be conveniently controlled by adjustment of the P_4S_{10} reaction conditions. These unique features are reminiscent of some previously observed solvent- and temperature-dependent product variations (Weintraub, 1973).

It is interesting to compare the above observations for the carbohydrate substrates to the previously mentioned results for lignocellulosic materials (Yalpani & Madgzinski, 1990). The S/P ratios of tetraphosphorus decasulfide-treated Kraft lignins and lignosulfonates were about 3:1 or lower, whereas P_4S_{10}-modified wood fibres had S/P ratios of about 4:1, the latter being similar to the values observed here for P_4S_{10}-modified cellulose. It appears, therefore, that the cellulosic components of the wood fibres displayed different reactivities towards P_4S_{10} than their polyphenolic counterpart.

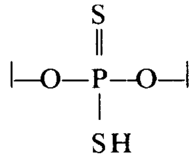
These observations raise the question about the nature of the incorporated functionalities under the different reaction conditions. The literature provides only limited information on P_4S_{10}-treated aliphatic alcohols for comparative purposes. Secondary dithiophosphates, $(RO)_2PSSH$, are the predominant products generally observed for low molecular weight alcohols and phenols, and products of the type $(RO)_2PSH$ and $(RO)_2PSSR$ have also been described (Weintraub, 1973). Yurchenko *et al.* (1989), for instance, obtained diademantyl-1-dithiophosphoric acid from P_4S_{10} modification of adamantanol in benzene. Methanol and ethanol have been shown to condense with P_4S_{10} to yield the corresponding *O*, *O*-dialkyl dithiophosphoric acids or dimeric species (Yousif *et al.*, 1984).

For the modified glycans described here, likely substituents can be anticipated to include thiophosphate residues of type 1 and cross-linked units of type 2, for which the S/P ratios should not exceed values of about three. However, when the tetraphosphorus decasulfide reactions were conducted in the absence of solvents, experimental S/P ratios of 3·9–5·6 were obtained for the resulting glycan derivatives. The higher than expected S/P ratios are therefore suggestive of the presence of additional thiol residues.



$$\overset{\displaystyle S}{\overset{\|}{|\!-\!O\!-\!P(SH)_2}}$$

1



$$|\!-\!O\!-\!\underset{\displaystyle SH}{\underset{|}{\overset{\displaystyle S}{\overset{\|}{P}}}}\!-\!O\!-\!|$$

2

When, on the other hand, the tetraphosphorus decasulfide modifications were performed in DMF, the S/P ratios of the resulting products were reduced by a factor of about 6–30 to values below unity (see Table 1), indicating the predominance of phosphate over thiophosphate residues. These observations are also corroborated by the IR spectra of the tetraphosphorus decasulfide-modified derivatives. For materials with high S/P ratios (>3·9, neat reactions), C-S adsorptions at 840–870 cm^{-1} were present, and the P-O-C adsorption bands at 1000 cm^{-1} were considerably less pronounced. This is presumably indicative of the incorporation of significant proportions of sulfide residues in addition to thiophosphate functions. In addition to solvent-dependent variations of S/P ratios, a time-dependency is also evidenced for the reactions conducted in DMF. For cellulose and starch, more prolonged condensations led to enhanced S/P ratios, while the opposite trend emerged for β-cyclodextrin. These observations indicate that the products formed during the initial stages of the modifications are sensitive to further alterations by P_4S_{10}.

A likely contribution to the high S/P ratios may arise from the generation of reactive S_2 and other sulfur products, which recent IR studies (Andrews *et al.*, 1990; Mielke *et al.*, 1991), conducted at albeit higher temperatures, have identified as thermal decomposition products of P_4S_{10}. These aspects of the P_4S_{10} method are currently subject to further examination.

In summary, it has been demonstrated here that tetraphosphorus decasulfide-based modifications offer a versatile and interesting alternative to some of the conventional techniques for the thiation and phosphorylation of carbohydrate polymers. The relatively high levels of phosphorus and sulfur incorporation attainable with this method will be of interest in applications, such as metal chelation, where the material performance is correlated to the degree of substitution. The functionalities of the modified materials described here are under separate investigation.

EXPERIMENTAL

Methods and materials

β-Cyclodextrin, starch and tetraphosphorus decasulfide were purchased from Aldrich Chemicals (Milwaukee, Wisconsin), cellulose powder was Whatman CF11, xanthan (Keltrol™) was from Kelco Co. (San Diego, California), sodium pyrophosphate 40 was from Monsanto Co. and chitin and chitosan powder were from Sigma Chemical Co. (St. Louis, Missouri). Elemental analyses were performed by Guelph Chemical Laboratories Ltd. (Guelph, Ontario).

General procedure for tetraphosphorus decasulfide modifications

Method A
Equal weight parts of tetraphosphorus decasulfide and the carbohydrate substrate were thoroughly mixed and then heated for two hours at 110°C. The solids were then dispersed or dissolved in hot water, dialyzed for several days and finally lyophilized.

Method B
The carbohydrate substrate was dispersed or dissolved in DMF and treated with equal parts of tetraphosphorus decasulfide for various periods (0·5–5 h). The resulting products were worked up as in Method A.

Preparation of modified cellulose derivatives

Elemental analysis for the product obtained by using method A, showed C 41·86%, H 5·52%, S 3·95% and P 0·71%.

IR (KBr): λ_{max} 3200–3600, 2930, 2350, 1680, 1630, 1440, 1380, 1345, 1325, 1295, 1240, 1210, 1170, 1120, 1000–1060, 900, 855 and 660 cm^{-1}.

Elemental analysis for the product obtained via method B (2-h reaction time), showed C 41·36%, H 3·88%, S 1·79% and P 10·27%.

IR (KBr): λ_{max} 3300–3500, 2930, 2330, 1670, 1620–1650, 1450, 1380, 1310, 1160, 1000–1200, 880, 780 and 640 cm^{-1}.

Elemental analysis for the product obtained after a 4-h reaction in DMF gave C 37·28%, H 4·94%, S 2·92% and P 8·69%.

IR (KBr): λ_{max} 3300–3500, 2925, 2330, 1670, 1620–1650, 1450, 1380, 1310, 1160, 1000–1200, 880, 770, 720 and 640 cm^{-1}.

Preparation of modified starch derivatives

Elemental analysis for the product obtained by using method A, showed C 40·55%, H 3·89%, S 18·79%, and P 4·80%.

IR (KBr): λ_{max} 3300–3600, 2940, 2650, 2330, 1670, 1640, 1395, 1130–1170, 980–1020, 850 and 650 cm^{-1}.

Elemental analysis for the product obtained by using method B (2-h reaction time) showed C 31·95%, H 4·90%, S 4·05% and P 10·61%.

IR (KBr): λ_{max} 3300–3600, 2930, 2650, 2300, 1660, 1630, 1470, 1410, 1200, 1140, 1000–1040, 840 and 640 cm^{-1}.

Elemental analysis of the product obtained after a 4-h reaction in DMF gave C 37·47%, H 4·81%, S 5·33% and P 8·60%.

IR (KBr): λ_{max} 3300–3600, 2940, 2650, 2300, 1660, 1630, 1470, 1410, 1200, 1140, 1000–1040, 860 and 830 cm^{-1}.

Preparation of modified β-cyclodextrin derivatives

Elemental analysis for the product obtained by using method A showed C 42·77%, H 3·06%, S 21·81% and P 5·03%.

Elemental analysis for the product obtained by using method B (0·5-h reaction time) showed C 27·51%, H 4·61%, S 6·09% and P 10·19%.

IR (KBr): λ_{max} 2940, 2630, 2300, 1670, 1640, 1470, 1400, 1205, 1150, 1000–1040, 860 and 620 cm^{-1}.

Elemental analysis of the product obtained after a 2-h reaction in DMF gave C 29·12%, H 4·18%, S 3·69% and P 10·31%.

IR (KBr): λ_{max} 2940, 2650, 2300, 1670, 1640, 1470, 1205, 1150, 1000–1040, 840, 740 and 645 cm^{-1}.

Preparation of xanthan phosphate

A sample of xanthan powder (5·0 g) was thoroughly mixed with sodium pyrophosphate (6·2 g) and then mildly heated at 60°C under moderate vacuum for two hours. The resulting mixture was suspended in aqueous methanol (3:1, 150 ml) for two hours, then dialyzed (2 days) and precipitated with methanol. The resulting material had a P-content of 4·01%.

Preparation of chitin and chitosan phosphates

Chitin and chitosan powder (5·0 g) were each thoroughly mixed with sodium pyrophosphate (6·1 g) and the mixtures were heated at 60°C under moderate vacuum for three hours. The resulting materials were suspended in aqueous methanol (3:1, 150 ml) for two hours, and then dialyzed (1 day), filtered, washed and dried. Elemental analysis of the modified materials gave phosphorus incorporations of 6–7%.

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