Applied Organometallic Chemistry (1987) 1 245–249
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0268–2605/87/01305245/$03.50

Synthesis of metal-containing carbohydrate polymers employing crown ether phase transfer catalyzed interfacial condensation

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Received 3 October 1986 Accepted 27 February 1987

Phase transfer catalyzed interfacial reaction of the polysaccharide dextran ($(C_6H_{10}O_5)_n$) with organotitanium and organotin dichlorides to form metal-containing carbohydrate polymers has been carried out in the presence of two bases, sodium hydroxide and triethylamine. Interfacial systems employing sodium hydroxide with a crown ether phase transfer catalyst (PTC) gave generally greater yields compared with the analogous systems without a PTC. The trend of maximum yield for triethylamine systems with organotin dichloride not containing a PTC was different from that observed for the sodium hydroxide systems without a PTC, probably because of the ability of triethylamine to act as a PTC.

Keywords: Polysaccharide, dextran, organotitanium, organotin, metal-containing carbohydrate polymers, phase transfer catalysis

INTRODUCTION

Carbohydrates are one of the most abundant renewable resources available in the world and are produced through natural photosynthesis by plants. As a group, carbohydrates represent a large source of under-used feedstock that should be investigated as an alternative feedstock to largely nonrenewable sources such as petroleum, natural gas or coal. Carbohydrates, beyond their renewable nature and abundance, may provide a valuable property such as three dimensional networks which are biodegradable. On the other hand, the metals may contribute a wide variety of chemical-, biological-, mechanical-, and electrical properties. Thus, the combination of carbohydrates and metals may yield products possessing thermal-, solvent-, electrical-, or biological characteristics not common to any other commercially available class of polymers. One objective is the synthesis of metal-containing polymers which show select biological activities for use in biomedical applications. Tin-containing polymers have been found to be active against a wide range of mildew and rot-causing organisms as well as a variety of cancer cell lines.[1–3] Potential applications include their use as additives to or components in bandages and topical creams. Titanium-containing polymers have shown good inhibition to a wide variety of cancer cell lines and may be of use as controlled release agents in the treatment of specific cancers.[2,3]

Recently Carraher, Naoshima and coworkers have synthesized metal-containing carbohydrate polymers through the reaction of cellulose and dextran with various organometallic halides under interfacial conditions.[4–8] In this investigation, the crown ether phase-transfer catalyzed interfacial reaction[9,10] of dextran ($(C_6H_{10}O_5)_n$) with both bis(cyclopentadienyl)titanium dichloride (BCTD, Cp_2TiCl_2) and dibutyltin dichloride (DBTD, Bu_2SnCl_2) was carried out, and the trend of the yield was compared with that obtained for the analogous interfacial reaction without a phase transfer catalyst (PTC).

MATERIALS AND METHODS

Reactions were carried out employing a one quart Kimex emulsifying jar placed on a Waring

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Blendor (Model 7011G) with a no-load stirring rate of about 20 000 rpm. The following organic chemicals were used as received (from Aldrich unless otherwise noted): bis(cyclopentadienyl) titanium dichloride, dibutyltin dichloride, 18-crown-6, dibenzo-18-crown-6, triethylamine (Wako Pure Chemical Industries), and dextran (Wako Pure Chemical Industries; molecular weight = 2 to 3×10^5). In a typical procedure, an aqueous solution of dextran containing a base and the crown ether PTC was added to rapidly stirred solutions of the organometallic dichloride in chloroform. The product was obtained as a precipitate employing suction filtration. Repeated washings with organic solvent and water assisted in the product purification. Molar ratios and other conditions are given in Tables 1–4. Elemental analyses for titanium and tin were con-

Table 1 Results as a function of base and amount of BCTD for the phase transfer catalyst 18-crown-6

Cp_2TiCl_2 (mmol)	Yield[a] (%)		Yield (g)		Ti (%)	
	PTC	None	PTC	None	PTC	None
A. Triethylamine						
0.5	0	24	0	0.03	—	7
1.0	4	56	0.01	0.14	12	9
2.0	16	67	0.08	0.33	15	12
3.0	25	46	0.18	0.34	17	21
4.0	39	1	0.38	0.01	21	18

(Dextran (3.0 mmol), TEA (9.0 mmol) and 18-crown-6 (0.9 mmol) in 50 cm^3 H_2O; Cp_2TiCl_2 in 50 cm^3 $CHCl_3$; 30 s stirring time.)

B. NaOH						
0.5	0	0	0	0	—	—
1.0	0	0	0	0	—	—
2.0	0	0	0	0	—	—
3.0	80	58	0.59	0.43	9	14
4.0	59	60	0.59	0.60	15	13

(Ibid above except employing NaOH (6.0 mmol) in place of TEA.)

C. NaOH						
0.5	0	0	0	0	—	—
1.0	0	0	0	0	—	—
2.0	21	0	0.11	0	17	—
3.0	86	48	0.64	0.36	17	17
4.0	86	53	0.86	0.53	21	21

(Ibid above except employing NaOH (9.0 mmol) in place of TEA.)

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[a] Yields based on the presence of three Cp_2Ti units per sugar unit for Tables 1 and 2

Table 2 Results as a function of base and amount of BCTD for the phase transfer catalyst dibenzo-18-crown-6

Cp_2TiCl_2 (mmol)	Yield (%)		Yield (g)		Ti (%)	
	PTC	None	PTC	None	PTC	None
A. Triethylamine						
0.5	0	24	0	0.03	—	7
1.0	15	56	0.04	0.14	14	9
2.0	40	67	0.20	0.33	14	12
3.0	37	46	0.27	0.34	20	21
4.0	46	1	0.46	0.01	20	18

(Dextran (3.0 mmol), triethylamine (9.0 mmol) in 50 cm^3 H_2O; Cp_2TiCl_2 and dibenzo-18-crown-6 (0.9 mmol) in 50 cm^3 $CHCl_3$; 30 sec stirring time.)

B. NaOH						
0.5	0	0	0	0	—	—
1.0	0	0	0	0	—	—
2.0	0	0	0	0	—	—
3.0	86	58	0.64	0.43	15	14
4.0	83	60	0.83	0.60	15	13

(Ibid above except employing NaOH (6.0 mmol) in place of TEA.)

Table 3 Results as a function of base and amount of DBTD for the phase transfer catalyst 18-crown-6

Bu_2SnCl_2 (mmol)	Yield[a] (%)		Yield (g)		Sn (%)	
	PTC	None	PTC	None	PTC	None
A. Triethylamine						
0.5	16	7	0.02	0.008	37	29
1.0	37	19	0.09	0.05	29	29
2.0	61	22	0.30	0.11	28	37
3.0	24	38	0.17	0.28	29	37
4.0	15	4	0.15	0.03	28	37

(Dextran (3.0 mmol), TEA (9.0 mmol) and 18-crown-6 (0.9 mmol) in 50 cm^3 H_2O; Bu_2SnCl_2 in 50 cm^3 $CHCl_3$; 30 sec stirring time.)

B. NaOH						
0.5	25	8	0.03	0.01	23	30
1.0	82	21	0.20	0.05	29	28
2.0	97	90	0.48	0.44	29	37
3.0	98	94	0.73	0.70	27	25
4.0	0	0	0	0	—	—

(Ibid above except employing NaOH (6.0 mmol) in place of TEA.)

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[a] Yields based on the presence of three Bu_2Sn units per sugar unit for Tables 3 and 4.

Table 4 Results as a function of base and amount of DBTD for the phase transfer catalyst dibenzo-18-crown-6

Bu_2SnCl_2 (mmol)	Yield (%)		Yield (g)		Sn (%)	
	PTC	None	PTC	None	PTC	None
A. Triethylamine						
0.5	30	7	0.04	0.008	26	29
1.0	67	19	0.17	0.05	29	29
2.0	88	22	0.44	0.11	36	37
3.0	24	38	0.18	0.28	22	37
4.0	17	4	0.17	0.03	31	37

(Dextran (3.0 mmol), TEA (9.0 mmol) in 50 cm^3 H_2O; Bu_2SnCl_2 and dibenzo-18-crown-6 (0.9 mmol) in 50 cm^3 $CHCl_3$; 30 sec stirring time.)

Bu_2SnCl_2 (mmol)	Yield (%) PTC	Yield (%) None	Yield (g) PTC	Yield (g) None	Sn (%) PTC	Sn (%) None
B. NaOH						
0.5	19	8	0.02	0.01	34	30
1.0	70	21	0.17	0.05	32	28
2.0	96	90	0.48	0.44	33	37
3.0	100	94	0.75	0.70	31	25
4.0	0	0	0	0	—	–

(Ibid above except employing NaOH (6.0 mmol) in place of TEA.)

ducted employing the usual wet analysis procedure with $HClO_4$. Infrared spectra were obtained using Hitachi 260-10 and 270-30 spectrometers and a Digilab FTS-IMX FT-IR. EI mass spectral analysis was carried out employing a JEOL JMS-D300 GC mass spectrometer connected with a JAI JHP-2 Curie Point Pyrolyzer. DT and TG analyses were performed employing a SINKU-RIKO ULVAC TGD-500M or a DuPoint 990 TGA and 900 DSC.

RESULTS AND DISCUSSION

Structural characterization was based on solubility, thermal and elemental analyses, and infrared and mass spectroscopic techniques. Characterization was in agreement with the product being a mixture composed of units including partially reacted units as depicted in Fig. 1.[6,8] For instance the products derived from BCTD had infrared bands characteristic of the dextran portions at 1650, 1480, 1440, 1360, 1275, 1240, 1160, 1100, 810 and 760 (all bands are given in units of cm^{-1}) and bands characteristic of the Cp_2Ti unit present at 1405, 1030 and 855. Mass spectral ion fragmentation patterns for the presence of the dextran and cyclopentadiene were in agreement with the literature values. The Ti-O-C ether associated band was found in the region of 1130. For the products derived from DBTD, infrared bands were present in the region 660–690 characteristic of the Sn-O-R asymmetric stretch and two bands between 555 and 598 characteristic of the Sn-O-R symmetric stretch. Bands characteristic of the presence of the dibutyltin moiety were present. For instance, bands characteristic of methylene deformation were present at 1470 and 1150 and bands characteristic of the methyl group were present at 1420 (asymmetric stretch) and 1380 (symmetric stretch). A quartet of bands characteristic of the C-H stretch in *n*-butyl groups was present at 2955, 2910, 2870, and 2855. Bands characteristic of the dextran moiety were also present. Mass spectral ion fragments characteristic of the presence of both the dextran and the Sn-O-R moieties were also found.

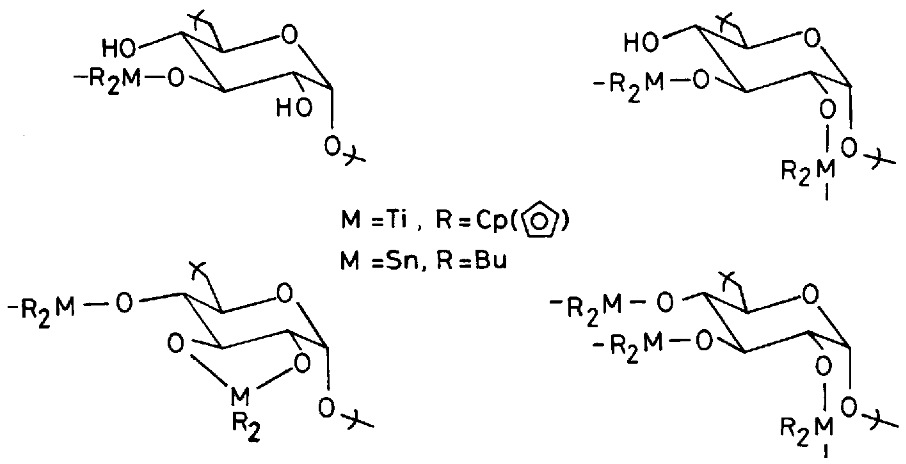

Figure 1 Probable structure units of metal-containing carbohydrate polymers.

Reactions of dextran with BCTD

Tables 1 and 2 show results as a function of the added base (sodium hydroxide or triethylamine) and of the amount of BCTD and PTC. Generally, interfacial reaction systems employing sodium hydroxide with a PTC gave greater yields than those obtained for the analogous systems without a PTC. The maximum yield for sodium hydroxide systems without a PTC was obtained at a BCTD to dextran ratio greater than about 4/3, while the sodium hydroxide systems employing a PTC provided the maximum yield around a ratio of 1 to 1, indicating that the added PTC did in fact function as a PTC. On the other hand, the maximum yield for triethylamine systems without a PTC was obtained at a ratio about 2/3, different from that observed for sodium hydroxide systems, and consistent with triethylamine itself acting as a PTC.[11] For triethylamine systems containing a PTC, the maximum was obtained at a ratio greater than 4 to 3 and differed significantly from the analogous systems without a PTC. The markedly different maximum resulting from addition of small amounts of the traditional PTC to the triethylamine systems seemed to attest to PTCs' greater efficiency compared with triethylamine for these systems.

While the term interfacial condensation systems is derived from the concept that reaction occurs at the interface of the two immiscible phases, reactions typically occur within either one or the other phase. For noncharged Lewis bases, such as amines, reaction occurs within the organic phase, while for charged species, such as salts of dicarboxylic acids, reaction occurs within the aqueous layer.[10] Carraher and coworkers have found that reactions involving organotin and organotitanium diclorides with alcohol-containing reactants, such as ethylene glycol and 1,6-hexanediol, occur within the organic phase.[12–16] The general activity of PTCs is to complex with one of the reactants, typically the water-soluble reactant, giving a complex that has a greater solubility in the organic phase. This is outlined in Fig. 2 for the present system.

Reactions of dextran with DBTD

Phase transfer catalyzed systems employing DBTD in the presence of both sodium hydroxide and triethylamine, as shown in Tables 3 and 4, gave generally increased yields compared with the analogous systems not containing a PTC. These results were consistent with the added PTC functioning as a PTC for the DBTD systems employing both sodium hydroxide and triethylamine. The maximum for triethylamine systems, whether or not a PTC was present, occurred at a DBTD to dextran ratio about 1/1, almost the same as that observed for the analogous sodium hydroxide systems. Further, triethylamine systems without a PTC gave lower yields than that obtained for the corresponding sodium hydroxide systems without a PTC, thus indicating that triethylamine itself apparently does not act as a PTC.

Analogous work with other types of metal species, experiments with other organic solvents and the investigations of the nature of nonprecipitated material have been carried out and this work was reported elsewhere.[17] In summary, reactions occurred within the organic phase giving almost only highly substituted products with the nonprecipitated reactants being largely the unreacted starting materials. It appeared that once reaction began on a dextran chain, the surrounding environment was polarized sufficiently to encourage further reaction. For the systems with BCTD other solvents were attempted, namely benzene, toluene, xylene, hexane, carbontetrachloride, and tetrachloroethylene but were unsatisfactory due to the poor solubility of BCTD. Thus typically greater yields were found in chloroform (BCTD solubility in $50\,\mathrm{cm}^3$ is 3.5–4.0 mmole at 25°C).

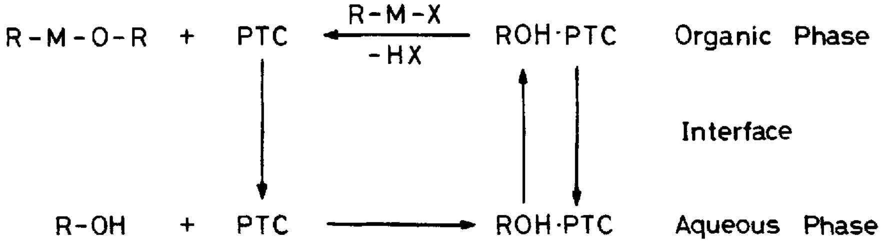

Figure 2 Reaction scheme involving PTC, alcohol-containing reactants and metal-containing reactants.

In conclusion, the trend of yields for the phase transfer catalyzed interfacial systems with BCTD was comparable with that observed for the corresponding interfacial systems employing DBTD, with the exception that for the DBTD systems, triethylamine itself did not function as a PTC. The use of classical PTCs typically allowed the synthesis of metal-containing carbohydrate polymers with generally greater yields.

These products are expected to inhibit a number of mildew and rot causing organisms.[1-3,18] Preliminary biological assays for the present metal-containing products are under way at the present time.

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