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Rapid N-phthaloylation of chitosan by microwave irradiation

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Abstract

Phthaloylation of chitosan with phthalic anhydride was achieved by microwave irradiation. The effects of reaction time and microwave outputs on the degree of substitution (DS) were studied and DS reached high only by a few minutes. Microwave irradiation brought more decrease in molecule weight than conventional heating technique.

Keywords: Microwave; Chitosan; Phthaloylation

1. Introduction

Chitosan [(1, 4)-2-amino-2-deoxy-D-glucan] is a linear polyaminosaccharide obtained by N-deacetylation of chitin, an abundant natural polymer. Recently much attention has been paid to chitosan for their advantageous properties such as biocompatibility, biodegradability, and antibacterial activity. However, the utilizations of chitosan have been delayed because chitosan is difficult to dissolve in general organic solvents except for some acids, owing to their rigid crystalline structures caused by the formation of intra- and/or inter hydrogen bonding between amino and hydroxyl groups.

N-phthaloylation of chitosan with phthalic anhydride is an efficient way to improve its organic solubility (Kurita, Ichikawa, Ishizeki, Fujisaki, & Iwakura, 1982; Nishimura, Kohgo, & Kurita, 1991). And *N*-phthaloylchitosan is a key precursor to prepare derivatives by regioselective and quantitative chemical modification, since the phthaloyl group could be deprotected easily to regenerate free amino group (Kurita, Akao, Kobayashi, Mori, & Nishiyama, 1997; Kurita, Kojima, Nishiyama, & Shimojoh, 2000; Kurita, Shimade, Nishiyama, Shimojoh, & Nishimura, 1998). What's more, *N*-phthaloylchitosan has been observed of lyotropic liquid crystalline characteristics (Rout, Pulapura, & Gross, 1993). The reaction of phthaloylation of chitosan was a heterogeneous reaction due to the solid-state morphology of the chitosan starting material, so it was difficult for the reactive amino functionalities to access the reagents. Though Rout et al. (1993) amend the synthesis course to enhance the reaction activity by the preparation of swollen chitosan, which followed a fussy solvent replacement, it commonly took over 5–7 or more hours above 100 °C to get *N*-phthaloylchitosan completed by conventional heating in the previously mentioned cases.

Microwave heating, as an alternative to conventional heating technique, has been proved to be more rapid and efficient. Considerable efforts have been devoted to investigate the microwave-assisted reaction in the synthesis and modification of polymer materials. Especially in the modification of nature polymers, a number of different polysaccharide derivatives, such as ester-cellulose (Satgé et al., 2002), starch acetates (Koroskynyi & McCarthy, 2002) and O-alkyl-chitosan, have been synthesized by the aid of microwave. In the present work, N-phthaloylation of chitosan was achieved successfully by microwave irradiation.

2. Experimental

2.1. Materials

Chitosan (degree of deacetylation = 85%) was purchased from Oceanary Biology Company of Zhejiang, China. Phthalic anhydride and hydrazine monohydrate were

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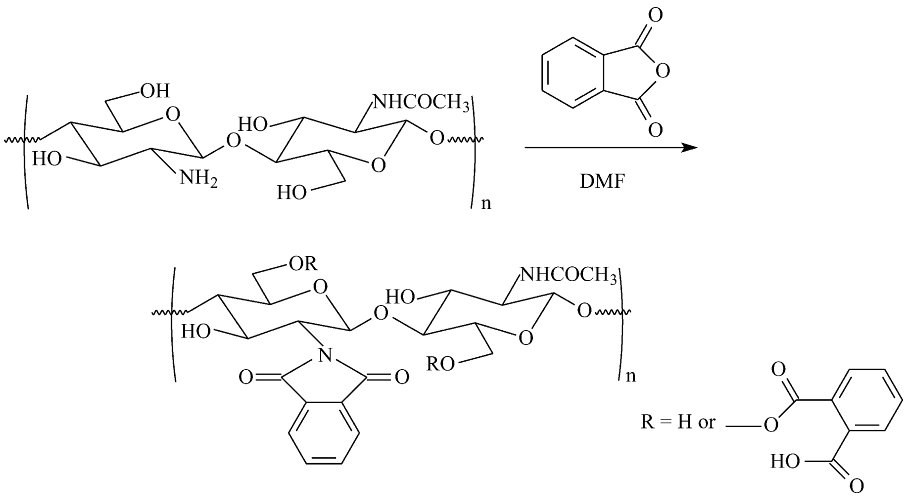

Scheme 1.

supplied by the First Reagent Factory of Shanghai, China. Dimethylformamide (DMF) was distilled under reduced pressure from calcium hydride and stored over molecular sieves (4A).

2.2. Phthaloylation of chitosan

Chitosan (1 g) and phthalic anhydride (2.7 g) were added in 10 ml DMF, and after phthalic anhydride was dissolved in DMF, the mixture was irradiated in microwave oven (Whirlpool, VIP 200) at pointed power for predetermined time under a nitrogen atmosphere (Scheme 1). The reaction product was precipitate in ice-water, washed completely with ethanol, and dried under vacuum at 40 °C.

2.3. Measurement

IR spectra were recorded on a fournier-transform infrared spectroscopy (Bruker, VECTOR-22). ^1H NMR spectra were recorded at 300.13 MHz, with a Bruker AV 300 spectrometer, using tetramethylsilane as an internal standard and DMSO-d_6 as the solvent. Elemental analyses were performed with an Elementar Vario EL-III elemental analyzer.

2.4. Deprotected reaction of phthaloylchitosan and determination of molecule weight

Phthaloylchitosan (0.5 g) was stirred with hydrazine monohydrate in water (5 ml) and heated to 100 °C under nitrogen for 12 h. The turbid solution was cooled to room temperature with another 5 ml water added, resulting in precipitation. The precipitate was collected and washed thoroughly with ethanol and dried in vacuum to yield chitosan. Then the intrinsic viscosity of chitosan was measured in 0.1 M acetate acid/0.2 M NaCl aqueous

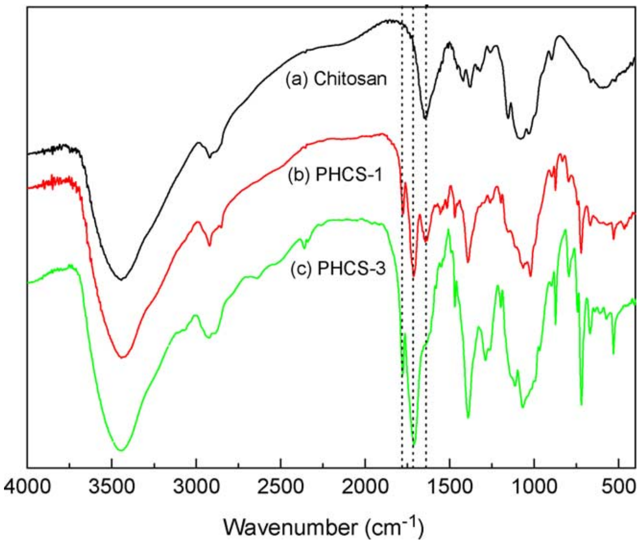

Fig. 1. IR spectra of chitosan (a) and Phthaloylchitosan (b,c).

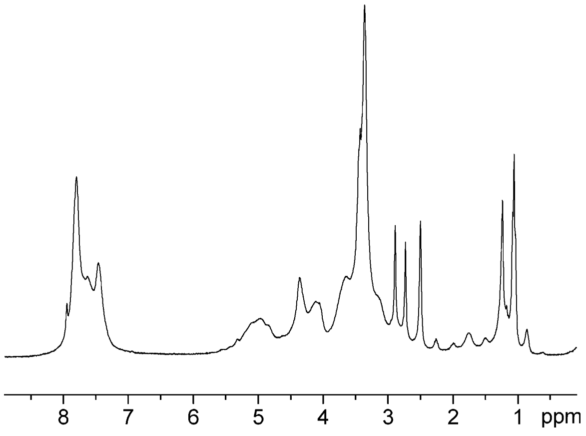

Fig. 2. ^1H NMR spectrum of Phthaloylchitosan (PHCS-3).

Table 1
Effect of microwave energy on DS values for phthaloylation of chitosan

Sample	Power (W)	Time (min)	DS	Elemental analysis, found (calc.) %		
				N	C	H
PHCS-1[a]	160	3	0.87	4.392 (4.08)	49.79 (58.16)	5.431 (4.30)
PHCS-2	160	6	1.41	3.633 (3.72)	54.82 (56.11)	4.994 (4.51)
PHCS-3	160	9	1.38	3.741 (3.77)	55.62 (56.01)	4.734 (4.53)
PHCS-4	160	12	1.34	3.747 (3.83)	54.60 (55.86)	4.714 (4.56)
PHCS-6	350	3	1.21	3.972 (4.04)	54.40 (55.36)	5.096 (4.66)
PHCS-7	350	6	1.19	4.113 (4.08)	55.73 (55.28)	4.741 (4.68)
PHCS-8	500	2	1.24	3.896 (3.99)	54.26 (55.48)	4.950 (4.64)
PHCS-9	500	3	1.39	3.681 (3.75)	54.98 (56.04)	4.831 (4. 52)
PHCS-10	500	4	1.46	3.569 (3.65)	55.11 (56.28)	4.584 (4.47)

[a] Partly dissolved in DMF.

solution at 25 ± 0.5 °C and the viscosity average molecule weight was calculated using the Mark-Houwink equation with $K = 1.81 \times 10^{-3}$ cm^3 g^{-1} and $\alpha = 0.93$ (Maghami & Roberts, 1988).

3. Results and discussion

3.1. Structural analysis of chitosan derivatives

The IR and ^{1}H NMR spectra of phthaloylchitosan were shown in Figs. 1 and 2, respectively. The characteristic absorptions at 1712 and 1777 cm^{-1} due to phthalimido groups and 721 cm^{-1} due to aromatic ring were observed in the IR spectrum of phthaloylchitosan compared with that of original chitosan. It was also observed that the peak of amide I at 1640 cm^{-1} decreased sharply with the increase of degree of substitution (DS) of phthaloylchitosan. The ^{1}H NMR of phthaloylchitosan showed mainly two sets of broad peaks: one set consisting of four peaks centering at 7.5, 7.6, 7.8 and 7.9 ppm assigned to the phthaloyl group and the other between 1.1 and 5.0 ppm belong to the chitosan backbone hydrogen (associated with DMSO-d$_6$ at 2.5 ppm, unremoved DMF at 2.7 and 2.9 ppm and impurity H_2O at about 3.4 ppm). The IR and NMR spectra of phthaloylchitosan prepared herein were in agreement with that of authoritative sample by the conventional heating method (Kurita et al., 1991; Rout et al., 1993).

Table 2
Comparison of microwave irradiation and heating method

Sample	Reaction condition	DS	MW
Chitosan	\	\	7.57×10^5
PHCS-h	120 °C, 5 h	1.40	2.02×10^5
PHCS-2	160 W, 6 min	1.41	6.31×10^4
PHCS-9	500 W, 3 min	1.39	7.13×10^4

3.2. Optimization of microwave irradiation

To investigate the effect of microwave energy on the DS of phthaloylchitosan, different reaction time and power outputs were examined. The results were displayed in Table 1. When microwave energy was beyond 160 W 6 min, samples have a much improved solubility in organic solvents, such as DMF, dimethyl sulfoxide (DMSO) and pydine. Moreover, the satisfactory high DS of phthaloylchitosan was obtained using rather short time by microwave irradiation, compared with the sample by conventional heating at 120 °C for 5 h ($DS = 1.40$). At the same level of microwave power, DS first increased quickly and then fell slowly with longer reaction time. The reason was that phthaloylation took place at the hydroxy groups to some extent in addition to the amino groups, as pointed out by Rout et al. (1993), and O-phthaloyl groups were less stable than ring phthalimido groups and would be eliminated with the reaction process. In the other hand, it was obvious that phthaloylation of chitosan went along more easily with the increasing microwave power out. But too higher power was unfavorable. It resulted charing of chitosan and evaporation of solvent so that the products grew deep color.

3.3. Comparison of microwave irradiation and conventional heating method

A number of phthaloylchitosan samples with almost the same DS were selected to give deprotected products—chitosan, and molecule weight of the resulted chitosan was measured. The results were listed in Table 2. It was observed that molecule weight of chitosan from samples by microwave irradiation showed a more decrease than that by conventional heating technique. This means that microwave accelerated splits of chitosan chains at the same time of the activation of phthaloylation reaction.

4. Conclusion

Microwave irradiation was a high efficient way for phthaloylation of chitosan. It improved speed of this heterogenous reaction remarkably and made reaction processing more smoothly. Moreover, microwave brought evident degradation of polysaccharide in the phthaloylation reaction of chitosan than the conventional heating technique.

Acknowledgements

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