

SYNTHESIS AND THERMAL PROPERTIES OF A NEW CHOLIC ACID-CONTAINING COPOLYMER*

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Abstract A new copolymer was synthesized by free radical polymerization in solution from methyl 3 α -methylacryloyl-7 α ,12 α -dihydroxy-5 β -cholan-24-oate (MACAME) and maleic anhydride (MAN). The copolymer was characterized by FT-IR and functional group analysis. The reactivity ratios of the two monomers were estimated [$r_1 = 11.6$ (MACAME), $r_2 = 0.01$ (MAN)] by conducting a series of copolymerizations with a variety of monomer feed compositions and analyzing the copolymer composition. Thermogravimetric and differential scanning calorimetric analyses of the samples indicate that the copolymer possesses good thermal stability. The temperature at which the copolymer samples experienced a 10% weight loss (T_{wt}) is over 287°C, and the T_g ranged from 174 to 185°C for the copolymers.

Keywords Cholic acid, Maleic anhydride, Copolymer, Photoresist, Polymer characterization

INTRODUCTION

Bile acids and their derivatives have been used in the development of new materials with applications as drug delivery systems^[1–3], artificial receptors^[4], molecular recognition^[5], asymmetric synthesis^[6], photogenerators^[7], etc. Various bile acid-containing polymers have been prepared in our laboratory in recent years^[8–15]. Bile acid-containing polymers have also been considered to be ideal candidates for the development of new deep UV-resist materials for memory storage and laser lithography devices^[16]. Cholic acid (CA) is the most common primary bile acid. CA-containing polymers can provide an alicyclic moiety for imparting photoresists high transparency, drying etching resistance, good adhesion properties to the substrates, specific groups which can switch the solubility of polymer resists by catalytically converting the photo-generated acid from a hydrophobic material into a hydrophilic one. Maleic anhydride (MAN) has been used in the synthesis of 193 nm photoresists^[17, 18]. The presence of MAN units in the molecular structure of polymeric resists may improve the thermal stability of the resist materials^[19], provide an easy way for the chemical modification of the resists and increase further the adhesion of the resists to the substrates. Based on the above considerations, we have studied the copolymerization of a CA-containing methacrylic monomer and MAN initiated by a free radical reaction in solution. This paper reports our preliminary work on the synthesis and thermal properties of the new copolymers.

EXPERIMENTAL

Materials

All the chemicals used in the synthesis were purchased from Aldrich. CA (3 α ,7 α ,12 α -trihydroxy-5 β -cholan-24-

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oic acid, 98% in purity) was used without further purification. Methacryloyl chloride was purified by vacuum distillation. MAN and 2,2-azo-bis-isobutyronitrile (AIBN) were purified before use by recrystallization in chloroform and methanol, respectively. Other reagents used were all of analytical purity and purified thoroughly by the conventional methods.

Methyl 3 α -methacryloyl-7 α ,12 α -dihydroxy-5 β -cholan-24-oate (MACAME, m.p. 180–182 °C) was prepared as described previously^[10].

Characterization

Fourier transform infrared (FT-IR) spectra were recorded from 4000–400 cm⁻¹ on a Bomen spectrometer (MB series). Thin pellets were made from 0.002 g of polymer sample and 0.100 g anhydrous potassium bromide.

The molecular weights of the copolymers were determined by size exclusion chromatography (SEC) using a Waters 1525 chromatograph equipped with a refractive index detector and a set of three columns, Styragel HR3, HR4 and HR6. Columns were calibrated using monodisperse polystyrene standard. Analysis was performed at 25 °C using tetrahydrofuran (THF) as solvent at a flow rate of 1.0 mL/min.

Glass transition temperatures (T_g) of the copolymers were determined with a differential scanning calorimeter (DSC 2910, TA Instruments). A polymer sample (*ca.* 10 mg) was weighed and sealed in an aluminum cell and an empty cell was used as reference. The temperature of the cells was raised from 25 to 250 °C at a rate of 5 K/min. Helium gas with a flow rate of 40 mL/min was introduced during the tests.

Thermogravimetric analyses (TGA) of the copolymers were carried out using a Hi-Res TGA 2950 (TA Instruments) under a flow of nitrogen (77 mL/min). Samples (*ca.* 2 mg) were heated from 25–700 °C at a rate of 20 K/min. Curves of the weight loss with the temperature were recorded. Temperatures at a 10% weight loss (T_{WL}) of the samples were used for the comparison of the thermal stability of copolymers with different compositions.

Composition analyses of the copolymers were conducted by acid-base titration of the maleic anhydride groups in the copolymers. The copolymer samples were dissolved in dioxane-water mixture solvent (1:1 *V/V*), an excess amount of sodium hydroxide solution was then added to drive the hydrolysis of MAN to completion. Superfluous sodium hydroxide was titrated with 0.005 mol/L hydrochloric acid (reverse titration), and a pH meter was employed to record the titration curves.

Preparation of the Copolymers

Copolymerization of MACAME and MAN was carried out in a 50 mL flask equipped with a magnetic stirrer and condenser. The flask was purged with nitrogen. MACAME and MAN of the desired amounts were added, along with 0.7 mol% of AIBN as the initiator. Then freshly distilled THF was injected into the flask. The mixture was heated to 50 °C at a rate of 5 K/min, then to 70 °C at a rate of 2 K/min, and maintained at 70 °C for as long as 24 h. During the polymerization, thin layer chromatography was used to verify the conversion of the monomers. After the reaction, the mixture was concentrated (to *ca.* 5 mL) under vacuum, and poured into diethyl ether. The precipitate was filtered out, and the crude products were purified twice by dissolution-precipitation. The final products were dried at 50 °C under vacuum.

RESULTS AND DISCUSSION

Synthesis and Composition of the Copolymer

A methacrylic monomer containing a cholic acid moiety (MACAME) was prepared by reacting methacryloyl chloride with the OH group on position 3 of cholic acid methyl ester. The free radical copolymerization of MACAME with maleic anhydride (MAN) was carried out in THF solution (Fig. 1).

FT-IR spectra of the synthesized copolymers P(MACAME-*co*-MAN)s and the corresponding homopolymers PMACAME and PMAN are shown in Fig. 2. The IR spectrum of PMAN shows three bands at 1712, 1783 and 1860 cm⁻¹ which are assigned to C=O stretching vibration, and the absorption band at 1231 cm⁻¹ corresponds to the C–O–C stretching vibration in the cyclic anhydride structure. The strong absorbance at 1725 cm⁻¹ in the IR spectrum of PMACAME is attributed to the ester groups in MACAME. In the

IR spectra of the copolymers the three bands at 1230, 1784 and 1862 cm^{-1} corresponding to the cyclic anhydride structure, characteristic of PMAN, become sharper and more intense. It is to be noted that the band at 1725 cm^{-1} corresponding to the characteristic peak of PMACAME becomes sensitive to the molar fraction of MACAME in the copolymers (comparing spectra 1, 3, 5 in Fig. 2).

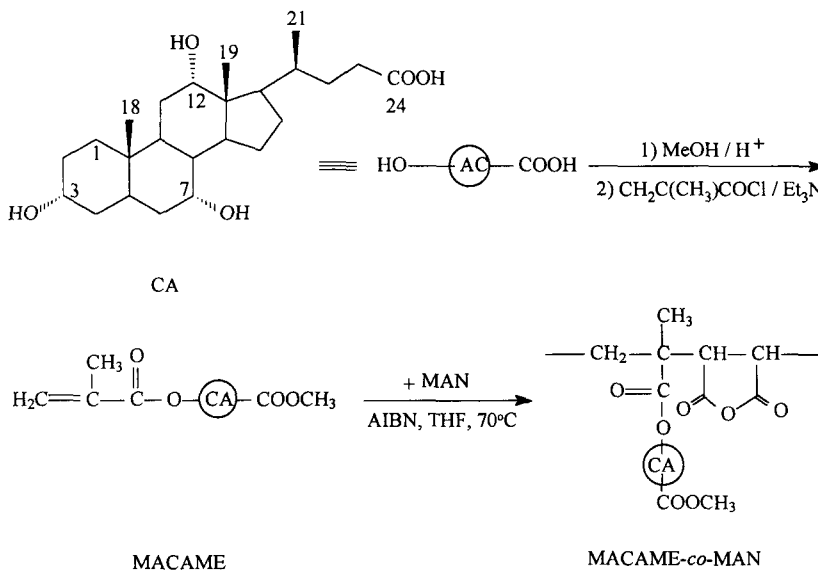


Fig. 1 Copolymerization of the cholic acid derivative (MACAME) with maleic anhydride (MAN)

The OH group in the abbreviated formula of cholic acid represents the one in position 3 of the steroid skeleton

Table 1. Composition and properties of PMACAME and the P(MACAME-co-MAN) copolymers^a

Polymer	F_1^b	M_w^c	M_w/M_n	T_g (°C)	T_{WL} (°C)
1	1.00	36200	3.23	192.2	342.1
3	0.63	3800	1.22	185.6	303.2
4	0.55	3000	1.21	180.2	302.0
5	0.50	2400	1.17	174.2	295.1

^a Reaction conditions: 70°C, 24 h, $[AIBN]_0/[M_1 + M_2]_0 = 0.07$ (molar ratio),

M_1 : MACAME, M_2 : MAN, F_1 : molar fraction of MACAME in the copolymer

^b Determined by reverse titration in dioxane-water

^c Measured by SEC method

The compositions and properties (M_w , T_g , T_{WL} , etc.) of some of the synthesized copolymers are listed in Table 1. As a comparison, the results for the corresponding homopolymer PMACAME synthesized under the same conditions are also listed. In general, NMR analysis is an efficient method for the analysis of the chemical composition of copolymers. In this case, $^1\text{H-NMR}$ cannot be used, since some of the characteristic peaks corresponding to the two monomers in the copolymer are overlapped. Elemental analysis is unsuitable because both monomers consist of the three elements carbon, hydrogen and oxygen. Therefore, functional group analysis based on acid-base titration was selected. The maleic anhydride groups in the copolymer can be easily hydrolyzed to carboxylic acid groups; the content of MAN in the copolymer can thus be determined by titration. The titration of the homopolymer PMACAME showed that the amount of hydrochloric acid consumed was exactly the same as that for a blank experiment. This indicates that the ester groups in MACAME moieties of the copolymers were not hydrolyzed. Since MAN is a weak diacid its reaction with NaOH is a two-step reaction, the inflection point of a direct titration would not be easy to detect.

Experiments demonstrate that the reverse titration method selected is an effective way for chemical composition analysis of the copolymer P(MACAME-co-MAN) and that the copolymerization proved to be more

difficult than the homopolymerization, and the molecular weight of the synthesized copolymer is much lower than that of the homopolymer PMACAME. To a large extent, this can be attributed to the large difference of reactivity ratios of the two monomers.

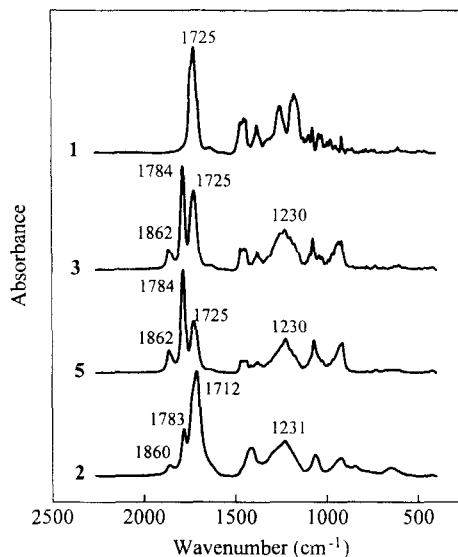


Fig. 2 FT-IR spectra of PMACAME, PMAN and the copolymers
The molar fractions of MACAME unit (F_1) in the polymers are 1 for **1**; 0.63 for **3**; 0.5 for **5**; 0 for **2** (PMAN)

Estimation of Monomer Reactivity Ratios

Based on the postulation mentioned above, the reactivity ratios (r_1 , r_2) of the two monomers in the copolymerization were estimated experimentally by conducting a series of copolymerizations with a variety of monomer feed compositions and analyzing the copolymer composition.

Assuming that the steady-state treatment applies to the copolymerization reaction, the copolymer composition equation may be expressed by

$$\frac{d[M_1]}{d[M_2]} = \frac{[M_1]}{[M_2]} \cdot \frac{r_1[M_1] + [M_2]}{r_2[M_2] + [M_1]} \quad (1)$$

Defining $A = \frac{d[M_1]}{d[M_2]}$, $B = \frac{[M_1]}{[M_2]}$, the following relationship is derived.

$$\left(B - \frac{B}{A}\right) = \frac{B^2}{A} r_1 - r_2 \quad (2)$$

A plot of $B - \frac{B}{A}$ against $\frac{B^2}{A}$ should yield r_1 from the slope and r_2 from the intercept (Fig. 3). Assigning M_1 = MACAME, and M_2 = MAN, the value of r_1 and r_2 can be estimated to be 11.6 and 0.01, respectively. This result demonstrates that in the copolymerization monomer **1** (MACAME) was incorporated into the copolymer exclusively in the early stage and the arrangement of the two monomer units on the copolymer chain was not statistically random.

Thermal Properties of the Copolymers

The thermal stability of the copolymer P(MACAME-co-MAN) was studied. TGA curves of the samples with different copolymer compositions are shown in Fig. 4. The temperature at which the copolymer samples

experienced a 10% weight loss (T_{WL}) is over 285°C (Fig. 5). This indicates that the copolymers synthesized possess good thermal stability. The experimental results also show that the T_{WL} of the sample is related to the copolymer composition, *i.e.*, T_{WL} decreases slightly with the increase in MAN content of the copolymers (Fig. 4).

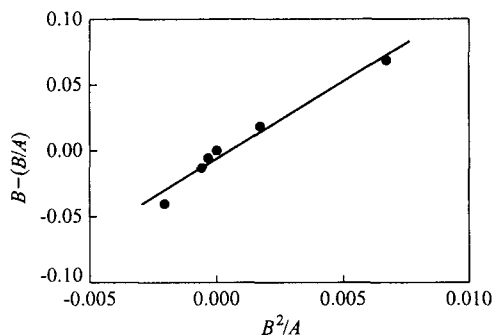


Fig. 3 Plot used in the calculation of the reactivity ratios of the monomers (Eq. 2)

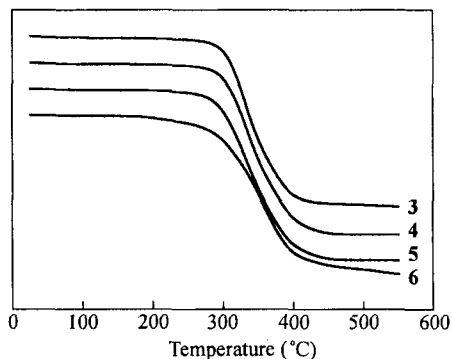


Fig. 4 Thermogravimetric analysis of P(MACAME-co-MAN) samples showing a sharp weight loss at about 330°C
MAN contents: 10.5% for sample 3; 14.2% for 4; 16.8% for 5 and 18% for 6

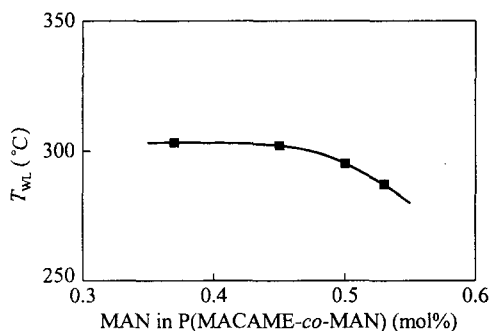


Fig. 5 Variation of the temperature at 10% weight loss (T_{WL}) with the composition of the copolymers

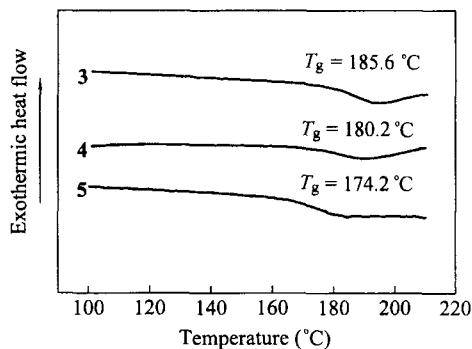


Fig. 6 DSC traces of the copolymers with different compositions
The molar fraction of MACAME in the copolymer samples are: 0.63 for 3; 0.55 for 4; 0.5 for 5

The glass transition temperature (T_g) of the copolymer ($F_1 = 0.63$) is determined as 185.6°C (Table 1).

The T_g values of the copolymers with different compositions were measured by DSC, and results are shown in Fig. 6. It is very clear that the T_g of the copolymers decreases with the increase of MAN content in the copolymers from 185.6 to 174.2°C. The highest T_g observed was 185.6°C for the copolymer with $F_1 = 0.63$.

CONCLUSIONS

Cholic acid-containing methacrylate monomers may be copolymerized with maleic anhydride, and the copolymers show good thermal stability. Clearly the T_g of the copolymers depends on their chemical compositions and can be adjusted by varying the monomer compositions, or adding a third co-monomer to better suit the requirements of their applications.

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