Synthesis and Characterization of Poly(butylene succinate-*co*-butylene malate): A New Biodegradable Copolyester Bearing Hydroxyl Pendant Groups

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A new biodegradable copolyester, poly(butylene succinate-*co*-butylene malate) P(BS-*co*-BM), has been preliminarily prepared with optically active centers and lateral hydroxyl functional groups via a four-step synthetic strategy. First, an optically active benzyl-protected dimethyl malate was synthesized from a starting material of (*S*)-dimethyl malate and purified with good yield. Then, copolyester poly(butylene succinate-*co*-benzyl-protected butylene malate), P(BS-*co*-BBM), was prepared through a skilled condensation copolymerization of the benzyl-protected dimethyl malate, dimethyl succinate, and 1,4-butanediol in the presence of titanium tetraisopropoxide as the catalyst. Finally, a Pd/C catalyzed hydrogenation was applied to eliminate the benzyl protection group in a mixed solution of THF and methanol; thus the target copolyester P(BS-*co*-BM) was attained. On the other hand, physical properties of the synthesized copolyesters were systematically characterized by means of nuclear magnetic resonance spectrometer, Fourier transformed infrared spectrometer, gel permeation chromatography, optical polarimeter, quantitative hydroxyl titration, and thermal analytical instruments. The experimental evidence demonstrated a successful construction of the product P(BS-*co*-BM) bearing lateral hydroxyl functional groups. It was also revealed that the lower BBM unit content was in the benzyl-protected optically active P(BS-*co*-BBM) copolyester, the higher melting point T_m, crystallinity, the broader molecular distribution, and the lower glass transition temperature T_g would be detected, and these results can be accounted for the presence of bulky lateral benzyl moieties. In contrast, the deprotected product P(BS-*co*-55 mol % BM) showed a higher T_m, crystallinity and lower T_g than its counterpart P(BS-*co*-55 mol % BBM). Interestingly, a thermal stability as high as that of the linear PBS was observed for P(BS-*co*-55 mol % BM) while a strong BBM unit content dependence of thermal stability was detected for the benzyl-protected copolyester P(BS-*co*-BBM)s. Therefore, these results may be beneficial for the new optically active P(BS-*co*-BM) bearing hydrophilic hydroxyl functional groups as a potential biomaterial.

Introduction

In the past two decades, there are a number of publications concerning poly(malic acid), an interesting biodegradable polyester.[1] Optically active (*S*)-malic acid has been known as an intermediate among the tricarboxylic acid cycle inside living organisms, and thus has been recognized as a kind of C-4 renewable natural resource.[2] In particular, besides its favorable physical and mechanical properties, poly(malic acid) has been revealed to be able to finally break down into the degradation product of nontoxic optically active malic acid under physiological conditions.[3] Hence, poly(malic acid) attracts much attention as a potential biomaterial which may be suitable for applications in biomedical and pharmaceutical fields. To date, there generally existed two separate methodologies for chemical synthesis of poly(malic acid): (i)

poly(α-malic acid),[4] a macromolecular architecture similar to that of poly(lactic acid), has been synthesized via a ring-opening polymerization (ROP) of a carboxylic group protected six-membered cyclic malide and a successive hydrogenation to eliminate the corresponding protection groups; (ii) Lenz and co-workers[5−7] developed various poly(benzyl β-malic acid) and poly(β-hydroxybutyric acid-*co*-benzyl β-malate)s, P(HB-*co*-BM), bearing different stereoregularities and comonomer sequence distributions from their constructed benzyl β-malolactonate and the corresponding β-butylactone comonomer. More recently, Bizzarri and co-workers[8] reported that poly(β-malic acid)s with various lateral chain structures designed on reaction sites of the pendant carboxylic groups were synthesized on the basis of a new class of malolactonate monomer toward biomedical applications.

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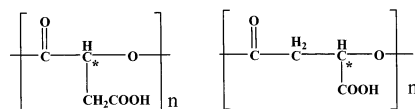
Nevertheless, although many reports have already been focused on polymer synthesis and a further modification at the carboxylic pendant sites for the natural malic acid based biodegradable polyesters and copolyesters, practically there are few studies reported on the construction of biodegradable polyester bearing pendant hydroxyl groups attributed to the malic acid unit. In the recent years, as a feasible synthetic way to precision polymerization, a "living" or controlled ROP has been intensively studied in the presence of Sn, Al organometallic catalysts on the basis of the cyclic monomers such as lactide, glycolide, ϵ-caprolactone, and so forth.[9−11] Furthermore, a coordination−insertion mechanism was thereby proposed and verified. In the case of living ROP of cyclic lactone and lactide, the hydroxyl groups originating from an added alcohol or a hydroxyl macromer has been recognized as the necessary initiators and play a key important role in tuning molecular weight, molecular distribution, and architecture of product polyester.[10] For a linear aliphatic polyester, the presence of lateral hydroxyl groups maybe bring the following benefits: (i) It can tune a hydrophilic−hydrophobic balance between the hydrophilic lateral group and the hydrophobic backbone chain, thus resulting in a variety of interesting polymer conformations such as the macromolecular self-assembled cylinder or core−shell shaped morphologies as recently reported.[12−14] (ii) A further living/controlled ring opening polymerization of reactive cyclic monomer grafted at the reactive hydroxyl sites can construct a functional brush- or comb-type macromolecular architecture through controlling the graft density and length.[15−17]

So far, poly(butylene succinate), PBS, has also been known as an important biodegradable aliphatic polyester, which can be synthesized through an AA/BB type of condensation polymerization from the C-4 compounds of succinic acid and 1,4-butanediol.[18] PBS has been reported to have a melting point of around 114 °C and excellent elongation at break as well as other properties similar to those of PE and recently has already been commercialized under a trademark of Bionolle as a very important green plastic (Showa Highpolymer, Ltd., Japan).[19] Hong and co-workers developed the microspheres of the PBS/PLLA blend and investigated their drug-releasing behavior.[20] However, the lack of hydrophilicity and lateral reaction active sites of the BS repeating unit practically limits further biomedical application for PBS.

In this study, a series of copolyesters, poly(butylene succinate-*co*-benzyl butylene malate) P(BS-*co*-BBM)s, have been synthesized with various benzyl butylene malate unit compositions by using a three-step synthetic strategy. Thus, the target linear aliphatic poly(butylene succinate-*co*-butylene malate), P(BS-*co*-BM)s, bearing lateral hydroxyl groups were preliminarily attained through a Pd/C catalyzed hydrogenation to eliminate the benzyl protection groups. In addition, the synthesized copolyesters were systematically characterized by means of NMR, gel permeation chromatography (GPC), hydroxyl titration, FT-IR, optical polarimeter, and thermal analytical instruments. As a result, the molecular structure dependence of physical properties were discussed for the natural malic acid based biodegradable P(BS-*co*-BBM) and P(BS-*co*-BM).
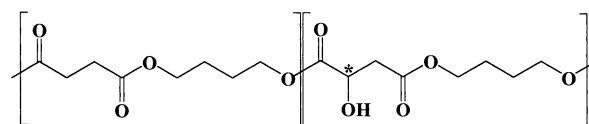
Experimental Section

(A) Materials. Trichloroacetonitrile, tetrabutylammonium hydrogen sulfate, and titanium tetraisopropoxide (AR grade) were purchased from Acros Organics. (*S*)-Dimethyl malate and trifluoromethane sulfonic acid (AR grade) were obtained from Aldrich Chemical. In addition, cyclohexane, benzyl alcohol, dichloromethane, and methanol (AR grade) were used as received. Pyridine and acetic anhydride were dried in advance and then distilled prior to experiment.

(B) Synthesis of Benzyl-Protected Dimethyl Malate (BDMM). *Benzyl 2,2,2-Trichloroacetimidate.* Into a mixed solution of 10 g of benzyl alcohol and 100 mL of dichloromethane was charged 100 mL of 50% aqueous potassium hydroxide solution and 15 mg of tetrabutylammonium hydrogen sulfate (catalytic amount), and then the resultant mixture was vigorously stirred under −15 to −10 °C (Scheme 1). After 5 min, trichloronitrile (1.2 equiv) was dropwise added, and the reaction mixture was further stirred for 30 min and then allowed to warm to the room temperature (25 °C) in 30 min. The organic layer was separated, and the aqueous layer was further extracted with dichloromethane (2 × 100 mL). Finally, the collected organic layer was dried with anhydrous sodium sulfate. The concentrated residue was purified via a column packed with silica gel using *n*-hexane/dichloromethane = 7:1 mixed solution as the eluent. The final product was a yellow oily compound with a yield of 95% (calcd). ^{1}H NMR (δ in ppm): 5.40 (−O−CH_2−C_6H_5, 2H, s), 7.47 (−CH_2−C_6H_5, 5H, m), 8.46 (−C(*NH*)−O−, 1H, s),

Benzyl-Protected Dimethyl Malate (BDMM). Furthermore, into a stirring cyclohexane and dichloromethane mixture solution (30 mL, *v/v* = 1:1) was added 15 mmol of (*S*)-dimethyl malate and 18 mmol of 2,2,2-trichloroacetimidate at ambient temperature under a nitrogen atmosphere. Continuously, 0.2 mL of trifluoromethane sulfonic acid was slowly added within 5 min, and then the reaction temperature was elevated to around 38 °C. The mixture was stirred until the starting material was completely converted as monitored through TLC (mobile phase: *n*-hexane/ethyl acetate = 8:1). Thus, the reaction mixture was quenched by addition of 5 mL of saturated NaHCO₃ aqueous solution and 100 mL of water, and then the white solid trichloroacetimide was removed via filtration. The aqueous layer was separated and extracted with ethyl acetate (3 × 20 mL). The organic layer was dried with anhydrous Na₂SO₄. Finally, the concentrated residue was purified with a silica gel column employing hexane/ethyl acetate (9:1) mixed solution as the eluent. The final product of BDMM monomer (Chart 1) was a yellow oily compound with a yield of 67% and purity of 99.2% as estimated by GC: [α]$_D$ −67.3° (1.4 g/dL,CHCl₃). ^{1}H NMR (δ in ppm): 7.34 (−CH_2−C_6H_5, 5H, m), 4.66 (−CH_2−C_6H_5, 2H, q), 4.40 (−*CH*(O)−,1H, dd), 3.77 (−CH−C(O)−O−CH_3, 3H, s), 3.68 (−CH₂−C(O)−O−CH_3, 3H, s), 2.81 (−CH_2−CH−, 2H, m)
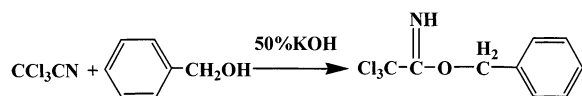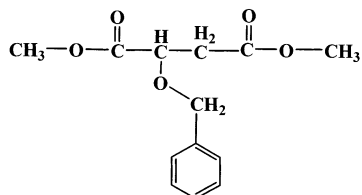
Scheme 1

Chart 1

***Poly(butylene succinate-co*-benzyl butylene malate),** **P(BS-*co*-BBM).** Ten millimoles of dimethyl ester and 15 mmol of 1,4-butanediol (BD) were placed into a flame-dried three-necked flask. Additionally, 0.01 mmol of titanium tetraisopropoxide was added as the catalyst, and then the flask was transferred to an oil bath under preset temperature. First, methanol as the esterification byproduct was removed under 200 °C for 3 h. Then, the polycondensation was carried out under a gradually reduced pressure and heated to 220 °C for 2−3 h. Finally, the resulting crude product was purified via pouring its chloroform solution into an excess amount of cold methanol and then dried under vacuum to constant weight.

PBS ^{1}H NMR as shown in Figure 1 (δ in ppm): 1.70 ($-CH_2-CH_2-O$-, 4H, m); 2.62 ($-CH_2-C(O)-$, 4H, s); 4.11 ($-CH_2-CH_2-O-$, 4H, t).

P(BS-*co*-BBM) ^{1}H NMR as seen in Figure 3 (δ in ppm): 1.71 ($-CH_2-CH_2-O$-,4H, t); 2.63 ($-CH_2-C(O)$-, 4H, s); 2.80 ($-CH-CH_2-C(O)$-,2H, m); 4.17 ($-CH_2-CH_2-O$-, 4H, m); 4.39 ($-CH_2-CH-C(O)$-,1H, dd); 4.65 ($-O-CH_2-C_6H_5$, 2H, q); 7.30 ($-O-CH_2-C_6H_5$, 5H, m).

PBBM ^{1}H NMR as shown in Figure 2 (δ in ppm): 1.72 ($-CH_2-CH_2-O$-, 4H, m); 2.79 ($-CH-CH_2-C(O)$-, 2H, m); 4.16 ($-CH_2-CH_2-O$-, 4H, m); 4.38 ($-CH_2-CH-C(O)-$, 1H, dd); 4.65 ($-O-CH_2-C_6H_5$, 2H, q); 7.32 ($-O-CH_2-C_6H_5$, 5H, m)

FT-IR (KBr): PBS 2946 (ν_{CH}^{as}), 2860 (ν_{CH}^s), 1714 ($\nu_{C=O}$), 1473 (ν_{CH}), 1260 (ν_{C-O-C}^{as}), 1046 (ν_{C-O-C}^s); P(BS-*co*-BBM) 3030 ($\nu_{=CH}$), 2962 (ν_{CH}^{as}), 1734 ($\nu_{C=O}$), 1640 ($\nu_{C=H}$), 1496 (ν_{CH}), 1261 (ν_{C-O-C}^{as}), 1030 (ν_{C-O-C}^s), 743 ($\delta_{=CH}$), 700 ($\delta_{=CH}$); PBBM 3032 ($\nu_{=CH}$), 2961 (ν_{CH}^{as}), 1736 ($\nu_{C=O}$), 1633 ($\nu_{C=H}$), 1460 (ν_{CH}), 1262 (ν_{C-O-C}^{as}), 1027 (ν_{C-O-C}^s), 740 ($\delta_{=CH}$), 698 ($\delta_{=CH}$).

Synthesis of Poly(butylene succinate-co-butylene malate), **P(BS-*co*-BM).** Sixty milligrams of 10 wt % palladium on charcoal was charged into 20 mL of methanol and tetrahydrofuran mixed solution (v/v = 1:1), including 1.5% (w/v) benzyl protected P(BS-*co*-BBM) bearing various BBM repeating unit molar compositions. The benzyl deprotection was implemented at room temperature under 5.0 MPa pressure of H_2 for 24 h. Then, the catalyst was removed with a combination of simple filtration and column, and the filtrate was further concentrated. As a result, a white powder product of benzyl-deprotected poly(butylene succinate-*co*-butylene malate) P(BS-*co*-BM) was obtained through precipitating the concentrated polymer solution in an excess amount of cold *n*-hexane. Results of NMR and IR characterization are listed below.

^{1}H NMR as shown in Figure 7 (δ in ppm): 1.72 ($-CH_2-CH_2-O-$, 4H, m), 2.63 ($-CH_2-C(O)-$, 4H, s), 2.83 ($-CH-CH_2-C(O)-$, 2H, m), 3.40 ($-CH-OH$, 1H, w), 4.14 ($-CH_2-CH_2-O-$, 4H, m), 4.51 ($-CH_2-CH-C(O)-$, 1H, t).

FT-IR (KBr): 3507 (ν_{OH}), 2946 (ν_{CH}^{as}), 2865 (ν_{CH}^s), 1716 ($\nu_{C=O}$), 1460 (ν_{CH}), 1265 (ν_{C-O-C}^{as}), 1046 (ν_{C-O-C}^s).

(D) Analytical Procedures. Molecular Weight. Molecular weights were characterized on a Perkin-Elmer 200 series gel permeation chromatograph equipped with a refractive index detector (RI) and a network chromatography interface NCI 900. A Ultrastyragel HR 5E column purchased from Waters Inc. was hereby applied with $CHCl_3$ as the eluent at a flowing rate of 1.0 mL/min under 40 °C. Polystyrene standards (Showa Denko, Ltd., Japan) with narrow molecular weight distributions were employed to build a universal calibration curve. Accordingly, the molecular weights (M_w, M_n) and polydispersity indexes of the synthesized polymers were thus evaluated.

^{1}H and ^{13}C NMR. Measurements of NMR spectra were conducted in $CDCl_3$ solution under ambient temperature on a Varian VXR 300FT-NMR spectrometer operated at 300.055 and 75.475 MHz, respectively. Tetramethylsilane (TMS) was applied as internal chemical shift standard. Accordingly, the molar composition of the benzyl-protected butylene malate, BBM, or the deprotected butylene malate, BM, repeating unit was estimated from the corresponding methylene proton resonance intensities as shown in Figures 1−3 and 7.

Hydroxyl Titration. To determine the pendant hydroxyl content in the synthesized biodegradable P(BS-*co*-BM), a nonaqueous titration method was thus accordingly applied.[21,22] A 100 mg portion of the benzyl deprotected product of P(BS-*co*-BM) was added into 6.0 mL of pyridine/acetic anhydride (3:1 v/v) mixed solution and then the oil bath temperature was raised up to 100 °C for 1 h of acetylation. Subsequently, 1.5 mL of H_2O was added to the reaction mixture and the reaction mixture was allowed to stand for 0.5 h. The methanol solution of KOH (0.932 M) was used to titrate the polyester solution in triplicate, where thymol blue was applied as the indicator. In parallel, the blank titration was also conducted in a same manner as stated.

Infrared spectroscopy (IR). FT-infrared spectra of all products were recorded on a Nicolet AV-360 spectrometer with a TGS detector. When the polyesters were amorphous, the FT-IR samples of these polyesters were prepared through mixing their chloroform solution with KBr and then further dried under vacuum for 24 h under ambient temperature prior to the FT-IR measurement.

Gas Chromatography. The purity of the benzyloxy-protected dimethyl malate monomer, BDMM, was determined via a Hewlett-Packard 6890 gas chromatograph with a PEG20M chromatographic column and an EID detector.

Optical Rotation. Measurements of optical rotation were conducted for the BDMM monomer and the synthesized

polyesters on a Perkin-Elmer polarimeter 341 instrument under 20 °C (λ = 589 nm). CHCl$_3$ was hereby applied as the solvent.

Thermal Analysis. Thermal analyses of the synthesized P(BS-*co*-BBM)s and P(BS-*co*-BM)s were implemented on a Perkin-Elmer Pyris 1 differential scanning calorimeter DSC and a Perkin-Elmer Pyris 1 thermal gravimeter TG. Eight to ten milligrams of a prepared polyester was encapsulated in an aluminum pan and then heated to 150 °C to remove its thermal history. These differential scanning calorimeter (DSC) samples were kept under ambient temperature for more than 4 weeks to promote the crystallization to equilibrium state. Hence, DSC thermograms of the prepared polyesters were recorded from 40 to 200 °C at a heating rate of 20 °C/min (first heating scan). The temperature was continuously kept at 200 °C for 1 min and then rapidly quenched to −100 °C at −450 °C/min. The sample was reheated from −100 to 60 °C at a rate of 20 °C/min (the second scan). Therefore, melting points T_m and heat of fusion (ΔH_m) were estimated as the main peak tops and the integrals of the endothermic curve recorded by the first DSC run, respectively. Glass transition temperature (T_g) and cold crystallization temperature (T_{cc}) were evaluated respectively as the midpoint of heat capacity change and the cold crystallization peak top occurring in the second DSC trace. On the other hand, TG analyses were carried out for the as-prepared polyesters. Two to three milligrams of samples were scanned from 25 to 500 °C at a heating rate of 10 °C/min under flowing nitrogen (40 mL/min). Peak tops (T_d) of the differentiated TG curve denoted as the dTG trace were employed as an index to assess thermal degradation behavior and stabilities for the synthesized polyesters.

Results and Discussion

Syntheses of Poly(butylene succinate-*co*-benzyl-protected butylene malate)s. In the present study, poly(butylene succinate-*co*-benzyl-protected butylene malate)s were prepared through a three-step synthetic strategy. In the first step, an intermediate of benzyl 2,2,2-trichloroacetimidate was accordingly synthesized from the starting materials of trichloronitrile and benzyl alcohol as described in Scheme 1.[23] Consequently, a purified yellow oily compound of benzyl 2,2,2-trichloroacetimidate was attained with an overall yield of 95% and was further analyzed by means of ^{1}H NMR. The ^{1}H resonance signals occurring at 5.40, 7.47, and 8.46 ppm were assigned to the corresponding methylene, phenyl, and imino protons, respectively. Second, the benzyl-protected dimethyl malate monomer BDMM for a further condensation copolymerization of P(BS-*co*-BBM) was thus synthesized on the basis of the prepared benzyl 2,2,2-trichloroacetimidate and (*S*)-dimethyl malate.[24,25] It has been found that the synthesized product of BDMM monomer was also a yellow oily compound with a final yield of 67% and a purity of 99.2% (calcd) as analyzed by gas chromatography. Moreover, a further analysis of BDMM monomer by optical polarimeter revealed that the [α]$_D$ (1.4 g/dL, in CHCl$_3$) at 25 °C was −67.3°, indicating that the product BDMM monomer is an optical active monomer. The ^{1}H NMR resonance signals of
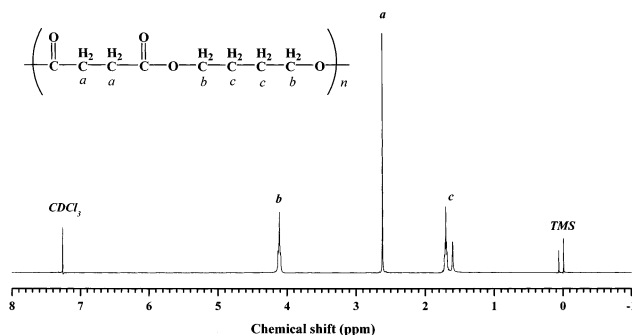

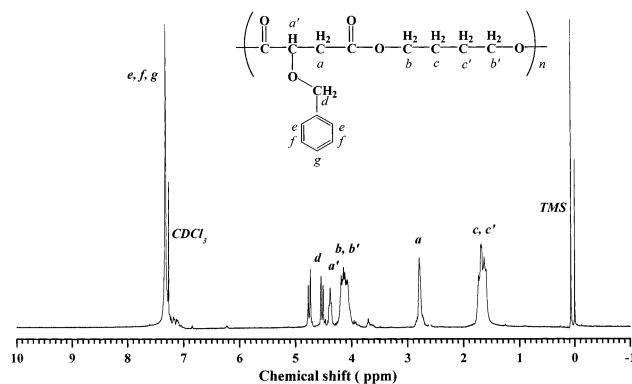**Figure 1.** 300.1 MHz ^{1}H NMR spectrum of poly(butylene succinate).

Figure 2. 300.1 MHz ^{1}H NMR spectrum of poly(benzyl-protected butylene malate).
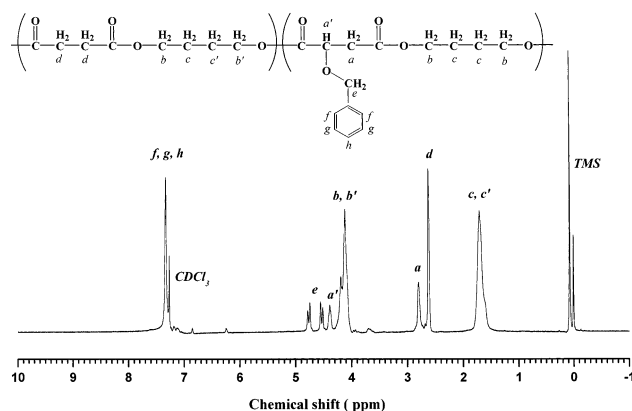

Figure 3. 300.1 MHz ^{1}H NMR spectrum of poly(butylene succinate-*co*-benzyl-protected butylene malate).

BDMM monomer appearing at 2.81, 3.68, 3.77, 4.40, 4.66, and 7.34 ppm were respectively assigned to the proton origins as −CH$_2$−CH−, −CH$_2$−C(O)−O−CH$_3$, −CH−C(O)−O−CH$_3$, −CH(O)−, −CH$_2$−C$_6$H$_5$, −C$_6$H$_5$ as shown in Chart 1.

On the basis of the prepared BDMM monomer, poly(butylene succinate-*co*-benzyl-protected butylene malate) bearing the lateral benzyl groups were synthesized through condensation copolymerization with dimethyl succinate DMS, BDMM, and 1,4-butanediol under 200−220 °C using titanium tetraisopropoxide as the catalyst (catalyst/ monomer molar ratio = 1/1000). Figures 1−6 depict the corresponding ^{1}H and ^{13}C NMR spectra of PBS, PBBM, and their copolyester P(BS-*co*-BBM), and the proton and ^{13}C resonance signals were hereby assigned as shown in Figures 1−6, referring to those of PBS as reported in our previous studies[26,27] and the results of PBBM. Moreover, FT-IR
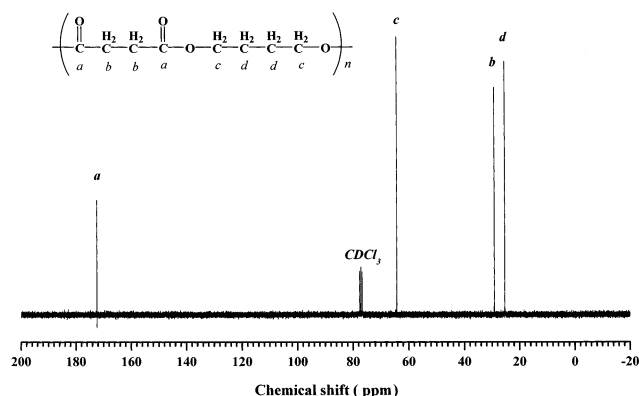
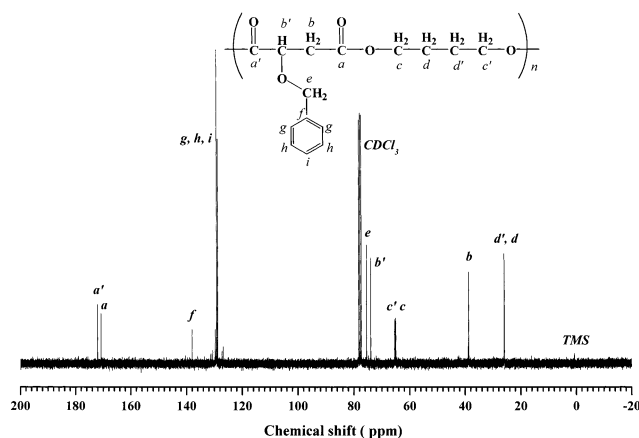**Figure 4.** 75.5 MHz ^{13}C NMR spectrum of poly(butylene succinate).

Figure 5. 75.5 MHz ^{13}C NMR spectrum of poly(benzyl-protected butylene malate).
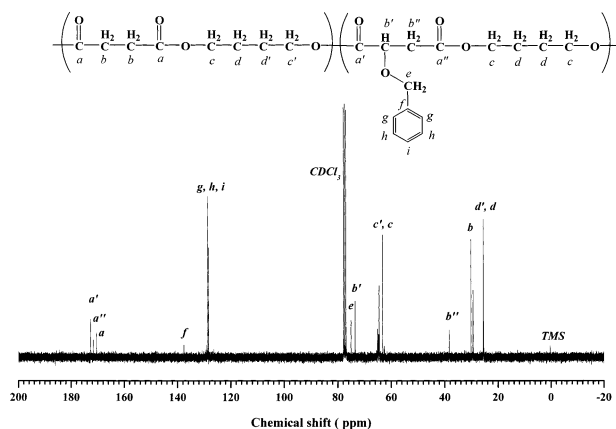

Figure 6. 75.5 MHz ^{13}C NMR spectrum of poly(butylene succinate-*co*-benzyl-protected butylene malate).

spectra (KBr) of the synthesized P(BS-*co*-BBM) were simultanously recorded in solid state. The IR absorptions were assigned to the respective vibration modes of individual bonds for PBS, PBBM, and P(BS-*co*-BBM) copolyester and were further generalized in the Experimental Section. Hence, the NMR and IR evidence demonstrated a successful construction of the product P(BS-*co*-BBM) copolyester. Furthermore, from the relative proton resonance intensities of methylene proton a and d as seen in Figure 3, the molar contents of the BBM unit were thus calculated for the synthesized copolyesters. Table 1 summarized the results of condensation copolymerization of P(BS-*co*-BBM) under an optimized initial diol/diester molar ratio of 1.5.[28] It can be

obviously seen that varying the feeding molar ratio of dimethyl succinate DMS monomer to BDMM monomer could prepare P(BS-*co*-BBM) copolyester with the BBM unit content spanning the whole range from 0 mol % of (PBS) to 100 mol % of PBBM. Approximately, there exists a linear correlation between the feeding molar ratio of DMS/BDMM and the BBM unit content in the product P(BS-*co*-BBM). On the other hand, GPC analyses using chloroform as the solvent indicated all unimodal eluent traces for PBS, PBBM, and P(BS-*co*-BBM) copolyesters with various BBM contents, and the higher the BBM content is in the P(BS-*co*-BBM) copolyester, the broader the GPC eluent trace or the higher apparent polydispersity index of M_w/M_n up to 6 will be observed. Here, another important parameter of polymer solubility should be taken into account for GPC analysis in an employed organic solvent.[12,29] In this study, chloroform with midpolarity was found to be a good solvent for linear PBS as previously reported.[26,27] However, increasing the BBM unit content of the product P(BS-*co*-BBM) indeed led to a relatively poor polymer solubility in chloroform, thus maybe concurrently influencing the polymer chain conformation and apparent molecular weight for the copolyester with high BBM unit content. In the present work, various solvents such as tetrahydrofuran (THF), DMF, and DMSO with higher polarities were also attempted, and similar polymer solubilities were indicated for the high BBM unit content P(BS-*co*-BBM)s. In addition, the results of optical rotation measurements exhibit $[\alpha]^{25}_D$ values from −8.0° of P(BS-*co*-19 mol % BBM) to −51.8° of PBBM, and there presents an approximately linear correlation between the $[\alpha]^{25}_D$ value and the BBM unit composition of copolyester. This result clearly demonstrated the products P(BS-*co*-BBM)s are optically active copolyesters.

Deprotection of Poly(butylene succinate-*co*-benzyl-protected butylene malate)s. To obtain the target product of poly(butylene succinate-*co*-butylene malate) bearing the lateral hydroxyl groups, deprotection of P(BS-*co*-BBM) was attempted in a mixed solution of THF and methanol through a Pd/C catalyzed hydrogenation. Tasaka et al.[15] reported a benzyl deprotection of the comb-type poly{[Glc-ser-(OBzl)]-LA} using TFMSA-thioanisole/TFA, and a slight main-chain cleavage concurrently occurred during the benzyl deprotection. Here, Table 2 and Figure 7 present the deprotection results for the P(BS-*co*-BM) copolyester by using a Pd/C catalyzed hydrogenation.[30] As compared with the proton resonance of P(BS-*co*-BBM) as shown in Figure 3, the ^{1}H NMR resonance signals at 7.32 and 4.65 ppm attributed to the lateral benzyl group completely disappeared with a weak hydroxyl signal newly occurring at 3.40 ppm. This result is in good agreement with the FT-IR experimental evidence that the IR absorption bands centered near 3030, 1630, 740, and 700 cm^{-1} as the intrinsic absorption of phenyl entirely disappeared for the benzyl deprotected copolyesters. In addition, a strong new IR absorption band emerging at 3507 cm^{-1} was attributed to the newly formed lateral hydroxyl groups. A quantitative assay of the hydroxyl content was also carried out by means of the hydroxyl titration and ^{1}H NMR, and the hydroxyl contents in the P(BS-*co*-55 mol % BM) were 5.36 mmol (hydroxyl titration method) and 5.73

**Table 1.** Syntheses of Biodegradable Poly(butylene succinate-*co*-benzyl-protected butylene malate)s

no.	feed molar ratio (DMS/BDMM/BD)	reaction time (min)[b]	BBM unit molar content (%)[c]	yield (%)	$[\alpha]_D^{25}$ [d]	molecular weight [e]		
						$M_w \times 10^{-4}$	$M_n \times 10^{-4}$	M_w/M_n
1[a]	1.00:0:1.50	230	0	83		5.84	2.78	2.1
2[a]	0.80:0.20:1.50	360	19	73	−8.0 (1.18)	14.75	2.55	5.8
3[a]	0.60:0.40:1.50	150	44	75	−25.0 (0.84)	19.68	3.12	6.3
4[a]	0.50:0.50:1.50	120	55	65	−31.6 (1.05)	13.55	2.11	6.4
5[a]	0.40:0.60:1.50	270	59	69	−36.7 (0.90)	9.23	1.55	6.0
6[a]	0.20:0.80:1.50	120	82	73	−40.8 (1.10)	7.57	1.71	4.4
7[a]	0:1.00:1.50	30	100	70	−51.8 (0.96)	10.38	1.72	6.1

[a] The P(BS-*co*-BBM)s were synthesized under 200∼220 °C with titanium tetraisopropoxide as the catalyst. [b] Indicates the polycondensation time. [c] The BBM unit molar contents were evaluated by ^{1}H NMR. [d] The $[\alpha]_D$ values were evaluated in chloroform, and the values in parentheses express the corresponding polymer concentration in g/dL. [e] The molecular weights were evaluated by GPC with PS standards.

Table 2. Physical Properties of the Benzyl-Protected P(BS-*co*-55 mol % BBM) and Its Corresponding Deprotected P(BS-*co*-55 mol % BM)

no.	BBM or BM unit in copolymers[c]	$[\alpha]_D^{25}$ [b]	T_m^c (°C)	ΔH_m^c (J/g)	T_g^d (°C)	T_d^e (°C)	molecular weight[f]		
							$M_w \times 10^{-4}$	$M_n \times 10^{-4}$	M_w/M_n
1	55 mol % BBM	−31.6 (1.05)	37.6	7.05	−24.6	364	13.55	2.11	6.40
2[a]	55 mol % BM	−4.3 (1.04)	63.9	40.5	−28.5	380	1.92	1.09	1.73

[a] Sample no. 2 was the corresponding deprotected product of sample no. 1 with Pd/C (10 wt %) as the catalyst. [b] The $[\alpha]^{25}_D$ values were obtained in CHCl$_3$, and the values in parentheses express the polymer concentration in g/dL. [c] T_m and ΔH_m were measured by the first scan at a heating rate of 20 °C /min. [d] T_g was estimated from the second DSC heating trace at 20 °C/min. [e] T_d values were measured by TG with a scanning rate of 10 °C/min. [f] Molecular weights were evaluated by GPC with PS standards.
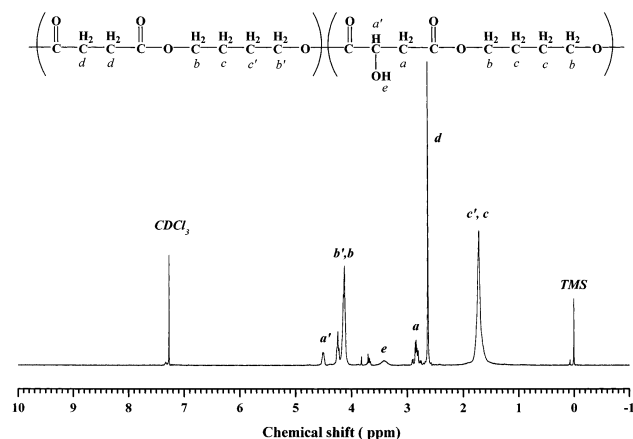
Figure 7. 300.1 MHz ^{1}H NMR spectrum of poly(butylene succinate-*co*- butylene malate).

mmol (^{1}H NMR method) per gram of copolyester, respectively, indicating a close agreement between two separate methods of hydroxyl titration and ^{1}H NMR. Therefore, these results demonstrated an efficient removal of the lateral benzyl-protection group and formation of the product P(BS-*co*-BM) copolyester. For instance, Table 2 shows the deprotection result for P(BS-*co*-55 mol % BBM). It can be seen that the deprotected P(BS-*co*-55 mol % BM) exhibited a polydispersity index M_w/M_n of 1.73, a value quite lower than 6.40 of its corresponding P(BS-*co*-55 mol % BBM) as well as the values of molecular weight. As aforementioned, the parameter of polymer solubility has been known to influence the molecular weight assay by GPC. In this study, the deprotected P(BS-*co*-BM)s were indeed found to resolve in both chloroform and THF much better than their benzyl protected counterparts, and this may be one reason for a more reasonable M_w/M_n value detected by GPC for the benzyl deprotected product. Moreover, an optical rotation value $[\alpha]^{25}_D$ of −4.3° was detected for the P(BS-*co*-55 mol % BM), indicating that the obtained P(BS-*co*-55 mol %BM) is an optically active copolyester.
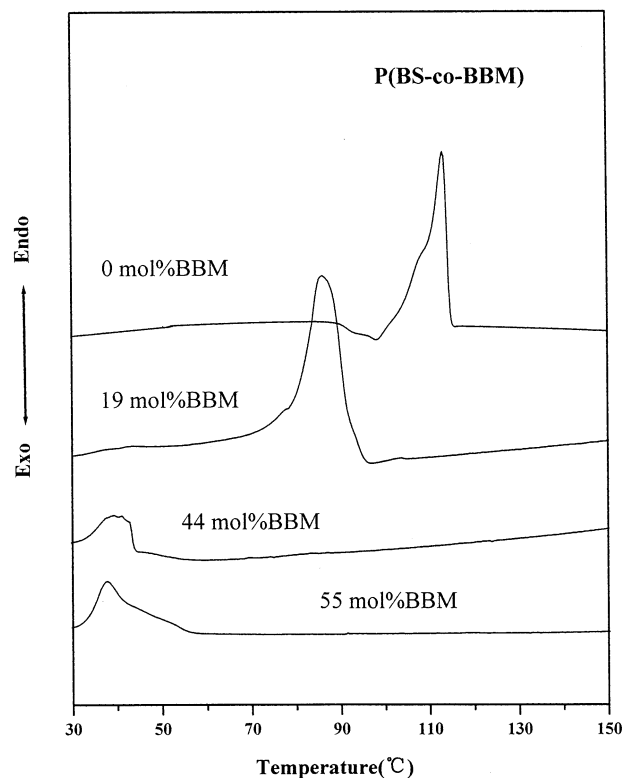

Figure 8. DSC traces of the poly(butylene succinate-*co*-benzyl-protected butylene malate)s recorded by the first heating run.

Thermal Characterization of P(BS-*co*-BBM)s and Their Deprotected P(BS-*co*-BM)s. Figure 8 depicts DSC thermograms for the P(BS-*co*-BBM)s bearing various BBM molar contents recorded by the first heating run, and the DSC results are summarized in Table 3. It can be seen that PBS exhibited a melting point around 114 °C as ever reported,[19,26−27] and that either T_ms or heat of fusion of the P(BS-*co*-BBM) copolyesters tend to remarkably decrease with increasing their BBM unit contents. As compared with the semicrystalline linear PBS, the endothermic peak of a
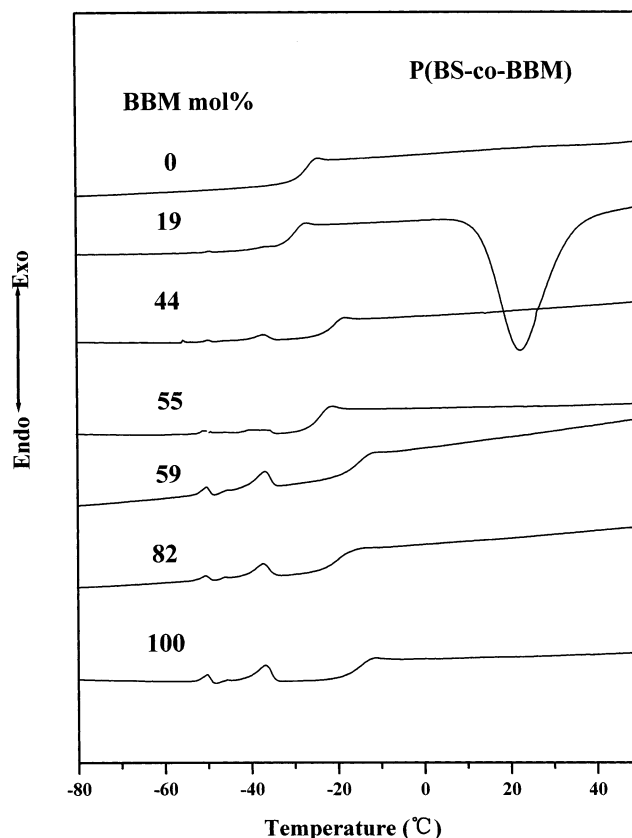
Table 3. Thermal Properties of Poly(butylene succinate-*co*-benzyl-protected butylene malate)s

no.	sample code	$T_m{}^a$ (°C)	$\Delta H_m{}^a$ (J/g)	$T_g{}^b$ (°C)	$T_{cc}{}^b$ (°C)	$T_d{}^c$ (°C)
1	PBS	114.6	97.2	−30.6		379
2	BBM = 19 mol %	86.0	41.2	−30.0	22.5	375
3	BBM = 44 mol %	41.2	11.37	−21.2	n.d.^{d}	367
4	BBM = 55 mol %	37.6	7.05	−24.6	n.d.^{d}	364
5	BBM = 59 mol %	n.d.^{d}	n.d.^{d}	−19.4	n.d.^{d}	359
6	BBM = 82 mol %	n.d.^{d}	n.d.^{d}	−25.3	n.d.^{d}	356
7	PBBM	n.d.^{d}	n.d.^{d}	−15.9	n.d.^{d}	355

^{a} The melting points and heat of fusion were measured by the first scan at a heating rate of 20 °C/min. ^{b} Glass transition temperature and cold crystallization temperature were estimated from the second DSC heating trace at 20 °C/min. ^{c} The thermal degradation temperature were measured by TG with a scanning rate of 10 °C/min. ^{d} Not detected.
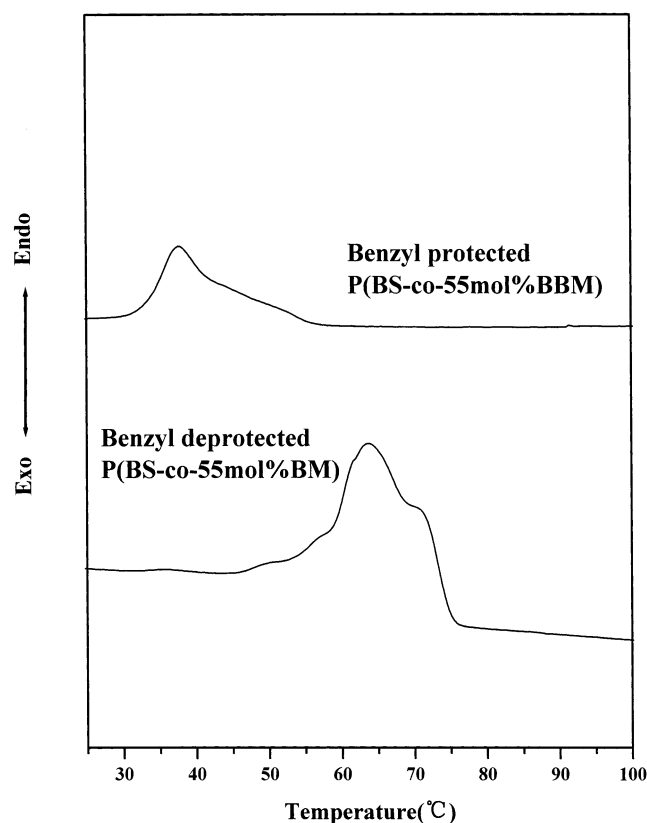
Figure 9. DSC trace of P(BS-*co*-55 mol % BM) as well as P(BS-*co*-55 mol % BBM) recorded by the first heating run.

Figure 10. DSC traces of the poly(butylene succinate-*co*-benzyl-protected butylene malate)s recorded by the second heating run.

P(BS-*co*-BBM) copolyester disappeared under ambient temperature when its BBM unit content was higher than 55 mol %, indicating an amorphous feature. When chain structure is taken into account, the lateral bulky benzyl group of the butylene malate unit significantly retarded main chain crystallizabilities of copolyester even though both BS and BBM repeating units share the same C4−C4 backbone chain structures. On the other hand, P(BS-*co*-55 mol % BM) exhibited T_m and ΔH_m higher than those of the benzyl-protected P(BS-*co*-55 mol % BBM) as shown in Figure 9 and Table 2. Ihn and co-workers have reported that linear PBS preferentially organizes a monoclinic crystal cell structure with $a = 0.523$ nm, $b = 0.908$ nm, $c = 1.079$ nm, and $\beta = 123.87°$, where two linear polyester chains oppositely oriented in parallel.[31,32] The higher melting point and crystallinity (heat of fusion) of P(BS-*co*-BM) can be

accounted for two possible reasons: (i) a hydroxyl side group with less steric hindrance will be more energetically favorable for accommodating a secondary BM unit than the BBM unit; (ii) an intermolecular interaction caused by the possible intermolecular hydroxyl bond between two neighboring hydroxyl and hydroxyl or carbonyl groups can stabilize the aggregated solid crystalline structure for P(BS-*co*-BM). Moreover, Figures 10 and 11 present the DSC traces for P(BS-*co*-BBM)s and the benzyl-deprotected P(BS-*co*-BM) by the second heating run. It seems that glass transition temperatures of the product P(BS-*co*-BBM)s tend to increase from −30.6 °C of PBS to −15.9 °C of PBBM and that the benzyl-deprotected P(BS-*co*-55 mol % BM) exhibited a glass transition temperature of −28.5 °C, lower than −24.6 °C of the corresponding P(BS-*co*-55 mol % BBM). These results indicated that the higher the BBM unit content is, the lower the chain/segmental mobility will be detected for copolyester P(BS-*co*-BBM). It can be accounted for a higher steric hindrance of molecular motions caused by the presence of lateral bulky benzyl groups as discussed above.

In particular, thermal degradation behavior and stability are of great importance for application of biodegradable aliphatic polyester. Here, to make a quantitative assay of thermal stabilities of the product copolyesters, peak top temperatures (T_d) of the corresponding differentiated TG traces (dTG) were applied as shown in Figures 12 and 13 and Tables 2 and 3. It can be seen that the linear PBS showed a high T_d of 379 °C as previously reported, and T_d of the product P(BS-*co*-BBM) tends to monotonically decrease to 355 °C of PBBM with an increase in the BBM unit content.
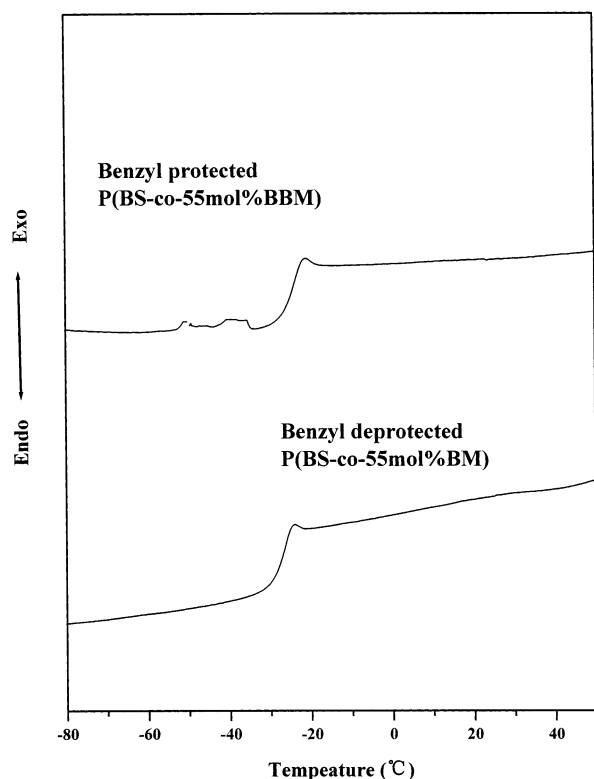
Figure 11. DSC trace of P(BS-*co*-55 mol % BM) as well as P(BS-*co*-55 mol % BBM) recorded by the second heating run.
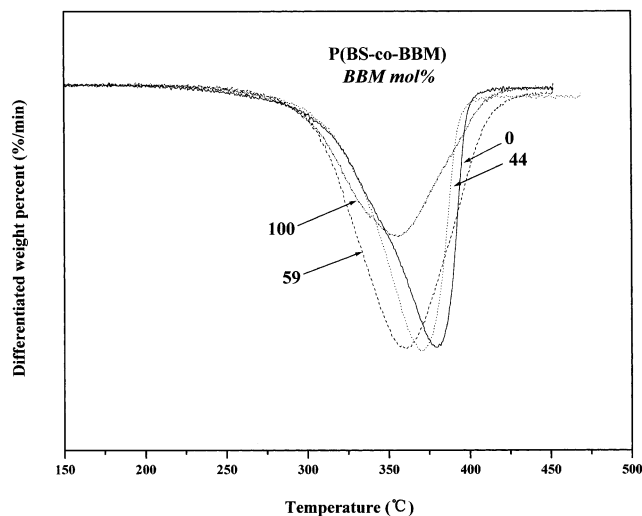

Figure 12. dTG traces of the poly(butylene succinate-*co*-benzyl-protected butylene malate)s.

With respect to P(BS-*co*-55 mol % BBM) and P(BS-*co*-55 mol % BM), it is worthy to note that a higher T_d of 380 °C was detected for P(BS-*co*-55 mol % BM) than 364 °C of its benzyl-protected counterpart. This result indicates that the product P(BS-*co*-BM)s bearing a lateral hydroxyl group have high thermal stabilities as PBS and that an incorporation of the benzyl-deprotected BM comonomer unit imparts optical active centers and a large amount of hydroxyl active sites to the product P(BS-*co*-BM).

Conclusions

A new optically active biodegradable poly(butylene succinate-*co*-butylene malate) (C4−C4) bearing pendant hy-
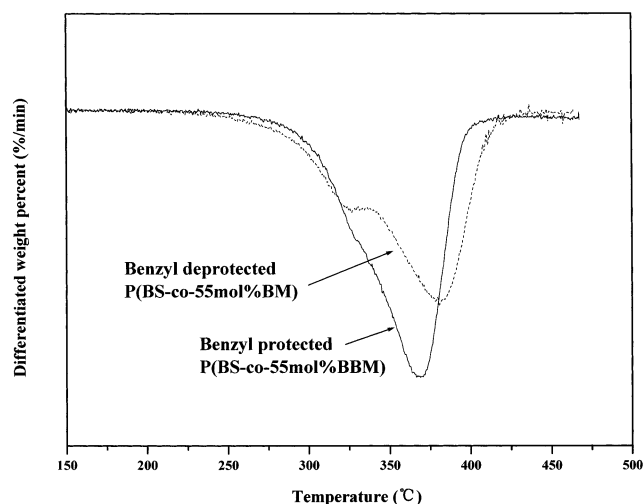

Figure 13. dTG trace of P(BS-*co*-55 mol % BM) as well as P(BS-*co*-55 mol % BBM).

droxyl functional groups has been chemically prepared through a four-step synthetic strategy. First, an optically active benzyl-protected dimethyl malate BDMM monomer was synthesized from (*S*)-dimethyl malate and purified; thus the copolyesters of poly(butylene succinate-*co*-benzyl-protected butylene succinate)s were further attained via a condensation copolymerization of BDMM, dimethyl succinate (DMS), and 1,4-butanediol (BD) in the presence of titanium tetraisopropoxide as the catalyst. ^{1}H, ^{13}C NMR, and FT-IR (KBr) physical characterization demonstrated a successful construction of the P(BS-*co*-BBM) copolyester, and approximately a linear correlation was detected between the BBM unit molar content in the product copolyester and the feeding molar ratio of BDMM to DMS comonomer during the condensation copolymerization. Measurements of optical rotation revealed that the synthetic P(BS-*co*-BBM)s were also optically active polymers regardless of their different BBM unit contents. Moreover, GPC analyses using chloroform as the solvent indicated that all benzyl-protected P(BS-*co*-BBM) copolyesters showed unimodal eluent traces; however much broader molecular distribution was detected for copolyester with a higher BBM unit content, and this may be accounted for another important parameter of polymer solubility. With regard to thermal properties, the lower melting point, crystallinity, and higher glass transition temperature were detected for the copolyester bearing higher BBM content, and P(BS-*co*-BBM)s with BBM unit content higher than 55 mol % were found to be amorphous. Furthermore, employing a Pd/C catalyzed hydrogenation methodology, a new benzyl-deprotected P(BS-*co*-BM) bearing lateral hydroxyl functional groups was preliminarily prepared and verified by means of ^{1}H NMR, FT-IR, and a quantitative hydroxyl titration. It is noted that the benzyl-deprotected P(BS-*co*-BM)s exhibited higher melting points and crystallinities than their P(BS-*co*-BBM) counterparts and that high thermal stability similar to that of PBS was observed for the benzyl deprotected P(BS-*co*-55 mol % BM) while a remarkable decrease in thermal stability was found for the P(BS-*co*-BBM) with increasing BBM molar content. Therefore, the synthesized P(BS-*co*-BM), a new copolyester with interesting optically active centers and lateral hydrophilic hydroxyl functional groups,

will be beneficial for a further chemical modification and construction of a new biomaterial.

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