Synthesis of Hydroxyl-Terminated Poly(lactic acid) via Polycondensation: An Equation to Predict Molecular Weight Based on the Reaction Parameters

Hossein Izadi-Vasafi,[1] Gity Mir Mohamad Sadeghi,[1,2] Hamid Garmabi[2]

[1]Amirkabir University of Technology, Mahshahr Branch, P. O. Box: 415, Mahshahr, Iran
[2]Department of Polymer Engineering and Color Technology, Amirkabir University of Technology, P. O. Box: 15875-4413, Tehran, Iran

ABSTRACT: Low-molecular-weight hydroxyl-terminated poly(lactic acid)s (PLA-OHs) were synthesized via the condensation polymerization of L-lactic acid (LA) with stannous octoate [$Sn(Oct)_2$] as a catalyst along with a small amount of 1,4-butanediol (1,4-BDO). The effect of three reaction parameters (i.e., reaction time, catalyst concentration, 1,4-BDO concentration) on the molecular weight (MW) and molecular weight distribution (MWD) of the PLA-OHs were investigated with response surface methodology. Three levels for each parameter were selected: 6, 8, and 10 h for reaction time, 0.05, 0.10, and 0.15 mol % catalyst concentrations based on LA content, and 2, 3, and 4 mol % 1,4-BDO concentrations based on LA content. The physicochemical structures of the polymers were investigated by Fourier transform infrared spectroscopy. The MW and MWD values of the synthesized polymers were investigated by ^{1}H-NMR and gel permeation chromatography. The results show that when the reaction time was increased, the MW of the PLA-OHs increased reasonably. The MW of polymers also increased with decreasing amount of catalyst. Increasing the amount of 1,4-BDO resulted in a decrease in the MW of the prepolymers. The only exception was observed when the lowest reaction time (6 h) was chosen along with a high concentration of 1,4-BDO; in this case, increasing the catalyst amount resulted in an increase in MW. Also, when we chose a reaction time of 10 h, a catalyst concentration of 0.10 mol % based on LA content, and a 1,4-BDO amount of 2 mol % based on LA content, we observed the highest MW among the other samples. Finally, an equation was developed by MINITAB software to predict the MWs of the PLA-OHs on the basis of the reaction parameters. © 2012 Wiley Periodicals, Inc. J Appl Polym Sci 000: 000–000, 2012

**Key words:** biopolymers; polycondensation; polyesters

INTRODUCTION

Poly(lactic acid) (PLA), one of the major types of biocompatible and biodegradable polymers,[1] has many applications both in medical and nonmedical fields,[2] and its applications are becoming increasingly widespread. One of the most important approaches for L-lactic acid (LA)-based polymers is to make PLA-based polyurethanes (PUs) to create a biodegradable PU with desirable properties, and many studies have been focused on this purpose.[3–9] Poly(ester urethanes) based on PLA are made by a two-step process including, first, the synthesis of hydroxyl-terminated poly(lactic acid) (PLA-OH) followed by the synthesis of PU.[10] In the first step, a low-molecular-weight telechelic polymer is synthesized via condensation polymerization in the presence of a catalyst with 1,4-butanediol (1,4-BDO) for hydroxyl termination and control of the molecular weight (MW) of the prepolymer. This prepolymer can be used as a polyol for the synthesis of biodegradable PU. In the following step, the final PU is produced by the linking of the prepolymer chains with a chain extender such as a diisocyanate.[10]

Telechelic PLA, having two functional groups at its chain ends, can be made by the polycondensation of LA[11–13] or by the hydrolytic degradation of high-molecular-weight PLA.[14] The polycondensation route is a convenient process and has been studied by many researchers during the last 2 decades.[4–8,15] The MWs of synthesized telechelic polymers are highly dependent on some of the reaction parameters, such as the reaction time, reaction temperature, pressure, catalyst type, and amount (based on the LA content used) and molar ratio of butanediol (BDO) to LA.[3] From the catalyst standpoint, it has been proved that tin(II) octoate [$Sn(Oct)_2$] is one of the most efficient catalysts for attaining a reliable MW.[3] The effect of the BDO content (molar ratio of BDO to LA monomer) on the MW of PLA-OH was also been investigated by Hiltunen et al.[11] However, to our knowledge, the simultaneous effects of the reaction conditions (e.g., reaction time, catalyst

Correspondence to: G. M. M. Sadeghi (gsadeghi@aut.ac.ir).
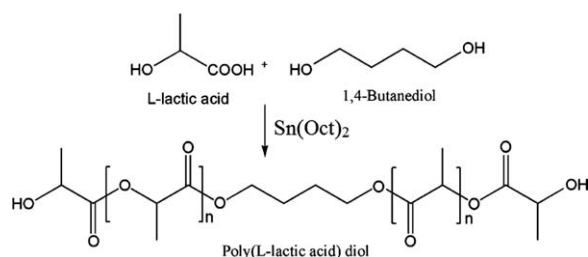
Scheme 1   Process for synthesizing PLA-OH.

concentration, BDO concentration) on the MW of PLA-OH have not been discussed in detail so far. Yoo and Kim[16] synthesized low-molecular-weight PLA and studied the effects of the catalyst and temperature on the reaction rate. They confirmed that the reaction kinetics increased with temperature up to 210°C and the maximum polymerization reaction rate was achieved by the catalyst sulfuric acid. Very recently, Sedlarik et al.[17] investigated the effect of the reaction time and reaction temperature on the MW of low-molecular-weight PLA with a nonmetal-based catalyst (methanesulfonic acid). They also investigated the effect of the catalyst concentration on the MW of PLA.

In this study, we investigated the effects of the aforementioned parameters on the MW of PLA-OH. The procedure was based on experimental design to reduce the number of runs. In the second step, the MW of the synthesized PLA-OH was investigated by ^{1}H-NMR and gel permeation chromatography (GPC) to obtain an acceptable equation to determine the MW of the PLA-OH as a function of the reaction parameters.

EXPERIMENTAL

Materials

LA (88% LA in water, 99% optically pure) was purchased from Sigma Chemical Co. United States. Excess water was removed before use by distillation under reduced pressure at 85°C. 1,4-BDO (+98%, Merck) and tin(II) octoate [$Sn(Oct)_2$] as the catalyst (Sigma Chemical) were used without further purification.

Synthesis of PLA-OH

PLA-OH was synthesized via the condensation polymerization of LA in a rotary evaporator equipped with a nitrogen inlet purge. The rotation speed was approximately set to 120 rpm. BDO was added to the flask after 4.5, 6.25, and 8 h for 6-, 8-, and 10-h runs, respectively. For all runs, the temperature range was 140–170°C, and the reduced pressure ranged from 700 to 200 mbar.

The structures of the PLA-OH samples synthesized by the condensation polymerization of LA and 1,4-BDO are shown in Scheme 1 in a reaction proposed by Hiltunen et al.[11]

Design of the experiment

To investigate the simultaneous effect of the reaction time, catalyst concentration, and BDO content on the MW of PLA-OH, the design expert methodology was used. In this study, three 3-level factors for the reaction time, molar ratio of $Sn(Oct)_2$ to LA monomer, and molar ratio of BDO to LA monomer were used. For the experimental design, response surface methodology (RSM) based on Box–Behnken design was used; this was specially made to require only three levels, which were coded as −1, 0, and +1. So, the number of reactions containing three center points was reduced to 15 experiments. This procedure creates designs with desirable statistical properties but, most importantly, with only a fraction of the experiments required for a three-level factorial. The Box–Behnken design also considers interactions between three parameters, which cannot be assumed in three 3-level factors in the Taguchi method.

The different levels of each factor are shown in Table I. The response for this design mode would be the MW of the PLA-OH samples, which was determined by both ^{1}H-NMR and GPC.

All of the experiments and values of the parameters based on the Box–Behnken RSM are listed in Table II. It should be noted that runs 1, 8, and 9 are the center points of Box–Behnken design.

After the polymerization of each PLA-OH sample, the molten polymer was allowed to cool down to room temperature before characterization.

Characterization and determination of the MW

To identify the physicochemical structures of the PLA-OH samples, Fourier transform infrared (FTIR) spectroscopy was conducted with a PerkinElmer 65 (Waltham, United States) FTIR spectrometer (resolution = 8.0 cm^{-1}, number of scans = 5). The ^{1}H-NMR spectra of the PLA-OH samples were recorded on a Bruker 500 NMR spectrometer with deuterated

TABLE I
Three Levels of Reaction Parameters for the PLA-OH Synthesis

Parameter	Level 1	Level 2	Level 3
Reaction time (h)	6	8	10
Catalyst concentration (mol %)[a]	0.05	0.10	0.15
BDO concentration (mol %)[a]	2	3	4

[a] Molar percentage based on the LA monomer amount.

TABLE II
Values of the Variables on the Basis of the Box–Behnken RSM

Experiment	Input variable		
Run	Time (h)	Catalyst (mol %)	BDO (mol %)
1	8	0.10	3
2	8	0.05	4
3	10	0.10	4
4	8	0.15	4
5	10	0.15	3
6	6	0.10	4
7	6	0.15	3
8	8	0.10	3
9	8	0.10	3
10	6	0.10	2
11	10	0.05	3
12	6	0.05	3
13	10	0.10	2
14	8	0.05	2
15	8	0.15	2

acetone as the solvent. The number-average degree of polymerization (DP_n) and number-average molecular weight ($M_{n,NMR}$) of the PLA-OHs were calculated from ^{1}H-NMR spectroscopy.[11] The number-average molecular weight (M_n), weight-average molecular weight (M_w), and polydispersity index (PDI) of the PLA-OHs were also determined by GPC (Agilent 1100 series instrument; the column was calibrated with polystyrene standards, the solvent was chloroform, the temperature was set to 30°C, and the flow rate was 1 mL/min).

RESULTS AND DISCUSSION

Structure of the PLA-OH samples (FTIR results)

The FTIR spectrum of the first PLA-OH sample (sample No. 1) is shown in Figure 1. The presented spectra were characterized as follows. The peaks located at 2995 and 2945 cm^{-1} were related to asymmetric and symmetric —CH— stretching, respectively. —CH— asymmetric and deformation banding was present at 1360 and 1380 cm^{-1}, respectively. The sharp peak at 1756 cm^{-1} was related to the C=O group, and the one occurring at 1455 cm^{-1} was for —CH$_3$ banding. The poor but clear peak appearing at 1268 cm^{-1} was attributed to the C—O stretching of the ester groups along the polymer chains. There were also four peaks located in the region between 1300 and 1040 cm^{-1}; at 1183, 1130, and 1090 cm^{-1} (C—O—C stretching); and at 1045 cm^{-1} (—OH bending). The two peaks appearing at 870 and 750 cm^{-1} were assigned to the —C—C— stretching, which were located in the amorphous and crystalline phases, respectively, as described by Auras et al.[18] Finally, the peak occurring at 3520 cm^{-1} was attributed to the —OH group that were expected to be at the chain ends.

The FTIR spectra of the other samples were similar to the first one described previously. For instance, four of them (samples 1, 4, 5, and 7) are shown in Figure 2. It can be seen that the other samples had the same peaks as sample 1, and so we concluded that the structures of all of the samples were similar to each other.

MWs of the PLA-OH samples (H-NMR and GPC results)

The DP_n and $M_{n,NMR}$ values of the synthesized polymers were calculated from ^{1}H-NMR spectroscopy. The signals occurring at different chemical shifts were as follows:[6]

- The chemical shifts at 5.18 ppm (δH^a) and 4.36 ppm ($\delta H^{a'}$) were assigned to methine protons in the repeating unit and at the terminus of the PLA-OH chains, respectively.
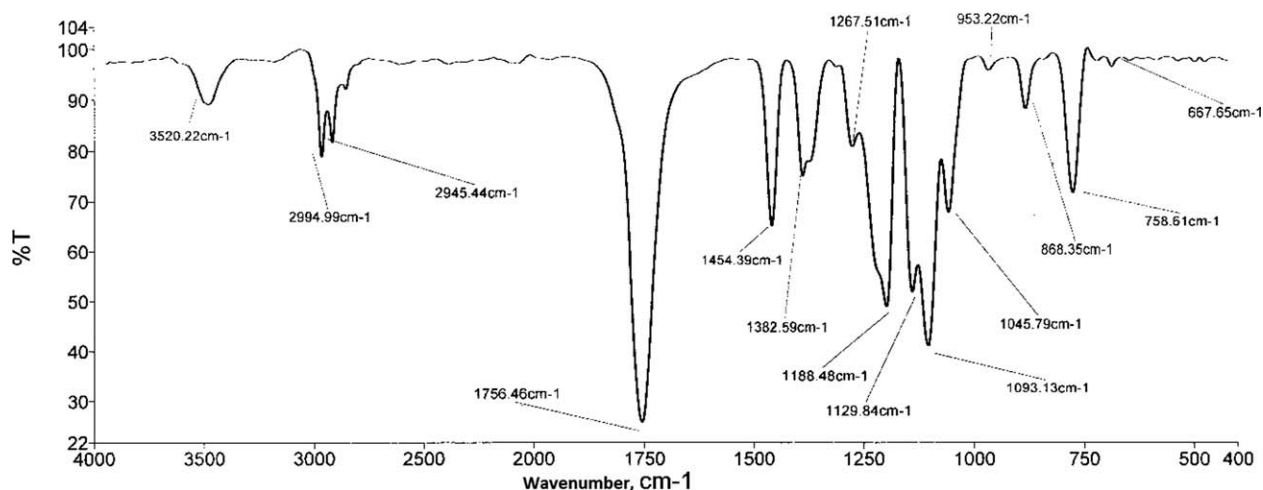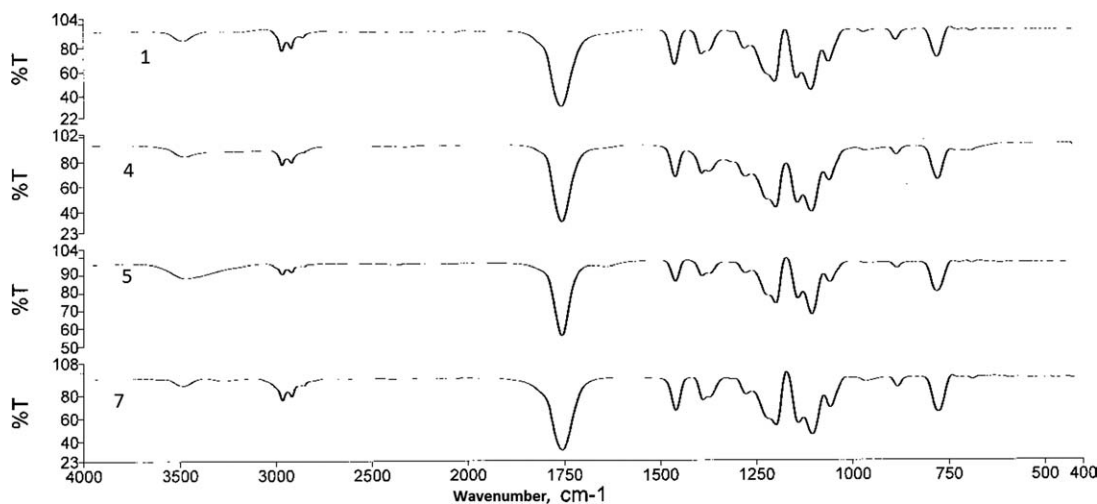

Figure 1 FTIR spectrum of PLA-OH1.

Figure 2 FTIR spectra of samples 1, 4, 5, and 7.

- The chemical shifts at 1.58 ppm (δH^b) and 1.48 ppm ($\delta H^{b'}$) were related to methyl protons in the repeating unit and at the terminus of the PLA-OH chains, respectively.
- The chemical shifts at 4.11 ppm (δH^c) and 1.68 ppm (δH^d) were attributed to the outer and inner methylene protons, respectively, of 1,4-BDO in the chain.
- The chemical shifts at 5.06 ppm (δH^i) and 1.70 ppm (δH^{ii}) were related to the formation of cyclic lactide, which was due to the randomness of the ester exchange reaction and, consequently, the formation of cyclic derivatives along with linear chains.[19]

The chemical structure having different protons and the corresponding chemical shifts for one of the samples (e.g., run 1, PLAOH1) are shown in Figure 3, and the data related to the intensities of the peaks for the other samples are listed in Table III.

DP_n and $M_{n,\mathrm{NMR}}$ of each sample could be calculated according to the following equations [eqs. (1) and (2)]:[6]

$$D_p = 2(I_{5.18} + I_{4.36})/I_{4.36} \qquad (1)$$

$$M_n = 72D_p + 88 + 2 \qquad (2)$$

where D_p is the average degree of polymerization, and I is the peak intensity of chemical shift. $I_{5.18}$ and $I_{4.36}$ are the intensities of the methine groups inside the chain and at end of the PLA-OH chain, respectively; 2 and 72 are the masses of hydrogen at the chain end and the repeating unit of PLA chains, respectively; and finally, 88 is the mass of residue of 1,4-BDO inside the chain.[6]

The $M_{n,\mathrm{NMR}}$ values of the samples are shown in Table IV. It can be seen that the variation of the reac-tion parameters through the ranges seen in Table IV resulted in MWs of the samples between about 1130 and 2130 g/mol.

The MWs of the PLA-OH samples were also investigated by GPC. The results, including M_n, M_w, and PDI, are listed in Table IV. As shown in the table, the PDIs of all of the samples were between 1 and 2, which are acceptable values for condensation polymers. The GPC spectrum of the first sample (run 1, PLA-OH1) is shown in Figure 4. The other GPC spectra of the samples were similar to the that of the first sample and are not shown here. As shown in Figure 4, the molecular weight distribution (MWD) curve was almost wide; this confirmed the condensation polymerization nature. Another important issue was that all of the MWs from GPC were greater than those from NMR analysis. Furthermore, no monotonic behavior was observed for the MWs from the GPC results. The reason was that the
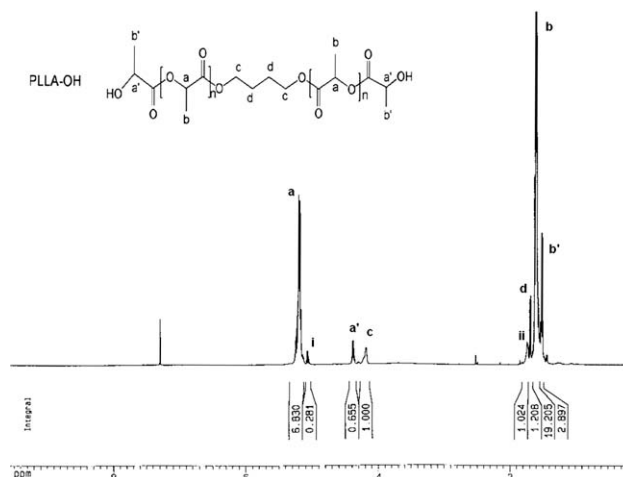

Figure 3 Chemical structure of PLA-OH and the corresponding ^{1}H-NMR chemical shifts for the first sample (run 1, PLAOH1).

TABLE III
Peaks Intensities at Different ^{1}H-NMR Shifts

Run	Sample	$I_{5.18}$	$I_{4.36}$	$I_{1.58}$	$I_{1.48}$	$I_{4.11}$	$I_{1.68}$	$I_{5.06}$	$I_{1.70}$
1	PLAOH1	9.7050	0.9812	24.183	4.070	1.000	2.441	0.323	—[a]
2	PLAOH2	5.6094	0.7023	14.577	2.574	1.000	1.485	—[a]	1.485
3	PLAOH3	6.4491	0.5691	17.379	2.300	1.000	0.816	0.229	0.816
4	PLAOH4	5.0876	0.6034	13.656	2.329	1.000	0.939	0.125	0.939
5	PLAOH5	8.9619	0.8382	24.699	2.824	1.275	1.357	—[a]	1.357
6	PLAOH6	4.8003	0.7722	12.162	1.994	1.000	1.428	0.176	1.428
7	PLAOH7	7.4107	0.8978	20.878	3.833	1.000	1.888	0.284	—[a]
8	PLAOH8	7.3032	0.7623	18.385	3.106	1.000	1.004	0.291	1.020
9	PLAOH9	6.3561	0.6545	19.205	2.897	1.000	1.208	0.281	1.024
10	PLAOH10	8.7925	1.0976	23.762	3.663	1.000	1.064	0.459	1.042
11	PLAOH11	6.5164	0.5445	17.170	2.209	1.000	0.988	0.272	0.989
12	PLAOH12	7.7028	1.0239	22.142	4.210	1.000	1.870	0.224	—[a]
13	PLAOH13	11.915	0.904	33.296	4.075	1.000	1.550	0.454	1.371
14	PLAOH14	11.498	0.927	32.713	3.994	1.000	1.236	0.587	1.236
15	PLAOH15	9.0021	0.9770	25.528	4.190	0.976	2.157	0.403	—[a]

[a] Not identified (zero value)

calibration for GPC was difficult, especially at low MW. This observation was also reported by Yoo and Kim.[16] In this work, we analyzed the MWs of samples obtained by both the ^{1}H-NMR and GPC techniques by experimental design and found that the MW variations were more monotonic and also liable in case of NMR analysis. So, because of these observations and also because the scale of NMR was much lower than that of GPC, we used $M_{n,\text{NMR}}$ to analyze and predict the final formula, as discussed in the following sections.

Comparing MWs of the different synthesized samples

The reaction parameters for analysis were reaction time, catalyst concentration, and 1,4-BDO concentration. The first reaction parameter was reaction time. It was clear that increasing the reaction time would reasonably result in an increment of MW of the final polymer.[20] As shown in Table IV, in comparisons of samples PLAOH10 and PLAOH13, samples PLAOH3 and PLAOH6, or samples PLAOH5 and PLAOH7, for instance, an increase in the reaction time, with the two other parameters fixed, led to an increase in MW.

In the case of catalyst concentration, we expected that an increase in the catalyst amount would lead to a decrease in MW because a higher catalyst concentration would produce more active centers to initiate the polymerization reaction, so the proportion of monomers for each active center would decrease and lead to a lower MW for each chain. This could also be seen from the data presented in Table IV; for example, in a comparison of PLAOH14 and PLAOH15, in which the time and 1,4-BDO amount were fixed, a catalyst increase led to an M_n decrease. The same trend was also observed in a comparison of PLAOH5 and PLAOH11.

TABLE IV
Data Obtained from ^{1}H-NMR and GPC Analysis

| Run	Sample no.	DP_n	$M_{n,\text{NMR}}$ (g/mol)	M_n (GPC; $\times 10^3$)	M_w (GPC; $\times 10^3$)	PDI
1	PLAOH1	21.78	1658	2.6	4.1	1.58
2	PLAOH2	17.97	1384	2.4	3.6	1.49
3	PLAOH3	24.66	1866	3.0	5.0	1.68
4	PLAOH4	18.86	1449	2.5	3.8	1.55
5	PLAOH5	23.38	1774	3.1	5.1	1.65
6	PLAOH6	14.43	1129	2.0	2.9	1.46
7	PLAOH7	18.51	1422	2.5	4.6	1.86
8	PLAOH8	21.16	1614	2.7	4.1	1.52
9	PLAOH9	21.42	1632	2.6	4.1	1.59
10	PLAOH10	18.02	1387	2.5	3.7	1.49
11	PLAOH11	25.94	1958	3.0	5.0	1.66
12	PLAOH12	17.05	1317	2.3	3.3	1.43
13	PLAOH13	28.36	2132	3.0	4.8	1.61
14	PLAOH14	26.81	2020	2.8	4.3	1.54
15	PLAOH15	20.43	1561	2.9	4.6	1.61
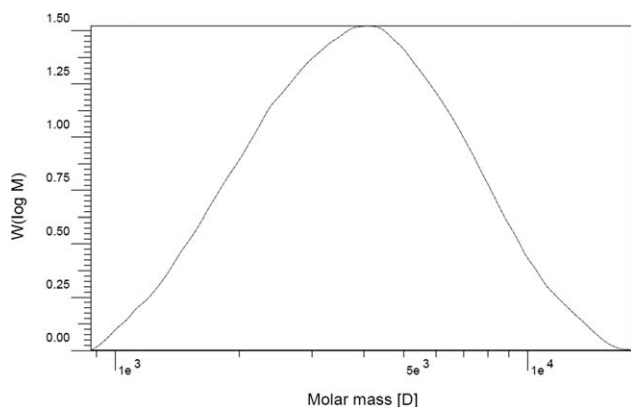
Figure 4 GPC spectrum of the first PLAOH sample (run 1, PLAOH1). W is the distribution function and M is molecular weight.

For the last parameter, 1,4-BDO, its concentration could affect the MW of the polymer.[21,22] A greater concentration of 1,4-BDO in the reaction mixture resulted in a decrease in the MW of the PLA-OH polymer chains because an increase in BDO concentration interfered with the routine polymerization path of LA and caused the chains to have fewer monomers. This trend can be seen in Table IV, for instance, in a comparison of PLAOH4 and PLAOH15. The same behavior can also be seen in comparisons of PLAOH6 and PLAOH10 and PLAOH3 and PLAOH13.

It can also be seen in Table IV that samples PLAOH1, PLAOH8, and PLAOH9, which were the

center points of the experimental design, had almost the same MW (ca. 1630 g/mol), so the repeatability of the experiments was verified.

Analysis of the MWs on the basis of Box–Behnken design

All of the MWs listed in Table IV were analyzed on the basis of the Box–Behnken RSM with MINITAB software (Release 13.1, Pennsylvania State University, Pennsylvania, US).

Effect of the reaction time

Figure 5 shows the different MWs of the PLA-OH samples at a 6-h hold value. For samples with 6 h of reaction time, when the 1,4-BDO concentration was increased up to 3 mol %, the MW sensitivity to 1,4-BDO gradually increased; after that, the MW sensitivity decreased as the 1,4-BDO concentration was increased up to 4 mol %. In fact, up to a 3 mol % 1,4-BDO concentration, the MW decreased with increasing catalyst concentration (Fig. 4), which is a usual trend. However, after that, that is, for 1,4-BDO concentrations greater than 3 mol %, an increase in the catalyst concentration led to an increase in MW, which is an unusual and unexpected trend based on conventional findings. The possible reason is as follows: the high concentration of catalyst produced more active centers to initiate polymerization when compared to lower catalyst concentrations, so the number of chains
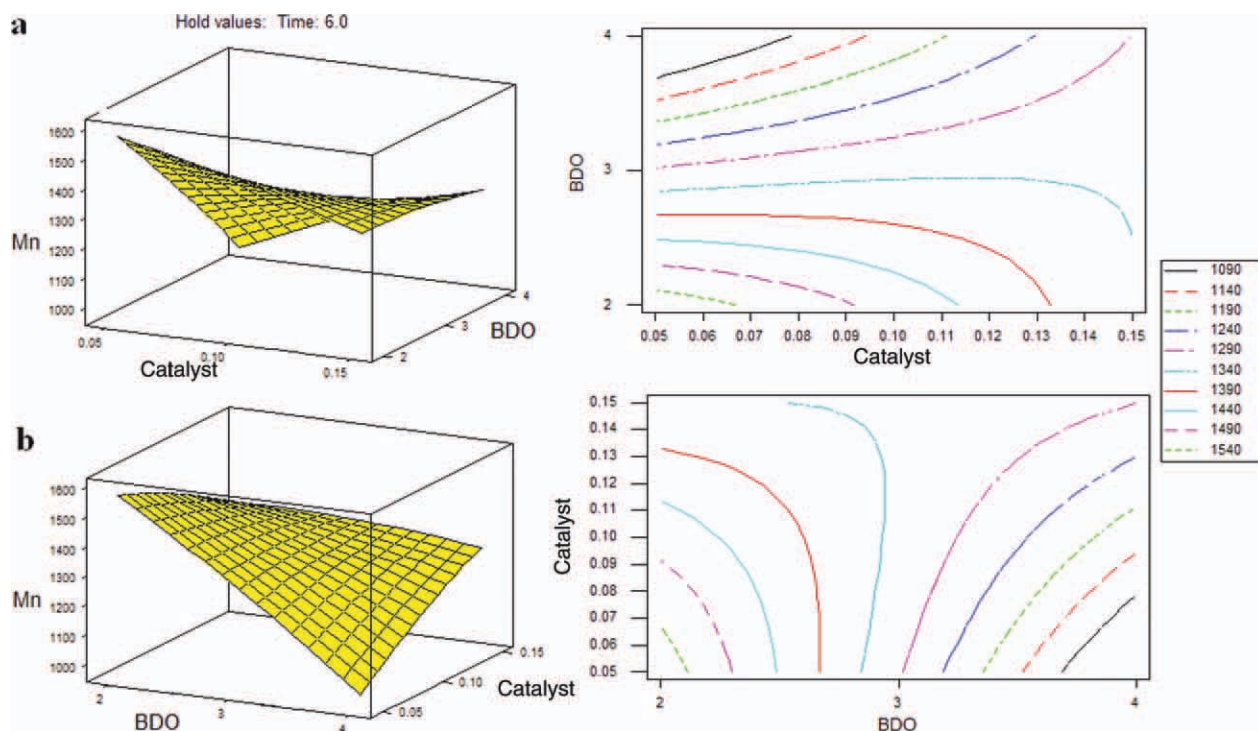

Figure 5 MW changes obtained in a fixed 6 h of reaction time. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]
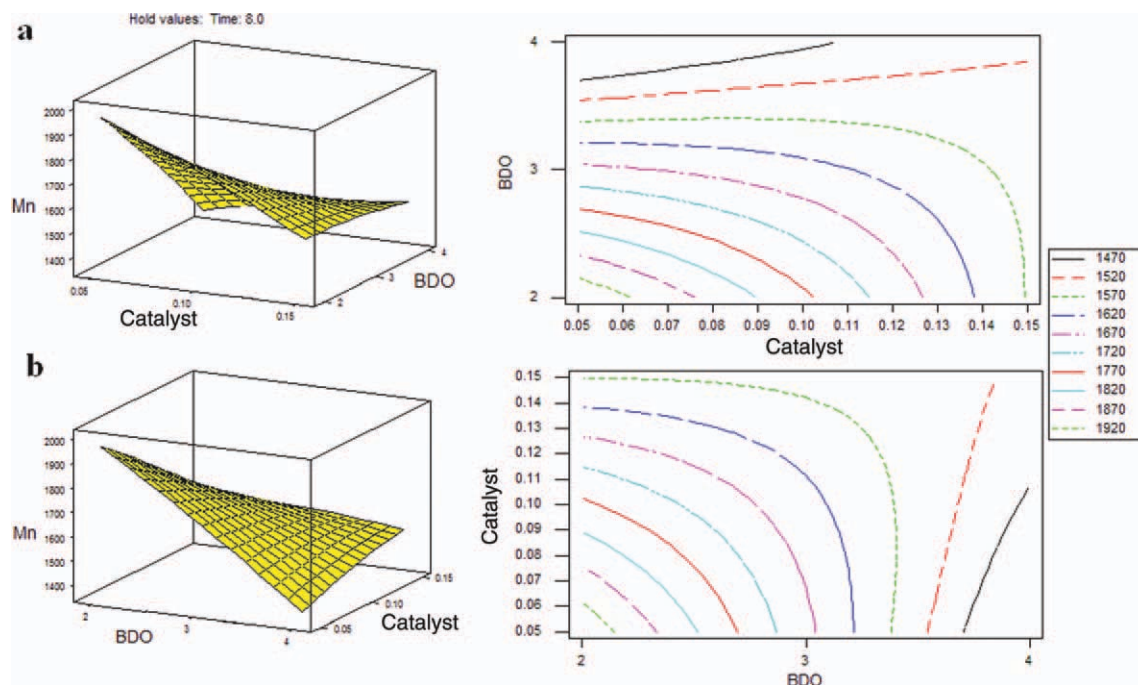
Figure 6 MW changes for a fixed 8 h of reaction time. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

increased, and the proportion of monomers for linking to active centers decreased. This resulted in a lower MW of the polymer. In this situation, if the reaction does not proceed for a long time (i.e., low reaction times, e.g., 4.5 h, for 6-h reaction time conditions), the resulting chains may have a low degree of polymerization, and they have still the potential to react with each other or another reactant inside the mixture. That is, they have the same reactivity as the monomers and low-molecular-weight reactants, and their rate constants are comparable to that of the monomers. Therefore, when we added high amounts of 1,4-BDO (e.g., 4 mol %) to the reaction mixture after 4.5 h after the beginning of the polymerization, it could react with the polymer chains of short lengths to produce longer chains instead of making PLA-OH polymers. Consequently, the MW of the final polymer increased at the end of the reaction. This unusual behavior occurred for 6 h of reaction time and 3 mol % of 1,4-BDO.

For 8 h of reaction time, the usual trend, discussed previously, was observed for 1,4-BDO concentrations up to around 3.5 mol %, and the unusual trend for BDO concentrations higher than 3.5 mol % was observed (Fig. 6). In other words, for 8 h of reaction time, which was higher than 6 h of reaction time, 1,4-BDO concentrations higher than 3 mol % caused the unusual trend (we called it the *critical BDO concentration*).

Therefore, it seemed that increasing reaction time caused the critical 1,4-BDO concentration to shift to higher values. This was made clear by an investigation of the data presented in Table IV and analysis of the 10-h reaction time (Fig. 7), for which the usual

trend was observed for all 1,4-BDO concentrations used in our study (2, 3, and 4 mol %).

So, we concluded that increasing the reaction time, in general, caused the MW of the prepolymers to increase. Another conclusion we drew in our study was that the MW sensitivity to reaction time was greater than that of the two other reaction parameters (i.e., catalyst and 1,4-BDO concentrations).

Effect of the catalyst concentration

From the data presented in Table IV and also from the graphs related to the different hold values of the catalyst, it was obvious that a normal trend was observed for this parameter. Figures 8–10 show this finding. The only point worth considering is that the MW sensitivity to reaction time was higher than that to 1,4-BDO concentration, and this behavior became stronger with increasing catalyst concentration.

In the case of the catalyst, another important conclusion is that the effect of time on this parameter was more than that of 1,4-BDO. Changing the catalyst concentration to higher values made the MW of the samples more sensitive to time rather than 1,4-BDO in such a way that for 0.15 mol % catalyst, the MW of the samples was almost independent of the 1,4-BDO changes (see Fig. 8).

Effect of the 1,4-BDO concentration

For low concentrations of this parameter (i.e., 2 mol %), a normal trend was observed (Fig. 11); this was
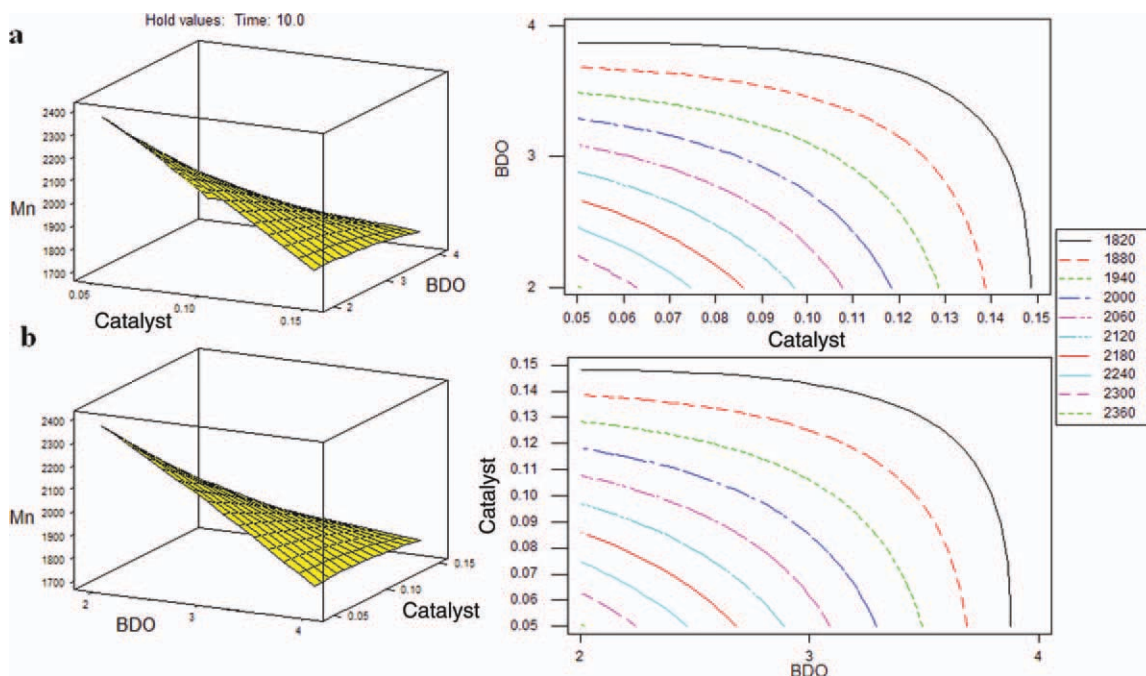
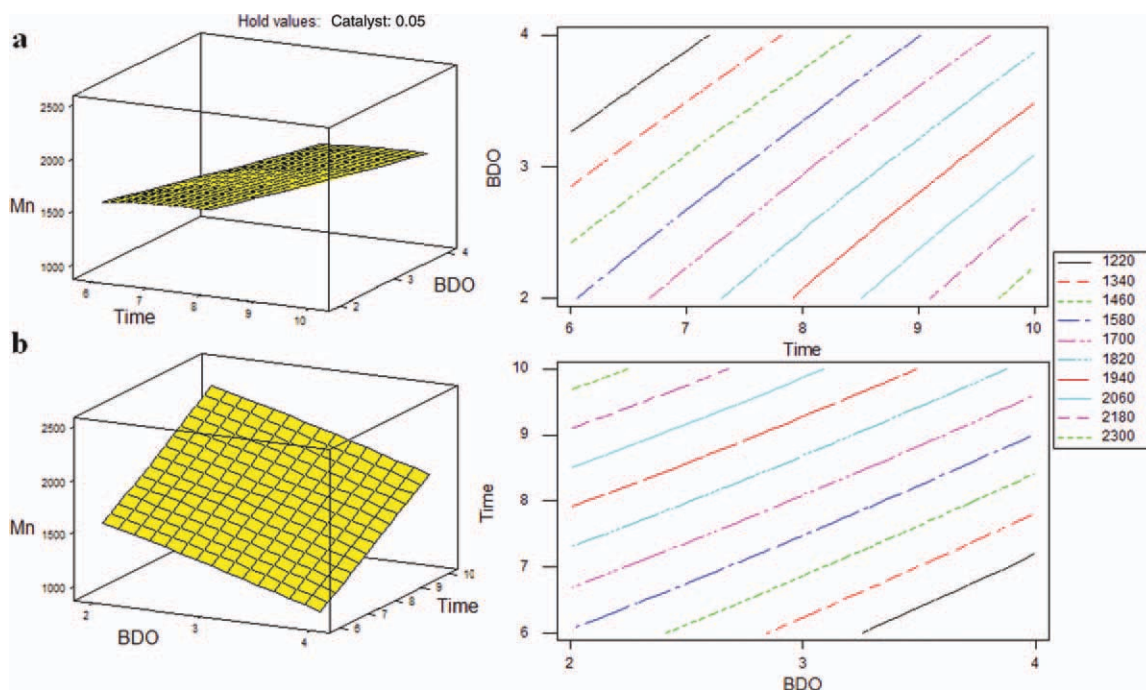**Figure 7** MW changes for a fixed 10 h of reaction time. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

concluded earlier in the reaction time analysis. Here, the only note is that the MW sensitivity to reaction time was greater than that to catalyst concentration. This behavior was also observed when we analyzed the catalyst concentration. This kind of behavior led us to the conclusion that the MW sensitivity to reac-

tion time was greater than that to the other two parameters.

When the BDO concentration was increased to 3 mol %, no catalyst sensitivity for MW was observed at low reaction times (Fig. 12), whereas at higher reaction times, a little sensitivity to the catalyst

Figure 8 MW changes for a fixed 0.05 mol % catalyst amount. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]
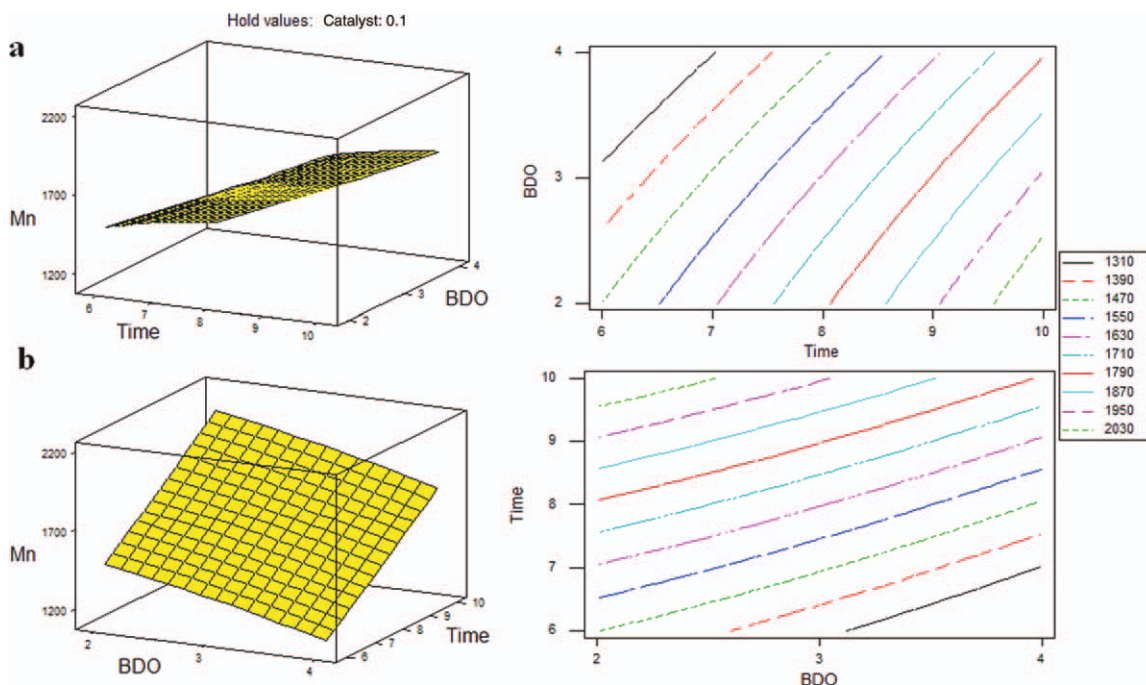
Figure 9 MW changes for a fixed 0.10 mol % catalyst amount. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

amount was observed, and the time sensitivity decreased. In fact, we slowly reached the BDO critical concentration. These behaviors can be seen in Figure 11.

For 4 mol % of 1,4-BDO, the sensitivity to reaction time gradually increased, and the sensitivity to catalyst concentration decreased so that for 10 h of reac-

tion time, no sensitivity to the catalyst was observed (Fig. 13).

For the 1,4-BDO amount, we concluded that when the 1,4-BDO concentration was changed, the MW sensitivity to time was still greater than that to the catalyst. This sensitivity gradually increased with up to 3 mol % of BDO and, after that, decreased until
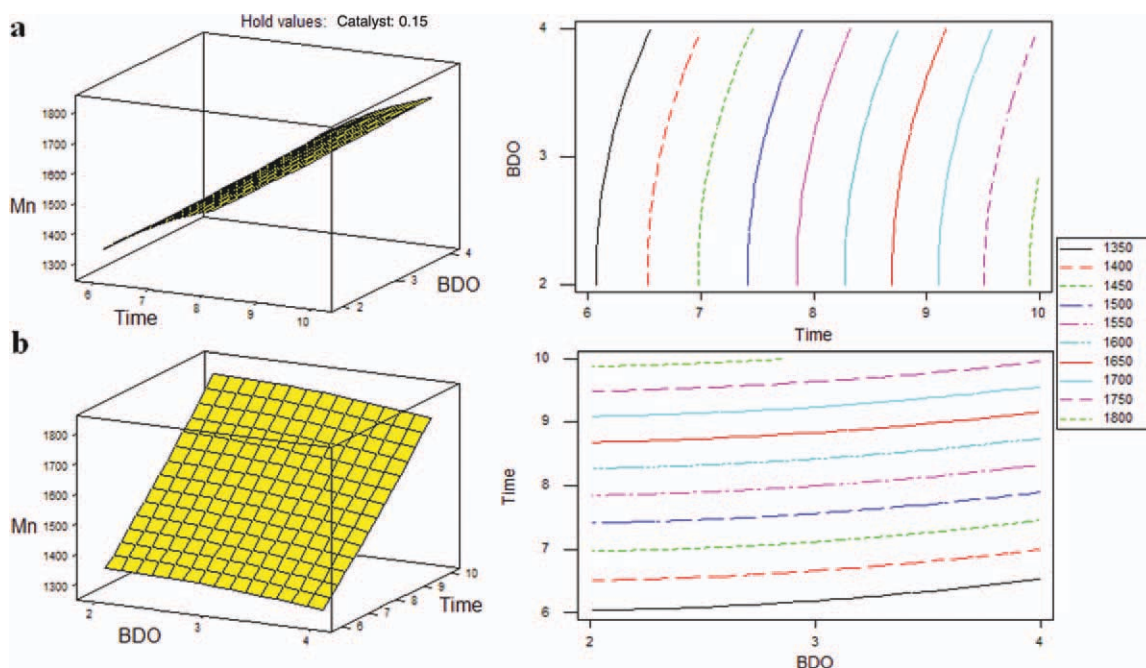

Figure 10 MW changes for a fixed 0.15 mol % catalyst amount. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]
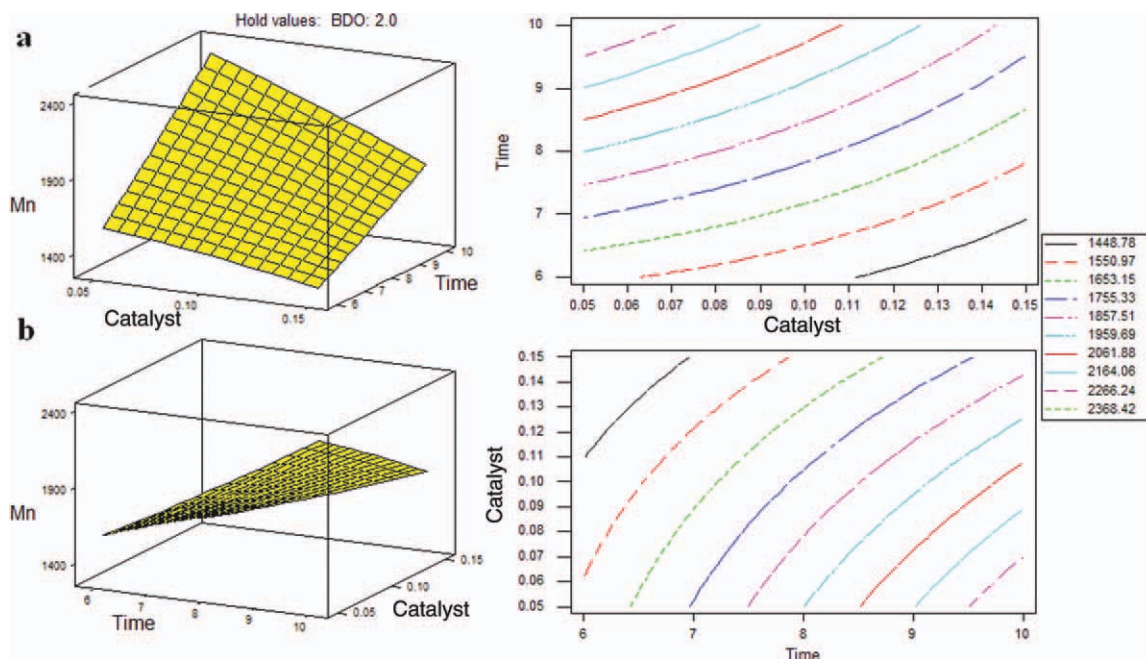
Figure 11 MW changes for a fixed 2 mol % 1,4-BDO amount. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

the BDO concentration reached 4 mol %. Another important result was that for 1,4-BDO concentrations higher than 3 mol %, the unusual trend was observed at low values of reaction time, whereas this trend was normal for long reaction times.

Finally, we came to the conclusion that the catalyst and 1,4-BDO concentrations had almost the

same effect on the MWs of the PLA-OH samples, and increasing their concentrations made this effect stronger.

At the end of our experiment, an equation for MW of the PLAOH samples as a function of these three reaction parameters, including the reaction time, catalyst concentration, and 1,4-BDO concentration, was
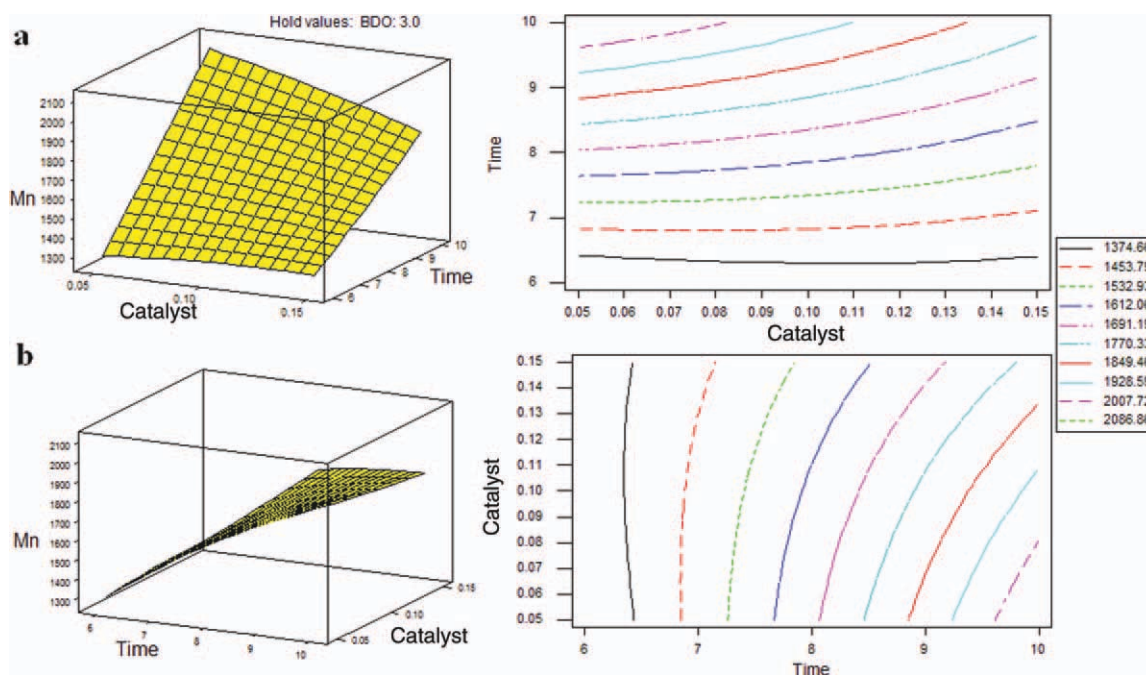

Figure 12 MW changes for a fixed 3 mol % 1,4-BDO amount. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]
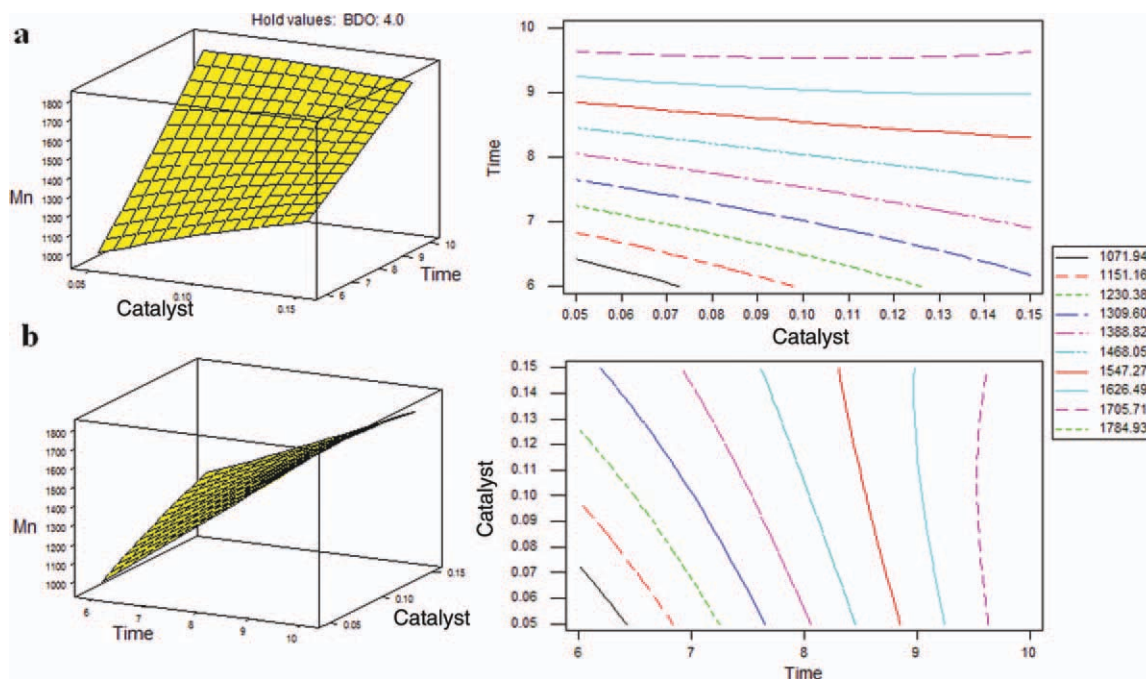
Figure 13 MW changes for a fixed 4 mol % 1,4-BDO amount. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

extracted by MINITAB software with Box–Behnken [eq. (3)]:

$$1154.9 + 188.7T - 1673.9C - 350.7B + 3.3T^2 \\ - 4645.8C^2 - 10.3B^2 - 817.1TC - 1.0TB - 2620.7CB \tag{3}$$

where T is the reaction time (h), C is the molar percentage of catalyst based on the LA amount, and B

is the molar percentage of 1,4-BDO based on the LA amount. The analysis for our response was statistically significant at greater than 99% of confidence, with $R^2 = 0.944$. Figure 14 shows the predicted values [the values of MWs calculated by eq. (3)] versus the actual values (the actual values of MW calculated with the ^{1}H-NMR peak intensities) of the response. As shown in this figure, the actual values and the values predicted from the software were fairly acceptable.

On the basis of our experimental design analysis, we found that the highest MW of PLA-OH was obtained when the reaction parameters were follows: 2 mol % of 1,4-BDO, 0.07 mol % of catalyst, and 9 h 40 min of reaction time.

CONCLUSIONS

In this study, we synthesized low-molecular-weight PLA-OHs via the condensation polymerization of LA with stannous octoate [Sn(Oct)$_2$] as a catalyst along with small amount of 1,4-BDO, and the effects of the reaction time, molar ratio of catalyst based on the LA content, and molar ratio of 1,4-BDO based on the LA content on the MW and MWD of PLA-OH were investigated by RSM. The structure of the polymers was identified by FTIR spectroscopy. The MW and MWD values of the synthesized polymers were investigated by ^{1}H-NMR and GPC. The results show increasing reaction time results with increasing MW of the PLA-OHs. The MWs of the PLA-OH polymers also increased with decreasing amounts of catalyst.
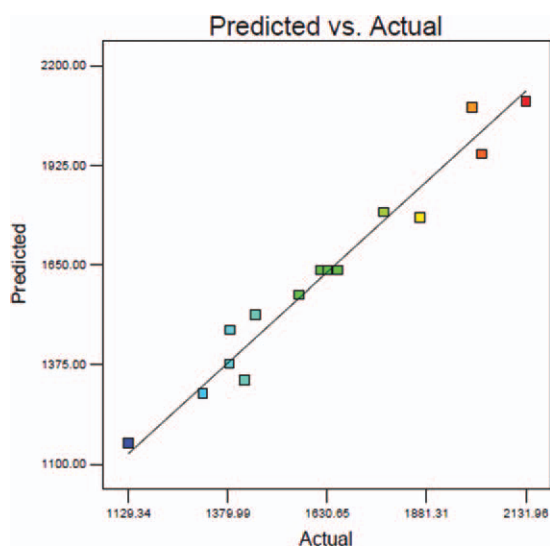

Figure 14 Predicted versus actual values of the response (MW of PLA-OH). The solid line shows the predicted values, and the rectangular dot points show the actual values. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Finally, an equation was developed to predict the MWs of the PLA-OHs on the basis of the reaction parameters, including the reaction time, amount of catalyst, and 1,4-BDO content.

References

1. Nair, L. S.; Laurencin, C. T. Prog Polym Sci 2007, 32, 762.
2. Gupta, B.; Revagade, N.; Hilborn, J. Prog Polym Sci 2007, 32, 455.
3. Cooper, T. R.; Storey, R. F. Macromolecules 2008, 41, 655.
4. Borda, J.; Bodnar, I.; Keki, S.; Sipos, L.; Zsuga, M. J Polym Sci Part A: Polym Chem 2000, 38, 2925.
5. Gu, S. Y.; Yang, M.; Yu, T.; Ren, T. B.; Ren, J. Polym Int 2008, 57, 982.
6. Zeng, J.-B.; Li, Y.-D.; Zhu, Q.-Y.; Yang, K.-K.; Wang, X.-L.; Wang, Y.-Z. Polymer 2009, 50, 1178.
7. Rich, J.; Tuominen, J.; Kylmä, J.; Seppälä, J.; Nazhat, S. N.; Tanner, K. E. J Biomed Mater Res (Appl Biomater) 2002, 63, 346.
8. Ren, J.; Wang, Q.; Gu, S.; Zhang, N.; Ren, T. J Appl Polym Sci 2006, 99, 1045.
9. Helminen, A.; Kylmä, J.; Tuominen, J.; Seppälä, J. V. Polym Eng Sci 2000, 40, 1655.
10. Hiltunen, K.; Seppälä, J. V.; Härkönen, M. J Appl Polym Sci 1997, 63, 1091.
11. Hiltunen, K.; Härkönen, M.; Seppälä, J. V.; Väänänen, T. Macromolecules 1996, 29, 8677.
12. Tuominen, J.; Seppälä, J. V. Macromolecules 2000, 33, 3530.
13. Hiltunen, K.;Seppal a, J. V. J Appl Polym Sci 1998, 67, 1011.
14. Li, S. M.; Garreau, H.; Vert, M. J Mater Sci Mater Med 1990, 1, 123.
15. Kylmä, J.; Tuominen, J.; Helminen, A.; Seppälä, J. Polymer 2001, 42, 3333.
16. Yoo, D. K.; Kim, D. Macromol Res 2005, 13, 68.
17. Sedlarik, V.; Kucharczyk, P.; Kasparkova, V.; Drbohlav, J.; Salakova, A.; Saha, P. J Appl Polym Sci 2010, 116, 1597.
18. Auras, R.; Harte, B.; Selke, S. Macromol Biosci 2004, 4, 835.
19. Montaudo, G.; Montaudo, M. S.; Puglisi, C.; Samperi, F.; Spassky, N.; LeBorgne, A.; Wisniewski, M. Macromolecules 1996, 29, 6461.
20. Odian, G. Principles of Polymerization, 4th ed.; Wiley: Hoboken, NJ, 2004.
21. Rudin, A. Elements of Polymer Science and Engineering; Elsevier Science & Technology: New York, 1998.
22. Sandler, S. R.; Karo, W. Polymer Syntheses; Gulf Professional: Oxford, United Kingdom, 1992; Vol. 1.