Journal of Applied Polymer Science

Radiopaque polyurethanes with flexible iodine-containing chain extender

Teng Wang,[1] Zhihua Zhang,[1] Ran Song,[1] Xinlin Tuo,[1] Jigong Wu[2]

[1]Key Laboratory of Advanced Materials (MOE), Department of Chemical Engineering, Tsinghua University, Beijing, People's Republic of china

[2]Department of Orthopaedics, the 306th Hospital of PLA, Beijing, People's Republic of china

Correspondence to: X. Tuo (E-mail: tuoxl@tsinghua.edu.cn)

ABSTRACT: Iodinated polyurethanes (IPUs) with radiopaque property were prepared using poly(oxytetramethylene) glycol, 4,4′-diphenylmethane diisocyanate, and a novel chain extender. The chain extender, described as N-(1,3-dihydroxypropan-2-yl)-2,3,5-triiodobenzamide, was synthesized in two steps from 2-aminopropane-1,3-diol and 2,3,5-triiodobenzoic acid with a high yield. A thorough study on the chemical structure, mechanical properties, radiopacity, and physiological properties of the IPUs was conducted. It is revealed that with increasing content of chain extender, the molecular weights of IPUs decreased slightly while the tensile modulus and breaking strength of IPUs increased significantly, illustrating an excellent comprehensive performance. With iodine content high to about 16 wt %, the IPU sample is equal to the aluminum plate with the same thickness in X-ray radiopacity, meaning that the synthesized polyurethanes are promising as radiopaque materials. The oxidative degradation and cytotoxicity tests illustrated a good performance of stability and biocompatibility for the IPUs. It confirmed that the as-synthesized IPUs are promising for biomedicine applications. © 2015 Wiley Periodicals, Inc. J. Appl. Polym. Sci. **2015**, *132*, 42693.

KEYWORDS: biomedical applications; polyurethanes; X-ray

Received 31 March 2015; accepted 2 July 2015

DOI: 10.1002/app.42693

INTRODUCTION

Owing to their highly designable properties, polyurethanes (PUs) have been used increasingly as medical materials. However, the fact that conventional PUs are radiolucent and cannot be noninvasive evaluated significantly limits their further applications. Nowadays, radiopaque PUs are highly concerned for their potential applications as implanted materials in various medical fields, such as cardiovascular implants, prostheses, orthopedic implants, and controlled drug release devices, for the possibility of postoperative assessment in the fate of the medicine using X-radiography.[1]

The key to enduing PUs with radiopacity lies in introducing high-atomic-number elements to PUs to increase the absorption of X-ray. A primary method to approach radiopaque PUs is blending PUs with metal powders, metal salts,[2–4] or nanoparticles.[5] However, this method encounters the potential risk that inorganic ions can leach into the body fluid, leading to poor mechanical strength and systemic toxicity in long-term implants.[6] To improve the stability of the process, metal complexes are introduced in this method, which reduces the exudation of metal to a certain extent. However, the radio pacifying atoms of the complexes can still run off in a long term due to absorption of water, which leads to unexpected hydrolysis.[7]

Another approach to prepare radiopaque PUs is covalently attaching certain heavy elements to the polymer chains. Halogen is widely applied in this method due to its high radiopacity, sufficient atomic number, and comprehensive chemical and medical influence. It has been reported that a catheter made by PUs with brominated glycols could be used as cardiovascular, balloon wedge pressure and balloon pacing catheters.[8] Tetrabromo dipentaerythritol was also used to endue PUs with radiopacity.[9,10] The main limitation of brominated chain extenders is that the useful radiopaque properties are accompanied with a high amount of brominated chain extender, which may result in a relatively large hard segment ratio, leading to stiffness and toxicity of the resulting PU.

Since iodine has a greater mass attenuation coefficient than bromide, there are more investigations about iodine in the medical field. There are numerous of reports about preparing radiopaque polymers through copolymerization with iodinated block, such as derived tyrosine,[11] ε-caprolactone,[12] cellulose mixed esters,[13] acrylate,[14] etc. Blends of PUs with diiodobenzoate and/

or tetraiodobenzoate were used to form medical surgical tubing with radiopacity.[15] Radiopaque thermoset polymer was prepared using triiodobenzoyl glycerol monoester and so on.[16] 2,2-Bis (hydroxymethyl) propane-1,3-diyl bis(2,3,5-triiodobenzoate) combined with lactide or caprolactone was used to prepare the electrospinning fibers of radiopaque poly(ester-urethanes), but the tensile strength of melt-spun poly(ester-urethane) monofilaments needed to be improved for potential textile applications.[17] Pendant-cleavable iodine substituted groups were used to prepare core–shell nanoparticles with radiopacity.[18] By reaction with active groups on the backbone, iodinated segments were introduced into PUs. Iodinated polyurethanes (IPUs) were prepared by the ammonolysis of pentaiodopropyl aromatic compounds onto Tecoflex.[19] The steric effect of rigid structure was avoided, but the ammonolysis reaction had low yield, resulting in low iodine content and broken hydrogen bonds, which weakened the mechanical strength of IPUs.

Moreover, the preparation of radiopaque PUs using iodinated chain extender has a broader scope and a higher reaction efficiency. In some reports, IPUs were prepared by adding 4,4′-isopropylidinedi- (2,6-diiodophenol) during PUs synthesis to realize a high radiopacity, with poly (oxytetramethylene) glycol as a soft segment.[1,20] Iodinated bisphenol A with poly(ε-caprolactone) diol was also used as a soft segment to prepare radiopaque PUs.[21,22] Some researchers used Iodinated hydroquinone bis(2-hydroxyethyl) ether as chain extender to prepare radiopaque PUs for biomedical application.[23] In another case, a chain extender of N,N′-bis-(3hydroxypropxyl)-2,3,5,6-tetraiodoterephthal-amide was designed to obtain radiopaque PUs with great radiopacity and favorable cytotoxicity.[24] However, the yields of preliminary reactions for the synthesis of chain extender and the mechanical properties of IPUs in the previous reports were not satisfactory.

Application of this type of IPUs was limited by the content of iodine and the harsh conditions of the reaction, which was due to the stiffness of iodinated aromatic structures in the main chain. It is a better approach to prepare IPUs using flexible chain extender to introduce the iodine to the side chain of IPU. Previously, IPUs were prepared using iodinated olefins (2,3-diiodo-2-butene-1,4-diol).[25] However, the existence of double bonds damaged the thermal stability of the materials greatly. Until now, researches on the flexible chain extender for IPU synthesis and property development are quite limited.

In this work, a novel iodinated aromatic compound, N-(1,3-dihydroxypropan-2-yl)-2,3,5-triiodobenzamide (DHTIBA) was synthesized by a two-step reaction and was used as a flexible chain extender to achieve radiopaque PUs. The chemical structure, mechanical properties, radiopacity, stability, and cytotoxicity of the obtained IPUs were studied and discussed. The as-synthesized IPUs had satisfactory radiopacity and physicochemical properties, illustrating a great potential for the application in biomedical fields.

EXPERIMENTAL

Materials

4,4′-Diphenylmethane diisocyanate (MDI, TCI Shanghai Development Co.) was filtrated after calefaction. Poly(tetramethyleneglycol) (PTMG, M_n=650, BASF China Co.) was dried under vacuum. Tetrahydrofuran (THF), dichloromethane, and dimethylformamide (DMF) (Beijing Chemical Reagent Co.) were kept over 4 Å molecular sieves. 2-Amino-1,3-propanediol (APDO, Adamas Reagent), 2,3,5-triiodobenzoic acid (TIBA, Internet Aladdin Reagent Database), and other reagents were used as received.

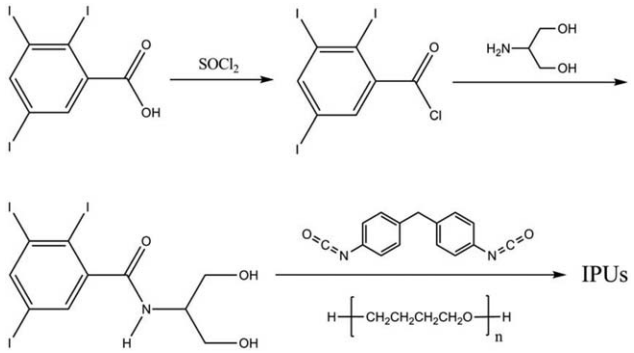
Characterization

Infrared spectra were obtained using a Fourier transform infrared spectrum instrument Nicolet 560-IR in transmission mode. Nuclear magnetic resonance (NMR) spectra were detected by a JEOL 600 MHz or 300 MHz instrument, JEOL JNM-ECA600 or ECA300, with tetramethylsilane (TMS) as the internal standard and DMSO-d_6, $CDCl_3$, or DMF-d_7 as the solvent, and D_2O as additive agent. Thermogravimetric analysis (TGA) was determined using TGA-Q5000 (TA Instruments, USA) in nitrogen atmosphere at a heating rate of 10°C/min. Differential scanning calorimetry (DSC) was determined using DSC-Q2000 (TA Instruments, USA) in nitrogen atmosphere at a heating rate of 10°C/min. Molecular weight distribution was obtained by refractive index detector Wyatt Optilab WREX-06 (Wyatt Technology Co., USA) and was fitted with a PL gel 5 μm mixed-D column, which was calibrated with linear polystyrene standards. THF was used as mobile phase at a flow rate of 1 mL/min.

In order to determine the mechanical properties, the samples were dissolved in DMF and cast to dumbbell-shaped spline. The thickness and width of samples were 1.0 mm and 6.6 mm, respectively. The tensile modulus and breaking strength were detected by TengDa Multifunction Tensile Testing Instrument in the stretching rate of 50 mm/min,

Table I. Feed Ratio, Molecular Weight, and Mechanical Properties of IPUs

Samples	Molar ratio of			Mn (×10^4)	PDI	Ideal iodine contents (wt %)	Experimental iodine contents (wt %)	Breaking strength (MPa)	Tensile modulus (MPa)	Hardness (HA)
	MDI	PTMG	DHTIBA							
IPU-1	1.1	1	0.1	7.9	2.0	3.9	2.8	6.0	0.4	69
IPU-2	1.2	1	0.2	7.6	2.8	7.2	4.3	6.8	0.6	70
IPU-3	1.3	1	0.3	6.7	2.0	10.0	7.1	17.5	2.6	74
IPU-4	1.4	1	0.4	6.6	2.4	12.4	10.1	17.1	3.3	79
IPU-5	1.5	1	0.5	5.4	2.1	14.5	12.2	38.4	8.1	88
IPU-6	1.6	1	0.6	4.9	2.5	16.4	15.9	39.1	9.7	92



Scheme 1. Schematic procedure of the synthesis of IPUs.

according to the testing standards GB528-76. The preset length between the two pneumatic grips of testing machine was 30 mm. The hardness of IPU samples was measured by Shore Hardness Tester TH200.

X-radiographs were detected with a standard clinical X-ray machine, General Electric XR/A, equipped with 2.5 mm aluminum filtration set at 60 kV with 10 mA current for 0.25 s. The samples were casted from DMF solution in mold of 2 cm × 2 cm to a thickness of 2 mm. An aluminum plate of the same thickness was chosen as the control group. Both experimental and control groups were covered with an extra 2.5 mm aluminum plate under the X-ray irradiation during the detection procedure. Graphics were progressed to obtain images with white background from the original X-radiographs with black background.

The samples for oxidative degradation were casted from DMF solution in mold of 2 cm × 2 cm to a thickness of 0.5 mm, and immersed in a 1 : 1 mixed solution of 10% H_2O_2 and 0.05 M $CoCl_2$ for 4 weeks. The solution was replaced every 4 days. Afterwards, the oxidized samples were thoroughly washed with deionized water, then detected by gel permeation chromatography (GPC) and scanning electronic microscopy (SEM).

The cytotoxicity of samples was detected by Cell Counting Kit-8 (CCK-8) method according to GB/T16175-2008. The cells were

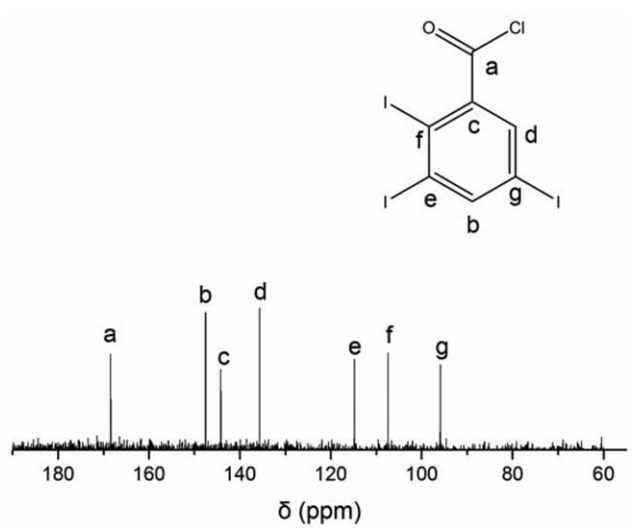


Figure 1. ^{13}C NMR spectra (300 MHz, $CDCl_3$) of TIBC.

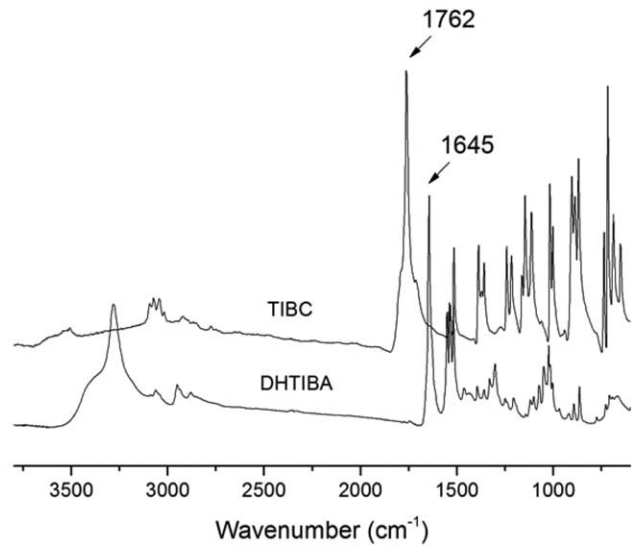


Figure 2. IR spectra of DHTIBA and TIBC.

C2C12 myoblasts from Peking Union Medical College Hospital. The samples were pretreated by phosphate buffered saline for three 5-min washes and immersed in ethanol solution of 75% for 30 min, then air-dried in the super-clean bench. After disinfected by ultraviolet, the samples were immersed in Dulbecco modified Eagle medium (DMEM) culture medium with 10% fetal bovine serum for 24 h in an incubator to obtain the material extract, according to the proportion of 1 mL DMEM culture medium per 6 cm^2 of sample. All the incubators that mentioned were set at 37°C. The cell suspension with the density of 1 × 10^4/mL was inoculated into a well plate, 100 μL cell suspension per well. The well plate was kept in the incubator for 6 h, then the wells on the plate were divided into groups of four. In the blank group, the agent was replaced by DMEM culture medium without cells. Different additive agent were added into the last three groups: 100 μL material extract was added in the experiment group, 100 μL DMEM culture medium in the negative control group, and 100 μL dimethyl sulfoxide in the

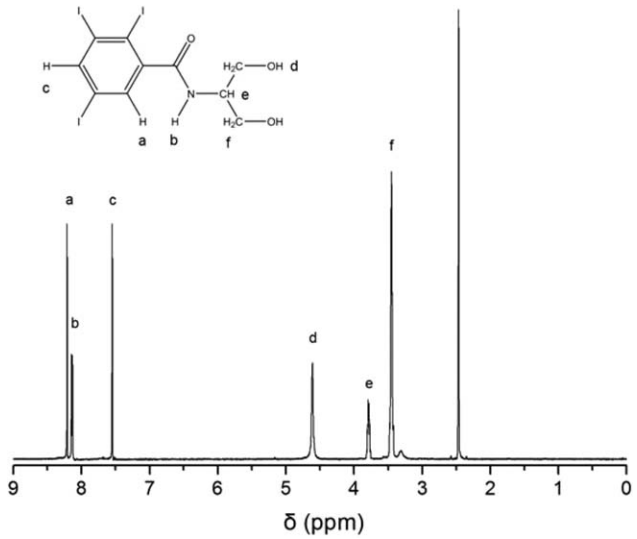


Figure 3. ^{1}H NMR spectra (600 MHz, DMSO-d_6) of DHTIBA.

positive control group. All the groups were cultivated for 72 h. After that, each well was added with 10 μL CCK-8 and cultivated for another 3 h. The absorbance was determined by the enzyme mark instrument Model 680 (Bio-Rad Laboratories Co., USA) at the wavelength of 450 nm. The relative growth rate, R, was calculated as the equation below:

$$R = \frac{A_s - A_b}{A_c - A_b} \times 100\% \quad (1)$$

where A_s, A_c, and A_b were the absorbance of experiment group, negative control group, and blank group, respectively. The state that $R \geq 100\%$ is defined as level 0; when $80\% \leq R \leq 99\%$, it is defined as level 1.

Synthesis of 2,3,5-Triiodobenzoyl Chloride (TIBC)

TIBC was obtained by the acylation of TIBA, according to the procedure in the literature.[26] A mixture of TIBA (4 g) and thionyl chloride (50 mL) was reacted at 60°C for 3 h. The gases generated were absorbed into the lye. Excessive thionyl chloride was distilled under reduced pressure. The crude was dissolved in dichloromethane and filtered, and then evaporated in vacuum to obtain the TIBC in a yield of 90%. Infrared spectra (IR) (KBr, cm^{-1}) v: 3074 (w), 1762 (s), 1516 (m), 1390 (m), 1360 (m), 1240 (m), 1147 (m), 1112 (m), 1018 (m), 904 (m), 870 (m), 717 (s). ^{13}C NMR (300 MHz, $CDCl_3$, ppm) δ: 168.5 (C^a), 147.6(C^b), 144.2(C^c), 135.7(C^d), 114.8(C^e), 107.4(C^f), 95.9(C^g).

Synthesis of N-(1,3-Dihydroxypropan-2-yl)-2,3,5-Triiodobenzamide (DHTIBA)

2-Aminopropane-1,3-diol (4 g) was dissolved at 60°C in THF (150 mL) with $MgSO_4$ as drier, filtrated, and then cooled down to room temperature. TIBC (4 g) dissolved in THF (5 ml) was added dropwise into 2-aminopropane-1,3-diol solution at room temperature and kept overnight. The products was obtained after rotary evaporation, washed with dichloromethane and deionized water, and dried in a yield of 87%. IR (KBr, cm^{-1}) v: 3280 (m), 2950 (w), 1645 (s), 1550 (m), 1537 (m), 1519 (m), 1024 (w). ^1H NMR (600 MHz, DMSO-d_6, ppm) δ: 8.21 (d, $J = 2$Hz, 1H, Ar-H), 8.14 (d, $J = 8$ Hz, 1H, NH), 7.55 (d, $J = 2$ Hz, 1H, Ar-H), 4.61 (s, 2H, OH), 3.78 (m, 1H, CH), 3.45 (m, 4H, CH_2).

Synthesis of IPUs

The PUs were synthesized by reaction of MDI, PTMG, and DHTIBA in different feed ratios as shown in Table I. In the case of IPU-1, MDI (2.753 g) and DHTIBA (0.573 g) were dissolved in DMF (10 mL) separately and mixed with PTMG (6.5 g) at room temperature for 1 h with mechanical stir under nitrogen atmosphere. Then the system was kept at 60°C for 6 h. The reaction mixture was washed by excess deionized water for three times and dried in an oven at 60°C to obtain the product.

RESULTS AND DISCUSSION

Preparation of IPUs

The synthesis procedure of IPUs was shown in Scheme 1. MDI, PTMG, and the newly synthesized chain extender of DHTIBA were utilized to synthesize the IPUs. The iodine-containing benzene ring of DHTIBA is linked in the side chain instead of main chain, which is different from the most previous reports. The flexible chemical structure of DHTIBA was designed to make the main chain of IPU softer, thus to reduce the steric hindrance of iodine during the IPU polymerization, and subsequently endue IPUs with higher molecular weight. To prepare DHTIBA, TIBC was obtained in advance by the acylation of TIBA, confirmed by ^{13}C NMR in Figure 1. Carbonyl was identified at $\delta = 168.5$ ppm, affected by chlorine atom. Six characteristic shifts for carbon atoms of benzene appeared between $\delta = 147.6$ and 95.9 ppm.

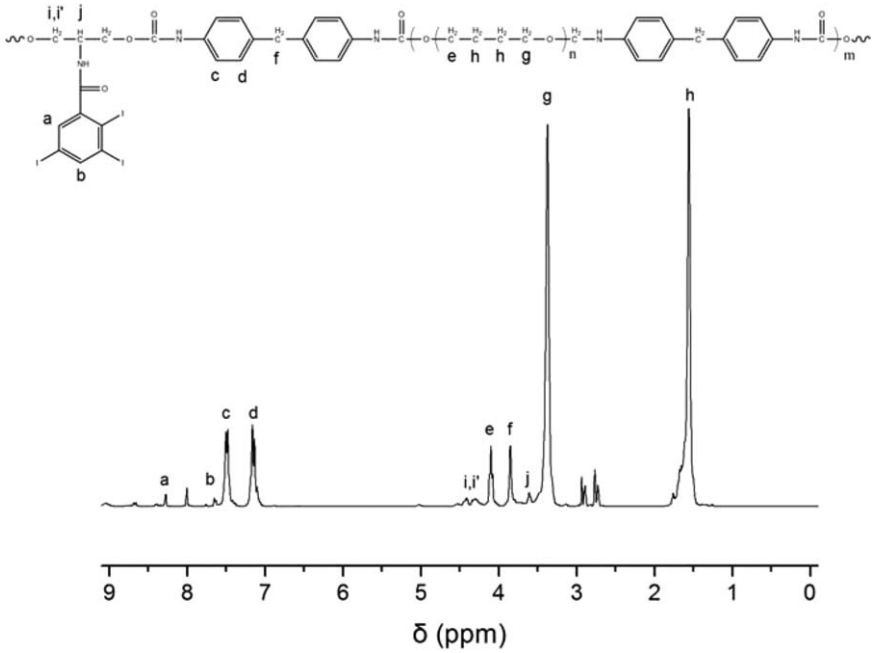


Figure 4. ^1H NMR spectra (600 MHz, DMF-d_7) of IPU-6.

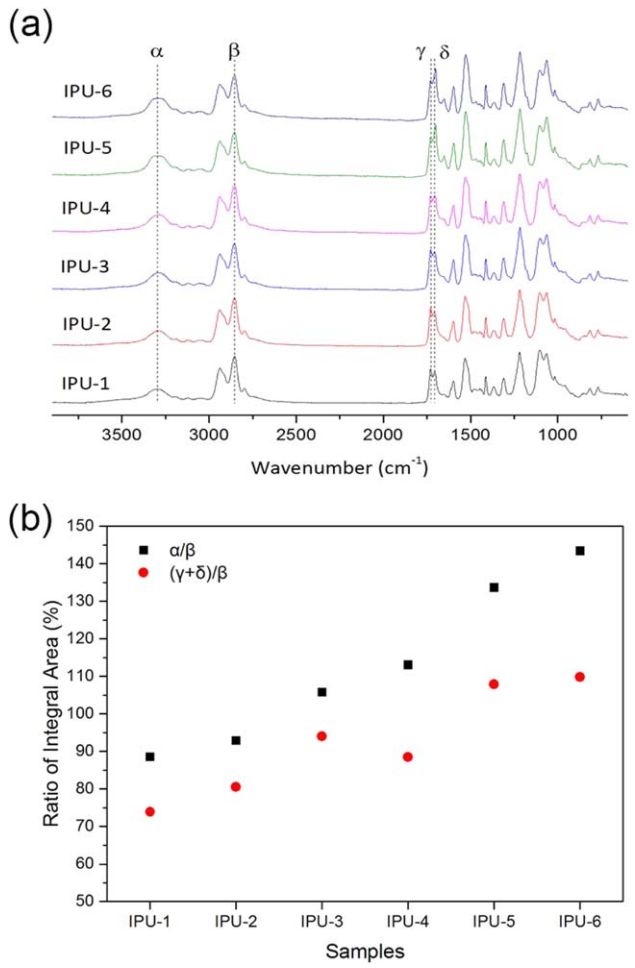


Figure 5. IR spectra of IPUs (a) and ratios of integral area of peaks (b). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

DHTIBA was obtained by the reaction between 2-aminopropane-1,3-diol and TIBC. Generally, both the alcohol and the amine have enough reactivity to combine with acyl chloride. To reduce the incidence of esterification, the reaction was conducted at a relatively low temperature without alkali. The structure of DHTIBA was confirmed by the IR spectra in Figure 2. The peak of 1645 cm^{-1}, -C=O stretching of amino link, was found in the IR spectra of DHTIBA, while no peak between 1730 cm^{-1} and 1740 cm^{-1} was found, illustrating that no ester was produced. The spectra of ^1H NMR in Figure 3 also confirmed this result. The characteristic shifts for the two protons of benzene appeared at $\delta = 8.21$ and 7.55 ppm. Amino was identified at $\delta = 8.14$ ppm with $J = 8$ Hz. The characteristic shifts for CH and CH_2 appeared at $\delta = 3.78$ and 3.45 ppm. The group of hydroxyl was identified at $\delta = 4.61$ ppm, which disappeared in ^1H NMR spectra with D_2O added. The ratio of integration area of the above mentioned peaks was 1 : 1 : 1 : 2 : 1 : 4, which is in accordance with the chemical structure of DHTIBA. Furthermore, this also demonstrated the purity of DHTIBA.

IPUs were obtained by polyaddition of MDI, PTMG, and DHTIBA. The chemical structure of the obtained IPUs was

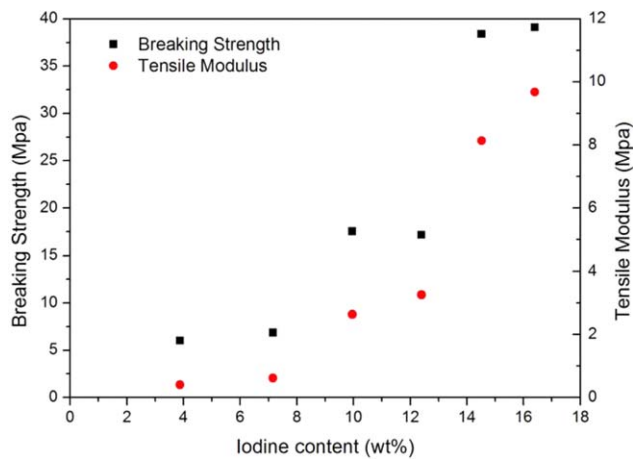


Figure 6. Variation of tensile modulus and breaking strength of IPUs with the iodine content in IPUs. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

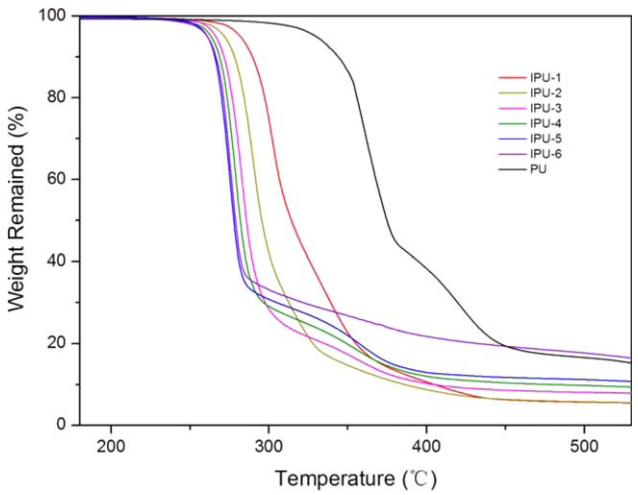


Figure 7. TGA curves of IPUs and PU for comparison at heating rate of 10 K/min. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

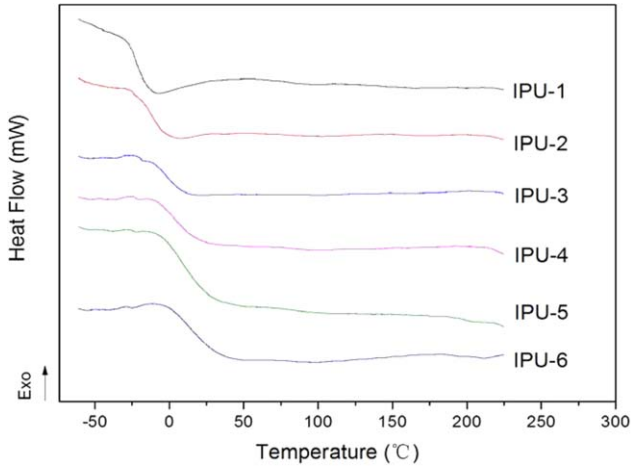


Figure 8. DSC curves of IPUs at heating rate of 10 K/min. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

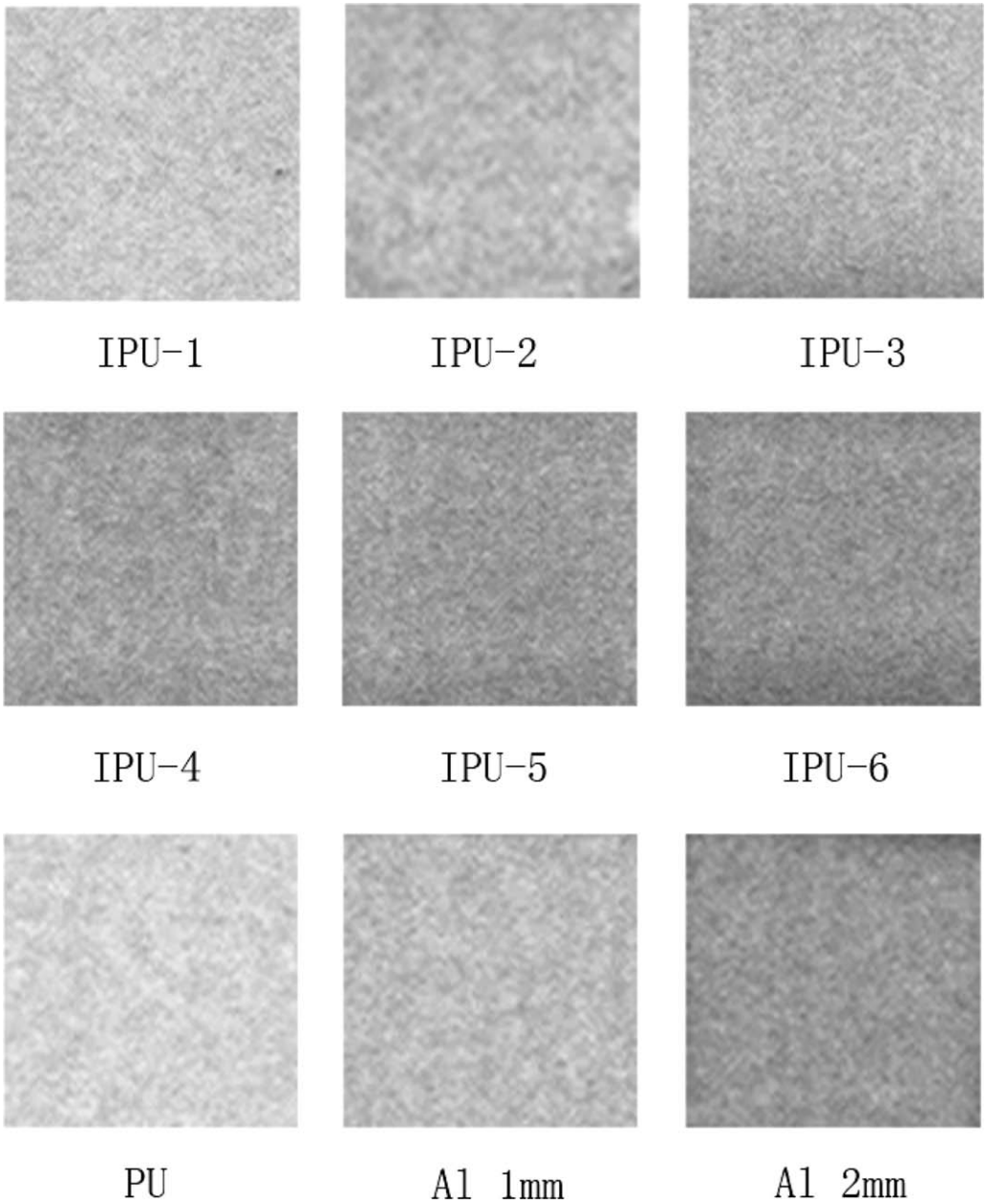


Figure 9. Radiopaque properties of IPUs and the aluminum plates with different thickness.

confirmed by ^{1}H NMR spectra as shown in Figure 4. The peaks due to the structure of DHTIBA in IPUs were at $\delta = 8.27(H^a)$, $7.65(H^b)$, $4.41(H^i)$, $4.30(H^{i'})$, and $3.61(H^j)$ ppm. The peaks due to the structure of MDI were identified at $7.48(H^c)$, $7.14(H^d)$, and $3.85(H^f)$ ppm. The characteristic shifts of $4.10(H^e)$, $3.37(H^h)$, and $1.57(H^g)$ were assigned to the protons of PTMG. The solvent peaks were shown at $\delta = 8.01$, 2.93, and 2.73 ppm. The experimental iodine contents in Table I were detected by ^{1}H NMR, based on the ratio of integration area of peaks at $\delta = 8.27(H^a)$ ppm and $\delta = 7.14(H^d)$ ppm, as shown in Figure 4, taking IPU-6 as an example. The experimental iodine contents of IPUs are slightly lower than the ideal iodine contents, which were calculated by the feed ratio in Figure 1. But DHTIBA was not detected in the washings. Besides, the pureness of DHTIBA has been proved by ^{1}H NMR spectra. Therefore, the deviation of iodine content should be attributed to the experimental error, maybe caused by the low sample concentration in ^{1}H NMR test.

IR spectra of IPUs are shown in Figure 5(a). The peak of 3295 cm^{-1} (α) belongs to the N–H stretching vibration. The peak of 2855 cm^{-1} (β) belongs to the C–H stretching vibration of CH_2 chain. The peak of 1725 cm^{-1} (γ) belongs to the C=O stretching vibration without hydrogen association. The peak of 1700 cm^{-1} (δ) belongs to the C=O stretching vibration associated with hydrogen. With the change of raw materials ratio, the content of PTMG decreased, and the content of DHTIBA increased. Thus, the ratio of integral area of peak α to peak β supposes to be raised. So does the ratio of total integral area of peak γ and peak δ to that of peak β. The ratios were shown in

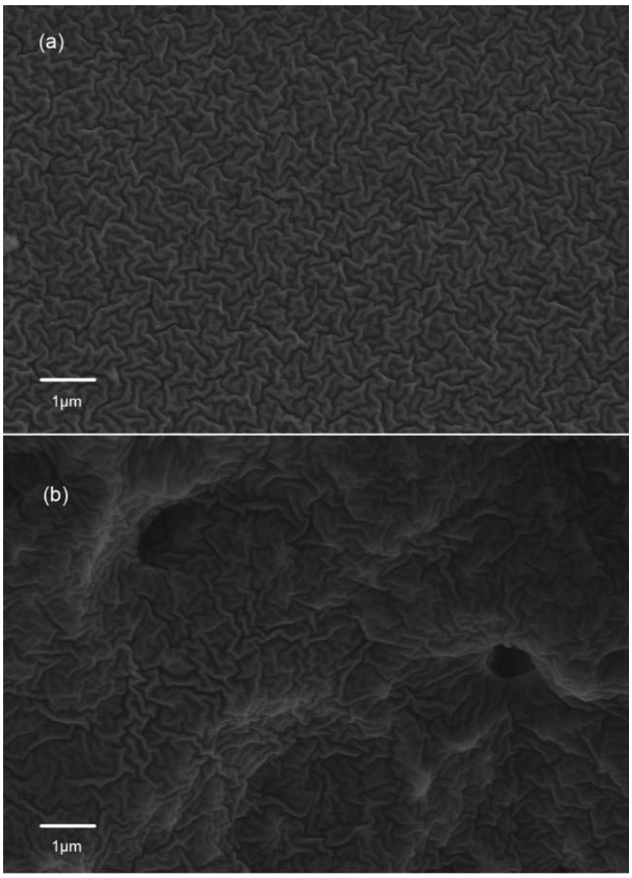


Figure 10. SEM images of IPU-6 (a) before and (b) after oxidative degradation.

Figure 5(b) with expectations. All the results above demonstrated the successful synthesis of IPUs.

The Molecular Weight and Mechanical Properties of IPUs

To determine the influence of DHTIBA on the molecular weight of IPU, series of IPUs with different ratios of MDI, PTMG, and DHTIBA were polymerized as shown in Table I. GPC analysis showed that with the gradual increase of DHTIBA content, the molecular weights (Mn) of IPUs reduced accordingly (from 7.9×10^4 Da to 4.9×10^4 Da). This result reveals that iodine has steric effect on the IPU polymerization procedure even though the iodine-containing benzene is side linked with IPU main chain.

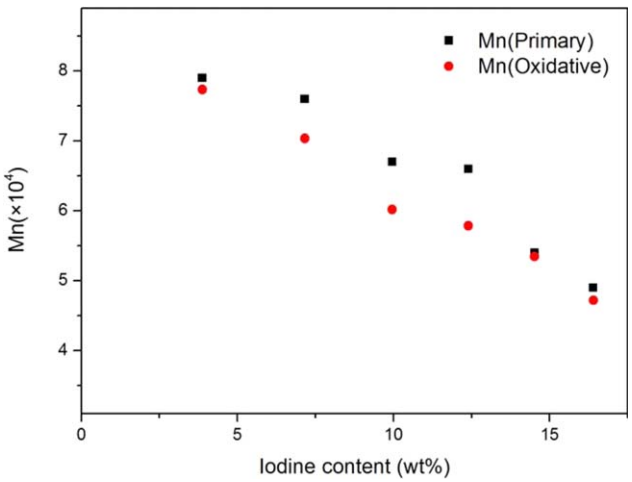


Figure 11. Variation of the molecular weights of IPUs during oxidative degradation. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

To evaluate the mechanical properties of IPUs, the tensile modulus and breaking strength were detected, as shown in Figure 6. With the increase of iodine content in IPUs from 3.9 wt % to 16.4 wt %, the breaking strength rose from 6.0 MPa to 39.1 MPa, and the tensile modulus rose from 0.4 MPa to 9.7 MPa. The hardness of IPUs also showed the same tendency. As shown in Table I, the hardness increased from 69 Å to 92 Å with increasing iodine content. All of these results demonstrate that there is a negative correlation between the mechanical properties and the molecular weight of IPUs, i.e., with the increase of DHTIBA content, the molecular weights of IPUs decreased, while the breaking strength and the tensile modulus of IPUs increased. That was contrary to the previous reports,[24] where the molecular weight and the breaking strength of the obtained IPUs both dropped with the increase of iodine content. The probable reason was that the flexible chain structure of DHTIBA promoted the movement and arrangement of hard segment and enhanced the strength of hard segment region. Besides, with the increase of iodine content, the proportion of hard segments increased at the same time. It also contributed to the enhancement of mechanical properties.

The Thermal Properties of IPUs

The Thermal stability of IPUs was determined by TGA and shown in Figure 7 as follows. The TGA curves of IPUs showed two stages during the decomposition process. The initial degradation from 260°C was the depolymerization of carbamate in the hard segments, while the later period of degradation from over 280°C was related to the soft segments. Comparing IPU-1 and PU, it was found that with the introduction of DHTIBA the temperature at which 5% weight loss occurred dropped from 329°C to 281°C. When the iodine content increased to 16.4 wt %, the temperature dropped to 261°C, which was still very meaningful for practical application. The decrease of temperature might be because the DHTIBA broke the crystallization of hard segment and impacted the stability of the carbamate.

To confirm this assumption, DSC tests of IPUs were conducted. Generally, the glass transition appears in DSC spectra in usual PUs. And the melt peaks are showed when crystallized. In Figure 8, we can see that the DSC spectra of IPUs showed only the glass transition peak in the temperature around 0°C, while nearly no melting endotherm was showed. This result suggested that the IPUs have low crystallization tendency. What's more, the iodinated phenyl groups of DHTIBA on the side chain could affect the movement of PUs due to its rigid structure and relatively large volume. Therefore, with the growth of DHTIBA content from 4.5% to 18.8% in molar fraction, the glass transition temperature increased greatly from −20°C to 17°C as shown in Figure 8. The iodinated phenyl groups increased the possibility of chain tanglement, which could be the reason why the IPUs can keep the ability of recovery after stretching in minutes, akin to the typical PU elastomer.

Radiopaque Properties of IPUs

To determine the radiopaque properties, the prepared IPUs were examined by a clinical X-ray machine. The samples of IPUs were made into 2 mm slices, and the radiopacity was compared with that of aluminum plates of 1 mm and 2 mm in thickness. Figure 9 showed that the radiopacity of IPUs was improved with the increase of iodine content and the sample of IPU-6 with iodine content at 16.4 wt % had the equal radiopacity to the aluminum plate with the same thickness, which demonstrated the IPUs had favorable radiopaque property.

Oxidative Degradation of IPUs

The stability of IPUs as implant materials was determined and simulated by oxidative degradation *in vitro*. The IPUs were soaked in $CoCl_2/H_2O_2$ solution for 4 weeks for oxidative degradation. The treated IPUs were compared with initial IPU by SEM, as shown in Figure 10. Fold phenomenon could be observed from the photograph of primary IPUs, which suggested the existence of microphase separation of IPUs on surface. After oxidation, although holes showed up on the surface of IPUs, the fold phenomenon still existed, demonstrating the stability of IPUs. For further verification, the molecular weights of IPUs were detected, as shown in Figure 11. Compared with the primary IPUs, the molecular weights of oxidative IPUs only decreased by a small percentage, between 3.1% and 13.1%. It was suggested that the stability of polymer chain of IPUs could be kept after oxidation by $CoCl_2/H_2O_2$, thus the IPUs were satisfactory for implant application.

Cytotoxicity of IPUs

To evaluate the cell toxicity of IPUs, the C2C12 myoblasts was cultured in leach liquor of IPUs and detected by CCK-8 method. The relative growth rate affected by IPUs was calculated to be 101% of the normal rate, so the toxicity classification of IPUs was ranked to level 0, based on the definition of CCK-8 method. The specifically treated cells had normal morphology. It suggests that the leach liquor of IPUs is nontoxic for C2C12 myoblasts.

CONCLUSIONS

Series of radiopaque PUs were synthesized using a newly designed compound, N-(1,3-dihydroxypropan-2-yl)-2,3,5-triiodobenzamide (DHTIBA), as the chain extender. The chemical structures of DHTIBA and the related IPUs were determined by IR and NMR spectra. It was found that with an increasing proportion of the flexible chain extender, the IPUs exhibited stronger radiopacity, as well as higher tensile modulus and breaking strength. In the meantime, the number average of molecular weight and the thermal stability decreased slightly. The radiopacity of the IPUs with defined iodine content was comparable to an aluminum plate with the same thickness. The oxidative degradation and cytotoxicity tests verified that the IPUs had a good stability and physiological properties. It was confirmed that the IPUs are promising in medical field as implant materials.

ACKNOWLEDGMENTS

This work was financially supported by the NSF of China (Grant No. 21174078).

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