Synthesis of novel main-chain azo-benzene poly(ester amide)s via interfacial polycondensation

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Abstract

Two amino acid-based poly(ester amide)s (PEAs) with azobenzene moieties in the main chain were successfully synthesized via interfacial polycondensation of a dip-toluenesulfonic acid salt of bis-(L-leucine)-1,6-hexylene diester with azobenzene 3,3'-dicarbonyl chloride or azobenzene 4,4'-dicarbonyl chloride. The structures of the obtained polymers were confirmed and characterized by ^{1}H and ^{13}C NMR spectroscopy and gel permeation chromategraphy (GPC). The photo-induced cis-trans-isomerization of azobenzene containing PEAs in the DMF solution was studied by UV-Vis spectroscopy. Irradiation with U.V. light (365 nm) resulted in reversible cis-trans isomerization. The effect of cis-trans-isomerization on the glass transition temperature was investigated by differential scanning calorimetry (DSC). It is shown that glass transition temperature decreases by irradiation when changes from trans to cis-isomer. Synthesized polymers were used in the preparation of photoresponsive nanoparticles for targeted drug delivery application. Nanoparticles' average diameter (A.D.), polydispersity index (PDI), and zeta-potential (Z.P.) were determined by Dynamic Light Scattering (DLS). Moreover, the stability of the N.P.s over time at low temperatures and upon irradiation were investigated.

Keywords — *Biodegradable smart polyester amides, main chain azo-benzene polymers, trans-to-cis isomerization, U.V. irradiation.*

I. INTRODUCTION

Nowadays, there is an increasing interest in remotely controlled drug delivery systems due to their potential to reduce side effects and injection load, together with enhancing therapeutic selectivity and efficacy [1]-[4]. Remotely controlled delivery can be achieved in response to various external stimuli such as light, temperature, electric or magnetic fields, and ultrasound. Among the different stimuli, the sun is considered the most attractive due to its ability to provide spatial and temporal control over the desired response [5]-[7]. There are three main strategies for light-induced drug release: a) photoisomerization, where photon absorption leads to the change of molecular conformation (e.g., *cis-trans* isomerization and ring-opening reactions involving bond breaking, but without the release of molecules), b) photodegradation, where irradiation causes polymer backbone degradation followed by drug release (e.g., polymers containing o-nitrobenzyl- or coumarin-groups), and c) photothermal, where absorbed light is converted to local heat, triggering drug release by various mechanisms (e.g., phase change, demicellization, etc.) [7]-[10]. Among them, there is a particular interest to the photoswitchable systems based on the photoisomerization approach, allowing either one-time or repeatable on-off drug release by merely switching the excitation source on/off [4], [8], [11]. Photoswitchable polymers are designed by incorporating photochromic moieties such as azobenzenes, spiropyrans, diarylethenes, and dithienylethenes the polymer. Among these molecules, azobenzene (A.B.) is the most frequently used chromophore due to the degradation-free and completely reversible light-induced *trans-cis* isomerization resulting significant change in physical properties, such as molecular geometry and polarity [12]-[14]. Isomerization is accompanied by decrease in the distance between the para carbon atoms in AB from 9.0 Å in the *trans*-form to 5.5Å in the *cis*-form. Polarity change is a consequence of the increase in dipole moment from p_{trans}=0 Debye to p_{cis}=3 Debye [14]. The majority of the isomerization studies on the photoswitchable drug delivery systems are carried out by U.V. or visible light and in the most cases present proof-of-concept, as the application of U.V./Vis light is limited in most biological systems due to issues with penetration depth and phototoxicity [13], [15]-[18]. The depth of U.V./Vis light penetration is limited (<1 cm) due to the strong scattering, absorption by water, and especially by high absorption of endogenous chromophores including hemoglobin, oxyhemoglobin, myoglobin and melanin [11], [19], [20]. Thus, U.V./Vis triggering is applicable for transdermal drug delivery systems, sites just a few millimeters below the surface of the skin or eye [10], [18], [21]. Application of two-photon excitation (TPE) by near-infrared (NIR) light is a promising alternative to U.V./Vis triggering [22]-[24]. NIR light with a wavelength of 650−900 nm is lower in energy compared to U.V./Vis radiation, has a lower absorption and scattering by biological media

leading to higher penetration depth into tissue (in less-attenuating organs even higher than 10 cm) and minimal phototoxicity [5], [10], [20]. Thus, the development of this technology opens new perspectives for azobenzene-based polymers in drug delivery applications.

The critical requirements for drug delivery systems are their biocompatibility and biodegradability, where the degradation products are also non-toxic and biocompatible [1]. Thus, amino acid-based poly(ester amide)s are promising materials for application as drug delivery vehicles due to their excellent biocompatibility and biodegradability [25]. Another attractive feature of this class of polymers is versatility in structural design, which allows tuning charge, hydrophobicity/hydrophilicity, or side functionalization for further modification [1]. Herein, we report on the synthesis of main-chain azobenzene containing poly(ester amide)s on the basis of bis(L-Leucine)-1,6- hexylene diester via activated step-growth polymerization. The document is a template. An electronic copy can be downloaded from the conference website. For questions on paper guidelines, please contact the conference publications committee, as indicated on the conference website. Information about final paper submission is available from the conference website.

II. EXPERIMENTAL

A. Materials

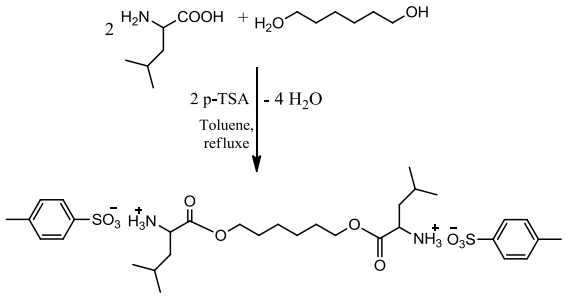
3-nitrobenzoic acid (99%, Alfa Aesar), 4-nitrobenzoic acid (99%, Alfa Aesar), D-(+)-Glucose (99%, Alfa Aesar), Sodium hydroxide (98%, Alfa Aesar), Dichloromethane (99.5%, Carl Roth), Phosphorus (V) Chloride (95-98%, Alfa Aesar), n-hexane (99%, Carl Roth), p-Toluenesulfonic acid monohydrate (98.5%, Aldrich), L-Leucine (98%, Aldrich), 1,6-hexanediol (99%, Aldrich), Toluene (99.5%, Carl Roth), Dimethyl sulfoxide (99.9%, Carl Roth), Tween 20 (Aldrich), all chemicals were used without further purification.

B. Synthesis

a) Synthesis of *a di-p-toluenesulfonic acid salt of bis-(L-leucine)*-1,6-hexylene diester (L6)

Di-p-toluenesulfonate of bis-(L-leucine)-1,6-hexylene diester was prepared following the procedure described in the literature (Scheme 1) [26]: L-Leucine (0.12 mol), p-toluenesulfonic acid monohydrate (p-TSA) (0.12 mol), 1,6-hexanediol (0.06 mol) and 150 ml toluene were placed in 500 mL flask equipped with a Dean-Stark trap and overhead stirrer. The suspension was heated to reflux until no water was distilled. The excess of Toluene was removed, and the resulting material was recrystallized twice from the distilled water (150 ml), yielding in a white powder. The reaction yield was 80%. M_p=192-194°C. 1H NMR confirmed the chemical structure.

Di-p-toluenesulfonic acid salt of bis-(L-leucine)-1,6-hexylene diester: ^{1}H NMR (400 MHz, DMSO-d6): 0.90 (m, 12H) 1.34 (m, 4H) 1.59–1.67 (m, 8H), 1.73 (m, 2H), 2.29 (s, 6H), 3.96 (t, 2H), 4.14 (m, 4H), 7.13 (d, 4H), 7.49 (d, 4H), 8.29 (s, 6H).



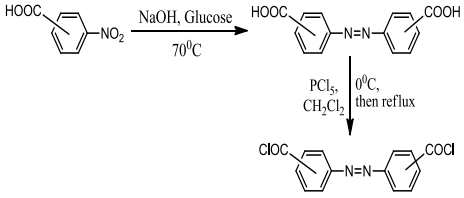
Scheme 1. Synthesis of *di-p-toluenesulfonate of bis-(L-leucine)*-1,6-hexylene diester

b) Synthesis of Azobenzene-3,3'-dicarboxylic Acid (m-AzoDCA).

Azobenzene-3,3'-dicarboxylic acid was prepared according to the procedure described elsewhere (Scheme 2) [27]: 3-nitrobenzoic acid (8.6 g, 0.051 mmol) and NaOH (28.6 g 0.715 mol) were placed in a two-necked flask and mixed in water (129 ml). The solution was heated to 80°C until the solid dissolved. Then, a hot aqueous solution of glucose (57.3 g in 86 mL of water) was added dropwise to the solution with vigorous stirring resulting in a yellow precipitate, which immediately changed to a brown solution upon further addition of glucose. Afterward, air was bubbled into the mixture for 10 h, and a light brown precipitate was obtained. The precipitate was collected by filtration, dissolved in distilled water, and acidified with acetic acid to reach a pH of 6, resulting in precipitation. The orange solid was collected by vacuum filtration, washed with water (300 ml), and dried in a vacuum oven to obtain azobenzene-3,3'-dicarboxylic acid (5.1 g, 74%).
^{1}H NMR (DMSO-d6, 400 MHz): 7.71 (t, J = 7.8 Hz, 2H), 8.19-8.06 (m, 4H), 8.37 (t, J = 1.7 Hz, 2H). ^{13}C NMR (DMSO-d6, 100 MHz): 122.9, 128.1, 130.5, 132.7, 132.9, 152.3, 167.2

c) Synthesis of Azobenzene-4,4'-dicarboxylic Acid (p-AzoDCA).

Azobenzene-4,4'-dicarboxylic acid was prepared according to the same procedure as for 3,3'-azodibenzoic acid described above (Scheme 2). ^{1}H NMR (DMSO-d6, 400 MHz): 8.01 (d, J = 8.2 Hz, 4H), 8.17 (d, J = 8.2 Hz, 4H), ^{13}C NMR (DMSO-d6, 100 MHz): 123.3, 131.2, 134.0, 154.7, 167.2. The yield was 75%.



Scheme 2. General scheme for the synthesis of azobenzene monomers.

d) Synthesis of Azobenzene 3,3′-dicarbonyl Chloride (m-AzoDCC).

To a suspension of Azobenzene 3,3′-dicarboxylic acid (1g, 3.7 mmol) in 75 mL of dichloromethane was added PCl5 (7.70 g, 37 mmol) at 0°C and then refluxed for 2 h (Scheme 2). This afforded orange crystals, which were repeatedly filtered and recrystallized from hexane to afford (0.461 g, 1.5 mmol, 41%). The melting point of Azobenzene 3,3′-Dicarbonyl Chloride was 100-101°C [28]. ^{1}H NMR (400 MHz, $CDCl_3$): 7.73 (t, 2H), 8.26 (m, 4H), 8.71 (s, 2H).

e) Synthesis of Azobenzene 4,4′-dicarbonyl Chloride [29] (p-AzoDCC).

Azobenzene 4,4′-dicarbonyl chloride was prepared according to the same procedure as for azobenzene 3,3′-dicarbonyl chloride described above (Scheme 2). Red crystals of azobenzene 4,4′-dicarbonyl chloride were obtained in a yield of 30% (0.366 g) with a melting point of 164°C [30]. ^{1}H NMR (400 MHz, $CDCl_3$): 8.07 (d, 4H), 8.33 (d, 4H).

f) Synthesis of m-Azobenzene-containing Poly(ester amide)s on the basis of bis(L-Leucine)-1,6- hexylene (m-AzoDC-L6).

Azobenzene 3,3′-Dicarbonyl Chloride (0.461 g, 1.5 mmol) was dissolved in anhydrous dichloromethane (32 mL) and then the solution was added dropwise (over 15 min) into an aqueous solution (32 mL) of the di-p-toluenesulfonic acid salt of L-6 (1.032 g, 1.5 mmol, 1.0 equiv) and potassium carbonate (0.415 g, 3.0 mmol). The reaction mixture was stirred at room temperature for 18 h. The DCM layer was separated using separating funnel, was washed several times with water, and dried over sodium sulfate. Afterward, sodium sulfate was filtered off, the solvent was removed under reduced pressure and the product was dried in vacuum oven leading to solid orange polymer (1.220 g, 98%).

^{1}H NMR (400 MHz, $CDCl_3$): 7.75-8.66 (8H, $CH_{arom.}$), 7.55 (2H, d, N<u>H</u>-CO), 4.98 (2H, dt, NH-C<u>H</u>), 4.25 (4H, t, O-C<u>H</u>$_2$), 1.44-2.20 (14H, O-CH$_2$-C<u>H</u>$_2$-C<u>H</u>$_2$-, CH$_3$-C<u>H</u>, CH-C<u>H</u>$_2$-CH), 1.07 (12H, d, C<u>H</u>$_3$-CH).

g) Synthesis of p-Azobenzene-containing Poly(ester amide)s on the basis of bis(L-Leucine)-1,6- hexylene (p-AzoDC-L6).

Azobenzene 4,4′-Dicarbonyl Chloride (0.366 g, 1.12 mmol) was dissolved in anhydrous dichloromethane (25 mL) and then the solution was added dropwise (over 15 min) into an aqueous solution (25mL) of the di-p-toluenesulfonic acid salt of L-6 (0.823 g, 1.12 mmol) and potassium carbonate (0.329 g, 2.24 mmol). The reaction mixture was stirred at room temperature for 18 h. The DCM layer was separated using separating funnel, was washed several times with water and dried over sodium sulfate. Afterward, sodium sulfate was filtered off, the solvent was removed under reduced pressure and the product was dried in vacuum oven leading to solid orange polymer (0.95 g, 98%).

^{1}H NMR (400 MHz, $CDCl_3$): 7.54-8.09 (8H, $CH_{arom.}$), 7.18 (2H, N<u>H</u>-CO), 4.84 (2H, NH-C<u>H</u>), 4.18 (4H, t, O-C<u>H</u>$_2$), 1.13-2.05 (26H, O-CH$_2$-C<u>H</u>$_2$-C<u>H</u>$_2$-, CH$_3$-C<u>H</u>, CH-C<u>H</u>$_2$-CH, C<u>H</u>$_3$-CH).

C. Preparation of nanoparticles

Nanosized drug delivery systems, viz. polymeric nanoparticles (N.P.s), were prepared by nanoprecipitation method under the optimal conditions previously established for amino acid-based biodegradable ester polymers [31]. 6.0 mg of polymer (**m-AzoDC-L6** or **p-AzoDC-L6)** was dissolved in 1.0 mL of DMSO (organic phase) and added dropwise (dropping rate 12 drops/min) to 10.0 mL of water (inorganic phase) containing 50.0 mg of the surfactant Tween 20 (organic/water phases ratio 1:10 v/v) at a stirring rate of 700 rpm using a magnetic stirrer. All manipulations were done at room temperature. In both cases, after adding the organic phase, the aqueous phase became turbid, indicating the formation of N.P.s. The suspensions of N.P.s, obtained after the complete addition of the organic phase, were stirred for 10-15 min and then dialyzed against distilled water for 2 h using the dialysis bag with MWCO 25 kDa to remove the organic solvent and residual surfactant. The obtained suspensions of N.P.s were stored in a refrigerator at 4-5°C.

D. Measurements

^{1}H and ^{13}C NMR spectra were recorded using JEOL ECA-400 MHz NMR spectrometer at room temperature with deuterated DMSO-*d*6 as a solvent and internal standard.

Molecular weight measurements were performed by gel permeation chromatography (GPC) using Waters 1525 system equipped with three consecutive Styragel columns (HR4, HR3, HR0.5 all 7.8 mm x 300 mm) calibrated by standard PMMA (Aldrich), refractive index (R.I.) detector (Waters 2414) and UV-detector (Waters 2487). GPC measurements were carried out in a 0.1 M solution of LiBr in DMF

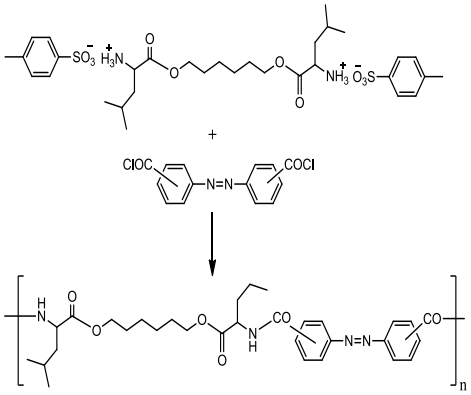
at a flow rate of 1.0 mL·min^{-1}, injection volume 100 µL, and sample concentration 5.0 mg·mL^{-1}.
Differential scanning calorimetry (DSC) measurements were carried out on a NETZSCH DSC 200 PC Phox under nitrogen at a heating rate of 10 K min^{-1}.
U.V./Vis absorption spectra were recorded using Shimadzu UV-1900 spectrophotometer.
Photoirradiation experiments were carried out using INTELLI-RAY 400 (Uvitron International). Samples were exposed to 365 nm U.V. light (115 mW cm^{-2}).

The N.P.s were characterized by size (Average Diameter, A.D.) and size distribution (Polydispersity Index, PDI), which were assessed by dynamic light scattering (DLS) using a particle size analyzer (Zetasizer Nano Z.S., Malvern Instruments) at 25°C.

III. RESULTS AND DISCUSSIONS

A. Synthesis

Poly(ester amide)s containing azobenzene groups in the main-chain were obtained via interfacial polycondensation of a di-p-toluenesulfonic acid salt of bis-(L-leucine)-1,6-hexylene diester with azobenzene 3,3′-dicarbonyl chloride or azobenzene 4,4′-dicarbonyl chloride (Scheme 3). Chemical structures of the synthesized polymers were confirmed by ^{1}H and ^{13}C NMR spectroscopy. A detailed synthesis of the monomers and polymers are given in the experimental part.



Scheme 3. General scheme for the synthesis of AzoDC-L6s

Synthesized polymers were obtained almost in quantitative yields (95–96%) and with rather high molecular weights (Tab. 1).

Table 1. Characteristics of the obtained AzoDC-L6s

Polymers	M_w (g mol^{-1})	M_n (g mol^{-1})	PDI (M_w/M_n)	T_g (°C)
p-AzoDBA-L-6	62800	28300	2.21	108.8
m-AzoDBA-L-6	47338	24067	1.98	92.4

B. Photoisomerization of m-AzoDC-L6 and p-AzoDC-L6

Azobenzene compounds and their derivatives undergo trans-cis isomerization upon irradiation with U.V. light (365 nm). The reverse cis-trans isomerization is induced by visible light (450 nm) or occurs thermally in the dark due to the thermodynamic stability of the trans isomer [16]. Photoisomerization behavior of synthesized AzoDC-L6s was studied by U.V./vis absorption spectroscopy. The UV-Vis spectra were recorded before and after irradiation by U.V. light (365 nm), irradiation was applied for two different times (120 and 300 sec) (Figure 1). Irradiated samples were transferred to the spectrometer in the dark to avoid reverse isomerization. The UV-Vis spectra of the synthesized Azo-polymers exhibited the strong absorption bands at around 325-330 nm characteristic for symmetry allowed π-π* electron transition of trans-form and the weak ones at around 450 nm for forbidden n-π* transition [16]. Upon U.V. irradiation of the Azo-polymer solutions, the absorption intensity at 325-330 nm corresponding to the π-π* transition of the trans-form decreased significantly, while the peak at around 450 nm corresponding to the n-π* transition slightly increased, indicating the trans-cis isomerization, as the azo-group in a cis-form absorbs stronger than trans-form [16]. Longer irradiation time (Figure 1) leads to an increase in isomerization. After 120 and 300 sec for both samples isomerization rate was significantly increased. Absorption band characteristic for a trans-azobenzene does not entirely disappear indicating incomplete photoisomerization in the applied irradiation time interval. The p-AzoDC-L6 polymer has significantly stronger absorption compared to the m-AzoDC-L6. Photoisomerization of both polymers, m-AzoDC-L6 and p-AzoDC-L6, is highly reversible process, as exposure to daylight for 24 h led to complete back-isomerization of thermodynamically less stable cis-forms to trans-forms (Figure 1).

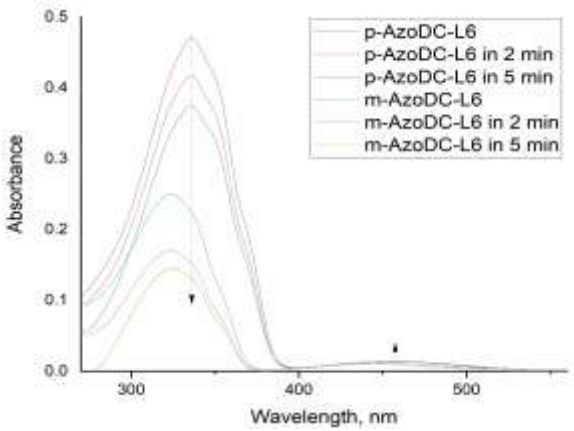


Figure 1. Changes in UV-Vis spectra of m-AzoDC-L6 and p-AzoDC-L6 in DMF under different irradiation times with 365 nm light at 25 °C.

C. Photoizomerization effect on the glass transition temperature of m-AzoDC-L6 and p-AzoDC-L6.

To study the effect of photoisomerization on the glass transition temperature of AzoDC-L6s, samples were dissolved in CH_2Cl_2, irradiated with 365 nm U.V. light for 5 min and then the solvent was removed under fully dark conditions (vacuum oven). Prior to the DSC analysis complete removal of CH_2Cl_2 was proved by ^1H NMR analysis. Dry samples were transferred to the DSC pan under fully dark conditions to avoid any back-isomerization. Glass transition temperature (T_g) of p-AzoDC-L6 before irradiation was 108.8 °C, while T_g of m-AzoDC-L6 was equal to 92.4 °C. Lower T_g of m-AzoDC-L6 compared to p-AzoDC-L6 is due to the unsymmetrically substituted benzene ring. Irradiated p-AzoDC-L6 showed T_g=104.9 °C and m-AzoDC-L6 - T_g=88.5°C, in both cases there is a decrease of T_g (Fig. 2), which can be due to the plasticizing effect of cis-isomer [32].

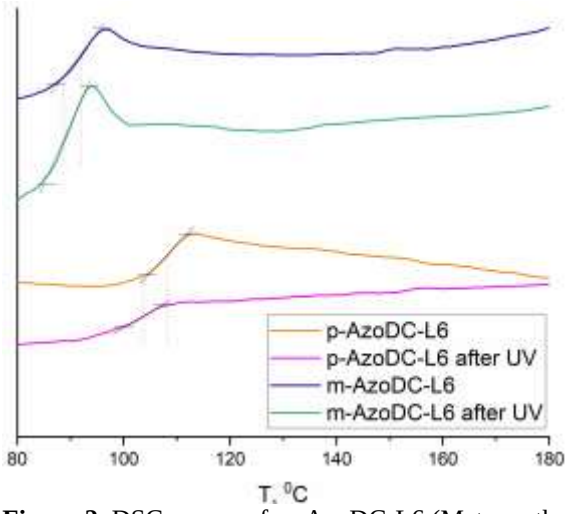


Figure 2. DSC curves of m-AzoDC-L6 (Meta on the graph) and p-AzoDC-L6 before and after irradiation with 365 nm light.

DSC studies, together with UV-Vis spectroscopy, indicate molecular changes that occur by irradiation. T_g decrease by trans-to-cis isomerization opens up the avenue for using this type of polymers as photo healing materials or transdermal delivery systems.

D. Nanoparticles based on m-AzoDC-L6 and p-AzoDC-L6 and their stability.

m-AzoDC-L6 and p-AzoDC-L6 based N.P.s (labeled as **m-AzoDC-L6 N.P.s** and **p-AzoDC-L6 N.P.s**) were prepared by a simple and cost-effective nanoprecipitation method. This technique is based on the precipitation mechanism. Polymer precipitation occurs after the addition of a polymer solution (organic phase) to a non-solvent (water phase) by a four-step mechanism: supersaturation, nucleation, growth by condensation, and growth by coagulation that leads to the formation of polymer N.P.s or aggregates [33]. Prepared m-AzoDC-L6 and p-AzoDC-L6 N.P.s were characterized by A.D. and PDI (Table 2) using DLS method.

Table 2. Characteristics of the freshly prepared N.P.s.

Sample	A.D. (nm) ± SD	PDI ± S.D.	Z.P. (mV) ± S.D.
m-AzoDC-L6 NPs	106.6 ± 0.9	0.275 ± 0.019	-13.4 ± 1.1
p-AzoDC-L6 NPs	111.0 ± 0.8	0.091 ± 0.011	-19.3 ± 0.7

Abbreviations*: AD, average diameter; PDI, polydispersity index; ZP, zeta-potential, SD, standard deviation.*
Note*: Data are presented as an average of five parallel measurements ± standard deviation.*

The results given in Table 2 show that the size of the obtained m-AzoDC-L6 and p-AzoDC-L6 N.P.s slightly differ and vary within 106.6 – 111.0 nm. The m-AzoDC-L6 N.P.s are characterized by wide particle distribution (PDI>0.16), while p-AzoDC-L6 N.P.s have mean particle distribution ($0.04 \leq PDI \leq 0.16$). As regards the surface charge (zeta-potential) of the obtained N.P.s, they both have a moderate negative charge. We suppose that the negative charge of the N.P.s is caused by partial hydrolysis of the ester links of the polymers generating free carboxyl groups (carboxylate anions –COO−).

The stability of the prepared N.P.s was investigated versus time and U.V. irradiation. Particle size and distribution of N.P.s were measured as for freshly prepared samples and after one-, two- and three-month storage at 4-5 °C. There was almost no chance of A.D. and PDI values, indicating the high stability of prepared N.P.s (Table 3).

Table 3. The stability of the prepared N.P.s upon storage at 4-5°C.

Sample	Time			
	Freshly prepared	After 30 days	After 60 days	After 90 days
	A.D. (nm) ± S.D. [PDI ± S.D.]			
m-AzoDC-L6 NPs	**106.6 ± 0.9** [0.275 ± 0.019]	**115.1 ± 0.8** [0.337 ± 0.008]	**117.8 ± 1.1** [0.356 ± 0.011]	**116.5 ± 1.5** [0.342 ± 0.012]
p-AzoDC-L6 NPs	**111.0 ± 0.8** [0.091 ± 0.011]	**112.8 ± 1.2** [0.088 ± 0.026]	**112.6 ± 0.8** [0.095 ± 0.013]	**113.7 ± 0.8** [0.100 ± 0.014]

Abbreviations*: AD, average diameter; PDI, polydispersity index; SD, standard deviation.*
Note*: Data are presented as an average of five parallel measurements ± standard deviation.*

In addition, the stability of the N.P.s made of AzoDC-L6 and p-AzoDC-L6 was evaluated versus

irradiation. N.P.s were irradiated by U.V. light (365 nm) for 5, 15, and 30 minutes and for each irradiation time, A.D. and PDI were measured. As it is obvious from the table 4, there is almost no change by irradiation independent of exposure time.

Table 4. The stability of the prepared N.P.s versus UV-irradiation.

Sample	Irradiation time			
	Before irradiation	**After 5 min**	**After 15 min**	**After 30 min**
	A.D. (nm) ± S.D. [PDI ± S.D.]			
m-AzoDC-L6 NPs	**106.6 ± 0.9** [0.275 ± 0.019]	**107.6 ± 0.8** [0.269 ± 0.013]	**108.3 ± 0.4** [0.272 ± 0.012]	**109.5 ± 0.4** [0.321 ± 0.010]
p-AzoDC-L6 NPs	**111.0 ± 0.8** [0.091 ± 0.011]	**108.8 ± 0.6** [0.063 ± 0.014]	**108.2 ± 0.2** [0.075 ± 0.009]	**109.9 ± 0.8** [0.099 ± 0.030]

Abbreviations*: AD, average diameter; PDI, polydispersity index; SD, standard deviation.*
Note*: Data are presented as an average of five parallel measurements ± standard deviation.*

Stability of nanoparticles versus time and U.V. radiation is an asset, as it may facilitate to the controlled drug delivery and dosage.

IV. CONCLUSIONS

Two new biodegradable amino acid-based polyester amides (PEAs) with azobenzene moieties in the main chain were successfully synthesized via interfacial polycondensation of a di-p-toluenesulfonic acid salt of bis-(L-leucine)-1,6-hexylene diester with azobenzene 3,3′-dicarbonyl chloride or azobenzene 4,4′-dicarbonyl chloride. Obtained polymers in the solution undergo trans-to-cis isomerization by irradiation with U.V. light (365 nm), the absorption intensity at 325-330 nm corresponding to the π-π* transition of the trans-form decreased significantly, while the peak at around 450 nm corresponding to the n-π* transition slightly increased, indicating the trans-cis isomerization. It was shown that by longer irradiation time isomerization rate increases. These types of materials are interesting for the fabrication of drug delivery systems.

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