Available online at www.sciencedirect.com
ScienceDirect
Polymer 49 (2008) 225–233
polymer
www.elsevier.com/locate/polymer

Electrochemical synthesis and characterization of novel bile acid functionalized polypyrroles

Yan Li [a,b], Weixia Zhang [a], Guangtao Li [a,*], Yong Ju [b,**]

[a] Key Lab of Organic Optoelectronics and Molecular Engineering, Department of Chemistry, Tsinghua University, Beijing, 100084, China
[b] Key Laboratory of Bioorganic Phosphorus Chemistry and Chemical Biology, Department of Chemistry, Tsinghua University, Beijing, 100084, China

Received 12 September 2007; received in revised form 1 November 2007; accepted 4 November 2007
Available online 3 December 2007

Abstract

A new series of pyrroles bearing bile acid moieties were synthesized and electrochemically polymerized in acetonitrile with tetrabutylammonium hexafluorophosphate ($TBAFP_6$) as the supporting electrolyte. It is found that these functionalized monomers could form polypyrrole films, but their electrochemical properties and the stability of the films are strongly dependent on the length of the alkyl spacer between pyrrole ring and the pendant bile acid moiety. Each of the resulting polymers with different bile acid groups shows a distinctive behaviour in terms of its microstructure of surface, as well as electrochemical and optical properties. Compared to other analogous polypyrroles, the optical property of the cholic acid functionalized polymer is sensitive to the polarity of the used solvents, exhibiting solvatochromic behaviour. This phenomenon is probably derived from its unique facial amphiphilic structure.

Keywords: Bile acid; Conjugated polymer; Electrochemistry

1. Introduction

Bile acid is a class of natural origin steroidal compounds and plays a very important role in biological systems [1]. In the past years, bile acids and their derivatives have been extensively explored for pharmacological applications [2]. Besides its biological importance, it is well recognized that such molecules are useful components for the construction of functional supramolecular systems [3]. It is especially true for the case of cholic acid, which is one of the primary bile acids found in human and a rare naturally occurring molecule exhibiting facial amphiphilicity [3]. This molecule has a rigid concave of hydrophobic backbone and a hydrophilic face pointing to the opposite direction through disposition of three hydroxyl groups. This unqiue contrafacial amphiphilic feature makes cholic acid conformationally sensitive to environmental conditions and as an ''ideal'' solvent-induced responsive molecule [4].

The interesting properties of bile acids and their derivatives have also prompted researchers to use these compounds in the design of new polymeric materials. The synthesis of bile acids derived polymers was first demonstrated in 1988 [5], followed by a lot of contributions by Zhu and Nichifor [6] and Zhu et al. [7], due to important biomedical applications. These polymers are expected to preserve some properties of bile acids, such as facial amphiphilicity, biocompatibility, capacity of self-assembling and high chemical stability of the steroid nucleus, exhibiting great promise for drug delivery and biomedical engineering applications [6]. So far, however, most of the bile acid polymers synthesized rely on the radical polymerization of methacryloyl group or the direct condensation between carbonyl and hydroxyl groups. The residue of initiator and coupling agents may not be tolerated or even toxic for biosystems [8].

Conductive polymers (CPs) have been the subject of intense research and development because of their academic interest and tremendous technological applications [9].

* Corresponding author. Tel./fax: +86 10 62792905.
** Corresponding author. Tel.: +86 10 62792795.
E-mail addresses: lgt@mail.tsinghua.edu.cn (G. Li), juyong@tsinghua.edu.cn (Y. Ju).

0032-3861/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.polymer.2007.11.010

Electrodeposition of conducting polymers offers a simple and attractive approach for preparing functional materials [10]. Among conducting polymers, polypyrrole is the most thoroughly studied and applied due to its ease of modification, excellent environmental stability and relatively low oxidation potential [11]. It has been reported that the homopolymerization of cholesterol functionalized pyrrole derivatives has been achieved in CH_3CN solution [12], whereas has failed for thiophene analogues [13]. In addition, polypyrrole derivatives exhibit some unique advantages for potential medical applications because of their excellent electrical properties and biocompatibility [14,15]. The facial amphiphilic nature of bile acid could allow the polypyrrole matrix to interact favorably with the biological environment, thus enhancing its biocompatibility.

In this respect, we are interested in exploring the electrochemical oxidation as new synthetic utility for the construction of novel bile acid functionalized macromolecules. In this work, the synthesis of new *N*-substituted pyrrole derivatives bearing cholic, deoxycholic and dehydrocholic acid moieties as well as their electropolymerization was demonstrated. The resulting polymers were characterized by CV, water contact angle, microscopy and spectral methods. We also found that the cholic acid functionalized polypyrrole is sensitive to polarity of the used solvents, exhibiting modest solvatochromic behaviour. To the best of our knowledge, our work is the first report on the bile acid derived conjugated polymers.

2. Experimental

2.1. Materials

Tetrabutylammonium hexafluorophosphate ($TBAPF_6$), cholic acid, deoxycholic acid, dehydrocholic acid, phthalimide potassium, 1,10-dibromodecane and 1,4-dibromobutane are purchased from Sigma Company and were used without further purification. Pyrrole and other solvents were received from Beijing Chemicals Company and purified according to standard procedures. The synthetic protocols of *N*-(10-bromodecyl)pyrrole [16] and *N*-(10-aminodecyl)pyrrole [17] were adapted from published reports.

2.2. Characterization

IR spectra were recorded on AVATAR 360 ESP FTS spectrophotometer with KBr pellets. ^{1}H NMR spectra were recorded at 300 MHz for protons on JOEL JNM-ECA300 spectrometer. Chemical shifts (δ) are given in ppm relative to TMS ($\delta = 0.0$). The HRMS (ESI) was measured on Bruker APEX spectrometer in positive mode. SEM experiments were performed with JEOL-6301F scanning electron microscope. Contact angles were measured with a Dataphysics contact angle system. The roughness parameter Rms was determined by AFM, using SPA-400 scanning probe in dynamic force mode. The perspective view is 10 μm × 10 μm. UV–vis characterization was carried out on a Perkin–Elmer Lambda35 spectrometer. The electropolymerization was carried out with a HEKA PG310 potentiostat (Dr. Schulz GmbH, Germany) in a three-electrode single-compartment cell. The working electrode was button platinum sealed in a Teflon holder with a surface of 4 mm^2 and was polished with Al_2O_3 polishing paste prior to use. The counter electrode is a platinum wire, and a saturated Ag/AgCl electrode was chosen as reference electrode.

2.3. Synthesis of pyrrole monomers bearing bile acid moieties

2.3.1. N-[10-(3α, 7α, 12α-trihydroxy-5β-cholan)decyl]-pyrrole (**4a**)

Cholic acid (0.816 g, 2.0 mmol), DCC (0.794 g, 2.2 mmol) and HOBt (0.297 g, 2.2 mmol) were dissolved in 6 ml dry DMF. After 10 min stirring at 0 °C, compound **3a** (0.475 g, 1.9 mmol) was added and the resulting reaction mixture was kept at ambient temperature for further 20 h. After separated from precipitate, the solution was poured into 30 ml ethyl acetate. The filtrate was washed with brine and dried over $MgSO_4$. The crude product was purified on silica gel, using CH_2Cl_2/CH_3OH (30:1 to 15:1) as eluent. Concentration of the product-containing fractions gave a white solid (755.8 mg) in 65% yield. Amorphous white powder. IR (KBr): 3394.7, 2925.9, 2853.1, 1646.8, 1465.6, 719.9 cm^{-1}. ^{1}H NMR ($CDCl_3$): $\delta = 6.64$ (t, 2H, pyrrole), 6.13 (t, 2H, pyrrole), 5.81 (br, s, 1H, NH), 3.97 (br, s, 1H, 12α-CH), 3.72 (m, 3H, 7α-CH, NHCH_2), 3.44 (br, s, 1H, 3α-CH), 3.21 (m, 2H, NCH_2), 1.10–2.32 (m, 40 H, aliphatic H), 1.00 (d, 3H, 21-CH_3), 0.89 (s, 3 H, 19-CH_3), 0.68 (s, 3H, 18-CH_3). HRMS (ESI) found: 630.5214, $[C_{38}H_{64}N_2O_4 + NH_4]^+$ calcd: 630.5210.

2.3.2. N-[10-(3α, 12α-dihydroxy-5β-deoxycholan)decyl]-pyrrole (**5a**)

This compound was synthesized using the same procedure as described for **4a**, with deoxycholic acid instead of cholic acid.

Yield: 67%. Amorphous white powder. IR (KBr): 3385.0, 2927.0, 2825.0, 1647.2, 1553.9, 1043.6, 719.6 cm^{-1}. ^{1}H NMR ($CDCl_3$): $\delta = 6.64$ (t, 2H, pyrrole), 6.12 (t, 2H, pyrrole), 5.56 (br, s, 1H, NH), 3.96 (br, s, 1 H, 12α-CH), 3.74 (t, 2H, NHCH_2), 3.58 (br, s, 1H, 3α-CH), 3.22 (m, 2H, NCH_2), 1.25–2.26 (m, 42H, aliphatic H), 0.97 (d, 3H, 21-CH_3), 0.90 (s, 3H, 19-CH_3), 0.67 (s, 3H, 18-CH_3). HRMS (ESI) found: 614.5263, $[C_{38}H_{64}N_2O_3 + NH_4]^+$ calcd: 614.5261.

2.3.3. N-[10-(3α, 7α, 12α-trioxo-5β-dehydrocholan)decyl]-pyrrole (**6a**)

This compound was synthesized using the same procedure as described for **4a**, with dehydrocholic acid instead of cholic acid. Yield: 70%. White solid. IR (KBr): 3292.6, 2926.4, 2853.1, 1723.4, 1706.9, 1738.4, 1279.3, 839.7, 724.1 cm^{-1}. ^{1}H NMR ($CDCl_3$): $\delta = 6.57$ (t, 2H, pyrrole), 6.05 (t, 2H, pyrrole), 5.56 (br, s, 1H, NH), 3.79 (t, 2H, NHCH_2), 3.15 (m, 2H, NCH_2), 1.06–2.90 (m, 43H, aliphatic H), 0.10 (s, 3H, 18-CH_3), 0.77 (d, 3H, 21-CH_3). HRMS (ESI) found: 624.4747, $[C_{38}H_{58}N_2O_4 + NH_4]^+$ calcd: 624.4740.