

## Synthesis and Characterization of Novel Multifunctional Acylthiourea Polymers

Xue Pu MAO<sup>1,2</sup>, Jin Feng HUANG<sup>2</sup>, Zhi Fang DUAN<sup>1</sup>, Zhi Yun DU<sup>1</sup>, Zhi Shu HUANG<sup>2</sup>, Lin MA<sup>1</sup>, Lian Quan GU<sup>1,2\*</sup>

<sup>1</sup>School of Chemistry and Chemical Engineering, Sun Yat-sen University, Guangzhou 510275

<sup>2</sup>School of Pharmaceutical Sciences, Sun Yat-sen University, Guangzhou 510080

**Abstract:** Several thiourea polymers have been synthesized through the reaction of diamine with 1, 4- or 1, 3- benzenedicarbonyl chloride and ammonium thiocyanate by solid-liquid phase transfer catalysis of polyethylene glycol-400 (PEG-400). The polymers were characterized and identified by elemental analysis, IR, <sup>1</sup>HNMR and GPC. The multifunctional polymers have potential value as an ideal support for immobilized enzymes.

**Keywords:** Synthesis, acylthiourea polymers, solid-liquid phase transfer catalysis.

Disubstituted thiosemicarbazides exhibited wide spectrum of biological activities. Some of them have been used in pesticide and plant-growth regulators<sup>1</sup>. Previous reports suggested that thioureas may have improved properties as hydrogen-bond donors, form more flexible hydrogen-bonding networks, and show lower tendency to self-associate than the corresponding urea analogues<sup>2</sup>. Therefore, replacing the urea moieties in the polymers by thiourea is of interest to increase the extent of hydrogen bonding with the urea functionalized guests, compared to the native state<sup>3</sup>. All of these prompt us to synthesize a new series of polymers bearing both polyamides containing aryl rings and thiosemicarbazide moiety, with the object of obtaining new multifunctional polymers which would have value in the enzyme immobilization.

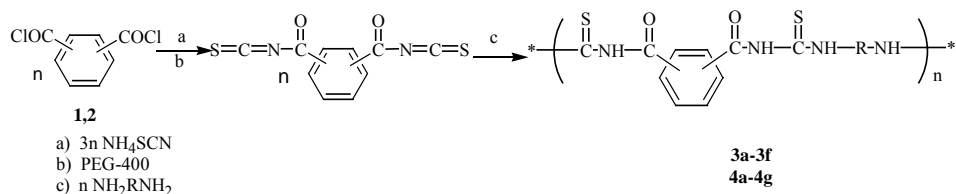
In this paper, we report for the first time the preparation of novel acylthiourea polymers containing aryl rings and thioureas by a convenient and efficient method under the condition of solid-liquid phase transfer catalysis using polyethylene glycol 400(PEG-400) as the catalyst<sup>4</sup> (**Scheme 1**).

Synthesis was conducted as follows: a suspension of 1,4- or 1,3-benzenedicarbonyl chloride (5 mmol), ammonium thiocyanate (15 mmol) and PEG-400 (3% based on ammonium thiocyanate) in methylene chloride was stirred for 1 h at room temperature, then diamines (5 mmol) was added. The mixture was stirred for another 1 h, the yellow precipitate was formed. The reaction mixture was filtered and washed with water, ethanol and a small quantity of THF successively to remove the inorganic salts and unreacted monomers. The data of polymers were shown in **Table 1, 2**.

---

\* E-mail: cdc42@zsu.edu.cn

Scheme 1



1, <i>p</i> -form		2, <i>m</i> -form	
Compd.	R	Compd.	R
<b>3a</b>	<i>p</i> -phenylenediamine	<b>4a</b>	<i>p</i> -phenylenediamine
<b>3b</b>	benzidine	<b>4b</b>	benzidine
<b>3c</b>	4,4'-methylenedianiline	<b>4c</b>	4,4'-methylenedianiline
<b>3d</b>	1,5-diaminonaphthalene	<b>4d</b>	4,4'-ethylenedianiline
<b>3e</b>	2,6-diaminopyridine	<b>4e</b>	1,5-diaminonaphthalene
<b>3f</b>	ethylenediamine	<b>4f</b>	2,6-diaminopyridine
		<b>4g</b>	ethylenediamine

Table 1 IR and  $^1\text{H}$  NMR spectra of the polymers

Polymer	IR <sup>a</sup> , $\tilde{\nu}(\text{cm}^{-1})$	$^1\text{H}$ NMR <sup>b</sup> , $\delta$ ppm
<b>3a</b>	3167,3037,1675,1517,1261,1152	Not soluble
<b>3b</b>	3371,3155,1672,1528,1258,1147	Not soluble
<b>3c</b>	3227,3166,1673,1516,1260,1146	Not soluble
<b>3d</b>	3156,3101,1677,1527,1254,1154	Not soluble
<b>3e</b>	3204,3108,1668,1535,1259,1149	12.85(s, 2H, NHCO), 11.74(s, 2H, NHAr), 8.04~6.28(m, 7H, ArH)
<b>3f</b>	3237,3140,1676,1521,1259,1162	11.66(s, 2H, NHCO), 10.86(s, 2H, NHAr), 7.99~7.91(m, 4H, ArH), 2.56~2.64(m, 4H, RH)
<b>4a</b>	3223,3036,1674,1515,1218,1143	Not soluble
<b>4b</b>	3223,3033,1674,1525,1340,1142	Not soluble
<b>4c</b>	3227,3032,1675,1516,1248,1144	12.47(s, 2H, NHCO), 11.53(s, 2H, NHAr), 8.52~7.29(m, 12H, ArH), 3.85~4.16(m, 2H, RH)
<b>4d</b>	3228,3033,1675,1515,1246,1141	12.49(s, 2H, NHCO), 11.58(s, 2H, NHAr), 8.54~6.92(m, 12H, ArH), 1.25~1.40(m, 4H, RH)
<b>4e</b>	3153,3024,1674,1523,1227,1150	12.61(s, 2H, NHCO), 11.82(s, 2H, NHAr), 8.04~6.71(m, 19H, ArH)
<b>4f</b>	3179,3035,1679,1530,1229,1154	13.12(s, 2H, NHCO), 11.08(s, 2H, NHAr), 8.49~6.32(m, 7H, ArH)
<b>4g</b>	3237,3025,1680,1522,1232,1175	11.24(s, 2H, NHCO), 10.83(s, 2H, NHAr), 8.30~7.97(m, 4H, ArH), 3.15~3.42(m, 4H, RH)

<sup>a</sup> Infrared spectra were recorded on a bruker EQUINOX-55 infrared spectrophotometer with KBr disks.

<sup>b</sup>  $^1\text{H}$  NMR spectra were made on a UNITYINOVA 500 MHz instrument using DMSO- $d_6$  as solvent and  $\text{Me}_4\text{Si}$  as internal standard.

**Table 2** The elemental analysis and some molecular weight of the polymers

Polymer	Elemental analysis (calcd.) %			Molecular weight <sup>a</sup>		
	Found(Calculated)			Mn <sup>b</sup>	Mw <sup>b</sup>	P.D <sup>c</sup>
	C	H	N			
<b>3a</b>	53.21(53.92)	3.51(3.39)	15.04(15.72)	/	/	/
<b>3b</b>	59.85(61.09)	4.02(4.28)	12.39(12.52)	/	/	/
<b>3c</b>	60.29(61.86)	4.23(4.06)	12.05(12.55)	/	/	/
<b>3d</b>	58.42(59.10)	3.68(3.47)	13.10(13.78)	/	/	/
<b>3e</b>	49.45(50.41)	3.85(3.79)	20.30(19.59)	/	/	/
<b>3f</b>	46.01(46.74)	4.17(3.92)	18.96(18.17)	/	/	/
<b>4a</b>	53.05(53.92)	3.75(3.39)	14.85(15.72)	/	/	/
<b>4b</b>	59.04(61.09)	4.12(4.28)	12.64(12.52)	/	/	/
<b>4c</b>	61.11(61.86)	4.05(4.06)	11.81(12.55)	16584	26535	1.600
<b>4d</b>	61.44(62.59)	4.34(4.38)	11.81(11.78)	/	/	/
<b>4e</b>	58.66(59.10)	3.87(3.47)	13.08(13.78)	8158	8173	1.002
<b>4f</b>	49.25(50.41)	3.75(3.79)	18.56(19.59)	2330	2908	1.25
<b>4g</b>	45.89(46.74)	4.52(4.67)	16.96(17.32)	8341	8369	1.003

<sup>a</sup> The molecular weight (**4c**, **4e**, **4f** and **4g**) was determined by GPC using THF as the solvent.

<sup>b</sup> Mn and Mw are the number-average and weight-average molecular weight, respectively.

<sup>c</sup> P.D is the polydispersity index of molecular weight distribution.

**Table 3** The activity of immobilized enzymes

Immobilized enzyme	Polyphenol oxidase	Papain	Urease	Stomach protease
Obtained activity (u/g)	356	85	346	115
$E_{spe}(\%)$	72.5	46.7	73.5	52.4

The thirteen kinds of polymer were all nonsoluble in following solvents: methanol, ethanol, isopropylalcohol, ethylene glycol, acetone, ethyl acetate, methylene chloride, chloroform, benzene, *etc.*. **3e** and **3f** were soluble in dimethyl sulfoxide (DMSO), N, N-dimethylformamide (DMF) and pyridine. **4c-4g** were soluble in DMSO, DMF and pyridine. **4c**, **4e**, **4f** and **4g** were soluble in tetrahydrofuran (THF).

The test of the enzyme immobilization was as follows: support activation with 1 mL of glutaraldehyde (5%) was performed at pH 6.86 at room temperature for 90 min. After centrifugation at 12000 rpm for 5 min, the support was washed three times with distilled water and placed in contact with 500  $\mu$ L of the enzyme solution in 0.1 mol/L buffer at pH 6.86 at 4°C for two hours. The enzyme-support complex was washed three times with buffers to remove the free enzyme. The best results were gained using **4f** as the support. As seen in the **Table 3**, immobilized polyphenol oxidase, urease and stomach protease showed good activity ( $a_{imm}$ ) and specific activity ( $E_{spe}$ )<sup>5</sup>. The immobilized activity of papain is relatively lower probably due to enzyme was absorbed relatively weak by the polymers.

**Acknowledgment**

This project is supported by the National Natural Science Foundation of China (Contract grant number: 29872061, 20032020).

**References**

1. G. Sridevi, R. P. Jayaprasad, R. K. Kondal, *Synth. Commun.*, **1989**, 19 (5), 965.
2. P. Buhlmann, S. Nishizawa, K. P. Xiao, Y. Umezawa, *Tetrahedron*, **1997**, 53(5), 1647.
3. (a) Y. Tobe, S. Sasaki, K. Hirose, K. Naemura, *Tetrahedron Lett.*, **1997**, 38(27), 4791. (b) Y. Tobe, S. Sasaki, M. Mizuno, K. Hirose, K. Naemura, *J. Org. Chem.*, **1998**, 63(21), 7481.
4. X. C. Wang, L. Zhang, Y. X. Da, *Synth Commun.*, **1999**, 29(23), 163
5. F. M. Bautista, M. C. Bravo, J. M. Campelo *et al.*, *J. Mol. Cat. B: Enzyme*, **1999**, 6(5), 473.

Received 23 August, 2004