Synthesis of Polymers with Pyrrolidone-Containing Side Chains and the Spacer Effect on Their Interaction with Phenols

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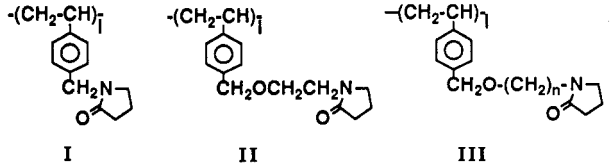
ABSTRACT: Three polymers with pyrrolidone-containing side chains (**NPES**, **NPHS**, and **NPDS**) with different spacer lengths between the main chain and the pyrrolidone group were synthesized by the reaction of cross-linked poly[styrene-*co*-4-(chloromethyl)styrene] with 1-(2-hydroxyethyl)-, 1-(6-hydroxyhexyl)-, and 1-(12-hydroxydodecyl)pyrrolidones, respectively. Interaction of these polymers with phenols was investigated in terms of the effect of the length of the spacers. The interaction strength was estimated by the binding constant K obtained from Klotz plots in water and chloroform solutions. K values with phenol were greater in water (28.2 mol/L for **NPES**, 30.1 mol/L for **NPHS**, 35.5 mol/L for **NPDS**) and were larger than in chloroform (17.2, 22.8, and 22.3 mol/L, respectively). Hydrophobic interaction in water is suggested as an additional effect besides hydrogen bonding and charge-transfer interaction. The order of K values in water (**NPDS** > **NPHS** > **NPES**) may arise from differences in degree of freedom and hydrophobicity of the spacer. In chloroform, K values for **NPHS** and **NPDS** were similar but larger than those of **NPES** with all the phenols. Small differences in K between **NPHS** and **NPDS** might be explained by the steric hindrance effect of the spacer of **NPDS**. The dihydroxy compounds catechol and 2,3-dihydroxynaphthalene showed 4–10 times larger K values than phenol and β-naphthol. There is a clear correlation between K and the acidity of the phenol.

Introduction

Interaction between poly(vinylpyrrolidone) [poly(vinyloxazolidone)] and low molecular weight compounds such as phenols, carboxylic acids, and alkyl halides has been extensively investigated. This interaction is actually applied in practice to drug delivery systems, chromatography, and fixation of dyes.[1–8] We have reported in detail the interaction between phenols and bifunctional pyrrolidones prepared as model compounds for poly(vinylpyrrolidone).[9] The results obtained suggested that the interaction between phenols and poly(vinylpyrrolidone) is partially suppressed by the steric hindrance of the polymer main chain, since the pyrrolidone moiety is bound directly to the main chain. On the basis of the results of the model study, we synthesized pyrrolidone polymers (**I**, **II**) with spacers between the main chain and the pyrrolidone moiety to evaluate their capacity in absorption–desorption equilibria of phenols.[10] The polymers with the spacers exhibited adsorption capability superior to that of polymers without such a spacer. Therefore, it is of interest to clarify the effect of the length of the spacer on the interaction. In this paper, the synthesis of cross-linked polymers with spacers between the main chain and the pyrrolidone moiety [**III**: **NPES** (n = 2), **NPHS** (n = 6), and **NPDS** (n = 12)] and the effect of the length of the spacers on the interaction of these polymers with phenols are described.



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Experimental Section

Materials. Cross-linked poly[styrene-*co*-4-(chloromethyl)-styrene] was obtained from Mitsubishi Kasei Corp. (20.15 wt % Cl content, 5.68 mmol/g (chloromethyl)styrene unit, and 0.17–0.43-mm grain diameter). Solvents (1,2-dichloroethane, dimethylformamide) were purified by distillation and stored over drying agents. Reagent-grade 2-bromoethanol, 6-bromohexanol, 12-bromododecanol, 2-pyrrolidone, phenol, β-naphthol, catechol, and 2,3-dihydroxynaphthalene were purified by distillation or recrystallization by conventional methods. Other chemicals were reagent grade and were used without further purification.

Synthesis of Bromoalkyl Pyranyl Ethers. 6-Bromohexyl 2-pyranyl ether was prepared according to the procedure of Manabe et al.[11] with some modifications. To a solution of 6-bromo-1-hexanol (50.7 g, 0.28 mol) in 400 mL of dry 1,2-dichloroethane was added a small amount of *p*-toluenesulfonic acid as an acidic catalyst. 3,4-Dihydro-2*H*-pyran (24.4 g, 0.29 mol) was added dropwise to the mixture at room temperature with stirring. The resulting mixture was stirred at room temperature for 3 h and poured into water. The oily material was extracted with ether, and the combined organic layer was dried over anhydrous magnesium sulfate. The organic layer was evaporated to give a yellow oil (73.0 g, 99%). The crude product was used for the synthesis of 1-(6-hydroxyethyl)pyrrolidone without further purification.

12-Bromododecyl 2-pyranyl ether was prepared from 12-bromo-1-dodecanol (74.3 g, 0.28 mol) by the same procedure as 6-bromohexyl 2-pyranyl ether. Crude yield 97.5 g (99%).

Synthesis of (Hydroxyalkyl)pyrrolidones. 1-(2-Hydroxyethyl)pyrrolidone was prepared according to the method of the previous paper.[12]

1-(6-Hydroxyethyl)pyrrolidone was synthesized by the procedure used for 1-(2-hydroxyethyl)pyrrolidone[12] with some modifications. To a suspension of sodium hydride (55 wt % mineral oil dispersion, 13.2 g, 0.33 mol) in 300 mL of dry dimethylformamide (DMF) was added dropwise 2-pyrrolidone (23.5 g, 0.28 mol) in 50 mL of dry DMF with stirring at room temperature. The mixture was kept at room temperature for 5 h. 6-Bromohexyl 2-pyranyl ether (73.0 g) in 50 mL of dry DMF was added dropwise to the mixture at room temperature with stirring. The resulting mixture was stirred at 60 °C for 5 h. DMF was removed by distillation under reduced pressure, the residue was extracted with ether, and the organic layer was dried over anhydrous magnesium sulfate. The solvent was evaporated and

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the residue was treated with Amberlite IR118(H) in 300 mL of methanol. The mixture was stirred at the methanol reflux temperature for 2 h. Methanol was evaporated and the residual product was subjected to column chromatography using ethyl acetate as eluent. Yield 35.2 g (68%, orange viscous oil). IR (neat): 3406 (OH), 2934 (CH_2), 2864 (CH_2), 1671 (C=O) cm^{-1}. ^1H-NMR ($CDCl_3$): δ 3.68–3.58 (t, J = 6.7 Hz, 2H, $HOCH_2$), 3.44–3.33 (t, 2H, J = 7.3 Hz, NCH_2–(ring)), 3.33–3.22 (t, 2H, J = 7.3 Hz, NCH_2), 2.45–2.33 (t, 2H, J = 7.9 Hz, $COCH_2$), 2.27–2.20 (s, 1H, OH), 2.10–1.95 (m, 2H, $COCH_2CH_2$), 1.66–1.20 (m, 8H, CH_2 × 4). Anal. Calcd for $C_{10}H_{19}NO_2$: C, 64.86; H, 10.27; N, 7.57. Found: C, 64.56; H, 9.88; N, 7.45.

1-(12-Hydroxydodecyl)pyrrolidone was prepared according to the same procedure as 1-(6-hydroxyhexyl)pyrrolidone. Yield 24.1 g (32%, white solid). MP 46.5–47.5 °C. IR (KBr): 3406 (OH), 2928 (CH_2), 2858 (CH_2), 1672 (C=O) cm^{-1}. ^1H-NMR ($CDCl_3$): δ 3.68–3.59 (t, 2H, J = 7.3 Hz, $HOCH_2$), 3.44–3.32 (t, 2H, J = 7.3 Hz, NCH_2–(ring)), 3.32–3.24 (t, 2H, J = 7.3 Hz, NCH_2), 2.45–2.34 (t, 2H, J = 7.9 Hz, $COCH_2$), 2.10–1.93 (m, 2H, $COCH_2CH_2$), 1.93–1.75 (s, 1H, OH), 1.70–1.15 (m, 20 H, CH_2 × 10). Anal. Calcd for $C_{16}H_{31}NO_2$: C, 71.38; H, 11.52; N, 5.20. Found: C, 71.18; H, 11.52; N, 4.77.

Synthesis of Cross-Linked Polymers Containing the Pyrrolidone Moiety in Side Chains. Typical Procedure (for NPES). To a suspension of sodium hydride (55 wt % mineral oil dispersion, 4.01 g, 0.10 mol) in 100 mL of dry DMF was added dropwise 1-(2-hydroxyethyl)pyrrolidone (11.1 g, 0.086 mol) dissolved in 50 mL of dry DMF with stirring at room temperature. The mixture was stirred at room temperature for 5 h. Cross-linked poly[styrene-*co*-4-(chloromethyl)styrene] (12.5 g, 0.072 mol) was added to the mixture with stirring at room temperature. The resulting mixture was stirred at room temperature for 5 h. The suspended polymer was collected by filtration and washed by Soxhlet extraction with methanol and *n*-hexane. The resulting polymer was dried under reduced pressure at 60 °C for 24 h. Material with grain size ranging from 0.17 to 0.43 mm in diameter was collected by sifting. IR (KBr): 2928 (CH_2), 2860 (CH_2), 1685 (C=O), 1100 (–O–) cm^{-1}. Anal. Found: N content, 2.55% (4-[2-(2-oxo-1-pyrrolidinyl)ethoxy]methylstyrene unit: 1.93 mmol/g).

By similar procedures, **NPHS** and **NPDS** were prepared from 1-(6-hydroxyhexyl)- and 1-(12-hydroxydodecyl)pyrrolidones and cross-linked poly[styrene-*co*-4-(chloromethyl)styrene], respectively.

NPHS: IR (KBr) 2926 (CH_2), 2858 (CH_2), 1685 (C=O), 1100 (–O–) cm^{-1}. Anal. Found: N content, 4.04% (4-[6-(2-oxo-1-pyrrolidinyl)hexyloxy]methylstyrene unit: 2.89 mmol/g).

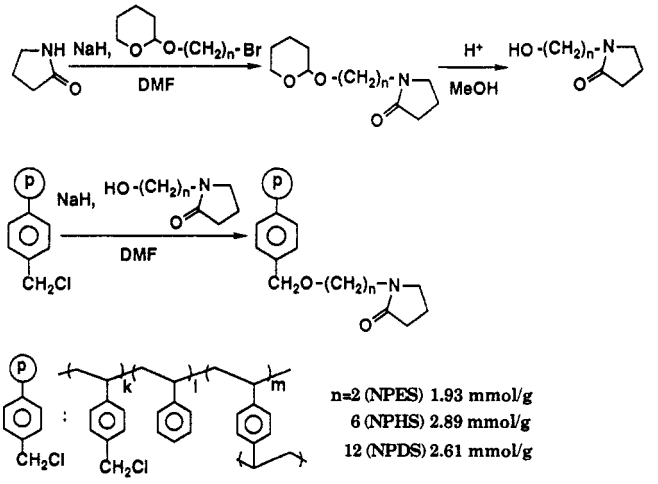
NPDS: IR (KBr) 2928 (CH_2), 2860 (CH_2), 1685 (C=O), 1100 (–O–) cm^{-1}. Anal. Found: N content, 3.66% (4-[12-(2-oxo-1-pyrrolidinyl)dodecyloxy]methylstyrene unit: 2.61 mmol/g).

General Procedure for Evaluation of the Interaction between the Polymers and Phenols. Cross-linked polymer containing the pyrrolidone moiety (100 mg) was added to 10 mL of a water or chloroform solution of a phenol (concentration ranging from 0.02 to 0.2 mol/L). The heterogeneous mixture was agitated by a shaker at 22 °C for 5 h. The polymer was separated by filtration, and concentration of the phenol remaining in the filtrate was measured by UV spectroscopy (using absorptions at 270 (phenol), 275 (β-naphthol), 277 (catechol), and 283 nm (2,3-dihydroxynaphthalene)).

Measurements. ^1H NMR spectra were recorded on a Bruker AC-P300 (300 MHz) using tetramethylsilane as an internal standard. FT-IR spectra were obtained with a Jasco FT/IR-5000 spectrophotometer. UV spectra were measured with a Hitachi U-3200 spectrophotometer.

Results and Discussion

Preparation of Polymers Containing the Pyrrolidone Moiety. Three cross-linked polymers (**NPES**, **NPHS**, and **NPDS**) with spacers between their polymer main chain and the pyrrolidone moiety were synthesized by the reaction of cross-linked poly[styrene-*co*-4-(chloromethyl)styrene] [5.68 mmol/g of 4-(chloromethyl)-styrene unit] with (ω-hydroxyalkyl)pyrrolidones, according to the following scheme.



Reaction of 2-pyrrolidone with ω-bromoalkyl pyranyl ether in the presence of sodium hydride in DMF afforded ω-pyrrolidonylalkyl pyranyl ether, which subsequently decomposed to (ω-hydroxyalkyl)pyrrolidone in methanol by treatment with an acid catalyst. The ω-pyrrolidonylalkoxy group was introduced into the cross-linked polymer by reaction of the (chloromethyl)phenyl moiety of the polymer with (ω-hydroxyalkyl)pyrrolidone in the presence of sodium hydride in DMF.

The introduction of the pyrrolidonylalkoxy moieties into the cross-linked polymers was confirmed by the IR spectra in which new absorptions characteristic of the pyrrolidonylalkoxy moiety at 1685 and 1100 cm^{-1}, corresponding to the lactam carbonyl and alkyl ether bonds, were observed in every case. A typical example (**NPES**) is shown in Figure 1.

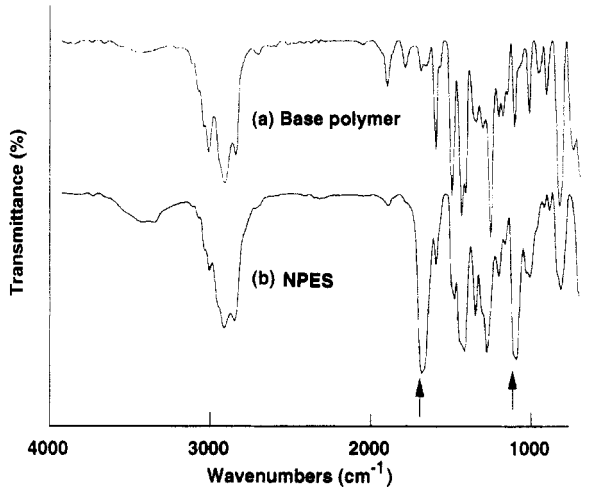


Figure 1. IR spectra of (a) cross-linked poly[styrene-*co*-4-(chloromethyl)styrene] (base polymer) and (b) **NPES**.

The content of pyrrolidonylalkoxy group in the cross-linked polymers ranged from 1.93 (**NPES**) to 2.89 mmol/g (**NPHS**) as determined by elemental analyses. The cross-linked polymers obtained were sieved to obtain grain sizes ranging from 0.17 to 0.43 mm in diameter and were used for the experiments of the interaction with phenols.

Interaction of Polymers with Phenols. The pyrrolidone-bearing cross-linked polymers were added to a solution of a phenol in water or chloroform, and the heterogeneous mixture was shaken at 22 °C for 5 h. The concentration of the phenol in the filtrate obtained on removal of the polymer was measured by UV absorption.

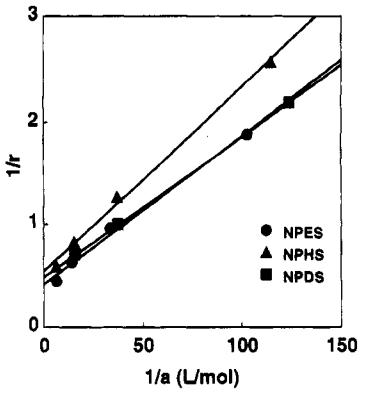


Figure 2. Plots of $1/r$ vs $1/a$ for interaction of polymers with phenol in water at 22 °C.

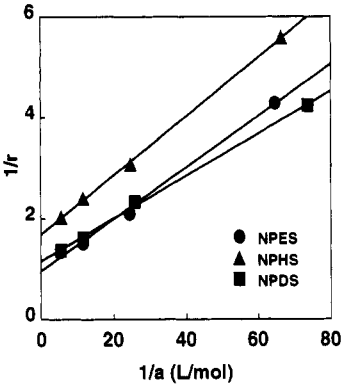


Figure 3. Plots of $1/r$ vs $1/a$ of the interaction of the polymers with β-naphthol in chloroform at 22 °C.

The shaking time required was determined to be 5 h, because the system was confirmed to reach an equilibrium within 5 h by independent experiments in varying shaking periods (ranging from 1 to 10 h). The strength of the interaction between the polymer and phenol was evaluated by the binding constants K obtained from the Klotz plots according to the Klotz equation:[13]

$$\frac{1}{r} = \frac{1}{nKa} + \frac{1}{n}$$

Here, r is the number of phenol molecules bound to the polymer per pyrrolidone unit, n is the number of binding sites per pyrrolidone unit, and a is the molar concentration of free phenol at equilibrium. Both r and a values were obtained from experiments over a range of phenol concentrations.

Plots of $1/r$ vs $1/a$ of the interaction of the polymers with phenol in water and with β-naphthol in chloroform are shown in Figures 2 and 3, respectively. The good linear relationship obtained in both cases indicates that the Klotz equation can be applied to these experimental systems. Similar linear relationships were also confirmed for phenol, catechol, and 2,3-dihydroxynaphthalene in chloroform.

From the Klotz plots $1/r$ for phenol in water was *ca.* 0.5 mol of pyrrolidone/mol of phenol, while in chloroform $1/r$ was *ca.* 1–2. The number of binding sites in water was much more than that in chloroform. For other phenols in chloroform $1/r$ was *ca.* 1–2. It has been reported that in the case of poly(vinylpyrrolidone) $1/r$ was 10;[1] however, in that study, the phenol concentration was different.

K values obtained from the Klotz plots are summarized in Table 1. In the case of phenol, the K value in water is larger than in chloroform for all of the polymers. This result supports our previous result[9,10] that the interaction between the pyrrolidone moiety and phenol in water is stronger than in chloroform. Probably the interaction

Table 1. Binding Constant K between Polymers with a Pyrrolidone Side Chain Moiety and Phenols in Water or Chloroform at 22 °C[a]

run	polymer	n[b]	phenol	solvent	K (mol/L)	pK_a[c]
1	**NPES**	2	phenol	water	28.2	9.98[d]
2	**NPHS**	6	phenol	water	30.1	
3	**NPDS**	12	phenol	water	35.5	
4	**NPES**	2	phenol	chloroform	17.2	
5	**NPHS**	6	phenol	chloroform	22.8	
6	**NPDS**	12	phenol	chloroform	22.3	
7	**NPES**	2	β-naphthol	chloroform	19.2	9.93[e]
8	**NPHS**	6	β-naphthol	chloroform	28.2	
9	**NPDS**	12	β-naphthol	chloroform	27.8	
10	**NPES**	2	catechol	chloroform	64.0	9.13[e]
11	**NPHS**	6	catechol	chloroform	93.3	
12	**NPDS**	12	catechol	chloroform	89.9	
13	**NPES**	2	2,3-dihydroxy-naphthalene	chloroform	100	8.68[f]
14	**NPHS**	6	2,3-dihydroxy-naphthalene	chloroform	292	
15	**NPDS**	12	2,3-dihydroxy-naphthalene	chloroform	285	

[a] Each polymer (100 mg) was added to 10 mL of a water or chloroform solution of the phenol (concentration from 0.02 to 0.2 mol/L) and the mixture was shaken for 5 h at 22 °C. [b] Number of methylene groups in the spacer chain. [c] Values measured in aqueous solution at 25 °C. [d] Reference 14. [e] Reference 15. [f] Reference 16.

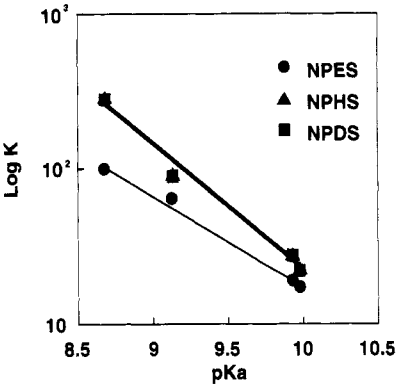


Figure 4. Plots of log K between the polymers and phenols in chloroform vs pK_a of the phenols.

between the polymers and phenol in chloroform is caused mainly by hydrogen bonding and charge-transfer (C-T) stacking, while the interaction in water can be attributed not only to hydrogen bonding and C-T stacking but also to hydrophobic interaction. For a given phenol, the K value in water increases with increasing methylene chain length of the spacer in the polymer's side chain (runs 1–3). In chloroform, however, the binding constants are in the order **NPES** < **NPHS** ≃ **NPDS** (runs 4–6). Thus, extension of the methylene chain length from 6 to 12 does not contribute to the further enhancement of the interaction in chloroform with any of the phenols (Table 1, runs 4–15). Therefore, it might be suggested that the long methylene chain of **NPDS** acts to suppress the interaction with phenol as a sterically hindered group and consequently counteracts any favorable effect on interaction associated with enhanced freedom of the pendant group due to the long spacer, so that the binding constant of **NPDS** is nearly equal to that of **NPHS**. Since the hydrophobic interaction between **NPDS** and phenol should appear in water but not in chloroform, the binding constant of **NPDS** more than that of **NPHS** in water would be attributed to the increase of the binding capacity due to the hydrophobic interaction of the methylene chain, as well as the enhancement of the freedom of the pendant group by the long spacer. This is consistent with the results in chloroform.

The dependence of the K value on the structure of the phenols is confirmed quite clearly (Table 1). The K value in chloroform decreases in the order 2,3-dihydroxynaphthalene > catechol > β-naphthol > phenol for each polymer. The K values of the dihydroxy compounds, catechol and 2,3-dihydroxynaphthalene, are 4–10 times larger than those of the corresponding monohydroxy compounds, phenol and β-naphthol. Figure 4 shows that the increase in log K is correlated clearly with decreasing acidity of the phenols. This correlation suggests that there is no special effect for the dihydroxy compounds. Thus, the more acidic the phenols are, the more the interaction is strengthened. This relation is reasonable, provided the interaction depends predominantly on hydrogen bonding.

To summarize, this study has clarified the importance of the spacer between the polymer main chain and the pyrrolidone group and the effect of its length in the adsorption of phenols with the polymers having the pyrrolidone moiety in the side chains.

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