Use of an Aromatic Polyimide as a Non-Cross-Linked Molecular Imprinting Material

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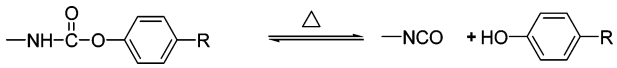
Introduction. Mechanically stable materials that can selectively recognize target molecules have potential uses in applications such as chemical sensors, stationary phases for high-performance chromatography, catalysts, and membranes for separating toxic chemicals.[1−6] Molecular imprinting constitutes a valuable method of preparing such materials, in which a specific binding site is introduced into an organic or inorganic polymer matrix. In the process, a target molecule (template) is first complexed with a functional monomer and then frozen into a matrix by polymerization. The removal of the template from the matrix generates a cavity, which can recognize the template.

The recognition ability of the cavity is greatly influenced by the structure of the matrix and the nature of the bond used for the template−monomer complexation. Most imprinted polymeric matrices reported so far are vinyl polymers, having cross-linked network structures, so as to prevent structural changes of the cavity occurring by relaxation or diffusion of the matrix molecules. Their microscopic structures depend primarily on the nature of the functional monomer and cross-linking agent as well as on the polymerization conditions. An excess of cross-linking agent is generally used to increase the rigidity of the imprinted matrix, but which sometimes has an adverse effect on the interaction between the template and the matrix, resulting in low recognition capacity.[7] There are only a few examples for non-cross-linked molecularly imprinted polymers. Recently, Kobayashi et al. reported a phase inversion molecular imprinting method, in which linear polymers were used as a matrix and template molecule information was encoded by the polymer phase inversion process.[8,9]

In this study, we explored the use of an aromatic polyimide as the imprinted matrix and a thermally reversible bond between the template and the monomer in the process of template−monomer complexation. Aromatic polyimides are prepared by condensation polymerization of aromatic dianhydrides and aromatic diamines. Depending on the selection of a dianhydride−diamine pair, a wide variety of physical properties can be conferred on the polyimide matrix. Aromatic polyimides are known as well-packed materials due to the strong interactions between the polymer chains, and most of them are insoluble and infusible.[10] Thus, we expected that an aromatic polyimide would produce a satisfactory non-cross-linked imprinted matrix.

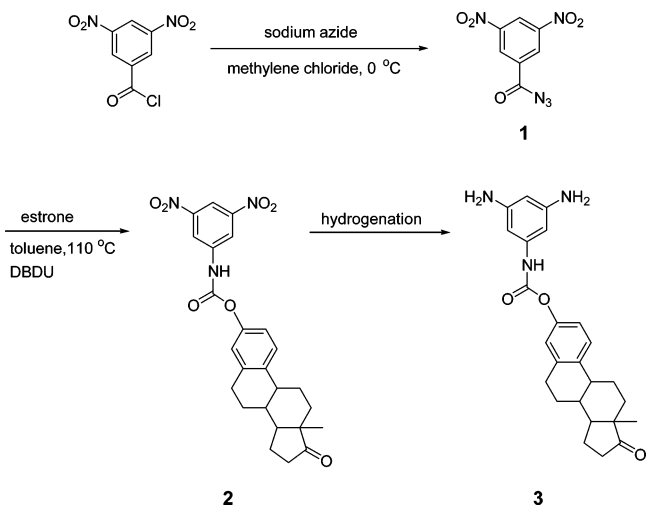
The template molecule, estrone, was attached to the polyimide chain by means of a urethane bond. The urethane bond was stable at room temperature but was cleaved at elevated temperature, as shown in Scheme 1.[11] The use of a thermally reversible bond has certain advantages in that it is possible to easily remove the template molecule from the matrix and to introduce various functional groups into the cavities.[12] Estrone is one of several naturally occurring estrogens. It influences the normal development and maturation of the female. Estrone has been suspected of having carcinogenic properties and adverse environmental effects.[13−15]

Scheme 1



Monomer Synthesis.[16] Diamine **3** having estrone was synthesized according to Scheme 2. 3,5-Dinitrobenzoyl chloride in methylene chloride was reacted with sodium azide in water at 0 °C to yield azide **1**.[17] A solution of **1** in toluene was refluxed in the presence of estrone and dibutyltin dilaurate. The reaction occurred between an isocyanato group formed by thermal rearrangement of an azide and a phenol moiety of estrone, resulting in urethane **2**.[18] The nitro groups of **2** were reduced to diamino groups by catalytic hydrogenation in tetrahydrofuran.[19] 3,5-Diaminobenzoyl azide (**4**) was synthesized according to the literature.[20]

Scheme 2



Preparation of Polyimide. Estrone imprinted polyimide was prepared according to Scheme 3. Polymerization was carried out in *N*,*N*-dimethylacetamide (DMAc) at room temperature using a stoichiometric amount of the diamine (1:19 mole ratio of **3** to 4,4′-oxydianiline) and pyromellitic dianhydride. The highly viscous solution was cast on a glass plate and dried in a vacuum oven for 48 h at room temperature. The poly(amic acid) film was thermally imidized for 0.5 h each at 80, 130, 170, 220, and 270 °C to yield a polyimide film (thickness: ca. 20 μm). A control polyimide film was fabricated in the same manner as the imprinted polyimide film.

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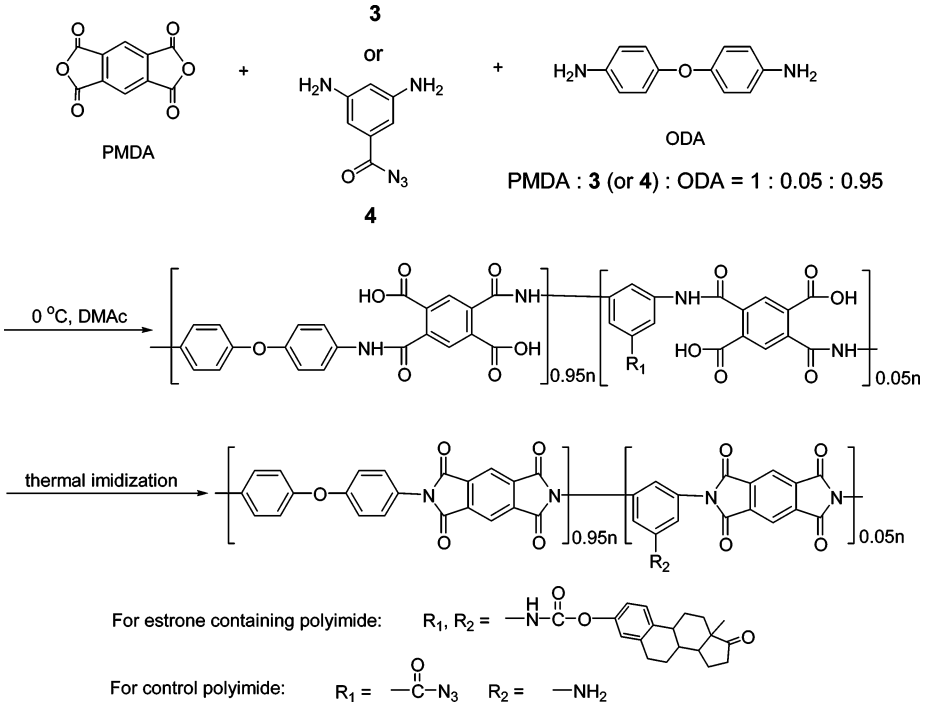
Scheme 3



For the control polyimide, 3,5-diaminobenzoyl azide **(4)** was used as a diamine in place of compound **3**.

The thermal behaviors of the polyimide films were evaluated by thermogravimetric analysis (Figure 1).[21] In the thermogram of the estrone-containing film, about 3% weight loss was observed between 220 and 320 °C, corresponding to the decomposition of estrone. This value coincides with the calculated weight percent of estrone contained in the films (3.4%).

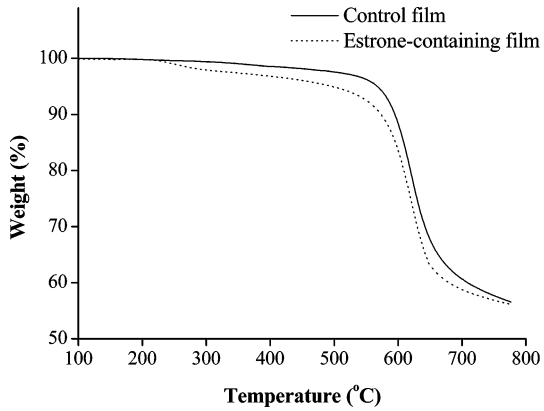


Figure 1. TGA thermograms of the estrone-containing and control polyimide films.

Extraction of Estrone. The thermal cleavage of the urethane bond was investigated by ^{1}H NMR spectroscopy and FT-IR spectroscopy. Compound **3** was dissolved in DMSO-d_6 and the ^{1}H NMR spectra were measured at 25 and 110 °C (Figure 2). The ^{1}H NMR spectrum obtained at room temperature showed the N−H peak of the urethane bond at 9.5 ppm and aromatic ring proton peaks of the estrone group at 7.3 and 6.9 ppm. After increasing the sample temperature to 110 °C, the N−H peak decreased remarkably while new peaks appeared at around 6.5 and 7.1 ppm, corresponding to the aromatic ring protons from the dissociated estrone, showing that the urethane bond had been thermally cleaved.

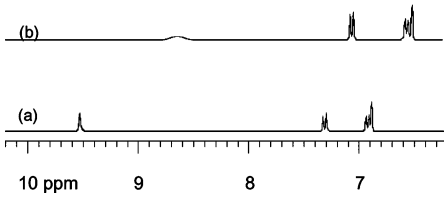


Figure 2. ^{1}H NMR spectra of compound **3** (a) at 25 °C and (b) at 110 °C.

It is believed that part of the template molecules were dissociated during the process of imidization and remained in the matrix. The template molecules in the film were extracted by refluxing in 1,4-dioxane in the presence of a small amount of water. In this process, undissociated template molecules were removed as well. The isocyanato groups formed by the dissociation were converted to amino groups through their reaction with water.[12] The extraction process was continued until the UV absorbance at 282 nm, corresponding to estrone in the solution, became constant.

Rebinding Experiment. Polyimide films (0.1 g) were added to the solutions of estrone or its structural analogues (testosterone, testosterone propionate, 98%, purchased from TCI) in chloroform (20 mL) at various concentrations (1, 2, and 3 mM). After incubating for 12 h at room temperature, the polyimide films were isolated by filtration. The filtrate was concentrated to dryness by evaporation of the solvent before HPLC analysis.[22]

Figure 3 shows the result of the rebinding experiment on the imprinted and control polyimide films. The concentrations of estrone were 1, 2, and 3 mM in 20 mL of chloroform. For the same estrone concentration, more estrone was bound to the imprinted polymer than the control. Figure 4 shows the results of selectivity tests on the imprinted polymer and control polyimide. A 0.1

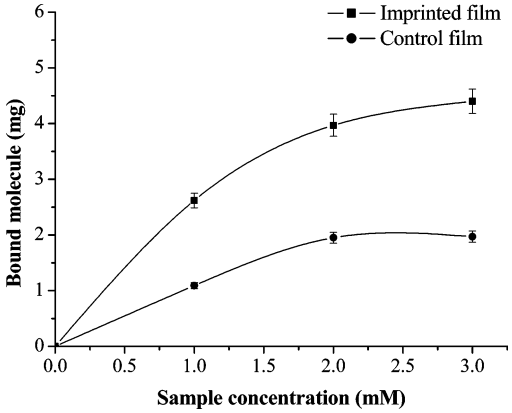


Figure 3. Amount of bound estrone by the imprinted and control polyimide films. In all experiments, the amount was analyzed by HPLC after 0.1 g of the polymers were added to 20 mL of the 1, 2, and 3 mM estrone solutions in chloroform for 12 h at room temperature. All experiments were repeated three times.

g of polyimide film was added to the 3 mM sample solution in 20 mL of chloroform. The tests were conducted using testosterone and testosterone propionate, which are the structural analogues of estrone but do not have a phenolic group. The imprinted film showed higher specific recognition ability for estrone than for its structural analogues. The results indicate that template-shaped cavities were imprinted in the polyimide matrix. The amino group inside the cavity would form a hydrogen bond with the phenol moiety of Estron in the rebinding process.

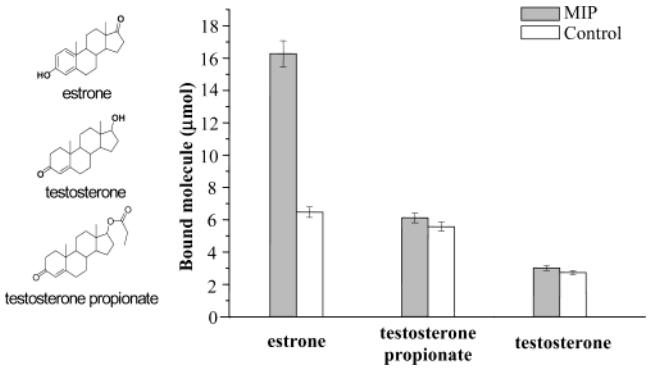


Figure 4. Amount of bound molecules by the imprinted (MIP) and control polyimide films. In all experiments, the amount was analyzed by HPLC after 0.1 g of the polymers were added to 20 mL of the 3 mM sample solutions in chloroform for 12 h at room temperature. All experiments were repeated three times.

Conclusion. We explored the use of a rigid non-cross-linked polymer in molecular imprinting. Aromatic polyimides have excellent thermal stability and mechanical strength, which have contributed to their successful application in several areas, such as films, moldings, coatings, adhesives, and resin matrices. The template molecule was attached to the polyimide chain by means of a thermally reversible urethane bond. The removal of the template was accomplished by a simple thermal reaction. Most imprinted materials obtain their rigidity through a cross-linking reaction, which it is not easy to control. Our results are quite encouraging as regards the use of non-cross-linked high-performance polymers, such as aromatic polyimides, in molecular imprinting.

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References and Notes

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(16) Sodium azide (99%) and dibutyltin dilaurate (95%) were purchased from Aldrich Chemical Co. Estrone (98%) and 3,5-dinitrobenzoyl chloride (99%) were purchased from TCI. Methylene chloride and tetrahydrofuran were used after purification by standard methods. Other chemicals were used as received without further purification.
(17) Compound **1**: Anal. Calcd for $C_7H_3N_5O_5$: C, 35.46; H, 1.28; N, 29.53. Found: C, 35.56; H, 1.29; N, 29.66. ^{1}H NMR (DMSO-d_6): δ 8.89 (s, 2H benzene ring protons), δ 9.02 (s, 1H benzene ring proton). ^{13}C NMR ($CDCl_3$, 500 MHz): 123.0, 129.2, 134.3, 149.0, 168.9. IR (KBR pellet, cm^{-1}): 3168 (aromatic C−H stretching), 2157 (N_3), 1691 (C═O), 1548, 1358 (N═O stretching).
(18) Compound **2**: Anal. Calcd for $C_{25}H_{25}N_3O_7$: C, 62.62; H, 5.26; N, 8.76. Found: C, 62.80; H, 5.32; N, 8.45. ^{1}H NMR (DMSO-d_6): 0.85 (s, 3H), 6.99 (s, 1H), 7.01 (d, 1H), 7.34 (d, 1H), 8.50 (s, 1H), 8.73 (s, 2H), 11.17 (s, 1H). ^{13}C NMR ($CDCl_3$, 500 MHz): 13.4, 21.0, 25.4, 26.0, 28.9, 31.2, 35.2, 37.8, 43.3, 47.2, 49.4, 112.7, 114.9, 117.7, 118.8, 121.5, 126.0, 137.3, 137.9, 141.1, 148.4, 219.6.
(19) Compound **3**: Anal. Calcd for $C_{25}H_{29}N_3O_3$: C, 71.57; H, 6.97; N, 10.02. Found: C, 71.62; H, 7.14; N, 9.63. ^{1}H NMR (DMSO-d_6): 0.84 (s, 3H), 4.68 (s, 4H), 5.53 (s, 1H), 6.00 (s, 2H) 6.86 (s, 1H) 6.91 (d, 1H), 7.28 (d, 1H), 9.5 (s, 1H). ^{13}C NMR ($CDCl_3$, 500 MHz): 14.0, 21.8, 26.0, 26.5, 29.6, 30.5, 31.7, 36.1, 38.3, 44.3, 50.7, 96.5, 97.7, 119.1, 121.9, 125.7, 126.6, 137.4, 138.2, 139.4, 148.4, 148.67, 221.0.
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(21) The thermogravimetric analysis was performed with a TGA 2050 thermogravimetric analyzer (TA instruments, Inc.) at a heating rate of 10 °C/min under a dried N_2 atmosphere.
(22) Reverse phase HPLC analysis was carried out using a M930 solvent delivery system, a M720 UV−vis detector (YOUNG LIN Instrument Co. Ltd., Korea), a MetaSil 5u ODS column from Metachem (Torrance, Canada) with methanol as an eluent at a rate of 1.0 mL/min at room temperature. For each analysis 20 μL of sample was injected.

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