Communications to the Editor

New Molecular Imprinting Materials: Liquid Crystalline Networks

J.-D. Marty,* M. Tizra, M. Mauzac, I. Rico-Lattes, and A. Lattes

Laboratoire des Interactions Moléculaires et Réactivité Chimique et Photochimique, U.M.R. CNRS 5623, Université Paul Sabatier, 118 Route de Narbonne, 31062 Toulouse Cedex 4, France

Received April 16, 1999
Revised Manuscript Received July 28, 1999

1. Introduction. Molecular imprinting was a valuable polymerization method for preparing synthetic materials able to exhibit the molecular recognition phenomenon present in living systems (enzymes, antibodies).[1,2] In this technique, a template was associated with one or more functional monomers to form a complex by means of covalent linkages or noncovalent interactions. A bifunctional monomer (cross-linker) was added and the polymerization/cross-linking reaction was realized around the complex previously formed. Upon removal of the template species, functionalized cavities, which have remembered the spatial features and bonding preferences of the template, were left inside the polymer network. Such imprinted networks showed high selectivity in rebinding their template. They were used as chromatographic stationary phases, in particular for the resolution of racemates,[4] as well as materials for stereoselective reactions or as catalysts.[5]

Despite all these possibilities, the molecular imprinting technology presents some drawbacks.[6] Most of them were linked to the fact that a large amount of cross-linking agent was needed (around 80−90%) to restrict the relaxation phenomena of the polymer backbones and to obtain an effective molecular recognition.[1] As a result, the imprinted network was very stiff; this lowered the probability of interactions between the template and the network and hindered the mechanism of extraction of the template from the imprinted cavities. Therefore, only a part of the imprinted sites remained available, and the capacity of the network was reduced, sometimes drastically (around 10−20% of the sites were active).[1]

To improve this technique, the challenge was to rationalize the necessary stiffness of the network with the expansion of its capacity. From this perspective, the use of liquid crystalline networks should be a useful tool in the search for systems developing cohesive effects in addition to cross-linking points.[7] Such networks were already used successfully as reaction media[8] or as supports for HPLC.[9] In the following, we developed a preliminary study of such a kind of network applied to molecular imprinting. For that purpose, we chose side chain liquid crystalline polymers in which mesogenic units were fixed laterally to a polymer backbone (here a polysiloxane chain). These networks could practically exhibit all the mesogenic phases.[10,11] In such systems, the interactions that developed between mesogenic substituents conferred on the network a stiffness from non covalent interactions and allowed the cross-linker proportion to be very low. As a result, while the rate of cross-linkers decreased, larger amounts of template should be introduced and the template should be easily extracted.

For this study, acetophenone, which has already been used in previous studies with polyacrylates imprinted networks,[12−14] was chosen as a template. It was linked covalently to the mesomorphous network thanks to a ketal link. The capacity and the specificity of the molecularly imprinted networks obtained were estimated.

2. Experimental Section. 2.1. Synthesis. The networks investigated were synthesized as shown in Figure 1. The precursor polymer backbone (**3**) was a poly(hydrogenmethyl-*co*-dimethyl)siloxane with 50% of hydrogenmethylsiloxane units, synthesized in the laboratory as previously described.[15] The average number molecular weight (M_n) of the polymers was determined by tonometry experiments and corresponds to an average number degree of polymerization of 80 units. The polydispersity, characterized by means of size exclusion chromatography, was relatively narrow ($M_w/M_n = 1.2$). For these copolymers, the random distribution of the units was checked by ^{29}Si NMR.[15] 4-Hydroxymethyl-4′-(3-butenyloxy) phenylbenzoate (**1**), which formed a ketal with the acetophenone that was chosen as a template, was synthesized as shown in Figure 2. The alcohol function of 4-hydroxymethyl benzoic acid was first protected.[16] Monoalkylated hydroquinone was prepared as previously described,[17] and an esterification reaction was then performed with the protected acid in dichloromethane using *N*,*N*′-dicyclohexylcarbodiimide (DCC) and 4-dimethylaminopyridine (DMAP). **1** was obtained after deprotection of the alcohol function, filtration, and recrystallization in ethanol (yield 30%).[16] This compound exhibits no mesomorphic behavior as checked by polarized optical microscopy. To obtain a mesomorphic network, the 4-methoxy-4′-(3-butenyloxy) phenylbenzoate mesogenic compound (**2**) was also synthesized.[17] As shown by optical microscopy and differential scanning calorimetry, this compound exhibits a monotropic nematic phase: crystal 92 (nematic 52) isotropic (enthalpy variation, $\Delta H_{I-N} = 1.87$ J/g). The cross-linking agent was a commercial available one: 1-21 docosadiene (Aldrich).

The first step in the synthesis of the imprinted polymer network (Figure 1) involved the formation of a ketal function between the template and **1** with para-toluene sulfonic acid as catalyst (Dean−Stark; yield < 10%).[18] In the second step, ketal previously obtained and **2** were fixed on the siloxane chain, by an hydrosilylation reaction performed at 60 °C in toluene, and catalyzed

* Corresponding author: J. D. Marty.

10.1021/ma990592+ CCC: $18.00
Published on Web 11/13/1999

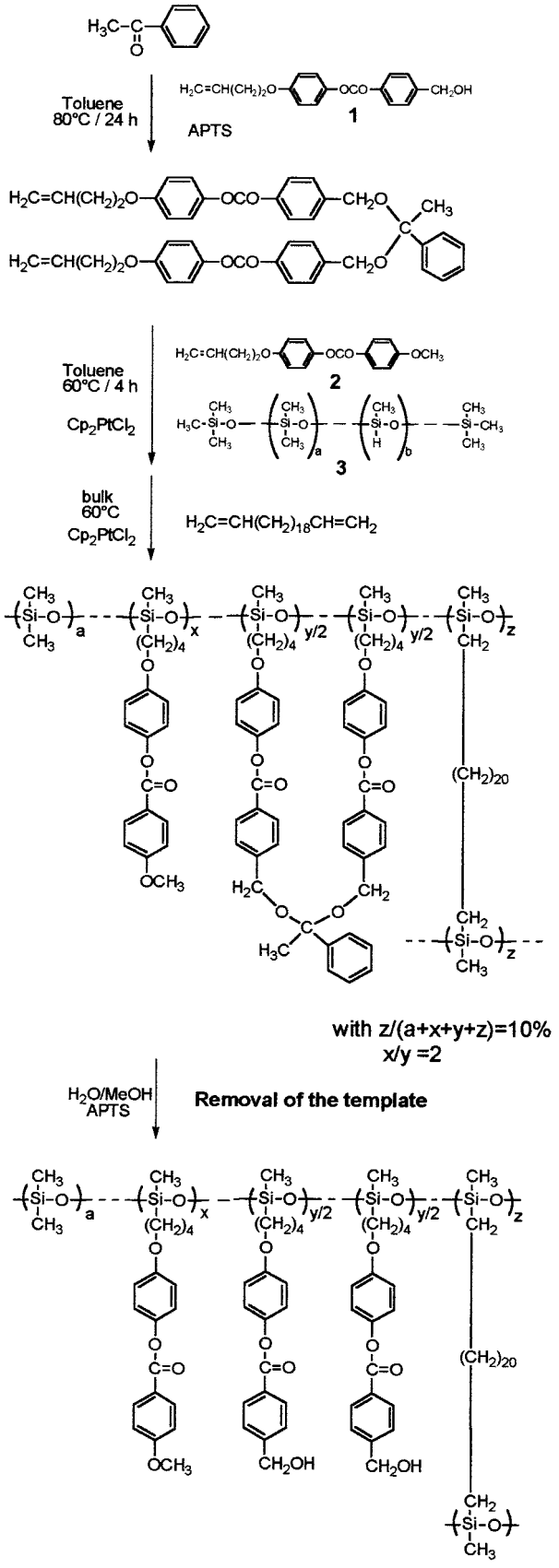

Figure 1. Scheme of the realization of the samples.

by a platinum complex.[17] This reaction occurs between the hydrogenmethylsiloxane units and the vinyl end groups of either the mesogen or the ketal. Vinyl groups were put in deficit so that 10% of silane functions still remained unsubstituted. After removal of the solvent at room temperature by evaporation under vacuum, the polymer network was obtained via the addition of the cross-linking agent, in bulk at 60 °C, on the remaining 10% silane functions. The removal of the template was performed at room temperature in an acidic solution: methanol/water/*p*-toluenesulfonic acid. This solution was a nonsolvent of the network; it was used in order to not disturb the mesomorphic structure of the network.

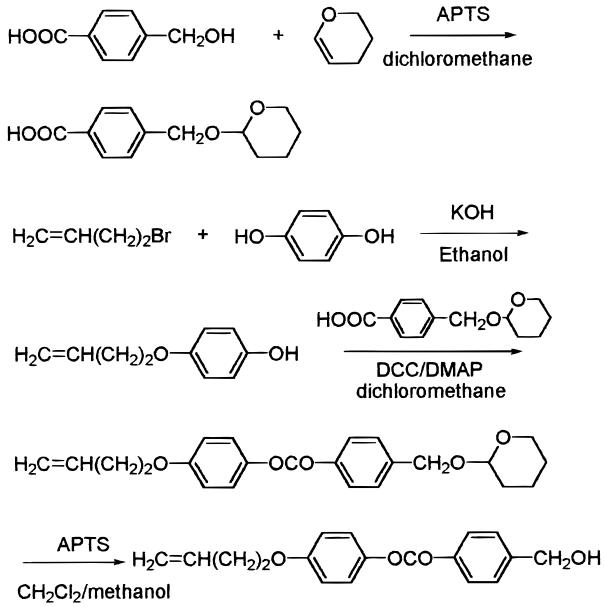

Figure 2. Scheme of the synthesis of substituent **1**.

Two series (**A** and **B**) of polymer networks were synthesized using two different proportions of dimethylsiloxane units (*a*), respectively 50% and 25%. In each series, one sample (**A′** and **B′**) was prepared with only mesogenic moieties as pending groups. A mesogen-free network (**A″**) was also realized in comparison. In samples **A** and **B**, the amount of mesogenic groups was twice as much as the amounts of groups **1**. The proportion of introduced cross-links was 10% for all the networks. The materials were obtained as a solid mass and were analyzed without sieving.

2.2. Characterization. Phase transitions determinations were performed by differential scanning calorimetry (Perkin-Elmer PYRIS 1). The transition temperatures reported in Table 1 correspond to those determined from the position of the peaks as the temperature fell at a rate of 5 °C/min. Infrared measurements were performed on Perkin-Elmer IR FT 1600, NMR ^{1}H analysis was obtained from a Brucker ARX 400 MHz.

3. Results and Discussion. 3.1. Polymorphism. The thermal behaviors of all the networks synthesized were summarized in Table 1. The mesogen-free sample (**A″**) exhibits no mesomorphic behavior, as expected. All the other networks are mesomorphous and display one or two liquid crystalline phases, the nature of which are still under investigation. In Table 1, the indices specified the state of the network: 0 means blank, i.e., without any template during the synthesis, 1 refers to samples synthesized with the template and analyzed before extraction of the template, 2 corresponds to samples after extraction of the template. The comparison between **A** and **A′** (or **B** and **B′**) as given in Table 1, shows that T_g increases for a same rate of mesogen, due to toughening of the backbones achieved by substituents **1**; these groups have a structure close to that for the

Table 1. Characteristics of the Samples[a]

network		*a*, %	*x*, %	*y*, %	T_g, °C	M1 → M2, °C	I → M1, °C	ΔH_{M1-M2}, J/g	ΔH_{I-M1}, J/g
A	$\mathbf{A_0}$	50	26.5	13.5	−20	8.3	19.5	1.7	2.9
	$\mathbf{A_1}$	50	26.5	13.5	−15		21[b]		<0.3
	$\mathbf{A_2}$	50	26.5	13.5	−16		22[b]		<0.3
A′		50	26.5	0	−28		8		1.5
A″		50	0	40	−10				
B	$\mathbf{B_0}$	25	43	22	2.7	6	26	2.6	5.3
	$\mathbf{B_1}$	25	43	22	4	5[b]	20[b]	2.4	4.6
	$\mathbf{B_2}$	25	43	22	4	5[b]	21[b]	<0.3	≈1
B′		25	43	0	−10		40		2

[a] Key: y (%), proportion of substituents **1** linked on the polysiloxane chain (with or without template); T_g, glass transition temperature; I, isotropic phase; M1, high-temperature mesophase; M2, low-temperature mesophase; ΔH, enthalpy variation for phase transition (J/g). [b] Broad peak.

mesogen, which should explain this behavior. On the other hand, we can observe (**A_0**, **A_1**, **A_2** or **B_0**, **B_1**, **B_2**) that the introduction of the template into the network modifies the polymorphism, i.e., the template plays the role of an impurity: the DSC peaks appear with a lower enthalpy variation and are broader. However, the important point that should be noted is that samples **A_1** and **A_2** (**B_1** and **B_2**) exhibit the sample mesomorphism: the introduction of the template modifies the interactions between mesogens and this phenomenon persists after extraction of the template. This result reveals a significant memory effect inside the imprinted network.

3.2. Extraction of the Template and Batch-Rebinding Studies. The amounts of template incorporated during the synthesis of samples **A_1** and **B_1** correspond to 350 and 380 μmol/g of polymer, respectively. These amounts are notably higher than those of the usual imprinted materials (around 100 μmol/g of polymer[13]) in which high cross-linker rates are needed. This amount should be increased by decreasing the rate of mesogen, but this rate cannot be too low; indeed in sample **A**, the mesomorphic order appears weaker than for **B** (in the former, ΔH is too small to be determined).

The amount of template that should still remains inside the network after extraction (samples **A_2** and **B_2**) was evaluated by ^{1}H NMR. The disappearance of the peak at 8.1 ppm relative to the phenyl group of acetophenone proves that the template was completely removed under acidic conditions.

To evaluate the ability of the networks to recognize specifically the template molecule, batch-rebinding studies were performed with, in one case the template, and in the other case, another ketone: a diketone 4,4′-diacetyl biphenyl. Each ketone was separetely placed in the presence of the imprinted network, at room temperature, during 1 day, without stirring in order to avoid breaking the material. Acetophenone was added without any solvent, whereas diketone was previously dissolved in a minimum of toluene. The toluene induced a small swelling of the network (swelling ratio lower than 2) that is not enough to destroy the mesomorphic order.[20] The resulting network was then washed with methanol (a nonsolvent that does not swell the network) and dried under vacuum. The amount of introduced ketone can be evaluated by weighing the resin before and after introduction. The accuracy of this determination was increased by using FT-IR spectroscopy. This technic allows to evaluate the amount of nonrebound acetophenone or of monolinked diketone present in the network after the extraction steps. First a calibration curve was realized by mixing a blank nonimprinted network with various amount of ketone (under these conditions, no ketal formation was observed). The various samples were then analyzed: each of the FT-IR spectra (KBr suspension) was submitted to the same baseline correction, and residual H_2O absorption was removed by spectral subtraction. The net peak area of the carbonyl group of the ketone was determined in the absorbance mode between the integration limits of 1710 and 1670 cm^{-1}. The area was normalized against the net reference absorption of the ester group of the both *x* and *y* benzoate groups between 1710 and 1760 cm^{-1}. The normalized carbonyl peak area was then plotted against the micromoles of ketone function per gram of polymer. This method allowed to verify that no free acetophenone still remained in the network after the rebinding process and that the amount of diketone rebound was under 10 μmol/g. A complete study was performed with samples **A** (Table 2). For these networks, the amount of template incorporated during synthesis corresponded to 350 μmol/g of polymer. The amount of acetophenone rebound was found to be 150 μmol/g of polymer (40% of the initial sites ± 10%) whereas the amount of 4,4′-diacetyl biphenyl introduced was minor at 10 μmol/g of polymer. For the corresponding nonimprinted network (sample **A_0**), no significant rebinding of acetophenone or diketone was observed. So the imprinted network showed a good selectivity for the template with an amount of rebound sites of 40% (±10%). Moreover this rebinding rate was certainly still limited by some problems of diffusion inside these solid mass materials.

Table 2. Capacity and Specificity of Samples A vs Ketone Molecules[a]

network	α, μmol/g of polymer	β, μmol/g of polymer	δ, μmol/g of polymer	
			acetophenone	diketone
A0	0	≈0	<20	<10
A1−A2	350	≈0	150	<10

[a] Key: α, amount of acetophenone incorporated during synthesis; β, amount of acetophenone remaining in the network after extraction; δ, amount of ketone molecule rebound in the network.

Conclusion. The imprinted materials studied here gave some encouraging perspectives. These networks remain mesomorphous even with high amounts of template. The liquid crystalline character increases the interactions between the polymer backbones and avoids high cross-linking densities. So the initial capacity of the network is much more important than in the previously studied systems. Moreover, the liquid crystalline behavior is almost not modified by the extraction of the template, which proves a memory effect inside the network. The first experiments, performed to define the selectivity of these materials, showed a good specificity toward the template molecule. The best compro-

mise between the mesogenic units rate and the template amount has yet to be found. Moreover in order to optimize the conditions of use and to enhance the accuracy in the determination of the selectivity of this kind of network, chromatography studies are under consideration.

This preliminary study showed the potential uses of liquid crystalline polymer networks as materials for the molecular imprinting technique. Some questions arise from these first results. The first remark that should be pointed out is that all the experiments described in this study were realized with samples in the mesomorphic state. Another works have to be performed in the glassy state in which the liquid crystalline organization can be frozen. Then, what is exactly the role of the pending mesogenic groups? Is it the liquid crystalline interactions that toughen the network and increase its selectivity, or is it the bulkiness of the pending groups and their chemical interactions that play the main role? This point will to be clarified in the next study. Moreover the final aim of this work is to specifically turn the liquid crystalline character introduced to good account, either to easily modify the orientation of all the substituents or to induce chiral structures inside the cavities.

References and Notes

(1) Wulff, G. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1812 and reference therein.
(2) Shea, K. J. *TRIP* **1994**, *2*, 166.
(3) Sellergren, B. *Trends Anal. Chem.* **1997**, *16*, 310.
(4) Ekberg, B.; Mosbach, K. *TIBTECH* **1989**, *7*, 92.
(5) Morihara, K.; Takigushi, M.; Shimata, T. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 1078.
(6) Ramström, O.; Ansell, R. J. *Chirality* **1998**, *10*, 195.
(7) Davis, F. J. *J. Mater. Chem.* **1993**, *3*, 551.
(8) Weiss, R. G. *Tetrahedron* **1988**, *44*, 3413 and references therein.
(9) Saito, Y.; Jinno, K.; Pesek, J. J.; Chen, Y.-L.; Luehr, G.; Archer, J.; Fetzer, J. C.; Biggs, W. R. *Chromatographia* **1994**, *38*, 295.
(10) (a) Finkelmann, H.; Koch, H.; Rehage, G. *Makromol. Chem. Rapid Commun.* **1981**, *2*, 317. (b) Zubarev, E. R.; Talroze, R. V.; Yuranova, T. I.; Plate, N. A.; Finkelmann, H. *Macromolecules* **1998**, *31*, 3081.
(11) Dubois, J. C.; Le Barny, P.; Mauzac, M.; Noel, C. In *Handbook of liquid crystal*; Demus, D., Goodby, J. W., Gray, G. W., Spiess, H. W., Eds. Wiley-VCH: London, 1998; Vol, IV, Chapter 5.
(12) Shea, K. J.; Sasaki, D. Y. *J. Am. Chem. Soc.* **1989**, *111*, 3442.
(13) Shea, K. J.; Sasaki, D. Y. *J. Am. Chem. Soc.* **1991**, *113*, 4109.
(14) Shea, K. J.; Sasaki, D. Y.; Stoddard, G. J. *Macromolecules* **1989**, *22*, 1722.
(15) Leroux, N.; Mauzac, M.; Noirez, L.; Hardouin, F. *Liq. Cryst.* **1994**, *3*, 421.
(16) Miyashita, N.; Yoshikoshi, A.; Grieco, P. A. *J. Org. Chem.* **1977**, *42*, 3772.
(17) Mauzac, M.; Hardouin, F.; Richard, H.; Achard, M. F.; Sigaud, G.; Gasparoux, H. *Eur. Polym. J.* **1986**, *22*, 137 and references therein.
(18) Meskens, A. J. *Synthesis* **1981**, 502.
(19) Stille, J. K.; Morgan, R. A.; Whitehurst, D. D. *J. Am. Chem. Soc.* **1965**, *87*, 3282.
(20) Zanna J. J.; Mauzac, M.; Boué, F. *Macromolecules* **1999**, *32*, 2962.

MA990592+