Solid-State Hosts by the Template Polymerization of Columnar Liquid Crystals: Locked Supramolecular Architectures around Chiral 2-Amino Alcohols

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Abstract: The cross-linking of multi-component liquid crystals could be applied to the synthesis of nanometer-sized porous materials with a well-defined structure. In this work we demonstrate the template polymerization of columnar liquid crystals composed of the salts of a carboxylic acid and enantiopure 2-amino alcohols, and the application of one of them as a solid-state host. The salts of 3,4,5-tris(11-acryloyloxyundecyloxy)benzoic acid with (S)-2-amino-1-propanol and with (1R,2S)-norephedrine showed hexagonal and rectangular columnar liquid-crystalline structures, respectively. The successful application of γ-ray-induced polymeri-
zation to the cross-linking of the liquid-crystalline salts, which was more advantageous than photoinduced polymerization from the standpoint of the retention of the original structural order in the gram-scale preparation of the polymers with a homogeneous columnar structure. The cross-linked polymer thus obtained from the gallic acid derivative and (1R,2S)-norephedrine was applicable as a heterogeneous host to capture amines from a guest solution
through acid–amine interactions. When (1R,2S)-norephedrine was replaced with other amines through the guest-exchange reaction, a "template effect" was observed; the size and shape of the guests were determining factors for the efficiency of the guest exchange. The guest adsorption was found to proceed in an enantioselective manner when racemic 2-amino alcohols were used as guests, especially in the cases of substrates possessing a bulky substituent at the C1-position. The guest preference was again elucidated by the template effect, although the enantioselection mode was switched depending on the presence of a C2 substituent.

**Keywords:** chiral recognition · host–guest systems · liquid crystals · nanostructures · template synthesis

Introduction

Architectures with an ordered structure on the submicrometer scale have recently attracted increasing attention.[1] Among them, organic materials with nanometer-sized pores are of special interest because of the characteristics of organic compounds, such as physical robustness and processability, as well as tunability in size and shape, and chemical/physical properties; they provide us with a new type of porous material and find various applications as selectors,[2] sensors,[3] and catalysts.[4] For the development of such materials, the cross-linking of multicomponent liquid crystals (LCs) is one of the most promising methods.[5] When a poly-
merizable mesogen (matrix) and another component (template) noncovalently interact with each other to form a liquid-crystalline (LC) structure, cavities with a well-defined structure complementary to the template are expected to be created by the in situ cross-linking of the matrix. Although polymerization reactions do not necessarily proceed in constrained architectures, such as in crystals,[6] the dynamic nature of the LC materials would permit an efficient cross-linking to "freeze in" the desired structure. In addition, considering the noncovalent nature of the linkage between the matrix and the template, the cross-linked materials should be applicable as solid-state hosts by removing and/or exchanging the template moiety (Scheme 1). Compared with the conventional molecular imprinting method, the present strategy will achieve further improved monoclonality of cavities, owing to the well-controlled alignment of components in anisotropically ordered LC structures.[7]

In the last few decades, several solid-state hosts have appeared based on the in situ cross-linking of LC materials. For example, the cross-linking of lyotropic LCs (reversed micelles) with a columnar structure has been extensively

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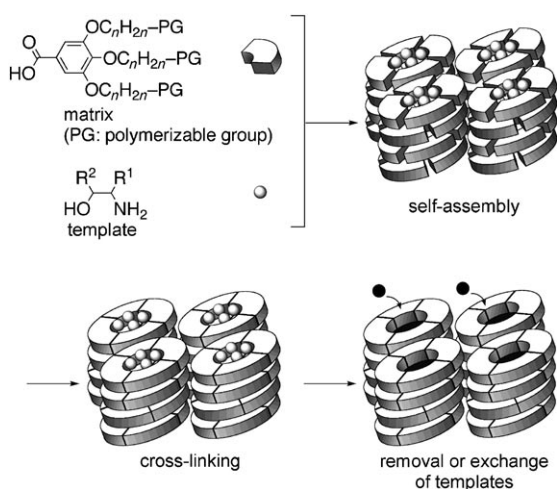
Scheme 1. Schematic representation of the preparation of the cross-linked polymer with an ordered structure and its application as a solid-state host.

studied by Gin et al., and afforded various sophisticated materials, including organic zeolite analogues,[2a,b] heterogeneous catalysts,[4b–e] and optical devices.[8] In addition, the application of a similar concept to thermotropic LCs has also been reported. As a typical example, Kim et al. used a columnar liquid crystal (CLC), composed of an aromatic heterocycle with a D_{3h} symmetric structure and an amphiphilic carboxylic acid possessing polymerizable groups, to develop an organic zeolite analogue with a hexagonal channel.[5c] In these examples, however, there are some problems with the generality and utility of the core unit. In the case of the lyotropic LC systems, the inner spaces of the columnar structures should be occupied by an uncertain number of solvent molecules, the arrangement of which is very difficult to predict. On the other hand, for the formation of thermotropic LC architectures, core units with a special structure are generally required, which is a serious obstacle for further sophisticated manipulation of these motifs.

Recently, we have briefly reported a novel thermotropic CLC system, which could be conveniently prepared through the salt formation of two easily available components, a gallic acid derivative and a 2-amino alcohol.[5a,b] A template polymerization approach was successfully adapted to our CLC system, and the preliminary application of the resultant material as a solid-state host

has been demonstrated by taking advantage of the exchangeable nature of the 2-amino alcohol unit with other amines (Scheme 1). Considering the characteristic properties of the core unit, a 2-amino alcohol, our system would have special relevance compared with the precedent systems from the following viewpoints: 1) 2-Amino alcohols are one of the most readily available classes of enantiopure materials, which allows us to prepare various chiral architectures just by changing the core unit. 2) The separation of the regio-/stereoisomers of 2-amino alcohols is of significant importance, because they are indispensable materials in most areas of chiral technology. Therefore, we thoroughly investigated the synthesis, properties, and characteristics of this material, and discuss the results in terms of the optimal conditions for its preparation, the scope and limitations of the template unit, the detailed guest-removing/exchanging process, and the application to the separation of amines.

Results and Discussion

Phase-transition behavior of the salts of the polymerizable carboxylic acid 1 with amines: To probe the scope of amines applicable as a core unit of the present LC-based template polymerization, the phase-transition behavior and lattice parameters of the salts of the polymerizable carboxylic acid **1** with various amines (**2–8**) were investigated (Table 1).[9] Cross-polarized optical microscopy, X-ray diffraction (XRD), and differential scanning calorimetry (DSC) revealed that the salts **1·(S)-3** and **1·(1R,2S)-5** took hexagonal ($P6mm$, 42.3 Å)[10] and rectangular ($P2m$, 45.2 × 26.8 Å) CLC structures, respectively, which were unambiguously

Table 1. Phase-transition behavior of the salts of a polymerizable carboxylic acid **1** with various 2-amino alcohols.

Amine	Phase transition[a]	Amine	Phase transition[a]
HO—NH₂ (R)-2	I	HO—NH₂ (S)-6	$M \xrightarrow{43} I$
HO—NH₂ (S)-3	$Col_h \xrightarrow{47} I$ $P6mm; a = 42.3$ Å	HO—NH₂ (S)-7	$K \xrightarrow{45} I$
HO—NH₂ (R)-4	$K \xrightarrow{43} I$	HO—NH₂ (1R,2S)-8	$K \xrightarrow{77} M \xrightarrow{91} I$
HO—NH₂ (1R,2S)-5	$Col_r \xrightarrow{73} I$ $P2m; a = 45.2, b = 26.8$ Å		

[a] Data were determined during the first heating scan (10 °C min⁻¹). K: crystalline phase; Col_h: columnar hexagonal phase; Col_r: columnar rectangular phase; M: mesophase; I: isotropic phase. Transition temperatures [°C] are given above the arrows.

characterized by three and nine refractions in the small-angle regions (Figure 1).[5a,b] According to the lattice parameters and the molecular models, the numbers of acid–base pairs included in one layer of a cylinder were estimated to
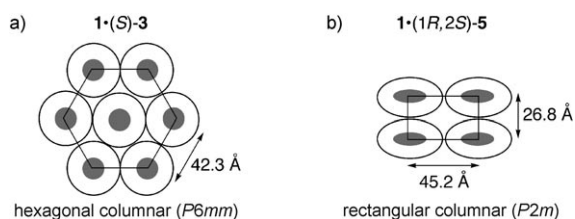

Figure 1. Representation of the arrangement of columns in the a) *P6mm* and b) *P2m* space groups.

be four for the hexagonal CLC structure and three or four for the rectangular CLC structure. On the other hand, by introducing a bulky substituent at the C2-position of a 2-amino alcohol, the formation of a CLC structure was significantly inhibited. The salt with (*S*)-**7** existed as a crystal at room temperature and directly transformed into an isotropic liquid upon raising the temperature, whereas the salts with (*S*)-**6** and (1*R*,2*S*)-**8** showed unknown metastable phases, displaying only a few XRD peaks with a low intensity. For the formation of a stable CLC structure, such an unfavorable effect of a bulky substituent at the C2-position of a 2-amino alcohol was also observed in the case of the salts with 3,4,5-tris(dodecyloxy)benzoic acid, an unpolymerizable analogue of **1**.[5b]

Cross-linking of the salts in the liquid-crystalline state: In general, the in situ polymerization of LCs is conducted by the photoinitiated radical polymerization of acryloyl group(s) embedded at the end of the aliphatic chain(s) in mesogens.[2,4b,c,e,5] For this method, a small portion of a photoinitiator should be added to LC materials in order to generate radical species efficiently. Therefore, in our previous study, the cross-linking of the salt **1**·(1*R*,2*S*)-**5** was accomplished by the photoinitiated polymerization of acrylic ester moieties in **1** with the aid of a radical initiator, 2-hydroxy-2-methylpropiophenone.[5a,b] However, for the preservation of the structural order in the resultant cross-linked polymer, there were several problems in the photoinitiated polymerization. 1) Addition of a photoinitiator, even approximately 2.5 wt% only, often gives rise to the undesired distortion of the ordered structure in a LC material. 2) The low penetration nature of UV/Vis light tends to cause the partial polymerization of a LC material at the surface domain, which could not guarantee the homogeneity of the resultant cross-linked polymer. 3) The amount of a sample applicable for each batch is limited to no more than several hundred milligrams whenever a usual light source is used. As an alternative method, γ-ray-induced polymerization is known, but its effectiveness has not yet been adequately proved in the cross-linking of LC materials.[11] Therefore, we applied γ-ray-induced polymerization to the cross-linking of the LC

salt **1**·(1*R*,2*S*)-**5**, and the properties of the resultant polymer were compared with those of the polymer obtained by conventional photoinitiated polymerization.

The γ-ray-induced polymerization of **1**·(1*R*,2*S*)-**5** was carried out (dose rate, 1.7 kGy h^{-1}; irradiation time, 48 h) in evacuated and sealed glass tubes at room temperature. The polymerization of the acryloyl groups in **1** proceeded smoothly, which was confirmed by FTIR spectroscopy (Figure 2b, iii). The resultant solid mass was hardly soluble in most solvents, which also supports our expectation that the degree of cross-linking was at a satisfactory level. The cross-linked polymer thus obtained was mechanically milled and
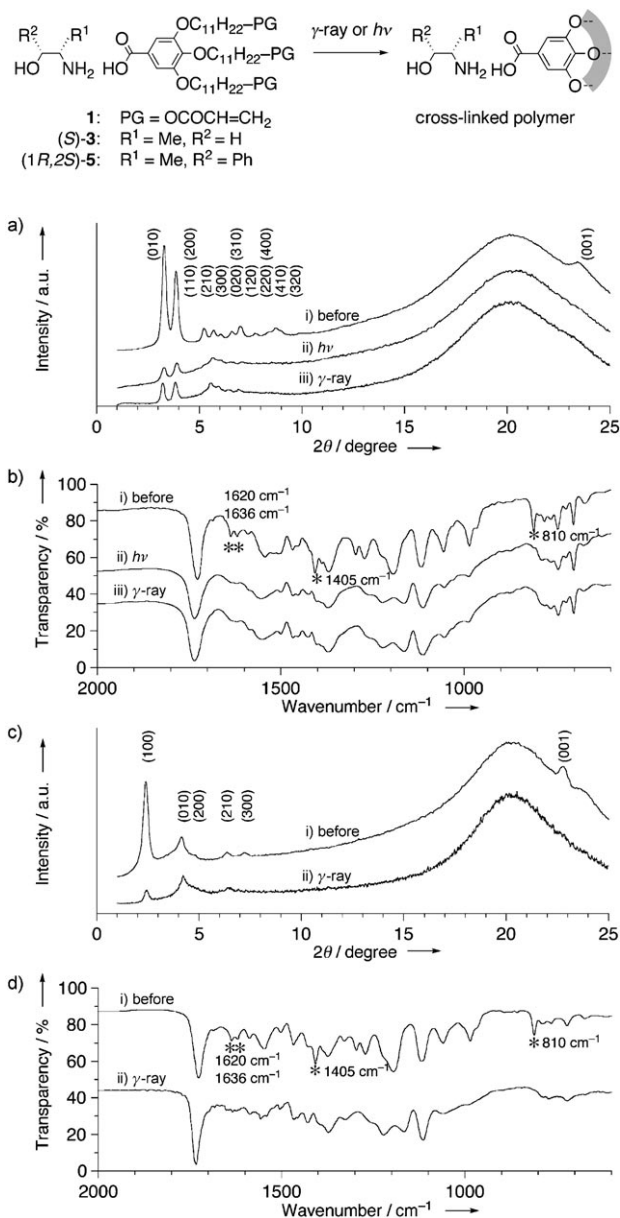

Figure 2. In situ polymerization of the LC salts **1**·(1*R*,2*S*)-**5** and **1**·(*S*)-**3**. a) XRD and b) IR profiles of **1**·(1*R*,2*S*)-**5** i) before polymerization, ii) after photoinduced polymerization, and iii) after γ-ray-induced polymerization. c) XRD and d) IR profiles of **1**·(*S*)-**3** i) before polymerization and ii) after γ-ray-induced polymerization.

washed with CHCl₃, in which trace amounts of unreacted **1** and (1*R*,2*S*)-**5** (<2%) were leached out from the polymer.

The XRD analysis showed that the original structural order in **1**·(1*R*,2*S*)-**5** was retained through the γ-ray-induced polymerization process, although the intensity of the XRD peaks was diminished compared with those of the initial state (Figure 2a, iii). Such a decrease in intensity of the XRD peaks, which were most likely due to the structural perturbation induced by the polymerization, were commonly observed in the cases of the γ-ray-induced and photoinitiated polymerization methods. In addition, the extension of the γ-ray irradiation time (four days) had little influence on the XRD and IR properties of the resultant polymer. Notably, there was a significant difference in structural order between the cross-linked polymers obtained by the two polymerization methods, as we expected (Figure 2a, ii and iii); in the small-angle region, the polymer obtained by the γ-ray-induced polymerization exhibited reflections undoubtedly stronger than those of the polymer obtained by the photoinitiated polymerization. Such good preservation of the original ordered mesostructure through the γ-ray-induced polymerization is most likely due to the beneficial properties of the ⁶⁰Co γ-ray.

From the viewpoint of scalability, the γ-ray-induced polymerization was also advantageous when compared with photoinitiated polymerization. The former method was proved to be applicable to a gram-scale preparation of the cross-linked polymer (up to 2.0 g). Contrary to this, in the case of the latter method, the thickness of the sample should be no more than approximately 1 mm in order to promote the photoinitiated polymerization sufficiently and to guarantee the homogeneity of the resultant polymer. Taking account of these advantages compared with photoinitiated polymerization, we adopted γ-ray-induced polymerization for the following studies.

The γ-ray-induced polymerization method was successfully applied to the cross-linking of **1**·(*S*)-**3** (Figure 2d), which exhibited a hexagonal CLC structure at room temperature. XRD analysis of the resultant polymer strongly suggested that the ordered hexagonal columnar structure was preserved throughout the cross-linking process (Figure 2c). However, the amine template (*S*)-**3** was easily volatilized from the cross-linked polymer, especially under low-pressure conditions, which was confirmed by monitoring the changes in the intensity of the IR adsorption peaks attributable to the ammonium carboxylate salt and the free carboxylic acid. On the other hand, such a phenomenon was not observed in the case of the cross-linked polymer from **1**·(1*R*,2*S*)-**5**. Although there remains a question of whether or not the packing mode of columns relates to the volatility of the core unit, this is most likely due to the difference in boiling point between the two core compounds and/or the effect of noncovalent interaction(s) involving the aromatic groups.

Removal of the template from the cross-linked polymer by treatment with an acid/base: In the cross-linked polymer thus obtained, the carboxylate units were immobilized by cross-linking with each other, whereas the amine units were incorporated in the matrix by noncovalent interactions. Owing to such structural characteristics, the cross-linked polymer was potentially applicable as a solid-state host to capture amines through acid–base interactions. As the beginning of host–guest chemistry in the cross-linked polymer, we studied the mass transfer between the cross-linked polymer and an external solution.

To promote the dissociation of a carboxylic acid–amine salt, the cross-linked polymer obtained from **1**·(1*R*,2*S*)-**5** was treated with various acidic/basic solutions, and the amount of (1*R*,2*S*)-**5** released from the cross-linked polymer was monitored by HPLC (Table 2). Typically, the cross-linked

Table 2. Removal of (1*R*,2*S*)-**5** from the cross-linked polymer by treatment with acids/bases.[a]

Entry	Acid/base	Method	Desorbed guest [%][b]
1	HCOOH	sonication	74
2	HCl	sonication	57
3	HBr	sonication	17
4	HClO₄	sonication	19
5	NH₄Cl	sonication	18
6	NH₃	sonication	73
7	HO(CH₂)₂NH₂ (**9**)	sonication	84
8	HO(CH₂)₂NH₂ (**9**)	RT	84
9	HO(CH₂)₂NH₂ (**9**)	50°C	86
10[c]	HO(CH₂)₂NH₂ (**9**)	50°C	82

[a] Conditions: amount of polymer = 45.0 mg (calculated to contain 45 μmol of the carboxylic acid–amine pair); amount of external acid/base = 7500 μmol (1.5 M, 5.0 mL in methanol/water = 1:1, v/v), 4 h. [b] Data are given with respect to the initial amount of the original guest (1*R*,2*S*)-**5** in the cross-linked polymer (45 μmol). [c] The cross-linked polymer before mechanical milling was used. Reaction time: 8 h.

polymer (45.0 mg, calculated to contain 45 μmol of the carboxylic acid–amine pair) was suspended in a solution containing a large excess of acid or base (1.5 M, 5 mL in methanol/water = 1:1, v/v), and the mixture was subjected to ultrasound sonication. The system reached a steady state within four hours, which was confirmed by HPLC detection. Notably, the efficiency of the extraction was significantly influenced by the choice of acid/base. In the case of acid treatment, the most determinant factor was undoubtedly the hydrophilicity/size rather than the pK_a. In the case of the treatment with HCOOH, 74% of (1*R*,2*S*)-**5** was extracted (Table 2, entry 1), whereas the extraction with HCl, HBr, and HClO₄ stopped at a moderate to poor level (57, 17, and 19%, respectively) although they are relatively strong acids (Table 2, entries 2–4). On the other hand, the treatment with amines realized efficient extraction comparable or superior to the case of HCOOH (Table 2, entries 6 and 7).

Among them, the treatment with 2-aminoethanol (**9**), which may be regarded as a "skeleton" of the original template (1*R*,2*S*)-**5**, achieved the extraction to an exceptional degree (84%; Table 2, entry 7). The difference between these entries might be elucidated by the degree of preservation of the structural order in the cross-linked polymer during the template-removal process. As we have recently reported, the removal of the template caused a dramatic change in the structure of the polymer (Figure 3a, ii and iii), and such
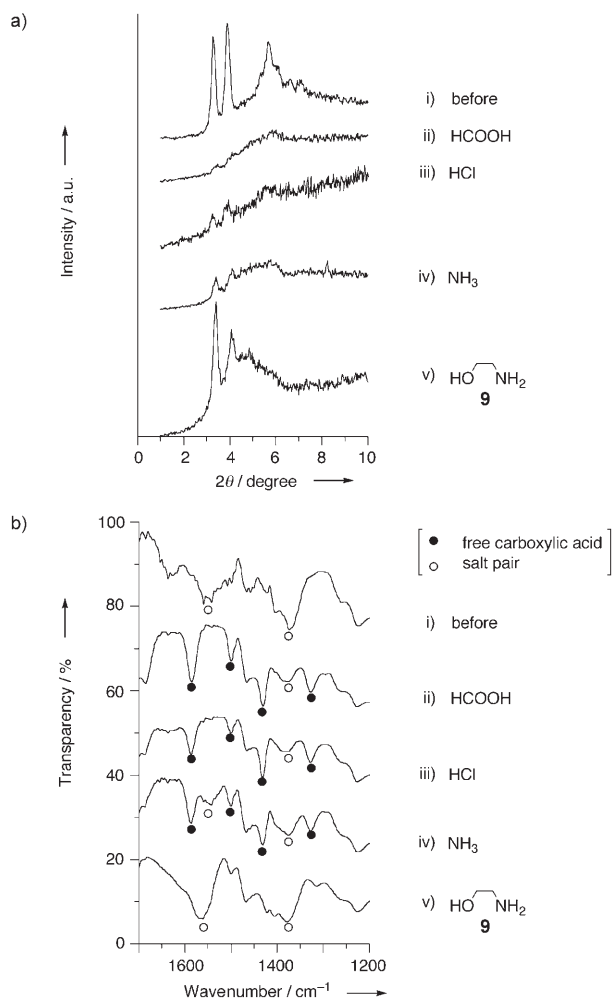
Figure 3. Removal of the template (1*R*,2*S*)-**5** from the cross-linked polymer. a) XRD and b) IR profiles of the polymer i) before extraction, and ii–v) after extraction with a methanol/water (1:1, v/v) solution (1.5 M) of ii) HCOOH, iii) HCl, iv) NH₃, and v) 2-aminoethanol (**9**).

an alteration was likely to prevent the template from being released.[5a] However, owing to its structural resemblance to the template (1*R*,2*S*)-**5**, the 2-amino alcohol **9** could efficiently fill the vacant sites which were originally occupied by (1*R*,2*S*)-**5** molecules so that a serious structural change would not occur. In fact, among the cross-linked polymers after these treatments, the polymer treated with **9** exhibited exceptionally strong XRD reflections. These results suggest that some structural order was well preserved only in the

case of the treatment with **9**, although the *d* spacings slightly decreased. In addition, the IR spectra of the polymers clearly showed that most of the carboxylic acid units existed as a salt form after treatment with **9**, whereas the other treatments generated free carboxylic acids (Figure 3b).

In order to realize the complete removal of the original template, several methods were applied by using **9** (Table 2, entries 8–10). However, these modifications did not bring an essential influence on the amount of (1*R*,2*S*)-**5** released (82–86%), but only on the reaction rate. In addition, a control experiment showed that the average size of the polymer particle was not a crucial factor to determine the efficiency of the extraction; even when a polymer sample before the milling process was used in place of a sample of fine powder, no less than 82% of (1*R*,2*S*)-**5** was leached out (Table 2, entry 10). From these observations, it can be clearly deduced that at least 86% of (1*R*,2*S*)-**5** did not take part in undesired side reactions during the polymer preparation processes (the formation of LCs and the γ-ray-induced cross-linking).

Exchange of the original guest in the cross-linked polymer with another 2-amino alcohol: Taking into account the results described above, we then attempted to evaluate the molecular recognition ability of the cross-linked polymer by using the guest-exchange reaction. As an initial model, we chose the exchange reaction of the original guest with (*R*)-**4**. Owing to the strong structural resemblance of (1*R*,2*S*)-**5** to (*R*)-**4**, the guest-exchange reaction was expected to proceed efficiently without involving complicated side reactions or unexpected phenomena. For example, the cross-linked polymer (45.0 mg, calculated to contain 45 μmol of the carboxylic acid–amine pair) was soaked in a methanol solution of (*R*)-**4** (18 mM, 5.0 mL, 2.0 equiv with respect to original guest) at room temperature, and the conversion of the guest-exchange reaction was monitored by checking the amounts of the template (1*R*,2*S*)-**5** and guest (*R*)-**4** in the supernatant. As can be seen in the time-course plot, a steady state was attained within three days, after which 18 μmol of the guest (39% with respect to the amount of the template) was incorporated in the polymer (Figure 4a, ● and ○). The reaction rate was increased by one order of magnitude by raising the temperature to 50°C or by ultrasound irradiation, but the conversion at a steady state was not influenced so much. The XRD and IR profiles of the resultant polymers were essentially identical to those of the polymer before the guest-exchange reaction, which indicates that (*R*)-**4** was incorporated in the sites originally occupied by (1*R*,2*S*)-**5** (Figure 4b and c, ii and iii).[12]

Unexpectedly, the amount of (*R*)-**4** incorporated in the polymer sometimes exceeded the amount of (1*R*,2*S*)-**5** leached out to the supernatant, depending on the conditions and polymer lot.[13] This phenomenon strongly suggests that some adsorption processes other than those we envisaged were involved; if certain amounts of the guest and template once leached out to the solution were adsorbed in the polymer in a nonspecific manner, the apparent quantity of adsorbed (*R*)-**4** will increase, whereas the quantity of released
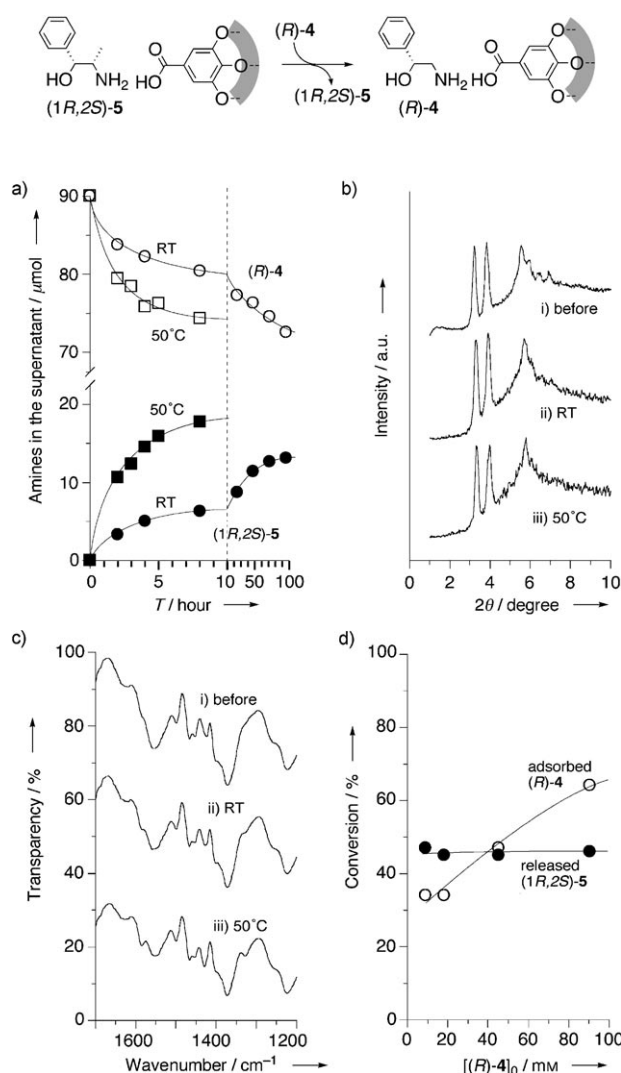
Figure 4. Guest-exchange reaction of (1R,2S)-**5** in the cross-linked polymer with (R)-**4**. a) Time-course plots of the guest-exchange reaction ((1R,2S)-**5**, ● and ■; (R)-**4**, ○ and □). b) XRD and c) IR profiles of the cross-linked polymer i) before exchange, ii) after exchange at room temperature, and iii) after exchange at 50 °C. d) Effect of the concentration of (R)-**4** on the conversion of the exchange at room temperature ((1R,2S)-**5**, ●; (R)-**4**, ○). Conditions: amount of polymer = 45.0 mg (calculated to contain 45 µmol of the carboxylic acid–amine pair); amount of external amine = 90 µmol (in methanol, 18 mm for (a–c) and 9.0–90 mm for (d)), 30 °C, 96 h.

(1R,2S)-**5** will become smaller than it should be.[14] Nevertheless, considering the very small changes in the structural order and in the hydrogen-bonding patterns, which were confirmed by XRD and IR measurements, such an unknown adsorption process seems to be an event hardly related to salt-pair formation between carboxylic acid moieties and amines.[12] Then, we scrutinized the influence of the initial conditions on this phenomenon and found that the concentration of (R)-**4** in a methanol solution was a crucial factor to control such undesired process(es). Upon increasing the concentration of (R)-**4** while maintaining its molar ratio in a methanol solution, the amount of (R)-**4** adsorbed increased
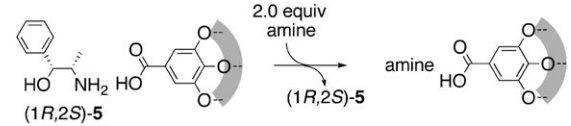
in a proportional manner, whereas the amount of (1R,2S)-**5** released was almost constant (Figure 4d). Thus, as long as the guest-exchange reaction was performed at a satisfactorily low concentration of (R)-**4** (less than approximately 20 mm), the main reaction was likely to be the simple replacement of (1R,2S)-**5** with (R)-**4**, and the progress of the unknown adsorption process(es) could be restricted to a low degree.[13]
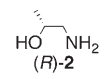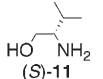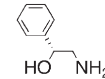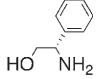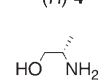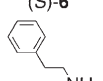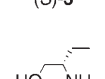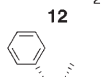
Molecular recognition through the guest-exchanging process: Considering the preparation method of the cross-linked polymer similar to that of general molecularly imprinted polymers,[7] the functional groups in this ordered material were likely to be arranged complementarily to the structure of the template. This expectation prompted us to investigate the molecular recognition ability of the cross-linked polymer through the guest-exchanging process; the guest-exchange reaction was conducted by using various amines in place of (R)-**4**, and the amounts of the guests adsorbed at a steady state were compared.

As summarized in Table 3, the topological shape of the guests was one of the most crucial factors for the efficiency of guest exchange. In the cases of guests for which the C2-position was unsubstituted ((R)-**2**) or substituted with a relatively small group, such as a methyl ((S)-**3**) or ethyl ((S)-**10**) group, the guest exchange proceeded smoothly as in the case of (R)-**4** to achieve incorporation of about 30 % (Table 3, entries 1, 3, and 4). Contrary to this, another family of guests, (S)-**11** and (S)-**6**, bearing an isopropyl group and a phenyl group at the C2-position, respectively, showed much lower affinity (22 and 10 % incorporation, respectively) toward the polymer (Table 3, entries 5 and 6). Thus, as a substituent at the C2 position, an isopropyl group and its equivalent in bulkiness were likely to be the borderline for smooth incorporation into the polymer matrix. Even in competitive guest-exchange reactions, the same tendency in guest preference was again observed, which clearly demonstrates the potential for the practical utility of the polymer as a selector for the separation of amines. For example, when the polymer was soaked in a methanol solution of an equimolar mixture of the regioisomers (R)-**4** and (S)-**6**, the incorporated amounts of (R)-**4** and (S)-**6** at a steady state were 22 and 6 %, respectively.

In order to discover the effect of hydrogen-bonding interactions on the guest exchange, two analogues of (R)-**4**, in which the hydrogen-donating functional groups (OH/NH$_2$) were removed/protected, were employed for the guest-exchange reaction. Unexpectedly, however, the OH-lacking guest **12** and the N-methylated guest (1R,2S)-**13** were incorporated in the cross-linked polymer at a level comparable to that of (R)-**4** (32 % adsorption in both cases). These results suggest that the acid–base interaction between the matrix polymer and the guests was the main driving force to capture guests in the polymer, and that the additional hydrogen-bonding interactions between the C=O group and the OH/NH group had little influence on the efficiency of the guest exchange.

Table 3. The guest-exchange reaction of (1R,2S)-**5** in the cross-linked polymer with various amines.[a]

Entry	Amine	Adsorbed guest[b] (desorbed template) [%]	Entry	Amine	Adsorbed guest[b] (desorbed template) [%]
1	HO NH₂ (R)-**2**	33 (37)	5	HO NH₂ (S)-**11**	22 (35)
2	HO NH₂ (R)-**4**	39 (29)	6	HO NH₂ (S)-**6**	10 (30)
3	HO NH₂ (S)-**3**	31 (35)	7	NH₂ **12**	32 (36)
4	HO NH₂ (S)-**10**	33 (34)	8	HO NHMe (1R,2S)-**13**	32 (42)

[a] Conditions: amount of polymer = 45.0 mg (calculated to contain 45 μmol of the carboxylic acid–amine pair); amount of external amine = 90 μmol (18 mM, 5.0 mL in methanol), 30 °C, 96 h. [b] Data are given with respect to the initial amount of the original guest (1R,2S)-**5** in the cross-linked polymer (45 μmol).
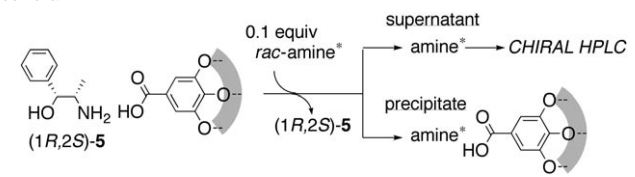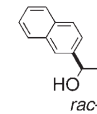
**Chiral recognition through the guest-exchanging process**: As a further intriguing target of guest selection, we next investigated the enantioseparation of racemic amines through the guest-exchange reaction; the racemates of several chiral amines were used for these reactions, and the compositions of the enantiomers in the supernatants were monitored by chiral HPLC. For easy evaluation of the enantiomeric excess (*ee*) of the guest remaining in the supernatant, 0.1 equivalents of the guest (9.0 mM, 1.5 mL) with respect to the amine–carboxylic acid pair in the polymer (135.0 mg, calculated to contain 135 μmol of the carboxylic acid–amine pair) was used for the guest-exchange reaction. Although the enantiomeric composition of the adsorbed guest could not be directly measured, it was unambiguously calculated on the basis of the amount of the adsorbed guest and the enantiomeric excess of the guest remaining in the supernatant (Table 4). As we expected, guest adsorption proceeded in an enantioselective manner, especially in the cases of substrates possessing a bulky substituent at the C1-position (Table 4, entries 2 and 3). In the case of the guests having a substituent only at the C1-position, the enantiomer preferentially adsorbed was of the absolute configuration at the C1-position which is identical to that of the original template (1R,2S)-**5**. This observation strongly suggests that a "template effect" certainly works in this system. In the cases of guests possessing only a C2 substituent, the enantioselections observed were at an unsatisfactory level regardless of the bulkiness of the substituent, and yet the favorable enantiomers were of the same configuration at the C2-position as that of the template (Table 4, entries 4–6). From these results, we can deduce that the stereochemistry at the C1-position is a determinant factor of the enantioselection, whereas

the substituent at the C2-position is likely to bring little influence, as long as either the C1- or C2-position of a 2-amino alcohol was substituted with an alkyl/aryl group. However, when both the C1- and C2-positions were substituted, the enantioselection occurred in an unexpected manner; in the case of **15**, the preferential guest was of the same configuration at the C2-position and at the same time of the opposite configuration at the C1-position, compared with those of the original template (Table 4, entry 7). Moreover, among the enantiomers of **8**, the favorable one was that with the same configurations at both the C1- and C2-positions as those of the template (Table 4, entry 8).

Some of these results are apparently inconsistent with each other, but the phenomenon might be fully elucidated by the template effect of the original guest, as follows: Assuming that the cross-linked polymer possesses cavities in which the shape is complementary to the template (1R,2S)-**5**, each cavity is likely to have a vacant site suitable to accommodate the aromatic group at the C1-position, as well as the carboxylic acid group arranged on the surface of the cavity to make a salt pair with the amino group (Figure 5, top). When the guest-exchange reaction is conducted by using a 2-amino alcohol possessing an aromatic substituent at the C1-position, the orientation of the guest in the cavity is roughly fixed by two interactive sites, the amino group and the aromatic substituent, in order to realize the acid–base interaction and to avoid steric repulsion of the bulky C1 substituent. As a result, the enantioselection takes place under the influence of the fitting of substituents other than the amino group and the aromatic substituent. In the case of a 2-amino alcohol possessing only a C1 substituent, the enantiomer with the same orientation of the OH group is a favorable guest (Figure 5a). On the other hand, when both of the C1- and C2-positions are occupied by substituents, there are two possible manners of substitution, the *erythro* and *threo* types (Figure 5b and c). When a guest substituted in the *erythro* manner is employed, the enantiomer with the same configurations at both of the stereogenic centers should be more preferential, owing to the fitting of the OH group and the C2 substituent (Figure 5b). Contrary to this, in the case of a guest substituted in the *threo* manner, both of the enantiomers cannot realize "best-fitting", and the guest preference is governed by the orientation of the C2 substituent rather than that of the OH group at the C1-position (Figure 5c); in this case, the orientation at the C2-posi-

Table 4. Enantioselection through the guest-exchange reaction of (1R,2S)-**5** in the cross-linked polymer with various 2-amino alcohols.[a]

Entry	Amine	Adsorption [%][b]	In the supernatant[c]			In the polymer[d]		
			ee [%]	C1	C2	ee [%]	C1	C2
1	rac-**2**	66	1.6	S	–	0.8	R	–
2	rac-**4**	64	24	S	–	14	R	–
3	rac-**14**	57	13	S	–	6.8	R	–
4	rac-**3**	60	2.2	–	R	1.4	–	S
5	rac-**10**	59	1.6	–	R	1.2	–	S
6	rac-**6**	37	0.6	–	R	1.0	–	S
7[e]	rac-**15**	52	6.2	S	S	5.8	R	R
8	rac-**8**	23	8.6	S	R	29	R	S

[a] Conditions: amount of polymer = 135 mg (calculated to contain 135 μmol of the carboxylic acid–amine pair); amount of external amine = 13.5 μmol (9.0 mm, 1.5 mL in methanol), room temperature, 96 h. [b] Data are given with respect to the initial amount of the external guest in the methanol solution (13.5 μmol). [c] Data are based on an HPLC analysis of the supernatant. [d] Data were deduced from the ee/stereochemistry of the amine in the supernatant. [e] As the template, (1S,2R)-**5** was used instead of its antipode (1R,2S)-**5** because of the convenience in HPLC analysis; (1R,2S)-**5** was eluted with a similar elution time to that of (1R,2R)-**15** under the HPLC conditions used here.

tion works prior to that of the C1-position, most likely because the C2-position is located next to the strongest interactive site, the ammonium–carboxylate salt bridge.

With these results in mind, we next attempted to extract the guest incorporated in the polymer and to estimate its enantiomeric excess. This operation may be a more direct evaluation of the efficiency of the enantioseparation through guest exchange, although there remains an ambiguity that all of the incorporated guests were not necessarily recovered. In order to obtain the extracted guest in sufficient quantity to be analyzed by HPLC, an excess amount of the guest was used so that adequate conversion of the guest-exchange reaction was achieved. For example, the cross-linked polymer (27.0 mg, calculated to contain 27 μmol of the carboxylic acid–amine pair) was soaked in a methanol solution of a guest (18 mm, 15.0 mL, 10 equiv with respect to the amine–carboxylic acid pair in the polymer), and after a steady state was realized the resultant polymer was separated by centrifugation and treated with ultrasound sonication in a solution of **9** in methanol (1.0 m) in order to extract the guest once incorporated in the polymer. The amount and enantiomeric excess of the extracted guest in the solution was measured by HPLC (Table 5). As we expected, detectable enantiomeric enrichment was observed for all of the guests thus extracted (**4**, **8**, **14**, and **15**, 3–9% ee), and the stereochemistry of the enriched isomers in the extracts was in good agreement with that expected from the results in Table 3. Although the ee values observed here were apparently too small for practical application, they were the result of only a one-batch process; the differences in the adsorption energy ($\Delta\Delta G$) between the pairs of enantiomers were calculated to be no less than 0.14–0.48 kcal mol^{-1}. This result implies the potential utility of the present polymer as a selector for multistage separations, such as a stationary phase for chiral chromatography, in which $\Delta\Delta G \geq$ 0.1 kcal mol^{-1} is a criterion for practical use.[15]

Conclusion

We have demonstrated that the LC salts **1**·(1R,2S)-**5** (rectangular columnar) and **1**·(S)-**3** (hexagonal columnar) polymerized upon γ-ray irradiation to give cross-linked polymers, which retained the ordered structures of the original CLC states. Through the studies, γ-ray-induced polymerization was proven to be a reliable method to prepare LC cross-linking materials, and several advantages were found compared with conventional photoinitiated polymerization. The cross-linked polymer from **1**·(1R,2S)-**5** was found to be applicable as a solid-state host, of which the original template could be removed/replaced with other guests by treatment with acids/bases (up to 86% conversion). Furthermore, the cross-linked polymer had an ability to recognize the size, shape, and chirality of amine guests through guest-exchange
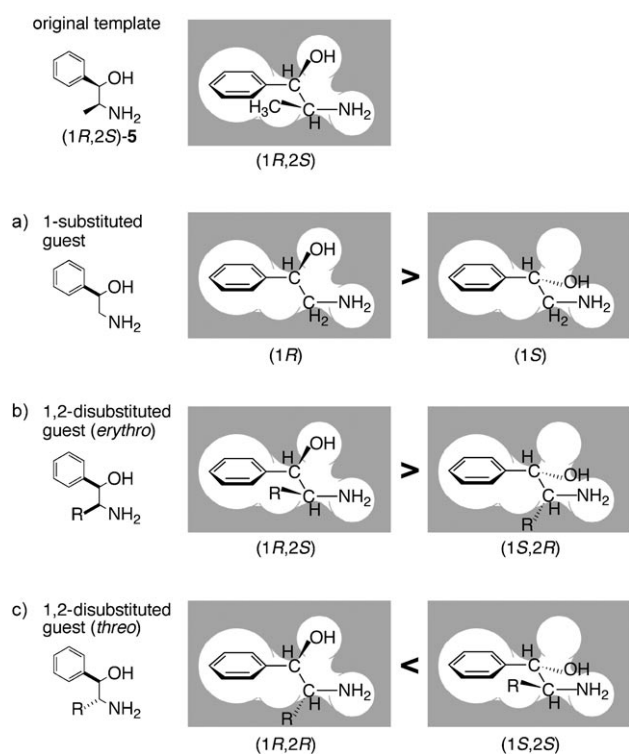
Figure 5. Schematic representation of the elucidation of the guest preference of the cross-linked polymer.

reactions. In the tendency for guest preference, a "template effect" was clearly observed. In addition to practical application as a selector for chromatographic separation, the cross-linked polymer, based on the template polymerization of CLCs with well-ordered structure, could shed some light on the problem in the traditional molecular imprinting method concerning polyclonality of cavities.

Table 5. Direct observation of the enantiomer ratio of the guest incorporated in the cross-linked polymer.[a]

Entry	Amine	Extracted guest [%][b]	ee [%]	C1	C2
1	rac-4	43	3	R	–
2	rac-14	22	9	R	–
3[c]	rac-15	43	7	R	R
4	rac-8	16	6	R	S

[a] Conditions: amount of polymer = 27.0 mg (calculated to contain 27 μmol of the carboxylic acid–amine pair); amount of external amine = 270 μmol (18 mM, 15 mL in methanol), room temperature, 72–96 h. [b] Data are given with respect to the initial amount of the original guest (1R,2S)-**5** in the cross-linked polymer (27 μmol). [c] As the template, (1S,2R)-**5** was used instead of its antipode (1R,2S)-**5** because of the convenience in HPLC analysis; (1R,2S)-**5** was eluted with a similar elution time to that of (1R,2R)-**15** under the HPLC conditions used here.

Experimental Section

Materials: The polymerizable carboxylic acid **1** was synthesized according to the method described in the literature.[8c] (R)-1-Amino-2-propanol ((R)-**2**), racemic 1-amino-2-propanol (rac-**2**), (S)-2-amino-1-propanol ((S)-**3**), racemic 2-amino-1-propanol (rac-**3**), (R)-2-amino-1-phenylethanol ((R)-**4**), racemic 2-amino-1-phenylethanol (rac-**4**), (1R,2S)-norephedrine ((1R,2S)-**5**), (1S,2R)-norephedrine ((1S,2R)-**5**), 2-aminoethanol (**9**), (S)-2-amino-1-butanol ((S)-**10**), racemic 2-amino-1-butanol (rac-**10**), (S)-2-amino-3-methylbuthanol ((S)-**11**),[16] 2-phenylethylamine (**12**), ephedrine ((1R,2S)-**13**), and racemic norpseudoephedrine (rac-**15**)[17] were purified by distillation just before use. (S)-2-Amino-2-phenylethanol ((S)-**6**), racemic 2-amino-2-phenylethanol (rac-**6**), and racemic 2-amino-1,2-diphenylethanol (rac-**8**) were purified by recrystallization.

Measurements: ¹H NMR spectra were obtained on a Varian Mercury 300 spectrometer, and the chemical shifts were given in ppm downfield from the internal standard tetramethylsilane. A Nicon Optiphoto polarized optical microscope (POM) equipped with a Mettler Toledo FP90 central processor, a Mettler FP 82HT hot stage, and a Polaroid PDMC Ie i was used to verify thermal transitions and to characterize anisotropic textures. DSC measurements were conducted on a Mettler DSC30 system to determine thermal transitions. FTIR spectra were recorded on a JASCO

FTIR-480 Plus spectrometer and were recorded as KBr mulls. XRD profiles were obtained with a Rigaku R-AXIS IV instrument by using $Cu_{K\alpha}$ radiation and equipped with a Mettler Toledo FP90 central processor and a Mettler FP 82HT hot stage. HPLC experiments were performed at 0°C with a JASCO PU-980 intelligent HPLC pump equipped with a UV-970 intelligent UV/Vis detector and a Hitachi D-2500 Chromato-Integrator, by using a Daicel CHIRALCEL CROWNPAK CR (+) column (4.6×153 mm); eluent, aqueous $HClO_4$ solution (pH 1.0–2.0); flow rate, 0.60 mL min⁻¹; detection of amines possessing aromatic substituent(s), UV absorption (200 nm); detection of amines lacking an aromatic substituent, UV absorption (345 nm) of a derivative formed by post-column derivatization with o-phthalaldehyde.

Synthesis and characterization of racemic 2-amino-1-(2-naphthyl)ethanol (rac-14):[18] A 300-mL, two-necked, round-bottomed flask equipped with a magnetic stirrer was charged with 2-naphthaldehyde (4.00 g, 25.6 mmol), CH_2Cl_2 (150 mL), ZnI_2 (256.2 mg, 0.80 mmol), and trimethylsilyl cyanide (3.8 mL, 28.2 mmol) under an argon atmosphere. After stirring for 3 h at room temperature, the reaction mixture was concentrated in vacuo and then diluted with diethyl ether (70 mL). The solution was added dropwise to a suspension of lithium aluminum hydride (2.60 g, 65.1 mmol) in diethyl ether (220 mL) under an argon atmosphere, and the mixture was refluxed for 2 h. Water (2.5 mL), aqueous NaOH

(15 wt %, 2.5 mL), and water (7.5 mL) were successively added dropwise to the resultant mixture. The suspension formed was separated by filtration, and the solid was extracted with THF (100 mL) by using a Soxhlet extractor. The filtrate and the extract were combined and concentrated under reduced pressure. The remaining white solid was crystallized from ethanol/hexane (1:3, v/v; 20 mL) to yield *rac*-**14** (3.35 g, 17.9 mmol, 70 %). M.p. 116–118 °C (lit.[18b] 118 °C); FTIR (KBr): $\tilde{\nu} = 3388$, 3054, 1599, 1477, 1422, 1382, 1332, 1163, 1121, 1071, 1015, 948, 897, 860, 822, 739, 655, 617, 482 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): $\delta = 2.90$ (dd, $J_1 = 12.9$, $J_2 = 7.6$ Hz, 1H), 3.11 (dd, $J_1 = 12.9$, $J_2 = 3.9$ Hz, 1H), 4.81 (dd, $J_1 = 7.6$, $J_2 = 3.9$ Hz, 1H), 7.46 (m, 3H), 7.83 ppm (m, 4H); ^{13}C NMR (75 MHz, [D$_6$]DMSO): $\delta = 49.89$, 74.35, 124.25, 124.68, 125.48, 125.96, 127.44, 127.49, 127.72, 132.28, 132.81, 141.93 ppm.

Synthesis of *R*-enriched 2-amino-1-(2-naphthyl)ethanol (14) and determination of chiral HPLC elution order: *R*-enriched 2-amino-1-(2-naphthyl)-ethanol was synthesized from enantiopure (*R*)-2-naphthylglycolic acid via 2,2-dimethyl-5-(2-naphtyl)-1,3-dioxolan-4-one according to the methods described in the literature with some modifications (78 % *ee*).[19] By comparing the HPLC profile of the *R*-enriched sample thus obtained with that of the racemic one, the chiral HPLC elution order of the enantiomers was unambiguously determined. Retention time: (*R*)-**14**, 104 min; (*S*)-**14**, 118 min. (HPLC conditions: eluent, methanol/aqueous HClO$_4$ (pH 2.0) = 15:85, v/v; flow rate, 0.60 mL min^{-1}).

General procedure for the preparation of the salt of 1 with a 2-amino alcohol: A diethyl ether solution (1.0 mL) of a 2-amino alcohol (1.00 mmol) was added to a diethyl ether solution (10 mL) of **1** (843.2 mg, 1.00 mmol), and the resultant solution was stirred at room temperature for 3 min. The solvent was removed by an argon flow and finally by evaporation under reduced pressure. The molar ratio of **1** to the amine in the resultant residue was confirmed by ^{1}H NMR spectroscopy. Salt **1**·(1*R*,2*S*)-**5**: FTIR (KBr): 3440, 3230, 3030, 2920, 2852, 1721, 1637, 1621, 1579, 1541, 1520, 1501, 1472, 1409, 1396, 1375, 1295, 1275, 1197, 1120, 1058, 979, 811, 780, 743, 721, 700, 660 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): $\delta = 1.10$–1.90 (m, 57H), 3.32 (m, 1H), 3.51 (dd, 1H), 3.73 (dd, 1H), 4.00 (t, $J = 6.6$ Hz, 6H), 4.10–4.20 (m, 6H), 5.00 (br, 1H+1H+2H), 5.80 (d, $J = 10.2$ Hz, 3H), 6.15 (dd, $J_1 = 10.5$, $J_2 = 17.3$ Hz, 3H), 6.40 ppm (d×2, $J_1 = 17.3$, 15.9 Hz, 3H+1H).

General procedure for the γ-ray-induced polymerization of the salt of 1 with a 2-amino alcohol: A diethyl ether solution (10 mL) of **1** (843 mg, 1.00 mmol) and a 2-amino alcohol (1.00 mmol) was partitioned into three glass tubes (length 100 mm, diameter 20 mm), and the solvent was removed by an argon flow and subsequent evaporation under reduced pressure at room temperature to afford the LC salt. The glass tubes were evacuated, sealed, and applied to a ^{60}Co γ-ray irradiator (dose rate, 1.7 kGy h^{-1}; irradiation time, 48 h at room temperature). The irradiated samples were detached from the glass tubes, combined, mechanically ground, washed with CHCl$_3$ (20 mL), and collected by filtration (Advantec T050A047A PTFE membrane filter, 0.5 μm mesh). The resultant white powder was dried in vacuo to give the cross-linked polymer.

General procedure for the guest-exchange reaction of the cross-linked polymer: The cross-linked polymer (45.0 mg) was loaded into a centrifuge tube, and a methanol solution (18 mM, 5.0 mL) of an amine was added. The resultant mixture was left to stand at 30 °C for 96 h and centrifuged (3000 rpm, 3 min). The amounts of the template amine and the guest amine in the supernatant were estimated by HPLC.

General procedure for the extraction of the guest amine from the cross-linked polymer: The guest-exchange reaction was conducted in the same manner as described above. The cross-linked polymer was recovered by centrifugation (3000 rpm, 3 min) and suspended in a methanol solution (1.0 M, 5.0 mL) of 2-aminoethanol. The resultant mixture was sonicated for 2 h and centrifuged (3000 rpm, 3 min), and the amount of the guest amine extracted into the supernatant was estimated by HPLC.

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[9] As described in our previous report (reference [5b]), the salts of an unpolymerizable analogue of **1** with simple primary amines did not display any LC phases, implying that the existence of a hydroxyl group was essential for the formation of a stable LC structure. On the basis of this result, only 2-amino alcohols were used as the base part of salts in this study.

[10] Reflections observed for **1**·(*S*)-**3** on XRD measurement: *d* spacings (Å) calcd for Miller indices of (100), (110), (210), (300), and (001): 36.6, 21.2, 13.9, 12.2, and 3.9; found: 36.5, 21.2, 13.9, 12.2, and 3.9.

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[12] Our previous work (reference [5a]) showed that the presence of vacant sites generated by the release of (1*R*,2*S*)-**5** caused a significant alteration of the whole system, and the original structural order

was reconstructed only when the site was again occupied by a new guest in a similar manner to the original state.

[13] Different batches of the cross-linked polymer were found to vary the amounts of guest capable of releasing/capturing, most likely because of the difference in the average particle size, degree of cross-linking, and/or density of defects in the columnar-ordered structure. As a result, the range of concentration of guest solution suitable for the guest-exchange reaction depends on the batch. The polymer samples for the experiments shown in Figure 4a–c were from the same batch, and the samples for the experiments shown in Figure 4d were from another batch. For each of Tables 3–5, all the entries were conducted by using polymer samples from an identical batch.

[14] Although an adsorption process other than salt formation with the carboxylate moieties is still unknown, it is most likely to be adsorption via the hydrogen bonding of the carbonyl group of the poly-(acrylic ester) in the cross-linked polymer with the amino and/or hydroxyl group in the 2-amino alcohols. The aminolysis/hydrolysis of the poly(acrylic ester) were not main processes, because the IR ad-

sorptions attributable to the moiety were inert to treatment with amine solutions.

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