

# Template polymerization of columnar architectures based on the salts of a carboxylic acid and 2-amino alcohols: application to the molecular recognition of 2-amino alcohols†

Yasuhiro Ishida,<sup>a</sup> Sayaka Amano<sup>b</sup> and Kazuhiko Saigo<sup>\*ab</sup>

<sup>a</sup> Department of Chemistry and Biotechnology, Graduate School of Engineering, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113-8656, Japan. E-mail: saigo@chiral.t.u-tokyo.ac.jp; Fax: (+81) 3 5802 3348; Tel: (+81) 3 5841 7266

<sup>b</sup> Department of Integrated Biosciences, Graduate School of Frontier Sciences, The University of Tokyo, Bioscience Bldg. 702, Kashiwa, Chiba 277-8562, Japan

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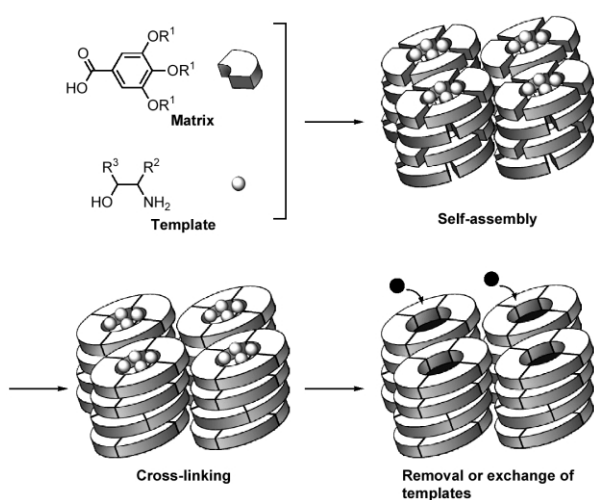
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The salts of trialkoxybenzoic acids and 2-amino alcohols showed a columnar liquid crystalline phase; in the case of the salt of a polymerizable acid and norephedrine, the photo-polymerization proceeded efficiently in the liquid crystalline state, and the resultant solid adsorbed 2-amino alcohols size, regio-, and enantio-selectively.

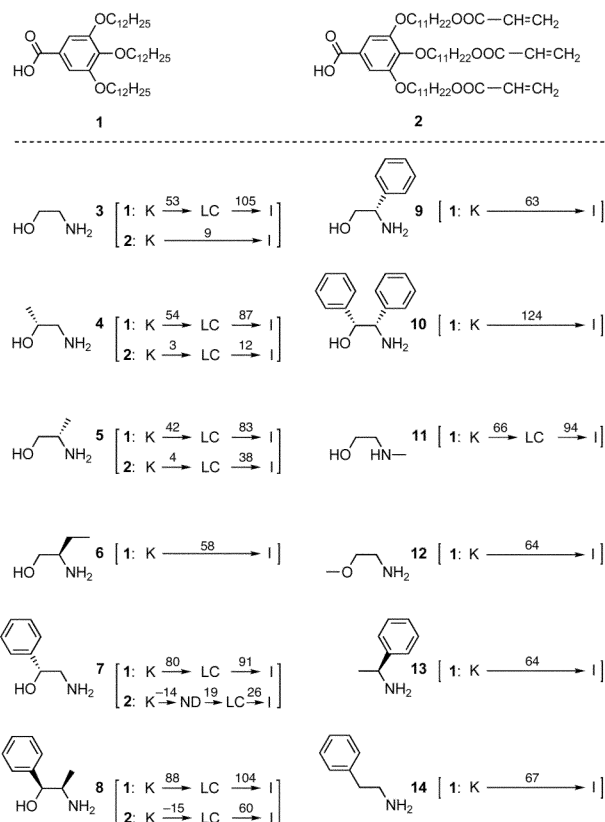
The cross-linking of columnar liquid crystals (CLC) is one of the most versatile methods to create porous organic materials.<sup>1–3</sup> When a polymerizable mesogen (matrix) and another component (template) are non-covalently interacted to form a CLC structure, cavities with well-defined structure complementary to the template will be created by *in situ* cross-linking of the matrix and subsequent removal and/or exchange of the template (Scheme 1).<sup>4</sup> From the viewpoint of monoclinality of the cavities, this approach is advantageous, compared with the conventional molecular imprinting method based on bulk polymerizations,<sup>5</sup> since the oriented state of the liquid crystals is “frozen-in” by the cross-linking reaction. However, most of the previous studies related to this concept have been restricted to lyotropic liquid crystalline systems, of which the cores usually consist of solvent molecules,<sup>1</sup> and the utilization of large molecules as templates has been surprisingly limited.<sup>3,6</sup> Here we describe a novel thermotropic CLC system, the salts of trialkoxybenzoic acids and 2-amino alcohols; the above strategy could be adapted to the CLC system, and the

resultant porous material was successfully applied for the separation of 2-amino alcohols (Scheme 1).

As matrix units for the construction of CLC structures, we used 3,4,5-trialkoxibenzoic acids (**1** and **2**), since such tapered molecules are known to show a CLC phase when their cores are connected by covalent or non-covalent interactions.<sup>7</sup> For these matrix units, amines are promising candidates of template units, because the salts of amines and carboxylic acids tend to form a columnar or layered structure through hydrogen-bonding interactions in the solid state.<sup>8,9</sup> In order to select suitable amines for the construction of stable CLC structures, the phase behavior of the salts of 3,4,5-tridodecanoxybenzoic acid (**1**) with various amines was investigated (Fig. 1).†† Cross-polarized optical microscopy, X-ray diffraction measurement (XRD), and differential scanning calorimetry (DSC) revealed that the salts of **1** with 2-amino alcohols formed a CLC structure, such as **3** (hexagonal), (–)-**4**, (+)-**5**, (–)-**7** (not determined), and (+)-**8**



**Scheme 1** Schematic representation of the preparation of ordered porous materials using the cross-linkable columnar assemblies.



**Fig. 1** Phase behavior of the salts of the carboxylic acids (**1** and **2**) with amines (**3–14**): K = crystalline phase; LC = liquid crystalline phase; I = isotropic phase; ND = not determined. The transition temperatures (°C) are given above the arrows.†

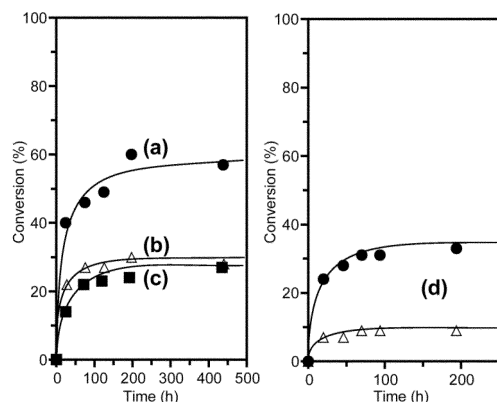
† Electronic supplementary information (ESI) available: optical textures, phase behavior, and XRD patterns of the salts; detailed explanations for the cross-linking of **2–8** and the exchange reaction of the amine units of cross-linked **2–8**. See <http://www.rsc.org/suppdata/cc/b3/b305625b/>

(rectangular). According to the lattice parameters and the molecular models, the number of acid–base pairs included in the layer of a cylinder was estimated; four pairs for the hexagonal CLC structure and three or four pairs for the rectangular CLC structure. § However, by introducing a bulky substituent at the C-2 position of the 2-amino alcohols, formation of a CLC structure was significantly inhibited, as no liquid crystalline phase was observed for the salts with (–)-6, (+)-9, and (–)-10.

When the amino or hydroxy group of the 2-amino alcohol was methylated, the resultant CLC phase became unstable; the salts with **11** and **12** showed a CLC phase at a quite narrow range of temperature compared with the salt with **3**. In addition, the salts with simple primary amines, (–)-13 and **14**, did not display any LC phase at all (Fig. 1). These observations indicate that hydrogen-bonding interactions between the carboxyl groups with the amino and hydroxy groups play an essential role for the stable CLC phase formation.

When polymerizable acid unit **2** was used in the place of **1**, the salts with 2-amino alcohols showed similar phase profiles to those of **1**, and CLC phases were again observed for the salts with (–)-4, (+)-5, (–)-7, and (+)-8 (Fig. 1). †‡ In the presence of a radical photoinitiator, the salt of **2** with (+)-8 (**2**-(+)-8) could be photopolymerized to give a cross-linked solid. For example, when a mixture of **2**-(+)-8 and 2-hydroxy-2-methylpropiophenone (2.5 wt.%), which showed a rectangular phase at a temperature range of –15 to 60 °C, was irradiated ( $\lambda > 300$  nm, a high-pressure mercury lamp) at 16 °C for 48 h, a solid mass insoluble in common organic solvents was obtained in quantitative yield. Consumption of the acryloyl groups of **2** was confirmed by IR spectroscopy; the absorption attributed to the  $\alpha,\beta$ -unsaturated carbonyl groups was significantly diminished after photoirradiation. The XRD analysis clearly showed that the cross-linked solid maintained the rectangular columnar structure, where the lattice constants slightly diminished after polymerization. †§

Taking advantage of the non-covalent nature of the interactions between the matrix unit and the template unit, **8** incorporated in the cross-linked material could be exchanged with other 2-amino alcohols. † For example, the solid obtained by the cross-linking of **2**-(–)-8 was milled and soaked in a solution of (–)-7 in methanol (25 mM). Upon standing the mixture at 4 °C, the original guest (–)-8 was released into the supernatant, whereas (–)-7 was adsorbed by the solid, which was monitored by HPLC. When the exchange reaction was attained at equilibrium (after 440 h), 57% of (–)-7, with respect to the original guest, was incorporated to the solid (Fig. 2a). The XRD analysis indicated that the rectangular columnar structure was retained even after guest exchange, although the intensity of the peaks became smaller presumably due to partial disorder of the original alignment.



**Fig. 2** The exchange reaction of the amine units of cross-linked **2**-(–)-8 in methanol at 4 °C. The ratio of the adsorbed 2-amino alcohols ((–)-7 [●], (+)-9 [△], and (–)-10 [■]) with respect to the original guest (–)-8. Initial conditions: (a) [(–)-7]<sub>0</sub> = 25 mM; (b) [(+)-9]<sub>0</sub> = 25 mM; (c) [(–)-10]<sub>0</sub> = 25 mM; (d) [(–)-7]<sub>0</sub> = [(+)-9]<sub>0</sub> = 12.5 mM.

Quite interestingly, the cross-linked material could be applied as “size- and shape-selective molecular sieves” for 2-amino alcohols. As described above, (–)-7 having a quite similar structure to the initial guest (–)-8 could efficiently substitute (–)-8 (Fig. 2a). Contrary to this, when substitution of (–)-8 with a bulky guest, (–)-10, was attempted, only 27% exchange was occurred under the same conditions (Fig. 2c). In the case of (+)-9, which possesses a similar size but a different shape compared with (–)-8, efficient exchange was again suppressed (28%, Fig. 2b). Thus observed guest selectivity motivated us to apply the cross-linked material for the separation of 2-amino alcohols. For example, from an equimolar mixture of (–)-7 and (+)-9 in methanol, (–)-7 was predominantly captured by the cross-linked solid, where the ratios of finally incorporated (–)-7 and (+)-9 were 33 and 9%, respectively (Fig. 2d).

Since optically active 2-amino alcohols can be used as templates in the present system, the resultant cross-linked materials have a potential for the enantioseparation of amines. As a preliminary study, we performed the resolution of racemic **7** through the guest-exchange reaction of the cross-linked **2**-(–)-8. Typically, the cross-linked solid was placed in a solution of racemic **7** (25 mM) until equilibrium was reached (59 % exchange), then the supernatant and the precipitate was separated by centrifugation, and the precipitate was extensively extracted with aqueous HCl. The supernatant and the collected polymer extract were analyzed by HPLC in order to estimate the optical purity of **7**. The supernatant and the polymer extract were (+)- and (–)-enriched (2 and 7% ee) respectively, which is consistent with our expectation that (–)-7, of which the stereochemistry at C-1 is the same as that of the initial template (–)-8, should be preferentially incorporated.

In conclusion, we found that the salts of trialkoxybenzoic acids and 2-amino alcohols generally show a CLC phase. When a polymerizable acid unit, **2**, was used, the resultant columnar structure could be fixed by an *in situ* cross-linking reaction, where the ordered structure was essentially maintained. Since various carboxylic acids and 2-amino alcohols are available, porous materials with well-controlled size, shape, and functional-groups could be created by careful choice of these units.

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## Notes and references

‡ The salts were prepared by dissolving equimolar amounts of the carboxylic acid and the amine in chloroform, followed by the evaporation of the solvent. The 1 : 1 stoichiometry was confirmed by <sup>1</sup>H NMR spectroscopy.

§ The lattice constants determined by XRD patterns. † **1-3** (hexagonal): *a* = 38.5 Å; **1-(+)-8** (ordered rectangular): *a* = 44.3, *b* = 25.2 Å; **2-(+)-5** (ordered hexagonal): *a* = 42.2 Å; **2-(+)-8** (ordered rectangular): *a* = 45.7, *b* = 26.9 Å; the cross-linked **2-(+)-8** (rectangular): *a* = 44.6, *b* = 26.6 Å.

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