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Nanostructured, Solid-State Organic, Chiral Diels–Alder Catalysts via Acid-Induced Liquid Crystal Assembly

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Chiral solid catalysts are valuable materials because they afford optically pure or enriched products and facile recovery of the often high-value catalyst.[1] One area that has recently received a great deal of attention is the design of enantio-selective, *nanostructured*, porous catalysts.[1] The benefits of such catalysts include improved active site accessibility, reactant size selectivity, and in some cases, enhanced enantio- and diastereoselectivity as a result of performing reactions in regular nanopores or molecularly confined environments.[2] These catalysts are generally formed by grafting chiral catalytic moieties onto nanostructured inorganic supports (e.g., zeolites,[3] mesoporous sieves,[4] layered metal salts).[2a] However, these supports have limited processability, and there are often limitations to the types of catalytic groups that can be attached.[2a] Chiral catalysts have also been prepared on organic solid polymer supports[5] as a means of obtaining heterogeneous systems with better chemical tunability and processibility,[6] but one common drawback of amorphous, nonporous polymer supports is limited access to the chiral ligands or active sites.[5c] Examples of chiral catalysts on nanostructured organic supports are rare. Chiral reactions in nanoporous or nanostructured organic solid media have been limited to photoreactions in porous chiral organic crystals and imprinted polymers.[2a] Herein, we present the preparation of nanoporous, heterogeneous, chiral Diels–Alder catalysts that are entirely organic in nature, via the acid-induced liquid crystal self-assembly and subsequent photopolymerization of a reactive chiral imidazolidinone derivative (**1**) (Figure 1). Compound **1** is non-mesogenic, but it was found that protonation not only activates the catalyst but also simultaneously induces lyotropic (i.e., amphiphilic) liquid crystal (LLC) behavior.[7] Depending on the type and amount of acid (HX) used, different nanoporous
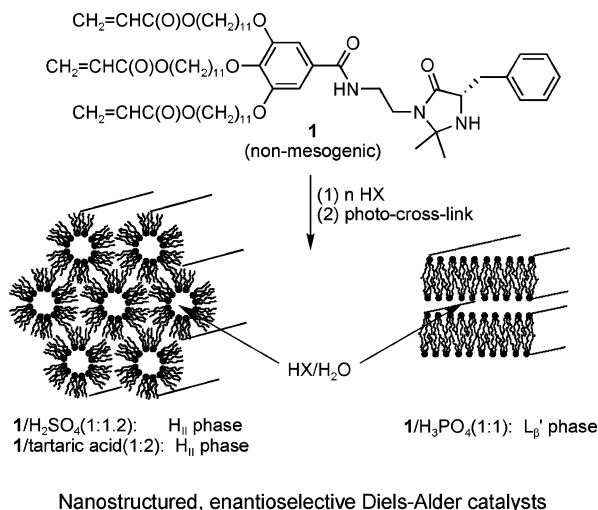
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Figure 1. Nanostructured, solid-state organic, chiral Diels–Alder catalysts via acid-induced LLC assembly and in situ photopolymerization.

Figure 2. XRD profiles of (a) the unpolymerized $1/H_2SO_4$ (1:1:2) system (H_{II} phase); (b) the cross-linked $1/H_2SO_4$ (1:1:2) system (H_{II} phase); (c) the unpolymerized $1/H_3PO_4$ (1:1) system (L_{β}' phase, the * peak is incommensurate with the other L peaks); and (d) the unpolymerized 1/tart (1:2) system (H_{II} phase). All systems were formed with 10 wt % water. Insets: POM optical textures.

geometries can be accessed, which is a unique feature compared to conventional catalyst supports. The resulting LLC assemblies ($1/n$HX) can be radically photo-cross-linked to afford nanostructured solid organic catalysts with very good reactive site accessibility (ca. 70%) and retention of the high enantioselectivities exhibited by the parent chiral imidazolidinone catalyst (2/HCl) in solution.[8]

Monomer 1 was synthesized by first designing a derivative of 2 containing a 2-aminoethyl linker and then coupling it to 3,4,5-tris(11′-acryloyloxy-1-undecyloxy)benzoic acid, a known polymerizable LLC starting unit[9] (see Supporting Information). This particular derivative was chosen as an initial test platform because MacMillan and co-workers have shown that 2/HCl (1:1) is highly selective for catalyzing asymmetric Diels–Alder reactions in mixtures of water and a polar organic solvent,[8] thus, making it potentially compatible with a water-based LLC architecture. Also, the active form of the catalyst is the protonated amine salt (usually the HCl salt)[8] and, thus, ideal for serving as a hydrophilic LLC headgroup. Finally, 2/HCl (1:1) has been successfully grafted onto solid polymer supports with retention of chiral catalytic activity.[5b]

The 1:1 HCl salt of 1 did not exhibit any LLC behavior in water, as determined by polarized optical microscopy (POM) and X-ray diffraction (XRD). However, when a slight excess of HCl was added, an inverted hexagonal (H_{II}) LLC phase formed that quickly became isotropic upon standing, presumably via evaporative loss of HCl. This suggested that a nonvolatile acid, as well as excess acid, might be required for stable LLC formation. To test this hypothesis, 1:1 salts of 1 were prepared using three nonvolatile acids of varying acidity: H_2SO_4, H_3PO_4, and tartaric acid (tart). Only the $1/H_3PO_4$ (1:1) salt exhibited LLC behavior when mixed with 10 wt % water. The material exhibits spherulite optical
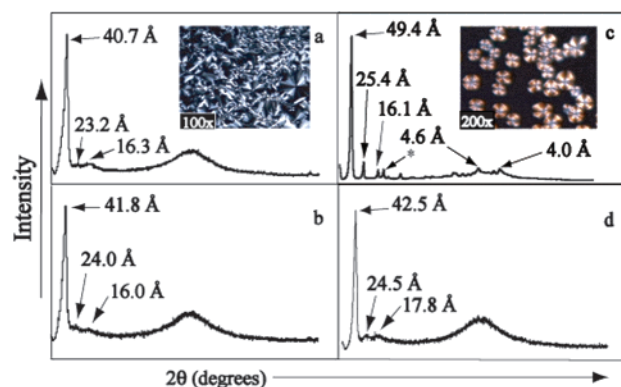
textures and XRD d spacings with the ratio 1:1/2:1/3, indicative of lamellar (L) phases (Figure 2).[7] However, there are also wide-angle XRD peaks and one incommensurate peak (*), suggesting that $1/H_3PO_4$ (1:1) forms an irregular lamellar gel (L_{β}') phase or a mixed L_{β}' phase (see Supporting Information).[7b] $1/H_2SO_4$ (1:1) and 1/tart (1:1) did not form LLC phases in water but rather required addition of excess acid. In the case of the H_2SO_4 salt, 1.2 molar equiv of H_2SO_4 is required to induce LLC behavior, whereas for the tartaric acid salt, 2 mol of acid are needed. The $1/H_2SO_4$ (1:1.2) and 1/tart (1:2) systems formed H_{II} phases, as confirmed by distinctive fanlike optical textures and XRD profiles with a $1:1/\sqrt{3}:1/\sqrt{4}$ d-spacing pattern.[7]

The type of LLC phase formed depends mostly on the nature of the counterion of the acid used to protonate 1, rather than the strength or amount of acid used. Only the medium-strength acid H_3PO_4 induced LLC phase formation as the stoichiometric 1:1 salt, whereas an excess of both the strongest (H_2SO_4) and weakest (tartaric) acids was required to induce phase formation, with concomitant formation of a different LLC phase altogether.[10] The excess acid needed appears to be related to forcing the acid–base equilibrium towards more salt formation (as seen in prior pH-dependent LLC systems),[11,12] rather than an ionic strength effect (which is important in forming inverse LLC phases).[7] Control experiments using high ionic strength NaCl solutions instead of excess acid did not induce LLC behavior in the salts of 1. The four $1/n$HX systems were also found to be catalytically active in solution. Unpolymerized 1/HCl (1:1), $1/H_2SO_4$ (1:1.2), $1/H_3PO_4$ (1:1), and 1/tart (1:2) are able to catalyze the cycloaddition of crotonaldehyde and 1,3-cyclopentadiene in solution with comparable overall reaction rates and essentially the same ee and de values as 2/HCl (1:1), irrespective of the counterion or presence of excess acid (Table 1). The stable LLC phases of the $1/H_2SO_4$ (1:1.2), $1/H_3PO_4$ (1:1), and 1/tart (1:2) systems can

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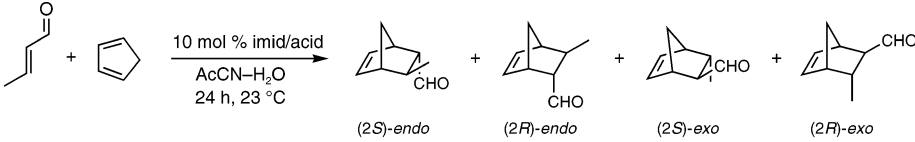
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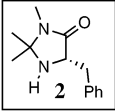
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Table 1. Yields and Stereoselectivities of Different Chiral Imidazolidinone Catalyst Variants in the Diels−Alder Reaction of Crotonaldehyde with 1,3-Cyclopentadiene

Imidazolidinone	Acid (equiv.)	Phase	Time (h)	Yield[a] (%)	*endo:exo*	*endo* ee (%)
(structure of **2**)	HCl (1.0)	sol'n	24	71	1.3:1	90
2	H_2SO_4 (1.0)	sol'n	24	66	1.3:1	87
1	H_2SO_4 (1.0)	sol'n	24	68	1.3:1	86
1	H_2SO_4 (1.2)	iso[b]	24	53	1.3:1	87
1	H_2SO_4 (1.2)	H_{II}[c]	24	50	1.3:1	87
2	H_3PO_4 (1.0)	sol'n	24	60	1.3:1	86
1	H_3PO_4 (1.0)	sol'n	24	72	1.3:1	90
1	H_3PO_4 (1.0)	iso[b]	24	58	1.3:1	88
1	H_3PO_4 (1.0)	L'_β[c]	24	54	1.3:1	88
2	tartaric (1.0)	sol'n	24	35	1.3:1	90
1	tartaric (2.0)	sol'n	24	60	1.3:1	90
1	tartaric (2.0)	iso[b]	24	48	1.3:1	88
1	tartaric (2.0)	H_{II}[c]	24	53	1.3:1	88

[a] Total yield of all four products by NMR. *[b]* Cross-linked isotropic powder. *[c]* Cross-linked LLC powder.

all be radically photo-cross-linked with retention of microstructure when a small amount of radical photo-initiator (2-hydroxy-2-methylpropiophenone) is included. Retention of the LLC structures after photo-cross-linking was confirmed by POM and XRD analysis (see Figure 2 and Supporting Information). The degree of acrylate conversion was determined to be >90% by Fourier transform infrared spectroscopy.[9] In powdered solid form, the cross-linked L'_β phase of **1**/H_3PO_4 (1:1) and the cross-linked H_{II} phases of **1**/H_2SO_4 (1:1.2) and **1**/tart (1:2) were found to give slightly lower overall reaction rates but nearly identical high enantioselectivity exhibited by the parent solution catalyst (Table 1). Titration of washed samples of cross-linked **1**/H_2SO_4 (1:1.2) and **1**/H_3PO_4 (1:1) with aqueous NaOH followed by elemental analysis revealed that about 72 and 66%, respectively, of the theoretical protonated amine active sites are accessible, indicating that more than just catalytic surface sites are involved.[14] These solid LLC catalysts can also be recovered and reused without significant loss of activity or stereoselectivity (see Supporting Information).

Unfortunately, enhancement of enantio- or diastereoselectivity was not observed as a function of catalyst nanostructure in these systems. This is not surprising because different soluble[13] and solid-state[5b,6a] derivatives of **2** have been found to exhibit similar stereoselectivities as the parent solution catalyst, suggesting that the immediate asymmetric substituent environment around the imidazolidinone plays the primary role in the stereocontrol process.[8] We are currently investigating the effect of chiral acids on the stereoselectivity of these LLC catalysts. The acid counterion provides an easy handle with which to manipulate the noncovalent interactions that give rise to additional selectivity seen in other systems. For example, having a sterically demanding, chiral anion in the channels may increase the asymmetry of the pores. Size-selective transport of molecules has also recently been demonstrated in similar nanoporous LLC networks.[15] Consequently, we are also examining the potential of these materials for molecular size-selective chiral catalysis of different size reactants.[16]

Supporting Information Available: Experimental details for the synthesis and characterization of **1**; LLC phase formation and cross-linking of the salt mixtures; and Diels−Alder catalysis and control experiments (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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