Hybrid Materials

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Comparison of Chiral and Racemic Forms of Zinc Cyclohexane *trans*-1,2-Dicarboxylate Frameworks: A Structural, Computational, and Calorimetric Study**

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The field of hybrid organic–inorganic framework materials is one of the major growth areas of materials chemistry. Hybrid frameworks show an enormous diversity of chemical and structural types, including coordination polymers, porous metal-organic frameworks (MOFs), and extended inorganic hybrids.[1–5] Chiral hybrid frameworks are of particular interest since they can readily be made from commercially available homochiral ligands[6] and show promise in applications such as enantiomerically selective catalysis and separations.[7–13] The comparative structures of racemic hybrid frameworks and their homochiral analogues have not been discussed in detail, but a few examples have been reported. In the nickel aspartates, for example, it has been found that the homochiral materials contain single-handed helical chains while the racemic phase contains both hands of the same chain.[14,15] However, there may be other ways of accommodating the constraints imposed by having only a single enantiomer with which to build the framework. For example, recent work on magnesium tartrates revealed entirely different architectures for the racemic materials and their D-tartrate analogues.[16] In the present work we explore the racemic and homochiral forms of zinc cyclohexane *trans*-1,2-dicarboxylate, $[Zn(C_8H_{10}O_4)]$. Recent work on the *cis* and *trans* zinc 4-cyclohexene-1,2-dicarboxylates has shown that these materials form under thermodynamic control and give rise to layered coordination polymers,[17] but the possibility of using the *R*,*R* or the *S*,*S* enantiomers of the *trans*-ligand was not examined at the time. In the present work we compare the structure and energetics of the chiral zinc *R*,*R*-cyclohexane *trans*-1,2-dicarboxylate with those of its racemic *R*,*R*/*S*,*S* analogue. This particular system was chosen for a detailed study of this type because of the availability of appropriate forcefields for the calculations and the availability of high-purity samples of each phase for calorimetric studies.

Reactions of the racemic mixture of *trans*-*R*,*R* and *trans*-*S*,*S*-cyclohexane dicarboxylic acids (1 equiv) with zinc acetate (1 equiv) heated hydrothermally in water at 150 °C for 48 h produced single crystals of a colorless phase, **1**, which was studied by single-crystal X-ray diffraction. Enantiomerically pure *trans*-*R*,*R*-cyclohexane dicarboxylic acid was prepared by resolution of commercially available racemic material following the procedure of Berkessel et al.[18] using (*R*)-(+)-1-phenylethylamine. A resolved sample having $>99\%$ *ee* was obtained after three recrystallizations from hot ethanol/toluene (1:1). Heating of the resolved acid with zinc acetate, as described for **1** above, led to the formation of a colorless solid product, **2**, which gave an X-ray powder pattern that was quite different from that obtained using the racemic mixture of dicarboxylic acids. X-ray intensity data were obtained from small single crystals of **2** on a laboratory diffractometer. The structures of **1** and **2** were solved and refined by conventional single-crystal methods.[19] Figure 1 shows the individual carboxylic acid ligands used in the hydrothermal synthesis, and their distinctive stacking in the layered hybrid structures, **1** and **2**.

The structure of **1** is centrosymmetric (space group $P\bar{1}$), while that of **2** is chiral in space group $P2_12_12_1$. Both **1** and **2** are layered 2-D coordination polymers, comprising double rows of ZnO_4 tetrahedra with the layers propagating in the *ab* plane (Figures 2 and 3). Pendant cyclohexane rings decorate the tops and bottoms of the layers, giving rise to non-covalent interlayer interactions. Assuming that the reactions proceed

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Supporting information for this article (crystallographic tables and powder X-ray diffraction patterns for **1** and **2**, the procedure for the resolution of the *trans*-1,2-dicarboxylate acids, details of the forcefield and simulation procedure, comparison of observed and calculated structures, hypothetical racemic structure) is available on the WWW under http://dx.doi.org/10.1002/anie.200802564.

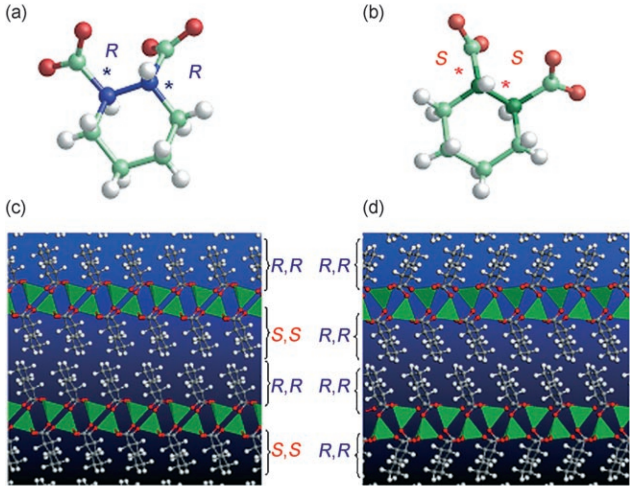

Figure 1. a,b) The *trans-R,R*-cyclohexane dicarboxylic acid (a) and *trans-S,S*-cyclohexane dicarboxylic acid (b). c) The racemic hybrid Zn-dicarboxylate structure **1**. d) The homochiral hybrid Zn-dicarboxylate structure **2**.

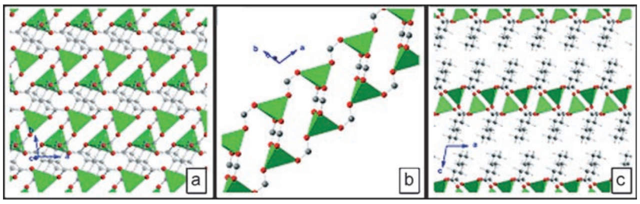

Figure 2. The crystal structure of **1**, the racemic *R,R/S,S*-zinc cyclohexane *trans*-1,2-dicarboxylate: a) Plan view of the layer; b) view of a chain showing zinc connectivity; c) side view showing the layer.

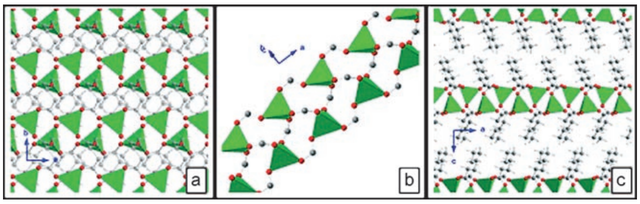

Figure 3. The crystal structure of **2**, the chiral *R,R*-zinc cyclohexane *trans*-1,2-dicarboxylate: a) Plan view of the layer; b) view of a chain showing zinc connectivity; c) side view showing the layer.

under thermodynamic control,[17] the racemic *R,R/S,S* product must be more stable than a 50:50 mixture of the *R,R* and *S,S* chiral phases. If the reverse were true, we would expect to see the racemic acid spontaneously resolve into its two chiral hybrids (*R,R* and *S,S*) on crystallization.

One of the most striking findings of our work is that the connectivities within the layers of **1** and **2** are fundamentally different. The layer of **1** is constructed from 4T-rings in which four tetrahedrally coordinated zinc ions are bridged by four carboxylate groups (Figure 2b), whereas the layers in **2** contain 3T-rings (Figure 3b). The bridging topology of ZnO_4 tetrahedra within each double row also differs between the two compounds. In the racemic compound, the tetrahedra are bridged by pairs of carboxylate groups whose O–C–O bonds run diagonal to the double rows and are parallel with all other O–C–O groups. In the chiral compound, the O–C–O bonds zigzag along the double rows, lying in two roughly perpendicular directions, both being diagonal to the chain.

The layer stacking is also very different between **1** and **2**. In **1**, the cyclohexane rings are arranged in a parallel fashion (Figure 2c), while those in the chiral compound adopt a herringbone geometry (Figure 3c). This results in the distance between neighboring sheets in the homochiral phase (13.12 Å) being significantly less than that in the racemic compound (13.63 Å), suggesting that there might be stronger interactions between the layers in **2**. In addition, the density is 1.862 $g\,cm^{-3}$ for the homochiral phase **2** compared with 1.721 $g\,cm^{-3}$ for the racemic phase **1**, a difference of 8.2%, raising doubts as to whether **1** is indeed more stable than **2**.

In order to explore this question more thoroughly, we have estimated the lattice energies of the two phases by using a recently developed forcefield for the Zn–O interaction[20] in combination with a standard cvff forcefield[21] for the organic parts of the structure. The total energies were decomposed into their respective contributions from the isolated layers and the interactions between the layers (Table 1). The results for the energy minimizations with geometry optimization (varying the cell parameters at constant pressure) for **1** and **2** are normalized to the cell content of the racemic structure, per $[Zn_2(C_8H_{10}O_4)_2]$ unit. Observed and calculated cell parameters, fractional coordinates, and bond lengths/angles, which agree rather well, are given in the Supporting Information. The results indicate that the less dense racemic structure **1** is indeed more stable than the chiral phase **2** by 21.9 $kJ\,mol^{-1}$, in agreement with our experimental observation that the racemic *R,R/S,S* phase forms in preference to a 50:50 mixture of the *R,R* and *S,S* chiral phases.

Table 1: Comparison between energies *E* (in $kJ\,mol^{-1}$) of the racemic (**1**) and homochiral structures (**2**), normalized to the unit-cell composition $[Zn_2(C_8H_{10}O_4)_2]$ of the racemic structure.

E	E_{Coulomb}	$E_{\mathrm{bonded+non\text{-}bonded}}$	Total E
racemic phase **1**	−2038.1	−202.4	−2240.5
single layer of **1**	−2037.7	−146.4	−2184.1
inter-layer energy in **1**	−0.4	−56.0	−56.4
homochiral phase **2**	−2041.3	−177.3	−2218.6
single layer of **2**	−2040.7	−106.0	−2146.7
inter-layer energy in **2**	−0.6	−71.3	−71.9

In order to corroborate the computational results and to assess their accuracy, the relative stabilities of racemic and chiral zinc cyclohexane *trans*-1,2-dicarboxylate were determined by solution calorimetry. A commercial CSC 4400 isothermal microcalorimeter operating at 298 K was used to measure the enthalpies of solution of phases **1** and **2**. Samples were pressed into pellets of about 15 mg and dropped into 25 g of 2 M NaOH (standardized solution, Alfa Aesar). Mechanical stirring was used for better sample dissolution. Calibration used the heat of solution of 15 mg pellets of KCl (NIST Standard Reference Material 1655)[22] in 25 g of deionized water under identical experimental conditions. Although the chiral zinc *S*,*S*-cyclohexane *trans*-1,2-dicarboxylate phase was used for the calorimetric experiments, the energetics of *R*,*R* and *S*,*S* chiral phases are identical. The calorimetric results are summarized in Table 2. Enthalpies of solution of structures **1** and **2** are exothermic, structure **1** (racemic) having a less exothermic ΔH_{sol} than structure **2** (chiral). This indicates that structure **1** is energetically more stable than structure **2** by an amount, $\Delta H_{\mathrm{trs}} = 19.6 \pm 1.3\ \mathrm{kJ\,mol^{-1}}$, which is in excellent agreement with the calculations ($21.9\ \mathrm{kJ\,mol^{-1}}$).

Table 2: Calorimetric data (in $\mathrm{kJ\,mol^{-1}}$) for the racemic (**1**) and chiral (**2**) zinc cyclohexane *trans*-1,2-dicarboxylates, normalized to unit-cell composition $[Zn_2(C_8H_{10}O_4)_2]$ of the racemic structure.

ΔH_{sol} (**1**)	ΔH_{sol} (**2**)	ΔH_{trs}
-137.5 ± 0.5	-157.1 ± 1.0	19.6 ± 1.3

The relative stabilities of the racemic **1** and chiral **2** phases can be rationalized in terms of the differences in the internal intra-layer energies of the component single layers and the non-bonded, inter-layer interactions (see Table 1). The inter-layer energy is stronger in phase **2** by $15.5\ \mathrm{kJ\,mol^{-1}}$ and is composed almost entirely ($> 99\,\%$) of dispersive interactions. However, the reason for the more favorable lattice energy of **1** stems from the intra-layer energy, which exceeds that in phase **2** by $37.4\ \mathrm{kJ\,mol^{-1}}$, yielding a greater stability for phase **1** of $21.9\ \mathrm{kJ\,mol^{-1}}$ measured relative to **2**.

It is interesting to speculate as to whether there might be other possible structures of similar or even lower energies. We examined a number of candidates, of which one was quite stable and could be energy minimized. Specifically, a racemic structure in which the stable layers of **1** are preserved, but alternate sheets are inverted so that *R*,*R* faces *R*,*R* and *S*,*S* faces *S*,*S* across the non-bonding regions (as in the closer packed single enantiomer structures) gives a total energy of $-2235\ \mathrm{kJ\,mol^{-1}}$, only $5\ \mathrm{kJ\,mol^{-1}}$ less stable than the observed racemic structure. The inter-layer interaction is indeed stronger ($-68\ \mathrm{kJ\,mol^{-1}}$), as in **2**, but the energy-minimized single layer energy is significantly less favorable than that in **1** ($-2167\ \mathrm{kJ\,mol^{-1}}$). Details are given in the Supporting Information. The calculations on alternative models underline the interplay between the layer–layer packing interactions and the energies within the individual layers. They also give us added confidence in the ability of the calculations to test the viability of different structural models.

In summary, we report the first integrated study of hybrid organic–inorganic framework materials involving synthesis, structure, computer simulation, and calorimetry. We have shown that the chiral zinc *R*,*R*-cyclohexane *trans*-1,2-dicarboxylate is less stable than its racemic *R*,*R*/*S*,*S* analogue and adopts a layered structure that has a fundamentally different topology. It is not yet clear whether such behavior is common in hybrid framework materials, but our observations point to the possibility that the structural diversity of racemic frameworks and their homochiral analogues may be much greater than has hitherto been suspected. In addition, we have shown that forcefield calculations on our hybrid structures made reliable predictions of their relative energies based upon the excellent agreement with our calorimetric results. Furthermore, we have shown that calculations of this kind can shed considerable light on the factors that control the energies of different crystalline forms.

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[19] Crystal data for **1**: $[Zn(C_8H_8O_4)]$, $M_r = 233.52$, crystal size $0.2 \times 0.15 \times 0.08$ mm; triclinic, $P\bar{1}$ (No. 2), $a = 4.9223(7)$, $b = 6.8499(11)$, $c = 13.864(2)$, $\alpha = 93.048(3)°$, $\beta = 99.600(2)°$, $\gamma = 98.501(2)°$, $V = 454.38(12)\ \mathrm{Å^3}$, $Z = 2$, $\mu = 2.680\ \mathrm{mm^{-1}}$, $\rho_{\mathrm{calcd}} = 1.721\ \mathrm{Mg\,m^{-3}}$, $F(000) = 240$, $R1 = 0.069$, $wR2 = 0.147$, GoF = 1.06. Bruker SMART CCD diffractometer, $\mathrm{Mo_{K\alpha}}$ radiation, $\lambda = 0.71073$ Å, $T = 293$ K, 3423 reflections scanned ($2\theta_{\mathrm{max}} = 52.7°$), 1746 unique ($R_{\mathrm{Int}} = 0.034$). Crystal data for **2**: $[Zn(C_8H_8O_4)]$, $M_r = 233.52$, crystal size $0.1 \times 0.04 \times 0.01$ mm; orthorhombic, $P2_12_12_1$ (No. 19), $a = 4.8436(2)$, $b = 6.6125(3)$, $c = 26.2382(13)$ Å, $\alpha = 90°$, $\beta = 90°$, $\gamma = 90°$, $840.37(7)\ \mathrm{Å^3}$, $Z = 4$, $\mu = 2.898\ \mathrm{mm^{-1}}$, $\rho_{\mathrm{calcd}} = 1.862\ \mathrm{Mg\,m^{-3}}$, $F(000) = 480$, $R1 = 0.069$, $wR2 = 0.130$, GoF = 1.04. Nonius KappaCCD diffractometer,

$\mathrm{Mo}_{K\alpha}$ radiation, $\lambda = 0.71073$ Å, $T = 293$ K, 5908 reflections scanned ($2\theta_{\max} = 54.9°$), 1919 unique ($R_{\mathrm{Int}} = 0.062$). All H atoms were geometrically placed and refined as riding with $U_{\mathrm{iso}}(\mathrm{H}) = 1.2\,U_{\mathrm{eq}}(\mathrm{C})$. CCDC 688064 (**1**) and 688065 (**2**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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