Herein we describe a molecular structure, formed from labile components, that exhibits structural memory. The macroscopic model in Figure 1 demonstrates this principle. The wooden icosahedral puzzle retains its structure (without any glue) despite dissociation of several pieces. These labile pieces can be removed and replaced without disassembly of the original structure. The structure itself is retained, or remembered, throughout the process of component substitution. In short, structural memory describes the substitution process itself and not merely the starting and ending states of the system.

Like the wooden puzzle, discrete supramolecular assemblies exhibit well-defined topologies, specified by the arrangement and connectivity of the constituent molecular components. If these molecular components can be substituted in a stepwise fashion and the supramolecular structure still persists, then there is structural memory. We describe such structural memory—as reported by retention of chirality—in

Figure 1. A 3D puzzle made of labile wooden components retains its structure despite dissociation of several pieces.
a chiral metallo-supramolecular assembly composed exclusively of labile achiral components. Although the molecular composition of the assembly is altered, chirality of the original assembly serves as a structural reporter, confirming that the original structure is preserved.

Chiral memory of self-assembled structures has been described previously.[2] In each of those examples, chiral molecular components induce supramolecular chirality in the original structure. Replacement of the chiral components by achiral analogues then creates a resolved structure, which is stable from days to years at room temperature. Importantly, without the initial chirally templated structure, the achiral components would assemble racemic, structural analogues. In contrast, we began with a resolved chiral assembly of achiral components in which chirality exists only at the supramolecular level. Stepwise replacement of the achiral components results in preservation of the original supramolecular chirality.

We have described the \([\text{Ga}_4\text{L}_1]\)^{12−} tetrahedron as the product of a rational design strategy; its labile metal and ligand components are programmed to form one predetermined structure.[1,4] The \(C_3\) symmetry of trisbidentate chelation at the four octahedral metal centers and the \(C_2\) symmetry of the six naphthyl-biscatecholamide \(L^1\) ligands drive formation of an \(M\text{L}_6\) tetrahedral cluster (Figure 2). An isolated cavity exists within the structure, and it encapsulates guest molecules such as tetraethylammonium. The assembly is truly supramolecular: the lability of the GaIII–catecholate interactions insures that self-assembly of the discrete structure is under thermodynamic control.

The chirality of the \([\text{Ga}_4\text{L}_1]\)^{12−} tetrahedron results from trisbidentate coordination of the metal ion. A simple \([\text{GaL}_3]\)^− catecholate complex exists in solution as two rapidly interconverting enantiomers (\(A\) and \(A\)).[5] Mechanical coupling of two such metal centers in a \([\text{GaL}_3]\)^− helicate complex slows the isomerization rate by a factor of 100 (Figure 3).[6] Assembly of the \([\text{Ga}_4\text{L}_1]\)^{12−} tetrahedron produces a racemic mixture of homochiral (\(\text{AA}\text{AA}\) and \(\text{DD}\text{DD}\)) structures. We have shown that these assemblies can be resolved by using chiral countercations.[7] Most remarkably, after exchange of the resolving agent for achiral countercations, an aqueous solution of the \(\text{AAA}\text{AA}\)-(\(\text{Et}_4\text{N})\text{GaL}_1\)^{12−} cluster retains its enantiopurity for at least eight months, even after extended boiling of the solution. The chirality of this structure, as measured from the circular dichroism spectra, persists even though there is evidence that partial dissociation of the complex occurs on the time scale of seconds.

The phenyl biscatecholamide \(L^2\) ligand does not form a tetrahedral structure itself but rather only forms an \(M\text{L}_2\) helicate when combined with octahedral metal ions (Figure 4). However, ligands \(L^1\) and \(L^2\) share very similar coordination chemistries, as both are biscatecholates. That such supramolecular components are programmed with the information specific to the formation of one self-assembled structure is a central tenet of supramolecular chemistry. In violation of this principle, the robustness of the \([\text{Ga}_4\text{L}_1]\)^{12−} tetrahedral framework is subjected to a radical test. Its ligands are replaced with the nontetrahedral \(L^2\) components in a stepwise fashion. Consequently, the formation of a series of \([\text{Ga}_4\text{L}_1\text{L}_2]^{12−}\) mixed-ligand tetrahedra from the homoleptic \([\text{Ga}_4\text{L}_1]^{12−}\) is followed in aqueous solution over time.

The \(L^2\) tetrahedral cluster was prepared and isolated as the \(\text{AAA}\text{AA}\)-(\(\text{Et}_4\text{N})\text{GaL}_1\)^{(11+)} salt, and the ligand \(L^2\) was introduced as the helicate complex \(K\text{[GaL}_1\text{]}^{3+}\) (Figure 4).
A D₂O solution of an equimolar ratio of the two complex (5.5 mm each) was prepared and buffered at pH 7.8. (The K₆[Ga₂L₂]₆ helicate provides a soluble source of L₂.)[9] This solution was heated to 75°C, and the ligand-exchange reaction was monitored over 24 h by ¹H NMR and CD spectroscopies (Figure 5 and Figure 6, respectively).

The encapsulated Et₄N⁺ ion acts as a structural probe in these experiments—it is only encapsulated in the M₄L₆ tetrahedra, as demonstrated by a large, characteristic upfield shift of its ¹H NMR resonance signals. The initial ¹H NMR spectrum of this reaction solution shows only one type of encapsulated Et₄N⁺ ion, corresponding to the ΔΔΔΔ-[(Et₄N)⁺Ga₄L₆]⁻¹⁺ starting material. The ¹H NMR data reveal formation of ΔΔΔΔ-[(Et₄N)⁺Ga₄L₆L₂⁻ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋₆₆₇

Figure 5. Left: schematic representation of L² ligand substitution into ΔΔΔΔ-[(Et₄N)⁺Ga₄L₆]⁻¹⁺. Right: ¹H NMR spectral region showing signals of the Et₄N⁺ guest. New guest signals appear as tetrahedra with different ligand combinations are formed. The methyl resonance signals of these guest species are labeled with the composition of the host tetrahedron.

Figure 6. The chirality of the ΔΔΔΔ-[(Et₄N)⁺Ga₄L₆L₂⁻ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋ₖ₋₆₆₇ tetrahedra is monitored by CD over time. Some change in the CD spectra is seen in the ligand-based absorptions due to the difference in chromophoric groups of the L¹ and L² ligands. However, these spectra show very little change in CD activity, demonstrating retention of chirality and thus structural memory of the tetrahedral system.

Experimental Section

General: ¹H NMR spectra were recorded on a Bruker DRX 500 MHz spectrometer. Circular dichroism spectra were measured with a Jasco J-500C spectropolarimeter, equipped with an IF-500 II A/D converter, and a Varian Cary 300 spectrophotometer was used to collect UV/Vis spectra. ΔΔΔΔ-[Et₄N]⁺[(Et₄N)⁺Ga₄L₆]⁻¹⁺ and K₆[Ga₂L₂]₆ were synthesized as previously reported.[7,8]

Ligand substitution: A solution of K₆[Ga₂L₂]₆ (5.5 mm) and ΔΔΔΔ-[Et₄N]⁺[(Et₄N)⁺Ga₄L₆]⁻¹⁺ (5.5 mm) was prepared in a K₂PO₄/D₂O buffer adjusted to pH 7.8 with NaOD. The solution was heated in an NMR tube at 75°C. At each time point the tube was cooled to room temperature, and an NMR spectrum was recorded.
For CD spectral measurements, aliquots of the reaction solution were removed at each time point and diluted to 0.52 mM with 2 mM KOH(aq). CD samples were measured in a 0.1 mm quartz cell. The absorption spectrum of each diluted aliquot was measured to verify aliquot concentration. Some material precipitated from the D2O solution over the course of the reaction. This material was redissolved and was found to contain the same mixture of species as the reaction solution (as evidenced by 1H NMR spectroscopy) and the same CD spectrum.

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[9] [Ga2L2]+ was used as the L2 source because of the poor D2O solubility of H4L2 itself. The excess GaIII introduced as a result presumably forms oligomeric products with the exchanged L1 ligand and excess L2. Regardless of the composition of these side products, they produce no CD signal since racemic [Ga2L2]+ helicate was used. Hence there is no change in CD activity.
[11] The CD spectra are cut off at 260 nm, because the bands at higher energies result from ligand π–π* transitions that are highly sensitive to the nature of the ligand present (L1 versus L2) rather than the configuration (A or D) of the metal centers.