

CHIRAL RECOGNITION VIA HELICAL SENSE AND PHASE IN A CRYSTALLINE SUPRAMOLECULAR ARRAY OF INTERMESHED TRIPLE-HELICES

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Publications:

Glaser, R. (1991) Helical Stereochemistry and Chiral Apple Halves, **Structural Chemistry**, 2, 479-483;

Glaser, R. (1993) Helical Stereochemistry and Chiral Apple Halves 2. La Coupe du Roi via Double Helical Complexation using Oligo(bipyridine) Strands and Cu(I)/Ag(I), **Chirality**, 5, 272-276;

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Abstract: *Hexatertiarybutyl-substituted C₃-symmetrical cage ligands composed of octahedral bidentate complexes of Ni(II) or Cu(II) ligated on either side to triskelion arrangements of three salicyl rings bound to a central nitrogen hub atom exhibit triple-helical conformations. Maximization of intermolecular aromatic-aromatic interactions between these complexes promote extended tongue-in-groove interleaving and afford a supramolecular array of diastereomeric intermeshed triple-helices perpetuating sideways throughout alternating enantiomeric layer stacks in the entire P-3 space group crystal lattice. The chiral recognition within the supramolecular ensembles is based upon the principles of helical sense and phase. A discussion of the symmetry, mechanical, and chemical factors and constraints influencing the formation of these self-assembled crystalline supramolecular ensembles will be presented.*

Metal complexes of a cage ligand (**1**) containing divalent nickel or copper atoms form right- or left-handed triple-helical molecules (Perkins *et al.* 2004; Perkins *et al.* 2006). The center of the complex consists of a right- or left-handed three-bladed propeller composed of three bidentate ligands with the metal atom at the hub. The chirality of the propeller is induced outward into triskelion moieties consisting of three salicyl rings ligated to

a central nitrogen atom. In solution these triple-helical complexes are palindromic [the same from both ends] and show D_3 -symmetry as evidenced by the nuclear magnetic resonance (NMR) spectrum. There is no NMR evidence for association in solution. Crystallization of these complexes affords crystals belonging to the trigonal $P-3$ space group. Two triple-helical complexes of opposite handedness afford the asymmetric unit of the crystal and each resides on a special position of three-fold rotational symmetry. Within the crystal the symmetry of the triple-helical entities has been reduced to C_3 -symmetry, thus making them non-palindromic. Intermeshing was observed between two triple-helical complexes of opposite handedness (see right-hand structure below) and the ensemble was described as a dimer (Perkins *et al.* 2004; Perkins *et al.* 2006). However, important stereochemical aspects of the molecular geometry with these crystals have not been previously commented upon.

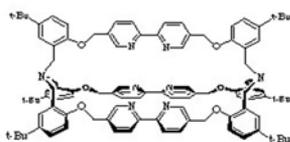


figure 1



figure 2

Edge-to-face interactions between aromatic rings provide the attractive force between the two intermeshed molecules. This was also not noted in the original work. Intermeshing can occur between two homochiral or two heterochiral triple-helices (Glaser 1993). Intermeshing provides a mechanism for chiral recognition (Glaser 1993) [your right foot fits better into your right shoe than into your left shoe]. The axes of two intermeshed homochiral triple-helices are tilted [right-hand drawing below] while those of two intermeshed heterochiral analogues are parallel [left-hand drawing below] (Glaser 1993). The magnitude of the aromatic interactions between the triple-helices differentiates the intermeshing between homochiral versus heterochiral assemblies. It is clear that these attractive interactions can occur in the top, center, and bottom regions of the ensemble in the case of heterochiral intermeshing, while they may exist solely in the localized central region for the homochiral arrangement.

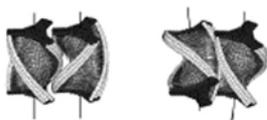


figure 3

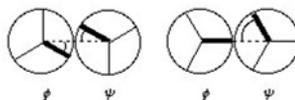


figure 4

For intermeshing to occur there must be a 60 degree phase difference between the two triple-helices where angles $\phi + \psi = 60^\circ$ [see arrangements above]. The inversion (*i*) symmetry operation of the $P-3$ space group provides a strong constraint against two *i*-symmetry enantiomeric triple-helical molecules intermeshing *over their entire lengths*. This is shown by the structure below in which the black colored inversion center generates

the enantiomeric 1/3-turn triple-helix with a 60° phase difference only if the helices intermesh over one-half of their lengths.



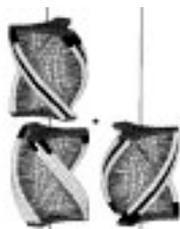
Figure 5

If the inversion center is placed at the mid-point of the triple-helical segment, then the two heterochiral triple-helices have a 0° phase difference and cannot intermesh [see left-hand arrangement below]. On the other hand, if they have a 60° phase difference and intermesh over their entire lengths, then there is no inversion center [see right-hand arrangement below].



Figure 6

Nature has placed two molecules in the asymmetric unit of the $P-3$ space group crystal to solve this dilemma. This means that there are two symmetry non-related triple-helices of the same handedness residing one on top of the other on the same C_3 -axis. These molecules are diastereomers since they have the same constitution [connectivity] but are not interconvertible by a symmetry operation. If the top triple-helix is related to the bottom one by a rotation of 60° , then the i -symmetry center between the axes will generate an enantiomeric copy of the top helix [see structure on the right below] which will be adjacent to the helix on the left below. In this manner, the two lower adjacent helices below will also be diastereomeric [and not enantiomeric] and they may now intermesh over their entire lengths to maximize the attractive aromatic interaction forces.



Finally, it is seen that the arrangement of molecules in the crystal is much more complex than the original description of a ‘dimer’ (Perkins *et al.* 2004; Perkins *et al.* 2006). Since the triple-helices each occupy special positions of three-fold rotational symmetry, this

obligates all the strands, and similarly, all the grooves to be symmetry equivalent. As a result a left-handed triple-helix must be surrounded by three diastereomeric right-handed intermeshing triple-helical neighbors [see partial structure below]. Similarly, each of the right-handed triple-helices will also be surrounded by three diastereomeric left-handed triple-helices. As a consequence, a supramolecular arrangement of intermeshing diastereomeric heterochiral helices is generated and forms a layer of the crystal. Where are the two enantiomeric entities? They reside in supramolecular ensembles stacked in layers on top or on bottom of the partial structure depicted below. Therefore, maximization of intermolecular aromatic-aromatic interactions between the oppositely handed complexes promoted extended tongue-in-groove interleaving and afforded a supramolecular array of diastereomeric intermeshed triple-helices throughout alternating enantiomeric layer stacks in the entire *P*-3 space group crystal lattice.



Figure 8

References

- Glaser, R. (1993) *Helical Stereochemistry and Chiral Apple Halves 2*. La Coupe du Roi via Double Helical Complexation using Oligo(bipyridine) Strands and Cu(I)/Ag(I), *Chirality*, 5, 272-276.
- Perkins, D. F., Lindoy, L. F., Meehan, G. V., Turner, P. (2004) "Inherent helicity in an extended tris-bipyridyl molecular cage". *Journal of the Chemical Society, Chemical Communications*, 152-153.
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