

# Supramolecular Chemistry with Chiral Pyridine-Type Ligands

Thomas Bark and Alex von Zelewsky\*

**Abstract:** Chiral pyridine-type ligands are readily available in enantiomerically pure form from enantiopure natural products via a Kröhnke reaction. The ease of synthesis allows numerous variations of the ligands which all display a particular coordination behavior. By these means, it is possible to synthesize 'tunable' series of molecules. Thus, mononuclear, as well as self-assembled polynuclear species can be obtained in enantiopure form. With these ligands, a significant step towards the systematic development of stereoselective synthesis in coordination chemistry was achieved, leading to a class of compounds that hold interest for various kinds of applications.

**Keywords:** Chirality · N ligands · Self assembly · Stereoselective synthesis · Supramolecular chemistry

## Introduction

The formation of compounds of 'higher order' (Verbindungen höherer Ordnung) was quite an enigma during the second half of the 19th century until Alfred Werner's introduction of coordination theory in 1893 [1]. The coordination compounds as species of higher order can be considered to be precursors to the modern supramolecular assemblies. Supramolecular assemblies go, of course, much beyond coordination chemistry, yet one possibility to assemble molecules in a well-defined way is through coordination by metal ions.

In our group at the University of Fribourg, we started a systematic study of the possibilities of stereoselective and stereospecific synthetic methods for coordination compounds about ten years ago with the purpose of fabricating multi-

nuclear coordination compounds with well-defined stereochemistry for the study of photochemically and photophysically interesting systems [2]. During this development, a large number of enantiopure chiral pyridine-type ligands were synthesized.

In this short account, we describe the development from the stereospecific synthesis of binuclear compounds following a conventional method to the self-assembled structures, which show predetermined configurations at the metal centers and beyond, e.g. in inherently chiral superstructures, like the helicates, using chiral pyridine-type ligands.

## Multinuclear Coordination Species with Defined Stereochemistry

Metals are often the chiral centers in multinuclear coordination species. In such cases the number of possible stereoisomers grows rapidly with the number of metal centers. The isomeric mixtures obtained using non-selective methods, are often difficult to separate. This explains the great interest in the stereoselective synthesis of such compounds. One approach that has been used in our group, consists in the use of enantiopure

complex fragments, so-called building blocks. To be of synthetic value, such building blocks must fulfill the following criteria:

- They must be easily accessible in high enantiomeric purity
- They must show specific and adequate reactivity
- No racemisation should occur during fabrication of the supramolecular assembly from the building blocks.

Hua and von Zelewsky [3] developed a method that provides the *cis*-Ru(bpy)<sub>2</sub> synthon [4] in enantiomerically pure form: *rac*-[Ru(bpy)<sub>2</sub>py<sub>2</sub>]Cl<sub>2</sub> is resolved with dibenzoyl tartrate, to yield  $\Delta$ -[Ru(bpy)<sub>2</sub>py<sub>2</sub>](*O,O'*-dibenzoyl-D-tartrate), or the  $\Lambda$ -L isomer, respectively. The two pyridine ligands are sufficiently labile to be substituted with bipyridine-type ligands in refluxing glycol. When light is excluded, no racemisation at the metal centers is observed under these reaction conditions.

Hua and von Zelewsky [5] used these building blocks in specific syntheses of the three possible isomers of the dimeric complex [Ru(bpy)<sub>2</sub>-( $\mu$ -dppm)-Ru(bpy)<sub>2</sub>](PF<sub>6</sub>)<sub>4</sub> (dppm=4,6-dipyridyl-pyrimidine) (Fig. 1).

Whereas both the chiral  $\Delta\Delta$ - and  $\Lambda\Lambda$ -isomers can be obtained directly in one-

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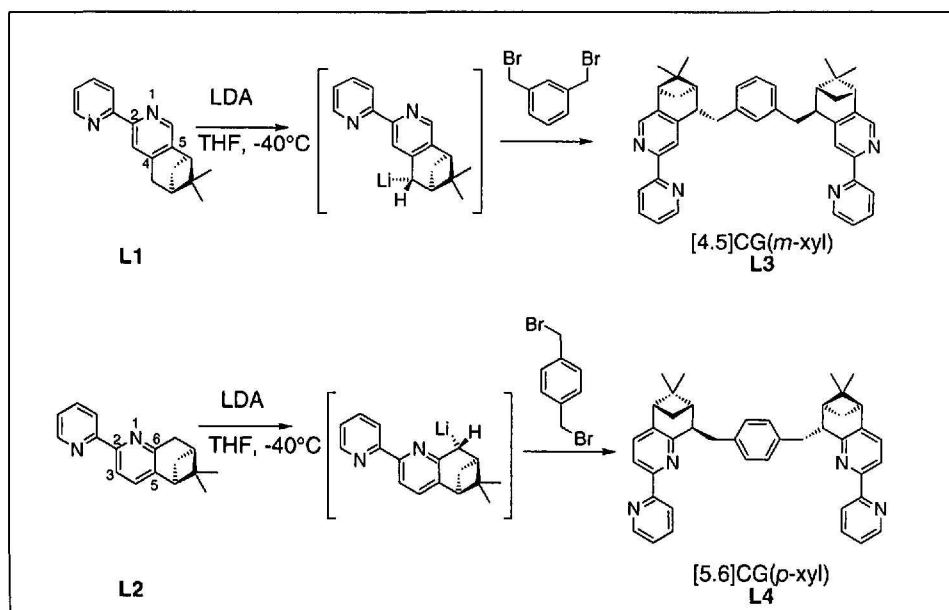
step reactions from the bridging ligand and the  $\Delta$ - (respectively:  $\Lambda$ -) form of the building blocks, the *meso*-form demands stepwise construction.

These versatile building blocks have also been used by other groups [6]. Drawbacks of this method are, on the one hand, the necessity of resolution of a racemate, and on the other hand, potential photoracemization of the building block. Also the multinuclear species are often configurationally unstable under various conditions (*e.g.* light or coordinating anions).

A different approach to chiral, enantiopure precursor complexes is diastereoselective complex formation, using enantiopure ligands. For this purpose, the so-called 'CHIRAGEN' ligands proved to be very useful (CHIRAGEN='generating chirality'). The basic idea of the CHIRAGENS is to link two bipyridine moieties through a chiral bridging group. Such ligands are predisposed for diastereoselective co-ordination to octahedral centers: The edge configuration [7] as well as the helicity of the obtained complexes are predetermined by the configuration of the chiral bridging group (Fig. 2).

Hayoz [8] translated this idea into real chemistry by the linkage of two pinene-fused bipyridine molecules (L1 or L2) with several dibromoalkanes or bis-(bromomethyl)-arenes (Scheme):

L1 and L2 are derived from commercially available, enantiopure terpenes. Both enantiomeric forms are easily accessible. The coupling reaction, in which a new chiral carbon is formed, proved to be completely diastereoselective.



Scheme.

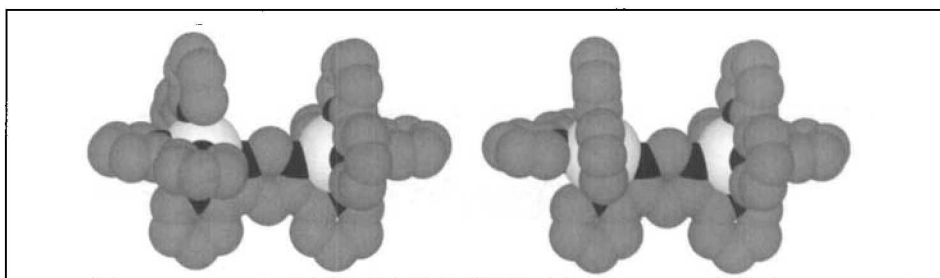


Fig. 1. The chiral  $\Delta\Delta$ -form (left), and the  $\Delta\Lambda$ -*meso*-form (right) of the  $[(Ru(bpy)_2)(dppm)]^{4+}$  complex ion (modeled structure).

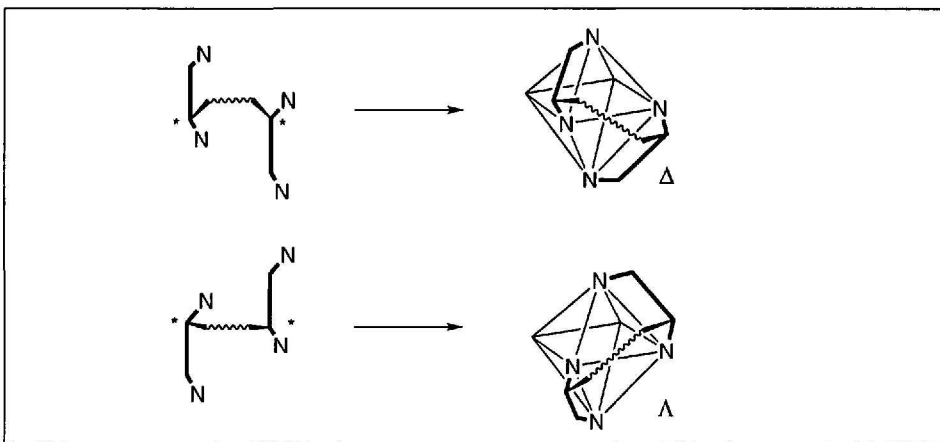


Fig. 2. Coordination mode of CHIRAGEN-type ligands at octahedral centers.

Mürner *et al.* [9] showed that xylene-bridged [4.5]CHIRAGENS form ruthenium(II) complexes with 100% diastereoselectivity, *i.e.* with total predetermination of the configuration at the metal center (Fig. 3).

An example for the application is the synthesis of all three possible isomers ( $\Delta\Delta$ ,  $\Lambda\Lambda$  and *meso*) of the dinuclear, 2,2'-bipyrimidine-bridged complex  $[RuCG(m-xyl)-(\mu-bpm)-RuCG(m-xyl)](PF_6)_4$  [10].

A special case is the CHIRAGEN [4.5]CG(5,5'-dm-bpy), which contains the 5,5'-dimethyl-bipyridine unit as spacer group. To this tritopic, hexadentate ligand, three  $\Delta$ - $[RuCG(m-xyl)Cl_2]$  units have been coordinated to result in a trinuclear ruthenium complex [11] (Fig. 4). This compound could be obtained isomerically pure, although it contains a total of 19 independent centers of chirality, of which eight are of natural origin and eleven are formed in diastereoselective reactions.

### Self Assembly with CHIRAGENS

Recently, CHIRAGEN ligands have also been used in the stereoselective construction of large supramolecular coordination species through self assembly.

Although the *meta*-xylyl-bridge in L3 is short enough for a monotopic complexation of  $Ru^{2+}$ , ditopic complexation with octahedral centers is observed for kinetically labile cations, such as  $Fe^{2+}$ ,  $Zn^{2+}$  and  $Cd^{2+}$ . Titration experiments, but also electrospray mass spectra reveal for all three metals formation of complexes with  $M_2L_3$  stoichiometry [12]. Several arrangements of the ligands and metals are in principle possible (Fig. 5).

Chirally predetermined ML3 fragments that are linked by a third ligand can be formed:  $[LM-(\mu-L)-ML]^{4+}$  (C5), and

also complexes with three bridging ligands:  $[M(\mu-L)_3M]^{4+}$ . For the latter case homo- (**C7**) and heteroconfigurational (**C6**) arrangements of the ligands around the metal ions are both in principle possible. Valuable information for the elucidation of the structure in solution comes from CD spectroscopy and NMR. The fact that the complexes obtained display distinct CD activity rules out the anti-helicate **C6**. Although chiral due to ligand centered chirality, these pseudo-*meso* complexes would show no or small  $\Delta\epsilon$  values, as they combine pairs of chromophores of opposite configuration. On the other hand, the  $^1H$  NMR spectrum comprises only one halfset of protons of the **C2** symmetrical ligand, therefore it does not corroborate with either the monobridged, heteroleptic complex **C5**, or the **C3** symmetrical anti-helicate **C6**. Only the  $D_3$  symmetrical helicate **C7** agrees with all spectroscopic data. The actual configuration at the metal centers can be elucidated by exciton coupling theory [13] from the sign of the CD band in the spectral region, that corresponds to ligand centered  $\pi-\pi^*$  transitions. It is actually  $\Delta$ , when (-)-**L3** is used.

CHIRAGEN ligands derived from [5.6]-pineno-pyridine **L2**, e.g. **L4**, have also been used successfully in spontaneous self assembly. These ligands are more appropriate for T-4 coordinated cations, as substituents in 6-position of 2,2'-bipyridines generally prevent coordination to OC-6 centers [14].

*p*-Xylene-bridged CHIRAGEN **L4** yields with both  $Cu^+$  and  $Ag^+$ , the highly interesting complexes **C8** and **C9** which possess aesthetically appealing solid-state structures [15] (Fig. 6). These cyclic, chiral hexameric assemblies, so-called circular helicates, form in a completely diastereoselective manner. The local configuration at the metal centers, as well as the helicity of the superstructure, are predetermined by the configuration of the ligand.

The behavior in solution of the silver complex has been studied in detail and is characterized by two main features: The hexamer is in equilibrium with a tetrameric form, as revealed by VT-NMR [16]. **L4** shows chiral self-recognition: An artificial racemate prepared from **L4** and *ent*-**L4** produces the same NMR-spectrum when combined with  $Cu^+$  as the enantiopure ligand. Formation of mixed species can therefore be excluded.

The cavity in the center of **C8** and **C9** is chiral, but due to its small diameter (0.84 nm), these complexes cannot accommodate guest molecules. Enlarge-

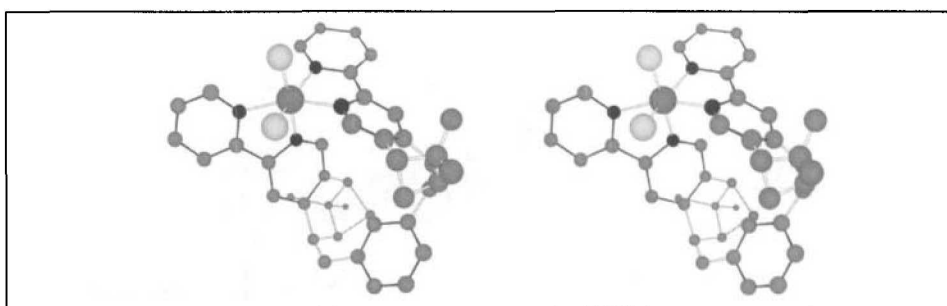


Fig. 3. Stereopair of the complex  $\Delta$ -[Ru([4.5]CG(*m*-xyl))Cl<sub>2</sub>] that can serve as an enantiopure building block in the fabrication of larger, oligonuclear coordination species (modeled structure).

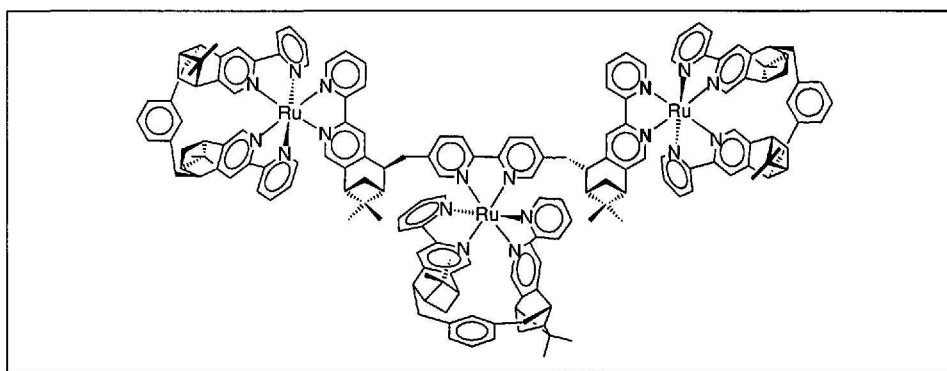


Fig. 4. The isomerically pure complex ion  $[[\Delta\text{-Ru}([4.5]\text{CG}(\textit{m}\text{-xyl}))]_3\text{-}\mu^3\text{-}([4.5]\text{CG}(5,5'\text{-dm-bpy}))]^{6+}$  obtained from a CHIRAGEN building block and another CHIRAGEN-type ligand.

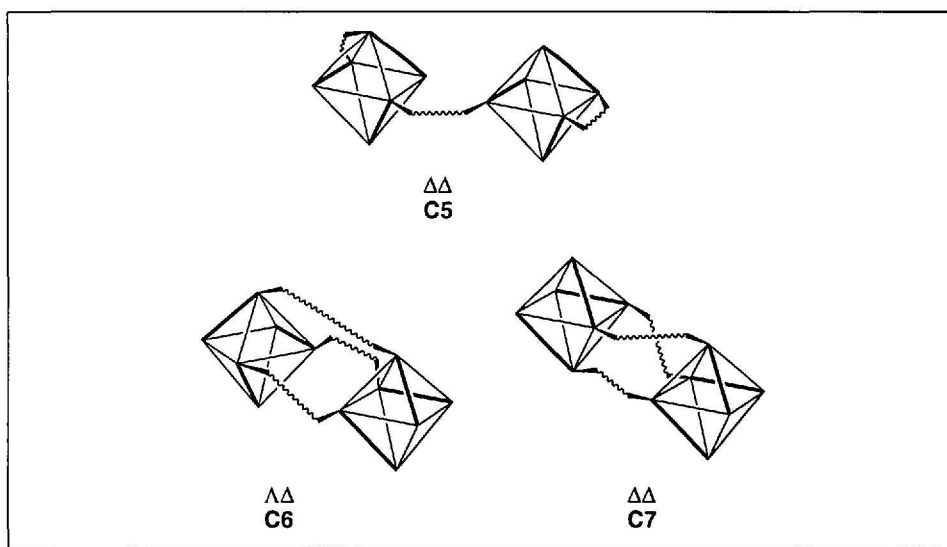
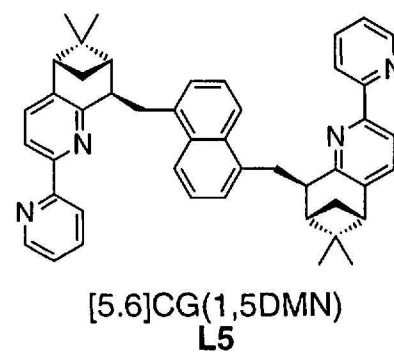


Fig. 5. Three possible coordination modes of complexes with  $M_2L_3$  stoichiometry, resulting from the combination of labile OC-6 centers and the enantiopure, tetradentate, ditopic ligand [4.5]CG(*m*-xyl).

ment of the cavity was attempted in a series of ligands similar to **L4** that contain bridging groups derived from dimethyl naphthalenes instead of xylene.

The outcome was unexpected: **L5**, which is closely related to **L4**, yields with silver salts a soluble complex **C10** with a polymeric solid-state structure [17] (Fig. 7).

In the crystal the unprecedented case of two polymeric, helical, intertwined strands is observed, resulting in an as-



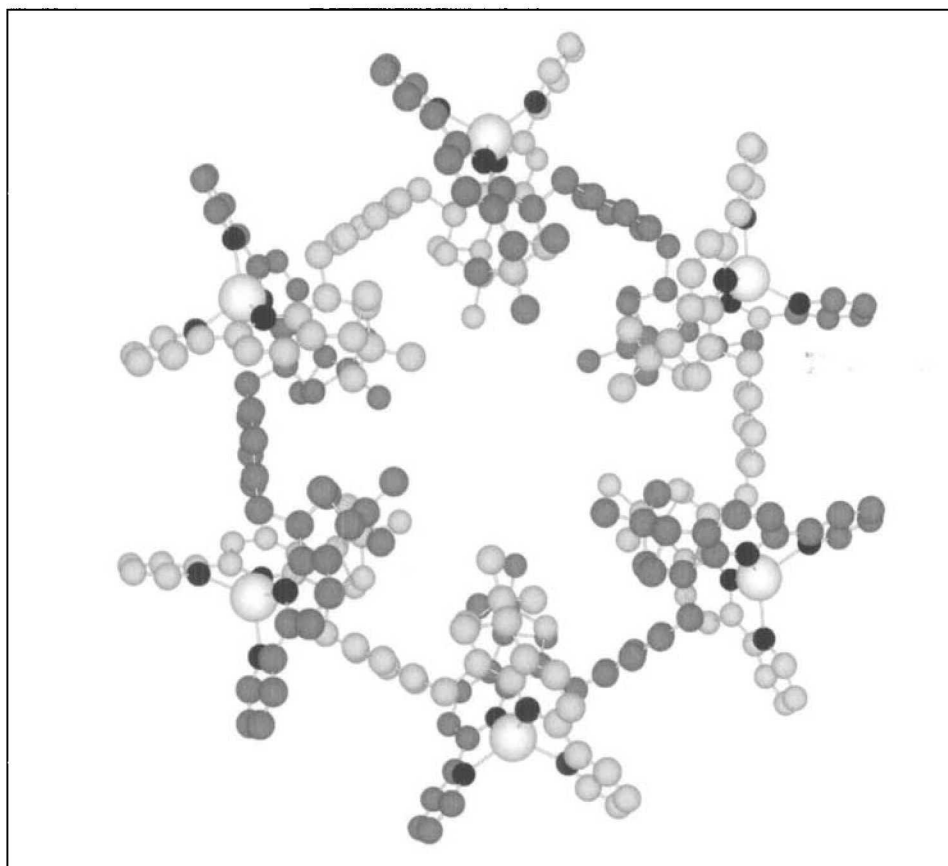


Fig. 6. The chiral, circular, hexameric complex ion  $[Ag_6L4_6]^{6+}$ , a so-called 'circular helicate', obtained in isomerically pure form from enantiopure **L4** (= [5.6]CG( $p$ -xyl)) and  $AgPF_6$ .

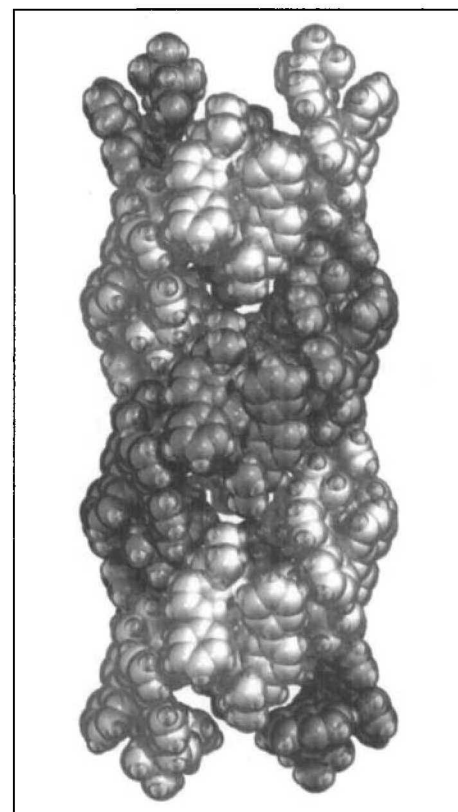


Fig. 7. A section that represents one and a half turns of the 'infinite' polymeric double-stranded helix  $[(Ag_nL5_n)_2]^{2n+}$ . The two independent strands are represented in different grayscales.

sembly that on first regard is reminiscent of double-stranded DNA. In contrast to the latter, the intertwined strands are not attached to each other by specific interactions, such as H-bonds or  $\pi$ -stacking. The stereochemical features of the complex are again determined by the configuration of the ligand. All metal centers are of the same configuration, and the helicity of the superstructure, the double helix, is predetermined. There is an interesting detail concerning the designation of chirality descriptors to the metal centers: Although **L4** and **L5** are derived from the same enantiomer of **L2**, the configuration at the metal centers in the hexamers **C8** and **C9** is *R*, but it is *S* for the polymer **C10**. Nevertheless, the descriptor is in both cases *A*, using the *skewed line system* [7] for definition of the helical arrangement of ligands around metal centers.

### Outlook

As we have shown, pineno-fused pyridine-type ligands are a valuable tool for the stereoselective synthesis of both 'classical' coordination compounds with kinetically inert metal ions, as well as self-assembled structures from kinetically labile metal ions. Due to this general applicability, our group is now using

CHIRAGEN-type ligands in new areas, such as the stereoselective synthesis of topologically interesting molecules or the development of complexes that can potentially serve as 'new materials'. We are specially interested in complexes that may display useful properties due to their enantiomeric purity. At the same time, we are developing mononuclear complexes as enantioselective catalysts for several types of reactions.

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