

# The bright future of stereoselective synthesis of co-ordination compounds

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Transfer of chirality during the build-up of molecules has been applied innumerable times in organic chemistry since the end of the 19th century, when it was introduced in the so-called asymmetric synthesis by E. Fischer. Although analogous reactions were introduced in co-ordination chemistry in its early development, diastereoselective reactions have not been applied in a very systematic way for co-ordination species. The highly versatile co-ordination geometry of metal centres makes the synthesis of a selected stereoisomer in general a formidable task. In the present article an account on new developments in the field is given, focussing on recently synthesized molecules, where natural chiral products are used to create a large number of chiral ligands which predetermine the chirality at metal centres.

## 1 Introduction

Stereoselectivity in its general meaning, which is the preferential formation of one stereoisomer over another in a chemical reaction, has been known in co-ordination chemistry for a very long time. A classical example, established in the early period of development of co-ordination chemistry, is reflected in the

*trans*-effect series, mainly applicable to square planar (*SP*-4)  $d^8$ -co-ordination centres. If one accepts the definition<sup>†</sup> that all stereoisomers are either enantiomers or diastereomers, the different forms of square planar (*SP*-4) co-ordination species (characterised either by a locant or by a configuration index) are clearly diastereomers (because they are not enantiomers), and the reactions can therefore be designated as diastereoselective in the widest sense. Since chirality does not play a role in this type of reaction, they can be called *regioselective reactions* (if they produce stereoisomers in non-statistical ratios). The *trans* influence has been used in innumerable examples for the preferential preparation of isomers of  $Pt^{II}$ ,  $Pd^{II}$ ,  $Ir^I$  and other co-ordination complexes. Yet, except for the *trans*

<sup>†</sup> Chemistry is becoming more and more a unified science. Since we should admit frankly that topographical stereochemistry has been developed in classical Organic Chemistry to a much higher level of sophistication (there are very good reasons for that) than in Inorganic Chemistry, it seems reasonable to adopt, whenever it is possible, the nomenclature of Organic Stereochemistry. Consequently, the not easily definable concept of geometrical isomerism, often applied to *SP*-4 complexes, should be avoided.

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influence series, there are not many other well documented, generally applicable, regioselective reaction types in coordination chemistry. There might be, at least at present, not enough general interest for the systematic study of the possibility to develop regioselective synthetic methods to a larger extent and we do not discuss here this type of reaction in any further detail.

In the present Perspective we want to emphasise another type of stereoselectivity: the focus of our interest is on reactions, in which a metal complex is synthesized, where the metallic centre constitutes an element of chirality. In order to fulfil the definition of stereoselectivity, the two possible configurations of this chirality element must not occur in a statistical (in most cases 1 : 1) ratio. Since electromagnetic force, on which chemical reactions is based to an almost exclusive extent, conserves parity, a stereoselective reaction of this kind requires at least in some of the reaction steps the presence of a chiral auxiliary or intermediate in a non-racemic form.‡ Reactions where new chirality centres are created with a preferential configuration of a carbon atom were invented by natural evolution aeons ago, probably soon after life had started on this planet. The question as to how nature arrived to synthesize chiral compounds in a preferential configuration is still a matter of speculation and it will probably never be known with absolute certainty how asymmetric synthesis started in natural systems. *Asymmetric synthesis* was the term introduced by Fischer in 1894<sup>1</sup> for the first laboratory preparation of a compound where a chirality element (an asymmetric carbon atom in the older terminology) was created artificially. During the past 106 years, diastereoselective and enantioselective synthesis has developed enormously in organic chemistry.

The art of making highly complex natural molecules in the laboratory, comprising many chirality centres, would not have been possible without highly stereoselective reaction steps. It was again natural evolution, which preceded similar human activities in the laboratory by billions of years in the field of *enantioselective catalysis*. Innumerable enzymatic reactions yield one enantiomer in a very high preference, propagating therewith the homochirality in the world of natural chiral molecules. Enantioselective catalysis was for the first time successful in the laboratory only in the 1950's.<sup>2</sup> It is noteworthy that a preponderant number of the laboratory enantioselective catalysts and also quite a few natural enzymes that perform enantioselective syntheses contain metal centres, which are often the active sites of the catalyst or the enzyme.

Chirality (called *Spiegelbildisomerie* by Alfred Werner) played an important role in the early days of co-ordination theory. The first resolution of a racemate of a co-ordination compound,<sup>3</sup> soon followed by the first resolution of a purely inorganic compound,<sup>4</sup> was the ultimate proof of the assumption of octahedral co-ordination geometry of various metal co-ordination centres. It took a few more years until stereoselective synthesis was first introduced into co-ordination chemistry. In a little known publication Smirnof, <sup>5</sup> one of the last collaborators of Alfred Werner, describes the diastereoselective synthesis of chiral octahedral platinum(IV) complexes in a clear way. By carefully measuring the optical rotation values, Smirnof deduces that  $[\text{Pt}(\text{pn})_2\text{Cl}_2]^{2+}$  and  $[\text{Pt}(\text{pn})_3]^{4+}$  are formed stereoselectively, if non-racemic 1,2-diaminopropane (pn) is used as a ligand. Smirnof quotes the classical work of Fischer in organic chemistry and he adds the phrase that comparable processes can certainly be carried out in co-ordination chemistry even with more efficiency than in organic chemistry.

Yet, after Smirnof, the field did not attract many researchers for several decades to come. The reason for this slow develop-

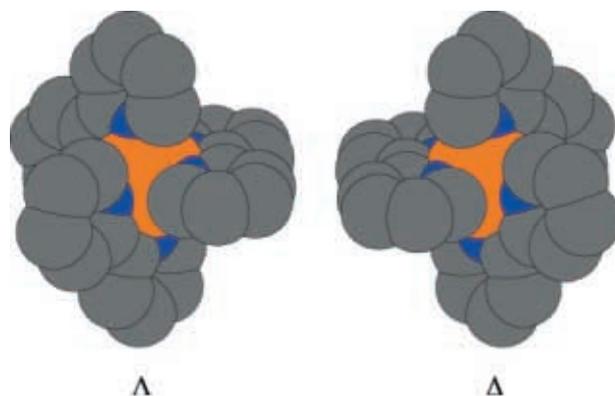


Fig. 1 The  $\Delta/\Lambda$  enantiomeric pair of the  $[\text{Ru}(\text{bpy})_3]^{2+}$  complex.

ment until quite recently is probably twofold. (i) Before the advent of enantioselective catalysis and of supramolecular chemistry, there were no incentives similar to those in organic chemistry to prepare species where the chirality at the metal centre is predetermined. (ii) The various possible co-ordination geometries, leading to an enormous number of possible configurations in a co-ordination complex, makes stereoselective synthesis of co-ordination species a formidable task. Only modern structural analytical methods like NMR spectroscopy in solution, and X-ray crystallography in the solid, make it possible really to know what is the outcome of a specific reaction. Consequently we have nowadays the possibility to investigate quite complicated systems in detail. A recent, fairly comprehensive review on examples where compounds have been prepared with predetermined chirality at the metal centre is available.<sup>6</sup>

The present Dalton Perspective gives a largely personal account of research carried out during the past ten years, which is all focussed on the synthesis of co-ordination species where the chirality at the metal centre is predetermined.

### 1.1 The Isomer Problem

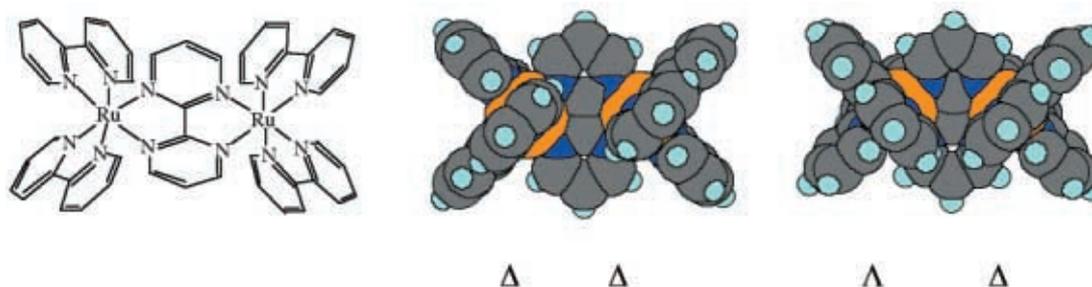
The subject caught our attention for the first time when we were involved in a three-centre collaboration with the groups of Vincenzo Balzani in Bologna and Fritz Vögtle in Bonn. It was the aim to synthesize multicentre systems that could perform various tasks, such as acting as antennas, harvesting light, switches for intramolecular electron transfer processes, *etc.* We soon found out that often precise characterisation of such species was hampered by the *Isomer Problem*. We called it this because our reaction products were often complicated mixtures of isomers, yielding extremely complicated, non-assignable NMR spectra. Moreover the compounds could not be obtained in single crystal form either. In most cases, the co-ordination species were extensions of metal tris-diimine units. These units (Fig. 1) are, of course, chiral and they can therefore occur in two configurations,  $\Delta$  and  $\Lambda$ . It can easily be calculated that a multinuclear species of 79 chirality centres yields up to (the detailed calculation must take into account symmetry)  $2^{79} = 6.0446 \times 10^{23}$  isomers. Thus, in one mole of such a substance each molecule would be, on a statistical basis, an individual.§

### 1.2 Possible solutions for the Isomer Problem

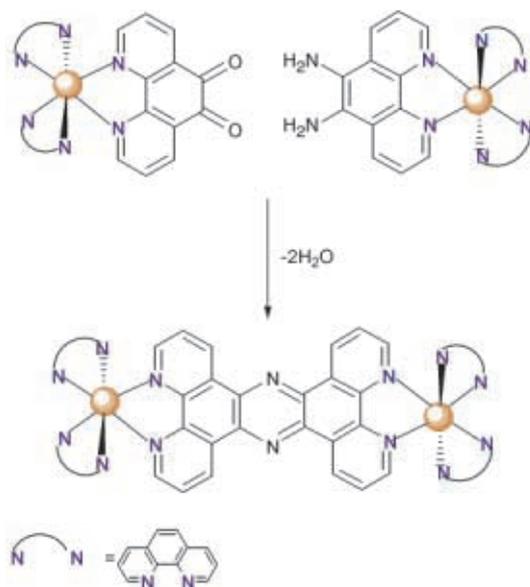
Looking to solutions for the Isomer Problem we found that it had not been studied in a really systematic way in co-ordination chemistry. In principle, the problem can be solved in an analytical way, *i.e.* through separation of the isomers formed

‡ Parity non-conservation in the weak interaction forces, nowadays often discussed as the possible origin of homochirality often found in living systems, has no consequences for laboratory syntheses, and it will therefore not be considered here.

§ From the point of view of possible information content, one mole of a substance, where each molecule is different from any other, could be an interesting sample, if one would be able to address each individual in some way.



**Fig. 2** The bridged dinuclear complex  $[(bpy)_2Ru(bpym)Ru(bpy)_2]^{4+}$  can be obtained in a stereospecific way as an heterochiral ( $\Lambda\Delta$ ) or homochiral ( $\Delta\Delta/\Lambda\Lambda$ ) complex if suitable chiral building blocks are used.



**Fig. 3** Enantiomerically pure complex obtained by MacDonnell and Bodige<sup>15</sup> *via* the condensation between tris-diimine ruthenium(II) building blocks. If the building block contains more than one functionalised phenanthroline type ligand, it can be used for the stereospecific synthesis of polynuclear complexes, *e.g.* metal dendrimers.<sup>16</sup>

during a synthesis. Obviously, this method is only practicable if the number of isomers is relatively small, and even then it is often of limited efficiency, and in addition the yield of a given isomer is always relatively low. We therefore looked from the beginning to synthetic pathways which would result in the selective formation of one and only one isomer. Starting from this point, we developed two strategies.

## 2 Enantiomerically pure chiral building blocks by resolution of a racemate

This strategy is extremely simple and straightforward, yet it had not been studied systematically before. It starts with a racemic complex with two bidentate and two monodentate ligands in *cis* positions, that can be substituted. If such a complex can be prepared in an enantiomerically pure form, and if the substitution reactions proceed in a stereospecific way (*i.e.* either with retention, or perhaps with inversion of configuration, but not with racemisation), then the resulting multinuclear species would be isomerically pure. For the complexes we were aiming at,  $[Ru(phen)_2(py)_2]^{2+}$  or  $[Ru(bpy)_2(py)_2]^{2+}$  seemed to be a suitable building block. The resolution of the former into the enantiomeric forms had been described by Bosnich and Dwyer.<sup>7</sup> The chiral auxiliary is arsoyl tartrate. The two complexes represent a rather typical example, where one given chiral auxiliary works well in one case and not at all in the other. All attempts to resolve  $[Ru(bpy)_2(py)_2]^{2+}$  with arsoyl tartrate failed. Benzoyl tartrate on the other hand works only with  $[Ru(bpy)_2(py)_2]^{2+}$  and not with  $[Ru(phen)_2(py)_2]^{2+}$ .<sup>8,9</sup>

It turned out that substitution reactions with these building blocks proceed indeed with retention of configuration. However, one has to take some precautions in order to avoid partial racemisation. Visible light, for example, can induce photo-racemisation with a rather high quantum yield. It is a general drawback of these chiral building blocks that they are not particularly stable towards racemisation. Nevertheless, it was possible to obtain for the first time a dinuclear species in any of the possible configurations in pure form. A simple example is  $[(bpy)_2Ru(bpym)Ru(bpy)_2]^{4+}$  ( $bpym = 2,2'$ -bipyrimidine) (Fig. 2). This method, which should be called stereospecific and not stereoselective synthesis, has since been used in several cases for the preparation of multinuclear species with well defined stereochemistry.<sup>10–12</sup>

Another method without replacement of ligands at the chiral centre is based upon the inertness of certain tris-diimine building blocks, containing functionalised ligands.<sup>13</sup> In this case the construction of polynuclear architectures involves reactions between the peripheral functional groups like the condensation between *o*-diamine (1,10-phenanthroline-5,6-diamine) and *o*-dione (1,10-phenanthroline-5,6-dione) (Fig. 3) ligands co-ordinated to different metal centres.<sup>14–16</sup>

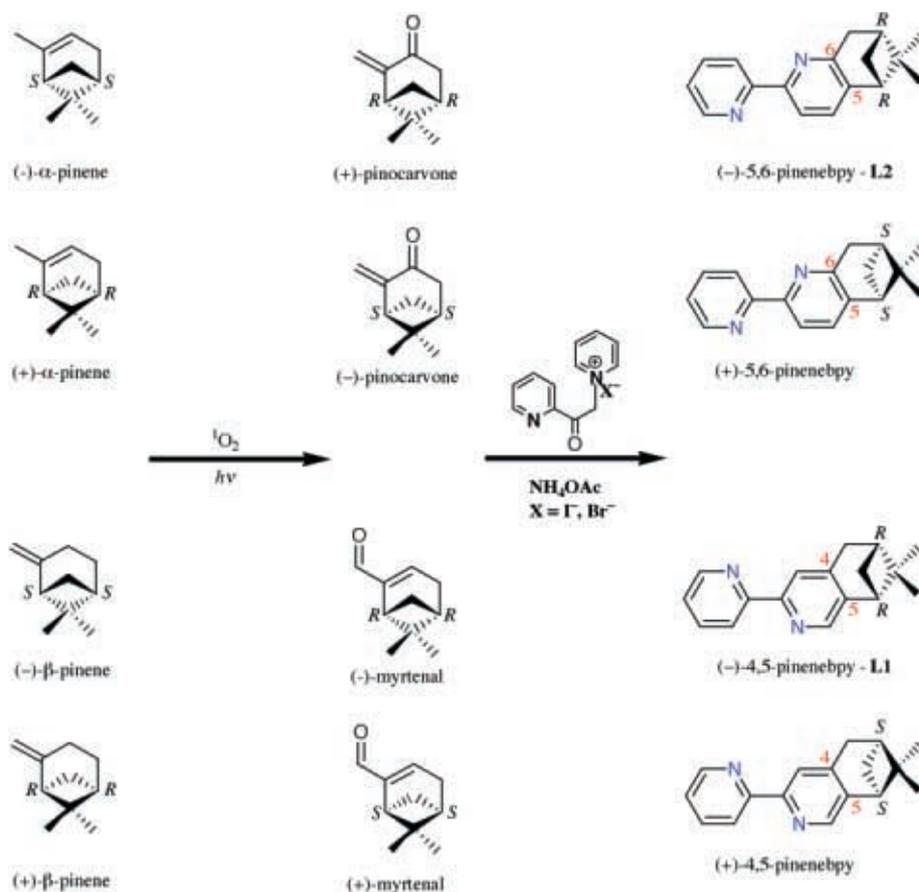
The stereospecific synthesis may very well have interesting applications and it will consequently be used in the future, whenever relatively simple multinuclear species are the target. A more general, and often also more useful, but definitely much more elegant method to generate stereochemically well defined metal complexes is the stereoselective synthesis described in the following section of this Perspective.

## 3 Creation of chiral metal centres in predetermined configurations

As already mentioned, the first report on a truly diastereoselective synthesis involving a metal centre appeared almost 80 years ago.<sup>5</sup> At that time there were no methods available to make these investigations in a quantitative manner. We therefore do not know in which ratio the diastereomers occurred. Indeed, we plan to repeat Smirnoff's historical syntheses and analyse the products with modern methods. The outcome of this analysis is of considerable interest, since we have recently found that in similar reactions, using chiralised bipyridine ligands and several metals as co-ordination centres, the preferred configuration can depend on whether the reaction is thermodynamically or kinetically controlled.<sup>17</sup> In the present contribution we want to show the way from our first realisation of a stereoselective synthesis of a co-ordination species to the multitude of metal complexes having metal centres of predetermined configuration.

### 3.1 Octahedral metal centres

Almost exactly ten years ago, one of us proposed to an incoming graduate student, Pascal Hayoz, for his PhD thesis the following problem: "synthesize a tetradentate ligand that is composed of two didentate subunits (preferably of the diimine type), which are connected through a chiral bridge in such a



Scheme 1 Synthetic route for the obtention of **L1**, **L2** and their enantiomers.

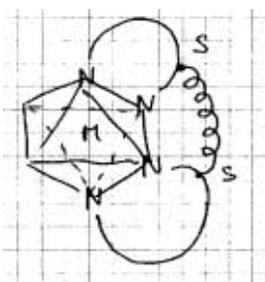


Fig. 4 Draft containing the idea of a chiral bridged tetradentate ligand for diastereoselective synthesis.

way that the ligand can wrap around the metal only in one of the two configurations,  $\Delta$  or  $\Lambda'$ . The sketch, which was drafted on a piece of paper, is reproduced in Fig. 4. Shortly after he presented an extremely elegant solution that has been the basis of our work in this field, and which is in our opinion just the beginning of a development that will yield many more interesting structures.

The key step to this development was the synthesis of the two molecules **L1** and **L2**. The synthetic pathway (Scheme 1) makes use of the general method for pyridine synthesis introduced by Kröhnke.<sup>18</sup> The chirality is introduced *via* the commercially available natural products, myrtenal or pinene. Since the terpene products occur in nature in both enantiomeric forms (nature is not homochiral in many of its terpene products, as opposed to amino acids and sugars), both enantiomers of these ligands are easily accessible.

Ligands **L1** and **L2** have the useful property that one proton is removable by strong base. This property makes them universally useable for further ligand syntheses. The target of preparing a ligand of the type represented schematically in Fig. 4 was hit for the first time with ligand **L4**, which was prepared according to Scheme 2. The deprotonation and consequently

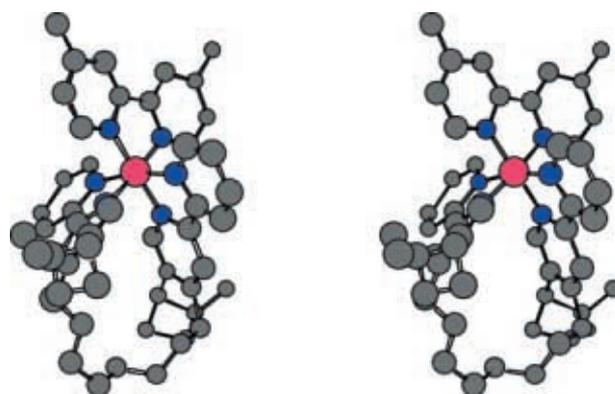
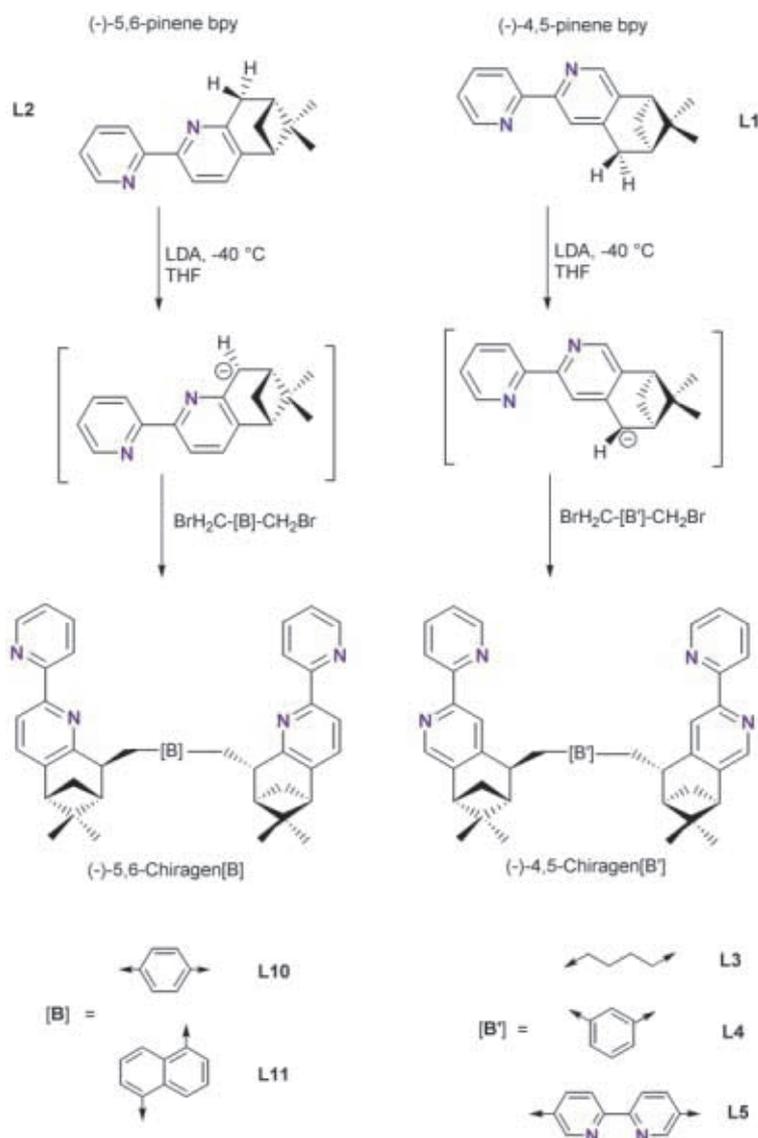


Fig. 5 Stereoview of the complex  $\{Ru((-)-4,5-Chiragen[6])(4,4'-dmbpy)\}^{2+}$ .

the coupling reaction with the bridging dibromoalkane is stereoselective. We never detected any trace of another isomer in the products, when a bridge is introduced between the two pinene bpy moieties (see below for other cases).

Is this tetradentate ligand capable of wrapping around a metal centre? The answer is in the affirmative and we were soon able to crystallise a complex, where the two remaining coordination sites were occupied by another didentate bpy ligand, 4,4'-dimethylbipyridine. A stereopair of the complex cation is depicted in Fig. 5. The complex turned out to be very rigid and highly stable. It could by no means be altered in its stereochemistry, neither by heating nor by irradiation with visible light. The ligand that generates chirality at the metal centre was baptized Chiragen, more specifically 4,5-Chiragen[6], taking into account in an obvious way some characteristics of the molecule.

The synthesis of the first chirally predetermined octahedral complex with ligand **L4** was not the end, but rather the begin-



**Scheme 2** Synthesis of Chiragen type ligands **L3**, **L4**, **L5**, **L10** and **L11**. LDA =  $\text{LiNPr}^i_2$ .

ning of an evolution in stereoselective synthesis of coordination compounds in our laboratories and elsewhere. In the meantime, we synthesized more than 100 different ligands, always following the same principles. The number of specific molecules to be synthesized for a certain aim is only limited by our imagination, and we believe that sometimes it will exceed the number of measures in Maurice Ravel's Bolero.¶ Fig. 6 gives a selection of some of the ligands so far synthesized. For the rest of this article we will concentrate on some of the metal complexes, so far obtained with some of these ligands.

The first ruthenium complex with a Chiragen ligand was not optimised with respect to steric requirements of the central metal. Some progress was achieved using xylyl bridging groups. All three, the *ortho*-, *meta*-, and *para*-xylyl bridged Chiragens form ruthenium(II) complexes. It could be shown that, not unexpectedly, **L4** forms the least strained co-ordination species. With this ligand, a useful building block,  $[\text{RuL4Cl}_2]$  (Fig. 7), which contains two quite labile ligands can be obtained.<sup>19,20</sup> This complex contains the bis-diimine synthon  $\text{RuL4}$ , which has a high configurational stability. It can be used to prepare multinuclear co-ordination species, where each centre has a well defined configuration. An example is the trinuclear complex

$\Delta\Delta\Delta\text{-}\{[(\text{bpy})_2\text{Ru}]_3\text{L5}\}^{6+}$  (Fig. 8), where a Chiragen molecule acts as bridging ligand.<sup>21</sup> This complex contains 27 elements of chirality: 16 of them are produced by nature in the biosynthesis of pinene, 8 more (at carbon centres) are created through stereoselective synthesis during preparation of the ligands, and finally three metal centres are formed stereoselectively.

The Chiragen ligands described so far are not only stereoselective with respect to chirality, but also with respect to the type of edge configuration. A topologically linear tetradentate ligand can wrap around an octahedron in three different edge configurations (Fig. 9).<sup>22</sup> Two of them #8 and #11 are chiral, with  $C_2$  and  $C_1$  symmetry, respectively. The bridged Chiragen ligands, being  $C_2$  symmetric, form in general complexes corresponding to the edge configuration number 8. In the case of a Chiragen ligand without a bridge (see below) complexes of edge configuration #11 and #14 have been obtained. The latter has an inherent  $C_{2v}$  symmetry that is broken down to  $C_2$  symmetry, if the ligand itself has  $C_2$  symmetry and it is therefore chiral. In this case, however, we cannot speak of an inherently chiral configuration at the metal centre.

Pluridentate ligands can wrap in 144 different ways around an octahedral metal centre.<sup>22</sup> More than half of these edge configurations, *i.e.* 74, are inherently chiral and they are shown together with their chirality descriptors in Fig. 10.|| Only a small

¶ A presentation of about 80 different molecules which was accompanied by Ravel's Bolero was given at the 33rd ICC in Florence, Italy in September 1998.

|| For more details about assigning chirality descriptors in some of these cases see ref. 22.

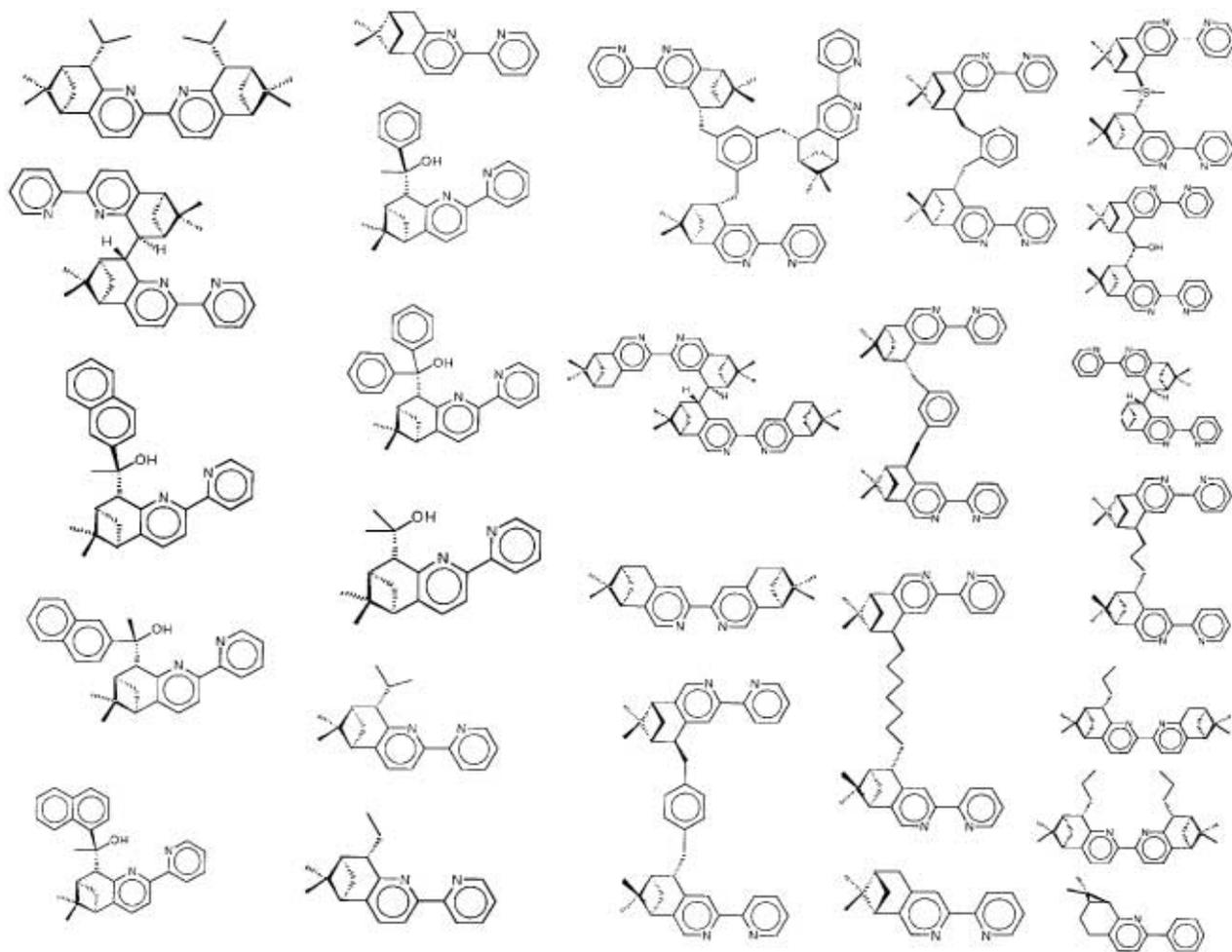


Fig. 6 26 of about 100 chiral ligands synthesized in our group after 1992.

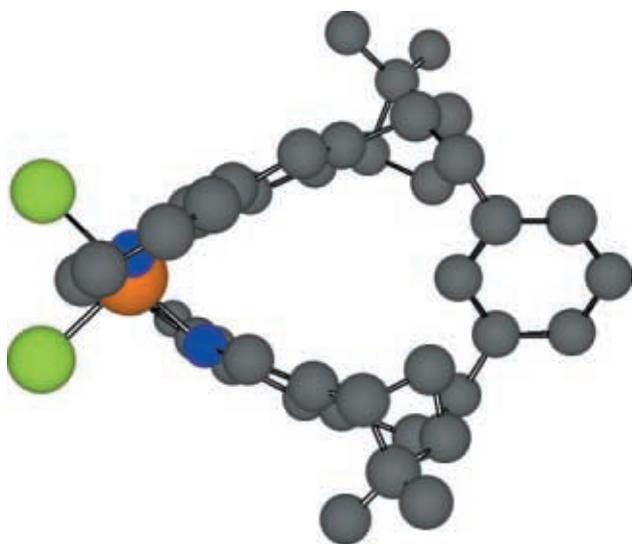


Fig. 7 The building block  $\Delta\text{-}\{\text{Ru}(-)\text{-}4,5\text{-Chiragen}[m\text{-xyl}]\text{Cl}_2\}$  containing two labile chloride ligands.

number of these different cases have been realised so far. It is a challenge for the molecular engineer to produce all of these configurations in a chirally predetermined way. We are quite confident that the chiralised bipyridine molecules can furnish ligands for many of those configurations. Examples are 83, which can be realised using ligand **L2**. Preliminary investigations indicate that it forms an octahedral nickel complex of the desired chirally predetermined structure.

### 3.2 Co-ordination number four

The two prevalent geometries with co-ordination number four are square planar ( $SP\text{-}4$ ) and tetrahedral ( $T\text{-}4$ ), respectively. Since these two structures are topologically the same, *i.e.* they can be transformed into each other by a continuous deformation, they will be considered together. This is particularly justified in discussing complexes with the chiral pyridine and bipyridine ligands, since they often yield structures that can be either described as distorted tetrahedra, or distorted square planar complexes.

**3.2.1 Cyclometallated platinum(II) complexes.** Platinum(II) as a  $d^8$  ion is one of the most typical representatives of those metal centres that form square planar complexes. The distortion modes from planarity towards a tetrahedral configuration seem to be rather soft, however. It was shown several years ago that ligands that prevent a coplanar arrangement through interligand interaction can give rise to a chirally distorted helicene-type structure. An example is 2,6-biphenylpyridine that yields a pure *cis* configuration as depicted in Fig. 11.

Using chiralised pyridine ligands, it is again possible to predetermine the chiral deformation of the square planar (Fig. 12) arrangement.<sup>23</sup> The absolute configuration of the two skew lines defined by the co-ordinating C,N atoms of the two ligands is  $\Delta$ . NMR and CD measurements indicate that the configuration is rigid and stable in solution. If the pinene groups are in the 4,5 positions of the pyridine ring (**L9**), the chiral configuration at the metal is fixed only in the solid state, whereas it is "floppy" in solution.<sup>24</sup>

A relation between chiral predetermination at a four-co-

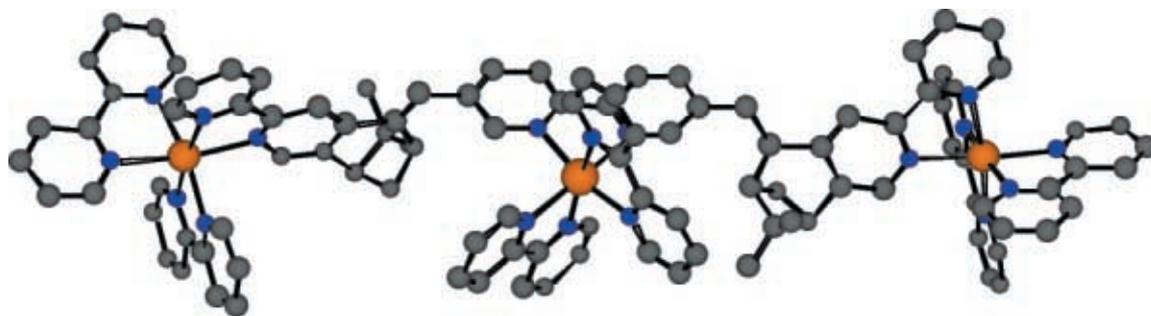


Fig. 8 Trinuclear complex  $\Delta\Delta\Delta\text{-}[(\text{bpy})_2\text{Ru}]_3(-)\text{-}4,5\text{-Chiragen}[5,5'\text{-bpy}]^{6+}$ .

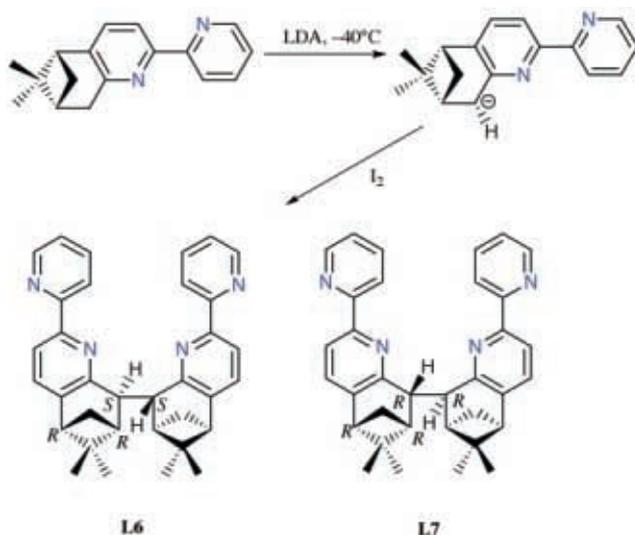


Fig. 9 The edge configurations of a metal centre in octahedral geometry co-ordinated by a tetradentate linear ligand.

ordinated platinum(II) centre and an octahedral complex of  $\text{Pt}^{\text{IV}}$  can be achieved through an oxidative addition reaction (Fig. 13), where the absolute configuration of the resulting octahedral species is predetermined by the “square planar” arrangement.

#### 4 The 5,6-Chiragen[0] ligand<sup>25</sup>

The 5,6-pinene bipyridine as well as the 4,5-pinene bipyridine can also be connected directly by forming a carbon to carbon bond in an oxidative coupling reaction. Scheme 3 shows this reaction sequence. Unlike the nucleophilic reaction that leads to the bridged Chiragen ligands, this oxidative coupling is not completely stereoselective. In the case of the  $(-)$ -5,6-Chiragen[0] ligand, the two ligands *RRS* (**L6**) and *RRR* (**L7**) are formed in a ratio of 9:1.



Scheme 3 Last reaction step in the synthesis of Chiragen[0] ligands **L6** and **L7**.

Both ligands form mononuclear complexes with metal centres that prefer normally *T*-4 or *SP*-4 co-ordination geometry. In any case, the structure of the complexes is neither *SP*-4, nor *T*-4, but in between. Fig. 14 shows the structures of various metal complexes of co-ordination number four. Compounds **L6** and **L7** form species of opposite absolute configuration, yet they are derived from the same natural precursor. The chirality of the metal centre is determined by the configuration at the

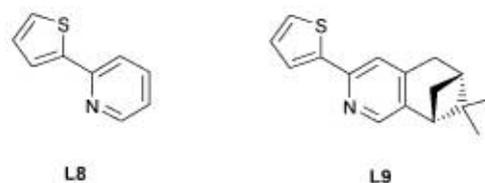
connecting C atoms between the two bipyridine moieties. If these last carbons have a *S* (or *R*) configuration the chirality of the metal centre is  $\Delta$  (or  $\Lambda$ ).

5,6-Chiragen[0] also forms a number of complexes with co-ordination number (CN) = 5. Fig. 15 shows as an example the structure of  $[\text{CuL6Br}]^+$  which is best described as a trigonal bipyramid with two nitrogen atoms in the apical positions. Again, the chiral configuration is predetermined in a similar way as in the four-co-ordinated species.

Some complexes with CN = 6 using 5,6-Chiragen[0] *RRS* were also studied. In these cases the predetermination concerns not only the chirality but also the edge configuration in the octahedron. Examples are a dinuclear  $\text{Cd}^{\text{II}}$  complex  $[(\text{ClO}_4)\text{-CdL6}(\mu\text{-ClO}_4)\text{CdL6}(\text{H}_2\text{O})][\text{ClO}_4]_2$  (Fig. 16a) and a mononuclear species  $[\text{ZnL6}(\text{NO}_3)][\text{NO}_3]$  (Fig. 16a), where one bidentate ligand completes the co-ordination sphere. The configuration is #11 (distorted) and if two monodentate ligands are co-ordinated the edge configuration is #14 distorted and chiralised because of the chiral ligands.

#### 5 Diastereoselective synthesis of polynuclear complexes

There are cases where diastereoselectivity is achieved in the synthesis of dinuclear complexes with chiralised pyridine ligands. The two or more chiralised bipyridine units do not have to be covalently linked. Diastereoselectivity is achieved, in a similar way as observed by Smirnov in 1920, *e.g.* through the formation of dinuclear cyclometallated rhodium(III) species obtained with **L9**. The dinuclear complex (Fig. 17) is obtained



with the non-chiral thienylpyridine ligand (**L8**) as a  $\Delta\Delta//\Lambda\Lambda$  racemate and a mesoform  $\Delta\Lambda$  in a statistical ratio of 1:1:2. It is formed in a completely regioselective way, yielding exclusively the *C,C-cis*, *N,N-trans* form.<sup>26,27</sup>

In addition to this regioselectivity a pronounced diastereoselectivity is observed with the chiralised thienylpyridine.<sup>24</sup> The two diastereomeric forms  $\Delta\Delta$  and  $\Lambda\Lambda$  are obtained in a ratio of 9:1. The pseudo-mesoform  $\Delta\Lambda$  is not observed.<sup>28</sup> Since  $\Delta\Delta$  and  $\Lambda\Lambda$  are now diastereomers, they are easily separable by crystallisation. The isomerically pure complexes can be used for further stereospecific syntheses, including transfer of chirality to new ligands that are used for cleaving the dichloro-bridge of the dimer. Qualitative modelling of these dinuclear species shows a strongly increased repulsive ligand/ligand interaction across the dichloro-bridge (Fig. 18), which can explain the absence of the  $\Delta\Lambda$  pseudo-mesoform.

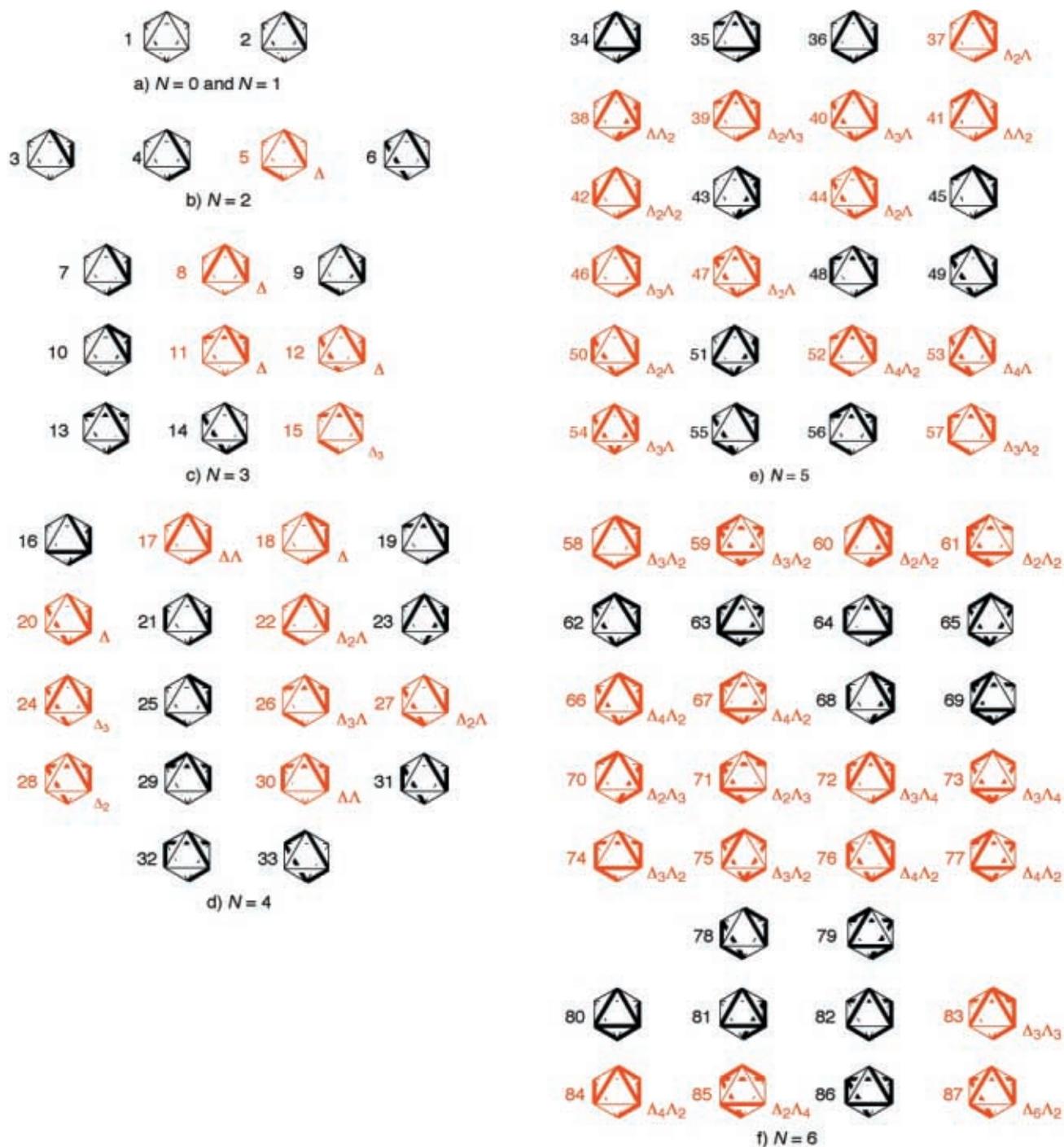


Fig. 10 Chiral edge configurations of octahedral metal centres with mono-, di-, tri-, tetra-, penta- and hexa-dentate ligands.

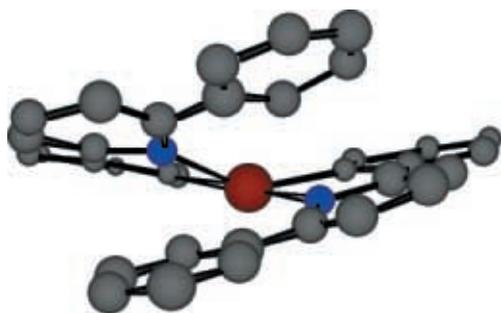


Fig. 11 The helical complex  $[\text{Pt}(\text{NC}_3\text{H}_3\text{Ph}_2-2,6)_2]^{2+}$ .

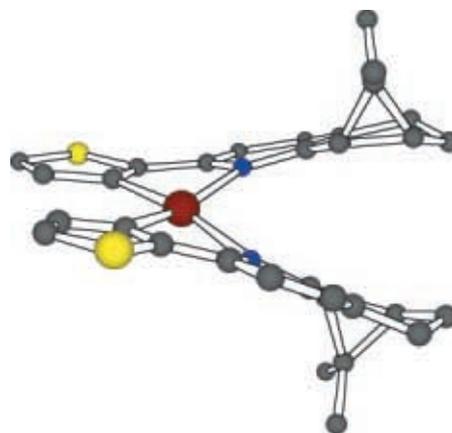


Fig. 12 The helical predetermined complex  $\Delta\text{-}\{\text{Pt}(\text{2-carene-thpy})_2\}$  (carene = trimethylbicyclo[4.1.0]hept-2-ene, thpy = thienylpyridine).

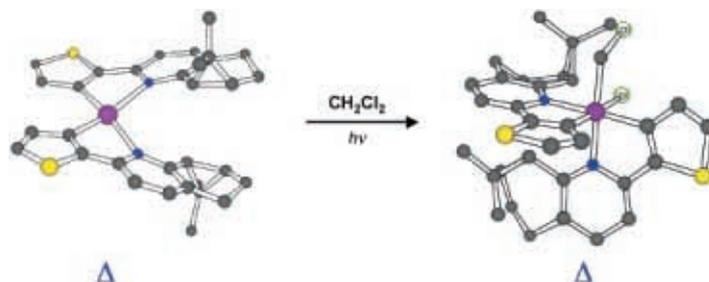


Fig. 13 The oxidation reaction of a platinum(II) to a platinum(IV) complex.

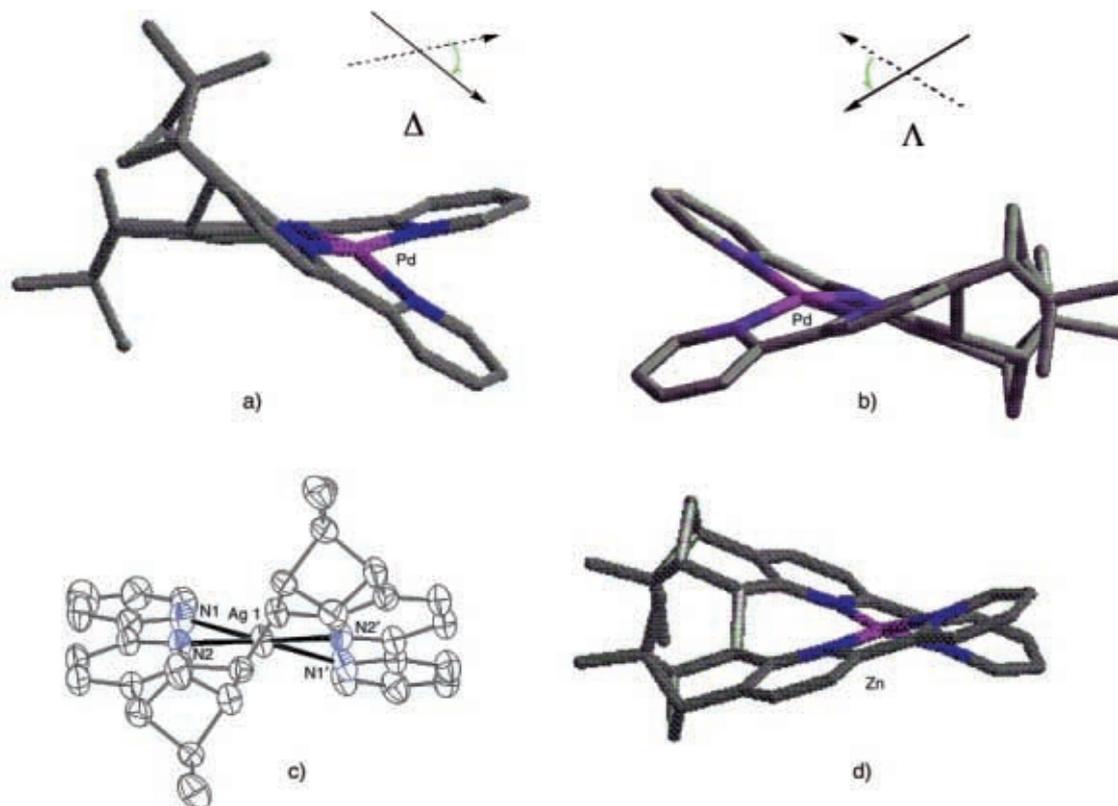


Fig. 14 Crystal structures of metal complexes of the ligand (–)-5,6-Chiragen[0] *RRS* with Pd<sup>II</sup> (a, perpendicular to the  $C_2$  axis), Ag<sup>I</sup> (c, parallel to the  $C_2$  axis), Zn<sup>II</sup> (d, perpendicular to the  $C_2$  axis) and the complex of Pd<sup>II</sup> with the ligand (–)-5,6-Chiragen[0] *RRR* (b, perpendicular to the  $C_2$  axis).

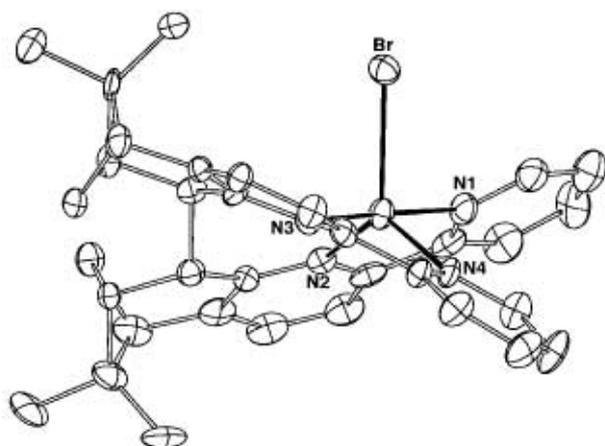


Fig. 15 A representation of the copper(II) complex with (–)-5,6-Chiragen[0] *RRS*.

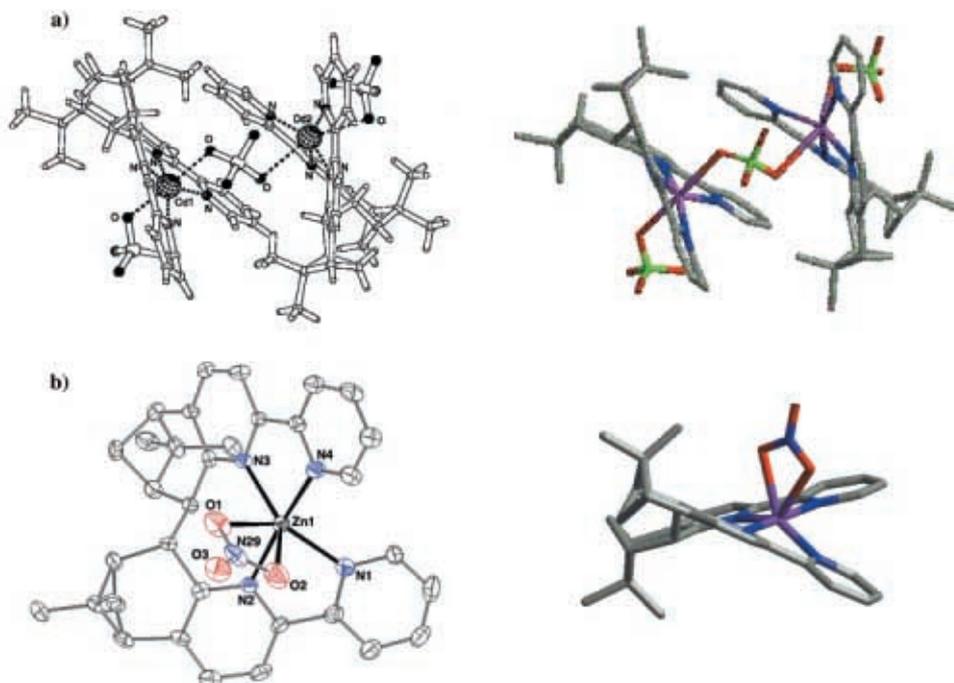
## 6 Diastereoselective self-assembly

A particularly fascinating field of co-ordination chemistry has been opened through the discovery that many systems yield well defined polynuclear species under thermodynamically con-

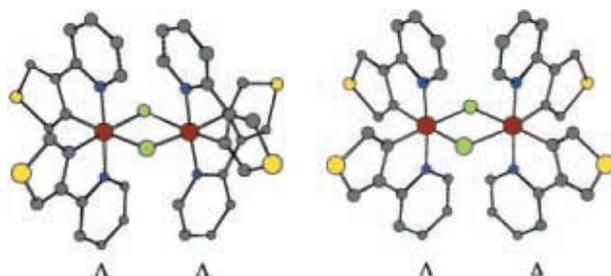
trolled conditions. Such structures may have their own interest through the architectures that they exhibit, or in other cases they can be used as precursors for even more complex molecules, like the well known case of molecular knots.<sup>20–31</sup> A necessary condition for self-assembly is a sufficiently high lability of the co-ordination units involved in the construction of an architecture which is thermodynamically selected from many possible arrangements. In addition, the formation mechanism has to comprise truly reversible steps, so that “wrong” steps can be “repaired” through new trials in other directions.<sup>32</sup>

The molecular objects obtained in self-assembly reactions are often, but by far not always, chiral. The molecular knot is an especially interesting example, since it is a topologically chiral molecule. Its self-assembled precursor is chiral, but not topologically chiral, however. An inherently chiral and recently often studied family of complex objects are the helicates which are obtained as racemates if no chiral induction is present. We have searched for systems where the Chiragen ligands yield helicates, because we were interested to test their ability to form such species in a diastereoselective manner.

The Chiragen ligands can indeed predetermine the configuration of self-assembled species, containing octahedral metal centres. An example is the formation of helicates of **L4** with Fe<sup>II</sup>, Ni<sup>II</sup>, and Cd<sup>II</sup> with the general formula [M<sub>2</sub>L<sub>3</sub>][PF<sub>6</sub>]<sub>4</sub>.<sup>33</sup> NMR and mass spectrometric investigations point clearly to a



**Fig. 16** Crystal structures of (a) the dinuclear complex of  $\text{Cd}^{\text{II}}$  with two  $(-)$ -5,6-Chiragen[0] *RRS*, one bridging perchlorate, one monodentate perchlorate and one water ligand, (b) the complex of  $\text{Zn}^{\text{II}}$  with  $(-)$ -5,6-Chiragen[0] *RRS* and one bidentate nitrate ligand.



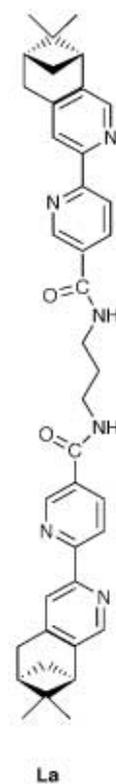
**Fig. 17** The dinuclear homochiral ( $\Lambda\Lambda$ ,  $\Delta\Delta$ ) and *meso*  $\Lambda\Delta$  rhodium(III) complex obtained in a statistical ratio upon reaction with non-chiralised thienylpyridine ligands.

dinuclear structure, while the CD spectra are indicative for a homochiral, *P* helical arrangement. A bis-bidentate ligand **La** containing two  $(-)$ -4,5-pinene bipyridines connected *via* a bridge in position 5 of the “free” pyridines was shown by others<sup>34</sup> to form with  $\text{Fe}^{\text{II}}$  a dinuclear *P* helicate also.

The  $d^{10}$  metal ions  $\text{Ag}^+$  and  $\text{Cu}^+$  offer particularly favorable conditions for self-assembled species. This is due to the fact that the tetrahedral co-ordination geometry exhibited by these ions in most of the cases is relatively soft, *i.e.* tolerant to distortions. A large number of helicates<sup>35</sup> with  $\text{Cu}^+$  or  $\text{Ag}^+$  and oligopyridine<sup>36</sup> type ligands have been described. It has been observed that the presence of substituents in position 6 of the polypyridines increase the stability of self-assembled species,<sup>37</sup> especially in the case of copper(I) complexes where the sterical protection is important against oxidation to  $\text{Cu}^{\text{II}}$ .<sup>38</sup> In this respect the 5,6-Chiragens consisting of two 5,6-pinene bipyridine moieties connected through a bridge represent a good choice. However the bridge with its properties position, length, rigidity/flexibility dictates the final self-assembled architecture.

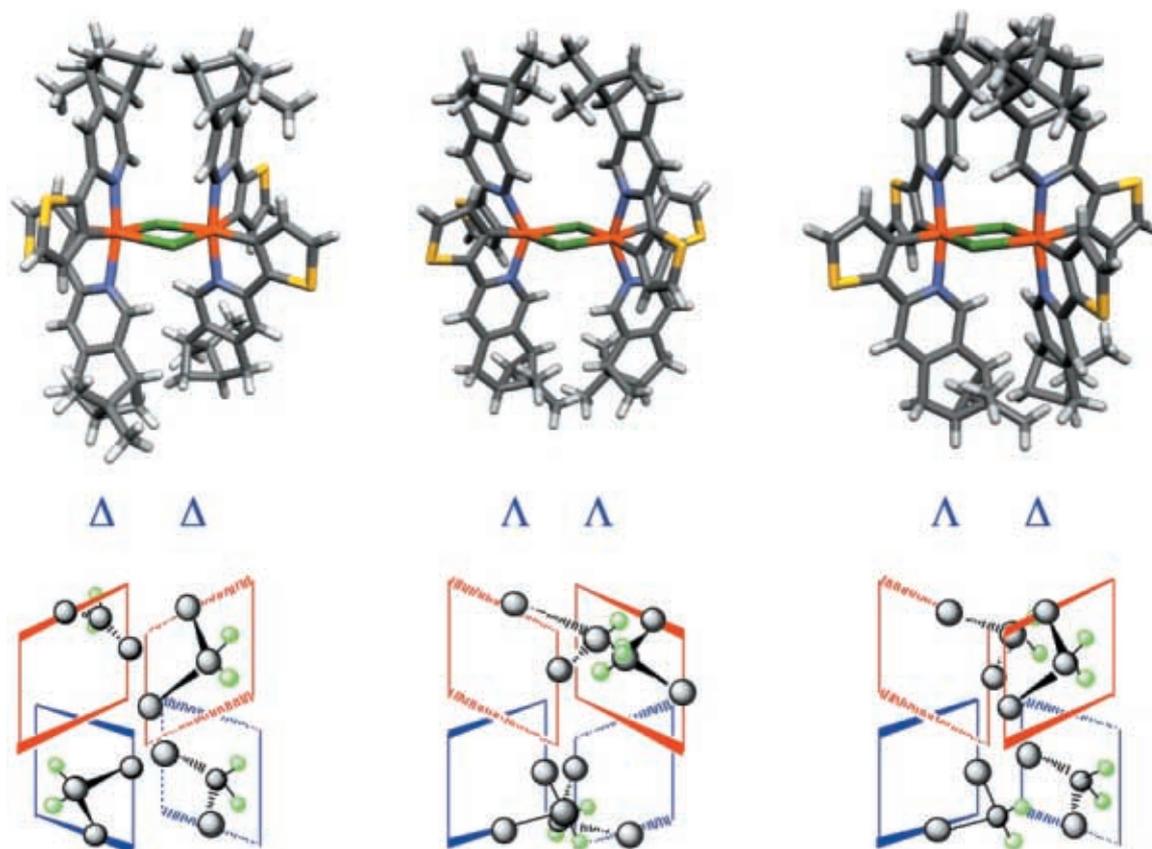
The ligand **L10** in reaction with  $\text{Ag}^{\text{I}}$ <sup>39</sup> or  $\text{Cu}^{\text{I}}$ <sup>40</sup> forms stereoselectively a circular, hexanuclear, monostranded helicate of *P* helicity (Fig. 19). The metal centres are situated in the corners of a hexagon, every bis-bidentate ligand wrapping around two adjacent metal cations. The 12 pinene groups, situated toward the central cavity, are disposed in two layers. The diameter of this discrete structure is about 3 nm and that of the chiral, empty cavity about 0.8 nm.

Other circular helicates of comparable dimensions have been

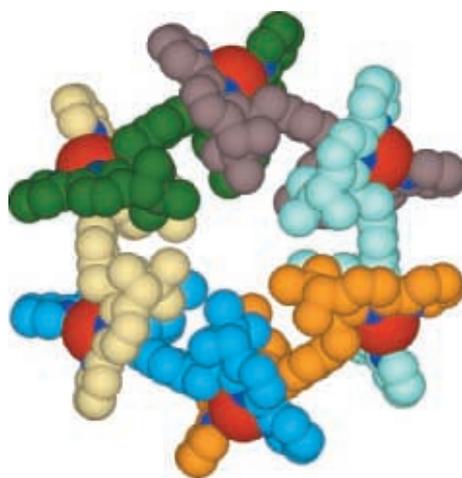


obtained *via* a template effect of the anions.<sup>41,42</sup> The anions have no influence in this case which is an example of a so called “structure-directed synthesis”.<sup>43</sup> The cascade of chiral induction starts from the enantiomerically pure,  $C_2$  symmetric ligand (*R,R,S*), which predetermines the local configuration at the metal centres ( $\Lambda$ ) and consequently the helicity *P* of the resulting helicate. Dissolution of the crystals in acetonitrile led, in the case of  $\text{Ag}^{\text{I}}$ , to an equilibrium between two highly symmetric species, which have been identified to be a hexanuclear circular helicate and a tetranuclear circular helicate.

If a ligand with a bridge derived from 1,5-dimethylnaphthalene, the ligand **L11**, reacts with  $\text{Ag}^{\text{I}}$  a double helical polymer is obtained in the solid state.<sup>44</sup> The polymer is com-



**Fig. 18** The three diastereoisomers of  $[\text{RhL9}_2\text{Cl}]_2$ .  $\Delta\Delta/\Lambda\Lambda$  is a pseudo-racemate, having nearly mirror image CD spectra. It is formed in a diastereomeric ratio of 9:1. The pseudo-mesoform  $\Lambda\Delta$  showing strong interligand steric repulsion is not obtained in measurable quantities.  $\Delta\Delta$  represents a crystal structure,  $\Delta\Lambda$  and  $\Lambda\Lambda$  are computer models.



**Fig. 19** Hexanuclear circular monostranded helicate  $[\text{Ag}_6\text{L10}_6]^{6+}$ .

posed of two intertwined helices (Fig. 20). Every helix can be considered as a monostranded, tridimensional helicate. In the linear, unidimensional helicates the metal centres are collinear, in the circular helicates they are planar. In our case they are disposed in three dimensional space building up a spiral. The helical pitch contains six metal centres, three from one strand and three from another, the architecture possessing a  $C_6^4$  helical axis (Fig. 21). Between the two strands are no interactions (except van der Waals). The cohesion of this structure is due to the crystalline packing. Every double helix is connected to neighbouring double helices by  $\pi$  bonds. The weakness of this kind of bond is overcome by their number: there are 12  $\pi$  interactions per turn of double helix (Fig. 22). As in the case of the circular helicate the helicity is predetermined, the metal centres are homochiral, the local configuration being  $\Lambda$ . The resulting double helix is  $P$ .

Other helical polymers are known,<sup>45–53</sup> some of them obtained in stereoselective syntheses,<sup>54–57</sup> however none of them represents a double helix stabilised by interhelix interactions.

The determining role of the bridge position in the case of the bis-bidentate ligands containing pinene has been highlighted by Constable and co-workers.<sup>58</sup> They synthesized ligands formed by two **L1** connected through the 5 positions of the pyridine rings. In this way the carbons at the head of the bridge are not chiral as in the 5,6-Chiragens and the consequences for diastereoselectivity are important. The ligand **L12** containing an ethylene bridge forms in reaction with  $\text{Ag}^{\text{I}}$  a dinuclear, double stranded  $P$  helicate. The reaction with  $\text{Cu}^{\text{I}}$  led to cyclic and linear helicates (Fig. 23). The diastereomeric excess in the solid state is zero, mixtures of  $P$  and  $M$  helicates being obtained in 1:1 ratio.

A similar ligand, **L13**, with direct connection between the two bipyridine halves, gave in reaction with  $\text{Ag}^{\text{I}}$  a dinuclear, double stranded  $P$  helicate (Fig. 24) in 95.3% diastereoisomeric excess.<sup>59</sup> In this case the origin of diastereoselectivity<sup>60</sup> is not the chiral interaction between two pinene substituents as assumed for other compounds, but the interaction between the pinene group belonging to a strand and the adjacent pyridine belonging to the second strand.

Chiral information is passed in these self-assembly processes from the ligand to the metal and finally to the helical structure as a whole. We can speak of a *cascade* of chiral information, or of *primary* (ligands), *secondary* (metal centres), and *tertiary* (whole structure) chirality.

## 7 Conclusions and outlook

At the end of the 20<sup>th</sup> century, stereoselective synthesis of Co-ordination Compounds is still a wide-open field that has by far not yet reached the level of perfection of stereoselective

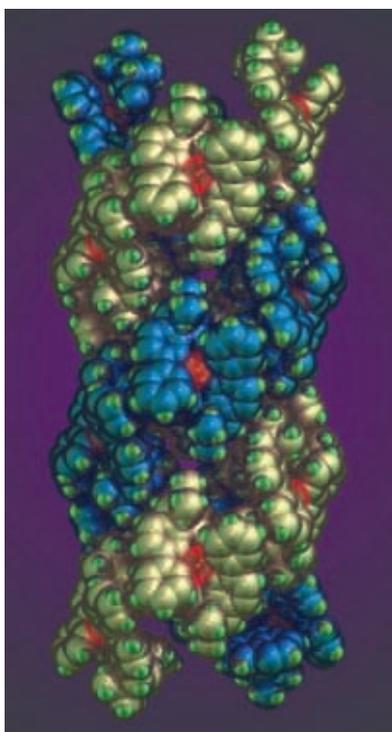


Fig. 20 Lateral view of the polymeric double helix  $\{[AgL11]^+\}_\infty$ .

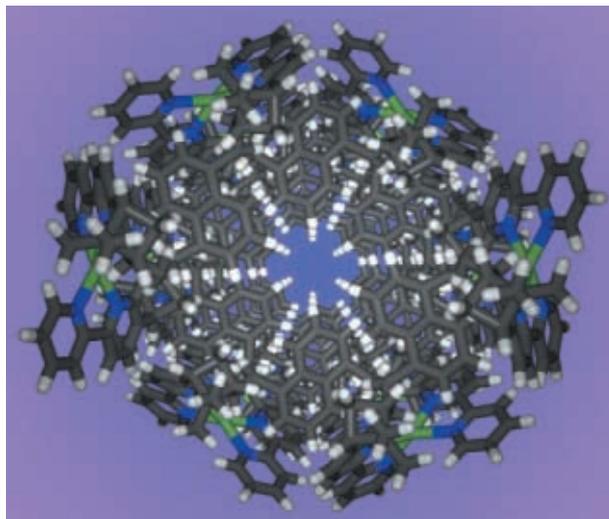


Fig. 21 View perpendicular to the  $C_6^4$  axis of the polymeric helix.

synthesis in organic chemistry and the same is true for many parts of organometallic chemistry. The chemistry of the metallic elements of the periodic system has developed enormously in the past few decades and a large number of applications spun off of basic research in this field. Yet, stereochemical questions were not very often considered in detail in this research. Syntheses with enantiopure chiral ligands that are natural products have been carried out in many cases, for example with amino acids. The Chiragen family of ligands, which is emphasised in the present Perspective, is an example of a class of ligands that is derived from enantiopure natural compounds, yet the ligating properties are very different from the natural products themselves. We believe that there are possibilities for numerous similar developments. The pyridine and bipyridine ligands described here are only one class, an especially versatile one, which can be rendered chiral by the natural products and they therefore yield metal complexes with highly interesting stereochemical properties. Thus, a large number of new chiral complexes and molecules will be accessible that may have important

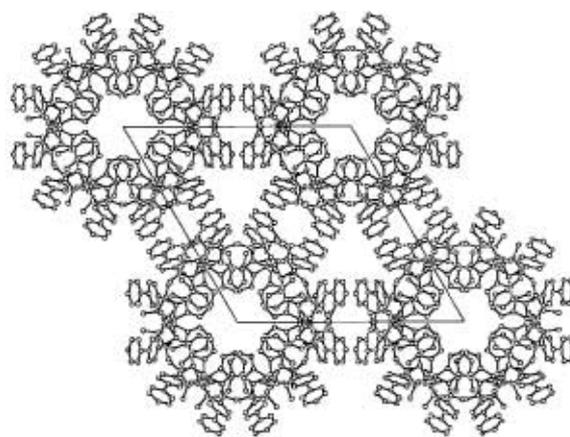


Fig. 22 Molecular packing of the cationic polymer along the crystallographic  $c$  axis. The  $PF_6^-$  anions occupying the channels between adjacent helices are omitted for clarity.

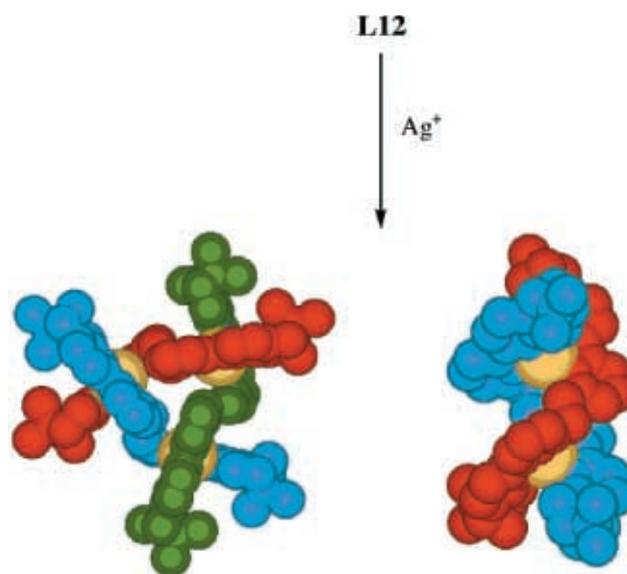
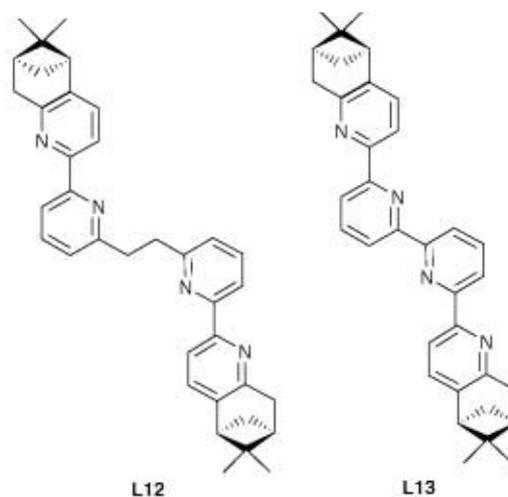
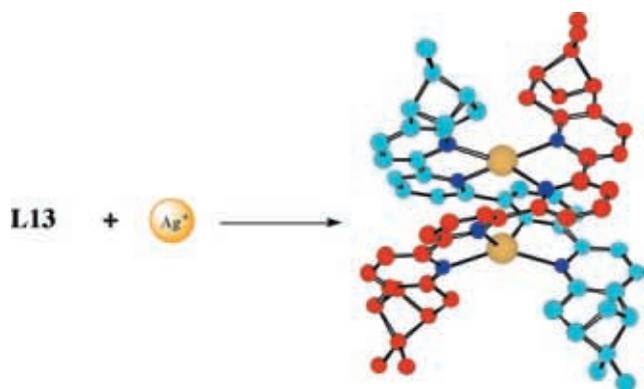


Fig. 23 The crystallisation of the solution obtained by the reaction between **L12** and  $Ag^+$  gave two types of crystals, one containing the dinuclear helicate and the other a trinuclear circular helicate. No diastereoselectivity was observed, the compounds have been obtained as a racemate.



applications in many fields of chemistry. These fields range from enantioselective catalysts to materials with non-linear optical properties, photonic materials and stereochemically well defined nanoscale molecular devices.



**Fig. 24** The chiral ligand **L13** forms in reaction with  $\text{Ag}^+$  only the dinuclear *P* helicate.

## 8 Acknowledgements

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