Non-Linear Effects in Asymmetric Reactions: Negative and Positive Stereoselectivity in the Formation of Homoleptic 1:2 Metal to Ligand Complexes of Chiral 1,9-Disubstituted Semicorrin Ligands

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Abstract: The stereoselectivity of the formation of bis-chelates with the 1,9-disubstituted chiral semicorrin ligands (1S,9S)-dimethyl-5-cyanosemicorrin-1,9-dicarboxylate (1) for Co2+, Ni2+, Cu2+, and Pd2+ and with its (1S,9R)-diethyl analogue 2 for Co2+ and Cu2+ have been measured by the method of continuous variation of enantiomers, and with 1 for Zn2+ by NMR. Positive selectivities were found for Co2+, Ni2+, and Zn2+ complexes, whereas very high negative selectivities prevail in the complexes of Cu2+ and Pd2+. These results are rationalised by X-ray structural determinations of some of the corresponding complexes. The optically active Cu2+ and Pd2+ complexes show distorted square planar structures with chirality predetermined by the chirality of the ligand. Ni2+ complexes are five or hexacoordinated and exhibit a distorted tetrahedral arrangement of the four coordinated nitrogen atoms. In the optically active compound the ester moiety is coordinated by the oxygen atom of the alkoxy group and the arrangement of the two N-N chelate rings shows \( \Lambda-(S,S) \) chirality. Interestingly, with the racemic ligand, it is not the more stable heterochiral, but the racemic complex containing the two homochiral enantiomers which is obtained. The coordination of the ester groups occurs by the carbonyl oxygen and the chirality is opposite to the optically active compound, e.g. \( \Lambda-(S,S) \)/\( \Lambda-(R,R) \). The structure of the optically active zinc compound shows very weak interaction with the alkoxy group of one ester moiety of each ligand molecule and the chirality of the N-N-chelate rings is \( \Lambda-(S,S) \). Again, the compound obtained with the racemic ligand contains the enantiomers of the homochiral complex, the chirality of which is \( \Lambda-(R,R) \)/\( \Lambda-(S,S) \). The results are discussed with respect to the possibility to perform asymmetric amplifications of the 1:1 complexes of semicorrin ligands as enantioselective catalysts.

Keywords: Asymmetric reactions · Negative and positive stereoselectivity · Non-linear effects

Introduction

In asymmetric reactions the enantiomeric excess (\( \%ee \)) usually depends linearly upon the enantiomeric purity of the stereoselective catalyst or reagent. In several cases however, non-linear effects, first described in 1986 by Kagan and coworkers have been observed [1]. In order to explain these phenomena Kagan suggested mainly two models: the MLn and the reservoir model [2]. Both models are based on the non-statistical distribution between the heterochiral \([M(R)(S)]\) and the homochiral, optically active \([M(R,R)]\) and \([M(S,S)]\) molecular forms according to Scheme 1. In the former the non-linearity can for example occur due to different stability and/or reactivity of the homo and the heterochiral forms, whereas in the latter only the 1:1 species is catalytically active. A non-statistical distribution in the 1:2 complexes then yields a \([M(R)]\)/\([M(S)]\) ratio different from that of the free ligand. Used as catalyst or as a reagent, the enantiomeric excess in the product can be higher than expected from enantiomeric purity of the reacting system. This is known as asymmetric amplification. Until now, most studies focused on non-linear effects with the aim to unravel reaction mechanisms based on Kagan’s model [3]. More recently, the kinetic behaviour, in addition to thermodynamic effects, has been taken into account [4]. Despite the interest in non-linear effects observed in enantioselective reactions, quantitative analyses of the relationship between optical purities of the products and the reacting species are almost nonexistent. In a first study this relationship has been reported for the reduction of acetophenone by \( \beta \)-chlorodiisopinocamphenylborane [5].
In that case the reagent is formed in a non-reversible way using different ratios of (+)- and (−)-α-pinene. Similar studies involving labile metal complexes as the catalytic system are not known. In the present communication we report stereoselectivity measurements of the complex formation of Co³⁺, Ni³⁺, Cu²⁺, Zn²⁺, and Pd²⁺ with the chiral semicorrines (1S,9S)-dimethyl 5-cyanoseminicorrin-1,9-dicarboxylate (1) and its (1S,9S)-diethyl analogue 2, a ligand system developed by Pfaltz [6], frequently used in asymmetric catalysis. The selectivity data are compared to structural properties of some of the corresponding solid compounds.

Stereoselectivity

Stereoselectivity of the 1:2 metal to ligand complexes of 1,9-disubstituted semicorrin ligands 1 and 2 with the bivalent metal ions Co³⁺, Ni³⁺, Cu²⁺, and Pd²⁺ were determined by circular dichroism (CD) measurements using the method of continuous variation of enantiomers [7][8]. Corresponding values for Zn²⁺ were obtained from NMR spectra of 1:2 mixtures of anhydrous Zn(CH₃COO)₂ with either optically active or the racemic 1 in CD₃OD. The results are given in the Table.

The differences measured for the complexes of Cu²⁺ and Pd²⁺ with 1 are very close to the theoretical maximum, and the values given in the Table have to be considered as upper limits. The real stereoselectivity with these two metal ions might therefore be higher than indicated, which means that the heterochiral form of the bis-complex is present at less than 5% in the equilibrium mixture.

It seems reasonable to admit that the change from positive to negative stereoselectivity is a consequence of a different arrangement of the ligand molecules in the coordination sphere of the metal ion. In the case of tetra-coordination, two basic geometries are possible, square planar and tetrahedral. The schematic representation in Scheme 2 makes clear that for chiral C₂ symmetric ligands the homochiral species is favoured for the square planar arrangement, whereas the heterochiral isomer should be more stable in the tetrahedral arrangement.

X-ray Structural Determinations

The data given in the Table suggest square planar structures for Cu²⁺ and Pd²⁺ complexes and tetrahedral structures for the Co³⁺, Ni³⁺, and Zn²⁺ complexes. In order to examine this hypothesis, we determined the X-ray molecular structure of some of the [M(1)₂] complexes obtained with both the optically active and the racemic ligand. The crystal structure of the copper complex with the analogous ligand (1S,9S)-1,9-bis(1-hydroxy-1-methylethyl)semicorrin-5-carbonitrile has been published [6]. The structure is described as tetrahedrally distorted with the two ligand planes tilted rel-

**Table. α-Values of ML₂ complex formation of 1 and 2 with various metal ions (α = K₀meso/(2·K₀rac))**

<table>
<thead>
<tr>
<th>M²⁺</th>
<th>L = 1</th>
<th>L = 2</th>
<th>% [M(R,R)(S,S)-1]</th>
<th>% [M(S,S)-1] =</th>
<th>% [M(R,R)-1]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co²⁺</td>
<td>2.1</td>
<td>8.1</td>
<td>67.4</td>
<td>16.2</td>
<td>60.2</td>
</tr>
<tr>
<td>Ni³⁺</td>
<td>2.8</td>
<td>–</td>
<td>–</td>
<td>13.2</td>
<td>–</td>
</tr>
<tr>
<td>Cu²⁺</td>
<td>&lt;0.05</td>
<td>0.17</td>
<td>&lt;4.8</td>
<td>&gt;47.6</td>
<td>&gt;47.6</td>
</tr>
<tr>
<td>Zn²⁺</td>
<td>3.7</td>
<td>–</td>
<td>78.8</td>
<td>10.6</td>
<td>&lt;5.6</td>
</tr>
<tr>
<td>Pd²⁺</td>
<td>&lt;0.06</td>
<td>–</td>
<td>&lt;5.6</td>
<td>&gt;47.2</td>
<td>&gt;47.2</td>
</tr>
</tbody>
</table>

a from NMR measurements.
Fig. 1. a) Molecular structure of molecule A of \([\text{Pd}((S,S)-1)_2]\). Bond distances (Å) Pd(1)-N(1) 2.045(5), Pd(1)-N(2) 2.011(6), Pd(1)-N(4) 1.922(5), Pd(1)-N(5) 2.058(5); bond angles (°) N(2)-Pd(1)-N(4) 89.5(2), N(2)-Pd(1)-N(5) 92.9(2), N(4)-Pd(1)-N(5) 96.9(2), N(2)-Pd(1)-N(5) 163.8(19), N(1)-Pd(1)-N(5) 153.4(18). b) Molecular structure of molecule B of \([\text{Pd}((S,S)-1)_2]\). Bond distances (Å) Pd(2)-N(21) 2.010(5), Pd(2)-N(22) 2.054(5), Pd(2)-N(24) 2.045(5), Pd(2)-N(25) 2.014(6); bond angles (°) N(21)-Pd(2)-N(22) 88.8(2), N(21)-Pd(2)-N(24) 92.9(2), N(24)-Pd(2)-N(25) 89.1(2), N(22)-Pd(2)-N(25) 96.9(2), N(21)-Pd(2)-N(25) 163.8(19), N(22)-Pd(2)-N(25) 152.1(18).

Fig. 2. a) Molecular structure of molecule A of \([\text{Ni}((S,S)-1)_2]\). Bond distances (Å) Ni(1)-N(1) 2.108(3), Ni(1)-N(2) 1.964(4), Ni(1)-N(4) 2.102(4), Ni(1)-O(4) 2.413(3), Ni(1)-O(13) 2.448(4); bond angles (°) N(1)-Ni(1)-N(2) 89.10(17), N(1)-Ni(1)-N(5) 108.73(16), N(4)-Ni(1)-N(5) 90.9(2), N(2)-Ni(1)-N(5) 153.42(18). b) Molecular structure of molecule B of \([\text{Ni}((S,S)-1)_2]\). Bond distances (Å) Ni(2)-N(31) 1.957(4), Ni(2)-N(32) 2.088(3), Ni(2)-N(34) 1.992(4), Ni(2)-N(35) 1.987(4), Ni(2)-O(34) 2.392(3), Ni(2)-O(36) 2.640(4); bond angles (°) N(31)-Ni(2)-N(32) 89.59(17), N(31)-Ni(2)-N(35) 148.91(19), N(34)-N(2)-N(35) 92.75(17), N(31)-Ni(2)-N(34) 114.32(18), N(32)-Ni(2)-N(35) 107.65(16).

As observed for the analogous copper(II) complex [6], the two ligand planes are inclined to each other by an angle of 64.06(12)° for molecule A and 61.82(12)° for molecule B.

The case of the nickel complexes is more complicated. The crystals obtained from an ethanolic solution containing two
equivalents of the optically active ligand crystallise with two independent molecules per asymmetric unit. Molecule A is hexacoordinated, each ligand molecule is, in addition to the two nitrogen atoms, coordinated by one ester group. The coordination occurs via the oxygen atom of the methoxy group. Molecule B, on the other hand shows pentacoordination with only one ligand molecule coordinated by one of its ester groups, again via the methoxy oxygen. The influence on the length of the Ni-N bonds by this additional coordination is rather small. In both molecules the Ni-N bond of the five-membered ring carrying the coordinated ester group is slightly shortened by about 2% with respect to the nitrogen atoms of the five-membered rings with the non-coordinated ester group. On the other hand, strong distortion from a regular tetrahedral arrangement of the four nitrogen atoms occurs due to the coordination of one or two ester groups. The structures of the pentacoordinated hexacoordinated forms are shown in Fig. 2.

The case of the Ni²⁺ complex, obtained from an alcoholic solution of the racemic ligand, shows some interesting features. From selectivity data one would expect the racemic [Ni(\(R,R\)-L,S,S-L-L)] to crystallise from solution, the equilibrium concentration of which being about three times as high as that of the homochiral compounds (cf. Table). This is obviously not the case, the solid obtained contains the equimolar mixture of the two homochiral complexes. Despite the identical chemical composition of the respective molecular units of the optically active and the racemic complex, some striking differences are observed in their molecular structures. The racemic complex, which crystallises with one molecule of the solvent, contains only one hexacoordinated molecular form of the complex. Interestingly, the ester group is not coordinated with the oxygen of the methoxy group as in the optically active compound, but by the carbonyl oxygen. The Ni-N bonds of the five-membered rings carrying the ester groups are clearly shortened by about 4% compared to the other Ni-N bonds and the distortion of the NiN₃ arrangement is increased. Fig. 3 shows the structure of the enantiomer with \(\Delta-(R,R)\) configuration.

As observed with Ni²⁺, no solid heterochiral complex could be obtained from the racemic ligand with Zn²⁺, despite that it is present by nearly 80% in solution. No difference between the ligand molecules is observed by NMR in solution indicating identical coordination of both ligand molecules. On the other hand, for the solid complexes the question arises whether they are to be considered as tetra- or hexacoordinated. The Zn-N bond lengths are almost identical and the distance between the oxygen atoms of the ester group and the coordination center is much longer than in the corresponding Ni²⁺ complexes. Nevertheless, the non-equivalence of the two substituents of the \(C_2\) symmetric ligands and the resulting deviation of the N-Zn-N angles from a regular tetrahedral arrangement indicates some bonding interaction between one ester group of each ligand with the metal ion. The molecular structure of the optically active complex is shown in Fig. 4 and that of the racemic compound in Fig. 5. The presence of two methoxy oxygens near the Zn²⁺ centre increases the tetrahedral distance of the Ni(1)-Zn(12) angle to 128.4°, whereas a similar distortion to 132.8° is observed for the N(1)-Zn(N1') angle in the racemic compound due to the presence of the carbonyl oxygen atoms. This distortion allows the attribution of \(\Lambda-(S,S)\) chirality to the optically active and \(\Lambda-(S,S)\)/\(\Delta-(R,R)\), chirality to the racemic complex, opposite to what is observed for the corresponding Ni²⁺ complexes with the same coordination pattern.

**Discussion**

Stereoelctivity data for the equilibrium reactions in methanolic solutions indicated a clear change in the basic structure of the 1:2 complexes of 1,9-disubstituted semicorrinates with the metal ions Cu²⁺ and Pu²⁺ on one side and Co²⁺, Ni²⁺, and Zn²⁺ on the other. According to Scheme 2, square planar structures are expected for the former and tetrahedral structures for the latter, in agreement with the usual coordination pattern for tetracoordination of these metal ions. Even if one needs to be careful in comparing solid state structures with the behaviour of labile systems in solution, some interesting features arise from the present measurements. Unfortunately, no heterochiral complex, which clearly exists in solution, could be obtained in the solid state for any of the metals studied. This is easily explained for Pu²⁺ the equilibrium in solution being strongly in favour of the homochiral form. On the other hand, with Ni²⁺ and Zn²⁺, despite the higher stability of the heterochiral form, only the homochiral complex crystallises from the solution containing the racemic ligand.

The structural influence of the substituents is clearly visible in the complexes with metal ions favouring tetrahedral and square planar arrangements as well, but seems especially high for the latter leading to angles of 64° resp. 62° between the ligand planes in the Pu²⁺ compound. In the Zn²⁺ complex, for which a tetrahedral arrangement is expected, the observed angle formed by the two ligand planes is 82°, corresponding to a deviation of only 8° from a regular arrangement, as it should exist in the corresponding heterochiral compound. The different stereochemical influence of the substituents for metals...
favouring square planar arrangements as Cu\(^{2+}\) and Pd\(^{2+}\) compared to metal ions of tetrahedral coordination geometries like Co\(^{2+}\), Ni\(^{2+}\), and Zn\(^{2+}\), in agreement with the observed strong negative stereoselectivity of the former, and only moderate preference of the latter. Similar results have recently been reported for Cu\(^{2+}\) and Ni\(^{2+}\) with the chiral ligand 1,2-bis(2-benzimidazolyl)-1,2-ethanediol [9].

Finally, the results reported in this work show that the realisation of an asymmetric amplification according to Scheme 1, using semicorrin metal complexes as a catalytic system, strongly depends on the metal ion involved. With metal ions favouring tetrahedral ligand arrangements, like Co\(^{2+}\), Ni\(^{2+}\), and Zn\(^{2+}\) among others, asymmetric amplification would be possible. On the other hand, with metal ions preferring the square planar coordination geometry, a negative effect would be observed.

**Supplementary Data**

Crystallographic data (excluding structure factors) for the five structures described here are deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 212279 (PdSS1), CCDC 212280 (NiRSS1), CCDC 212281 (NiRSS1), CCDC 212282 (ZnSS1), CCDC 212283 (ZnSSRR1). Copies of the data can be obtained free of charge on application to the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) +44-1223/336-033; E-Mail: deposit@ccdc.cam.ac.uk].

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