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The Concept of Prochirality Applied to Coordination Compounds

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The concept of prochirality, widely used for organic molecules, is extended here to mononuclear octahedral (OC-6), square pyramidal (SP-5), square planar (SP-4) and trigonal bipyramidal (TB-5) coordination compounds.

A prochiral coordination compound (C_s symmetry) is characterized by a prochiral center, namely the metal atom, and by the existence of two heterotopic elements. The elements can be ligands, faces or planes, depending on the geometry of the complex.

The most common reactions that can transform the prochiral metal center into a chiral one are treated in detail. Interactions of prochiral complexes with prochiral organic molecules are also treated.

Applications of particular interest for prochiral coordination compounds can be envisaged in the fields of asymmetric synthesis and bioinorganic chemistry.

Key Words: *prochiral complex, prochiral metal atom, pro-pseudoasymmetric metal atom, stereochemical descriptors, prochiral catalyst, enantiotopic ligands, diastereotopic ligands*

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INTRODUCTION

The concept of prochirality was introduced by Hanson in 1966.[1] Although widely used for organic molecules, it has seldom been used explicitly for coordination compounds. This concept has been applied in particular to tetrahedral and trigonal assemblies.

A prochiral tetrahedral assembly of ligands (e.g., CABXX in Fig. 1), characterized by the presence of two homomorphic heterotopic ligands (X) [Refs. 2–4, see Ref. 5 for definitions], be-

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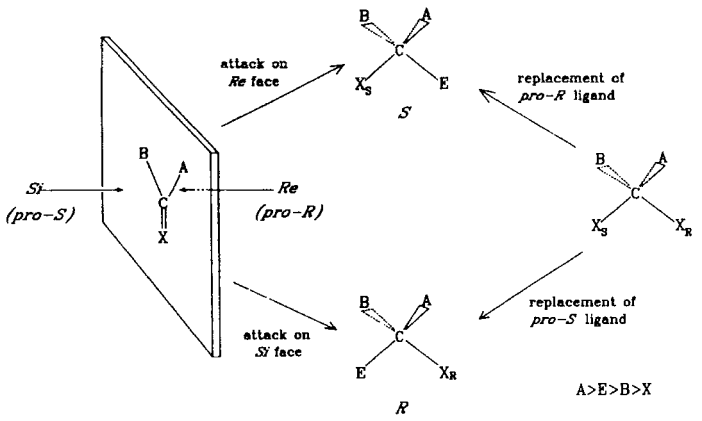

FIGURE 1 Schematic example of tetrahedral and trigonal prochiral assemblies of ligands and of the formal reactions that transform the prochiral center into a chiral one. The enantiotopic elements are named according to Ref. 1; configurations of the chiral carbon atoms are assigned according to CIP rules (Ref. 6), the priority order being A > E > B > X.

comes chiral by replacement of one homomorphic ligand by a new achiral one not already present in the assembly. The central atom (C in Fig. 1) is defined as the prochiral center. The two heterotopic ligands can be formally distinguished by the following procedure: one of them is arbitrarily elevated to a higher priority over the other, without affecting the priorities of A and B, to create a hypothetical chiral center to which the CIP chirality rules[6] are applied. If the resulting center has an R configuration, then the selected ligand is called *pro-R* (Fig. 1) and may be denoted by adding a subscript R as X_R. By default the other X ligand is *pro-S* (X_S). Note that there does not have to be a correlation between the prochirality descriptor (e.g., X_S) and the configuration of the product arising from the replacement of the heterotopic ligands (see, for example, Fig. 1).

A prochiral trigonal assembly of ligands is characterized by two heterotopic faces.[7] Addition of the same achiral reagent to either face will give rise to enantiomeric products. Therefore, the two faces can be defined as prochiral and the central atom as the prochiral center. According to the rule introduced by Hanson,[1] the two faces can be distinguished as *pro-R* (or *Re*) and *pro-S* (or *Si*) (Fig. 1).

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Geometrical criteria can be applied to further classify heterotopic elements (ligands and faces). When such elements can be interchanged by a rotation–reflection (S_n) operation, most often a plane ($\sigma = S_1$) or a center ($i = S_2$), they are called enantiotopic. When such heterotopic elements cannot be interchanged by any symmetry operation, they are called diastereotopic.[3] For example, if A or B in Fig. 1 possesses a chiral center, the heterotopic elements are diastereotopic. The descriptors *pro-R* and *pro-S* are used for both enantiotopic and diastereotopic elements.[1,3]

Differentiation of enantiotopic ligands and faces occurs in the presence of a chiral reagent or catalyst. Several examples can be found in enzymatic reactions, where only one of the two enantiotopic elements of a molecule is recognized by an enzyme.[2] Moreover molecules bearing prochiral centers are commonly used as synthons in asymmetric synthesis and catalysis. For a given chiral reagent or catalyst, the enantioselectivity of the reaction will depend on the nature of the substituents on the prochiral center.

It should be pointed out that the concept of prochirality, even though currently used in synthetic chemistry, is essentially geometrical in nature and it is not necessarily an expression of a precursor–product relationship. In fact, there exist stereoselective reactions at prochiral elements that do not generate elements of chirality.[2,8]

By extending the concepts as used in organic chemistry to some selected classes of coordination compounds with C_s symmetry, the metal center can be defined as prochiral. A coordination compound having a prochiral metal atom will have at least two homomorphic heterotopic elements, namely ligands, faces or planes, depending on the geometry of the complex. For each of these elements, a reaction can be identified that transforms the prochiral metal center into a chiral center. In particular, enantiomeric products having opposite chirality at the metal atom can be formed by replacement of either one of the enantiotopic ligands by a different achiral ligand, addition of the same achiral ligand to either one of the two enantiotopic faces, or ligand rearrangement along either one of the two enantiotopic planes. Where appropriate, we point out obvious extensions of these concepts to other elementary reactions typical of coordination compounds, such as oxidative additions, electrophilic additions, migration reactions, etc.

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We will consider the cases of octahedral (OC-6), trigonal bipyramidal (TB-5), square pyramidal (SP-5) and square planar (SP-4) complexes. To simplify the discussion, the following restrictions will be applied to the nature of the complexes: (i) only mononuclear complexes are considered; (ii) chelate ligands are not considered, but some results on bidentate chelate complexes are used for illustrative purposes (therefore we will not treat those classes of dissymmetric complexes whose chirality arises from chelate ring distribution and is labelled by Δ for a right-handed and Λ for a left-handed helix); and (iii) all the monodentate ligands are achiral and are assumed to have free rotation about the metal–ligand bond axis unless otherwise stated. Following Hirschmann and Hanson, we will treat all ligands as achiral points placed at the sites of the ligating atoms.[2] Such points are to be regarded as distinct if the ligands that they represent are heteromorphic. Heteromorphic ligands will be designated by different capital letters, while homomorphic ligands will be designated by identical capital letters.

Even though the term "prochiral molecule" has been discouraged,[1] it is commonly used by biochemists and organic chemists; in the text that follows we will use the term "prochiral complex" to designate a complex having a prochiral metal center and bearing achiral ligands.

When all the ligands are achiral, the reactions involving the heterotopic elements will convert the prochiral complex to a racemic mixture of two optical isomers having opposite chirality at the metal atom. In the examples to follow, if one of the ligands has a chiral center of given configuration, two diastereoisomers will be obtained.

Prochiral complexes could find appealing applications in reactions with chiral molecules, in particular those of biological interest such as aminoacids, proteins, mono- and poly-nucleotides. Prochiral complexes, in fact, although bearing only achiral ligands, should be able to give highly diastereoselective or, even, diastereospecific reactions with such biological molecules. The diastereoselectivity of such reactions will depend on the nature of the achiral ligands, since they become substituents of a chiral metal center.

The interactions of prochiral complexes with prochiral ligands

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and the involvement of prochiral complexes in catalytic cycles deserve particular attention and are treated in a separate section.

PROCHIRAL COMPLEXES

Two classes of *prochiral octahedral complexes* can be defined: *cis,cis,trans*-ML_2Z_2XY (I) and *trans*-ML_2XYWZ (II) (Fig. 2). Complexes of class I have two pairs of enantiotopic ligands, L and Z, but we will assume that only L can be substituted. The following sub-classes can also be usefully defined: Ia when X (or Y) = Z; Ib when X (or Y) = L; IIa when two equatorial cis ligands are identical (e.g., Z = W). Configurational descriptors for enantiotopic ligands can be defined by extending the Hanson prochirality rules for tetrahedral assemblies[1] and adopting the CIP priority rules for determination of the absolute configuration of an octahedral center.[6] Since the chirality symbols C (clockwise) and A (anticlockwise) are used to denote absolute stereochemistry in coordination compounds other than tetrahedral,[9] the enantiotopic ligands L can be defined as *pro-C* (L_C) and *pro-A* (L_A) (Fig. 3).

Substitution of either one of the two enantiotopic ligands with an achiral entering ligand E will give octahedral enantiomeric products (the following restrictions on the nature of E apply: for complexes of class I and Ib: $E \neq Z$; for complexes of class Ia: $E \neq Z, X$). Similarly, migration reactions that involve the enantiotopic ligands will give enantiomeric square pyramidal derivatives. More specifically, migration of either X or Y to L (or vice versa) for complexes of class I (see Fig. 4), and migration of any equatorial ligand to L (or vice versa) for complexes of class II.

Prochiral square pyramidal complexes are of the type *cis, cis*-ML_2Z_2X (III), with L and Z ligands in the square plane (Fig. 2). They can be regarded as octahedral complexes of class I, where one of the axial ligands has been replaced by a phantom atom. Besides the two enantiotopic ligands, L, this class of complexes also possesses two enantiotopic planes containing the L, X and Z ligands. The narrowing of the L–M–Z angle from 180° to 120° in either one of the two enantiotopic planes will transform the prochiral square pyramidal complex into a chiral trigonal bipyramid (Fig. 5). It is of interest to note that the two enantiomeric trigonal

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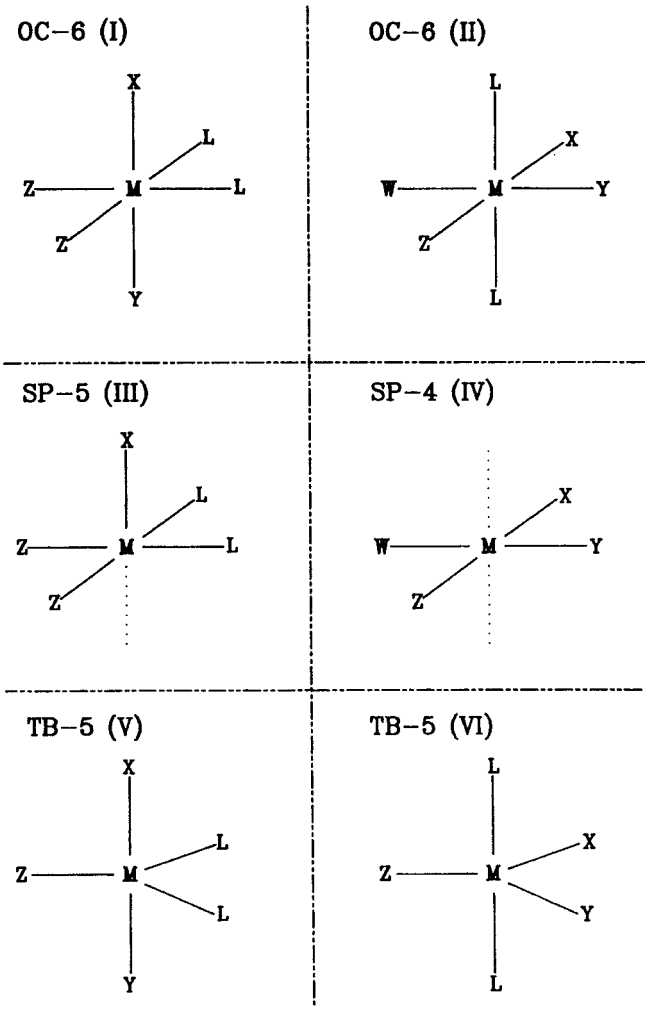

FIGURE 2 Schematic representation of the classes of prochiral octahedral (I, II), square pyramidal (III), square planar (IV) and trigonal bipyramidal (V, VI) coordination compounds.

bipyramids can interconvert through a prochiral square pyramidal complex.

Prochiral square planar complexes are of the type MXYWZ (IV) (class IVa when two cis ligands are identical, e.g., W = Z) (Fig.

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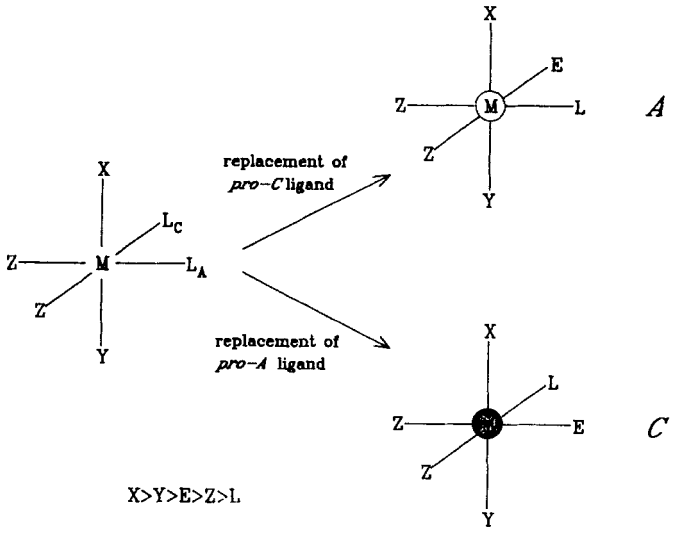

FIGURE 3 Schematic example of a prochiral octahedral complex of class I and of the formal substitution reaction that transforms the prochiral metal center into a chiral one. Configurations of the chiral metal atoms are assigned according to CIP rules for octahedral assemblies ("the chirality symbol *C* is assigned to that configuration in which the CIP priority numbers of the ligating atoms in the plane perpendicular to the principal axis increase in a clockwise direction when viewing the plane from the most preferred atom of CIP priority 1 on the principal axis" (Ref. 9). The enantiotopic elements are named according to an extension of the rules reported in Ref. 1. The ligand priority order according to CIP rules is: X > Y > E > Z > L. Metal atoms circled with different shadings represent optical isomers throughout the paper.

2) and can be treated as octahedral complexes of class II, but with the two equal axial ligands replaced by two phantom atoms. The two phantom atoms are the enantiotopic ligands; alternatively, the prochiral SP-4 complex can be regarded as having two enantiotopic faces. Replacement with E of either one of the enantiotopic phantom atoms (or, alternatively, addition of E to either of the enantiotopic faces) will give rise to enantiomeric square pyramidal complexes (Fig. 6).

The configurational descriptors for prochiral SP-5 and SP-4 complexes can be defined by applying the same rules as adopted for octahedral complexes (the phantom atom has obviously the lowest priority).

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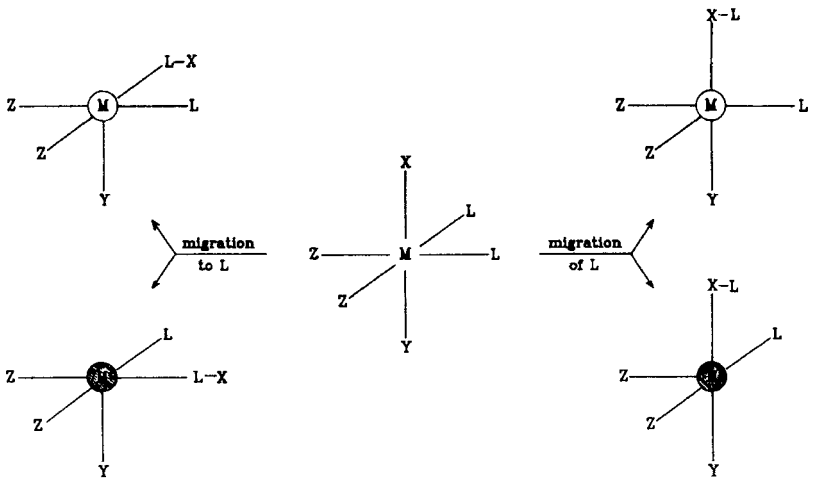

FIGURE 4 Schematic representations of migration reactions involving the enantiotopic ligands of a prochiral octahedral complex of class I producing enantiomeric square pyramidal derivatives.

Finally, two classes of *prochiral trigonal bipyramidal complexes* of the type ML_2XYZ can be defined (Fig. 2). In the first class (V) the two enantiotopic ligands L are in the trigonal plane. The complex is still prochiral if either Y = Z (Va) or Y = L (Vb). This class of complexes also has two enantiotopic faces, defined by the plane containing the X, Y and Z ligands. In the second class (VI), the two enantiotopic ligands occupy apical positions and there are no enantiotopic faces. The configurational descriptors for prochiral TB-5 complexes can be determined by applying the usual prochirality rules and the priority rules defined by Mislow for determination of the absolute configuration of trigonal bipyramidal assemblies.[10] In the case of structure VI, the prochiral descriptors correspond to those defined for prochiral trigonal assemblies, where *Re* = *pro-C* and *Si* = *pro-A*.

For both class V and class VI complexes, replacement of either one of the enantiotopic ligands with E will give TB-5 derivatives of opposite chirality (for class V only, E ≠ Z). Similarly, for complexes of class V, coordination of E in the trigonal plane to either one of the enantiotopic faces will give enantiomeric octa-

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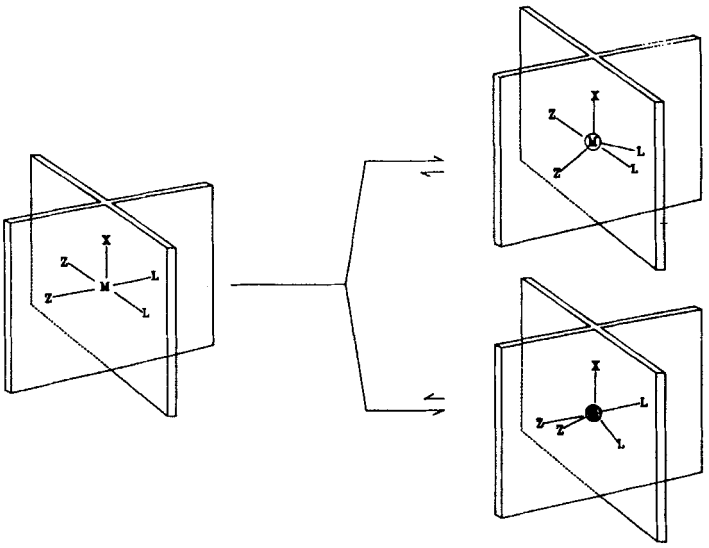

FIGURE 5 Schematic representation of the isomerization of a prochiral square pyramidal complex to two enantiomeric trigonal bipyramids. The two enantiotopic planes are indicated.

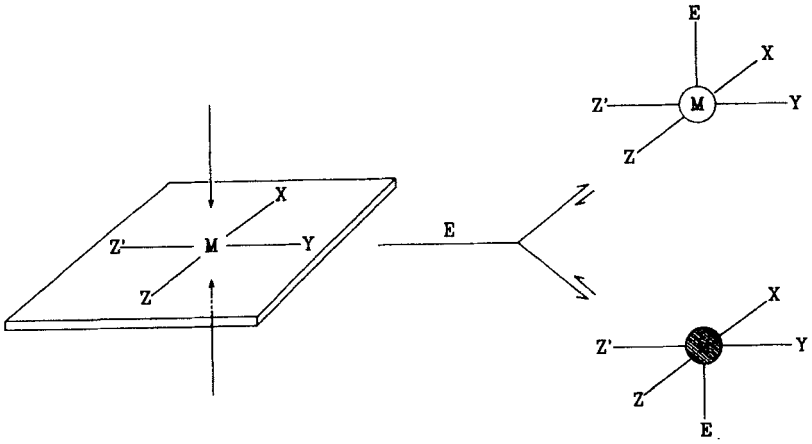

FIGURE 6 Schematic representation of ligand coodination to a prochiral square planar complex of class IV producing two enantiomeric square pyramids. The enantiotopic attack directions are indicated.

hedral complexes. Examples for class V complexes are schematically reported in Fig. 7.

Trigonal bipyramidal complexes of class V can be also defined as prochiral with respect to the isomerization that permutes two equatorial ligands (L and Y) with the two axial ligands. This isomerization is currently thought to occur through a pseudorotation process that simultaneously interchanges the two pairs of ligands (Berry mechanism[11]). The enantiomer formed depends both on which of the two L ligands participates in the pseudorotation process and on the direction of the rotation.

When the complex with a prochiral metal atom has at least one chiral ligand, the heterotopic elements become diastereotopic. The case of octahedral complexes is treated in detail. For complexes of class I, the heterotopic ligands L become diastereotopic when: (i) either X or Y (or both) are chiral, or (ii) both Z ligands are chiral with the same absolute configuration. For complexes of class II, these ligands are diastereotopic when (i) at least one of the ligands in the equatorial plane is chiral. (These can be either homomorphic or enantiomorphic ligands.[5])

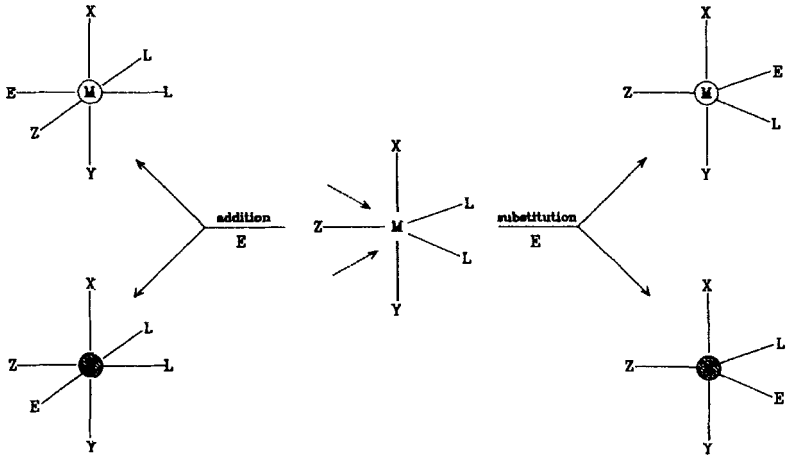

FIGURE 7 Schematic representation of enantiotopic ligand substitution and of ligand coordination in the case of a prochiral trigonal bipyramidal complex of class V, in both processes, producing two enantiomeric trigonal bipyramidal or octahedral derivatives, respectively. The enantiotopic attack directions in the trigonal plane are indicated.

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When, in complexes of class I, X and Y are enantiomorphic ligands, the metal atom is a pro-pseudoasymmetric center.[3] In fact, substitution of either one of the diastereotopic ligands L by a new achiral ligand gives two diastereomeric meso forms. The same case applies to complexes of class II when X and Y are enantiomorphic ligands and Z = W. In agreement with the nomenclature used for tetrahedral assemblies, when the metal atom is a pro-pseudoasymmetric center the configurational descriptors of prochiral ligands adopt lower case letters: *pro-c* and *pro-a*.[3,12] Examples of two cis enantiomorphic ligands can be commonly found among bidentate chelating systems with chiral donor atoms of opposite configuration (meso forms), such as diphosphines (e.g., (dipamp)) and disulfoxides (e.g., 2,5-dithiahexane 2,5-dioxide ($DTHO_2$)). As an example of a pro-pseudoasymmetric octahedral complex of class II, we note the ruthenium (II) derivative *trans*,*cis*,*cis*-$RuCl_2$(R,S-$DTHO_2$)$(Im)_2$ (Im = imidazole) recently synthesized in our laboratories.[13]

Having defined the various classes of "prochiral complexes," we now treat some of them in more detail, within the context of the most common reactions that can transform the prochiral metal center into a chiral one.

We will begin by considering the replacement of one of the heterotopic ligands of a prochiral octahedral complex. All the substitution reactions will be assumed to occur without formation of geometrical isomers. An obvious requirement is that the two heterotopic ligands must be labile, while the other ligands are inert. The key steps of a substitution reaction, which goes through a dissociative path, are: (i) the dissociative step to give a square pyramidal or a trigonal bipyramidal intermediate and (ii) the associative step (Fig. 8). If the substitution reaction proceeds through a square pyramidal intermediate, the complex will become chiral during the dissociation of one of the two enantiotopic ligands, L. If the reaction proceeds through a prochiral trigonal bipyramid intermediate, the complex will become chiral during the coordination of the entering ligand, E, which can attack either one of the two enantiotopic faces. Moreover, if in this latter case E is a phantom atom, an isomerization reaction from a prochiral TB-5 to a chiral SP-5 occurs.

It is worth stressing at this point that an initially achiral octa-

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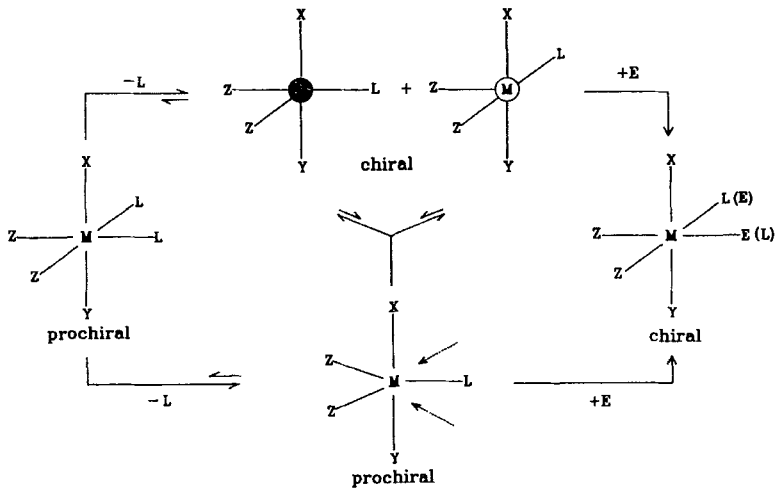

FIGURE 8 Schematic representation of the dissociative path in the substitution reaction of an enantiotopic ligand on a prochiral octahedral complex. The possible chiral (square pyramidal) and prochiral (trigonal bipyramidal) intermediates are indicated.

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hedral complex with proper features, in the absence of isomerization reactions, can evolve in two subsequent substitution steps to a prochiral and finally to a chiral derivative (for a detailed treatment of the step-by-step evolution of an achiral assembly of ligands to a chiral one, see Ref. 14). This case is well illustrated by the behavior of the complex *trans*-$RuCl_2(DMSO)_4$.[15] In aqueous solution this complex immediately releases two cis DMSO molecules to give the *trans*-dichloro *cis*-bis(dimethylsulfoxide) *cis*-diaquo derivative (1) (Fig. 9). This complex is still achiral, having C_{2v} symmetry. The subsequent dissociation of a chloride ligand lowers the complex symmetry from C_{2v} to C_S and gives the prochiral class IB cationic complex (2). Substitution of a water molecule in the equatorial plane by an achiral ligand will lead to enantiomers with opposite chirality at the metal atom (3a, 3b). The strong trans-directing effect[16] of S-bonded DMSO will minimize the possible formation of other geometrical isomers.

As an example of the interaction of a prochiral octahedral complex with chiral molecules, we studied in detail the reaction of *trans*-$RuCl_2(DMSO)_4$ with the mononucleotide 5′-dGMP and found

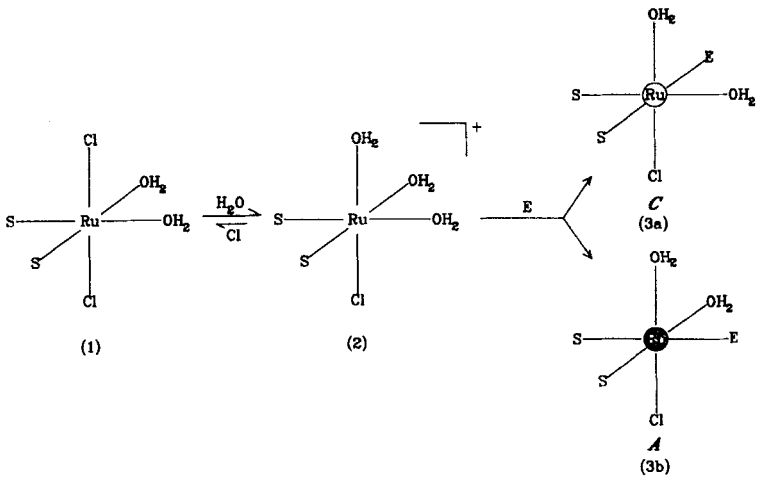

FIGURE 9 Example of a step-by-step evolution of a symmetric octahedral complex (1) to a prochiral (2) and eventually chiral (3a, 3b) derivatives; S = S-bonded dimethyl sulfoxide. The capital letters *A* and *C* under the complexes represent the chirality symbols according to Ref. 9, with the assumption that the entering ligand coordinates through a nitrogen atom.

that at acidic pH two N7 coordinated diastereoisomers are actually formed, their equilibrium constant being ≈ 0.6.[17]

As examples of octahedral complexes with either enantiotopic or diastereotopic ligands we report the ruthenium(II) derivatives *fac*-[Ru(DMSO)$_3$Cl$_2$(R–NH$_2$)]° (R = H, (R)–CH(CH$_3$)–Ph or (S)–CH(CH$_3$)–Ph), recently synthesized and characterized by our group.[18,19] Of interest, such complexes can be thought of as belonging either to class Ia, when the chlorine atoms are assumed as the heterotopic ligands, or to class Ib, when the two DMSO's trans to Cl are assumed as the heterotopic ligands. The first point of view is convenient when the chemical behavior of the complexes in aqueous solution is considered. In fact, upon dissolution in water, these complexes slowly release a chloride ligand, producing the corresponding aquo-derivatives as a pair of enantiomers (R = H) or of diastereoisomers (R = (S) or (R)–CH(CH$_3$)–(C$_6$H$_5$)). In this latter case the two diastereoisomers should form with different rates and in different amounts (Fig. 10). The second point of view is more conveniently adopted for the interpretation of the complex ^{1}H NMR spectrum. In fact, for R = H, each enantiotopic DMSO

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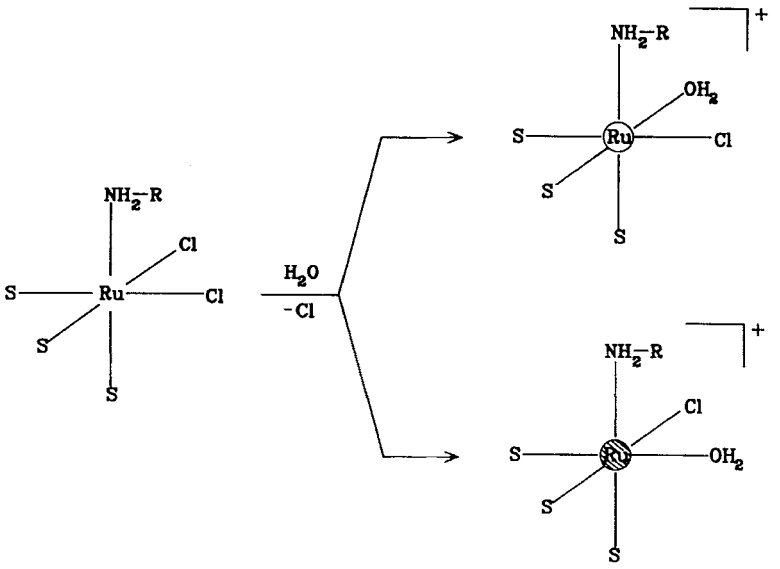

FIGURE 10 Example of a prochiral Ru(II) octahedral complex of class Ia; S = S-bonded dimethyl sulfoxide. A pair of enantiomers (R = H) or diastereoisomers (R = (S)- or (R)-CH(CH_3)-Ph) is obtained upon hydrolysis of one enantiotopic ligand (Cl).

brings two diastereotopic methyl groups (the complex lacks the "horizontal" symmetry plane); on the other hand Me_A is enantiotopic with Me_C and Me_B with Me_D (Fig. 11) (the same situation can be found in organic molecules such as the methylene protons of diethyl sulfoxide[3]). Each pair of enantiotopic methyls is expected to give a different signal in the ^1H NMR spectrum of the complex; moreover, due to ^1H-{^1H} coupling between diastereotopic methyls on the same DMSO, each signal should be split into a quartet.

In fact, the ^1H NMR spectrum of a fresh D_2O solution of the ammonia complex consists of three peaks of equal intensity in the methyl region for S-bonded DMSO's.[19] A sharp singlet at 3.42 ppm is easily attributed to the equivalent methyl groups of the DMSO trans to NH_3, while two unresolved multiplets at 3.46 and 3.40 ppm can be attributed to the two enantiotopic pairs of diastereotopic methyls of the enantiotopic DMSO's. A very similar spectrum was also reported for an aqueous solution of *cis*-$RuCl_2(DMSO)_4$, where an H_2O molecule sits in the place of NH_3.[20]

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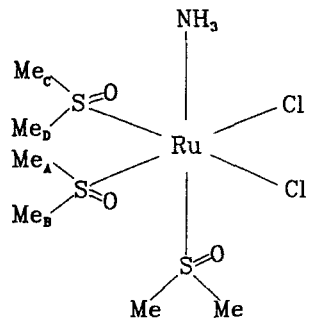

FIGURE 11 *cis,fac*-$RuCl_2(DMSO)_3(NH_3)$ can be conveniently considered as a class Ib prochiral complex for the interpretation of its ^1H NMR spectrum. The two enantiotopic pairs of diastereotopic methyl groups (Me_A and Me_C; Me_B and Me_D) are indicated.

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Having treated the substitution reaction on prochiral octahedral complexes and, consequently, the coordinative addition to trigonal bipyramidal and square pyramidal derivatives, we turn now to examine these same processes for square planar species. Substitution reactions of prochiral square planar complexes will always give final products that are achiral at the metal center. However, for an associative mechanism, the trigonal bipyramidal intermediates formed during the reaction are chiral when E is different from the ligand trans to the leaving group, since the leaving and entering ligands occupy equatorial positions. Square planar Pt(II) complexes such as *cis*-$[Pt(NH_3)_2X(H_2O)]^+A^-$ (X = Cl, OH), since they are metabolites of the widely used anticancer agent *cis*-$Pt(NH_3)_2Cl_2$,[21] represent particularly interesting examples of a class IVa prochiral complex. As depicted in Fig. 12, substitution of the water ligand by a chiral ligand (E*, e.g., DNA) can proceed through two pentacoordinated diastereoisomeric intermediates. The complex will therefore preferentially undergo reaction at one of its two enantiotopic faces. On the other hand, in the case of the corresponding trans square planar isomer, the metal atom is an achiral center throughout the substitution process. In fact, when a complex bears two trans homomorphic non-labile ligands the metal center always remains achiral.

On the other hand, coordination of an entering ligand, E to either one of the enantiotopic faces of a prochiral square planar

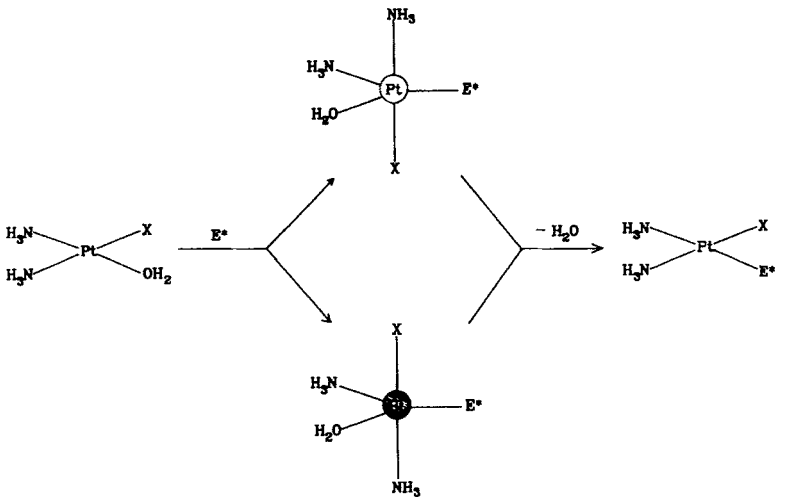

FIGURE 12 An illustration that a substitution reaction of a prochiral square planar complex can proceed through two pentacoordinated chiral intermediates.

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complex will give rise to chiral square pyramidal products or intermediates, which can easily isomerize to trigonal bipyramidal final products. It is interesting to consider the consequences of this type of isomerization reaction on coordinative (or oxidative) addition reactions of square planar complexes of the general formula *cis*-ML_2X_2 (C_{2v} symmetry, i.e., not prochiral). Association of E with such square planar complexes gives rise to a chiral trigonal bipyramid (or a chiral octahedron) through the formal intermediate formation of a prochiral square pyramidal species. The case of coordinative addition is schematically reported in Fig. 13. Several examples of such reactions are known in the literature, such as the addition of small molecules to square planar d^8 complexes of the type $[M(L-L)_2]^+$ or $[M(L-L)(L'-L')]^+$.[22]

The coordinative and oxidative additions of small molecules (e.g., H_2, O_2, $CH_2{=}CH_2$) to d^8 square planar prochiral complexes deserve particular consideration at this point. For example, molecular hydrogen can coordinate[23] on either of the two enantiotopic faces of a prochiral complex of class IV, the H–H bond being oriented either along the Z–M–X or the Z–M–Y axis. The oxidative addition will result in two octahedral geometrical isomers, each as a

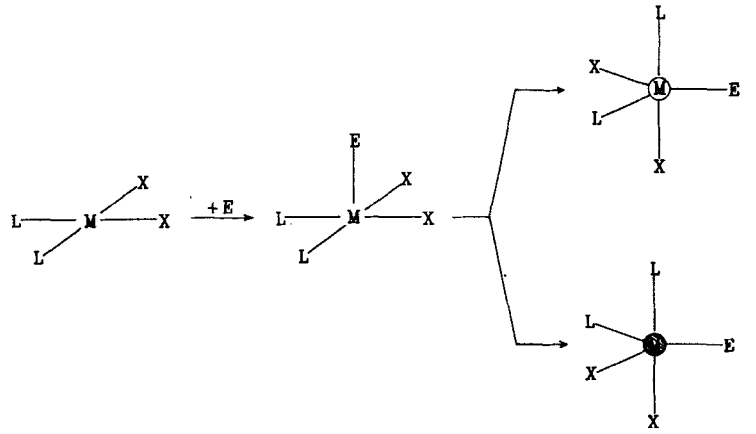

FIGURE 13 Schematic representation of the two elementary steps (ligand coordination followed by isomerization) which can transform an achiral (C_{2v}) square planar complex into a chiral trigonal bipyramid.

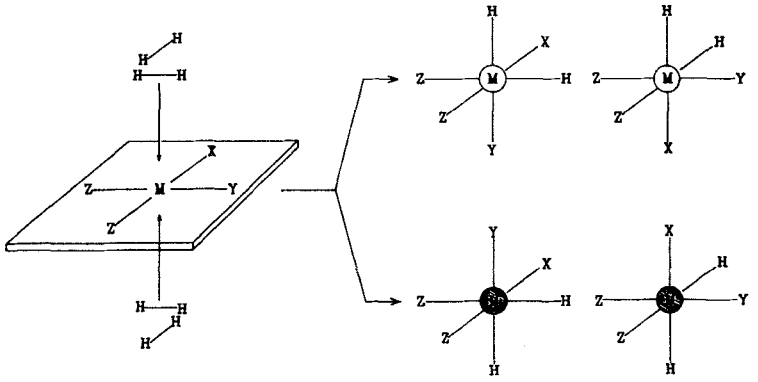

FIGURE 14 Schematic representation of H_2 oxidative addition on a prochiral square planar complex of class IVa. Two geometrical isomers, each as a pair of enantiomers, may be obtained.

pair of enantiomers (Fig. 14). An interesting example of this reaction has been reported for iridium(I) derivatives with diphenylphosphinoethane (DPE) of general formula *cis*-[Ir(CO)(X)DPE] (X = Cl, Br, I, CN) (Fig. 15). In this case only one geometrical isomer was found, due to a stereoselective attack of the hydrogen molecule along the P–Ir–CO axis.[24]

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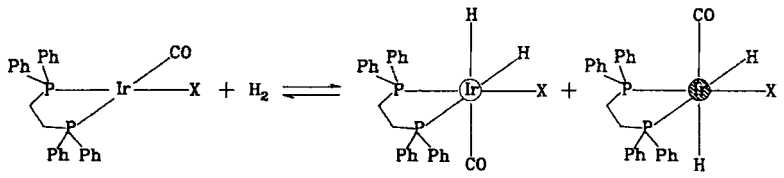

FIGURE 15 Example of H_2 oxidative addition on a prochiral square planar Ir(I) complex of class IVa (X = Cl, Br, I, CN) (Ref. 24).

The same considerations used for H_2 can be easily extended to the coordination of O_2 (side-on) and ethylene. Finally, E can be an electrophile, such as in the first associative step of an oxidative addition reaction of E–X molecules (e.g., CH_3–I).

INTERACTIONS OF PROCHIRAL COMPLEXES WITH PROCHIRAL MOLECULES

Of the most common substrates with prochiral centers (olefins, thioethers, ketones), the case of olefins will be treated in detail. Prochiral olefins are characterized by two enantiotopic faces; when they bind to a metal center, each of the unsaturated carbon atoms which bears two different substituents becomes asymmetric (and therefore a chiral center).[25] Accordingly, if the metal center is symmetric and not prochiral, two diastereoisomers will form (two enantiomers if the olefin has only one prochiral center), depending on which enantiotopic face is coordinated.[26] In this case the metal center can be formally compared to the oxygen atom in chiral epoxides.

Coordination of a prochiral olefin to a prochiral complex will produce one further chiral center, namely the metal atom, and the number of possible stereoisomers increases accordingly.

The interaction of a prochiral square planar complex with a simple prochiral olefin such as propylene will be treated in detail. The olefin is assumed to bind to the metal with the carbon–carbon double bond parallel to the Z–M–Y axis.

Coordination of propylene with the same enantiotopic face (e.g., *Re* face) to either of the two enantiotopic faces of the complex will give two pentacoordinated diastereoisomers, namely CR and

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AR,[27] with opposite chirality at the metal atom and the same chirality (R) at the carbon atom (Fig. 16). The two other diastereoisomers, CS and AS, will be obtained upon coordination of the olefin with its *Si* face. An equal distribution of the four diastereoisomers should be obtained. In the absence of free rotation about the metal–olefin bond, the positions trans to Y and trans to Z are different. In the present case, two sets of four diastereomers are possible, giving eight total species. Diastereoisomers interconverted by rotation of 180° about the olefin–metal bond axis without bond rupture can be referred to as rotamers.[28] Coordination of the olefin along the Z–M–X axis will give the corresponding geometrical isomers, where Y occupies an apical position and X occupies an equatorial position.

The same situation applies in the case of prochiral 1,2-disubstituted olefins of C_S symetry (e.g., CHR=CHR′, R ≠ R′) which, upon coordination to the metal center, give rise to two different chiral carbon atoms. On the contrary, in the case of prochiral 1,2-disubstituted olefins of C_{2h} symmetry (e.g., *trans*-2-butene), the

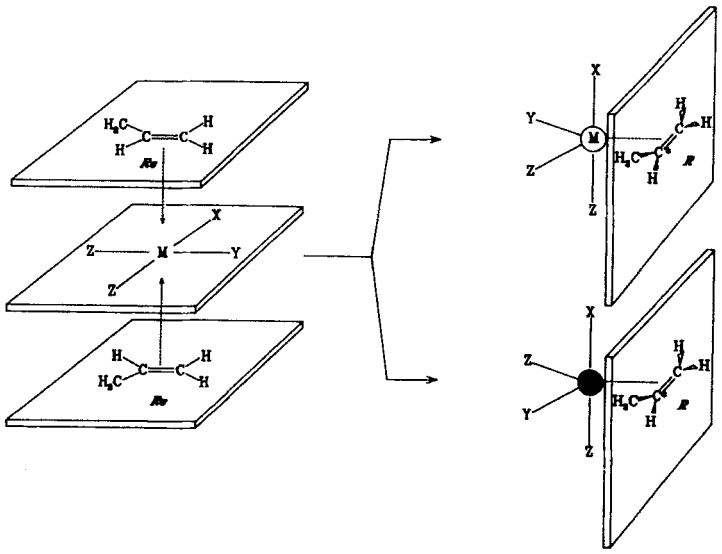

FIGURE 16 Schematic representation of the formation of two pentacoordinated diastereoisomers upon coordination of the *Re* enantiotopic face of propylene to either of the enantiotopic faces of a prochiral square planar complex of class IV.

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rotamers are equivalent and the number of diastereomers is reduced to four for each attack direction.

We turn now to the consideration of a square planar complex with propylene displacing Y from the prochiral complex. In the hypothesis of olefin free rotation, the square planar symmetry plane is maintained and the metal atom becomes achiral. On the contrary, in the absence of free rotation the symmetry plane is lost and the metal atom becomes chiral; two diastereoisomeric rotamers, with oposite chirality at the metal atom and the olefin always perpendicular to the plane of the complex are formed (Fig. 17). The two other diastereoisomers (not illustrated) are obtained when propylene coordinates with its other enantiotopic face.

Assignment of the metal atom absolute configuration can be easily accomplished by viewing the complex as a pseudo trigonal bipyramid with the olefin coordinated in a metallacyclic fashion in the trigonal plane. Accordingly, the formation of the diastereoisomeric rotamers can be envisioned as the coordination of the prochiral olefin to a prochiral trigonal bipyramid having two free enantiotopic coordination positions (Fig. 18).

When either the olefin or the metal complex bears a chiral sub-

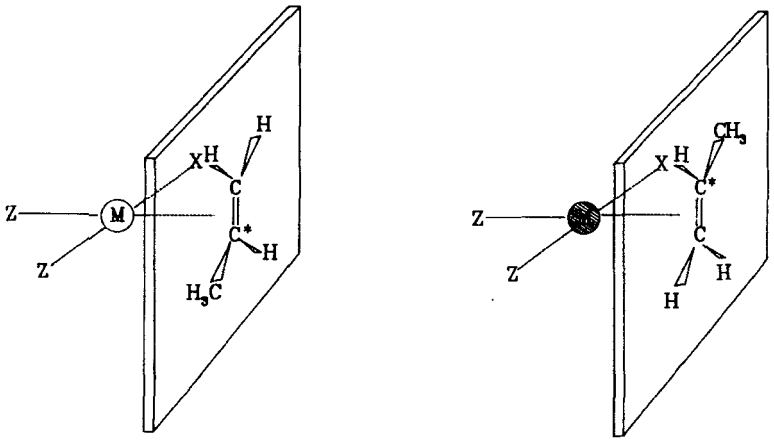

FIGURE 17 Schematic representation of two diastereoisomeric rotamers obtained upon substitution of a ligand by propylene in a prochiral square planar complex. Coordination of propylene with only one of its enantiotopic faces is represented.

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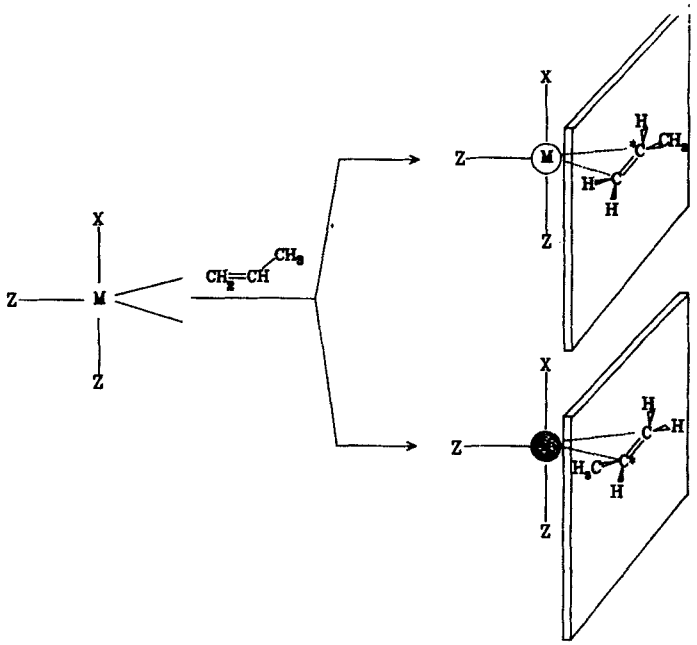

FIGURE 18 A rotamer of a square planar complex with a coordinated olefin can be envisaged as a pseudo trigonal bipyramid with the olefin bound in a metallacyclic fashion in the trigonal plane.

stituent of given configuration, the number of possible stereoisomers will not change, but their distribution will be altered. The case of prochiral olefins coordinated to a square planar complex bearing a chiral ligand has been treated in detail by Bosnich,[28] but without consideration of the chirality acquired by the metal center.

The case of prochiral thioethers can be treated as that of prochiral olefins, since the sulfur atom becomes chiral upon coordination to the metal center.

On the contrary, prochiral ketones bind to the metal center through the oxygen atom and therefore the carbonyl carbon atom becomes chiral only upon attack of a nucleophile (e.g., hydride). If the ketone being attacked is bound to a prochiral metal center, four diastereoisomeric activated complexes are formed.

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PROCHIRAL CATALYSTS

A distinctive characteristic of coordination compounds is that they can behave as catalysts. From a general point of view, transition metal complexes involved in catalytic cycles are commonly divided into two main classes: achiral and chiral catalysts. Usually the chiral catalysts have a stable chiral signature with a given configuration on one of the nonleaving groups, often a chelating ligand (e.g.: $[Rh(Chiraphos)(S)_2]^+$ (S = solvent)[29]; $[M(PPEI)(COD)]^+$ (M = Rh,[30] Ir[31]; PPEI = 2-pyridinal-1-phenylethylimine; COD = 1, 5-cyclooctadiene); $PtCl_2/SnCl_2/(-)-BPPM$ ((−)−BPPM = (2S,4S)-N-(tert-butoxycarbonyl)-4-(diphenylphosphino)-2-[(diphenyl-phosphino)methyl]pyrrolidine.[32]

Of course, there is no chiral signature for achiral catalysts. However, when the ligand distribution about the metal atom is also taken into account, achiral catalysts can be distinguished according to whether they have an achiral or a prochiral metal center. In this latter case, the prochiral complex might be called a "prochiral catalyst."

"Prochiral catalysts" could find useful applications in the field of diastereoselective catalysis with substrates having a prochiral center and a chiral substituent of given configuration (e.g., the catalytic reduction of chiral ketones, oxidation of chiral thioethers, epoxidation of chiral olefins). A prochiral complex, in fact, could coordinate the substrate to give either one stereoisomer predominantly or one diastereoisomer that is much more reactive than the other(s). In this way, the prochiral catalyst promotes the reaction and at the same time amplifies the chiral information brought by the substrate. Such a catalytic process could give rise to one of the two diastereoisomeric products with a selectivity higher than that obtained with an achiral catalyst. For a given substrate the diastereoselectivity of the reaction will depend on the nature of the achiral ligands, which become substituents of a chiral metal center. Examples of the application of prochiral complexes in catalysis can be found in the isotactic and syndiotactic polymerization of propylene catalyzed in homogeneous phase by Group 4B metallocene/methylalumoxane systems.[33,34]

In the case of chiral catalysts, the metal atom is usually achiral;

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very often, however, in the course of the proposed catalytic cycles, the metal atom becomes a prochiral and then a chiral center in subsequent sequential steps. The metal center returns obviously to its initial achiral form at the end of the cycle. If in the catalytic cycle the metal atom becomes a chiral center before or during the stereo-determining step, the enantiomeric excess of the reaction will depend also on the nature of the achiral ligands.

CONCLUSIONS

Several classes of coordination compounds of various geometries have been defined as prochiral, and the most common reactions that can transform the prochiral metal atom into a chiral center have been considered.

The importance of recognizing a complex as prochiral becomes evident when it interacts with chiral molecules of given configuration to form two diastereoisomers. The diastereoselectivity of such reactions can be tuned not only by changing the substituents at the chiral center but also, more easily, by changing the nature of the achiral ligands. They become, in fact, substituents of the chiral metal center.

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