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2,2′-Bipyrrolidine versus 1,2-Diaminocyclohexane as Chiral Cores for Helically Wrapping Diamine−Diolate Ligands

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The synthesis of chiral tetradentate dianionic diamine−diolate ligands assembled around either *N*,*N*′-dimethyl-*trans*-1,2-diaminocyclohexane or 2,2′-bipyrrolidine is described. These ligands wrap in a fac−fac helical mode around octahedral titanium and zirconium centers giving chiral-at-metal complexes. Diaminocyclohexane was found to be a poor chiral motif for diastereoselective helical wrapping, and all complexes of this family were obtained as mixtures of stereoisomers. In contrast, bipyrrolidine was found to be a perfect chiral motif for helical wrapping, and the corresponding diamine−diolate complexes were obtained as (enantiomerically pure) single diastereomers.

trans-1,2-Diaminocyclohexane has enjoyed vast popularity as the chiral motif of chelating ligands, following the introduction of Jacobsen's asymmetric catalysts based on the tetradentate−dianionic Salen ligands.[1,2] Linear tetradentate ligands may form three isomers when wrapping around octahedral metal centers designated as mer−mer (trans), fac−fac (cis-α), or fac−mer (cis-*β*), as shown in Figure 1. The planar array of donor atoms in the mer−mer isomer renders the metal nonstereogenic, whereas the helical ligand wrapping in the two other isomers leads to stereogenic metal centers, often referred to as *chiral-at-metal* complexes.[3] The key factor in the design of chiral-at-metal complexes is the chiral induction from the ligand backbone to the ligand wrapping mode attempting to achieve a single diastereomeric complex of an enantiomerically pure ligand. Salen ligands tend to bind in a mer−mer geometry,[4] and therefore no such chiral induction is required from the *trans*-diamino-cyclohexane core. However, for helically wrapping ligands, it is often found that the chiral induction of this fragment is either absent (Ti complexes of *N*-Me Salan ligands),[5] weak (Ti and Zr complexes of "fluorous" diamine−diolate ligands),[6] or occurring only within a certain range of structural demands (Ti complexes of *N*-H Salan ligands, Zr complexes of Salan ligands).[7] A prediction of the degree of diastereoselectivity, and, in fact, of which of the two (Δ or Λ) diastereomers will prevail, is currently unavailable.[8]

In an attempt to design chiral tetradentate dianionic ligands that will wrap in a single predictable helical sense around metal centers, we turned to the chiral 2,2′-bipyrrolidine motif.[9,10] Having a direct bridge between the almost flat and rigid five-membered rings, this core is conformationally constrained relative to the diaminocyclohexane core. A mechanical molecular model (e.g., "Framework" or "Dreiding") of this core clearly shows that only specific faces of the endocyclic *N*-donors may converge, namely, have the ability to form a chelate with a metal center. Two "external" donors anchored to these donors should emerge via the opposite faces and complete a defined chiral wrapping around the metal. Very recently, we have synthesized the first dianionic ligands around this motif, that is, diamine−diphenolate (Salan) ligands, and demonstrated that they bind in a fully diastereoselective manner.[11] In comparison to chiral Salans, chiral diamine−diolate ligands have been much less explored.[12] A recent example is a "fluorous" ligand consisting of a diaminocyclohexane chiral core and $N(CH_3)-CH_2C(CF_3)_2OH$ arms that led to diastereomer mixtures around titanium (6:1) and zirconium (1:1).[6] In this work, we set out to expose the relative success of bipyrrolidine and diaminocyclohexane

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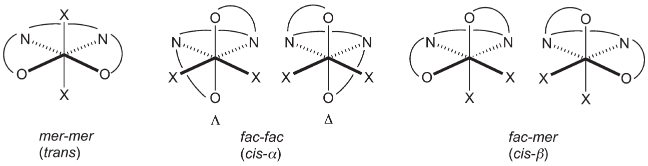
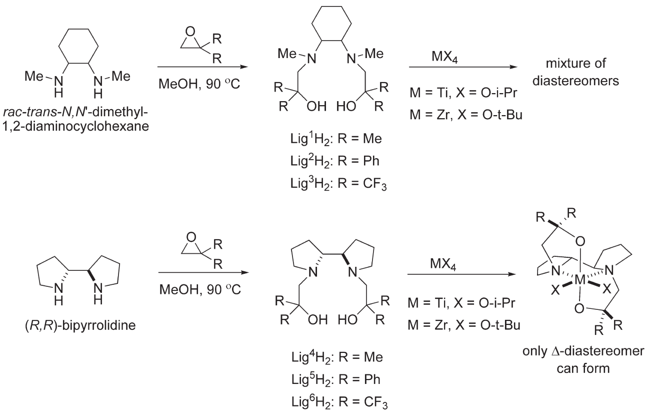


Figure 1. Possible wrapping modes of linear tetradentate ligands in an octahedral environment.

Scheme 1. Diamine Diolate Ligands and Their Group 4 Complexes



as the chiral motifs in diamine–diolate ligands that lead to chiral-at-metal octahedral complexes around titanium and zirconium.

Toward this end, we synthesized three ligands around each skeleton by reacting either *rac-trans-N,N'*-dimethyl-1,2-diaminocyclohexane or enantiomerically pure 2,2'-bipyrrolidine with 2,2-disubstituted epoxides (Scheme 1). To address the influence of different steric and electronic environments, the epoxide substituents included dimethyl, diphenyl, or bis(trifluoromethyl) groups. Lig^3H_2 was previously reported.[6] For a modified synthesis that does not produce a monosubstituted side product, see the Supporting Information. Each ligand was reacted with tetra(isopropoxide)titanium and with tetra(*tert*-butoxide)zirconium to give the mononuclear complexes of the type [(ONNO)Ti(O-*i*-Pr)$_2$] and [(ONNO)Zr(O-*t*-Bu)$_2$], respectively (Scheme 1).

NMR characterization of the six complexes of the diaminocyclohexane-based ligands revealed that they had all formed as mixtures of diastereomers. The mixtures consisted of essentially two C_2-symmetric isomers (i.e., fac–fac diastereomers) with ratios ranging between 1:5.5 and 1:1.[13] No clear trend for metal- or ligand-dependent diastereoselectivity could be found. Namely, *trans*-diaminocyclohexane is a poor motif for diastereoselective helical wrapping of diamine–diolate ligands. In contrast, the six complexes of the bipyrrolidine-based ligands had all formed as single diastereomers of C_2 symmetry; that is, chiral 2,2'-bipyrrolidine is a perfect motif for helical wrapping of diamine–diolate ligands around octahedral metal centers. The difference between these two series of diamine–diolate ligands is demonstrated in Figure 2, which depicts the ^{19}F NMR spectrum of [Lig^3Ti(O-*i*-Pr)$_2$] (that had formed with the highest diastereoselectivity of the diaminocyclohexane series) relative to that of [Lig^6Ti(O-*i*-Pr)$_2$] (a typical single diastereomer).

The X-ray structures of the complexes [(*R,R*)-Lig^4Zr(O-*t*-Bu)$_2$], [(*R,R*)-Lig^6Ti(O-*i*-Pr)$_2$], and [(*S,S*)-Lig^6Zr(O-*t*-Bu)$_2$] were solved.[13] Molecular views of the two zirconium complexes and some bond lengths and angles are shown in Figure 3. Consistently with the molecular model, the (*R,R*) ligands wrapped in a Δ helix and the (*S,S*) ligand wrapped in a Λ helix around the octahedral metal centers irrespectively of the α-carbon substituents or the particular metal. The bond lengths and angles are unexceptional for such complexes, signifying an unhindered binding. It is noteworthy that, except for the α substituents, and minor differences in bond lengths due to electronic effects, these two structures are practically superimposable (being however mirror images).

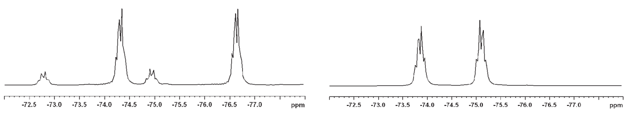


Figure 2. ^{19}F NMR (188.16 MHz, C_6D_6) of a diastereomer mixture of [Lig^3Ti(O-*i*-Pr)$_2$] (left) versus that of a single diastereomer of [Lig^6Ti(O-*i*-Pr)$_2$] (right).

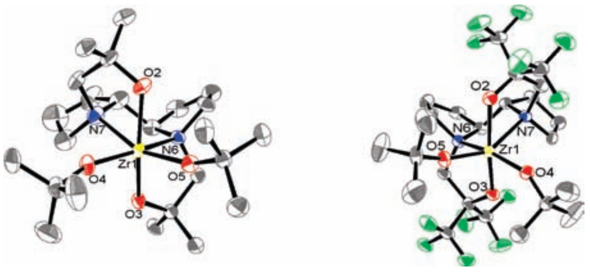


Figure 3. ORTEP representation of two bipyrrolidine-based diamine–diolate complexes with 50% probability ellipsoids and hydrogen atoms omitted for clarity. Selected bond lengths (Å) and angles (deg). (*R,R*)-Lig^4Zr(O-*t*-Bu)$_2$ (left): Zr–O2, 2.050(2); Zr–O3, 2.047(2); Zr–O4, 1.947(2); Zr–O5, 1.945(2); Zr–N6, 2.438(3); Zr–N7, 2.425(3); O2–Zr–O3, 153.27(9); O4–Zr–O5, 108.37(9). (*S,S*)-Lig^6Zr(O-*t*-Bu)$_2$ (right): Zr–O2, 2.076(2); Zr–O3, 2.101(2); Zr–O4, 1.930(2); Zr–O5, 1.917(3); Zr–N6, 2.437(3); Zr–N7, 2.459(3); O2–Zr–O3, 160.86(9); O4–Zr–O5, 107.08(11).

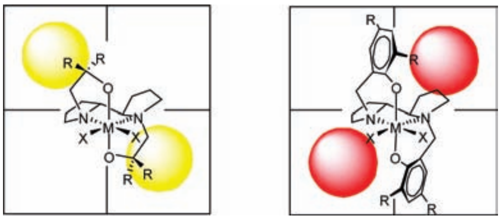


Figure 4. The opposite quadrant hindrance exhibited by the R groups in a diamine–diolate complex (left) and a Salan complex (right) based on a bipyrrolidine core of the same absolute configuration.

It is instructive to compare these diamine–diolate ligands and the corresponding Salan ligands[11] according to the "quadrant view",[14] which outlines, for C_2-symmetric complexes, which pair of opposite quadrants of space is relatively hindered, thus controlling substrate approach to the chiral metal center. The diamine–diolate ligands feature short N–C–C–O bridges leading to five-membered chelates, and the substituents reside on an "inner" α-carbon atom of the bridge, whereas the Salan ligands feature a longer N–C–C–C–O bridge, and the substituents reside on an "outer" phenolate atom beyond the *O* donor. This signifies that, for a given enantiomer of bipyrrolidine, which induces an identical helical sense of wrapping for the two families of ligands, an opposite

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[13] See the Supporting Information.

[14] Corradini, P.; Guerra, G.; Cavallo, L. *Acc. Chem. Res.* **2004**, *37*, 231.

quadrant picture is obtained, and accordingly, an opposite substrate approach to the chiral pocket is expected (Figure 4).

In conclusion, we have shown that, by employing 2,2′-bipyrrolidine (rather than diaminocyclohexane) as a chiral core, well-defined chiral-at-metal complexes of diamine−diolate ligands are obtained. This chemistry can obviously be extended to other metals and different coordination environments. We are currently exploring the applications of these complexes.

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Supporting Information Available: Experimental details for the synthesis of ligands and complexes in PDF format and crystallographic data for the three X-ray structures in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.