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Chiral Induction via the Disassembly of Diruthenium(II,III) Tetraacetate by Chiral Diphosphines

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Supporting Information

ABSTRACT: $[Ru_2(\mu\text{-}O_2CCH_3)_4(MeOH)_2](PF_6)$ reacts with chiral diphosphines (*R,R*)- and (*S,S*)-chiraphos, leading to disassembly and production of the enantiomers Λ-$[Ru(\eta^2\text{-}O_2CCH_3)(\eta^2\text{-}(R,R)\text{-chiraphos})_2](PF_6)$ and Δ-$[Ru(\eta^2\text{-}O_2CCH_3)(\eta^2\text{-}(S,S)\text{-chiraphos})_2](PF_6)$ in high yield and purity. X-ray crystallography and solid-state circular dichroism (CD) show that only the indicated isomers are present in the solid state. Solution CD measurements also indicate their predominance in solution.

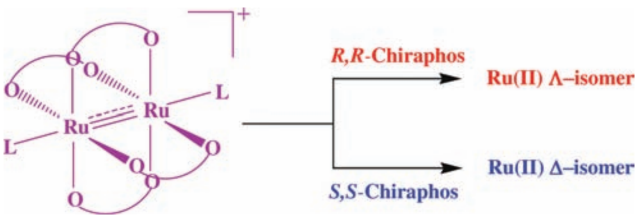
Chiral induction (chirality transfer), from a tetrahedral center to an octahedral metal center, has been an underexplored area of transition-metal stereochemistry and has, in all of the cases that we have encountered, been generated by adding chiral ligands to mononuclear metal centers. We present here a unique, easy method of generating an enantiomerically pure material using a "dimer disassembly" process involving chiral diphosphines reacting with a mixed-valent diruthenium(II,III) tetraacetate.

While Smirnoff first demonstrated the principle of "predetermination of chirality" in octahedral platinum(IV) complexes in reactions with "tetrahedrally" chiral (*S*)- and (*R*)-1,2-diaminopropane in the 1920s,[1] it was not until the work of von Zelewsky et al. in the 1990s that a systematic approach to this important area of enantioselective synthesis was initiated.[2] von Zelewsky et al. studied reactions with chiral tetradentate "chiragen" ligands and were able to induce delta (Δ) or lambda (Λ) chirality on an originally achiral, octahedral, monoruthenium(II) starting material, with the stereoselectivity, Λ or Δ, being dictated by the chirality of the reacting chiragen ligand. Many papers have appeared covering such aspects as chiral induction in porous solids, metallamacrocycles, and metallopolymers,[3] as well as applications in chiroptical and magnetochiral switching, chiral metallomesogens,[4] and chiral auxiliaries for asymmetric synthesis.[5]

Work in our group has centered on the reaction chemistry of mixed-valent diruthenium(II,III) tetracarboxylates, $[Ru_2(\mu\text{-}O_2CR)_4]^+$, and their adducts.[6] Recently, we expanded on a synthetic methodology (discovered in the 1980s by Robinson et al. but not exploited)[7] whereby the diruthenium paddlewheel structure is "disassembled" using mono- or bidentate π-acid ligands, such as phosphines or pyridines.[8] We have used this methodology as a facile and high-yield means of constructing mononuclear ruthenium(II) species with bulky R groups, such as metallocenyls. (Yields were higher than those obtained using more conventional methods that employ mononuclear ruthenium(II) starting materials.) Previous work in our laboratory[9] has looked at the reaction of $[Ru_2(\mu\text{-}O_2CR)_4]^+$ (where R = CH_3 or metallocenyl) with a series of achiral diphosphines (P−P), such as 1,2-bis(diphenylphosphino)ethane (dppe). In all cases, the final product was of the form $[Ru(\eta^2\text{-}O_2CR)(\eta^2\text{-}P{-}P)_2]^+$, or more generally $[M(A{-}A)(B{-}B)_2]^+$, for which both Δ and Λ isomers exist. Where achiral diphosphines were used to initiate the disassembly, a racemic mixture of Δ and Λ products was found, with both forms existing in the crystal structure (a *racemate*). This prompted us to use the new strategy with chiral diphosphines in an effort to preferentially form one metal-centered isomer over the other.

The reaction of chiral diphosphines (*R,R*)- and (*S,S*)-chiraphos [2,3-bis(diphenylphosphino)butane] with the PF_6^- salt of the diaquo adduct of diruthenium(II,III) tetraacetate, $[Ru_2(\mu\text{-}O_2CCH_3)_4(H_2O)_2](PF_6)$, in methanol produces the mononuclear ruthenium(II) species Λ-$[Ru(\eta^2\text{-}O_2CCH_3)(\eta^2\text{-}(R,R)\text{-chiraphos})_2](PF_6)$ [Λ-(*R,R*)-**1**] and Δ-$[Ru(\eta^2\text{-}O_2CCH_3)(\eta^2\text{-}(S,S)\text{-chiraphos})_2](PF_6)$ [Δ-(*S,S*)-**1**], respectively (Scheme 1; see the Supporting Information for full experimental details).

Scheme 1. Outline Showing the Disassembly Reaction Producing Chiral Induction



Both products are obtained in greater than 80% yield. The IR and NMR spectra are similar to those obtained for the achiral species $[Ru(\eta^2\text{-}O_2CCH_3)(\eta^2\text{-dppe})_2](PF_6)$,[9] and elemental analyses are consistent with the formulations given (see the Supporting Information for further spectral and analytical details). Crystals, for each product, were grown from methanol.

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In both cases, the space group is C_2, and so only pure rotations and screw rotations are possible. The crystal structures are, therefore, noncentrosymmetric and chiral.[10] The absolute structure parameters (Flack)[11] are 0.01(4) for Δ-(*S*,*S*)-**1** and −0.004(5) for Λ-(*R*,*R*)-**1**, confirming our assignment of Δ at the metal for the (*S*,*S*)-chiraphos disassembled product [Δ-(*S*,*S*)-**1**] and Λ for the (*R*,*R*)-chiraphos product [Λ-(*R*,*R*)-**1**], respectively, and we do, indeed, have a pair of enantiomers (Figure 1; see also Figure S1 in the Supporting Information).

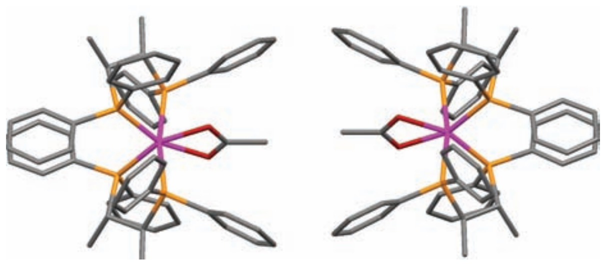

Figure 1. Solid-state structure of the enantiomeric pair Δ-(*S*,*S*)-$\mathbf{1}^+$ (left) and Λ-(*R*,*R*)-$\mathbf{1}^+$ (right). Hydrogen atoms and the PF_6^- counterion have been omitted for clarity.

The ligands maintain their *S*,*S* and *R*,*R* stereochemistry, and no evidence of the respective diastereomers, i.e., Λ-(*S*,*S*)-**1** and Δ-(*R*,*R*)-**1**, is seen in the solid state. As well, the bound (*S*,*S*)-chiraphos structures show *δ* conformations and the (*R*,*R*)-chiraphos structures show *λ* conformations. Six X-ray structures were determined on crystals (for each product) from three or four separate preparations as well as from different times during the crystallization process, and in all cases, the same, previously assigned, absolute configuration at the metal was found.

Both solid-state and solution circular dichroism (CD) spectra were run on each enantiomer, and the results, along with the UV−visible spectrum, can be seen in Figure 2. The free ligands (*S*,*S*)- and (*R*,*R*)-chiraphos do not show significant CD signals above 270 nm,[12] and hence the signals seen are exclusively due to metal complex chromophores. Clear Cotton effects are seen for both enantiomers [two positive and one negative for Λ-(*R*,*R*)-**1** and the mirror opposite for Δ-(*S*,*S*)-**1**] corresponding to three absorption bands seen in the electronic spectrum at 315, 368, and 420(sh) nm (a combination of d−d and ligand-to-metal charge-transfer transitions).[9] CD spectra run on the bulk sample and on the individual crystals used in X-ray analysis were identical, which confirms the enantiopurity (and diastereopurity) of the bulk compound in the solid state.

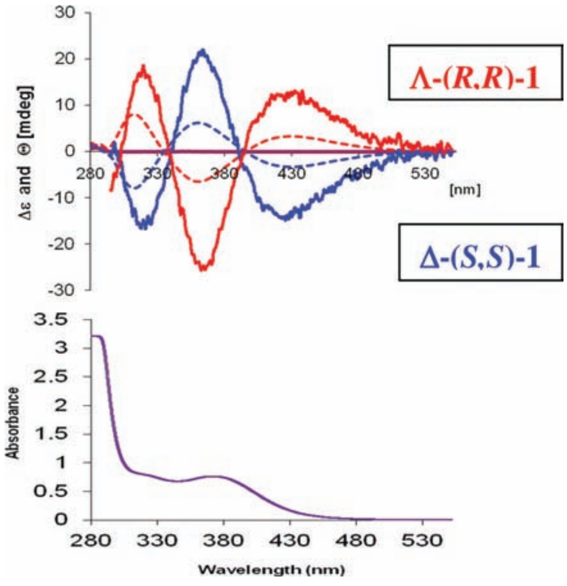

Figure 2. Top: CD spectra in solution (dashed lines) and in the solid state, KBr disk (solid lines), of Λ-(*R*,*R*)-**1** (red), Δ-(*S*,*S*)-**1** (blue), and the starting diruthenium(II,III) tetraacetate dimer (purple). Bottom: UV−visible spectrum of Λ-(*R*,*R*)-**1**/Δ-(*S*,*S*)-**1** (purple) in MeOH (all solutions run at 5.60×10^{-4} M).

The red shifts in the max/min wavelengths of the solid-state CD spectra versus the solution spectra (Figure 2) are not unusual and have been documented and studied in the past by Castiglioni et al.[13] They explain that the shifts are caused by "absorption flattening" due to inhomogeneity in the sample matrix. The smaller the red shift, the smaller these inhomogeneities. In our case, for example, for Λ-(*R*,*R*)-**1**, Cotton effects are seen at 312, 361, and 429 nm in solution and are only very slightly red-shifted to 320, 366, and 432 nm in the solid state.

The solution CD spectra run in methanol show behavior very similar to that of the solid, suggesting that the absolute molecular structure is the same in the solid state and in solution and no significant amount of the diastereomer is present. Again, as with the solid-state measurements, solution CD spectra run on selected crystals, for which the absolute configuration was known, are the same as those run on a bulk sample. Additionally, there is no evidence of any diastereomer in the ^{31}P and ^{1}H NMR of each enantiomer down to −50 °C in $CDCl_3$.[14] It should also be noted that both solution CD and NMR spectra do not change over periods of more than 1 week.

While epimerization at the metal center [Δ-(*S*,*S*)-**1** to Λ-(*S*,*S*)-**1** or Λ-(*R*,*R*)-**1** to Δ-(*R*,*R*)-**1**] in solution cannot be completely ruled out, it would seem highly unlikely. Complexes of the form $[Ru(A{-}A)_3]^{2+}$, where A−A is a neutral bidentate ligand, have been found to be stereochemically rigid. For example, $[Ru(bipy)_3]^{2+}$ racemizes slowly between Δ and Λ forms at elevated temperatures[15] or upon irradiation.[16] The racemization reaction is slow because the complex is low-spin d^6 Ru^{2+} (which has a large splitting of −24 Dq). The difference in the ligand-field absorption emission will be 4 Dq if the racemization reaction goes through a bond rupture mechanism [unlikely due to the inertness of tris-chelated ruthenium(II)] and will be even larger if the mechanism is the more likely Bailar or Ray-Dutt pseudorotations (trigonal or rhombic twists). Racemization/epimerization rates of $[Ru(A{-}A)(B{-}B)_2]^{2+}$-type complexes are very scarce in the literature. The most relevant and fastest rate of interconversion we could find was determined for ΔΛ-$[Ru(\delta\lambda\text{-}1,1'\text{-biiq})(bipy)_2]^{2+}$ (1,1′-biiq = 1,1′-biisoquinoline) by Ashby et al.,[17] who found a modest conversion (epimerization) rate of 12.8 s^{-1} at 80 °C, easily measurable using ^{1}H NMR techniques. In Ashby et al.'s case, as in ours, there is chirality at the metal (Δ/Λ) and at the ligand (*δ*/*λ*). The complex crystallized as an enantiomeric pair of the major diastereomer (Δ,*δ*/Λ,*λ*). In solution the ratio of the major diastereomer (Δ,*δ*/Λ,*λ*) to the minor diastereomer (Δ,*λ*/Λ,*δ*) was found to be 3:1 ($K = 2.88$). They were not able to confirm whether the isomerization was taking place at the metal or the ligand, although they do seem to feel that the latter is less likely, but both ligand (biiq) dissociation and an intramolecular ligand isomerization were postulated. In our case, as discussed earlier, there is no evidence of diastereomers (in the solid state or solution),[18] racemization of the ligand (certainly at room temperature) does not occur,[19] and racemization at the metal is predicted to be very slow.

We have presented here a unique and facile method of chiral induction at a metal center that occurs via the disassembly of an achiral complex *dimer* using diphosphine ligands that contain tetrahedral chirality on the ethylene spacers between the phosphorus centers. The method is highly diastereoselective, certainly in the solid state, and produces enantiomers when diphosphines of opposite chirality (*R*,*R* vs *S*,*S*) are used. This methodology works significantly better than the addition of chiraphos ligands to conventional *mononuclear* ruthenium starting materials because we have been unsuccessful in generating products in that fashion with significant enantiomeric excess. We are currently investigating the generality of this method by using diphosphine ligands that contain only one chiral center, as well as chirality at the phosphorus centers and hope to soon be able to "predict" the chirality induced at the metal center from the nature of the chiral ligand used to induce it.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Details of the preparation of the complexes, analytical data, crystallographic data (CIF), and additional structural diagrams. This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) Crystal data for Δ-(*S*,*S*)-**1**: crystal size 0.34 × 0.47 × 0.09 mm^3, monoclinic, C_2, a = 13.865(8) Å, b = 19.038(8)Å, c = 12.292(7) Å, β = 121.69(3)°, V = 2761(3) Å^3, Z = 2, ρ_{calc} = 1.393 g cm^{-3}, $2\theta_{\text{max}}$ = 60.1°, Mo Kα radiation, T = 213(2) K, μ = 0.490 mm^{-1}. Refinement on F^2 for 4180 reflections/356 parameters gave R1 = 0.0403 and wR2 = 0.1059 [for $I > 2\sigma(I)$] with $-0.992 < \Delta p < 0.680$ e Å^{-3}. Λ-(*R*,*R*)-**1**: crystal size 0.34 × 0.28 × 0.22 mm^3, monoclinic, C_2, a = 13.7603(6) Å, b = 18.9087(7) Å, c = 12.2024(6) Å, β = 121.6105(17)°, V = 2703.9(2) Å^3, Z = 2, ρ_{calc} = 1.426 g cm^{-3}, $2\theta_{\text{max}}$ = 72.4°, Mo Kα radiation, T = 123(1) K, μ = 0.501 mm^{-1}. Refinement on F^2 for 17 862 reflections/389 parameters gave R1 = 0.0207 and wR2 = 0.0237 [for $I > 3\sigma(I)$] with $-0.55 < \Delta p < 0.85$.

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