Reaction between (salen)TiCl$_2$ and Chiral α-Hydroxy Carboxylic Acids

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salen [*N,N'*-ethylenebis(salicylidenaminate)] is a common, tetradentate ligand which binds octahedrally coordinated metal ions in a *mer*, pseudo-planar configuration; the remaining two ligands adopt *trans* geometry about the metal. When salen is forced into *fac* geometry in an octahedral complex, it adopts a helical conformation, as shown, for example, in (salen)MoO$_2$,[1] (salen)Cr(oxalato)$^-$,[2] (salen)Fe(oxalato)$^-$,[2] and (salen)Co(acac).[3] Clearly, no preferential chirality is imparted to the salen "twist" in these species. We find that reaction of (salen)TiCl$_2$, **1**, with (*R*)- or (*S*)-α-hydroxy carboxylic acids gives octahedral Ti compounds, **2a–e**, in which the salen ligand is *fac* substituted and in which the sense of salen helical chirality in the adduct is determined (and can be predicted) by the absolute configuration of the bidentate hydroxy carboxylato ligand (Scheme 1). Formation of these adducts is, therefore, an example of the Pfeiffer effect.[4]

In a general procedure, (salen)TiCl$_2$ and an α-hydroxy carboxylic acid (1 equiv) were treated with aniline (2 equiv) in CH$_2$Cl$_2$ for 12 h at room temperature. Anilinium chloride was removed by filtration, and the filtrate was concentrated to small volume. Hexane was added to precipitate **2** in high yield (>80%). ^{1}H NMR spectra of **2a–e** show one isomer for each present in solution,[5] in which *fac* substitution of the salen ligand is clearly demonstrated by the nonequivalence of the azomethine (*H*—C=N) and ethylene moiety protons. NMR data for **2a** and **2a'**, **2c** and **2c'**, and **2e** and **2e'** are identical, indicating enantiomeric pairs. That is, helicities of the salen ligand are complementary for coordination of (*R*)-α- and (*S*)-α-hydroxy carboxylates. Although several isomers of (*fac*-salen)MoO$_2$ are present in solution which slowly interconvert on the NMR time scale,[1] variable-temperature NMR studies of **2a–e** failed to reveal the existence of additional diastereomers.

Circular dichroism (CD) measurements provide a rapid means to determine the helical chirality of salen complexes **2a–e** (Table 1) and are consistent with the predominance of one isomer in solution. An exciton couplet at ~360 nm, which had been previously assigned to the π–π* transition of the azomethine chromophore,[6] is indicative of helical deformation of the salen moiety. The sign of this couplet has been empirically related to ligand conformations in a variety of Schiff base-metal complexes.[6] The opposite signs of couplets measured for **2a** and **2a'**, **2c** and **2c'**, and **2e** and **2e'**, respectively, indicate complementary helicities for each pair: for complexes resulting from (*R*)-α-hydroxy carboxylates this sign is (–), and it is (+) for those resulting from *S*-enantiomers. From these data, we can predict that the favored helical conformation of the salen ligand is Δ when the metal coordinates (*R*)-α-hydroxy carboxylates and is Λ when it coordinates *S*-enantiomers.

Chiral exciton theory has been used to relate the CD amplitude of the split Cotton effect, *A* [defined as Δ(Δϵ) for a couplet], to the magnitude of distortion from planarity for a variety of organic chromophores.[7] By this account, and with assumption of single diastereomer present in solution for each α-hydroxy carboxylate, the magnitude of the helical deformation of the salen might be expected to decrease on metal complexation of RCH(O–)COO– in the order R = PhCH$_2$ > i-Bu > Cy ~ i-Pr > Ph, consistent with decreasing steric bulk of the R groups. However, another possible interpretation of these CD measurements is that two diastereomers are present in solution for a given α-hydroxy carboxylate, by equilibrium of Δ and Λ helices of the salen: For large R, a single diastereomer predominates, and with decreasing size of R, the equilibrium ratios of major to minor diastereomers approach unity. For example, it has been reported that L-amino acids (L-aa) and Co(salen) form an equilibrium mixture of favored (Λ-salen)Co(L-aa) and disfavored (Δ-salen)Co(L-aa) in solution, with the ratio of (Λ-salen)Co(L-aa) to (Δ-salen)Co(L-aa) decreasing as steric size decreases.[8]

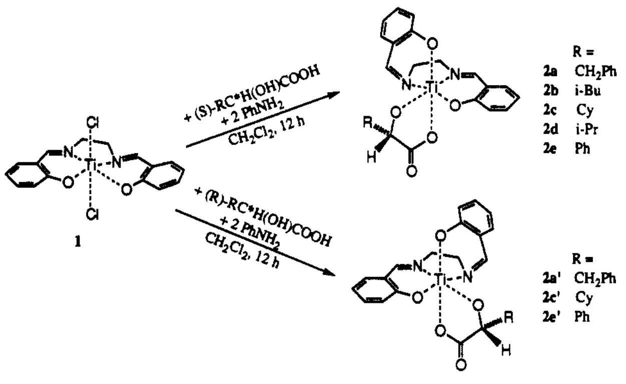
For a definitive study of the relationship between helical deformation and the sign of the CD couplet for these (salen)Ti complexes, *R,R*-salchxn analogs (using (*R,R*)-1,2-diaminocyclohexane in place of ethylenediamine) were prepared. Such salchxn species have been reported to yield only a single helical "twist" on *fac* coordination because of conformational constraints

Table 1. CD Results for **2a–e**, **3**, and **4**

compd	λ, nm (Δϵ)[a]		*A* (Δϵ^2 – Δϵ^1)
2a	340 (–55)	385 (+135)	+190
2a'	340 (+60)	385 (–150)	–210
2b	339 (–22)	383 (+63)	+85
2c	340 (–11)	380 (+29)	+40
2c'	340 (+10)	380 (–27)	–37
2d	339 (–11)	381 (+30)	+41
2e	348 (+1)[b]	377 (+5)	+4
2e'	348 (–1)[b]	377 (–5)	–4
3	380 (–13)	450 (+42)	+55
4	340 (+95)	405 (–110)	–205

[a] CD spectra for the azomethine π–π* transition measured at 4.2 × 10^{-4} M. [b] Measurement at 348 nm is complicated by overlap with bands from another transition.

Scheme 1. Reaction of (salen)TiCl$_2$ with (*R*)- or (*S*)-α-Hydroxy Carboxylic Acids



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(5) Selected ^{1}H NMR (CD$_2$Cl$_2$) data. **2a**, **2a'**: 8.43 (*H*C=N, 1H, s); 8.22 (*H*C=N, 1H, s). **2b**: 8.53 (*H*C=N, 1H, s); 8.51 (*H*C=N, 1H, s). **2c**, **2c'**: 8.51 (*H*C=N, 1H, s); 8.50 (*H*C=N, 1H, s). **2d**: 8.67 (*H*C=N, 1H, s); 8.66 (*H*C=N, 1H, s). **2e**, **2e'**: 8.57 (*H*C=N, 1H, s); 8.53 (*H*C=N, 1H, s).

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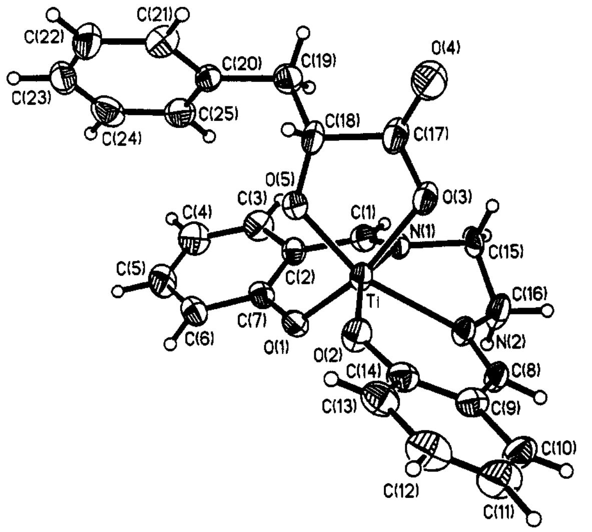

Figure 1. ORTEP diagram for compound **2a′** with labeling scheme showing 50% thermal ellipsoids. Selected bond lengths (Å) and angles (deg): Ti–O(1) = 1.899(3), Ti–O(2) = 1.859(4), Ti–N(1) = 2.128(4), Ti–N(2) = 2.204(4), Ti–O(3) = 1.997(3), Ti–O(5) = 1.843(3), C(1)–N(1) = 1.278(6), C(8)–N(2) = 1.285(6); O(1)–Ti–O(2) = 100.2(1), O(1)–Ti–N(1) = 82.3(1), O(2)–Ti–N(1) = 156.0(1), O(1)–Ti–N(2) = 107.7(1), O(2)–Ti–N(2) = 82.9(1), N(1)–Ti–N(2) = 73.6(1), O(1)–Ti–O(3) = 161.0(1), O(2)–Ti–O(3) = 97.3(1), N(1)–Ti–O(3) = 84.8(1), N(2)–Ti–O(3) = 81.7(1), O(1)–Ti–O(5) = 88.9(1), O(2)–Ti–O(5) = 103.6(2), N(1)–Ti–O(5) = 100.3(1), N(2)–Ti–O(5) = 161.0(1), O(3)–Ti–O(5) = 79.7(1).

present in the diaminocyclohexyl backbone:[9] *R*,*R*-salchxn should result in a Δ helical deformation, and *S*,*S*-salchxn, in a Λ one.[9] Reaction between oxalic acid and (*R*,*R*-salchxn)TiCl$_2$, **3**, gave a single product, **4**, by NMR.[10] As for **2**, *fac* coordination was demonstrated by the nonequivalence of the azomethine (*H*—C═N) protons. Also as for **2**, CD analysis (Table 1) showed an exciton couplet for the π–π^* transition of this chromophore. The (–) sign of this couplet indicated a Δ helical salchxn deformation; *A* [Δ(Δε)] = –205, comparable to **2a′** (*A* = –210), suggesting similar chiral deformations from planarity for both complexes.

To confirm the relationship between *A* and helicity, X-ray crystallographic structures for **2a′** and **4** were determined.[11] The ORTEP diagram of **2a′** (Figure 1) shows the presence of a single diastereomer. The geometry about Ti is a distorted octahedron, with the two O atoms of the 3-phenyllactato ligand occupying cis positions about the metal. The coordination angles at Ti, which range from 73.6° for N(1)–Ti–N(2) to 107.7° for O(1)–Ti–N(2), indicate a distorted octahedral environment at the metal. Bond distances fall within the expected range for compounds of this type, O(salen)–Ti = 1.88 Å (average), and N(salen)–Ti = 2.17 Å (average). The helical deformation of the salen was indeed Δ, as predicted by CD.

The X-ray structure of compound **4** showed the expected presence of a single diastereomer (see Figure 2). As in **2a′**, the geometry about Ti is a distorted octahedron, with Δ helical deformation of the salchxn. Coordination angles around Ti range from 73.7° for *N*(1)–Ti–N(2) to 113.6° for O(1)–Ti–N(2) and bond distances, O(salen)–Ti = 1.85 Å (average) and N(salen)–Ti = 2.17 Å (average), are comparable to those in **2a′**. Thus, the configuration of ethylenediamine substitution in salchxn complexes, the configuration of the α-hydroxy carboxylate ligand in simple salen species, and the sense of the salen ligand helical twist in either series can all be easily correlated, qualitatively.

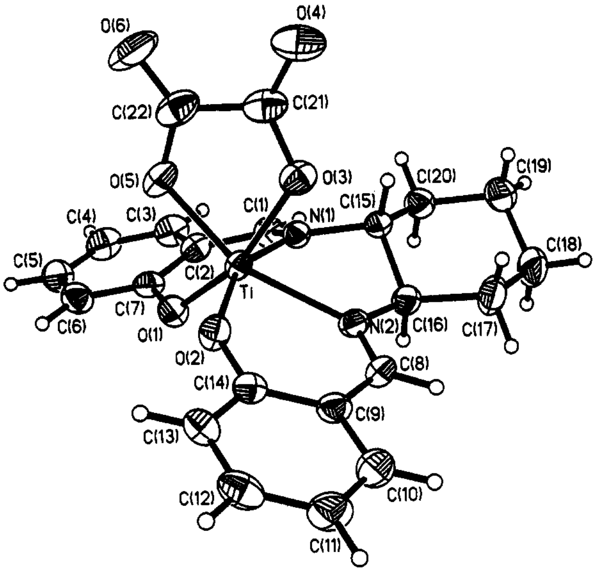

Figure 2. ORTEP diagram for compound **4** with labeling scheme showing 50% thermal ellipsoids. Selected bond lengths (Å) and angles (deg): Ti–O(1) = 1.860(1), Ti–O(2) = 1.832(2), Ti–N(1) = 2.134(2), Ti–N(2) = 2.203(2), Ti–O(3) = 1.991(2), Ti–O(5) = 1.974(2), C(1)–N(1) = 1.276(2), C(8)–N(2) = 1.282(3); O(1)–Ti–O(2) = 96.4(1), O(1)–Ti–N(1) = 83.0(1), O(2)–Ti–N(1) = 154.5(1), O(1)–Ti–N(2) = 113.6(1), O(2)–Ti–N(2) = 83.4(1), N(1)–Ti–N(2) = 73.7(1), O(1)–Ti–O(3) = 159.1(1), O(2)–Ti–O(3) = 100.1(1), N(1)–Ti–O(3) = 87.4(1), N(2)–Ti–O(3) = 81.1(1), O(1)–Ti–O(5) = 84.8(1), O(2)–Ti–O(5) = 106.5(1), N(1)–Ti–O(5) = 98.9(1), N(2)–Ti–O(5) = 158.5(1), O(3)–Ti–O(5) = 78.3(1).

Chiral exciton theory predicts that compounds with similar dihedral angles between the chromophores that produce an exciton couplet should have similar *A* values. Conversely, the dihedral angle between the azomethine units of the salen ligand (measured from the planes determined by the three atoms H—C═N) should be comparable for **2a′** and **4**, since *A* values are similar. For **2a′**, this dihedral angle was measured to be 138.4°, and for **4** the angle was 142.9°. The torsion angle of the azomethine fragments, defined by C═N···N═C, can also be employed as a measure for nonplanar distortion of the salen ligand. These torsion angles were calculated to be –85.4° for **2a′** and –82.7° for **4**. [For comparison with the pseudoplanar starting materials, the dihedral angle for the azomethine units in (salen)TiCl$_2$ is 12.6°,[12] and *A* = 55 for [*R*,*R*-salchxn]TiCl$_2$.] Structural results correlate with the larger *A* value demonstrated for **2a′**, and they suggest that compound **2a′** is a single diastereomer in solution.[13]

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Supplementary Material Available: NMR spectral data, figures showing unit cells, and tables of atomic coordinates, anisotropic thermal parameters, crystallographic data, bond lengths and angles, and least-squares planes for **2a′** and **4** (23 pages). Ordering information is given on any current masthead page.

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(10) Selected ^{1}H NMR for **4** (CD$_2$Cl$_2$): 8.70 (*H*C═N, 1H, d); 8.49 (*H*C═N, 1H, d).

(11) Crystal data for **2a′**: C$_{25}$H$_{22}$N$_2$O$_5$Ti, *M* = 478.3, *P*2$_1$ (No. 4), *a* = 7.039(3) Å, *b* = 18.042(6) Å, *c* = 8.979(3) Å, β = 104.89(3)°, *V* = 1102.0(6) Å^3, *Z* = 2, *D*$_c$ = 1.442 g cm^{-3}, *T* = 230 K, μ = 0.429 mm^{-1}. With all non-hydrogen atoms anisotropic and hydrogen atoms in calculated positions, *R*(*F*) = 4.88%, *R*$_w$(*F*) = 5.32%, and GOF = 1.07. Crystal data for **4**·CH$_2$Cl$_2$: C$_{23}$H$_{22}$Cl$_2$N$_2$O$_6$Ti, *M* = 541.2, *P*2$_1$ (No. 4), *a* = 8.536(1) Å, *b* = 16.922(3) Å, *c* = 8.630(1) Å, β = 107.75(1)°, *V* = 1187.3(3) Å^3, *Z* = 2, *D*$_c$ = 1.514 g cm^{-3}, *T* = 230 K, μ = 0.628 mm^{-1}. With all non-hydrogen atoms anisotropic and hydrogen atoms in calculated positions, *R*(*F*) = 2.66%, *R*$_w$(*F*) = 3.67%, and GOF = 1.04.

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(13) The classical Pfeiffer effect[4] involves trapping a rapidly equilibrating pair of enantiomers by a chiral reagent to give preferentially a single diastereomer. Because helical deformations in Δ- and Λ-(salen)TiCl$_2$ are small (*ca.* 12°) relative to those found for (salen)Ti(α-hydroxy carboxylato) products (ca. 40°), this diastereoselective complexation could be viewed as an "enhanced" Pfeiffer effect.