Communication

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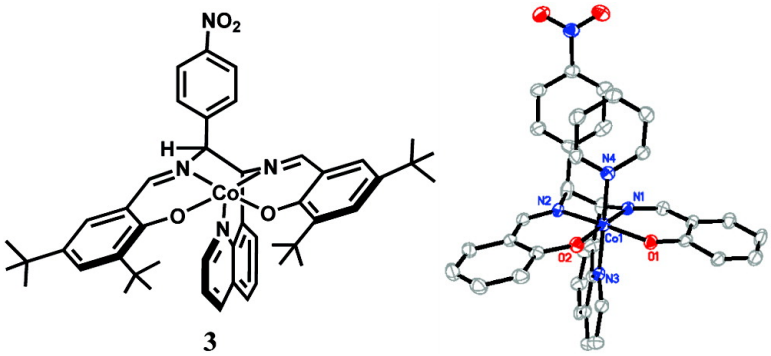

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A Cobalt(III)−Salen Complex with an Axial Substituent in the Diamine Backbone: Stereoselective Recognition of Amino Alcohols

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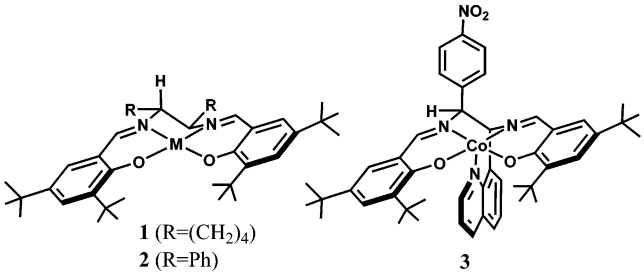
Over the past two decades, there has been considerable interest in chiral (salen)metal [Mn(II), Co(III), Cr(III), Al(III), Y(III), Ti-(IV), V(IV)] complexes as catalysts for a wide range of organic reactions (epoxidation, epoxide opening, Strecker, cycloaddition, aldol, etc.).[1] In most of the studies, the salen ligand is made from the reaction of 1,2-diaminocyclohexane (**1**) or 1,2-diphenylethylenediamine (**2**) with a variety of substituted salicylaldehydes. The axial substituents in the diamine backbone are hydrogens in **1** and **2**. Here we report an amino alcohol receptor based on a Co(III)−salen complex with an aromatic substituent in the axial position of the diamine backbone (**3**).



In general, it is difficult to place alkyl or aryl groups in the axial positions of the diamine backbone in **1** and **2** since these substituents prefer to occupy equatorial positions to avoid steric crowding around the metal. One way to overcome this difficulty is to use tetrasubstituted diamines[2] instead of disubstituted diamines, but their synthesis can be challenging. We envisioned that, by coordinating one of the substituents in the diamine backbone to the metal, the other substituent could be forced to occupy the axial position (**3**). Since the axial substituent is close in proximity to the metal coordinating site, it is ideally positioned to affect the stereoselective binding of the substrate.

The diamine in **3** was synthesized by diaza-Cope rearrangement reaction in a one-pot reaction (Scheme 1).[3] Sequential addition of the two aldehydes to **4** results in efficient formation of the mixed diimine (**6**) followed by the rearrangement reaction to give **7**. The two resonance-assisted hydrogen bonds in **7** drive the rearrangement reaction to completion.[4] We first synthesized a Co(III) complex of **7** using pyridine as a base. The crystal structure of the Co(III) complex[5] (Figure 1) shows that the quinoline group coordinates to the metal, thereby forcing the nitrophenyl group to occupy the axial position as desired. Interestingly, a pyridine molecule is coordinated to the cobalt complex and positioned almost parallel to the nitrophenyl group. The two groups are about 3.26−3.90 Å apart.

The salen ligand in **3** was prepared by hydrolyzing **7** and reacting the mixed diamine with 3,5-di-*tert*-butylsalicylaldehyde.[3] The

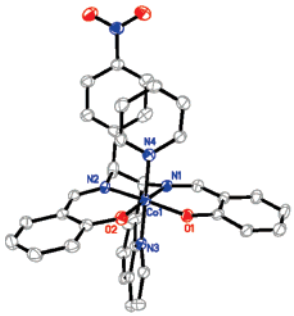
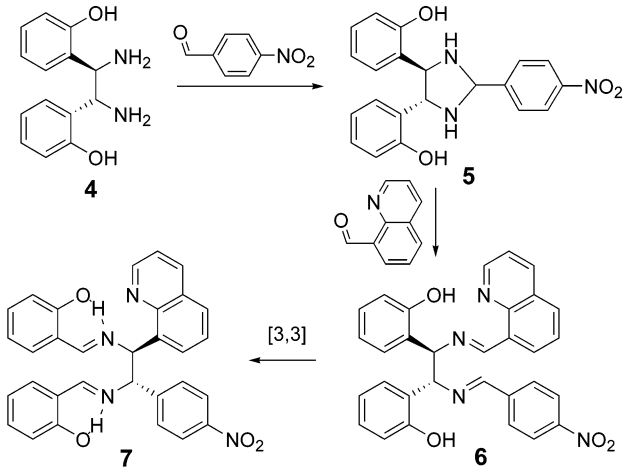


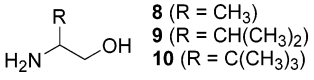
Figure 1. ORTEP representation (30% probability) of the crystal structure of [(**7**)Co(III)(pyridine)](NO$_3$). Selected bond angles (°) and distances (Å): O1−Co1−N1 94.14 (1.886, 1.894); O2−Co1−N2 94.23 (1.894, 1.870); N3−Co1−N4 178.59 (1.953, 1.964).

Scheme 1



crystal structure (Figure S2) and enantiopurity (>99% ee, Figure S1) of this ligand (**L3**) have been determined.[3,6] The salen ligand (**L3**) was mixed with Co(II) nitrate in methanol and air oxidized to obtain the Co(III) complex.[3]

To systematically evaluate the effect of the nitrophenyl group in **3**, we compared the stereoselective coordination of three amino alcohols (**8**−**10**) to two Co(III) complexes, (*R*,*R*)-**1** and (*S*,*S*)-**3**. Although the two cobalt complexes have opposite configurations, it is evident that the two complexes have the same sense of folding of the diamine backbone.[7] In all of the cases, reversible coordination of the amino alcohols to the cobalt complexes is rapid but slower than the NMR time scale.[8] Thus, the diastereomeric complexes give distinct ^{1}H NMR signals.



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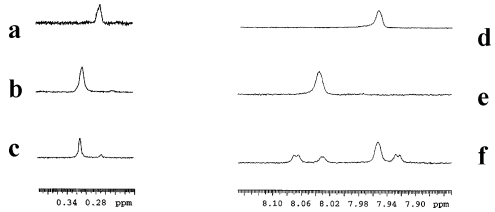

Figure 2. (a−c) ^{1}H NMR (in CD_3CN) of the *tert*-butyl group of *t*-leucinol coordinated to (*S*,*S*)-**3** (a, (*R*)-*t*-leucinol; b, (*S*)-*t*-leucinol; c, *rac*-*t*-leucinol). (d−f) ^{1}H NMR of the host imine C−H when valinol is coordinated to (*R*,*R*)-**1** (d, (*S*)-valinol; e, (*R*)-valinol; f, *rac*-valinol).

Table 1. Stereoselectivity of **1** and **3** for Binding Amino Alcohols **8**−**10**

	(*R*,*R*)-**1**	(*S*,*S*)-**3**
8	$(K_S/K_R) = 2.6{:}1$	$(K_S/K_R) = 2.9{:}1$
9	$(K_S/K_R) = 2.6{:}1$	$(K_S/K_R) = 6.2{:}1$
10	$(K_S/K_R) = 2.6{:}1$	$(K_S/K_R) = 36{:}1$

In a typical experiment, 2 equiv of *t*-leucinol was added to (*S*,*S*)-**3** (10 mM). Figure 2a−c shows the ^{1}H NMR signals of the *tert*-butyl group of the coordinated amino alcohol. When (*R*)-*t*-leucinol is added, the signal appears at about 0.27 ppm (Figure 2a), whereas when (*S*)-*t*-leucinol is added, the signal appears at about 0.33 ppm (Figure 2b). The two signals appear in a ratio of about 1:6 when a racemic mixture of *t*-leucinol is added (Figure 2c). This indicates that the equilibrium constant for binding of (*S*)-**10** to (*S*,*S*)-**3** (K_S) is about 36 (6^2) times greater than that for binding of (*R*)-**10** to (*S*,*S*)-**3** (K_R).[9]

In the case of coordination of the amino alcohols to (*R*,*R*)-**1**, we monitored the host imine signals by ^{1}H NMR. Figure 2d−f shows the imine proton signals when 4 equiv of valinol (**9**) is added. Under our experimental conditions, two amino alcohols are coordinated to (*R*,*R*)-**1**. Each of the two homocomplexes (two coordinated amino alcohols with the same configuration) gives just one imine ^{1}H NMR signal due to C_2 symmetry of the complexes (Figure 2d and e). The heterocomplex (two coordinated amino alcohols with opposite configuration) gives two imine proton signals of equal intensities since the C_2 symmetry is broken. The concentrations of the homo- and heterocomplexes (Figure 2f) are in binomial distribution ($a^2 + 2ab + b^2$).[10] Thus, the stereoselectivity of the two sites is independent with little or no cooperativity. When 4 equiv of racemic **9** is added to (*R*,*R*)-**1**, the observed ratio of all the bound (*S*)-**9** to all the bound (*R*)-**9** is 1.6. The equilibrium constant for binding of the (*S*) amino alcohol to (*R*,*R*)-**1** (K_S) is about 2.6 (1.6^2) times greater than that for binding of the (*R*) amino alcohol to (*R*,*R*)-**1** (K_R).

Table 1 shows that (*R*,*R*)-**1** and (*S*,*S*)-**3** bind amino alcohols with the same sense of stereoselectivity. We suggest that folding of the complex is an important factor for determining the sense of the stereoselectivity. The stereoselectivity of (*S*,*S*)-**3** increases from about 2.9 to 36.0 with increasing steric bulk of the amino alcohol (**10** > **9** > **8**). In contrast, the stereoselectivity of (*R*,*R*)-**1** remains low (selectivity ≈ 2.6) independent of the size of the amino alcohol. Since the nitrophenyl group in **3** is much bigger than the hydrogen in **1**, the binding cavity should be smaller for **3**. As larger amino alcohols fill the small cavity in **3**, the stereoselectivity is expected to increase.

Over the years, there has been considerable interest in making stereoselective receptors for amines, amino acids, and amino alcohols.[11] Although much progress has been made, it remains a challenge to develop highly stereoselective receptors for these substrates based on simple organic compounds or metal complexes. An oxazoline-based organic receptor and a chiroporphyrin-based Co(III) complex have been shown to bind amino alcohols with stereoselectivities approaching 5.0.[12]

In conclusion, we have developed a simple method for placing axial substituents on the diamine backbone of metal−salen complexes. The axial substituents are well positioned to directly affect the stereoselective coordination of the substrates. In this communication, we have demonstrated this effect using sterically bulky amino alcohols.

Acknowledgment. We thank the Natural Sciences and Engineering Research Council of Canada and the Korean Science and Engineering Foundation (H.-J.K.) for financial support of this work.

Supporting Information Available: Experimental data, including crystallographic data for **L3** and **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(5) Crystal structure of [(**7**)Co(III)(pyridine)](NO$_3$)1/2(CH_2Cl_2): $C_{36.50}H_{28}ClCoN_6O_7$, T = 150(2) K, monoclinic, *C*2/*c*, Z = 8, a = 25.5931(12) Å, b = 10.2487(5) Å, c = 27.0553(13) Å, α = 90°, β = 91.349(2)°, γ = 90°, V = 7094.5(6) Å^3, $R1$ = 0.0654, $wR2$ = 0.1515 for $I > 2\sigma(I)$, GOF on F^2 = 0.933. Compound **3** is also expected to be octahedral with a solvent molecule completing the coordination.

(6) Crystal structure of **L3**: $C_{47}H_{56}N_4O_4$, T = 150(1) K, monoclinic, *P*21/*c*, Z = 4, a = 14.1133(10) Å, b = 24.338(2) Å, c = 13.7730(6) Å, α = 90°, β = 118.090(4)°, γ = 90°, V = 4173.6(5) Å^3, $R1$ = 0.0900, $wR2$ = 0.2207 for $I > 2\sigma(I)$, GOF on F^2 = 1.015.

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(8) The host−guest complexes were heated for 10 s at 70 °C in order to rapidly reach equilibrium. The value of the equilibrium constant did not change within experimental error (±10%) even after 1 day.

(9) K_S = [(*S*,*S*)-**3**-(*S*)-**10**]/([(*S*,*S*)-**3**][(*S*)-**10**]) and K_R = [(*S*,*S*)-**3**-(*R*)-**10**]/([(*S*,*S*)-**3**][(*R*)-**10**]). Thus, when 2 equiv of racemic alcohol is added, K_S/K_R = ([(*S*,*S*)-**3**-(*S*)-**10**][(*R*)-**10**])/([(*S*,*S*)-**3**-(*R*)-**10**][(*S*)-**10**]) = ([(*S*,*S*)-**3**-(*S*)-**10**]/[(*S*,*S*)-**3**-(*R*)-**10**])^2.

(10) Where a^2 and b^2 represent mole fraction of the homocomplexes and 2*ab* represents the mole fraction of the heterocomplex. The ratio of (*S*) and (*R*) amino alcohols bound to (*R*,*R*)-**1** can be obtained by taking the square root of the ratio of the two homocomplexes ($a/b = (a^2/b^2)^{1/2}$). Alternatively, this ratio can be obtained from all of the bound (*R*)- and (*S*)-amino alcohols ($a/b = (a^2 + ab)/(b^2 + ab) = [a(a + b)]/[b(a + b)]$).

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