

Electronic and Steric Effects in Diamine Recognition with a Highly Rigid Zn(II) Complex

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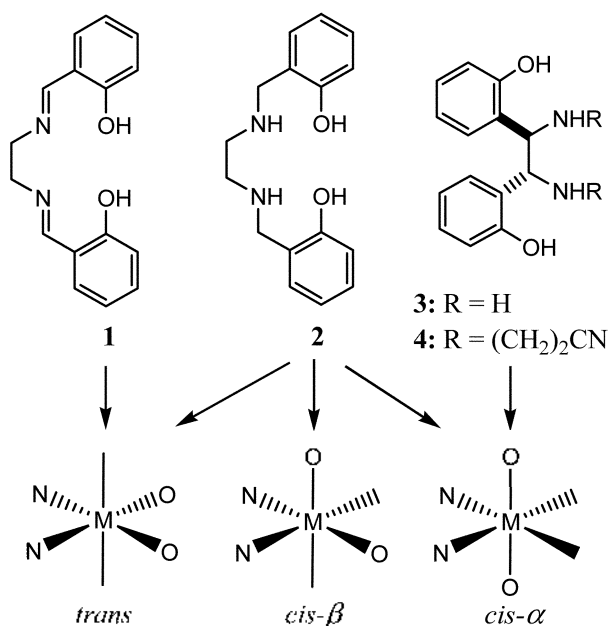
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Rigid and C_2 symmetric chiral ligands are useful for crafting stereoselective catalysts.¹ Binol, binap, dpen, dach, pybox, and salen ligands¹ are just some of the 'privileged'² C_2 symmetric ligands that have been used to construct a wide variety of interesting metal complexes as stereoselective catalysts. The C_2 symmetric N_2O_2 salen ligand (**1**) forms *trans* octahedral complex (Scheme 1). It is uncommon to find C_2 symmetric N_2O_2 ligands that form only one kind of *cis* octahedral complexes. For example, **2** (Scheme 1) can in principle form three isomers of octahedral complexes (*cis- α* , *cis- β* or *trans*).^{3,4} In contrast, **3** and **4** (Scheme 1) should form only the C_2 symmetric *cis* octahedral complexes (*cis- α*) due to the connectivity of the ligand. The *cis- α* topology is particularly attractive for stereoselective recognition of bidentate substrates and for stereoselective catalysis that requires two free metal coordination sites in *cis* orientation.^{3,4} Our interest in molecular recognition of small molecules⁵ led us to investigate the stereoselective recognition of vicinal diamines with Zn(II) complexes of **3** and **4**.

Compound **3** was prepared according to a literature procedure⁶ and the reaction of **3** with two equiv of acrylonitrile

provided compound **4**. Figure 1 shows the crystal structure of a ternary complex formed between (*R,R*)-dpen, Zn(ClO₄)₂, and the disodium salt of (*S,S*)-**4**.⁷ The two phenoxy groups occupy the less favored axial positions in the Zn(II) complex allowing the phenolic oxygens to coordinate to the metal and form the highly rigid *cis- α* octahedral structure. In contrast, the crystal structure of a Pt(II) complex of **3** showed that the ligand binds to the metal as a bidentate ligand (*N* coordination) forming a square planar structure.⁸ The two phenol groups in the Pt(II) complex occupy the more favored equatorial positions. Vicinal diamines generally form tetrahedral Zn(II) complexes.⁹

¹H NMR was used to study the stereoselectivity of ternary complex formation between **3** or **4** with Zn(OTf)₂ and 1,2-diphenylethylenediamine (dpen).¹⁰ In a typical experiment, equimolar amounts of Zn(OTf)₂ (10 mM) and disodium salts of **3** or **4** (host) were mixed with two equiv of dpen (guest) in methanol-d₄. ¹H NMR shows that the guest diamine does not displace the host diamines even when excess of guest diamine is used. This supports the idea that the host diamines bind tightly to the metal as a tetradentate ligand in solution as depicted in the crystal structure (Figure 1). Figure 2a shows the chiral carbon C-H signals of the heterochiral



Scheme 1. Three different octahedral complexes that can be formed by C_2 symmetric N_2O_2 tetradentate ligands **1**, **2**, **3** and **4**.

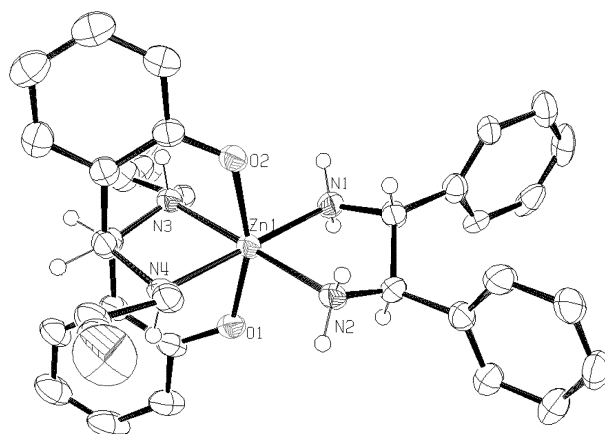


Figure 1. Ortep representation of the Zn(II) complex formed between (*S,S*)-**4** and (*R,R*)-dpen at 50% probability. Hydrogen atoms on amine nitrogens and chiral carbons are shown for clarity. Selected bond distances: Zn1-N1 = 2.130(2); Zn1-N2 = 2.144(2); Zn1-N3 = 2.222(2); Zn1-N4 = 2.213(3); Zn1-O1 = 2.094(2); Zn1-O2 = 2.109(2). Selected bond angles: O1-Zn1-O2 = 162.07(8); N1-Zn1-N2 = 80.95(9); N3-Zn1-N4 = 85.30(9).

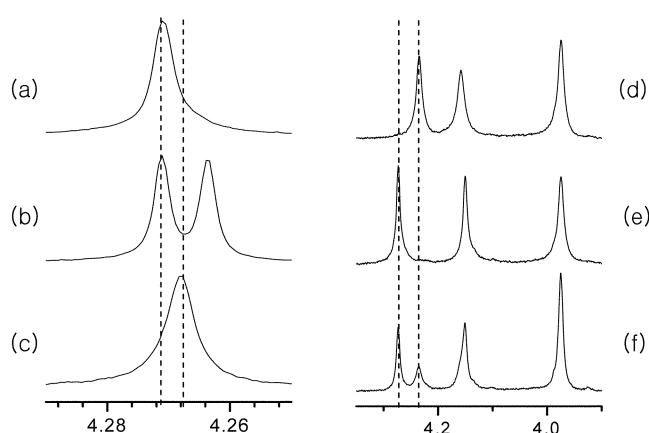


Figure 2. Partial ^1H NMR (in methanol- d_4) of the ternary complexes formed between (a) (S,S) -**3** and (R,R) -dpen, (b) racemic **3** and (R,R) -dpen, (c) racemic **3** and racemic dpen, (d) (S,S) -**4** and (S,S) -dpen, (e) (S,S) -**4** and (R,R) -dpen, (f) racemic **4** and racemic dpen.

ternary complex formed between (S,S) -**3** and (R,R) -dpen. Only the host signals are shown in Figures 2a, 2b and 2c. The free and bound guest signals (not shown in Figures 2a, 2b and 2c) are averaged and appear as a singlet due to the rapid ligand exchange rate compared to the nmr time scale.¹¹ Figure 2b shows the chiral carbon C-H signals due to the homochiral and heterochiral ternary complexes formed between racemic **3** and (R,R) -dpen. The host signal of the homochiral complex is slightly upfield shifted (δ 4.263) relative to the host signal of the heterochiral complex. When the ternary complex is formed between the racemic mixtures of both **3** and dpen (Figure 2c), the host signal of the ternary complex appears as a singlet almost exactly at the midpoint (δ 4.267) between the host signals of the homochiral and the heterochiral complexes. Here again the averaging of the signals is due to rapid equilibration of the homochiral and heterochiral complexes and the fact that the peak appears at the midpoint indicates that there is little or no stereoselectivity for coordination of dpen to the zinc complex of **3**.¹¹

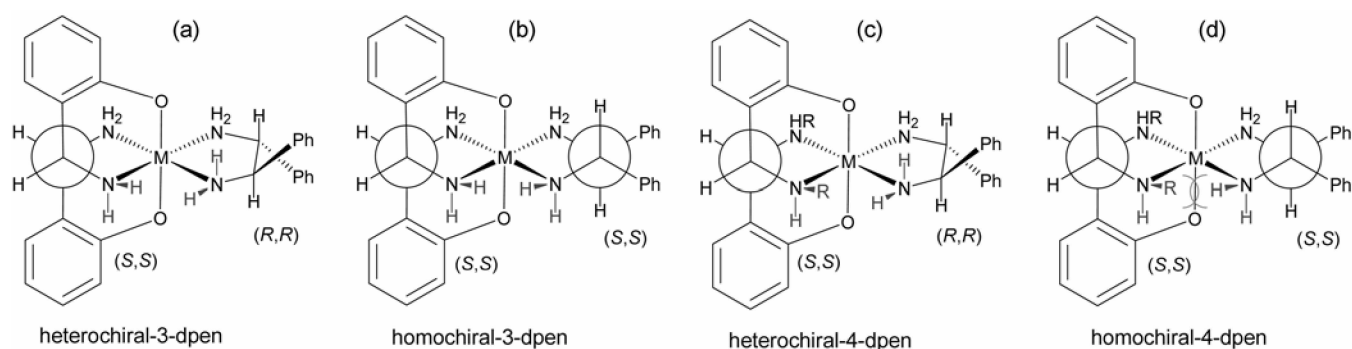
Interestingly, the results are strikingly different when **4** is used instead of **3** to form the ternary complex. This is rather surprising in view of the fact that the structures of **4** and **3** are so closely related. Figure 2d shows the chiral carbon C-H

signals of the homochiral ternary complex formed between (S,S) -**4** and (S,S) -dpen. The host signal appears as a singlet at δ 4.24 ppm. The free (δ 4.16) and bound (δ 3.98) guest signals are not averaged and appear well separated as two distinct singlets indicating that the ligand exchange rate is slow compared to the nmr time scale.¹¹ Figure 2e shows the chiral carbon C-H signals due to the heterochiral ternary complex formed between (S,S) -**4** and (R,R) -dpen. The host signal of the heterochiral complex is slightly downfield shifted (δ 4.27) relative to the host signal of the homochiral complex while the guest signal of the heterochiral complex appears at about the same place as that of the homochiral complex. Here again the free and bound guest signals are not averaged and appear as two distinct singlets. When the ternary zinc complexes are formed between the racemic mixtures of **4** and dpen (Figure 2f), both host signals of the heterochiral complex and the homochiral complex appear in a ratio of about 2 : 1. These two signals are not averaged since the rate of interconversion of the diastereomeric complexes is slow compared to the nmr time scale.

Two interesting questions may be raised at this point. First, why should the diamine exchange rate be faster with the zinc complex of **3** than with the zinc complex of **4**? Second, why should the heterochiral ternary complex be more stable than the homochiral ternary complex when **4** is used while the two complexes are about equal in energy when **3** is used? It would be difficult to answer such questions for flexible complexes that can form many isomers. However the zinc complexes of **3** and **4** are highly rigid making it simpler to dissect and isolate the steric and electronic effects.

Compound **4** is expected to be less basic than **3** due to the electron withdrawing nature of the nitrile groups.¹² Thus the zinc complex of **4** is expected to be more Lewis acidic than that of **3**. It follows that the guest diamine should dissociate more slowly from the zinc complex of **4** than from the zinc complex of **3**. We suggest that this electronic effect may be a reason why the diamine exchange rate is faster with the zinc complex of **3** than with the zinc complex of **4**.

Scheme 2 shows the side views of the homochiral and heterochiral ternary zinc complexes formed between **3** or **4** with dpen. The phenoxy groups occupy axial positions due to metal coordination while the phenyl groups and the



Scheme 2. Side views of ternary complexes between (a) (S,S) -**3** and (R,R) -dpen; (b) (S,S) -**3** and (S,S) -dpen; (c) (S,S) -**4** and (R,R) -dpen; and (d) (S,S) -**4** and (S,S) -dpen.

cianoethyl groups are expected to occupy equatorial positions to avoid steric congestion with the metal (Figure 1).¹³ Molecular mechanics computation¹⁴ reveals that the heterochiral-3-dpen complex (Scheme 2a) is only slightly more stable than the homochiral-3-dpen complex (0.8 kcal/mol which translates to about 4 : 1 selectivity) while the heterochiral-4-dpen complex is significantly more stable than the homochiral-4-dpen complex (3.8 kcal/mol which translates to about 600 : 1 selectivity). This increase in selectivity going from 3 to 4 is in qualitative agreement with the nmr data. In the homochiral-4-dpen complex, one of the guest N-H and the host N-CH₂ groups are pointing directly at each other whereas in the heterochiral-4-dpen complex, these two groups are not pointing directly at each other. We suggest that the homochiral-4-dpen complex is less stable than the heterochiral-4-dpen complex because of the steric interaction between the guest N-H and the host N-CH₂ group of the former complex.

In conclusion we have developed a C₂ symmetric N₂O₂ ligand (**4**) that forms only a single isomer of an octahedral Zn(II) complex. The rigidity of the complex allows detailed understanding of molecular recognition of dpen and dach. The tactical placement of *N*-(2-cyanoethyl) substitution in the host diamine was found to be critical in the chiral recognition for both electronic and steric reasons: the electronic effect of the cyanoethyl groups in **4** results in slowing down the rate of dissociation of dpen from the metal and the steric effect of the cyanoethyl groups results in increasing the stereoselectivity of the recognition.

Experimental Section

Synthesis of **4**: Acrylonitrile (10.2 mmol) was added to a solution of **3** (4.1 mmol) dissolved in methanol (14 mL). The mixture was stirred for 48 hours at room temperature. After removal of the solvent, ether was added and the resulting solution was allowed to stand at room temperature for 3 days to give yellow crystals.

¹H NMR (400 MHz, CDCl₃) δ 7.19 (ddd, *J* = 8.0, 7.5 and 1.9 Hz, 2H), 6.88 (dd, *J* = 8.1, 0.9 Hz, 2H), 6.82 (dd, *J* = 7.5 and 1.8 Hz, 2H), 6.75 (ddd, *J* = 8.1, 8.0 and 1.1 Hz, 2H), 3.99 (s, 2H), 2.87 (m, 4H), 2.50 (td, *J* = 6.9 and 1.8 Hz, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 156.1, 130.0, 129.9, 123.3, 120.4, 118.0, 117.7, 68.4, 43.7, 18.4; HRMS (EI) calcd for C₂₀H₂₃N₄O₂⁺ (M+H⁺) 351.1821, found 351.1825.

Synthesis of (*S,S*)-**4**-Zn-(*R,R*)-dpen: Equimolar amounts of Zn(ClO₄)₂ (10 mM), dpen, and **4** (host) were mixed in methanol. The ternary complex precipitated out of solution upon addition of two equiv of NaOH to the reaction mixture. The crude product was recrystallized from methanol by slow evaporation to give colorless needles of the ternary complex. ¹H NMR (400 MHz, CD₃OD) δ 7.03-7.26 (m, 14H), 6.81 (ddd, *J* = 9.0, 4.5, 1.5 Hz, 2H), 6.55 (td, *J* = 7.1 Hz, 2H), 4.27 (s, 2H), 4.10 (s, 2H).

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- C₃₆H₄₄N₈O₅Zn, T = 150(1) K, orthorhombic, P 2₁ 2₁ 2₁, Z = 4, a = 11.5201(3) Å, b = 13.8898(3) Å, c = 23.1504(6) Å, α = 90°, β = 90°, γ = 90°, V = 3704.34(16) Å³, R₁ = 0.0420, wR₂ = 0.0838 for I > 2σ(I), GOF on F² = 0.943. Crystallographic data for the structure reported here have been deposited with the Cambridge Crystallographic Data Centre (Deposition No. CCDC-627889). That data can be obtained free of charge via www.ccdc.cam.ac.uk (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).
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