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Chiral Tropocoronands: Synthesis and Metal Complex Formation

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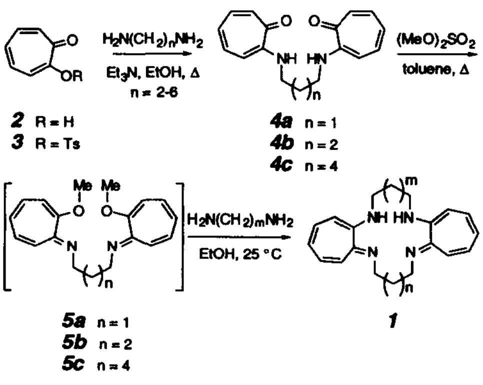
Abstract: The synthesis of several chiral tropocoronands based on 1,2-cyclohexanediamine (**7**) and 1,2-diphenylethylenediamine (**8**) has been accomplished. X-ray crystallography has confirmed the structure of two metallated derivatives, Cu(II)(TC-4,cyhex) (**9**) and Ni(II)(TC-4,cyhex) (**10**), that are indicative of the types of chiral complexes that can be formed from these systems. © 1997 Elsevier Science Ltd.

The use of metal complexes of chiral ligands to promote catalytic, asymmetric reactions for the generation of chiral molecules as single enantiomers continues as an active area of investigation.[1] Tropocoronands (**1**) represent of a ligand class with the potential to be modified with a chiral moiety and applied to enantioselective reactions.

Tropocoronands are macrocycles containing two cycloheptatriene rings and four nitrogens linked by two chains. They were first synthesized by Nakanishi, Lippard, and Nozoe.[2,3] Symmetrical tropocoronands where m = n = 2-6 have been made in a four-step synthesis from tropolone (**2**, Scheme 1). Either 2-tosyloxytropone (**3**)[4] or 2-chlorotropone can be made from tropolone and then reacted with the appropriate diamine to give diaminodiketones **4**. These diketones then give dialkoxydiimines **5** by treatment with dimethyl sulfate in refluxing toluene or with triethyloxonium tetrafluoroborate in refluxing chloroform/hexamethylphosphoramide. The resulting dialkoxides can then undergo amine displacement and ring closure at 25 °C to give the tropocoronands **1**. Reported yields in the cyclization are generally 20-40%, but only 2% when m = n = 2. However, Nozoe has demonstrated yields of 55-65% for closure to **1** (m = n = 3) using methyl fluorosulfate in methylene chloride as the alkylating agent.[5]

Scheme 1

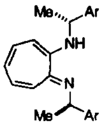


Recently unsymmetrical tropocoronands have been synthesized where the number of carbons of the simple straight-chain linkages is different (m ≠ n).[6] Compounds H_2(TC-3,4) (**1**, where m = 3, n = 4) and H_2(TC-4,5) (**1**, m = 4, n = 5) are the only unsymmetrical tropocoronands reported to date.

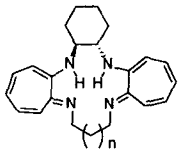
Lippard has studied tropocoronands as ligands for copper(I) and (II), rhodium(I), nickel(II), and cobalt(III).[6] The structures of these complexes have been characterized in detail. Ethanol solutions of salts of Fe(II) through Zn(II) have been found to form intense colors with methylene chloride solutions of tropocoronands where the linker chains contain 3-6 methylenes, suggesting that complexation of these substances with transition metal ions is general. Lippard has studied only simple achiral linker chains in tropocoronands. Incorporation of a chiral moiety into the tropocoronand macrocycle and subsequent study of metal complexes derived from such chiral ligands have not been reported. The only uses of a related ligand in asymmetric catalysis are those described by Brunner[7] and Lippard.[8] Tropolone derivative **6** was shown to induce asymmetry during the course of ketone hydrosilylation and 1,4-addition of cuprates to enones, respectively.

Many potential applications of chiral tropocoronand ligands to catalytic, enantioselective reactions can be envisioned. As a prelude to exploring these possibilities we describe here the synthesis of a set of chiral tropocoronand ligands, in both racemic and non-racemic form and the preparation of two metal complexes of one such system.

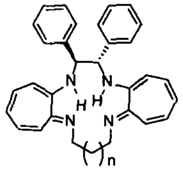
We have synthesized five tropocoronands that have chiral diamines incorporated into their macrocycle. These are unsymmetrical where one linker chain is chiral and the other is derived from simple straight chain α,ω-diamines containing 3, 4, or 6 carbons. Series **7a-c** is derived from *trans*-1,2-diaminocyclohexane and series **8b-c** from (*R**,*R**)-1,2-diphenyl-1,2-ethanediamine, both commercially available as either enantiomer. Using the synthesis outlined in Scheme 1, but substituting *trans*-1,2-diaminocyclohexane in the final step, we have made both racemic and non-racemic samples of H_2(TC-3,cyhex) (**7a**), H_2(TC-4,cyhex) (**7b**), and H_2(TC-6,cyhex) (**7c**). In analogous fashion we have used (*R**,*R**)-1,2-diphenyl-1,2-ethanediamine to synthesize H_2(TC-4,diphen) (**8b**) and H_2(TC-6,diphen) (**8c**). The syntheses proceeded well, although the yields in the cyclization step are low, as is typical for the synthesis of the simple achiral analogs like **1**. The diaminodiketones **4** are easily prepared in large quantities and are stable. The dimethoxydiimines **5** were prepared and used in the cyclization step the same day. All of the tropocoronands **7** and **8** are high melting, yellow to yellow-orange, crystalline compounds that can be isolated and purified easily by chromatography or recrystallization. Spectroscopic properties are in accord with their structure. Isolated yields of recrystallized material range from 12-31% in the cyclization. The H_2(TC-n,cyhex) series (**7**) seems to be more easily purified than the H_2(TC-n,diphen) derivatives (**8**).



6



7a n = 1
7b n = 2
7c n = 4

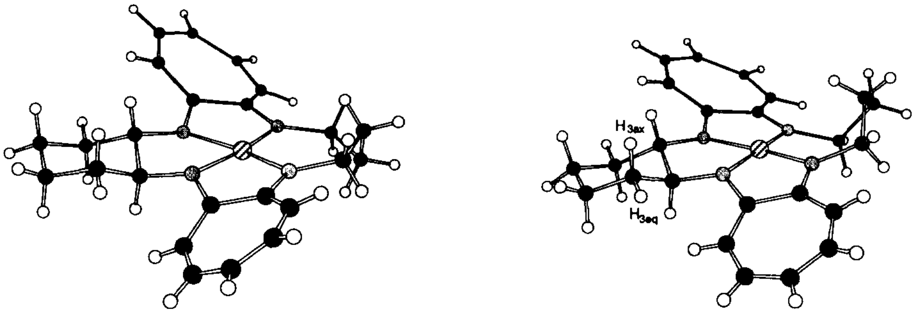


8a n = 1
8b n = 2
8c n = 4

Tropocoronand H_2(TC-6,cyhex) (**7c**) has been reacted with a variety of metal salts in the presence of a base to form solutions of colored complexes. For example, treatment of **7c** (THF, 0 °C) with two equivalents of *n*-BuLi followed by $CoCl_2$ (0 °C, THF), a dark brown solution was generated, indicative of complex formation. Also, when **7c** itself was mixed with $RhCl_3{\bullet}(H_2O)_3$/NaOAc, $FeBr_3$/NaOAc, or $Mn(OAc)_2{\bullet}(H_2O)_4$, colored solutions were immediately generated. We have not yet succeeded in structurally characterizing products from these reactions. The ligand H_2(TC-4,cyhex) (**7b**) also forms complexes with $Cu(OAc)_2{\bullet}(H_2O)$ and $Ni(OAc)_2{\bullet}(H_2O)_4$. In these two cases the resulting complexes **9** and **10** could be crystallized from a methylene chloride/ethanol mixture to give material suitable for X-ray crystallographic analysis. Chem 3D representations taken from the coordinates of the crystallographic structures of **9** and **10** are shown in Figure 1.

Complexes **9** and **10** represent the first structurally characterized metal complexes of chiral tropocoronands. They are also the first to contain a bridge as short as two carbons between two of the nitrogen atoms. The stereogenic centers on the cyclohexane ring impart chirality elsewhere in the molecule. In the solid state the carbon backbone of the 1,4-butanediyl bridge adopts a gauche$^+$ geometry in the complex derived from *S,S*-1,2-diaminocyclohexane. In the ^{1}H NMR spectrum for the nickel complex **10** the vicinal coupling constants through this backbone are typically either ~10 and ≤3 Hz. These data suggest that in solution the bridge is sufficiently mobile to render each of the four diastereotopic pairs of protons equivalent, yet the conformational preferences are strong enough to lead to well-defined anti- and gauche-like H-C-C-H dihedral angles through this bridge. Likewise, the two nearly planar tropylium rings are canted in a gauche$^+$-like fashion. Protons H_{3ax} and H_{3eq}, the cyclohexyl axial and equatorial pair nearest the tropylium rings (Figure 1), have a very large chemical shift difference, resonating at δ 1.25 and 2.69 ppm, respectively. Anisotropic effects from the cycloheptatriene ring are most likely responsible. The stereogenic elements create a chiral environment that meridially surrounds the metal. We hope to exploit this topology as we examine possible catalytic roles for these and similar complexes.

Figure 1 Chem3D™ Representations of the X-ray Crystal Structures of Cu Complex **9** and Ni Complex **10**.



9

10

In summary, we have achieved a synthesis of chiral tropocoronands. We have also shown that this class of ligands forms metal complexes quite easily. We plan to design and synthesize additional chiral tropocoronands and their metal complexes and to investigate their utility in asymmetric catalysis.

Representative Experimental Procedures:

(±)-H_2(TC-4,cyhex) (7b). Following the general procedure of Nozoe and Nakanishi,[3] dimethyl sulfate (2.77 g, 22.0 mmol) was added over 1 min to crude diaminodiketone **4b** (2.96 g, 10.0 mmol) in toluene (50 mL) at reflux. The mixture was refluxed for an additional 45 min. A dark insoluble oil was formed, which solidified on cooling. The mixture was extracted with water (3 x 100 mL), in which the solid dissolved. The combined aqueous layers were washed with chloroform (2 x 100 mL) and then made alkaline with 5% sodium carbonate (250 mL) to a pH of 9-10. The aqueous phase was extracted with chloroform (3 x 75 mL). The combined chloroform extracts were dried with anhydrous potassium carbonate, filtered, and concentrated to give crude dimethoxydiimine **5b** as a dark oil. The oil was dissolved in absolute ethanol (375 mL) in an addition funnel. In a second funnel (±)-*trans*-1,2-diaminocyclohexane (1.37 g, 12.0 mmol) was also dissolved in absolute ethanol (375 mL). The two solutions were added at the same rate over 3 h to a flask containing absolute ethanol (100 mL) with magnetic stirring. The resulting solution was stirred overnight. Removal of ethanol yielded 3 g of crude material, which was dissolved in chloroform (100 mL) and filtered through a 2-cm long column of basic alumina. The alumina was rinsed with chloroform (150 mL) to give a crude product containing **7b** as an orange solid (2.64 g). This crude tropocoronand was recrystallized from acetone to give **7b** (0.78 g, 2.09 mmol, 21%) sufficiently pure for further studies. Two additional recrystallizations from acetone gave analytically pure **7b**: mp 231-233 °C; ^{1}H NMR ($CDCl_3$, 400

MHz) δ 7.80 (br s, 2H), 6.75 (m, 4H), 6.30 (d, J = 11.0 Hz, 2H), 6.12 (m, 4H), 3.46 (m, 2H), 3.34 (ddd, J = 13.5, 2.5, and 2.5 Hz, 2H), 3.07 (t, J = 12.4 Hz, 2H), 2.50 (br d, J = 13.2 Hz, 2H), 1.90 (m, 4H), 1.60 (m, 2H), 1.47 (m, 2H), and 1.30 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 155.0, 154.9, 133.3, 132.7, 117.5, 110.4, 110.2, 61.5, 46.3, 30.2, 26.5, and 25.2; IR (KBr) 3436, 3248, 2929, 2857, 1587, 1546, 1513, 1463, 1381, 1271, 1212, and 727 cm^{-1}. HRMS (EI) calcd for $C_{24}H_{30}N_4$ 374.2470, found 374.2471. Anal. Calcd for $C_{24}H_{30}N_4$: C, 76.97; H, 8.07. Found: C, 77.13; H, 7.75.

(±)-Cu(TC-4,cyhex) (9). To a 50-mL round-bottom flask equipped with a stir bar was added (±)-**7b** (0.050 g, 0.134 mmol) and CH_2Cl_2 (16 mL). To this was added a 40 °C solution of $Cu(OAc)_2•1H_2O$ (0.027 g, 0.134 mmol) in absolute ethanol (11 mL). The resulting deep brown/burgundy solution was gently warmed with a heat gun and then allowed to stir for 15 minutes. The reaction was then concentrated to an approximate volume of 2 mL. The mixture was filtered, and the solid cake was washed with 1 mL of cold absolute ethanol to give analytically pure **9** as small burgundy crystals (46 mg, 80 %). X-ray quality single crystals (burgundy needles) were grown by slow diffusion of absolute ethanol into a methylene chloride solution of **9** (70 % recovery); IR (KBr) 2931, 1586, 1506, 1436, 1417, 1263, 1229, and 724 cm^{-1}. HRMS (FAB) calcd for $C_{24}H_{28}N_4Cu$ [M+1]$^+$ 436.1610, found 436.1667. Anal. Calcd for $C_{24}H_{28}CuN_4$: C, 66.11; H, 6.47, N, 12.85. Found: C, 66.22; H, 6.51, N, 12.66.

(±)-Ni(TC-4,cyhex) (10). ^{1}H NMR ($CDCl_3$, 500 MHz, assignments supported by ^{1}H-^{1}H COSY) δ 6.71 (dddd, J = ~10, ~9.5, 3.5 ,1 Hz, 2H, NC=CH-CH), 6.68 (dddd, J = ~10, ~9.5, 4.0, 1.5 Hz, 2H, N'C=CH-CH), 6.24 (brd, J = 10.8 Hz, 2H, NC=CH), 6.18 (brd, J = 11.3 Hz, 2H, N'C=CH), 6.08 (dd, J = 9.3, 9.3 Hz, 2H, NC=CH-CH=CH), 3.73 (m, 2H, R_2CHN), 3.25 (dddd, J = 13.9, ~2, ~2, ~2 Hz, 2H, NCHH'R), 3.15 (dd, J = 13.7, 9.6 Hz, 2H, NCHH'R), 2.69 (br d, J = 13.3 Hz, 2H, H_{3eq}), 2.03 (m, 2H, $NCH_2CHH'R$), 1.83 (m, 2H, $NCH_2CHH'R$), 1.75 (m, 2H), 1.43 (m, 2H), and 1.25 (m, 2H, H_{3ax}); IR (thin film) 2930, 1581, 1505, 1424, 1419, 1394, 1229, and 725 cm^{-1}. HRMS (FAB) calcd for $C_{24}H_{28}NiN_4$ [M+1]$^+$ 431.1667, found 431.1725. Anal. Calcd for $C_{24}H_{28}N_4Ni$: C, 66.85; H, 6.55, N, 12.99. Found: C, 66.94; H, 6.85, N, 12.72.

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