

Effect of Ligand Constraints upon the Stabilities and Potentials of Macrocyclic Polythiaether Complexes. Copper(II) and Copper(I) Complexes with Cyclohexyl and Phenyl Derivatives of [14]aneS₄ in Water, 80% Methanol, and Acetonitrile

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Synthetic procedures are described for the preparation of all 11 of the possible derivatives of the 14-membered macrocyclic tetrathiaether [14]aneS₄ (1,4,8,11-tetrathiacyclotetradecane), in which one or both of the ethylene bridges have been replaced by 1,2-benzene and/or *cis*- or *trans*-1,2-cyclohexane. The visible spectra of the copper(II) complexes formed with the derivatized ligands have been recorded in aqueous solution, in 80% methanol, and in acetonitrile; and the Cu^{II}L potentials have also been determined in these three solvents. Limited solubility of the uncomplexed ligands has hindered the measurement of the Cu^{II}L or Cu^IL stability constants in aqueous solution. However, it has proved possible to measure the Cu^{II}L stability constants in 80% methanol with all ligands except the dibenzo derivative using a spectrophotometric approach; and the Cu^IL stability constants have been measured by pulsed square-wave cyclic voltammetry in acetonitrile. The stability constants for the Cu^IL complexes in 80% methanol and the Cu^{II}L complexes in acetonitrile, though too large to be measured directly by these approaches, were calculated indirectly for each ligand system by means of the Nernst equation. The trends in the stability constant values in these two solvent matrices are relatively uniform with the Cu^{II}L stability constants for the cyclohexyl and phenyl derivatives *increasing* by about 10⁷-fold and 10⁸-fold, respectively, on going from 80% methanol to acetonitrile while the Cu^IL stability constants *decrease* by about 10⁸-fold. These solvent dependencies are primarily attributed to the differing abilities of the two solvents to coordinate with the two oxidation states of copper. For the Cu(II) complexes with the derivatized [14]aneS₄ ligands, the following trends are noted: (i) incorporation of a single cyclohexyl group increases the stability constant by 1.5 orders of magnitude as a result of a more favorable enthalpy; (ii) incorporation of a second *trans*-cyclohexyl group increases the stability constant by more than an additional 1.5 orders of magnitude for a total increase of more than 10³; (iii) for the *cis,cis*-dicyclohexyl derivatives, the *syn* isomer increases the overall stability by 4 orders of magnitude, but the *anti* isomer yields only a 10-fold increase; (iv) incorporation of a single benzene lowers the stability by about 3 orders of magnitude, while two benzenes lower the stability to the point where measurements could not be obtained. In the Cu(I) complexes, incorporation of either a cyclohexane or benzene increases the stability constant by about 10-fold. The effect of introducing a second cyclohexane ring results in stability constant increases of about 1- to 10-fold with no pattern apparent.

Introduction

The copper(II/I) complexes formed with macrocyclic polythiaethers exhibit some of the most positive potentials ever observed for this redox couple in aqueous solution ($E^{\circ} \approx 0.5$ – 0.8 V vs NHE).^{2,3} These high potential values, coupled with the intense visible absorption bands of the Cu^{II}L species, have materially aided the study of the electron-transfer kinetics and mechanisms of copper(II/I) systems⁴ and have made it feasible to probe the intriguing dual-pathway mechanism which appears to be characteristic of this redox couple.^{5–7}

Studies on the copper polythiaethers have been hampered by the very small stability constants of the Cu(II) complexes in aqueous solution. This feature is largely attributable to the weakness of Cu(II)–thiaether sulfur bonds.⁸ In addition, the uncomplexed cyclic polythiaethers tend to adopt an *exo* conformation in which the lone pairs on the sulfur donor atoms are oriented away from the ligand cavity,^{9,10} resulting in unfavorable enthalpic contributions to the complex formation process.^{8,10} It has been noted that the addition of appropriate

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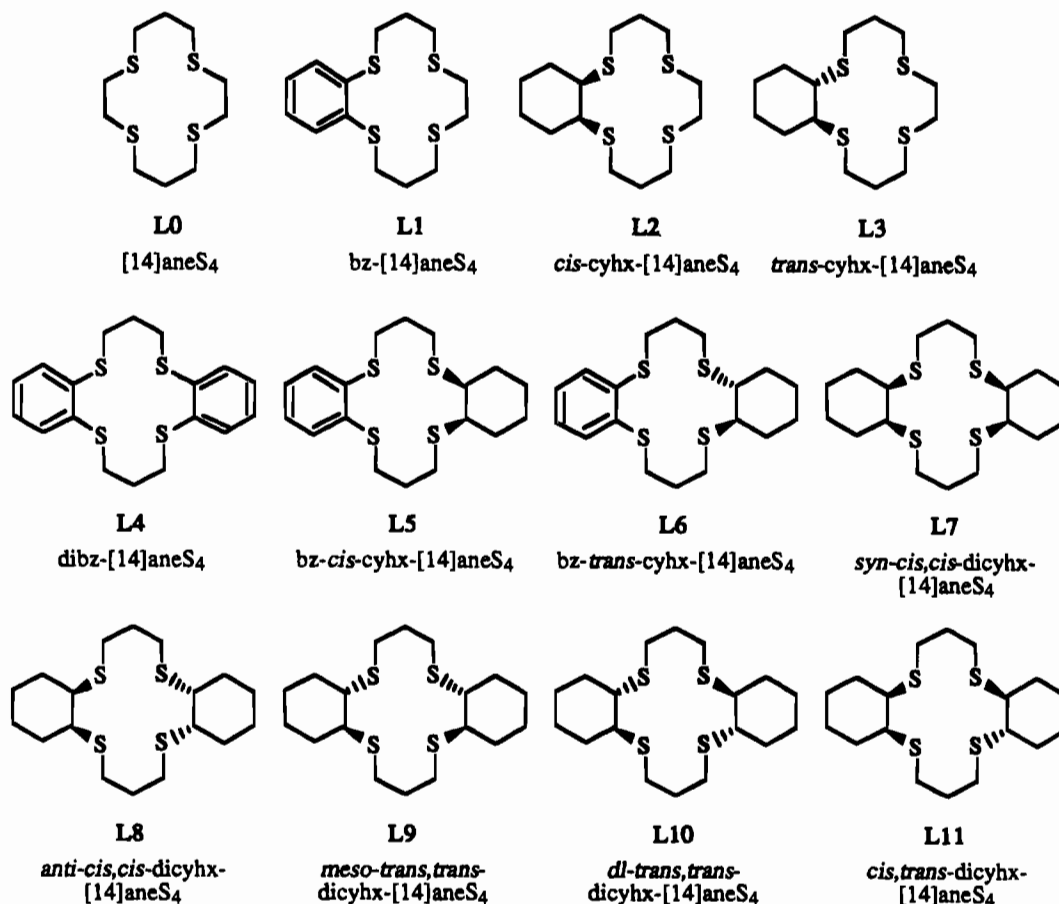


Figure 1. Ligands included in this work.

ring substituents should assist in the pre-organization of the ligand toward an *endo* conformation in which the lone pairs on the sulfurs are oriented toward the ligand cavity.¹¹ This should induce a more negative enthalpy of complexation resulting in increased stability constants.

Two series of derivatized ligands have been previously reported involving ring substitution on the central carbon of the trimethylene bridges in the 14-membered cyclic tetrathiaether 1,4,8,11-tetrathiacyclotetradecane ([14]aneS₄), a macrocycle with a cavity of optimal size to accommodate first-row transition-metal ions.¹² For the alcoholic derivatives, [14]aneS₄-ol and *syn*- and *anti*-[14]aneS₄-diol,¹³ we observed a decrease in the Cu(II) stability constants in aqueous solution with increasing -OH substitution, although no thermodynamic parameters were measured. Gellman^{11,14,15} prepared the corresponding *gem*-dimethyl derivatives, Me₂- and Me₄-[14]aneS₄ and succeeded in enhancing the stability constant of Ni^{II}L in nitromethane and Cu^{II}L in 80% methanol by a factor of about seven for each *gem*-dimethyl addition. Izatt and co-workers¹⁶

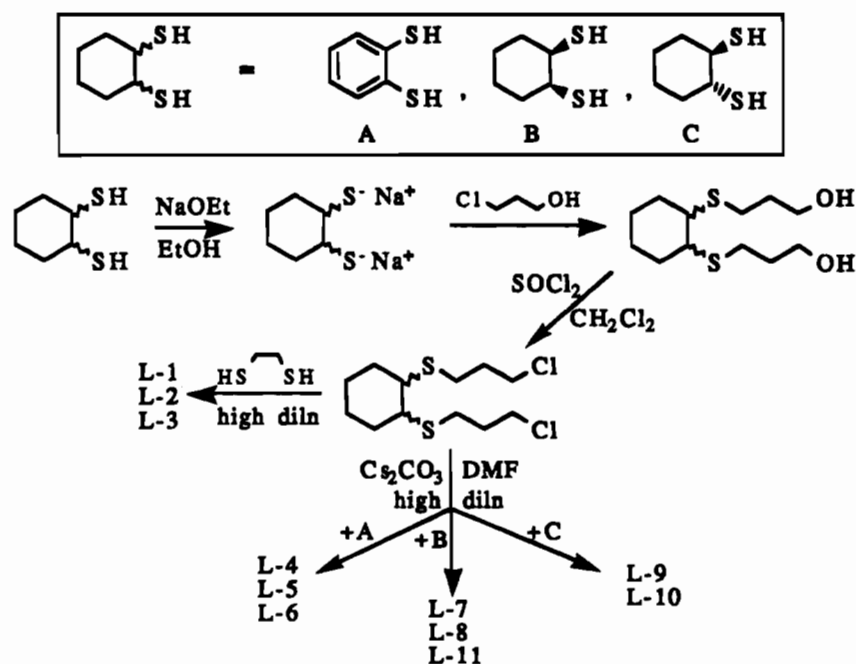
carried out subsequent thermodynamic measurements on the Cu(II) complexes in methanol-water mixtures and in acetonitrile and observed an increase in the enthalpy term for each *gem*-dimethyl group—with a small decrease in entropy partially counteracting the stability enhancement.

In the current work, synthetic procedures have been developed to substitute 1,2-benzene or *cis*- or *trans*-1,2-cyclohexane rings in place of one or both of the ethylene bridges in [14]aneS₄. The 11 new ligands reported herein (Figure 1), representing all possible combinations of these substituents, are expected to exhibit enhanced pre-organization toward an *endo* conformation. Since each of the five different diastereomers of dicyclohexyl-[14]aneS₄ exhibits a slightly different "twist" in the orientation of the four sulfur donor atoms, it was anticipated that these various derivatives would differ in their tendencies to pre-organize the donor atoms in a planar or non-planar array. Thus, the relative influence upon the Cu^{II}L and Cu^IL stability constants and, therefore, upon the Cu^{II}L potential values, should be significant.

In investigating the various substituted ligands, we have determined the formal potential values for these Cu^{II}L systems in aqueous solution, in 80% methanol-20% water (by weight), and in acetonitrile. The stability constants of the Cu^{II}L complexes in 80% methanol and of the Cu^IL complexes in acetonitrile were measured directly, the former being determined as a function of temperature. These values have then been combined with the potential measurements to permit the indirect calculation of the stability constants for the Cu^IL complexes in 80% methanol and the Cu^{II}L complexes in acetonitrile. Thus, we have now generated a nearly complete set of data for both oxidation states of copper in these two solvents, permitting

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Scheme 1



several useful comparisons regarding the effects of both the ring substituents and the solvent upon the complex stabilities.

Experimental Section

General Approach to Ligand Syntheses. Scheme 1 illustrates the generalized synthetic strategy exploited for all 11 ligands investigated in this study. Classical Williamson thioether condensation of bis(sodium thiolates) with 2 equiv of 3-chloropropanol affords the bis(3-hydroxypropyl) sulfides; these, in turn, are converted to the bis(3-chloropropyl) sulfide intermediates by thionyl chloride in nearly quantitative overall yields. Unlike the potent vesicant β -chloro sulfides, which are also prone to intrachain polymerization,¹⁷ the γ -chloro sulfides are stable and pose minimal vesicant hazard. In the absence of deprotonating base to form reactive thiolate anions, thiol reaction with γ -chloro sulfides is negligible at room temperature in DMF solution. This low reactivity facilitates the equimolar, single-solution addition of 1,2-dithiols and the bis(3-chloropropyl) sulfides to a large diluting pool of DMF containing suspended activating carbonate base at 80–110 °C. This method, initially demonstrated by Kellogg,¹⁸ affords the desired smallest macrocyclic oligomer in greatest yield as the first eluted condensation product, conveniently resolvable from higher molecular weight polymers during preparative column chromatography. However, when both synthones contain chiral centers, diastereomeric sets of products (L7, L8 and L9, L10) arise, which require more demanding resolution and X-ray crystallographic structure assignment.

General Separation and Characterization Techniques. Commercially available starting compounds were used as obtained from Aldrich Chemical Co., Milwaukee, WI. Preparative column chromatography was performed on J. T. Baker Inc. analyzed reagent silica gel (60–200 mesh) with Fisher Scientific or EM Science reagent solvents. All solvent mixtures for the following synthetic procedures are reported as volume percents. TLC assays were performed on 1 × 3 in., 250 μ m, MK6F Whatman glass plates (Catalog No. 4861-110) and observed by UV contrast at 254 nm or iodine vapor staining. Unless otherwise stated, routine characterizations of products were by the following: FT-IR (Nicolet 5 DXC); GC-mass spectrometry (Hewlett Packard 5971A, EI/CI mass selection detector/HP-5890 Series II GC system, with HP-5, part no. 19091J-433 capillary column) carried out

on dilute ether solutions of samples with injector temperatures of 180–220 °C and rapid temperature ramps up to 280 °C without significant decomposition of samples; and ¹H- and ¹³C-NMR run against TMS internal reference (Bruker AC, NR/80 or JEOL Eclipse 400 FT-NMR systems). For the NMR spectra, only ¹³C data are reported for convenience, since the complex overlapping ¹H-NMR patterns of the ligand series offer little *a priori* basis for distinction. Capillary melting points were determined with a Thomas-Hoover Uni-melt apparatus and are uncorrected. Elemental analyses were performed by analytical services of the University of Wisconsin–Milwaukee.

Preparation of Synthone Intermediates. The essential synthones 1,2-benzenedithiol¹⁹ and *trans*-1,2-cyclohexanedithiol²⁰ were prepared according to published procedures without complication at 10-fold increase in scale. Similarly, *cis*-1,2-cyclohexanedithiol was prepared according to a published procedure,²¹ but with several significant modifications. Precursor *cis*-1,2-cyclohexanediol was prepared by an improved method,²² which in turn was converted to *cis*-1,2-bis(*o*-tosyl)-cyclohexane by the method of Fieser.²³ On a 0.5 mol scale the bis-(tosylate) was converted to the *cis*-1,2-dithiocyanatocyclohexane by reaction with 6 molar equiv of KSCN per tosyl function in twice the reported proportional volume of diethylene glycol solvent at 70 °C for 2 weeks (rather than 100 °C for 3 days). Only in this fashion could isomerization to the *trans* product be minimized without limiting overall net conversion. Reductive cleavage of the dithiocyanato intermediate to the *cis*-1,2-cyclohexanedithiol proceeded as previously reported. The 1,2-bis(3-hydroxypropyl) sulfide derivatives of benzene and the cyclohexanes, as well as the corresponding 1,2-bis(3-chloropropyl) sulfide derivatives, were prepared in nearly quantitative yields by adaptation of our previously published procedures.²⁴ To minimize losses, the crude, filtered products were only stripped of solvents by Kugelrohr evaporation below 50 °C/0.05 Torr. After ¹³C-NMR confirmation of isomeric purity, they were utilized without further purification.

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Generalized Cyclocondensation Procedure Documented for 2,3-trans-Cyclohexano-1,4,8,11-tetrathiacyclotetradecane (L3). A mantle-heated, three-necked, 5 L flask was fitted with a T-line mechanical stirrer and two Claisen adapters. One of the Claisen adapters was fitted with an argon gas inlet adapter and an immersion thermometer. The other Claisen adapter was used to introduce reactants and also fitted to a Friedrich condenser through which the argon gas sweep was vented to an oil bubbler at about 1 mL/min. The flask was charged with finely milled anhydrous K_2CO_3 ,²⁵ 83 g (0.6 mol), suspended in 2 L of anhydrous DMF by efficient stirring, and heated to maintain 85–95 °C for the reaction duration. In 1 L of anhydrous DMF was dissolved *trans*-1,2-bis((3-chloropropyl)thio)cyclohexane, 75.3 g (0.25 mol), and 1,2-ethanedithiol, 20.95 mL (0.25 mol); this solution was then gravity filtered into a 2 L separatory funnel. From the bottom of the funnel the solution was delivered with a Waters/Millipore Model 590, dual-head, programmable HPLC pump into the reaction flask at a rate of 0.7 mL/min through a cork-mounted syringe needle in the remaining Claisen adapter opening. To inhibit air oxidation of the thiol, the argon stream was extended to bubble through the reagent mixture reservoir. After addition of reactants, heating was terminated and the reaction allowed to cool to room temperature with stirring; it was then suction filtered and DMF rotary vacuum evaporated at 80 °C/18 Torr. The filter cake and evaporation residue were dispersed in 1 L methylene chloride and 1 L water, and the aqueous phase discarded. The organic phase was washed twice with 0.5 L portions of 20% hydrochloric acid, dried with $MgSO_4$, vacuum filtered, and reconcentrated to 79 g of semi-solid residue. TLC analysis of the residue, 5:95 ethyl acetate/toluene, showed the major product component at $R_f = 0.55$. Elution chromatography through a 5 × 60 cm silica gel column, 50:50 cyclohexane/toluene, afforded combined elution fractions of the major component, 34.4 g, which was then recrystallized after charcoal treatment from 600 mL hexane to yield 28.8 g (35.8%) of colorless plates, mp = 91–92 °C. ^{13}C -NMR (20.15 MHz, $CDCl_3$), δ in ppm (multiplicity): 23.30(t), 29.51(t), 29.88(t), 29.95(t), 30.37(t), 31.42(t), 47.37(d). FT-IR (KBr), $\bar{\nu}$ in cm^{-1} (relative intensity): 2955(s), 2932(s), 1433(s), 1330(w), 1271(m), 1202(m), 1130(m), 1025(w), 902(w), 855(w), 826(w), 694(m). ET-MS, m/z (relative intensity): 322 M^+ (27), 106(100). Anal. Calcd for $C_{14}H_{26}S_4$: C, 52.12; H, 8.12. Found: C, 51.94; H, 8.20.

2,3-Benzo-1,4,8,11-tetrathiacyclotetradecane (L1). The washed residue, 12.2 g, from 0.04 mol scale condensation of 1,2-bis((3-chloropropyl)thio)benzene with 1,2-ethanedithiol in DMF/ Cs_2CO_3 showed the main product component at $R_f = 0.48$, 5:95 ethyl acetate/toluene. Gradient elution with cyclohexane, followed by 50:50 cyclohexane/toluene on a 2.5 × 55 cm silica gel column, resolved small amounts of intrachain condensation products, 2,3-benzo-1,4-dithiacycloheptane ($R_f = 0.60$), and 2,3-benzo-1,4,8-trithiacycloundecane ($R_f = 0.55$) from the desired component. The combined fractions were concentrated, 2.4 g, and twice recrystallized from 20:80 toluene/hexane with charcoal treatment to yield 1.38 g, 10.9%, colorless plates, mp = 116–117 °C. ^{13}C -NMR (20.15 MHz, $CDCl_3$), δ in ppm (multiplicity): 29.93(t), 29.99(t), 32.47(t), 33.01(t), 126.70(d), 129.55(t), 136.95(s). FT-IR (KBr), $\bar{\nu}$ in cm^{-1} (relative intensity): 3057(w), 2953(s), 2924(m), 2834(w), 1575(w), 1446(m), 1427(s), 1292(w), 1244(m), 1202(m), 1040(m), 843(w), 745(s). EI-MS, m/z (relative intensity): 316 M^+ (100), 153(81). Anal. Calcd for $C_{14}H_{20}S_4$: C, 53.12; H, 6.37. Found: C, 53.25; H, 6.40.

2,3-cis-Cyclohexano-1,4,8,11-tetrathiacyclotetradecane (L2). The washed residue, 31.0 g, from 0.1 mol scale condensation of *cis*-1,2-bis((3-chloropropyl)thio)cyclohexane and 1,2-ethanedithiol in DMF/ Cs_2CO_3 showed the main product component at $R_f = 0.45$, 5:95 ethyl acetate/toluene. Gradient elution as for L1 afforded 10.9 g of combined major component fractions as a waxy solid which was twice recrystallized with charcoal treatment from 300 mL 5:95 ethyl acetate/hexane to yield 9.1 g (28.5%) colorless plates, mp = 92–93 °C. ^{13}C -NMR (100.6 MHz, $CDCl_3$), δ in ppm (multiplicity): 23.37(t), 29.88(t), 30.14(t), 30.49(t), 31.33(t), 32.10(t), 49.63(d). FT-IR (KBr), $\bar{\nu}$ in cm^{-1} (relative intensity): 2926(s), 2880(s), 2841(m), 1440(m), 1415(m), 1250(m), 1200(w), 1140(w), 988(w), 906(w), 831(w), 762(w), 727-

(w), 692(w), 656(w). ET-MS, m/z (relative intensity): 322 M^+ (26), 106(100). Anal. Calcd for $C_{14}H_{26}S_4$: C, 52.12; H, 8.12. Found: C, 52.44; H, 8.30.

2,3,9,10-Dibenzo-1,4,8,11-tetrathiacyclotetradecane (L4). The washed residue, 33.8 g, from 0.1 mol scale condensation of 1,2-bis((3-chloropropyl)thio)benzene and 1,2-benzenedithiol in DMF/ K_2CO_3 showed the main product component at $R_f = 0.65$, toluene. Flash chromatography with toluene on a 2.5 × 55 cm silica gel column afforded 14.8 g of combined elution fractions of solid major component, which was recrystallized with charcoal treatment from 300 mL toluene to yield colorless plates, 13.08 g (35.9%), mp = 153–154 °C. ^{13}C -NMR (20.15 MHz, $CDCl_3$), δ in ppm (multiplicity): 27.16(t), 31.48(t), 126.69(d), 131.59(d), 136.45(s). FT-IR (KBr), $\bar{\nu}$ in cm^{-1} (relative intensity): 3052(w), 2924(w), 2911(w), 2832(w), 1588(w), 1447(m), 1427(s), 1244(m), 1236(w), 1138(w), 1040(m), 744(s). EI-MS, m/z (relative intensity): 364 M^+ (95), 182(100). Anal. Calcd for $C_{18}H_{20}S_4$: C, 59.33; H, 5.54. Found: C, 59.49; H, 5.66.

2,3-Benzo-9,10-cis-cyclohexano-1,4,8,11-tetrathiacyclotetradecane (L5). The washed residue, 32.9 g, from 0.095 mol scale condensation of 1,2-bis((3-chloropropyl)thio)benzene and *cis*-1,2-cyclohexanedithiol in DMF/ K_2CO_3 showed the main product component at $R_f = 0.48$, toluene. Flash chromatography as for L4 afforded 7.0 g of combined elution fractions of solid major component, which was three times recrystallized with charcoal treatment from 200 mL 20:80 ethyl acetate/hexane to yield colorless powder, 5.15 g (14.7%), mp = 103–104 °C. ^{13}C -NMR (100.6 MHz, $CDCl_3$), δ in ppm (multiplicity): 23.58(t), 27.94(t), 30.18(t), 31.10(t), 33.18(t), 48.18(d), 126.75(d), 130.82(d), 137.09(s). FT-IR (KBr), $\bar{\nu}$ in cm^{-1} (relative intensity): 3044(w), 2932(s), 2925(s), 2883(m), 2855(m), 1580(w), 1426(s), 1401(m), 1329(w), 1025(w), 997(w), 836(w), 735(s), 694(w). EI-MS, m/z (relative intensity): 370 M^+ (88), 182(100). Anal. Calcd for $C_{18}H_{26}S_4$: C, 58.36; H, 7.08. Found: C, 58.44; H, 7.05.

2,3-Benzo-9,10-trans-cyclohexano-1,4,8,11-tetrathiacyclotetradecane (L6). The washed residue, 24.5 g, from 0.068 mol scale condensation of 1,2-bis((3-chloropropyl)thio)benzene and *trans*-1,2-cyclohexanedithiol in DMF/ Cs_2CO_3 showed the main product component at $R_f = 0.60$, toluene. Flash chromatography as for L4 afforded 5.1 g of combined elution fractions of semi-solid major component, which was twice recrystallized with charcoal treatment from 200 mL 15:85 hexane/toluene to yield colorless needles, 4.68 g (18.6%), mp = 76–78 °C. ^{13}C -NMR (100.6 MHz, $CDCl_3$), δ in ppm (multiplicity): 23.17(t), 29.19(t), 29.75(t), 29.79(t), 33.18(t), 47.65(d), 126.68(d), 130.06(d), 137.19(s). FT-IR (KBr), $\bar{\nu}$ in cm^{-1} (relative intensity): 3051(w), 2928(s), 2916(s), 2847(m), 1574(w), 1450(m), 1440(s), 1403(m), 1244(m), 1202(w), 1075(w), 1005(w), 834(w), 745(s), 687(w). EI-MS, m/z (relative intensity): 370 M^+ (94), 182(100). Anal. Calcd for $C_{18}H_{26}S_4$: C, 58.36; H, 7.08. Found: C, 58.57; H, 7.11.

Separation of Diastereomeric Mixture of *syn*-2,3,9,10-cis,cis-Dicyclohexano-1,4,8,11-tetrathiacyclotetradecane (L7) and *anti*-2,3,9,10-cis,cis-Dicyclohexano-1,4,8,11-tetrathiacyclotetradecane (L8). The washed residue, 18.0 g, from 0.05 mol scale condensation of *cis*-1,2-bis((3-chloropropyl)thio)cyclohexane and 1,2-cyclohexanedithiol in DMF/ Cs_2CO_3 showed two main product components at $R_f = 0.55$ (isomer 1) and $R_f = 0.43$ (isomer 2), methylene chloride. Flash chromatography as for L4 afforded 5.5 g of a mixture of the two components separated from other condensation products. ^{13}C -NMR showed ten peaks consistent for the diastereomeric mixture, with relative intensities of the methine peaks indicating an approximate 6:4 isomer ratio. Resolution of isomers was achieved by careful methylene chloride elution chromatography on 4 × 60 cm silica gel columns. Two consecutive column runs were required to harvest combined crops of 3.44 g (isomer 1) and 1.69 g (isomer 2). Traces of alternative isomer were removed from the major isomer by charcoal treatment recrystallization. Isomers 1 and 2 are assigned as L8 and L7, respectively.

Recrystallization of isomer 1 (L8) from 150 mL 50:50 ethyl acetate/ethanol yielded colorless crystals, 2.91 g (15.5%), mp = 182–184 °C. ^{13}C -NMR (20.15 MHz, $CDCl_3$), δ in ppm (multiplicity): 23.40(t), 28.18(t), 30.34(t), 30.39(t), 48.82(d). FT-IR (KBr), $\bar{\nu}$ in cm^{-1} (relative intensity): 2925(s), 2855(s), 1444(m), 1416(w), 1294(w), 1250(m), 1202(w), 1005(w), 988(w), 829(w), 787(w), 695(w). EI-MS, m/z (relative intensity): 376 M^+ (28), 106(100). Anal. Calcd for $C_{18}H_{32}S_4$: C, 57.39; H, 8.56. Found: C, 57.31; H, 8.50.

(25) Superior yields are obtained with cesium carbonate (see ref 18); however, potassium carbonate is more cost effective for larger scale preparations.

Recrystallization of isomer 2 (L7) from 100 mL ethanol yielded colorless plates, 1.49 g (7.9%), mp = 113–114 °C. $^{13}\text{C-NMR}$ (20.15 MHz, CDCl_3), δ in ppm (multiplicity): 23.63(t), 29.17(t), 30.73(t), 31.55(t), 49.24(d). FT-IR (KBr): 2925(s), 2854(s), 1454(w), 1444(m), 1412(w), 1295(w), 1256(m), 1204(w), 991(m), 905(w), 834(w), 829(w), 779(w), 695(w) cm^{-1} . EI-MS, m/z (relative intensity): 376 (30), 106(100). Anal. Calcd for $\text{C}_{18}\text{H}_{32}\text{S}_4$: C, 57.39; H, 8.56. Found: C, 57.54; H, 8.64.

Separation of Diastereomeric Mixture of *meso*-2,3,9,10-*trans*-, *trans*-Dicyclohexano-1,4,8,11-tetrathiacyclotetradecane (L9) and *d,l*-2,3,9,10-*trans*-, *trans*-Dicyclohexano-1,4,8,11-tetrathiacyclotetradecane (L10). The washed residue, 21.4 g, from 0.06 mol scale condensation of *trans*-1,2-bis((3-chloropropyl)thio)cyclohexane and *trans*-1,2-cyclohexanedithiol in DMF/ Cs_2CO_3 showed the major product by TLC analysis as an unresolvable band at $R_f = 0.50$ – 0.55 , toluene; or $R_f = 0.45$ – 0.55 , methylene chloride. Flash chromatography as for L4 afforded 6.3 g of the major product component separated from other condensation products. $^{13}\text{C-NMR}$ analysis showed ten carbon peaks consistent for the diastereomeric mixture, with relative intensities of the methine peaks indicating an approximately equal isomer ratio. Separation of diastereomers was achieved by fractional recrystallization. $^{13}\text{C-NMR}$ was used to assay fractionation. X-ray crystallography established the identity of L9.²⁶

Recrystallization of the 6.3 g isomer mixture from 300 mL 40:60 hexane/toluene, followed by two recrystallizations with charcoal treatment of isolated solids, yielded colorless needles of L9, 2.67 g (11.8%), mp = 162–164 °C. $^{13}\text{C-NMR}$ (20.15 MHz, CDCl_3), δ in ppm (multiplicity): 24.06(t), 28.77(t), 29.02(t), 31.17(t), 46.38(d); FT-IR (KBr), $\bar{\nu}$ in cm^{-1} (relative intensity): 2924(s), 2855(s), 1441(m), 1420(w), 1329(w), 1300(w), 1250(w), 1194(w), 1117(w), 1040(w), 984(m), 829(w), 787(w), 752(w). EI-MS, m/z (relative intensity): 376 M^+ (32), 106(100). Anal. Calcd for $\text{C}_{18}\text{H}_{32}\text{S}_4$: C, 57.39; H, 8.56. Found: C, 57.26; H, 8.44.

Three recrystallizations of the filtrate residues from the initial 6.3 g isomer mixture in 200 mL hexane with charcoal treatment yielded L10 as a colorless powder, 2.13 g (9.4%), mp = 111–114 °C. $^{13}\text{C-NMR}$ (20.15 MHz, CDCl_3), δ in ppm (multiplicity): 23.67(t), 30.52(t), 30.73(t), 30.96(t), 49.17(d). FT-IR (KBr) 2930(s), 2855(m), 1441(m), 1422(w), 1292(w), 1250(m), 1202(m), 1125(w), 1010(w), 907(w), 829(w), 702(w), 617(w) cm^{-1} . EI-MS, m/z (relative intensity): 376 M^+ (26), 106(100). Anal. Calcd for $\text{C}_{18}\text{H}_{32}\text{S}_4$: C, 57.39; H, 8.56. Found: C, 57.66; H, 8.75.

2,3-*cis*-9,10-*trans*-Dicyclohexano-1,4,8,11-tetrathiacyclotetradecane (L11). The washed residue, 34.8 g, from 0.1 mol scale condensation of *trans*-1,2-bis((3-chloropropyl)thio)cyclohexane and *cis*-1,2-cyclohexanedithiol in DMF/ K_2CO_3 showed the major product component at $R_f = 0.52$, toluene. Flash chromatography as for L4 afforded 9.1 g of combined elution fractions of waxy solid main component, which was twice recrystallized with charcoal treatment from 300 mL hexane to yield a colorless powder, 7.96 g (21.2%), mp = 103–105 °C. $^{13}\text{C-NMR}$ (100.6 MHz, CDCl_3), δ in ppm (multiplicity): 22.68(t), 23.87(t), 24.15(t), 24.36(t), 27.32(t), 28.89(t), 28.97(t), 30.03(t), 30.52(t), 30.56(t), 30.73(t), 30.86(t), 30.97(t), 31.58(t), 47.01(d), 47.67(d), 47.72(d), 49.94(d). FT-IR (KBr), $\bar{\nu}$ in cm^{-1} (relative intensity): 2924(s), 2855(s), 1446(m), 1329(w), 1250(m), 1202(w), 1117(w), 1046(m), 928(w), 814(w), 787(w), 709(w), 694(w). EI-MS, m/z (relative intensity): 376 M^+ (27), 106(100). Anal. Calcd for $\text{C}_{18}\text{H}_{32}\text{S}_4$: C, 57.39; H, 8.56. Found: C, 57.42; H, 8.65.

Other Reagents. Copper(II) and mercury(II) perchlorate salts were prepared by the slow addition of reagent grade perchloric acid (G. Frederick Smith Chemical Co.) to reagent grade copper carbonate (MCB Manufacturing Chemists) or mercuric oxide (J. T. Baker) followed by recrystallization as previously described.²⁷ [WARNING: Metal perchlorate salts are potentially explosive; the salts should never be heated to dryness nor subjected to shock!] Sodium perchlorate was similarly prepared by the slow addition (with cooling) of perchloric acid to reagent grade sodium hydroxide followed by recrystallization. For the

preparation of $\text{CuClO}_4 \cdot 4\text{CH}_3\text{CN}$, copper(II) perchlorate was refluxed in acetonitrile with copper metal shot (99.99%, Fisher Scientific) at 90 °C over a water bath and cooled to form white crystals; these were collected by gravity filtration and allowed to dry on a filter paper before storing in a vacuum desiccator.²⁸ Solutions of both copper(II) and mercury(II) salts in water or 80% methanol were standardized by titration with aqueous EDTA. Similarly, copper(I) solutions in acetonitrile were first oxidized to copper(II) and then titrated with aqueous EDTA. All ligand solutions were standardized spectrophotometrically by either direct or displacement mol ratio plots as outlined in the next section. Reagent grade ferrocene was obtained from Sigma Chemical Co. and was used without further purification. All water utilized was distilled and then deionized. Reagent grade methanol and HPLC grade acetonitrile were obtained from EM Science and Fisher Scientific, respectively. No attempt was made to dry the latter solvent since it was shown that all experimental parameters were essentially unaffected by the addition of small amounts of water.

Instrumentation. All ultraviolet and visible spectra were obtained using a Hewlett-Packard 8452A Diode Array spectrophotometer. Quantitative absorbance measurements, including stability constant determinations, were made using a Cary Model 17D dual-beam recording spectrophotometer equipped with a thermostatted cell holder. All cyclic voltammetric measurements were made with a Bioanalytical Systems BAS-100 Electrochemical Analyzer (Bioanalytical Systems, Inc., Lafayette, IN) equipped with a glassy carbon disk working electrode, a platinum wire auxiliary electrode, and a Ag/AgCl reference electrode containing 3 M NaCl, for which $E^\circ = 0.197$ V vs NHE (the use of NaCl, rather than KCl, prevented the possible precipitation of KClO_4 at the liquid junction). The ferrocenium ion/ferrocene redox couple was used as an internal reference for all potentiometric measurements in 80% methanol and in acetonitrile. Potentiometric titrations were conducted using an Orion 720A pH meter equipped with a Pt wire indicating electrode and a Ag/AgCl reference electrode (as above). The solutions were contained in a jacketed beaker through which water was circulated from a constant temperature bath to maintain the temperature at 25.0 ± 0.1 °C.

Results

Ultraviolet–Visible Spectra. Dissolution of the 11 derivatives of [14]ane S_4 in solutions of $\text{Cu}(\text{ClO}_4)_2$ yielded colored solutions ranging from deep blue to rose in each of the three solvents investigated: water, 80% methanol, and acetonitrile. However, it was evident that the phenyl derivatives form very weak complexes which could not be adequately studied in aqueous solution or 80% methanol. In acetonitrile, the three monophenyl derivatives were studied only with difficulty; solutions of the diphenyl derivative bleached almost immediately, preventing the cumulation of useful data.

All spectral measurements were conducted in a medium of 0.10 M perchlorate ion. The visible spectrum for each Cu^{II} L complex was obtained at ambient temperature in all three solvents while the ultraviolet spectrum was examined only in acetonitrile. All Cu^{II} L species exhibited spectra similar to that previously noted for $\text{Cu}^{\text{II}}([\text{14}]\text{aneS}_4)$ ²⁹ with peaks occurring in the vicinity of 255, 390 and 570 nm. Typical molar absorptivity values for these three wavelengths are 2600, 8000, and 2100 $\text{M}^{-1} \text{cm}^{-1}$, respectively. For the peak in the vicinity of 390 nm (assigned to $\text{S} \rightarrow \text{Cu}(\text{II})$ charge transfer),³⁰ significant variations were noted in the molar absorptivity values as a function of both ligand and solvent. For the phenyl derivatives, the ultraviolet peak could not be easily distinguished from the strong ligand absorbance in this region; and, for these same systems, the peak near 570 nm tended to be obscured by the

(26) Aronne, L. A.; Heeg, M. J.; Ochrymowycz, L. A.; Rorabacher, D. B. Submitted for publication.
(27) Rorabacher, D. B.; Blencoe, B. J.; Parker, D. W. *Anal. Chem.* **1972**, *44*, 2339–2346.

(28) Hathaway, B. J.; Holah, D. G.; Postlethwaite, J. D. *J. Chem. Soc.* **1961**, 3215–3218.
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(30) Ferris, N. S.; Woodruff, W. H.; Rorabacher, D. B.; Jones, T. E.; Ochrymowycz, L. A. *J. Am. Chem. Soc.* **1978**, *100*, 5939–5942.

Table 1. Visible (and Ultraviolet) Absorbance Peaks and Molar Absorptivity Values for Copper(II)–Tetrathiaether Complexes in Aqueous Solution, 80% Methanol, and Acetonitrile at 25 °C, $\mu = 0.10 \text{ M} (\text{ClO}_4^-)^a$

complexed ligand	aqueous		80% methanol		acetonitrile		
	$\lambda_{\text{max}} [\epsilon/10^3]^b$	$\lambda_{\text{max}} [\epsilon/10^3]^b$	$\lambda_{\text{max}} [\epsilon/10^3]^b$	$\lambda_{\text{max}} [\epsilon/10^3]^b$	$\lambda_{\text{max}} [\epsilon/10^3]^b$	$\lambda_{\text{max}} [\epsilon/10^3]^b$	$\lambda_{\text{max}} [\epsilon/10^3]^b$
[14]aneS ₄ (L0)	390 [8.0]	570 [1.9]	390 [10.56(5)]	564 [1.56]	252 [2.6]	390 [8.52(3)]	560 [2.0]
bz-[14]aneS ₄ (L1) ^c			382	≈564 ^d	<i>e</i>	384 [4.97(1)]	580 [2.0]
<i>cis</i> -cyhx-[14]aneS ₄ (L2)	390 [7.4]	570 [2.0]	390 [8.40(3)]	572 [2.1]	258 [2.6]	394 [8.27(9)]	556 [2.4]
<i>trans</i> -cyhx-[14]aneS ₄ (L3)	388 [8.9]	558 [1.8]	388 [9.80(2)]	566 [1.3]	255 [2.6]	392 [11.5(1)]	538 [2.0]
bz- <i>cis</i> -cyhx-[14]aneS ₄ (L5) ^c	384 [5.7(7)]		388 [9.8(9)]	≈558 ^d	<i>e</i>	393 [6.19(6)]	562 [2.5]
bz- <i>trans</i> -cyhx-[14]aneS ₄ (L6) ^c	384 [8(1)]		388	≈580 ^d	<i>e</i>	391 [6.52(5)]	562 [2.4]
<i>syn-cis,cis</i> -dicyhx-[14]aneS ₄ (L7)	392 [8.6(4)]	570 [2.7]	392 [6.25(4)]	≥568 [1.4]	262 [2.7]	394 [8.04(2)]	557 [2.4]
<i>anti-cis,cis</i> -dicyhx-[14]aneS ₄ (L8)	396 [9.1]	552 [1.8]	394 [8.13(3)]	548 [1.2]	284 [2.3]	398 [12.0(3)]	520 [1.7]
<i>meso-trans,trans</i> -dicyhx-[14]aneS ₄ (L9)	388 [9.6(1)]	530 [2.0]	388 [12.17(5)]	538 [0.94]	258 [3.2] ^d	390 [13.8(1)]	520 [2.1]
<i>dl-trans,trans</i> -dicyhx-[14]aneS ₄ (L10)	390 [4.6]	564 [1.5]	394 [6.80(2)]	566 [1.2]	278 [3.1]	398 [8.09(8)]	556 [2.1]
<i>cis,trans</i> -dicyhx-[14]aneS ₄ (L11)	390 [8.1(1)]	560 [2.2]	390 [6.54(9)]	566 [1.5]	268 [2.7]	394 [9.71(7)]	548 [2.2]

^a The characteristic Cu^{II}L peak in the ultraviolet region is recorded here only for acetonitrile as solvent; the molar absorptivity values (in brackets) for this latter peak are typically in the range of $(2.6\text{--}3.1) \times 10^3 \text{ M}^{-1} \text{ cm}^{-1}$. ^b All wavelengths are in nm; all molar absorptivity values are in units of $\text{M}^{-1} \text{ cm}^{-1}$ and have been multiplied by 10^{-3} ; digits in parentheses following molar absorptivity values represent the standard deviation in terms of the last digit listed; thus, 10.56(5) represents 10.56 ± 0.05 . ^c The ligands containing benzene substituents are not sufficiently soluble in water and 80% methanol to permit an accurate determination of the molar absorptivity values by the approach used; estimated values are given where possible. ^d Peak is relatively broad and obscured by presence of large excess of solvated Cu(II). ^e The ultraviolet peaks for the benzyl derivatives tend to be buried under the ligand spectrum.

absorbance peak for solvated Cu(II) since a large excess of the metal ion was required to generate significant complex formation.

In water, reasonably accurate values of the Cu^{II}L molar absorptivities were obtained for the peak in the vicinity of 390 nm for each complex by means of a spectrophotometric displacement–mole ratio plot in which a standard Hg(II) solution was incrementally added to a ligand solution containing a large excess of solvated Cu(II) ion and 1 M HClO₄.³¹ The total ligand concentration was determined from the volume of Hg(II) solution required to displace the Cu(II) completely and the molar absorptivity was then calculated from the initial absorbance prior to the addition of any Hg(II).

In acetonitrile, the Cu(II) complexes were much more stable,¹⁶ thereby permitting the ligand concentration and the Cu^{II}L molar absorptivity to be determined from a direct mol ratio plot of ligand against a Cu(ClO₄)₂ solution. For 80% methanol, the molar absorptivity values were determined in conjunction with the stability constant determinations as outlined below. For all three solvents, molar absorptivity values for the peak in the vicinity of 570 nm (and the peak near 255 nm for acetonitrile) were then estimated from the ratio of the peak heights. Peak maxima and molar absorptivity values for all three solvents are listed in Table 1.

Potential Measurements. In both aqueous solution and acetonitrile, slow scan cyclic voltammograms (5–10 mV s⁻¹) provided direct measurements of the half-wave potentials for the Cu^{II}L systems. For CV measurements in acetonitrile, an aqueous Ag/AgCl electrode was utilized with the ferrocene/ferrocenium ion redox couple added as an internal reference standard; all potential values were referenced to this couple and were corrected to NHE based on the assumption that $E^f \equiv 0.340 \text{ V}$ for Fc⁺/Fc in acetonitrile.³² For both of these solvents, the $E_{1/2}$ values are assumed to approximate the formal potential values, E^f , for all systems studied.

In the case of the 80% methanol measurements, slow-scan CV measurements often did not provide unequivocal potential values since two overlapping anodic peaks appeared for some systems at the slowest accessible scan rates.³³ Thus, for the latter solvent, potentiometric titrations of the Cu^{II}L complexes were conducted using ferrocene as the reductant so that all Cu^{II}L potentials could be referenced to that of the Fc⁺/Fc redox couple. Although the potential breaks for these titrations were relatively small, accurate potential measurements could still be obtained provided that the concentrations of the initial Cu^{II}L and ferrocene solutions were known. The absolute potential values were referenced to an aqueous Ag/AgCl reference electrode and were corrected to aqueous NHE by adding 0.197 V to the measured potentials.³⁴

The apparent formal potential values for all Cu^{II}L systems in water, in 80% methanol, and in acetonitrile are listed in Table 2. All values are for 25 °C with an ionic strength of 0.10 M (NaClO₄ for acetonitrile and 80% methanol, NaClO₄/HClO₄ in water).³⁵

Stability Constant Measurements in 80% Methanol. Since the perchlorate ion concentration was maintained constant throughout this work, no corrections were made for the formation of perchlorate adducts of the type which have been previously detected.^{8,16,36} Thus, all Cu^{II}L stability constants are

- (31) Since some of the Cu^{II}L complexes were of relatively low stability, a large excess of Cu(II) was utilized to ensure the complete complexation of the ligand. Large excesses of perchlorate ion have also been shown to stabilize many of the Cu^{II}L species (see ref 8). In aqueous solution, the Hg^{II}L complexes were sufficiently stable to provide reasonably sharp breaks in the absorbance curves at the stoichiometric equivalence points.
- (32) Koeppe, H.-M.; Wendt, H.; Strehlow, H. *Z. Elektrochem.* **1960**, *64*, 483–491.

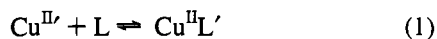
- (33) Similar results have been observed previously for [14]aneS₄ and its diol derivatives: Bernardo, M. M.; Robandt, P. V.; Schroeder, R. R.; Rorabacher, D. B. *J. Am. Chem. Soc.* **1989**, *111*, 1224–1231; cf. ref 3.
- (34) The 0.197 V potential for an aqueous saturated Ag/AgCl electrode is taken from: Ives, J. G. D.; Janz, G. J. *Reference Electrodes*; Academic: New York, 1961. For potentiometric measurements in 80% methanol using an aqueous reference electrode, corrections should also be made for the liquid junction potential which is estimated to be about -0.152 V {(a) Alfenaar, M.; de Ligny, C. L. *Recl. Trav. Chim. Pays-Bas* **1967**, *86*, 1185–1190; see Table II and Figure 1. (b) Douheret, G. *Bull. Soc. Chim. Fr.* **1968**, 513–521}. However, such corrections were not made in this work since the Cu(II)_{soln}/Cu(0) potential value utilized from the literature was presumed not to be corrected for the liquid junction potential (*vide infra*). Since the same values were applied to all measurements, any errors in these values should be consistent in all subsequent calculations; i.e., the relative values reported are internally consistent. In fact, all potential values in 80% methanol were assigned relative to the measured potential of ferrocene (0.525 V) as listed in Table 2.
- (35) In making the CV measurements, the scan rates were generally varied over the range of 10–500 mV for which the $E_{1/2}$ values at 25 °C were relatively constant.

Table 2. Formal Potentials for Copper(II)–Tetrathiaether Complexes in Aqueous Solution and Acetonitrile at Ambient Temperature (ca. 23 °C) and in 80% Methanol at 25 °C; $\mu = 0.10$ M (ClO_4^-)

complexed ligand	$E_{\text{Cu}^{\text{II}}/\text{Cu}^{\text{I}}}$, V vs aqueous NHE		
	H_2O^a	80% CH_3OH^b	CH_3CN^c
reference system: ferrocene	0.400 ^d	0.525 ^e	0.340 ^d
solvent	0.153/0.159 ^g	0.204 ^h	0.941
[14]aneS ₄ (L0)	0.58 ⁱ	0.697, 0.69 ^j	0.55
bz-[14]-aneS ₄ (L1)			0.80
cis-cyhx-[14]aneS ₄ (L2)	0.536	0.651	0.51
trans-cyhx-[14]aneS ₄ (L3)	0.600	0.697	0.54
bz-cis-cyhx-[14]aneS ₄ (L5)	0.890		0.73
bz-trans-cyhx-[14]aneS ₄ (L6)	0.784		0.72
syn-cis,cis-dicyhx-[14]aneS ₄ (L7)	0.569	0.581	0.422
anti-cis,cis-dicyhx-[14]aneS ₄ (L8)	0.665	0.619	0.55
meso-trans,trans-dicyhx-[14]aneS ₄ (L9)	0.584	0.737 ^k	0.435
dl-trans,trans-dicyhx-[14]aneS ₄ (L10)	0.694	(0.699) ^l	0.600
cis,trans-dicyhx-[14]aneS ₄ (L11)	0.600	0.646	0.480

^a Potential values in water were measured by cyclic voltammetry against an aqueous Ag/AgCl reference electrode; corrections to NHE are based on the assumption that the potential for this electrode is 0.197 V vs aqueous NHE without correction for the liquid junction potential (see text). ^b Potential values in 80% methanol were determined at a controlled temperature of 25.0 ± 0.2 °C by titration of the Cu^{II} species against ferrocene; thus, all values are relative to the potential shown for ferrocene (see footnote e). ^c Potential values in acetonitrile were measured by cyclic voltammetry using ferrocene/ferrocenium ion as an internal reference standard; corrections to NHE are based on the assumption that the potential for the ferrocene redox couple is 0.340 V vs NHE (see footnote d). ^d Potential value listed for ferrocene is that reported by Koepp et al.³² ^e The potential value listed for ferrocene in 80% methanol represents the average of values determined from the potentiometric titrations against the various $\text{Cu}^{\text{II}}\text{L}$ systems; this average value (std dev = 0.007 V) is used as the reference for all other potentials in this solvent; an independent ferrocene potential value of 0.532 V was determined by cyclic voltammetry. ^f Standard potential: Milazzo, G.; Caroli, S. *Tables of Standard Electrode Potentials*; Wiley: New York, 1978; p 23. ^g Standard potential: Bard, A. J.; Parsons, R.; Jordan, J. *Standard Potentials in Aqueous Solution*; Marcel Dekker: New York, 1985; p 292. ^h Value listed represents the concentration potential as determined in this work (see text). ⁱ Reference 3. ^j Reference 2. ^k Value determined from slow scan CV. ^l Precipitate observed after the equivalence point during potentiometric titration with ferrocene; thus, value shown may be unreliable.

reported as conditional constants, $K_{\text{Cu}^{\text{II}}\text{L}'}$, as defined by the reaction



$$K_{\text{Cu}^{\text{II}}\text{L}'} = \frac{[\text{Cu}^{\text{II}}\text{L}']}{[\text{Cu}^{\text{II}}][\text{L}]} \quad (2)$$

where $[\text{Cu}^{\text{II}}\text{L}']$ represents the sum of the concentrations of the various forms of the solvated complex species with or without ClO_4^- as an adduct, i.e.^{8,37}

$$[\text{Cu}^{\text{II}}\text{L}'] = [\text{CuL}(\text{H}_2\text{O})_2^{2+}] + [\text{CuL}(\text{H}_2\text{O})(\text{CH}_3\text{OH})^{2+}] + [\text{CuL}(\text{CH}_3\text{OH})_2^{2+}] + [\text{CuL}(\text{H}_2\text{O})(\text{ClO}_4)^+] + [\text{CuL}(\text{CH}_3\text{OH})(\text{ClO}_4)^+] \quad (3)$$

and $[\text{Cu}^{\text{II}}]$ represents the total concentration of the various solvated species of uncomplexed Cu(II) in this solvent mixture:³⁸

$$[\text{Cu}^{\text{II}}] = [\text{Cu}(\text{H}_2\text{O})_6^{2+}] + [\text{Cu}(\text{H}_2\text{O})_5(\text{CH}_3\text{OH})^{2+}] + [\text{Cu}(\text{H}_2\text{O})_4(\text{CH}_3\text{OH})_2^{2+}] + \dots \quad (4)$$

Based on our previous studies,^{8,16,36} $K_{\text{Cu}^{\text{II}}\text{L}'}$ values determined in 0.10 M ClO_4^- are expected to be approximately twice the magnitude of the concentration constants corrected for ClO_4^- adduct formation.³⁶ Due to the presence of multiple species of $\text{Cu}^{\text{II}}\text{L}$ and Cu^{II} , the enthalpies and entropies of formation represent *mixed* parameters which can not be rigorously interpreted.

As previously described,⁸ the spectrophotometric approach of McConnell and Davidson³⁹ was employed for the determination of $K_{\text{Cu}^{\text{II}}\text{L}'}$ values in 80% methanol using the peak in the vicinity of 390 nm. For each $\text{Cu}^{\text{II}}\text{L}$ system, a series of five or more solutions was prepared in which the ligand concentration was kept constant while the copper concentration was varied. The same set of solutions was used to obtain absorbance measurements at 15, 25 and 35 °C. The change of solution volume with temperature was insignificant relative to the experimental error of the measurements and no concentration correction was made.

The data for each system were plotted in the form of eq 5,⁸ where b represents the path length of the spectrophotometric

$$\frac{bC_L}{A} = \frac{1}{\epsilon_{\text{Cu}^{\text{II}}\text{L}'}} + \frac{1}{\epsilon_{\text{Cu}^{\text{II}}\text{L}'}K_{\text{Cu}^{\text{II}}\text{L}'}(C_{\text{Cu}(\text{II})} - [\text{Cu}^{\text{II}}\text{L}'])} \quad (5)$$

cell (in cm), A is the measured absorbance at the selected wavelength (in the vicinity of 390 nm), and $\epsilon_{\text{Cu}^{\text{II}}\text{L}'}$ is the apparent molar absorptivity value (in $\text{M}^{-1} \text{cm}^{-1}$) of the $\text{Cu}^{\text{II}}\text{L}'$ species. Due to the enhanced stability of most of the Cu(II) complexes with the cyclohexyl-derivatized ligands relative to that of the corresponding unsubstituted [14]aneS₄ complex, it was generally necessary to operate under conditions where the total Cu(II) concentration, $C_{\text{Cu}(\text{II})}$, was not in large excess over the total ligand concentration, C_L . Thus, $[\text{Cu}^{\text{II}}\text{L}']$ represented a significant fraction of $C_{\text{Cu}(\text{II})}$ and could not be ignored in the denominator of eq 5.

For most of the complexes studied in this work, the $\text{Cu}^{\text{II}}\text{L}'$ complexes were sufficiently stable to permit the value of $\epsilon_{\text{Cu}^{\text{II}}\text{L}'}$ to be determined directly by assuming complete complexation upon the addition of a ten-fold excess of Cu(II) to a solution of known ligand concentration. Under these circumstances, the value of $[\text{Cu}^{\text{II}}\text{L}']$ to be utilized in the denominator of eq 5 for

(36) Young, I. R.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.* **1986**, *25*, 2576–2582.

(37) Although all species in eq 3 represent Cu(II) as six-coordinate, some complexes tend to be five-coordinate with only one apical solvent molecule or perchlorate ion (Figure 4).

(38) Diaddario, L. L.; Zimmer, L. L.; Jones, T. E.; Sokol, L. S. W. L.; Cruz, R. B.; Yee, E. L.; Ochrymowycz, L. A.; Rorabacher, D. B. *J. Am. Chem. Soc.* **1979**, *101*, 3511–3520.

(39) McConnell, H.; Davidson, N. *J. Am. Chem. Soc.* **1950**, *72*, 3164–3167. Cf.: Benesi, H. A.; Hildebrand, J. H. *J. Am. Chem. Soc.* **1949**, *71*, 2703–2707.

Table 3. Experimentally Determined Stability Constants for Derivatized [14]aneS₄ Ligand Complexes with Copper(II) in 80% Methanol and with Copper(I) in Acetonitrile at 25 °C, $\mu = 0.10 \text{ M} (\text{ClO}_4^-)$

complexed ligand	80% methanol			acetonitrile $10^{-5}K_{\text{Cu}^{\text{I}}\text{L}}, \text{M}^{-1}$
	$10^{-5}K_{\text{Cu}^{\text{II}}\text{L}}, \text{M}^{-1}$	$\Delta H^{\circ}, \text{kJ mol}^{-1}$	$\Delta S^{\circ}, \text{J mol}^{-1} \text{K}^{-1}$	
[14]aneS ₄ (L0)	0.0300(2)	-8(2)	38(8)	0.158(5)
bz-[14]aneS ₄ (L1)	≈0.0001			2.7(1)
<i>cis</i> -cyhx-[14]aneS ₄ (L2)	1.61(2)	-15(6)	49(20)	0.91(3)
<i>trans</i> -cyhx-[14]aneS ₄ (L3)	1.12(1)	-17(3)	40(9)	2.7(1)
bz- <i>cis</i> -cyhx-[14]aneS ₄ (L5)	0.00055(5)			15(2)
bz- <i>trans</i> -cyhx-[14]aneS ₄ (L6)	≈0.0002			3.0(3)
<i>syn-cis,cis</i> -dicyhx-[14]aneS ₄ (L7)	553(23)			>10
<i>anti-cis,cis</i> -dicyhx-[14]aneS ₄ (L8)	0.501(3)	-16(2)	35(8)	1.95(9)
<i>meso-trans,trans</i> -dicyhx-[14]aneS ₄ (L9)	72(2)	-25(9) ^a	45(30) ^a	4.0(2)
<i>dl-trans,trans</i> -dicyhx-[14]aneS ₄ (L10)	50(3)	-40(17) ^a		^b
<i>cis,trans</i> -dicyhx-[14]aneS ₄ (L11)	74(5)	-27(10) ^a	41(35) ^a	2.87(6)

^a Thermodynamic data in italics for the very stable Cu^{II}L complexes in 80% methanol are relatively inaccurate; such values may not be meaningful.

^b Osteryoung square-wave voltammetry yielded two peaks for which the relative heights varied with repetitive scans.

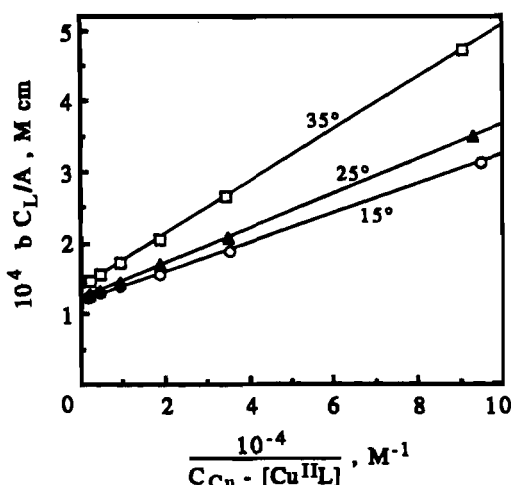


Figure 2. Typical “corrected” plots of eq 5 for the Cu^{II}(*anti-cis,cis*-dicyhx-[14]aneS₄) (L8) complex in 80% methanol at 15, 25 and 35 °C. The measurements shown were made in a 5.00 cm cell on solutions containing $C_L = 5.85 \mu\text{M}$ and $C_{\text{Cu(II)}}$ in the range 12.8–586 μM . The intercepts represent the reciprocal of the molar absorptivity for the Cu^{II}L’ species while the intercept/slope ratios yield the values of the conditional stability constant, $K_{\text{Cu}^{\text{II}}\text{L}'}$.

each solution could be calculated directly from the absorbance. For systems in which reliable values of $\epsilon_{\text{Cu}^{\text{II}}\text{L}'}$ were not determined directly, an approximate value of $\epsilon_{\text{Cu}^{\text{II}}\text{L}'}$ was obtained from the intercept of an uncorrected plot of eq 5 (i.e., a plot in which it was assumed that $C_{\text{Cu(II)}} \gg [\text{Cu}^{\text{II}}\text{L}']$). Final values of $\epsilon_{\text{Cu}^{\text{II}}\text{L}'}$ and $K_{\text{Cu}^{\text{II}}\text{L}'}$ were obtained by iteration. Corrected plots of eq 5 for the *anti-cis,cis*-dicyhx-[14]aneS₄ (L8) complex are illustrated in Figure 2.

Solutions containing approximately equal values of $C_{\text{Cu(II)}}$ and C_L were prepared and were sequentially diluted to determine the concentration level at which the complex was no longer fully formed. For the more stable complexes, relatively dilute solutions (<10 μM) were required to obtain satisfactory data and, even at that level, the percentage of ligand complexation was relatively large, thereby limiting the accuracy of the resultant stability constants. All 80% methanolic $K_{\text{Cu}^{\text{II}}\text{L}'}$ values are listed in Table 3 with standard deviations indicated in parentheses.

Also included in Table 3 are the enthalpies and entropies of Cu^{II}L’ formation. For systems with $K_{\text{Cu}^{\text{II}}\text{L}'}$ values greater than 10^6 M^{-1} , the trends as a function of temperature were generally unsatisfactory resulting in large standard deviations for ΔS° and ΔH° . Such values are listed in italics in Table 3 and should be regarded as semi-quantitative values only.

Stability Constant Measurements in Acetonitrile. In acetonitrile, the Cu^{II}L complexes were too stable to permit the use of eq 5. However, as a result of the strong solvation of Cu(I) by acetonitrile, the Cu^IL complexes were not fully formed for solutions in which Cu(I) and the ligand were present in close to stoichiometric quantities, provided that reasonably low concentration levels (ca. 10^{-5} M) were used. Therefore, the $K_{\text{Cu}^{\text{I}}\text{L}}$ values were determined experimentally.

Since Cu^IL complexes do not exhibit a visible spectrum (nor a useful ultraviolet spectrum), an electrochemical approach was utilized. For each ligand system, the concentration of the Cu^IL species was determined by Osteryoung square-wave cyclic voltammetric measurements⁴⁰ for a series of solutions containing constant $C_{\text{Cu(I)}}$ with increasing values of C_L . For a constant sweep rate, the Cu^IL oxidation peak current is directly related to the equilibrium Cu^IL concentration,⁴¹ the proportionality being determined from the limiting current, i_{∞} , as obtained at high C_L values where the total Cu(I) in solution is fully complexed {thus, $[\text{Cu}^{\text{I}}\text{L}] = C_{\text{Cu(I)}}(i/i_{\infty})$ }. This approach permitted the use of a modified form of eq 5 for the determination of $K_{\text{Cu}^{\text{I}}\text{L}}$ values

$$\frac{C_{\text{Cu(I)}}}{i} = \frac{1}{Y} + \frac{1}{YK_{\text{Cu}^{\text{I}}\text{L}'}(C_L - [\text{Cu}^{\text{I}}\text{L}'])} \quad (6)$$

where Y represents the product of several electrochemical parameters.⁴² A plot of eq 6 for the Cu^I(*meso-trans,trans*-dicyhx-[14]aneS₄) data is illustrated in Figure 3 where the value of $K_{\text{Cu}^{\text{I}}\text{L}'}$ is determined from the intercept/slope ratio. As listed in Table 3, all $K_{\text{Cu}^{\text{I}}\text{L}'}$ values in acetonitrile were determined only at 25 °C, $\mu = 0.10 \text{ M} (\text{NaClO}_4)$.

Stability Constant Calculations for Cu^IL Species in 80% Methanol. The $K_{\text{Cu}^{\text{I}}\text{L}'}$ values in 80% methanol were calculated using the Nernst equation³

$$E_{\text{Cu}^{\text{II}}\text{L}'} = E_{\text{Cu(II/I)}_{\text{solv}}} - \frac{2.303RT}{\mathcal{F}} \log \frac{K_{\text{Cu}^{\text{II}}\text{L}'}}{K_{\text{Cu}^{\text{I}}\text{L}'}} \quad (7)$$

(40) Christie, J. H.; Turner, J. A.; Osteryoung, R. A. *Anal. Chem.* **1977**, *49*, 1899–1903.

(41) The specific relationship between peak current, i , and the bulk Cu^IL concentration (C^*) is $i = n\mathcal{F}AC^*(\pi D\sigma)^{1/2}\chi(\sigma)$ where n represents the number of electrons transferred (i.e., $n = 1$), \mathcal{F} is the Faraday constant, A is the area of the electrode, D is the diffusion constant for Cu^IL, $\sigma = (n\mathcal{F}\nu/RT)$, ν is the sweep rate, R is the gas constant, T is the absolute temperature, and $\chi(\sigma)$ is the normalized current (see ref 40).

(42) Bard, A. J.; Faulkner, L. R. *Electrochemical Methods*; Wiley: New York, 1980; p 217.

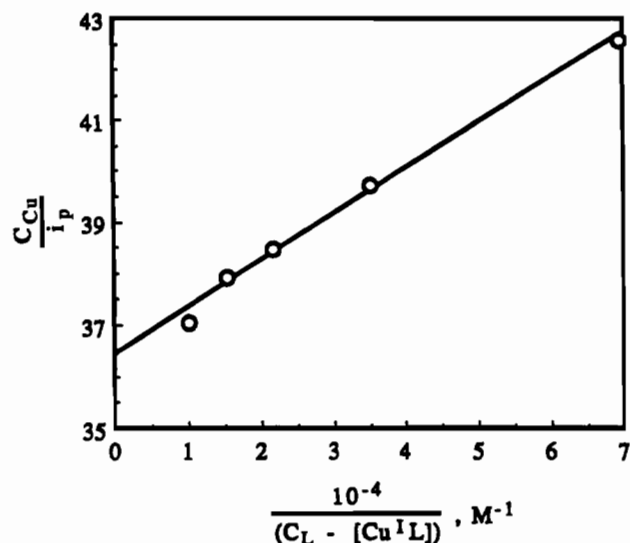
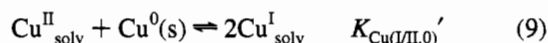


Figure 3. Typical plot of current values as a function of eq 6 for the $Cu^I(meso-trans,trans-dicyhx-[14]aneS_4)$ (L9) complex at 25 °C, $\mu = 0.10$ M ($NaClO_4$), in acetonitrile. Solutions contained $C_{Cu} = 0.251$ mM and $C_L = 0.165$ – 0.272 mM. The value of $K_{Cu^I L'}$ is determined from the intercept/slope ratio.

where $E_{Cu(II)_{sol}^f}$ represents the formal potential of the solvated $Cu(II/I)$ redox couple:



Previously, a value of $E_{Cu(II)_{sol}^f} = 0.13$ V was utilized in aqueous solution at 25 °C, $\mu = 0.10$ M.^{43,44} This value is not known for 80% methanol and a direct measurement cannot be made due to the instability of solvated $Cu(I)$. Therefore, we undertook the determination of the equilibrium constant for the comproportionation of Cu^I_{sol} (i.e., solvated $Cu(I)$) in this solvent:



Finely divided solid copper shot was shaken for several days in an 80% methanolic solution containing a known concentration of Cu^{II}_{sol} , maintained at 25 °C. After experimenting with several methods for determining the concentration of $Cu(I)$ present, we adopted a procedure in which several aliquots of this solution were drawn off with a syringe under nitrogen and mixed with a solution containing a very large excess (0.1 M) of 2,9-dimethyl-1,10-phenanthroline (i.e., neocuproine or 2,9-Me₂phen) to form the highly colored $Cu^I L_2$ complex which was then measured spectrophotometrically.⁴⁵ The large concentration of Cu^{II}_{sol} present in the equilibrated solutions caused a significant interference due to the rapid formation of $Cu^{II}(2,9-Me_2phen)_2$ which spontaneously reduced to the $Cu(I)$ complex (attributed to the reducing properties of methanol). To correct for this interference, the equilibrated $Cu(II)/Cu(I)$ solution was mixed with the neocuproine reagent in a stopped-flow spectrophotometer and the formation of the $Cu^I(2,9-Me_2phen)_2$ complex

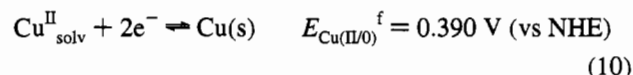
(43) Bernardo, M. M.; Heeg, M. J.; Schroeder, R. R.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.* **1992**, *31*, 191–198.

(44) This "formal concentration potential" value was calculated by correcting the standard potential for the aquocopper(II) redox couple ($E^\circ = 0.153$ V; Milazzo, G.; Caroli, S. *Tables of Standard Electrode Potentials*; Wiley: New York, 1978) by the activity coefficients for the aquated ions at an ionic strength of 0.10 M using the extended Debye-Hückel equation (assuming ionic diameters of 4 Å for each species). Use of the concentration potential rather than the activity potential alters the calculated ratio of the two stability constants by a factor of 2.

(45) Ahrland, S.; Rawsthorne, J. *Acta Chem. Scand.* **1970**, *24*, 157–172.

was monitored as a function of time. A corresponding blank solution, containing only Cu^{II}_{sol} , was run under identical conditions and the difference between the two rate curves was calculated by computer. The average of several determinations yielded an approximate value of $K_{Cu(I/II)_0'} = 5 \times 10^{-7}$ at 25 °C, $\mu = 0.10$ M ($HClO_4$).

The potential of the $Cu^{II}_{sol}/Cu(s)$ half-reaction has previously been reported for 80% methanol:⁴⁶



This value was combined with the comproportionation equilibrium constant to generate the formal potential value for $Cu(II/I)_{sol}$ in 80% methanol:

$$E_{Cu(II/I)_{sol}^f} = E_{Cu(II/0)}^f + \frac{2.303RT}{2F} \log K_{Cu(I/II)_0'} = 0.20_4 \text{ V} \quad (11)$$

The stability constant values for the $Cu^I L$ complexes in 80% methanol were then calculated using eq 7 where the $E_{Cu(II/I)_{sol}^f}$ values are those listed in Table 2. The calculated $\log K_{Cu^I L'}$ values in 80% methanol are listed in Table 4. To the extent that the $E_{Cu(II/I)_{sol}^f}$ potential value in eq 11 may be in error, all $K_{Cu^I L'}$ values will also be in error. However, it should be noted that all $K_{Cu^I L'}$ values are internally consistent and, thus, the relative trends should be reliable.

Stability Constant Calculations for $Cu^{II} L$ Species in Acetonitrile. The stability constant values for the $Cu^{II} L'$ complexes in acetonitrile were also calculated using eq 7. In this solvent, the stability of solvated $Cu(I)$ and $Cu(II)$ made it possible to make a direct measurement of $E_{Cu(II/I)_{sol}^f} = 0.601$ V vs Fc^+/Fc (or 0.941 V vs aqueous NHE)⁴⁷ at 25 °C, $\mu = 0.10$ M (ClO_4^-). This latter value differs markedly from the published value of 0.964 V vs aqueous SCE for Cu^{II}_{sol} in acetonitrile,⁴⁸ but it is internally consistent with all other values determined in this work. The resultant $\log K_{Cu^I L'}$ values are included in Table 4. Since the $Cu^I L$ stability constants in acetonitrile were determined by an electrochemical method and both $E_{Cu(II/I)_{sol}^f}$ and all $E_{Cu^{II} L'}$ measurements are referenced directly to the ferrocene potential, the values calculated for the $Cu^{II} L$ stability constants are unaffected by errors in the value of the ferrocene potential itself.

Discussion

Potential Values. In attempting to establish a suitable reference redox couple for comparing electrode potentials among various solvents, Koeppe, Wendt, and Strehlow³² concluded that the potential of the ferrocenium ion/ferrocene (Fc^+/Fc) half-reaction is nearly ideal as a reference standard. This couple is only slightly affected by solvation—principally due to the small charge-to-radius ratio involved and the relatively spherical nature of the exterior surface which ferrocene presents to the bulk

(46) Minc, S.; Jastrzebska, J. *Rocz. Chem.* **1954**, *28*, 519–520. In reporting the $Cu(II/0)$ potentials in methanol–water mixtures, the authors did not specify whether per cent methanol refers to weight, volume, or mole per cent. Although the potential values are reported to be referenced to aqueous NHE, the actual internal reference electrode used was not specified and there was no indication that a correction was made for the liquid junction potential. Since the actual values of the liquid junction potential for aqueous reference electrodes in methanol–water mixtures were not determined until a later date (see ref 34), it is presumed, in fact, that no correction was made for the liquid junction.

(47) The correction to NHE is based on Strehlow's published value of 0.340 V for the Fc^+/Fc redox couple in acetonitrile vs. aqueous NHE: see ref 32.

(48) Farha, F., Jr.; Iwamoto, R. T. *J. Electroanal. Chem.* **1964**, *8*, 55–64.

Table 4. Comparison of Experimental and Calculated Logarithmic Stability Constants for Copper(I)- and Copper(II)-Tetrathiaether Complexes in 80% Methanol and Acetonitrile at 25 °C, $\mu = 0.10$ M (ClO_4^-)

complexed ligand	80% methanol		acetonitrile		preferred sulfur non-bonded lone-pair orientn	preferred conformn ^a
	log $K_{\text{Cu}^{\text{II}}}$	log $K_{\text{Cu}^{\text{I}}}$	log $K_{\text{Cu}^{\text{II}}}$	log $K_{\text{Cu}^{\text{I}}}$		
[14]aneS ₄ (L0)	3.48	11.8	10.8	4.20		
bz-[14]aneS ₄ (L1)	≈0		7.8	5.43		
<i>cis</i> -cyhx-[14]aneS ₄ (L2)	5.21	12.8	12.2	4.96		
<i>trans</i> -cyhx-[14]aneS ₄ (L3)	5.05	13.4	12.2	5.43		
bz- <i>cis</i> -cyhx-[14]aneS ₄ (L5)	1.74		9.7	6.18		
bz- <i>trans</i> -cyhx-[14]aneS ₄ (L6)	≈1.3		9.2	5.48		
<i>syn-cis,cis</i> -dicyhx-[14]aneS ₄ (L7)	7.7	14.1	>14.8	>6	+++ +	C, D
<i>anti-cis,cis</i> -dicyhx-[14]aneS ₄ (L8)	4.70	13.7	11.9	5.29	+ + - -	none
<i>meso-trans,trans</i> -dicyhx-[14]aneS ₄ (L9)	6.86	13.3	14.2	5.60	- + + -	A
<i>dl-trans,trans</i> -dicyhx-[14]aneS ₄ (L10)	6.70	(15.1) ^b			- + - +	B
<i>cis,trans</i> -dicyhx-[14]aneS ₄ (L11)	6.87	14.3	13.3	5.46	+ + + -	D

^a For preferred conformations, see Figure 4. ^b Precipitate formed during potentiometric titration; thus, the $\text{Cu}^{\text{II}}/\text{L}'$ potential and the resultant calculation for $K_{\text{Cu}^{\text{II}}}$ are unreliable.

solvent. In view of the conclusions of Strehlow and co-workers, the potential of the Fc^+/Fc redox couple is included in Table 2 for each solvent matrix and, as noted in the preceding sections, serves as a benchmark potential value for all $\text{Cu}(\text{II}/\text{I})$ systems. For purposes of comparison, the measured potentials of the $\text{Cu}^{\text{II}}/\text{L}$ systems are "corrected" to an assigned potential value of zero for the H^+/H_2 couple—the corrections being based on several specific assumptions which are outlined in the footnotes to Table 2.³⁴ From an experimental standpoint, however, all $\text{Cu}^{\text{II}}/\text{L}$ potentials in 80% methanol and in acetonitrile are more accurately referenced to the ferrocene potential values listed.

Relative to ferrocene, the potentials of the $\text{Cu}^{\text{II}}/\text{L}$ systems with [14]aneS₄ and the monosubstituted ligands (i.e., L0, L1, L2, L3) are observed to be nearly constant (within 30 mV) in the three solvents tested in this work (Table 2). Thus, it appears that solvation does not have a significant influence on the redox properties of these copper complexes. This is somewhat surprising since the $\text{Cu}(\text{II})$ complexes involve either one or two coordinated solvent molecules, whereas many of the $\text{Cu}(\text{I})$ complexes are expected to have no coordinated solvent. The absence of a significant solvent effect in the potential values of these $\text{Cu}^{\text{II}}/\text{L}$ systems presumably reflects the fact that the solvent molecules are only very weakly coordinated.

By contrast, with the exception of the *dl-trans,trans*-dicyhx derivative (for which the potentials appear to be less trustworthy, particularly in 80% methanol), all di-substituted ligand systems (i.e., L7, L8, L9, L11) appear to exhibit uniform $\text{Cu}(\text{II}/\text{I})$ potentials relative to ferrocene in 80% methanol and acetonitrile but are significantly higher in water. These latter results suggest the possibility that, for these systems, the stable conformation of either the $\text{Cu}^{\text{II}}/\text{L}$ or the $\text{Cu}^{\text{I}}/\text{L}$ species may be significantly different in aqueous solution than in the other two solvents.

Stability Constant Trends as a Function of Solvent. In earlier work we have noted that the stability constants for $\text{Cu}(\text{II})$ macrocyclic tetrathiaether complexes in 80% methanol are approximately 1 order of magnitude smaller than in aqueous solution under the same conditions of temperature and ionic strength.³⁸ In the current studies, the $K_{\text{Cu}^{\text{II}}}$ values for the cyclohexyl derivatives in acetonitrile are consistently 7 orders of magnitude larger than in 80% methanol (Table 4). This observation leads to the conclusion that the uncomplexed $\text{Cu}(\text{II})$ ion is much more strongly solvated in 80% methanol (and in water) than in acetonitrile. For the phenyl derivatives the data are much less reliable, but a similar increase in $K_{\text{Cu}^{\text{II}}}$ of about 8 orders of magnitude is observed on going from 80% methanol to acetonitrile.

In contrast to the $\text{Cu}^{\text{II}}/\text{L}$ solvent trends, the $\text{Cu}^{\text{I}}/\text{L}$ stability constants with the cyclohexyl derivatives in acetonitrile are about 10^8 less stable than in 80% methanol (Table 4). This depen-

dence upon solvent is consistent with the strong solvation of uncomplexed $\text{Cu}(\text{I})$ by acetonitrile.⁴⁹ Thus, the relative stabilities of the complexes for the two oxidation states of copper are completely reversed when utilizing acetonitrile as solvent.

Stability Constant Trends as a Function of Cyclohexyl and Phenyl Substituents. An examination of the data in Table 4 reveals several general trends in the stability constant data as a function of ligand substitution. For the $\text{Cu}(\text{II})$ complexes, the incorporation of a single cyclohexyl group into the macrocycle (L2 and L3) increases $K_{\text{Cu}^{\text{II}}}$ by approximately 1.5 orders of magnitude regardless of the solvent. This agrees with the recent qualitative observation that these same two ligands enhance the stability of $\text{Ni}(\text{II})$ complexes in nitromethane by ≥ 100 -fold relative to [14]aneS₄.⁵⁰ Addition of a second *trans*-cyclohexyl group results in an additional increase in $K_{\text{Cu}^{\text{II}}}$ of more than 1.5 orders of magnitude. Thus, the overall stability enhancement of $\text{Cu}^{\text{II}}/\text{L}$ complexes with *trans,trans*- (L9 and L10) or *cis,trans*-dicyhx-[14]aneS₄ (L11) amounts to more than 3 orders of magnitude relative to the parent $\text{Cu}^{\text{II}}/[\text{14]aneS}_4$ complex.

The *cis,cis*-dicyclohexyl derivatives exhibit more unique behavior. The $\text{Cu}(\text{II})$ complex with the *syn-cis,cis* analogue (L7) is 10 times more stable than the corresponding complexes in which at least one of the cyclohexyl groups is *trans*. Thus, even in 80% methanol, this $\text{Cu}^{\text{II}}/\text{L}$ species approaches stability levels which become nearly quantitative at accessible concentration levels; and it is expected that the aqueous $K_{\text{Cu}^{\text{II}}}$ value for this complex will be close to 10^9 . On the other hand, $K_{\text{Cu}^{\text{II}}}$ for the *anti-cis,cis*-dicyclohexyl-[14]aneS₄ (L8) complex is 1000-fold smaller than for the *syn* derivative. This difference may be attributable to a significantly different orientation of the sulfur donor atoms in these two complexes as discussed below.

In sharp contrast to the influence of cyclohexyl substituents, the incorporation of a single benzene into the macrocyclic ligand structure causes a dramatic decrease in the stability of the $\text{Cu}^{\text{II}}/\text{L}$ complexes amounting to 5 orders of magnitude relative to a corresponding monocyclohexyl derivative. Approximate molecular mechanical calculations indicate that steric factors do not contribute to this phenomenon. The observed decrease is largely attributed to the negative inductive effect of the benzene ring upon the coordinating ability of the sulfur donor atoms. Incorporation of a second benzene group into the macrocyclic structure appears to destabilize the system even further, but quantitative data have been impossible to obtain.

(49) See, e.g.: Kratochvil, B.; Zatko, D. A.; Markuszewski, R. *Anal. Chem.* **1966**, *38*, 770–772.

(50) Desper, J. M.; Vyvyan, J. R.; Mayer, M. J.; Ochrymowycz, L. A.; Gellman, S. H. *Inorg. Chem.* **1993**, *32*, 381–382.

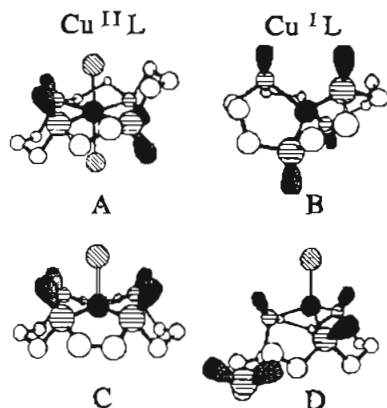


Figure 4. Schematic representations of the major configurations of $\text{Cu}^{\text{II}}\text{L}$ (left) and $\text{Cu}^{\text{I}}\text{L}$ (right) complex species involving $[14]\text{aneS}_4$ derivatives as they are believed to exist in solution. In each complex, the solid atom represents Cu, the horizontally striped atoms represent sulfurs and the diagonally striped atoms represent coordinated solvent molecules (or anions). The orientation of the shaded non-bonded lone electron pairs is designated as plus (+) if directed upward or minus (-) if directed downward in these representations. All configurations are shown here for the parent $[14]\text{aneS}_4$ ligand with one of the ethylene bridges in the foreground of each schematic so that the preferred orientation of the bridging carbon atoms can be readily observed. Species A and C represent six-coordinate (tetragonal) and five-coordinate (square pyramidal) $\text{Cu}(\text{II})$, respectively. Species B and D both represent four-coordinate (tetrahedral) $\text{Cu}(\text{I})$ with all four ligand donor atoms coordinated in B and one $\text{Cu}-\text{S}$ bond replaced by a solvent molecule in D.

In the case of the $\text{Cu}(\text{I})$ complexes, incorporation of either cyclohexyl or phenyl groups into the macrocyclic structure appears to increase the stability constant by about 1 order of magnitude relative to the parent $[14]\text{aneS}_4$ ligand, with little variation from one complex to the next. This is somewhat surprising in view of the marked differences in the behavior of the cyclohexyl and phenyl derivatives toward $\text{Cu}(\text{II})$. However, as a low-valent d^{10} system, the $\text{Cu}(\text{I})$ ion is known to exhibit dramatically different behavior in its donor atom preferences as has recently been noted in macrocyclic ligand complexes involving mixed nitrogen-sulfur donors.⁴³ As discussed in more detail below, the stability constants might also be expected to reflect the ease with which the various ligands can conform to a tetrahedral coordination sphere since $\text{Cu}(\text{I})$ generally tends to prefer the latter geometry. However, based on the data in Table 4 (as well as on semi-quantitative strain calculations), there is little evidence for such an influence in this work. As a result of the relative constancy of the $\text{Cu}^{\text{II}}\text{L}$ stability constants, it is obvious that the $\text{Cu}^{\text{II}}\text{L}$ redox potentials are principally influenced by the stability of the $\text{Cu}^{\text{II}}\text{L}$ species.

Ligand Conformations. Two conformations are expected to predominate for the current set of $\text{Cu}(\text{II})$ complexes. The first of these has been observed in the crystal structure for $\text{Cu}^{\text{II}}\text{L}$ ($[14]\text{aneS}_4$)⁵¹ in which the $\text{Cu}(\text{II})$ atom and the four sulfur donor atoms are co-planar while the two trimethylene bridges lie on opposite sides of the central plane. As illustrated by species A in Figure 4, the overall conformation of the complexed macrocyclic ligand resembles that of a chair with two axially coordinated anions or solvent molecules completing the tetragonal coordination sphere.⁵² In this conformation, the non-bonded electron pairs on the sulfur donor atoms adopt the pattern

$+-+-$ (for positions 1,4,8,11) where the plus and minus designations refer, respectively, to lone pairs above and below the plane defined by the four sulfur atoms.

In the alternative $\text{Cu}^{\text{II}}\text{L}$ structure (species C in Figure 4), the ligand adopts a boat conformation in which both trimethylene bridges are oriented on the same side of the sulfur donor plane. The relative orientation of the non-bonded electron pairs for the sulfur donors is then $++++$. In this conformation, the $\text{Cu}(\text{II})$ ion sits above the plane of the four sulfurs and is coordinated to a single apical solvent molecule or anion, resulting in a square pyramidal geometry. This geometry has previously been observed by us for $\text{Cu}(\text{II})$ complexes with several substituted macrocycles including *syn*- $[14]\text{aneS}_4$ -diol,⁷ *cis*- and *trans*-*cyhx*- $[14]\text{aneS}_4$ ⁵³ and the 12- and 13-membered S_4 -macrocycles.¹² Both conformations A and C have been observed by Desper and Gellman in a single crystal for the closely related $\text{Cu}^{\text{II}}(\text{Me}_4[14]\text{aneS}_4)$ complex.¹⁵

It is likely that both conformations A and C co-exist in solution for most of the $\text{Cu}^{\text{II}}\text{L}$ complexes involved in the current study. However, it is also presumed that the various phenyl and cyclohexyl substituents should cause the ligands to prefer one conformation relative to the other. For example, simple molecular models indicate that the sulfurs in the *meso-trans*-*trans*-*dicyhx*- $[14]\text{aneS}_4$ ligand (L9) are ideally adapted for the $+-+-$ arrangement of non-bonded lone electron pairs represented by species A in Figure 4 while the *syn-cis*,*cis*-*dicyhx*- $[14]\text{aneS}_4$ (L7) ligand would appear to be ideally suited for the $++++$ orientation required by the square pyramidal geometry designated as C. It is particularly interesting to note that these are two of the strongest $\text{Cu}(\text{II})$ complexes observed in this work.

Previously studied $\text{Cu}(\text{I})$ complexes with S_4 -macrocycles have also been observed to adopt two contrasting configurations. The most obvious of these is represented by B in Figure 4 in which the four sulfur donor atoms are coordinated to a single copper atom in a tetrahedral arrangement, resulting in a $+-+-$ arrangement of the non-bonded lone-pair electrons. This conformation has been observed in crystal structures for the $\text{Cu}^{\text{I}}([14]\text{aneNS}_3)$ ⁴³ and $\text{Cu}^{\text{I}}(\text{trans-cyhx}-[14]\text{aneS}_4)$.⁵³ Since the 14-membered ring is too small to permit the four donor atoms to achieve a symmetric tetrahedral array around the copper atom, the resulting complexes are considerably flattened and sample calculations indicate that such complexes are quite strained. This strain doubtless accounts for the alternative $\text{Cu}(\text{I})$ complex structure, first observed in a crystal structure of $\text{Cu}^{\text{I}}([14]\text{aneS}_4)$,⁵⁴ which involves the rupture of one $\text{Cu}-\text{S}$ bond to generate a distorted tetrahedral complex involving three coordinated sulfur donor atoms and (presumably) a coordinated solvent molecule (or anion) as represented by configuration D in Figure 4. The latter configuration corresponds to a $+++0$ arrangement of the non-bonded lone pairs on the sulfur donor atoms (where the "0" denotes the fact that the fourth sulfur donor atom is not coordinated to the central copper atom).

Of the *dicyclohexyl* derivatives, the *dl-trans*,*trans*-*dicyhx*- $[14]\text{aneS}_4$ ligand (L10) appears to be ideally suited to coordinate all four sulfurs in a tetrahedral array as in configuration B (see Table 4). By contrast, the *syn-cis*,*cis*- (L7) and the *cis*,*trans*-

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(52) Earlier stability constant measurements in aqueous solution give evidence for the formation of weak ClO_4^- adducts (presumed to be coordinated at an axial site) with an equilibrium constant of approx. 24 M^{-1} in aqueous solution: see refs 8, 16, 36.

(53) Salhi, C. S.; Heeg, M. J.; Ochrymowycz, L. A.; Rorabacher, D. B. *Inorg. Chem.*, submitted for publication. Cf: Salhi, C. S. Ph.D. Dissertation, Wayne State University, 1993.

(54) Dockal, E. R.; Diaddario, L. L.; Glick, M. D.; Rorabacher, D. B. *J. Am. Chem. Soc.* 1977, 99, 4530-4532. Although the crystal structure for $\text{Cu}^{\text{I}}([14]\text{aneS}_4)$ involved a polymeric species in which the fourth coordinated sulfur donor was from an adjacent ligand, it is presumed that, in solution, the fourth site involves a coordinated water molecule (since the properties of dilute solutions show no evidence of polymers).

dicyhx-[14]aneS₄ (L11) ligands should readily adapt to configuration D. However, as noted earlier, all Cu^IL complexes exhibit relatively consistent stability constants regardless of the predicted influence of the benzene and cyclohexane rings upon the preferred orientation of the non-bonded lone electron pairs of the sulfur donor atoms.

Comparison to Corresponding Macrocyclic Polyethers and Polyamines. No quantitative stability constant data have been located for complexes formed with the phenyl and cyclohexyl derivatives of the closely related macrocyclic polyether [14]aneO₄ (i.e., 14-crown-4). However, Moyer, Sachleben and co-workers⁵⁵ recently reported preliminary qualitative results for the complexation of Li⁺ with *syn*- and *anti-cis,cis*-dicyhx-[14]aneO₄ in which they found that the *syn* isomer forms a much stronger complex than does either the *anti* isomer or the unsubstituted ligand.⁵⁵ This parallels our own observations on the $K_{Cu^I L'}$ trends with the [14]aneS₄ analogues, although the marked differences in coordination requirements for Cu(II) and Li make this analogy somewhat tenuous. The crystal structure for the [Li(*syn-cis,cis*-dicyhx-[14]aneO₄)SCN] complex⁵⁶ shows that it is square pyramidal (having an apically coordinated SCN⁻) with the Li atom 0.55 Å above the O₄ plane. Although some ligand reorganization takes place upon complex formation,⁵⁶ the orientation of the free ligand appears to be favorably disposed for this coordination geometry relative to that of either the unsubstituted parent compound or the *anti-cis,cis*-dicyhx derivative. The crystal structure of the corresponding [Li(dibenzo-[14]aneO₄)SCN] complex⁵⁷ is very similar to that of the *syn-cis,cis*-dicyhx derivative and it has been suggested that the free dibenzo ligand is even better pre-organized for this type of complexation.⁵⁸

A few derivatives of the corresponding macrocyclic tetramine, [14]aneN₄, have also been reported which are pertinent to the current work. Lindoy and co-workers⁵⁹ prepared Me-dibz-[14]aneN₄, which is analogous to our ligand L4 with the addition of a methyl group on the central carbon of one trimethylene bridge. These workers obtained a stability constant of 6×10^3 for the Zn(II) complex in 95% methanol (25 °C, $\mu = 0.1$ M (NEt₄CIO₄)) which is nearly 12 orders of magnitude smaller than the value reported for Zn^{II}([14]aneN₄) in aqueous solution under these same conditions.⁶⁰ The difference in solvent may account for up to 2 orders of magnitude, but the remaining 10 orders of magnitude clearly reflect the electron-withdrawing influence of the benzene groups upon the donor ability of the anilino nitrogens. This is consistent with our observation of a 10⁵ decrease in $K_{Cu^I L'}$ for a single benzene substituent compared to a single cyclohexane. If a similar decrease is assumed to occur for the substitution of a second benzene in dibz-[14]aneS₄ (L4), complexation with Cu(II) would be negligible in 80% methanol. This is consistent with our findings.

Moriguchi and Sakata⁶¹ have determined the aqueous stability constants for the Ni(II), Cu(II) and Zn(II) complexes with the

two *cis,cis*-dicyhx-[14]aneN₄ diastereomers analogous to our ligands L7 and L8. For Cu(II), the complex formed with the *anti-cis,cis* derivative was nearly identical to that with the parent [14]aneN₄ ligand⁶² while the complex with the *syn-cis,cis* diastereomer was enhanced by only 4-fold. In the case of Ni(II), the complex formed with the *syn* derivative was only slightly more stable than that formed with [14]aneN₄⁶³ while the *anti* diastereomer showed a stability constant increase of about 3-fold. In contrast to this, the Zn(II) complexes with both the *syn* and *anti* isomers showed a 10⁴ increase in stability.

Kobiro and co-workers⁶⁴ have determined the crystal structures of the Ni(II) complexes with both *syn-cis,cis*- and *anti-cis,cis*-dicyhx-[14]aneN₄. Interestingly, these structures reveal that the Ni(II)-*anti* complex corresponds to conformation A in Figure 4 and the Ni(II)-*syn* complex to conformation C. (In the latter case, there is no apical atom as the Ni(II) is low spin and only four-coordinate.) The latter conformation is consistent with our prediction for the corresponding Cu(II) tetrathiaether complex (Table 4).

The contrasting influence of *cis,cis*-dicyclohexyl groups upon the stability constant trends for the Ni(II)- and Cu(II)-[14]aneN₄ complexes and the corresponding Cu(II)-[14]aneS₄ systems may be presumed to reflect basic differences in the N₄ and S₄ macrocycles. Several significant differences have been noted between these two types of macrocycles, *viz.*: (i) the cavity size is larger in the endodentate form of the tetramine ligands than in the corresponding tetrathiaethers, (ii) the preferred torsional angles for N-C-C-N and S-C-C-S are significantly different, and (iii) nitrogen donor atoms have a single lone pair of electrons for coordinate bond formation whereas sulfur donor atoms have two lone pairs, either of which may be donated to the metal ion. Of these properties, the second is probably the most influential in terms of the observed trends in the complex stability constants. As noted in the Introduction, the preferred torsional angles in cyclic polythiaethers tend to favor an *exo* conformation for the uncomplexed ligand¹⁰ whereas the cyclic tetramines preferentially adopt an *endodentate* conformation. Therefore, incorporation of cyclohexyl groups into the ligand structure might be expected to have a more dramatic effect upon complex stability constants in the case of the polythiaethers. However, we note that the large increase in the Zn(II) complex stability constants upon the incorporation of *cis,cis*-dicyclohexyl groups on [14]aneN₄ is not consistent with this explanation.

Thermodynamic Parameters for Copper(II) Complexes.

As our original premise, we suggested that the incorporation of cyclohexane rings into the macrocyclic ligand structure of the polythiaethers should result in more favorable enthalpies for Cu(II) complex formation. Suitable data relating to this prediction could not be obtained for complex formation in acetonitrile since the Cu^{II}L species are too stable to be determined directly; and indirect calculations using the Nernst equation result in too many uncertainties to yield viable temperature dependencies. However, the 80% methanol data are significant in this regard.

It is apparent from Table 3 that, in 80% methanol, the incorporation of a single cyclohexane ring into the [14]aneS₄ macrocycle results in an enthalpy gain of approximately 8 kJ mol⁻¹ relative to the unsubstituted complex. There is no

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significant entropy effect. Interestingly, the enthalpy for the formation of $\text{Cu}^{\text{II}}(\text{anti-cis,cis-dicyhx-[14]aneS}_4)$ is virtually identical to that for the monocyclohexyl derivatives. For the Cu^{I} complexes with the other dicyclohexyl-substituted ligands, $K_{\text{Cu}^{\text{II}}}$ $\gg 10^6$ which results in large experimental errors in the temperature dependencies and a high level of uncertainty for the thermodynamic parameters. Nonetheless, it appears that the incorporation of a second *trans*-cyclohexane ring into the tetrathiaether macrocycle yields an additional enthalpy gain of 8 kJ mol^{-1} or more. Thus, for the Cu^{II} complexes, a gain in enthalpy of 8 kJ mol^{-1} is achieved upon incorporation of each cyclohexane ring into the [14]aneS₄ macrocycle. The exceptional behavior of the *anti-cis,cis-dicyhx-[14]aneS*₄ system suggests that this ligand does not provide a good "fit" to the coordination geometry preferred by copper(II). This phenomenon will be investigated further in future work.

Conclusions. The more negative enthalpy values for the Cu^{II} complexes formed with the cyclohexyl-derivatized [14]aneS₄ ligands is consistent with our initial premise that the ring substituents might tend to force the donor atoms into a more endodentate conformation. In fact, molecular mechanical calculations indicate that the uncomplexed ligands tend to adopt conformations which are intermediate between *exo*- and *endo*-dentate.⁶⁵

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The relatively parallel changes in stability constants and potentials for all $\text{Cu}^{\text{II/L}}$ systems on changing from 80% methanol to acetonitrile indicates that inner- and outer-sphere solvation effects are of minimal importance. Thus, thermodynamic measurements made in one solvent may provide rough approximations of the properties in a second solvent. The complete reversal in relative stabilities of the $\text{Cu}^{\text{II/L}}$ and $\text{Cu}^{\text{I/L}}$ complexes in acetonitrile compared to 80% methanol suggests that the solvent of choice may vary for different types of applications.

Finally, the generation of reasonably large Cu^{II} complex stability constants with modified polythiaether ligands in aqueous-like media (i.e., water and 80% methanol) suggests that complexes of measurable stability may also be achieved by these ligands (or more highly modified analogues) with other divalent transition-metal ions. Such complexes would make it possible to probe the effects of thiaether sulfur donor atoms upon the specific spectral and electrochemical properties of such metal ion species without having to resort to poorly coordinating solvents such as nitromethane.

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