A Versatile Preparative Route to 5-Substituted-1,10-Phenanthroline Ligands via 1,10-Phenanthroline 5,6-Epoxide

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Polypyridine ligands such as 2,2′-bipyridine and 1,10-phenanthroline (phen) are some of the most widely used chelating ligands in modern coordination chemistry.[1] The ligands or their complexes have found application in areas such as molecular catalysis,[2] solar energy conversion,[3] colorimetric analysis,[4] herbicides,[5] molecular recognition,[6] self-assembly,[7] antineoplastic agents,[8] and nucleic acid probes.[9] We have embarked on a program to extend the application of metal–phen complex chemistry to the development of luminescence-based sensors for pH, anions, and cations. Although this luminophore approach to sensing has been widely exploited using organic materials,[10] few studies involving coordination complexes exist,[6a,11] and none to our knowledge involve the phen ligand. In order to realize this goal we have developed new chemistry based on the reactive precursor 1,10-phenanthroline 5,6-epoxide (**I**) that enables a variety of analyte binding sites to be linked to the 5-position of phen. We anticipate that this versatile chemistry will find many other uses.

We have prepared ligand **I** by a slight variation of the method of Krishnan et al,[12,13] which is convenient since phen can be reacted with commercial bleach under phase transfer conditions to obtain a good yield of **I**. We note that the ring-opening chemistry of **I** has been briefly presented as an integral part of a short synthesis of the marine alkaloid ascididemin.[14] In our studies, reaction of ligand **I** with a variety of nucleophiles results in the intermediate hydroxy–dihydro derivatives in 50–80% yields.[15] Dehydration under conditions appropriate for the substituent gives excellent yields of the 5-substituted-1,10-phenanthroline ligand (50–80%).[15] Figure 1 presents some representative examples. Of interest is that the reaction with excess cyanide (preparation 1 in Figure 1) gives 5-cyano-1,10-

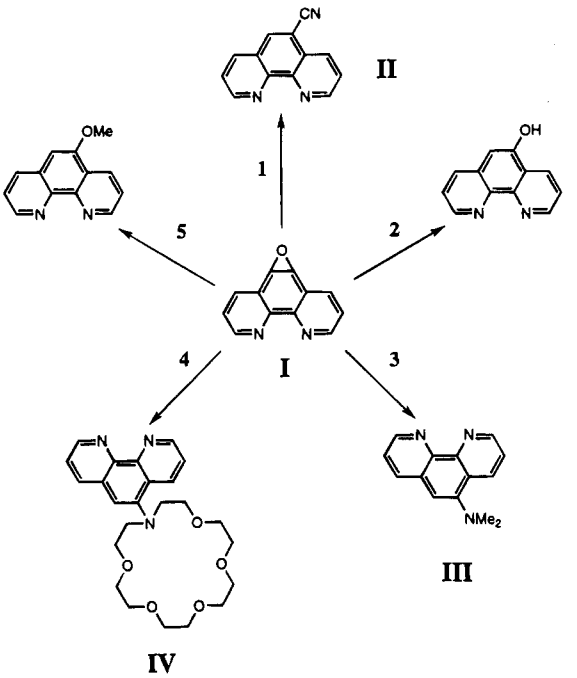

Figure 1. Examples of the new ligands prepared from 1,10-phenanthroline 5,6-epoxide via nucleophilic attack and dehydration of the hydroxy–dihydro intermediate. Numbers next to the arrows refer to synthetic preparations we have conducted.

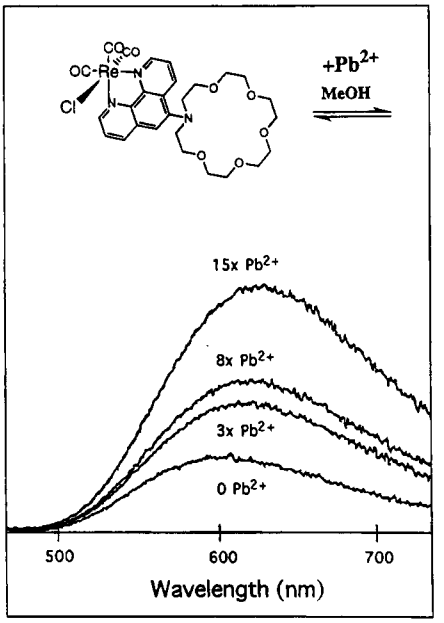

Figure 2. Perturbation of the emission spectrum of *fac*-Re(ligand **IV**)$(CO)_3Cl$ (1.4×10^{-4} M in MeOH) upon addition of $Pb(OAc)_2$. Concentrations of Pb^{2+} are 3, 8, and 15 times that of the metal complex.

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phenanthroline (**II**) directly in an overall yield of 80%, without isolation of the intermediate.[16] The method of dehydration in preparations 2−5 involves heating the hydroxy−dihydro derivatives in the presence of a strong base such as NaH. Characterization of both the dihydro intermediates and the 5-substituted-1,10-phenanthroline ligands has been done by ^{1}H and ^{13}C NMR, ultraviolet, infrared, and mass spectroscopies and by elemental analysis. Typical procedures for the preparations are found in the footnotes 13−16.

Reaction of $Re(CO)_5Cl$ with the ligands shown in Figure 1 or with ligand **I** itself in toluene gives the *fac*-Re(ligand)$(CO)_3Cl$ complexes in high yield.[17] Characterization of the complexes has been accomplished by ^{1}H NMR, infrared, UV−visible, and luminescence spectroscopies and by elemental analysis. A curious phenomenon, which is apparent by examination of the proton NMR of *fac*-Re(ligand **I**)$(CO)_3Cl$ in CD_2Cl_2, is the fluxional nature of the epoxide grouping. This is apparent upon examination of the proton NMR of the complex, where it is seen that the 5,6-protons appear as a single resonance.[18] At −20 °C this resonance broadens and by −60 °C it has split into two. We attribute this behavior to a relatively low barrier between the two isomers of the system, one having the epoxy group "pointing toward" the Cl and the other away. Furthermore, the effect of a low isomerization barrier is also seen in the X-ray crystal structure of Fe(ligand **I**)$_3(PF_6)_2$, which has disorder only around the epoxy oxygens due to the crystallization of all three possible structural isomers of the complex.[19]

Since our motivation in developing this chemistry was to provide versatile synthetic routes to luminescence sensors based on the metal-to-ligand charge transfer processes involving the phen ligand, we were intrigued to find that both 5-(dimethylamino)-1,10-phenanthroline (**III**) and 5-crown-1,10-phenanthroline (**IV**) are highly emissive in fluid solution. For example, in CH_3CN, ligand **III** emits at 503 nm and ligand **IV** at 498 nm. We note in passing that emission from Zn(ligand **III**)$_3^{2+}$ in CH_3CN is substantially red-shifted to 600 nm and that treatment of the complex with dilute CF_3SO_3H, conditions under which the lone pair is protonated, quenches this emission.

The rhenium complexes of ligands **III** and **IV** also luminesce, and it may be that this process is predominantly MLCT in nature. In fact, as we had anticipated, the direct connection of the amino substituent to the phen nucleus allows *fac*-Re(ligand **IV**)$(CO)_3Cl$ to be used as a metal ion sensor. As is shown in Figure 2, treatment of the complex with $Pb(OAc)_2$ in MeOH under just moderate excess conditions (15×) leads to a ca. 20 nm red shift and a 270% increase in integrated intensity of the emission. In striking contrast, the same reaction with $Ba(OAc)_2$ under 50-fold excess leads to a 10 nm red shift and only a 25% increase in integrated intensity. We are currently exploring the electronic structures of the ligands and their complexes as they apply to pH and cation sensing in water solution.

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(13) **Preparation of 1,10-Phenanthroline 5,6-Epoxide.**[12] A mechanically stirred mixture of 900 mL of CLOROX (regular) and 600 mL of water at 18 °C was adjusted to pH 8.5 with concentrated HCl. To this solution were added 2 g of tetrabutylammonium hydrogen sulfate and 5 g of 1,10-phenanthroline dissolved in 500 mL of chloroform. The pH of the reaction mixture was carefully maintained between 8 and 9. The conversion of the reaction was followed by NMR because the reaction time varies due to the quality of the bleach. Also, the yield decreases over time. After the reaction was complete, the organic layer was then isolated and washed with several portions of water. The washed organic layer was dried with sodium carbonate anhydrous and filtered, and the solvent was removed by rotary evaporation at room temperature. The crude epoxide was purified by recrystallization from a mixture of chloroform and hexanes (5:1) to give the pure product (2.6 g, 50% yield). Anal. Calc for $C_{12}H_8N_2O$: C, 73.46; H, 4.11; N, 14.28. Found: C, 73.31; H, 4.15; N, 14.37.

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(15) **Preparation of 5-(Amino- or alkoxy)-1,10-phenanthroline.** This is a typical procedure for the preparation of 5-substituted-1,10-phenanthroline via 1,10-phenanthroline 5,6-epoxide except for 5-cyano-1,10-phenanthroline. In this procedure, the hydroxy−dihydro intermediates can be isolated followed by treatment with NaH to regain the phenanthroline derivatives. **(a) 5,6-Dihydro-5-hydroxy-6-methoxy-1,10-phenanthroline.** The phenanthroline 5,6-epoxide (100 mg) was dissolved in 15 mL of methanol which contained a small amount of sodium methoxide. It was stirred at room temperature overnight. The solution was then removed by rotary evaporation. The residue was dissolved in methylene chloride, and the compound was purified by recrystallization from the mixture of methylene chloride and hexanes (2:5) to afford 86 mg of the compound (60% yield). Anal. Calc for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found: C, 67.60; H, 5.35; N, 12.14. ^{1}H NMR (δ/ppm, $CDCl_3$): 3.20 (br s, 1H), 3.70 (s, 3H), 4.50 (d, 1H), 5.00 (d, 1H), 7.30 (m, 2H), 7.85 (m, 1H), 8.00 (m, 1H), 8.73 (m, 2H). ^{13}C NMR (δ/ppm, $CDCl_3$): 59.9, 71.3, 82.2, 123.8, 124.2, 131.8, 133.3, 134.0, 134.1, 150.0, 150.1. UV−visible [λ/nm, CH_3CN (ϵ/M^{-1} cm^{-1})]: 298 (12 000), 254 (7000). **(b) 5-Methoxy-1,10-phenanthroline.** A 100-mg sample of 5,6-dihydro-5-hydroxy-6-methoxy-1,10-phenanthroline was dissolved in 10 mL of dioxane, and the solution was heated to 70 °C. To the stirred solution was added 120 mg of NaH in three portions at 0.5-h intervals. The reaction mixture was stirred overnight at 80 °C. After the mixture was cooled to room temperature the solvent was removed by rotary evaporation, the residue was dissolved in 30 mL of cold water, and the crude product was obtained by three extractions with 30-mL portions of chloroform. The product was purified by chromatography on a silica gel column eluted by a mixture of hexanes and ammonia-saturated chloroform (1:4). After removal of the solvent a yield of 53 mg (55%) was obtained. Anal. Calc for $C_{13}H_{10}N_2O$: C, 74.27; H, 4.79; N, 13.32. Found: C, 74.17; H, 4.84; N, 13.31. ^{1}H NMR (δ/ppm, $CDCl_3$): 4.07 (s, 3H), 6.91 (s, 1H), 7.53 (dd, 1H), 7.62 (dd 1H), 8.08 (dd, 1H), 8.64 (dd, 1H), 9.00 (dd, 1H), 9.17 (dd, 1H). ^{13}C NMR (δ/ppm, $CDCl_3$): 55.6, 100.6, 122.5, 123.0, 129.0, 130.7, 134.4, 142.7, 146.5, 147.7, 150.5, 152.8. UV−visible [λ/nm, CH_3CN (ϵ/M^{-1} cm^{-1})]: 352 (420), 336 (611), 302 (3000), 270 (15 000), 230 (20 000). **(c) 5-(Dimethylamino)-1,10-phenanthroline.** The preparation was the same as the above except the overall yield for both steps was 71%. Anal. Calc for $C_{14}H_{13}N_3 \cdot 0.5H_2O$: C, 72.36; H, 6.08; N, 18.09. Found: C, 72.42; H, 6.03; N, 18.00. ^{1}H NMR (δ/ppm, $CDCl_3$): 2.96 (s, 6H), 7.21 (s, 1H), 7.53 (dd, 1H), 7.64 (dd, 1H), 8.11 (dd, 1H), 8.61 (dd, 1H), 9.04 (dd, 1H), 9.17 (dd, 1H). ^{13}C NMR (δ/ppm, $CDCl_3$): 44.1, 111.0, 121.5, 122.4, 125.2, 128.3, 132.2, 134.1, 143.1, 146.5, 147.5, 148.0, 149.1. UV−visible [λ/nm, CH_3CN ($\epsilon/M^{-1}/cm^{-1}$)]: 324 (4800), 278 (16 000), 228. (38 000).

(16) **Preparation of 5-Cyano-1,10-phenanthroline.** Phenanthroline 5,6-epoxide (100 mg) was dissolved in 10 mL of water, and the solution was added to 10 mL of a 0.3 M KCN/water solution. The mixture was stirred at room temperature for 4 h. A white precipitate formed and was filtered off, washed with a large amount of water, dried, and recrystallized from methanol to give 84 mg of product (80% yield). Anal. Calc for $C_{13}H_7N_3$: C, 76.09; H, 3.44; N, 20.48. Found: C, 76.29; H, 3.23; N, 20.36. ^{1}H NMR (δ/ppm, $CDCl_3$): 7.80 (m, 2H), 8.36 (m, 2H), 8.66 (m, 1H), 9.34 (m, 2H). ^{13}C NMR (δ/ppm, $CDCl_3$): 109.6, 116.3, 124.1, 124.3, 126.4, 126.9, 133.9, 134.9, 136.9, 145.7, 147.4, 151.9, 153.2. UV−visible [λ/nm, CH_3CN (ϵ/M^{-1} cm^{-1})]: 342 (580), 326 (760), 298 (3200), 266 (13 000), 236 (17 000).

(17) **Preparation of Re(5-aza-18-crown-6-1,10-phen)$(CO)_3Cl$.** The preparation follows a typical procedure for synthesizing rhenium oomplexes.[18] Pure product (86% yield) was obtained by chromatography on neutral alumina eluting with 1:1 (v/v) toluene/acetonitrile. Anal. Calc for $C_{27}H_{31}N_3ClO_8Re$: C, 43.40; H, 4.18; N, 5.62. Found: C, 43.21; H, 4.18; N, 5.57. ^{1}H NMR (δ/ppm, $CDCl_3$): 3.50−3.80 (m, 24H), 7.75 (dd, 1H), 7.77 (s, 1H), 7.85 (dd, 1H), 8.45 (d, 1H), 9.19 (d, 1H), 9.21 (d, 1H), 9.34 (d, 1H). UV−visible [λ/nm, CH_3CN (ϵ/M^{-1} cm^{-1})]: 352 (7500), 290 (15 000), 252 (27 000). IR (CH_2Cl_2) (ν(CO)/cm^{-1}): 2022, 1918, 1896.

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