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NEW 1,10-PHENANTHROLINETHIOLS

Max Hunziker*[a] and Urs Hauser

Department of Physics, Stanford University, Stanford, CA 94305, USA

[a] current address: Zentrale Forschungslaboratorien, Ciba-Geigy AG,
CH-4002 Basel, Switzerland

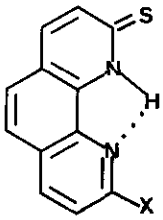
Abstract -- Reaction of KHS with 2-chloro- and 2,9-dichloro-1,10-phenanthroline in ethanol at elevated temperature and pressure afforded the corresponding phenanthrolinethiols which were characterized by spectroscopic and chemical methods. 2,2'-Thiobis(1,10-phenanthroline) and other heteroaryl sulfides derived from 1,10-phenanthroline-2-thiol were prepared by amide promoted nucleophilic substitution of aryl halide by thiolate anion.

INTRODUCTION

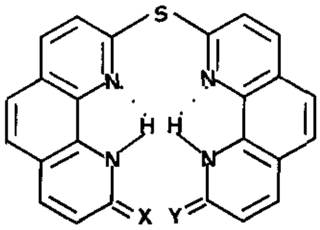
The chemistry of 1,10-phenanthroline has recently received more attention owing to the interest in the preparation of macrocyclic ligand systems incorporating the phenanthroline moiety[1-8]. A number of new 2,9-disubstituted 1,10-phenanthrolines were prepared for this reason by Ogawa et al.[1-4], Lewis et al.[6] and Chandler et al.[7]. In the course of our work for sulfur bridged macrocycles we prepared some new sulfur derivatives of 1,10-phenanthroline on which we are reporting below.

RESULTS AND DISCUSSION

1,10-phenanthroline-2-thiol (**1**) and 1,10-phenanthroline-2,9-dithiol (**2**) were prepared from 2-chloro-1,10-phenanthroline[9] and 2,9-dichloro-1,10-phenanthroline[3], respectively, with KHS in ethanol at elevated temperature and pressure. In 2- (and 4-) mercaptopyridines and other mercapto derivatives of six-membered nitrogen heterocycles it is well established[10] that tautomeric forms with hydrogen on nitrogen are favored at the expense of tautomers with hydrogen on sulfur. The same behavior was found for the two phenanthrolinethiols. The IR-spectra of both **1** and **2** show strong bands at 3330 and 3320 cm^{-1} respectively, attributed to the N-H stretching vibration of the thione form. In addition, the IR-spectrum of the



1 (X=H)
2 (X=SH)

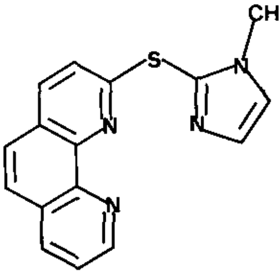


3 a (X=Y=S)
b (X=S ,Y=O)
c (X=Y=O)

dithiole **2** shows a weak band at 2600 cm^{-1} which was assigned to the S-H stretching vibration in agreement with the position reported for a number of other aromatic thiols[11]. The presence of both bands in **2** indicates that the molecule adopts the thione form on one side only. This is fully confirmed by ^{1}H NMR in $CDCl_3$ where one finds six nonequivalent aromatic protons. If, however, the ^{1}H NMR spectrum of **2** is recorded in DMSO-d_6 three pairs of equivalent aromatic protons are found, indicating interaction with the solvent such that the dithiole form is favored (DMSO is known as a hydrogen bond acceptor). The spectrum of **2** in DMSO-d_6 could, however, also be explained as that of 2,2',9,9'-bis-(1,10-phenantholinediyl)disulfide since it is well known that DMSO oxidation of aromatic thiols leads to disulfides[12-14]. Attempts to prepare the disulfides from **1** and **2** applying the standard DMSO oxidation procedure by Yannios[14] failed, however, and **1** was isolated unchanged after 18 h in DMSO at 90°C. Under the same conditions **2** gave a yellow precipitate with a crude melting point around 315°C with an elemental analysis and IR-spectrum consistent with **3a**.

The thiols **1** and **2** were further characterized by conversion to the corresponding alkyl thioethers with methyl and ethyl iodide (products **4**,**5**,**6**,**7**). The thioethers were obtained as the hydroiodides (from **1**) or the hydrotriiodides (from **2**) showing the N-H stretching vibration around 3330 cm^{-1}. The free 2,9-bis(alkylthio)-1,10-phenanthrolines were obtained from the hydrotriiodides by recrystallization from acetone or acetone-water mixtures.

Aryl sulfides may generally be prepared by nucleophilic substitution of aryl halide by thiolate anion[15]. The reaction is promoted by the use of amide solvents. Campbell[16] has shown that best results are achieved when alkali metal thiolates and the appropriate aryl halides are heated in DMA or DMF. Following this general procedure, we prepared several examples of diaryl sulfides. Thus 8 was obtained from 2-mercapto-1-methylimidazole and 2-bromo-1,10-phenanthroline, while the symmetrical compound 9 was prepared from 1 and 2-chloro-1,10-phenanthroline.



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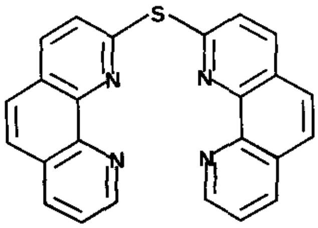
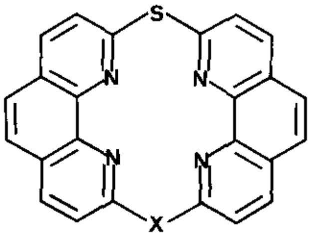


9



10 a (X=S), b (X=O)

The structure of 9 was confirmed both by spectroscopic methods and X-ray structure analysis[17]. As a tetradentate ligand, 9 forms stable complexes with transition metals. The Fe^{2+}-, Co^{2+}-, Ni^{2+}-, and Cu^{2+}-complexes were prepared in DMF solution and characterized spectroscopically. Table 1 contains UV/VIS absorption bands in aqueous solutions. Characteristic features are a very weak absorption in the visible and a new strong absorption around 273 nm with an extinction coefficient, log ε, of ca.4.75. This corresponds roughly to twice the extinction coefficient of the absorption band of the 1,10-phenanthrolinium ion (270 nm, log ε 4.5, dil. HCl[18]). As expected, the ferroin reaction is not observed.

When we applied Campbell's procedure for the preparation of macrocycle 10a (using 2,9-dichloro-1,10-phenanthroline and 1,10-phenanthroline-2,9-dithiol in a 1:1 molar ratio) we obtained a complex mixture containing 10a only in a low yield. IR-spectra of the carefully dried and solvent free crude reaction product showed typical amide bands at 3360, 1680 and 1625 cm^{-1} indicative of nucleophilic substitution by hydroxyl ions[19], resulting in 1,10-phenanthrolin-2(1H)-ones. This agrees with mass spectrometry where, in addition to the expected mass 420 for 10a, strong peaks at m/e 438, 422 and 404 were observed and tentatively assigned to 3b, 3c and 10b.

Table 1: Electronic spectra of M(9)Cl_2 complexes in aqueous solution and comparison with the ligand in $CHCl_3$. λnm(log ε)

Fe^{2+}	475sh(2.44), 378(4.07), 363sh(4.03), 327sh, 305(4.34), 290sh(4.71), 273(4.71), 249sh, 226(4.74), 203(4.74)
Co^{2+}	379(4.14), 361(4.07), 317sh, 307(4.33), 272(4.75), 247sh, 228(4.76),203(4.71)
Ni^{2+}	540(.46), 379(4.20), 362(4.09), 320sh, 307(4.26), 292sh, 273(4.74), 247(4.55), 224(4.63), 202(4.73)
Cu^{2+}	650(1.34), 470sh, 385(4.14), 368(4.06), 322sh, 309(4.27), 279(4.76), 250(4.67), 220(4.80), 208(4.86)
9 in $CHCl_3$	367(4.07), 350(4.03), 324(4.27), 308(4.38), 294sh, 265sh

Also observed was m/e 454 corresponding to 3a. The extremely low solubility in all solvents made separation of the various products impossible. Sublimation in vacuo at temperatures above 300°C did not separate the products satisfactorily and led to decomposition. Thermal dimerization by elimination of H_2S is often a successful method for the preparation of sulfides. However, heating of 2 under various conditions always gave the singly bridged bis-phenanthroline 3a and only traces of 10a were observed in the m.s. Other attempts for 10a (e.g. 2,9-dichloro-1,10-phenanthroline in DMF with Na_2S) also gave only small yields (m.s.) of 10a together with polymeric and other side products.

EXPERIMENTAL SECTION

Reagent grade substances and solvents were used in synthesis, analytical grade in spectroscopy. ^1H NMR spectra were obtained on a Varian XL-100 spectrometer with tetramethylsilane as internal standard. UV/VIS spectra of solutions were recorded on a Cary 14 spectrophotometer using quartz cells, and infrared spectra were obtained on a Perkin-Elmer model 621 from KBr pellets. Low resolution mass spectra were recorded on a Varian MAT-44 spectrometer using the direct inlet mode for all products. Melting points from a Thomas-Hoover capillary melting point apparatus are corrected. Elemental analyses were performed by E. Meier at the Microanalytical Laboratory of Stanford University.

1,10-phenanthroline-2-thiol (**1**): 2-chloro-1,10-phenanthroline[9] (200 mg), ethanol (6 ml) and KHS (560 mg) were heated in a sealed teflon cup at 140°C for 23 h. After cooling to room temperature the reaction mixture was evaporated to dryness and the resulting yellow residue suspended in water acidified to approx. pH 5 with acetic acid. The yellow product was filtered, washed with water and dried in vacuo over $CaCl_2$. Recrystallization from toluene afforded dark yellow needles of **1** (160 mg, 80 %); mp 221-222°C; ^1H NMR ($CDCl_3$) δ 7.65-7.53 (m,5H), 8.21 (dd,J=1.7, 8.3 Hz, 1H), 8.91 (dd,J=1.7, 4.3 Hz, 1H); M.S. m/e 212. Anal.Calcd. for $C_{12}H_8N_2S$: C,67.90; H,3.80; N,13.20; S,15.11; Found: C,67.93; H,4.05; N,13.19; S,15.14.

1,10-phenanthroline-2,9-dithiol (**2**): 2,9-dichloro-1,10-phenanthroline[2] (200 mg), ethanol (6 ml) and KHS (960 mg) were heated together in a sealed teflon cup at 140°C for 23 h. After cooling to room temperature the reaction mixture was evaporated to dryness. The resulting residue was dissolved in water and the product precipitated by the addition of glacial acetic acid to a pH of about 5. Dissolution in 1 M KOH and reprecipitation with acetic acid yielded a yellow microcrystalline product which was dried in vacuo over $CaCl_2$ to give the hemihydrate, **2**.1/2 H_2O (180 mg,88%); mp: upon fast heating melts at ca 217°C with decomposition to a new solid (see below) which melts at ca 325°C; ^1H NMR ($CDCl_3$) δ 7.54 (d,J=9.0 Hz, 1H), 7.55 (m, 3H), 7.84 (d,J=9.0 Hz, 1H), 8.10 (dd,J=9.0, 10.5 Hz, 1H); (DMSO-d_6) δ 7.40 (d,J=9.0 Hz,2H), 7.67 (s, 2H), 7.91 (d,J=9.0 Hz, 2H);M.S. m/e 244. Anal. Calcd. for $C_{12}H_8N_2S_2 \cdot 1/2H_2O$: C,56.89; H,3.58; N,11.05; S,25.31; Found: C,57.33; H,3.48; N,11.09; S,25.30.

9,9'-thiobis[1,10-phenanthrolin-2(1H)-thione] (**3a**): This compound was obtained by heating of **2** above approx. 220°C. The weight loss corresponded to 1 mole of H_2S per mole **3a** formed. mp: ca. 330°C with dec. (compare **2**); the product takes up water from the atmosphere; M.S. m/e 454. Anal. Calcd. for $C_{24}H_{14}N_2S_3 \cdot 3/4\ H_2O$: C,61.58; H,3.33; N,11.97; S,2o.54; Found: C,61.39; H,3.24; N,11.88; S,2o.69.

2-methylthio-1,10-phenanthroline hydriodide (**4**): 37 mg of **1** and 20 ml of methyl iodide were stirred at 30-35°C for 1 h. Fine yellow needles of **4** formed which were filtered and washed with ethanol and ether. Yield: 58 mg, 94%. Recrystallization from H_2O: mp 278-279°C; ^1H NMR (D_2O) δ 2.00 (s,3H), 6.87 (d,J=8.7 Hz, 1H), 7.19 (d,J=1.6 Hz, 2H), 7.39 (d,J=8.7 Hz, 1H), 7.45 (dd, 1H), ca. 8.3 (m, 2H).

Anal.Calcd. for $C_{13}H_{11}IN_2S$: C,44.08; H,3.13; I,35.83; N,7.91; S,9.05; Found: C,44.59; H,3.16; I,34.0; N,7.89.

2-ethylthio-1,10-phenanthroline hydriodide (**5**): This compound was prepared from **1** and excess ethyl iodide. Reaction time 4 h, yield 80%. Light yellow needles from H_2O mp 235-238°C; ^{1}H NMR (DMSO-d_6) δ 1.42 (t,J=7.4 Hz, 3H), 3.60 (dd,J=7.4 Hz, 2H), 7.87 (d,J=8.7 Hz, 1H), 8.25 (d,J=1.5 Hz, 2H), 8.36 (dd,J=5.4, 8.3 Hz, 1H), 8.51 (dd,J=8.7 Hz, 1H), 9.34 (dd,J=1.5, 8.3 Hz, 1H). Anal. Calcd. for $C_{14}H_{13}IN_2S$: C,45.66; H,3.56; I,34.46; N,7.61; Found: C,45.39; H,3.58; I,32.5; N,7.68.

2,9-bis(methylthio)-1,10-phenanthroline (**6**): **2** (50 mg) was dissolved in methyl iodide (15 ml) with stirring. After a few minutes an orange precipitate began to form. Stirring was continued for some 16 h at RT. The gold brown product was filtered off and washed with ether. Yield 62 mg, mp 178°C. The elemental analysis showed half a mole of hydrotriiodide and approx. one mole of water. Recrystallization from acetone gave **6** as light yellow needles, mp 192°C; ^{1}H NMR (DMSO-d_6) δ 2.83 (s, 6H), 7.65 (d, J=8.5 Hz, 2H), 7.86 (s, 2H), 8.30 (d,J=8.5 Hz, 2H); M.S. m/e 272. Anal. Calcd. for $C_{14}H_{12}N_2S_2$: C,61.74; H,4.44; N,10.29; S,23.54; Found: C,60.40; H, 4.45; N,10.14.

2,9-bis(ethylthio)-1,10-phenanthroline (**7**): **2** (39 mg) and ethyl iodide (25 ml) were stirred at 60-65°C for 15 h. After cooling to -10°C fine gold brown needles of the hydrotriiodide of **7** were filtered off and washed with ether. Yield 46 mg (42%); mp 167°C. Recrystallization from acetone-water afforded **7** as white needles: mp 71°C; ^{1}H NMR (acetone-d_6) δ 1.55 (t,J=7.3 Hz, 6H), 3.57 (q,J=7.3 Hz, 4H), 7.49 (d,J=8.5 Hz, 2H), 7.79 (s, 2H), 8.18 (d,J=8.5 Hz, 2H). Anal. Calcd. for $C_{16}H_{16}N_2S_2$: C,63.96; H, 5.36; N, 9.32; Found: C,62.83; H,5.33; N,9.21.

2-[(1-methylimidazol-2-yl)thio]-1,10-phenanthroline monohydrate (**8**): 2-mercapto-1-methylimidazole (200 mg) and KOH (100 mg) were heated in DMA (8 ml) until a dark blue solution resulted. 2-bromo-1,10-phenanthroline (370 mg) was added and the mixture refluxed for 8 h. After cooling to RT the mixture was filtered and the solvent removed by distillation until a thick slurry resulted. Water was added and the mixture extracted with toluene. Removal of the solvent left a noncrystallizable oil. Light yellow crystals of **8** were obtained from ethanol-water after prolonged cooling: mp 125°C dec.; ^{1}H NMR ($CDCl_3$) δ 3.76 (s, 3H), 7.03 (d,J=8.5 Hz, 1H), 7.20 (d,J=1.5 Hz, 1H), 7.33 (d,J=1.5Hz, 1H), 7.64 (dd,J=4.5, 8.5 Hz, 1H), 7.73 (s, 2H), 8.03 (d,J=8.5 Hz, 1H), 8.25 (dd,J=ca. 2, 8.5 Hz, 1H), 9.25 (dd,J=ca.2, 4.5 Hz, 1H). Anal. Calcd. for $C_{16}H_{12}N_4S \cdot 1H_2O$: C,61.92; H,4.55; N,18.05; S,10.33; Found: C,61.31; H,4.53; N,17.84; S,10.37.

2,2'-thiobis(1,10-phenanthroline) (9): 1 (420 mg), KOH (126 mg) and DMA (32 ml) were heated and the water plus approx. 15 ml of the DMA were distilled off. Then 2-chloro-1,10-phenanthroline (420 mg) was added and the mixture refluxed for 2.5 h. After cooling to ca. 80°C the solvent was removed under reduced pressure. The resulting residue was extracted with a mixture of chloroform and water. The chloroform phase was washed with water, dried over Na_2SO_4, concentrated to a few ml and refrigerated. 860 mg of crude product precipitated, were filtered and washed with ether. Recrystallization from $CHCl_3$ afforded colorless needles of 9 (666 mg, 53%) containing two equivalents of $CHCl_3$: mp 277-278°C. Concentration of the filtrate yielded a second crop of somewhat less pure product (112 mg), mp 273-275°C. The needles lost the $CHCl_3$ at 100°C in vacuo with deterioration. ^1H NMR ($CDCl_3$) δ 7.65 (dd,J=4.3, 8.1 Hz, 2H), 7.79 (s, 4H), 8.03 (d,J=8.4 Hz, 2H), 8.16 (d,J=8.4 Hz,2H), 8.27 (dd,J=1.8, 8.1 Hz, 2H), 9.24 (dd,J=1.8, 4.3 Hz, 2H). M.S. m/e (relative intensity): 390(85), 389(100). Anal. Calcd. for $C_{24}H_{14}N_4S \cdot 2CHCl_3$: C,49.63; H,2.56; N,8.90; S,5.10; Cl,33.81; Found: C,49.58; H,2.63; N,8.61; S,5.11; Cl,33.49.

Metal complexes of 9: 9 (40 mg) and DMF (3 ml) were heated to 100°C. An equivalent amount of metal chloride was added slowly with vigorous stirring. The mixture was allowed to cool to RT and the resulting precipitates (powders) were isolated and washed with DMF and ether. Yields: 50-70%. By this procedure complexes of the general formula $M(C_{24}H_{14}N_4S)Cl_2$ were obtained, with M= Fe, Co, Ni, Cu. All complexes gave satisfactory elemental analysis.

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19. Introduced into the reaction mixture as deprotonating agent.

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