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Facile one-step synthesis of a thia-bridged bis-1,10-phenanthroline macrocycle☆

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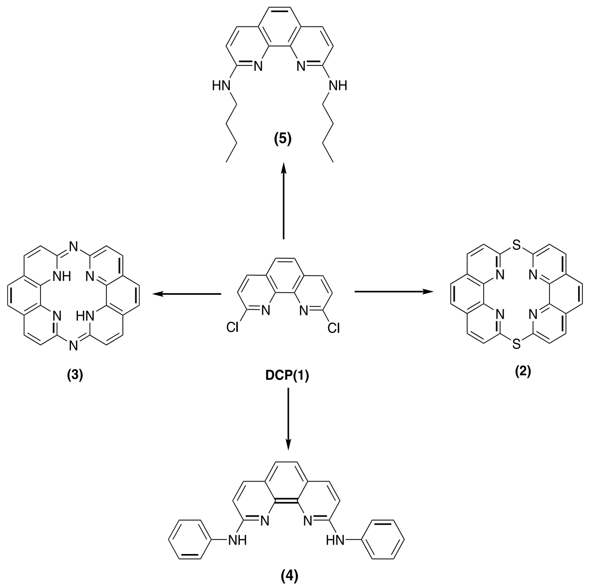
Abstract—An efficient one-pot synthesis of a macrocyclic ligand, consisting of two 1,10-phenanthroline nuclei bridged by sulfur, is described. A spectrophotometric investigation reveals the isolated compound to be the mono-trifluoroacetate salt. Symmetrical NH- and S-bridged tetradentate ligands were also synthesized by the new method.

There has been a great deal of interest in the preparation of macrocyclic ligand systems incorporating 1,10-phenanthroline moieties.[1,2] Transition metal complexes of these ligands have been extensively investigated for their photochemical,[3] electrochemical,[4] and biological properties.[5] The increasing interest in the specific DNA binding and cleavage activity mediated by metal complexes of 1,10-phenanthroline containing macrocycles has also provided fresh impetus for the design of novel synthetic routes leading to these desirable compounds.[2,6] Recently we reported an efficient one-pot synthesis of an aza-bridged bis-1,10-phenanthroline macrocycle which included its structural characterization by single-crystal X-ray analysis.[1h] Preparation of the thia-bridged bis-phenanthroline macrocyclic ligand [H_2DTPP (**2**)] has been reported by Ogawa et al.[1g,2,6] via a two-step procedure involving cyclization of 9-chloro-1,10-phenanthroline-2(1*H*)-thione. These workers quoted a yield of 71% using their synthetic protocol. The thermal dimerization procedure[1g] has been reported to give a very low yield of the desired compound with many, largely undefined, side products. We report here a simpler, more efficient synthesis of **2** that proceeds without the need for a metal template by direct reaction of 2,9-dichloro-1,10-phenanthroline [DCP (**1**)] with H_2S. Full characterization of the resulting product is also included.

The synthesis of **2** is as follows: Finely powdered **1** (1.02 g; 4.10 mmol) was heated at 170°C under an atmosphere of H_2S for 1 h. During the course of heating, the color of the solid changed from white to yellow and finally to orange-yellow. The crude product was washed successively with CH_2Cl_2 and CH_3OH, and dried in vacuum. Crystallization was effected by slow diffusion of diethyl ether into a concentrated TFA solution to afford an orange-yellow powder (0.89 g, yield: ∼80%).[7] The yield of product **2** could be



Scheme 1.

Keywords: thia; macrocycle; polythiocyclophane; phenanthroline.

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Table 1. Reaction conditions of DCP and CP

Entry	Substrate	Reagent	Time (h)	Temp. (°C)	Product	Yield (%)[a]
1	DCP (**1**)	H_2S	1	170	**2**	80
2	DCP (**1**)	NH_3	8	250	**3**	84[1h]
3	DCP (**1**)	Aniline	5	150	**4**	30[12]
4	DCP (**1**)	Butylamine	2	150	**5**	85[1h]
5	CP (**6**)	NH_3	6	240	**7**[b]	63
6	CP (**6**)	H_2S	10	180	**8**	60

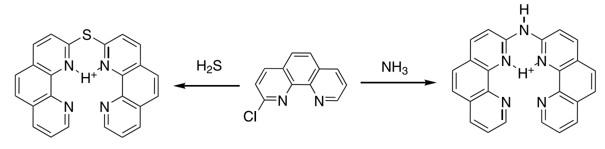
[a] After crystallization.

[b] Characterized by IR, UV–vis, ^1H and ^{13}C NMR, FAB-MS.

increased by using the hydrochloride salt of **1**. The mass spectrum (FAB) shows the expected peak at $m/e=421$ (100%). ^1H and ^{13}C NMR spectra show H_2DTPP to have a planar structure (C_{2h}) in solution. Its IR spectrum shows a very strong band at 1656 cm^{-1}, which is assigned to the stretching vibration of the counter ion CF_3COO^-, in agreement with the cationic form of the ligand. This is further corroborated by the presence of a N–H stretch at 3330 cm^{-1} and a N–H bending mode at 1607 cm^{-1}. A broad absorption at 2800–3000 cm^{-1} is an indication of the intramolecular N–H···N interaction as found for the aza-analogous (Scheme 1).[1]

The electronic spectrum is slightly dependent on solvents. The hydrogen located on the inner nitrogen has no effect on the π-conjugation system. The pK_{a2} value for **2**[8] determined here is 4.48, smaller than the pK_a value of 4.98 for 1,10-phenanthroline. The pK_{a1} is too small to be determined. The spectrophotometric titration experiment together with the infrared spectrum indicates that crystallization of the macrocyclic ligand from CF_3COOH affords the mono-protonated salt. The CV shows two irreversible peaks for the mono- and di-anion.[9] Similarly, 1,10-phen also shows two irreversible peaks at 2.12 and −2.70 V. The lone-pair electrons on the sulfur atoms and the greater conjugation resulted in lower reduction potentials for this macrocycle.

The reaction proceeded smoothly for H_2S and NH_3 to afford the thia- and aza-bridged macrocycles (entries 1 and 2) in very good yields (see Table 1) without any side products. However, application of the present method to aniline and *n*-butylamine led to formation of *N*,*N*′-diphenyl-1,10-phenanthroline-2,9-diamine **4**[10] and 2,9-dibutylamino-1,10-phenanthroline **5**,[1h] respectively under the conditions as shown in Table 1. In order to increase the scope and the utility of the method, we have synthesized bis(1,10-phenanthroline-2-yl)amine [DPA (**7**)][11] and 2,2′-thiobis(1,10-phenanthroline) [DPS (**8**)][12] from **CP** with NH_3 and H_2S in good yields (Scheme 2). Compound **8** directly obtained from the reaction vessel as yellow needles was shown to have a structure similar to that of **7**. Its IR spectrum shows a very strong band at 3330 cm^{-1} which was attributed to the N–H stretching vibration in agreement with the hydrochloride salt of DPS. The electronic spectrum indicates that the molecule also contains the hydrogen of cationic character similar to the spectrum obtained by the semi-empirical method[13] and that of **7** as well. This is further supported by the presence of a broad singlet at 12.3 ppm due to N–H proton in its ^1H NMR spectrum recorded in DMSO-d_6.



DPS(8) CP(6) DPA(7)

Scheme 2.

On the basis of these results, other macrocycles could be synthesized by proton-assisted template coupling of **1** with other nucleophilic agents.

In conclusion, we have developed a more efficient and convenient one-pot method for the synthesis of macrocycle **2** compared to those previously reported.[2]

Acknowledgements

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References

1. (a) Ogawa, S.; Yamaguchi, T.; Gotoh, N. *J. Chem. Soc., Chem. Commun.* **1972**, 577–578; (b) Ogawa, S.; Yamaguchi, T.; Gotoh, N. *J. Chem. Soc., Perkin Trans. 1* **1974**, 976–978; (c) Ogawa, S. *J. Chem. Soc., Perkin Trans. 1* **1977**, 214–216; (d) Seno, M.; Tsuchiya, S.; Ogawa, S. *J. Am. Chem. Soc.* **1977**, *99*, 3014–3018; (e) Bishop, M. M.; Lewis, J.; O'Donoghue, T. D.; Raithby, P. R. *J. Chem. Soc., Chem. Commun.* **1978**, 476–478; (f) Ogawa, S.; Shiraishi, S. S. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2527–2530; (g) Hunziker, M.; Hauser, U. *Heterocycles* **1982**, *19*, 2131–2138; (h) Wang, W.-J.; Chuang, K.-S.; Luo, C.-F.; Liu, H.-Y. *Tetrahedron Lett.* **2000**, *41*, 8565–8568.
2. Hirai, M.; Shinozuka, K.; Sawai, H.; Ogawa, S. *Chem. Lett.* **1992**, 2023–2026.
3. Kalyanasundaram, K. *Photochemistry of Polypyridine and Porphyrine Complexes*; Academic Press: New York, 1992.

4. Kelly, D. M.; Vos, J. G. In *Electroactive Polymer Electrochemistry Part* 2; Lyons, M. E. G., Ed.; Plenum Press: New York, 1994; pp. 173–232.
5. Sammes, P. G.; Yahioglu, G. *Chem. Soc. Rev.* **1994**, 327–334.
6. Hirai, M.; Shinozuka, K.; Ogawa, S.; Sawai, H. *Chem. Lett.* **1996**, 1113–1114.
7. **H_2DTPP**: IR (KBr, v/cm^{-1}): 3330 (N–H), 3030 (C–H Ar), 1656 (CF_3COO^-), 1607 (N–H bend), 1581 and 1547 (Ar C–H in-plane bend), 1500–1400 (C=C or C=N stretch), 850 (Ar C–H out of plane bend). ^{1}H NMR (CF_3COOD, δ): 9.20 (d, J=8.7 Hz, 4H); 8.61 (d, J=8.7 Hz, 4H); 8.44 (s, 4H). ^{13}C NMR (CF_3COOD, δ): 128.2, 145.7, 131.7, 159.2, 138.1, 132.9. FAB-MASS (m/z): 421 (M^+). The electronic spectrum measured for H_2DTPP in MeOH:CH_2Cl_2 (1:1) at room temperature shows absorption bands at 229 (1.22×10^5), 282.5 (6.52×10^4), 308 (3.47×10^4), 354 (1.68×10^4), 372.5 (1.67×10^4) and 395 nm (1.22×10^4) with their molar absorptivities (ε/dm^3 mol^{-1} cm^{-1}) given in parentheses. As may be noted, with the increase of pH, the three bands in the successive absorption curves undergo blue shifts during which they pass through three isosbestic points at 265.5, 327.5 and 330.5 nm.
8. A stock solution (1×10^{-5} M) in MeOH/CH_2Cl_2 mixture was titrated with standard HCl over the pH range 2–7 for pK_{a2} and over the pH range 9 to −0.31 for pK_{a1}. The pK_a values were determined from the relationship between the changes in the optical density with the pH for a given wavelength. The plot gave the pK_{a2} value of 4.48. Three isosbestic points at 265.5, 327.5 and 330.5 nm were observed. Acid titration with standard HCl in the range of pH 9 and −0.31, gave three isosbestic points at 262 nm, 317 nm, 345.5 nm. The pH variations stopped at pH −0.31, but increasing of absorbance at 282.5 nm continued. This observation suggests the occurrence of the second protonation.
9. Cyclic voltammogram of $HDTPP^+$ in propylene carbonate containing 0.1 M $LiClO_4$ shows two irreversible peaks at −1.35 and −1.72 V, forming two anionic radicals.
10. Wang, W.-J.; Luo, C.-F.; Chuang, K.-S.; Liu, H.-Y. *Molecules* **2000**, *6*, M230.
11. Kao, H. C. MSc. Thesis, Tamkang University, Taipei, Taiwan, 2002.
12. **DPS**: IR (KBr, v/cm^{-1}): 3330 (N–H), 3030 (C–H Ar), 1607 (N–H bend), 1589 and 1564 (Ar C–H in-plane bend), 1500–1400 (C=C or C=N stretch), 844 (Ar C–H out of plane bend). ^{1}H NMR (DMSO-d_6, δ): 12.28 (s, 1H); 9.05 (dd, J=1.5, J=4.4 Hz, 2H); 8.52 (dd, J=1.5, J=8.3 Hz, 2H); 8.04 (d, J=9.0 Hz, 2H); 7.87 (d, J=5.9 Hz, 4H); 7.80 (dd, J=4.41, J=8.3 Hz, 2H); 7.53 (d, J=9.0 Hz, 2H). UV–vis ($CHCl_3$) measured at room temperature, λ nm (ε/dm^3 mol^{-1} cm^{-1}): 249 (5.7×10^3), 307 (3.2×10^3), 318 (5.0×10^3), 358 (1.6×10^3), 418 (1.4×10^3).
13. CAChe® 4.4 Windows, Fujitsu Limited, Japan, 2000.