Synthesis of 4,7-Disubstituted Phenanthrolines as Key Building Blocks for the First Preparation of Macrocyclic Mono- and Bisphenanthrolines with *exo*-Coordination Sites

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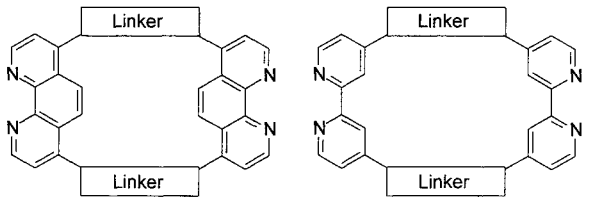
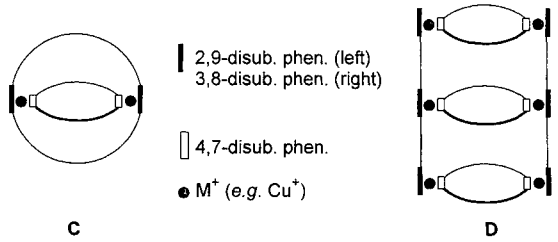
Abstract. The preparation of various 4,7-bisalkynylated phenanthrolines and 4,7-bis(4-hydroxyphenoxy)phenanthroline as well as their use in the synthesis of the first macrocyclic phenanthrolines and bisphenanthrolines with *exo*-coordination sites is described.

While macrocyclic phenanthrolines with *endo*-coordination sites have attracted much attention due to their key role in the formation of catenanes,[1] rotaxanes[2] and molecular knots,[3] macrocyclic bis- or oligophenanthrolines with *exo*-coordination sites (**A**) are not known so far. Macrocycles exhibiting the closest structural resemblance contain bipyridine ligands as *exo*-coordination sites (such as **B**) and have been reported from several laboratories.[4]



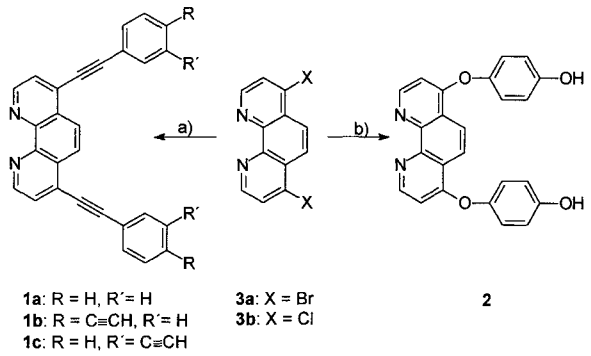
We have become interested in the coordination chemistry of macrocyclic bisphenanthroline ligands **A** because of their potential for the convergent construction of the novel redoxactive globes **C** and of the fascinating nanotubes **D** through the simple self-assembly of three reactants: i) Cu^{I} as coordinating metal ion with a tetrahedral complex geometry, ii) type **A** phenanthroline ligands, and iii) either macrocyclic bisphenanthrolines with *endo*-coordination sites (for **C**) or linearly connected 3,8-oligophenanthrolines (for **D**).



Scheme 1

The construction of such novel topological structures, however, relies decisively on a simple synthetic access to 4,7-disubstituted phenanthrolines that have only rarely been described in the literature.[5,6] Herein, we now describe the synthesis of the novel 4,7-disubstituted phenanthrolines **1a-c** and **2** that may serve as versatile building blocks for the desired macrocyclic ring systems and their use for the first preparation of macrocyclic phenanthrolines with *exo*-coordination sites.

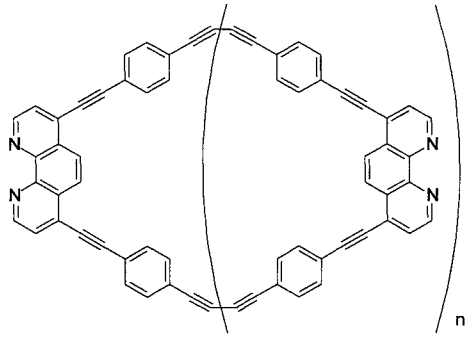
The synthesis of **1a-c** was realized through $Pd(PPh_3)_2Cl_2$-catalyzed alkynylation of 4,7-dibromophenanthroline (**3a**) in DMF. The highest yields of analytically pure compounds (**1a**: 95%, **1b**: 49%, **1c**: 39%) were achieved by employing a fivefold excess of the acetylene component (*i.e.* phenylacetylene, *p*-diethynylbenzene, *m*-diethynylbenzene).[7,8] Actually, the main problem of this synthetic route to **1** is the availability of *pure* **3a** that was prepared from the reaction of



Scheme 2. a) **3a** + $Pd(PPh_3)_2Cl_2$, CuI, 90 °C, arylacetylene; b) **3b** + *p*-hydroquinone, Na_2CO_3, 160 °C

4,7-dihydroxyphenanthroline with PBr_3 in PBr_5. When following the literature procedure,[9] the reaction afforded a mixture of various brominated phenanthrolines [4,7-dibromophenanthroline (30%), 3,4,7-tribromophenanthroline (17%), 3,4,7,8-tetrabromophenanthroline (7 %)] the separation of which proved to be extremely difficult. After testing 20 different solvent mixtures a highly efficient purification by chromatography could be developed using chloroform/acetone (100:1) on silica gel.

Unfortunately, the use of phenanthrolines **1b,c** for the construction of macrocyclic ring systems through oxidative coupling is limited. When we treated **1b** under typical Glaser conditions, the bis- and trisphenanthrolines **4** (n=1,2) were obtained as main products as demonstrated by MALDI-TOF experiments, but all efforts to purify the mixture of macrocycles failed because of the insolubility of these planar molecules.

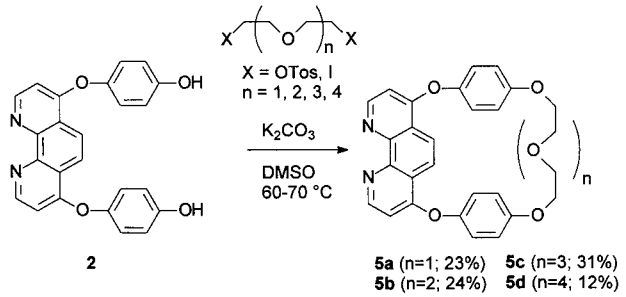


4a (n = 1), **4b** (n = 2)

As an alternative building block for the desired oligophenanthroline macrocycle **A** we have synthesized bis(4-hydroxyphenoxy)-phenanthroline (**2**). It was readily prepared from 4,7-dichlorophenanthroline (**3b**)[10] in presence of a large excess of *p*-hydroquinone and sodium carbonate as base in dry acetonitrile. Heating this mixture under nitrogen atmosphere at 150 - 160 °C in a sealed glass tube for 6 h led to complete formation of **2** (95%) whose purification was facilitated because of its insolubility in acetonitrile and water.[11] The

application of this slightly acidic phenanthroline ligand in amperometric pH sensors using the $Fe(\mathbf{2})_3^{2+}$ complex as a redoxactive component is under current investigation.[12]

In addition, phenanthroline **2** could be successfully utilized for the preparation of the desired mono- (**5**) and bisphenanthroline (**6**) macrocycles. Using a typical macrocyclization protocol, **2** was treated with various diiodides or ditosylates in presence of potassium carbonate to furnish **5** and **6** in acceptable yield.[13]



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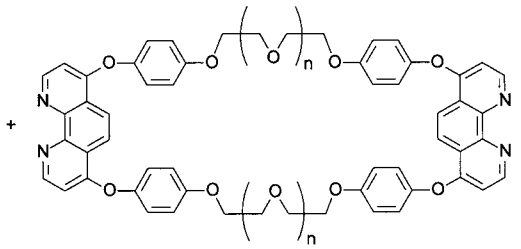
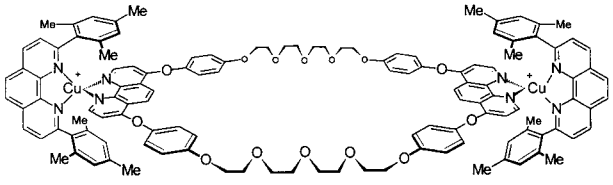
5a (n=1; 23%) **5c** (n=3; 31%)
5b (n=2; 24%) **5d** (n=4; 12%)



6a (n=1; 8%) **6c** (n=3; 10%)
6b (n=2; 6%) **6d** (n=4; 5%)

The bisphenanthroline macrocycles **6** now pave the way to the preparation of structures **C** by using a novel method for the clean and controlled generation of mixed phenanthroline copper(I) complexes developed by us recently. When reacting two equivalents of 2,9-dimesitylphenanthroline with **6c** in presence of Cu^I the redoxactive dinuclear copper(I) complex **7** was formed.[14] *En route* to **C** the 2,9-disubstituted phenanthrolines need only to be replaced by an appropriately sized macrocyclic bisphenanthroline exhibiting *endo*-coordination sites, a work that is currently underway in our laboratory.



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7.) Preparation of **1a**: A degassed solution of 4,7-dibromo-1,10-phenanthroline (**3a**) (600 mg, 1.78 mmol), phenylacetylene (850 mg, 8.33 mmol), copper(I) iodide (15.0 mg, 78 (mol), dichlorobis(triphenylphosphine)-palladium(II) (33.0 mg, 47 (mol) and triethylamine (1.00 ml, 7.50 mmol) in 15 ml of dry DMF was heated for 18 h at 90 °C. After standard work-up the crude compound was purified by column chromatography on silica gel (eluent $CHCl_3$/MeOH 100:1) and recrystallized from dry DMF, yielding 649 mg (96 %) of the pure product **1a** as pale yellow needles (mp 197-198 °C). ^{1}H-NMR (200 MHz, $CDCl_3$): δ = 7.43-7.46 (m, 6 H, 3'-H, 4'-H, 5'-H), 7.68-7.72 (m, 4 H, 2'-H, 6'-H), 7.80 (d, *J* = 4.6 Hz, 2 H, 3-H, 8-H), 8.46 (s, 2 H, 5-H, 6-H), 9.16 (d, *J* = 4.6 Hz, 2 H, 2-H, 9-H).

8.) All new compounds gave satisfactory elemental analyses and/or high resolution mass spectra. Some selected analytical data: **1b**: yellow crystals. ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.26 (s, 2H), 7.56 (d, *J* = 8.6 Hz, 4H), 7.66 (d, *J* = 8.6 Hz, 4H), 7.79 (d, *J* = 4.6 Hz, 2H), 8.45 (s, 2H), 9.18 (d, *J* = 4.6 Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 79.8, 83.0, 86.8, 98.5, 122.4, 123.3, 125.1, 125.6, 128.3, 129.6, 131.9, 132.4, 146.3, 149.9; IR (KBr): ν 3286, 3150, 2207, 2101, 831 cm^{-1}; MS: [M^+] calcd for $C_{32}H_{16}N_2$: 428.1313, found: 428.1322.

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11.) After recrystallization from water white needles of **2** were obtained. ^{1}H NMR (200 MHz, d_6-DMSO): δ 5.75 (s, 2H), 6.92 (d, *J* = 5.2 Hz, 2H), 6.96 (d, *J* = 8.7 Hz, 4H), 7.20 (d, *J* = 8.7 Hz, 4H), 8.46 (s, 2H), 8.93 (d, *J* = 5.2 Hz, 2H); calcd for $C_{24}H_{16}N_2O_4 \cdot H_2O$: C 69.56 H, 4.38 N, 6.76; found C 69.25, H 4.70, N 6.30.

12.) Schmittel, M.; Ganz, A.; unpublished results.

13.) General procedure for the preparation of **5,6**: 4,7-bis(*p*-hydroxyphenoxy)-1,10-phenanthroline **2** (400 mg, 1.02 mmol), 1,11-diiodo-3,6,9-trioxaundecane (460 mg, 1.10 mmol) and potassium carbonate (2.00 g, 15.0 mmol) were heated to 60-70 °C in 30 ml of dry DMSO for 4 days. After work up the residue was purified by chromatography (silica gel, dichloromethane : methanol : NH_3 = 10 : 1 : 0.01) providing the bisphenanthroline macrocycle **6c** (10%) and the cyclic monophenanthroline **5c** (31%) in analytically pure form. Data for **5c**: ^{1}H-NMR (250 MHz, $CDCl_3$): δ = 3.72 (m, 8H), 3.87 (m, 4H), 4.15 (m, 4H), 6.73 (d, *J* =

5.2 Hz, 2H), 6.98 (d, J = 9.2 Hz, 4H), 7.15 (d, J = 9.2 Hz, 4H), 8.36 (s, 2H), 8.85 (d, J = 5.2 Hz, 2H); ES-MS ($C_{32}H_{30}N_2O_7$+H^+): calcd. 555.21, found 555.43; data for **6c**: ^{1}H-NMR (250 MHz, $CDCl_3$): δ = 3.76 (m, 16H, 3''-H, 4''-H), 3.92 (m, 8H, 2''-H), 4.12 (m, 8H, 1''-H), 6.64 (d, J = 5.2 Hz, 4H, 3-H, 8-H), 6.93 (d, J = 8.85 Hz, 8H, 3'-H, 5'-H), 7.00 (d, J = 8.85 Hz, 8H, 2'-H, 6'-H), 8.17 (s, 4H, 5-H, 6-H), 8.84 (d, J = 5.2 Hz, 4H, 2-H, 9-H); ES-MS ($C_{64}H_{60}N_4O_{14}$+H^+): calcd. 1109.42, found 1109.25.

14.) Schmittel, M.; Ganz, A.; *Chem. Commun.* **1997**, in press.