# A Short Synthetic Route to Novel, Highly Soluble 3,8-Dialkyl-4,7-dibromo-1,10-phenanthrolines

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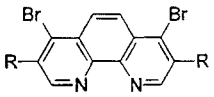
**Abstract.** A short and convenient synthesis of highly soluble 3,8-dialkyl-4,7-dibromo-1,10-phenanthrolines is described. These compounds are versatile key building blocks for the preparation of macrocyclic oligophenanthrolines with *exo*-coordination sites.

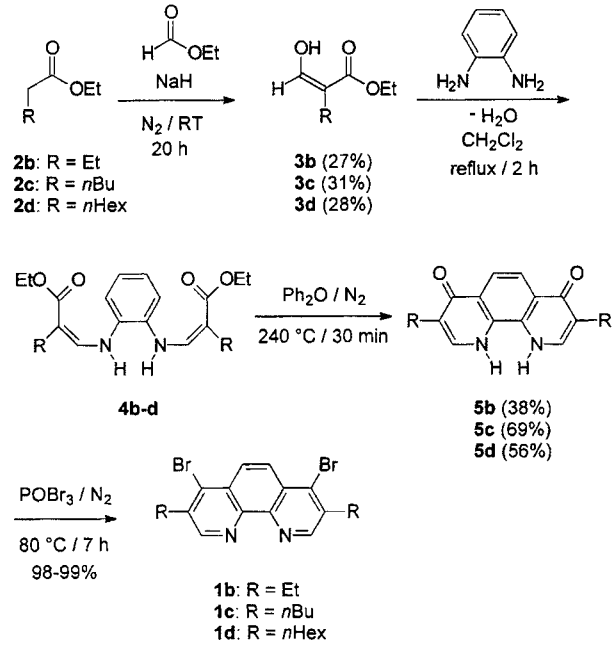
In view of their exciting coordination chemistry[1] macrocyclic oligophenanthrolines and oligobipyridines with *exo*-coordination sites are currently of great interest.[2-4] Mostly, 2,2´-bipyridines are preferred over phenanthrolines as exoreceptors because the former can be readily prepared and incorporated in flexible macrocycles.[3,4] In contrast, preparation of rigid macrocyclic oligobipyridines is obviously severely impeded by the preferred *anti* conformation of the central C-C bond of bipyridine building blocks.[4] Therefore, and in consideration of their stronger complexation constants we have concentrated on constructing rigid macrocyclic oligophenanthrolines[2] starting from 4,7-dibromophenanthroline **1a**,[5] the latter being available in 5 steps from 1,2-phenylenediamine. Heck-coupling of various dialkynes to **1a** furnished phenanthrolines with two acetylene termini that upon oxidative alkyne coupling afforded the desired macrocyclic oligophenanthrolines.[2] Unfortunately, their low solubility prevented any use in the self-assembly of supramolecular coordination complexes.[6]



**1a**: R = H
**1b**: R = Et
**1c**: R = *n*Bu
**1d**: R = *n*Hex

This frustrating finding stimulated our search for an efficient synthetic route to modified 4,7-dibromophenanthrolines exhibiting a greatly increased solubility. We expected that appropriate alkyl groups in the 3,8-position should increase solubility without changing the complexation properties, but such phenanthrolines had not been described yet. Despite the structural simplicity of phenanthrolines **1b-d**, our attempts to prepare them by modifying various known routes[7,8] failed. We finally succeeded by following old procedures outlined by Bell[9] and Case[10] that after major changes and improvements - as described in the present paper - provide synthetic access to 10 g of **1b-d** within 2.5 d. Moreover, these novel phenanthrolines, in particular **1d**, exhibit outstanding solubility which underlines their synthetic utility as key building blocks for the desired multireceptor macrocycles.

The required α-formylacetic esters **3b-3d** were readily obtained by a method of Spengler[11] although not in good yield. Fortunately, these compounds can be used without further purification in a reaction with 1,2-phenylenediamine in dichloromethane at reflux temperature removing the formed water in a Dean-Stark apparatus to furnish the corresponding 1,2-bis-(β-ethoxycarbonyl-β-alkylvinylamino)-benzenes **4b-4d** after only two hours in nearly quantitative yield (as detected by $^1$H-NMR-spectroscopy).[12] This is a major improvement over the preparation of similar compounds in presence of $P_2O_5$ as described by Bell[9] and Case,[10] since their reaction times ranged from several days to 3 months!




**Scheme 1**

Compounds **4b-4d** could - again without need for purification - be cyclized thermally in diphenylether at 240 °C to afford the corresponding 1,10-phenanthroline-4,7-diones **5b-5d** in good overall yield.[13] The cyclization **4** ⟶ **5** is very sensitive towards longer reaction times (a maximum of 30 min is recommended) and to high concentrations, both resulting in reduced yields. As an important benefit, compounds **5b-5d** proved to be highly insoluble in organic solvents; hence, they were obtained in an analytically pure form after extraction of the impurities into acetone. By this route, 10 g of **5** were prepared within 2 days.

Finally, in the presence of a great excess of $POBr_3$, phenanthrolines **5b-d** could be transformed to the corresponding 4,7-dibromo-1,10-phenanthrolines **1b-d**, which were obtained in analytically pure form (98-99% yield) after a simple work-up.[14,15] Our procedure constitutes a major improvement over the traditional bromination[5] of phenanthroline-4,7-diones using $POBr_3/PBr_3$ that only leads to the brominated products in 25-30% yield[2] and requiring extensive chromatographic separations.

Obviously, one may worry about the utility of phenanthrolines **1b-1d** in Heck-coupling reactions because of the alkyl substituents in 3,8-position. However, when **1d** was treated with an excess of phenylacetylene in the presence of catalytic amounts of $PdCl_2(PPh_3)_2$ and CuI the bisalkynylated phenanthroline **6** was afforded in 86% yield.[16] As such, the yield of the Heck-coupling was similar to that with the parent compound 4,7-dibromo-1,10-phenanthroline (95%).[2]

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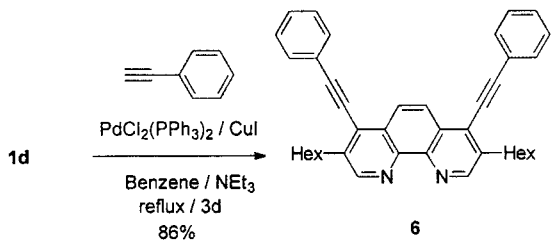


**Scheme 2**

Importantly, the dialkylated 4,7-dibromo-1,10-phenanthrolines **1b-1d** proved to be extremely soluble in organic solvents, much more than our original building block, 4,7-dibromo-1,10-phenanthroline (**1a**). For example, the solubility of **1a** in $CHCl_3$ was only 0.01 mol•l$^{-1}$ (<4 mg•ml$^{-1}$) while it was increased to 2.1 mol•l$^{-1}$ (1079 mg•ml$^{-1}$) for the analogous system **1d** with hexyl groups in the 3,8-positions, corresponding to an improvement in solubility of roughly 200!

In summary, we have described the synthesis of the highly soluble phenanthroline ligands **1b-d** that can be easily modified in the 4- and 7-positions. The highly efficient route is far superior to approaches to similar phenanthrolines, both in time and yield.[5] Work to use these ligands in macrocyclic oligophenanthrolines with *exo*-coordination sites is under way.

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**References and Notes**

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(12) *General procedure for the preparation of 1,2-bis-(β-ethoxycarbonyl-β-alkylvinylamino)-benzene* **4b-d**: 1,2-phenylenediamine (33 mmol) was added to a solution of **3b-d**[11] (75 mmol) in 100 ml of dichloromethane and kept to reflux in a Dean-Stark apparatus for 2 h. The solvent was evaporated and the oily brown residue used in the following reactions without purification.

(13) *General procedure for the preparation of 3,8-dialkyl-1,10-phenanthroline-4,7-diones* (**5b-d**): Crude **4b-d** (8-12 g) was added under nitrogen to 300 ml of diphenylether at a temperature of 200 °C. The temperature was raised to 240-250 °C for 30 min while a vigorous stream of nitrogen was bubbled through the solution. Thereafter, the reaction mixture was allowed to cool down and a colorless solid started to precipitate. Petroleum ether (50-70 °C) was added (200 ml) to complete precipitation, the solid was filtered off and washed twice with 100 ml of diethylether. To dissolve impurities the colorless residue was suspended in acetone (100 ml) and refluxed for 15 min. The precipitate was filtered off, washed with acetone and dried *in vacuo* to yield **4a-c** as colorless solids in 38-69% in analytically pure form.

(14) *General procedure for the preparation of 3,8-dialkyl-4,7-dibromo-1,10-phenanthrolines* **1b-d**: **5b-d** (3.00 mmol) was added under nitrogen to melted phosphoryl tribromide (30 ml) and the resulting solution was stirred at 80 °C for 7 h. The hot solution was then slowly added dropwise to a well stirred mixture of crushed ice (100 g) in water (200 ml). After 15 min chloroform (50 ml) was added and the resulting two-layer-system was carefully brought to a basic pH by adding a concentrated KOH solution. The organic layer was separated and the water layer extracted twice with 50 ml of chloroform. The combined organic layers were washed with 100 ml of concentrated KOH solution and dried over $MgSO_4$. After evaporation of the solvent and drying *in vacuo* for 8 h the 3,8-dialkyl-4,7-dibromo-1,10-phenanthrolines **1b-d** were obtained as colorless solids in 98-99% yield in analytically pure form.

(15) All novel compounds have been characterized by spectroscopic means and elemental analysis. Some selected data: *3,8-Di-n-hexyl-1,10-phenanthroline-4,7-dione* (**5d**): m.p. 196 °C. - IR (KBr): ν = 3344 cm$^{-1}$ (NH), 3253, 3184, 3063, 2956, 2923, 2853, 1670, 1609, 1558, 1491, 1409, 1218, 1201, 908, 835, 751, 722. - $C_{24}H_{32}N_2O_2$ (380.53): calcd. C 75.75, H 8.48, N 7.36; found C 75.68, H 8.80, N 7.30. - *4,7-Dibromo-3,8-di-n-hexyl-1,10-phenanthroline* (**1d**): m.p. 141°C. - $^1$H NMR ($CDCl_3$): δ = 0.86 (t, *J* = 6.9 Hz, 6 H, 6'-H), 1.24-1.51 (m, 12 H, 3'-, 4'-, 5'-H), 1.63-1.84 (m, 4 H, 2'-H), 2.99 (t, *J* = 7.5 Hz, 4 H, 1'-H), 8.24 (s, 2 H, 5-, 6-H), 8.89 (s, 2 H, 2-, 9-H). - $^{13}$C NMR ($CDCl_3$): δ = 14.0 (q, C-6'), 22.5 (t, C-5'), 29.0 (t, C-4'), 29.7 (t, C-3'), 31.5 (t, C-2'), 34.4 (t, C-1'), 126.3 (d, C-5, -6), 127.6 (s, C-3, -8), 134.6 (s, C-4a, -6a), 138.0 (s, C-4, -7), 144.8 (s, C-1a, -10a), 151.4 (d, C-2, -9). - $C_{24}H_{30}Br_2N_2$ (506.32): calcd. C 56.93, H 5.97, N 5.53; found C 56.65, H 6.29, N 5.50.

(16) *4,7-Diethynylphenyl-3,8-dihexyl-1,10-phenanthroline* (**6**): To a solution of **1d** (1.00 g, 1.95 mmol), phenylacetylene (0.67 ml,

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6.12 mmol) and 10 ml of dry triethylamine in benzene (20 ml) a mixture of $PdCl_2(PPh_3)_2$ (150 mg) and CuI (300 mg) was added. After refluxing the mixture for three days under nitrogen the solvent was evaporated. The black residue was dissolved in 100 ml of $CH_2Cl_2$, washed with 100 ml of 2% KCN solution, 100 ml of water and dried over $MgSO_4$. The residue was purified by column chromatography ($SiO_2$, 1. $CH_2Cl_2$, 2. ethyl acetate) to yield 0.94 g (86 %) of **6**: m.p. 136 °C. - IR (KBr): $\tilde{\nu}$ = 3056 $cm^{-1}$, 2917, 2852, 2205, 1598, 1559, 1499, 1467, 1421, 753, 686, 522. - $^1H$ NMR ($CDCl_3$): δ = 0.87 (t, *J* = 6.9 Hz, 6 H, 6'-H), 1.24-1.59 (m, 12 H, 3'-, 4'-, 5'-H), 1.73-1.94 (m, 4 H, 2'-H), 3.11 (t, *J* = 7.5 Hz, 4 H, 1'-H), 7.43-7.46 (m, 6 H, H-Ph), 7.66-7.71 (m, 4 H, H-Ph), 8.43 (s, 2 H, 5-, 6-H), 9.05 (s, 2 H, 2-, 9-H). - $^{13}C$ NMR ($CDCl_3$): δ = 14.0 (q, C-6'), 22.5 (t, C-5'), 29.1 (t, C-4'), 30.5 (t, C-3'), 31.6 (t, C-2'), 34.6 (t, C-1'), 84.0 (s, C-2''), 102.3 (s, C-1''), 122.5 (s, C-3''), 125.0 (d, C-6''), 127.6 (d, C-5, -6), 127.9 (s, C-3, -8), 128.6 (d, C-4''), 129.2 (d, C-5''), 131.8 (s, C-4a, -6a), 138.8 (s, C-4, -7), 144.4 (s, C-1a, -10a), 151.1 (d, C-2, -9).

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