Synthesis of new functionalized 1,10-phenanthrolines

E. N. Gulakova,[a] O. Yu. Kolosova,[b] and O. A. Fedorova[a,b]*

[a]*A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 28 ul. Vavilova, 119991 Moscow, Russian Federation. Fax: +7 (499) 135 5085. E-mail: gulakova@ineos.ac.ru*
[b]*D. I. Mendeleev University of Chemical Technology of Russia, 9 Miusskaya pl., 125047 Moscow, Russian Federation. Fax: +7 (499) 135 5085*

Styrylphenanthroline derivatives containing the fragments dithia-18-crown-6, aza-18-crown-6, and azadithia-15-crown-5 were obtained for the first time. The conditions for their synthesis were optimized.

Key words: 1,10-phenanthroline, styryl-containing neocuproine, crown compounds, dithia-18-crown-6 ether, aza-18-crown-6 ether, azadithia-15-crown-5 ether, formyl derivatives, benzaldehyde, 4-bromobenzaldehyde, condensation.

1,10-Phenanthroline is one of the most common ligands in supramolecular photochemistry. Its molecule contains two N atoms, which have lone electron pairs to be coordinated by metal cations. Because of its extended π system, a phenanthroline molecule can absorb light (π—π* transition) and sensitize coordinated metal ions, acting as a light antenna. In iron complexes, *o*-phenanthroline functions as a bidentate ligand to form stable chelate complexes.[1,2] Introduction of new functional groups into phenanthroline substantially extends its scope of application.

The goal of the present work was to develop methods for the synthesis of crown-containing styryl-1,10-phenanthrolines. These polydentate ligands are of interest as both sensing elements and building blocks for the design of various supramolecular complexes.

A survey of relevant literature data revealed that styrylazines are generally prepared by condensation of methyl-containing heterocyclic compounds with aromatic aldehydes under the action of various agents.[3—5] The presence of a crown ether fragment in the starting aldehyde can involve appreciable changes in the reaction conditions since macrocycles are often unstable, tending to break their polyether chains. In addition, condensation reactions in the presence of metal salts can be accompanied by metal—crown ether complexation, thus changing the activity of the metal reagents used.[6]

Condensation of neocuproine (**1**) with aromatic aldehydes remains virtually uninvestigated. For example, a heterocyclic analog of 9-methyl-2-styrylphenanthroline has been synthesized in 14% yield by heating compound **1** with pyrrolecarbaldehyde in DMF at 100 °C in the presence of piperidine.[7] Using Bu^{t}OK as a base in condensation reactions of compound **1** with benzaldehyde derivatives, we obtained mono- and bisstyrylphenanthrolines containing benzo-15-crown-5 fragments at room temperature, thus avoiding resinification of the reaction mixture.[8]

Under the same conditions, we carried out condensation reactions of compound **1** with formylbenzodithia-18-crown-6 ether **2a** and 4-bromobenzaldehyde **2d**. In an inert atmosphere, the yields of the target products were much higher. The reaction of compound **1** with aldehyde **2d** gave bisstyrylphenanthroline **4d** as the major product (Scheme 1, Table 1).

It is known[9—11] that lithium diisopropylamide (LDA) is widely used as a base in condensation of dimethyl-sub-

Table 1. Conditions of the synthesis and the yields of the condensation products obtained from compound **1** and substituted benzaldehydes **2a—d**

Benzaldehyde	Reaction conditions	Product, yield (%)	
		3	**4**
2a	Bu^{t}OK, DMF, 20 °C	**3a**, 16	**4a**, 0
	Bu^{t}OK, DMF, 20 °C, inert atmosphere	**3a**, 30	**4a**, 0
	LDA, THF, 0 °C, *p*-toluenesulfonic acid	**3a**, 10	**4a**, 0
	Ac_2O, 140 °C	**3a**, 12	**4a**, 0
2b	Ac_2O, 140 °C	**3b**, 15	**4b**, 0
	HCl, 120 °C	**3b**, 5	**4b**, 14
2c	Ac_2O, 140 °C	**3c**, 16	**4c**, 8
2d	Bu^{t}OK, DMF, 20 °C, inert atmosphere	**3d**, 19	**4d**, 25
	Ac_2O, 140 °C	**3d**, 0	**4d**, 0

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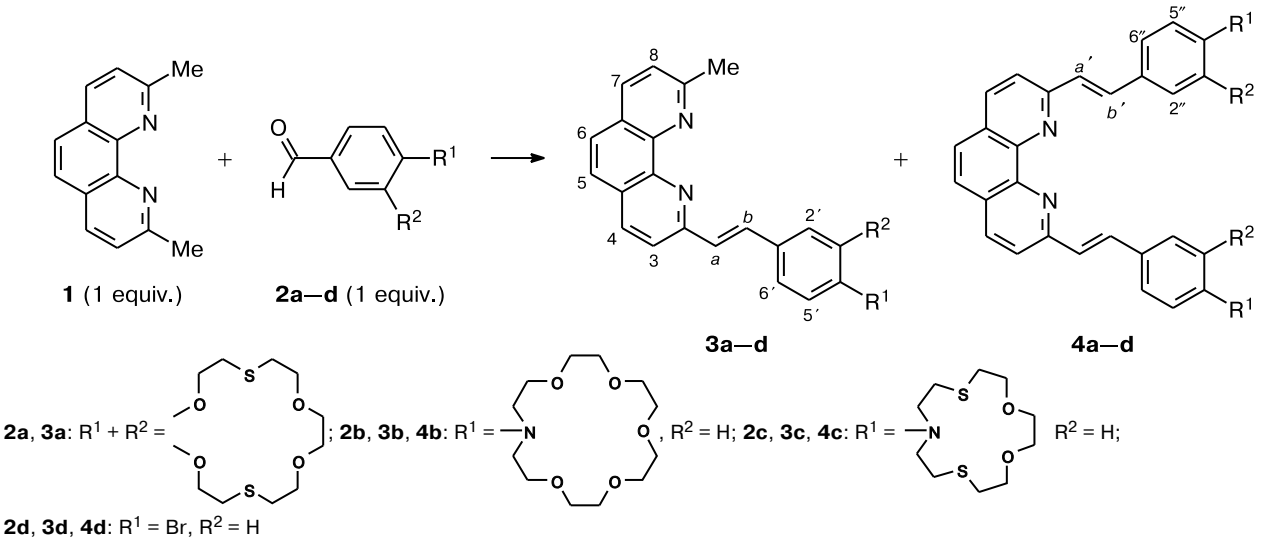
Scheme 1



stituted heterocycles with aromatic aldehydes. We attempted the synthesis of styrylphenanthroline **3a** containing dithia-18-crown-6 in the presence of LDA; however, the yield of the target product was only 10%.

Table 2. Spectroscopic characteristics of compounds **3a**—**d** and **4b**—**d**

Compound	^{1}H NMR (solvent, δ, *J*/Hz)	MS, *m/z*
3a	DMSO-d_6: 2.86 (s, 3 H, Me); 2.96, 3.12 (both m, 8 H, 4 SCH_2); 3.56, 3.68 (both m, 8 H, 4 OCH_2); 4.22, 4.31 (both m, 4 H, 2 $ArOC\underline{H}_2$); 7.06 (d, 1 H, H(5′), *J* = 8.4); 7.30 (d, 1 H, H(6′), *J* = 8.6); 7.50 (s, 1 H, H(2′)); 7.59, 7.86 (both d, 2 H, H(a), H(b), *J* = 16.3, *J* = 16.8); 7.68, 8.02 (both d, 2 H, H(4), H(7), *J* = 7.9, *J* = 8.4); 7.92 (s, 2 H, H(5), H(6)), 8.38, 8.46 (both d, 2 H, H(3), H(8), *J* = 8.2, *J* = 8.6)	563.2 $[M + H]^+$
3b	DMSO-d_6: 2.87 (s, 3 H, Me); 3.61 (m, 16 H, 8 OCH_2); 3.67(m, 8 H, 2 NCH_2, 2 OCH_2); 6.81, 7.63 (both d, 4 H, H(3′), H(5′), H(2′), H(6′), *J* = 8.7, *J* = 8.5); 7.37, 7.82 (both d, 2 H, H(a), H(b), *J* = 16.4, *J* = 16.7); 7.73, 8.06 (both d, 2 H, H(4), H(7), *J* = 8.5, *J* = 8.2); 7.90 (s, 2 H, H(5), H(6)), 8.38, 8.42 (both d, 2 H, H(4), H(7), *J* = 7.5, *J* = 8.0)	558.4 $[M + H]^+$
3c	CD_3CN: 2.75, 2.88 (both m, 8 H, 4 SCH_2); 2.84 (s, 3 H, Me); 3.60 (s, 4 H, 2 OCH_2); 3.67 (m, 4 H, 2 OCH_2); 3.74 (m, 4 H, 2 NCH_2); 6.71, 7.59 (both d, 4 H, H(2′), H(6′), H(3′), H(5′), *J* = 8.8, *J* = 8.6); 7.31, 7.76 (both d, 2 H, H(a), H(b), *J* = 16.2, *J* = 16.2); 7.57, 7.88 (both d, 2 H, H(3), H(8), *J* = 8.3, *J* = 8.3); 7.78 (s, 2 H, H(5), H(6)); 8.23, 8.26 (both d, 2 H, H(4), H(7), *J* = 8.1, *J* = 8.1)	546.43 $[M + H]^+$
3d	DMSO-d_6: 2.8 (s, 3 H, Me); 7.68—7.72 (m, 4 H, H(2′), H(6′), H(3′), H(5′)); 7.77, 7.92 (both d, 2 H, H(a), H(b), *J* = 15.3, *J* = 16.0), 7.81 (s, 1 H, H(8), *J* = 8.5); 7.96 (c, 2 H, H(5), H(6)), 8.15 (d, 1 H, H(3), *J* = 8.2); 8.41 (d, 1 H, H(7), *J* = 8.0); 8.51 (d, 1 H, H(4), *J* = 8.5)	376.27 $[M + H]^+$
4b	CD_3CN: 3.55, 3.65 (both m, 32 H, 16 OCH_2); 3.70 (m, 16 H, 4 OCH_2, 4 NCH_2); 6.83, 7.68 (both d, 8 H, H(3′), H(3″), H(5′), H(5″), H(2′), H(2″), H(6′), H(6″), *J* = 8.8, *J* = 8.6); 7.43, 7.95 (both d, 4 H, H(a), H(b), H(a′), H(b′), *J* = 16.1, *J* = 16.1); 7.82 (s, 2 H, H(5), H(6)); 7.92 (d, 2 H, H(3), H(8), *J* = 8.4); 8.33 (d, 2 H, H(4), H(7), *J* = 8.4)	907.6 $[M]^+$; 558.5
4c	DMSO-d_6: 2.75, 2.85 (both m, 16 H, 8 SCH_2); 3.57 (s, 8 H, 4 OCH_2); 3.65 (m, 8 H, 4 OCH_2); 3.70 (m, 8 H, 4 NCH_2); 6.70, 7.63 (both d, 8 H, H(2′), H(2″), H(6′), H(6″), H(3′), H(3″), H(5′), H(5″), *J* = 8.7, *J* = 8.6); 7.36, 7.85 (both d, 4 H, H(a), H(b), H(a′), H(b′), *J* = 16.2, *J* = 16.0); 7.82 (s, 2 H, H(5), H(6)); 7.98, 8.35 (both d, 4 H, H(3), H(8), H(4), H(7), *J* = 8.4, *J* = 8.4)	883.42 $[M + H]^+$
4d	DMSO-d_6: 7.73 (m, 4 H, H(2'), H(2"), H(6′), H(6″)); 7.84 (m, 4 H, H(3′), H(3″), H(5′), H(5″)); 7.75, 8. 02 (2 d, 4 H, H(a), H(a′), H(b), H(b′), *J*= 16.2, *J* = 16.7); 7.99 (s, 2 H, H(5), H(6)); 8.15 (d, 2 H, H(3), H(8), *J* = 8.5); 8.53 (d, 2 H, H(4), H(7), *J* = 8.5)	543.2 $[M + H]^+$

Earlier, it has been demonstrated that methyl derivatives of heterocyclic bases do not react with formylphenylaza-crown ethers under basic conditions.[12] This can be explained by the presence of a strong donor (dialkylamino group) in the *para*-position relative to the formyl substituent, which increases the electron density on the formyl C atom and makes it inert to the nucleophilic addition of the methyl group of the heterocycle. Nevertheless, this condensation occurs successfully under the conditions of acid catalysis. Heating of compound **1** with formylphenylaza-18-crown-6 ether **2b** and formylphenylazadithia-15-crown-5 ether **2c** in acetic anhydride gave the corresponding products; in the latter case, both mono- and bisstyrylphenanthrolines were obtained. The starting reagents were recovered in both cases. The condensation of compound **1** with ether **2b** in the presence of HCl gave monostyrylphenanthroline **3b** only in 5% yield, the major product being bisstyrylphenanthroline **4b**.

We also attempted the synthesis of styryl derivatives **3a** and **3d** by heating the reagents in acetic anhydride. The yield of product **3a** was only 12% because of considerable resinification of formylbenzodithiacrown ether **2a** under these reaction conditions. Bromostyrylphenanthroline **3d** was not obtained at all by acid-catalyzed condensation of compound **1** with 4-bromobenzaldehyde **2d**.

According to NMR data, the coupling constants of the olefinic protons are about 16 Hz (Table 2); therefore, mono- and bisstyrylphenanthrolines **3** and **4** were obtained in the form of *trans*-isomers.

To sum up, we obtained for the first time crown-containing mono- and bisstyrylphenanthrolines, potential receptors that can selectively form stable complexes and intensely absorb or emit light, which is peculiar to photosensitive groups. Although the yields of the target products are low, the advantages of the methods we proposed for their synthesis include accessible starting reagents, single-step reactions without side processes, and simple purification of products.

Experimental

Melting points were measured on a Mel-Temp instrument. ^{1}H NMR spectra were recorded on a Bruker DRX300 spectrometer (300.13 MHz) with Me_4Si as the internal standard. Chemical shifts and coupling constants were measured to within 0.01 ppm and 0.1 Hz, respectively. Elemental analysis was performed at the Microanalysis Laboratory of the A. N. Nesmeyanov Institute of Organoelement Compounds (Russian Academy of Sciences). Mass spectra were recorded on a Surveyor MSQ instrument (Thermo Finnigan; Waters column, XBridge C18 2.5 um 3.0×20 mm). Column chromatography was carried out on aluminum oxide (neutral, Brockmann activity I, STD grade, 150 mesh, 58 Å, Sigma—Aldrich).

Neocuproine (**1**), substituted benzaldehydes **2a—d**, potassium *tert*-butoxide, lithium diisopropylamide, THF (Acros Organics, 99.5%, extra dry, over molecular sieves, stabilized) were commercial chemicals and used as such.

Base-catalyzed condensation of compound 1 with aromatic aldehydes 2a and 2d (general procedure). A suspension of Bu^tOK (0.72 mmol) in DMF (4 mL) was slowly added dropwise under argon to a stirred solution of neocuproine (**1**) (0.72 mmol) and aldehyde **2a** or **2d** (0.65 mmol) in dry DMF (4 mL). The reaction mixture was kept at room temperature for 24 h and concentrated *in vacuo*. The residue was dissolved in distilled water (30 mL) and the product was extracted with chloroform (3×20 mL). The extracts were combined and concentrated; the residue was chromatographed on Al_2O_3 with benzene—ethanol (100 : 1) as an eluent.

This procedure was used to obtain 2-[2-(2,3,5,6,8,9,11,12,14,15-decahydrobenzo[1,7,10,16,4,13]tetraoxadithiacyclooctadecin-18-yl)ethenyl]-9-methyl-1,10-phenanthroline (**3a**), 2-[2-(4-bromophenyl)ethenyl)]-9-methyl-1,10-phenanthroline (**3d**), and 2,9-bis[2-(4-bromophenyl)ethenyl]-1,10-phenanthroline (**4d**). For the yields of the products, see Table 1. Their physicochemical characteristics are given in Tables 2 and 3.

Condensation of compound 1 with aldehyde 2a in the presence of LDA. A solution of compound **1** (0.1 g, 0.48 mmol) in dry THF (3 mL) was added dropwise under argon at 0 °C to a stirred solution of LDA (0.053 g, 0.49 mmol) in dry THF (2 mL). The mixture was kept at 0 °C for 1 h, whereupon a suspension of aldehyde **2a** (0.179 g, 0.48 mmol) in dry THF (5 mL) was added dropwise. The reaction mixture was kept at 0 °C for 2 h and then at room temperature for 18 h and diluted with distilled water (20 mL). The product was extracted with dichloromethane (3×20 mL). The organic extracts were combined and concentrated *in vacuo*. The residue was dissolved in toluene (20 mL) and *p*-toluenesulfonic acid (0.05 g) was added. The resulting solution was kept in a flask equipped with a Dean—Stark trap at 110 °C for 12 h, cooled to room temperature, and concentrated *in vacuo*. The residue was chromatographed on Al_2O_3 (gradient elution with C_6H_6—MeCN from 10 : 1 to 4 : 1). The yield of compound **3a** was 0.025 g (10%). For the yields of the products, see Table 1. Their physicochemical characteristics are given in Tables 2 and 3.

Acid-catalyzed condensation of compound 1 with aromatic aldehydes 2a—c (general procedure). A solution of aldehyde **2a—c** (0.54 mmol) and neocuproine (**1**) (0.54 mmol) in acetic anhydride (4 mL) was kept under argon at 140 °C for 6—10 h. The reaction mixture was cooled and diluted with distilled water (60 mL). The aqueous solution was neutralized with 15% NaOH to pH 7—8 and the product was extracted with benzene (3×35 mL). The organic extracts were combined and concentrated *in vacuo*. The residue was chromatographed on Al_2O_3 (gradient elution with C_6H_6—MeCN from 10 : 1 to 4 : 1). This procedure was used to obtain 2-[2-(2,3,5,6,8,9,11, 12,14,15-decahydrobenzo-[1,7,10,16,4,13]tetraoxadithiacyclooctadecin-18-yl)ethenyl]-9-methyl-1,10-phenanthroline (**3a**), 2-{2-[4-(1,4-dioxa-7,13-dithia-10-azacyclopentadecan-10-yl)phenyl]ethenyl}-9-methyl-1,10-phenanthroline (**3c**), and 2,9-bis{2-[4-(1,4-dioxa-7,13-dithia-10-azacyclopentadecan-10-yl)phenyl]ethenyl}-1,10-phenanthroline (**4c**). For the yields of the products, see Table 1. Their physicochemical characteristics are given in Tables 2 and 3.

Condensation of compound 1 with aldehyde 2b in the presence of HCl. A solution of neocuproine (**1**) (150 mg, 0.72 mmol) and HCl (0.1 mL) in ethanol (4 mL) was evaporated to dryness *in vacuo*. Then the resulting neocuproine hydrochloride was

Table 3. Physicochemical characteristics of compounds **3a—d** and **4b—d**

Compound	M.p. /°C	Molecular formula	Found / Calculated (%)		
			C	H	N
3a	75—78	$C_{31}H_{34}N_2O_4S_2$	65.02	6.24	4.14
			66.16	6.09	4.98
3b*	—	$C_{33}H_{39}N_3O_5$	71.43	6.99	7.10
			71.07	7.05	7.53
3c	87—89	$C_{31}H_{35}N_3O_2S_2$	68.34	6.40	7.85
			68.22	6.46	7.70
3d	100—103	$C_{21}H_{15}N_2Br\cdot 0.3H_2O$	66.32	4.42	7.03
			66.26	4.13	7.36
4b	52—55	$C_{52}H_{66}N_4O_{10}$	68.72	7.44	6.42
			68.85	7.33	6.18
4c	119—120	$C_{48}H_{58}N_4O_4S_4$	65.14	6.51	6.42
			65.27	6.62	6.34
4d	160—163	$C_{28}H_{18}Br_2N_2\cdot 0.2C_6H_6$	62.98	3.47	4.84
			62.86	3.47	5.02

* Isolated as an oil.

mixed with aldehyde **2b** (367 mg, 0.72 mmol). The reaction mixture was kept on an oil bath at 110 °C for 4.5 h, cooled, and diluted with distilled water (60 mL). The aqueous solution was neutralized with Na_2CO_3 to pH 7—8 and the product was extracted with benzene (3×35 mL). The organic extracts were combined and concentrated *in vacuo*. The residue was chromatographed on Al_2O_3 (gradient elution with C_6H_6—MeCN from 15 : 1 to 2 : 1). This procedure was used to obtain 9-methyl-2-{2-[4-(1,4,7,10,13-pentaoxa-16-azacyclooctadecan-16-yl)phenyl]-ethenyl}-1,10-phenanthroline (**3b**) and 2,9-bis{2-[4-(1,4,7,10,13-pentaoxa-16-azacyclooctadecan-16-yl)phenyl]ethenyl}-1,10-phenanthroline (**4b**). For the yields of the products, see Table 1. Their physicochemical characteristics are given in Tables 2 and 3.

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References

1. C. R. K. Glasson, L. F. Lindoy, G. V. Meehan, *Coord. Chem. Rev.*, 2008, **252**, 940.
2. M. W. Cooke, D. Chartrand, G. S. Hanan, *Chem. Rev.*, 2008, **252**, 903.
3. L. Kacmarek, P. Borowicz, A. Grabowska, *J. Photochem. Photobiol.*, 2001, **138**, 159.
4. S. Achell, I. Nouira, B. Pfaffinger, Y. Ramondenc, N. Ple, J. Rodriguez-Lopez, *J. Org. Chem.*, 2009, **74**, 3711.
5. V. M. Chapela, M. J. Percino, C. Rodriguez-Barbarin, *J. Chem. Cryst.*, 2003, **33**, 77.
6. E. N. Andryukhina, M. M. Mashura, O. A. Fedorova, L. G. Kuz´mina, J. A. C. Howard, S. P. Gromov, *Izv. Akad. Nauk, Ser. Khim.*, 2005, 1650 [*Russ. Chem. Bull., Int. Ed.*, 2005, **54**, 1700].
7. Y. Azechi, K. Takemura, Y. Shinohara, Y. Nishimura, T. Arai, *J. Phys. Org. Chem.*, 2007, **20**, 864.
8. O. A. Fedorova, E. N. Andryukhina, M. M. Mashura, S. P. Gromov, *ARKIVOC*, 2005, **15**, 12.
9. A. Juris, S. Campagna, I. Bidd, J. Lehn, R. Ziessel, *Inorg. Chem.*, 1998, **27**, 4007.
10. O. Maury, J.-P. Guegan, T. Renouard, A. Hilton, P. Dupau, N. Sandon, L. Toupet, H. Le Bozec, *New J. Chem.*, 2001, **25**, 1553.
11. T. Le Bouder, L. Viau, J.-P. Guegan, O. Maury, H. Le Bozec, *Eur. J. Org. Chem.*, 2002, 3024.
12. O. A. Fedorova, E. N. Andryukhina, A. V. Lindeman, S. S. Basok, T. Yu. Bogashchenko, S. P. Gromov, *Izv. Akad. Nauk, Ser. Khim.*, 2002, 302 [*Russ. Chem. Bull., Int. Ed.*, 2002, **55**, 319].

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