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Efficient Access to a Versatile 5,6-Dithio-1,10-phenanthroline Building Block and Corresponding Organometallic Complexes

Bertrand Chesneau, Angélique Passelande, and Piétrick Hudhomme*

Université d'Angers, CNRS, Laboratoire de Chimie et Ingénierie Moléculaire d'Angers, CIMA UMR 6200, 2 Boulevard Lavoisier, 49045 Angers, France

pietrick.hudhomme@univ-angers.fr

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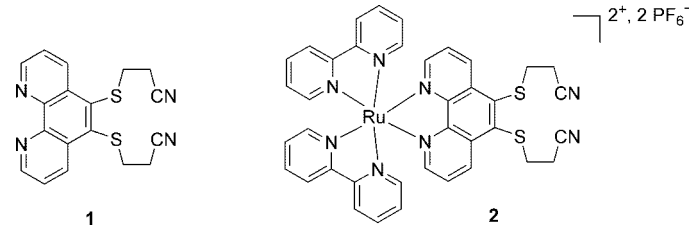
ABSTRACT



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A facile access to 5,6-bis(2-cyanoethylsulfanyl)-1,10-phenanthroline 1 and its ruthenium(II) bipyridil complex 2, as versatile building blocks for the straightforward synthesis of 5,6-dithio functionalized 1,10-phenanthroline based systems, is described.

Over the past few years, impressive development has been carried out on transition metal complexes containing a heterocyclic sp^2 nitrogen donor based upon 2,2′-bipyridine (bpy), [2,2′:6′,2″]-terpyridine (tpy) or 1,10-phenanthroline (phen) chelating ligands.[1] Among them, 1,10-phenanthroline ligand appears of particular interest for applications in coordination chemistry.[2] For instance, phenanthroline ligands have been successfully used as cationic ionophores[3] or for homogeneous catalytic reaction.[4] In addition, due to their electronic, photophysical, redox, and luminescence properties, these ligands have known important development in the field of supramolecular and macromolecular chemistry.[5] Fascinating architectures based on copper(I)[6] or ruthenium(II)[7] 1,10-phenanthroline complexes were designed in which photoinduced energy or electron transfer processes could occur, in particular for applications in the field of photonic devices.[8] Such organometallic complexes have also shown particular interest for their DNA-binding interactions,[9] and the inhibition of gene transcription was demonstrated with promising properties for the design of DNA markers in photochemotherapy.[10]

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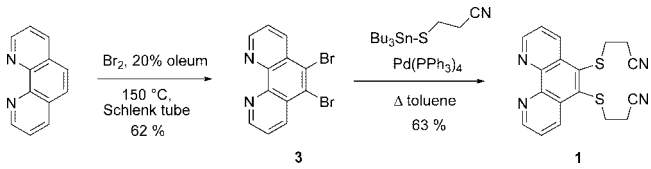
In this context, straightforward synthetic access to 1,10-phenanthroline building blocks appears of strong importance. The functionalization of the 1,10-phenanthroline ligand appears relatively limited.[11] Substitution at the 2,9-positions can be achieved using the nucleophilic addition of aryl-lithium[12] (or thienyl-lithium)[13] compounds followed by an oxidative rearomatization or using metal-catalyzed cross-coupling reactions from the 2,9-dihalogenated derivative.[14] Further extension of such organometallic reactions was carried out using 3,8-dibromo-1,10-phenanthroline giving rise to 3,8-disubstituted derivatives.[15]

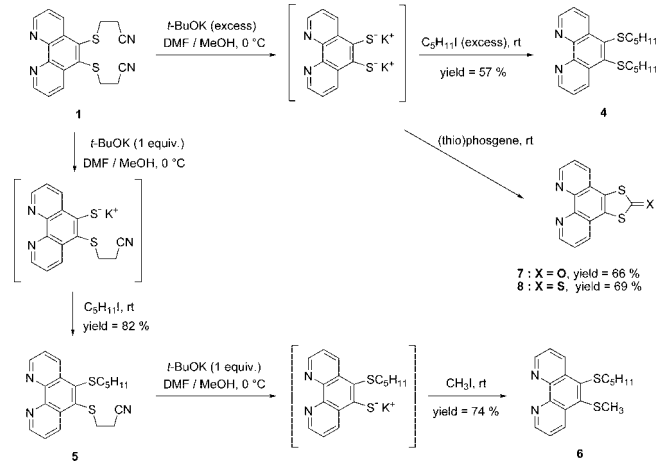
On the contrary, 5,6-disubstituted-1,10-phenanthroline derivatives have been less explored despite their attractivity. The most common functionalization corresponds to the oxidation affording 1,10-phenanthroline-5,6-dione,[16] which plays an important role as a versatile building block with well-known applications in biological chemistry and materials science. Also, preparation of 5,6-dibromo-1,10-phenanthroline was realized using bromine in fuming sulfuric acid (containing 60%[17] or 30%[18] oleum). Functionalizations from this starting material were carried out using the Suzuki cross-coupling reaction.[19] Very recently, a palladium cross-coupling reaction was also described to reach 5,6-bis(ethynylpyrene)-1,10-phenanthroline systems.[20]

In this context, the preparation of a 1,10-phenanthroline building block allowing an easy functionalization on the 5,6-positions by reaction with electrophilic species appears complementary to these methods. To our knowledge, only the synthesis of 5,6-dibenzylsulfanyl-1,10-phenanthroline was very recently described.[21] This work describes the synthesis of 5,6-bis(2-cyanoethylsulfanyl)-1,10-phenanthroline **1** as an attractive building block for further development of 5,6-dithio-1,10-phenanthroline derivatives (Scheme 1). The particular interest in this 2-cyanoethylsulfanyl group relies on a very efficient and selective deprotection−alkylation reaction of the highly nucleophilic thiolate groups (Scheme 2). This protecting group has been first introduced in the tetrathiafulvalene series[22] and then applied into the thiophene chemistry.[23] This work is extended to the synthesis of ruthenium(II) bipyridil complex **2** as an interesting model for developing new metal-coordinated 5,6-dithio-1,10-phenanthroline based architectures (Scheme 3).

Scheme 1. Synthesis of Building Block 5,6-Bis(2-cyanoethylsulfanyl)-1,10-phenanthroline **1**



Scheme 2. Applications of Compound **1** to the Synthesis of Symmetrical, Unsymmetrical, and Heterocyclic 5,6-Dithio Functionalized 1,10-Phenanthrolines



5,6-Dibromo-1,10-phenanthroline **3** was synthesized in 62% yield by treating 1,10-phenanthroline monohydrate with bromine in fuming sulfuric acid containing 20% oleum as a modified procedure of previous reported methods.[18] Preliminary attempts to synthesize building block **1** in a one-pot reaction from compound **3** after halogen−lithium exchange using butyllithium followed by addition of sulfur and then thioalkylation with 3-bromopropionitrile were unsuccessful. As an alternative, we investigated a palladium-catalyzed cross-coupling reaction. Compound **3** was treated in the presence of $Pd(PPh_3)_4$ with 3-(tributylstannylsulfanyl)propanenitrile, which was prepared according to the reported procedure.[24] Finally, key compound **1** was isolated in 63% yield (Scheme 1).

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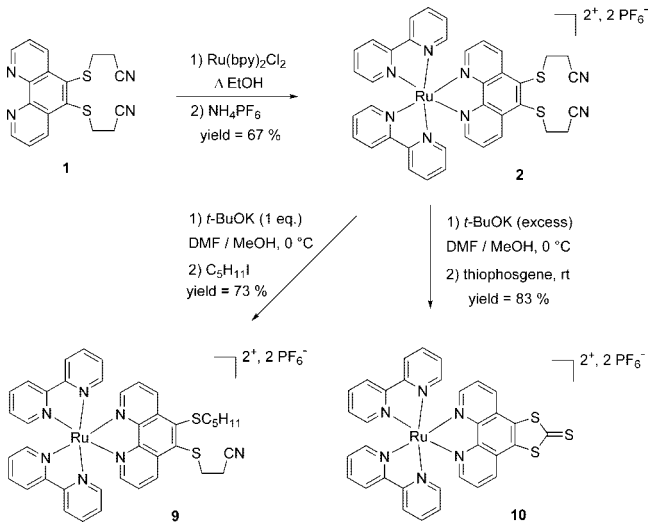
Scheme 3. Synthesis and Applications of 5,6-Bis(2-cyanoethylsulfanyl)-1,10-phenanthroline Ruthenium(II) Bipyridil Complex **2**



The 2-cyanoethylsulfanyl protecting group is well-known for its deprotection using cesium hydroxide as reagent.[25] Considering 1,10-phenanthroline derivative **1**, potassium *tert*-butoxide in DMF/MeOH (1:1 v/v) proved to be the most efficient reagent to generate selectively the corresponding mono- or dithiolate (Scheme 2).

After generation of the dithiolate by treatment with a slight excess of base, subsequent alkylation using 1-iodopentane afforded 5,6-bis(2-pentylsulfanyl)-1,10-phenanthroline **4** in 57% yield, demonstrating the efficiency of the deprotection−alkylation process.

The selective access to one thiolate group gives ready access to unsymmetrical derivatives. For instance, derivative **6** could be attained in two steps. First the mild and selective deprotection of one 2-cyanoethylsulfanyl group was cleanly achieved by treatment with 1 equiv of base. Subsequent quenching of the thiolate anion with 1-iodopentane afforded compound **5** in 82% yield. The second deprotection−alkylation sequence was carried out as above leading to unsymmetrical 1,10-phenanthroline **6** in 74% yield.

The presence of an intermediate vicinal dithiolate could be exploited to synthesize the 2-oxo or 2-thioxo-1,3-dithiole heterocycle fused to the 1,10-phenanthroline system.[26] The dithiolate intermediate was trapped by addition of phosgene or thiophosgene to give the 2-oxo-1,3-dithiole **7** or 2-thioxo-1,3-dithiole **8** as particularly insoluble materials in 66% and 69% yields, respectively. These two compounds constitute potential precursors for further applications in tetrathiafulvalene (TTF) chemistry.[27]

As extensive research is focused on applications of ruthenium(II) complexes from the 1,10-phenanthroline ligand, we were interested in the development of the new organometallic building block **2** (Scheme 3). For this purpose, compound **1** was treated in refluxing ethanol with *cis*-dichloro-bis(2,2′-bipyridine)ruthenium, which was prepared according to reported procedure.[28] Corresponding ruthenium(II) bipyridil complex **2** was isolated in 67% yield after anionic metathesis treatment using an aqueous solution of ammonium hexafluorophosphate. The selective monodeprotection−alkylation strategy was efficiently carried out to reach unsymmetrical complex **9** in 73% yield. Access to the dithiolate using the procedure described above and subsequent quenching with thiophosgene afforded the new complex **10** in 83% yield.

The ^{1}H NMR spectrum of compound **1** shows that the H_2 proton of the 1,10-phenanthroline moiety resonates at lowest field (δ = 9.26 ppm) with the expected ^3J coupling constant ($^3J_{H_2-H_3}$ = 4.5 Hz and $^4J_{H_2-H_4}$ = 1.5 Hz). The closed H_4 proton (δ = 9.21 ppm) presents the highest ^3J coupling constant ($^3J_{H_3-H_4}$ = 8.5 Hz and $^4J_{H_2-H_4}$ = 1.5 Hz), whereas the H_3 proton is shielded (δ = 7.78 ppm).

The ^{1}H NMR spectrum of complex **2** was assigned with the aid of ^{1}H−^{13}C HMQC experiments in the aromatic region (Figure 1). Concerning the three phenanthroline protons, the chemical shift of the H_2 proton is significantly highfield-shifted by 1.14 ppm (δ = 8.12 ppm) compared to ligand **1**, while H_3 and H_4 protons are not affected by the formation of the octahedral $[Ru(bpy)_2Phen]^{2+}$ complex. This shielding of H_2 by comparison with H_4 is in accordance with previous NMR assignments reported for $[Ru(bpy)_2Phen]^{2+}$ complexes.[29] This is also in agreement with the ^{13}C spectrum

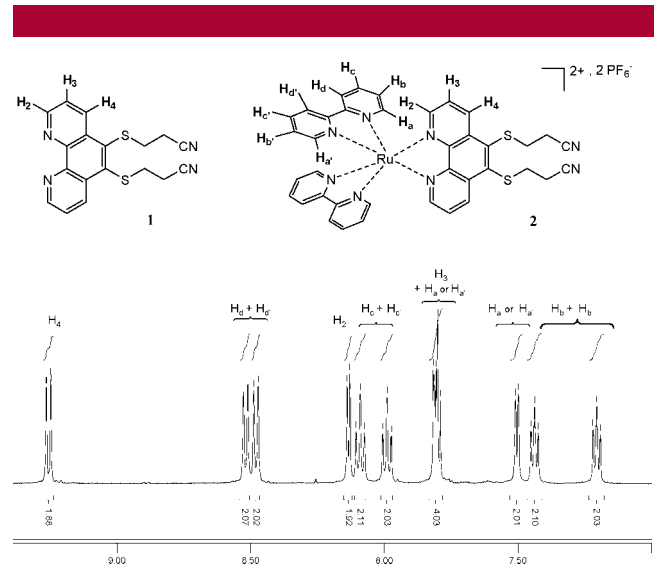


Figure 1. Aromatic part of the ^{1}H NMR spectrum of 5,6-bis(2-cyanoethylsulfanyl)-1,10-phenanthroline ruthenium(II) bipyridil complex **2**.

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and the expected chemical shift of C_2 at 152 ppm, which is deshielded compared to C_4 at 138 ppm. The ^1H NMR spectrum shows that the two bipyridil ligands are magnetically equivalent. This leaves eight signals identifiable with four protons for each bipyridil ligand defined as H_a, H_b, H_c and H_d for one pyridine unit ($H_{a'}$, $H_{b'}$, $H_{c'}$, and $H_{d'}$ for the second pyridine moiety). The protons of bipyridil ligands show characteristic chemical shifts with H_d and $H_{d'} > H_c$ and $H_{c'} > H_a$ and $H_{a'} > H_b$ and $H_{b'}$.

Whereas 1,10-phenanthroline presents a maximum absorption at 265 nm in CH_3CN, the UV−vis spectrum of **1** shows a maximum absorption band at 269 nm, and this band is bathochromatically shifted to 286 nm in corresponding ruthenium(II) complex **2**. Moreover, the UV−vis spectrum of complex **2** exhibits the characteristic metal to ligand charge transfer (MLCT) band between 400 and 500 nm (Figure 2).

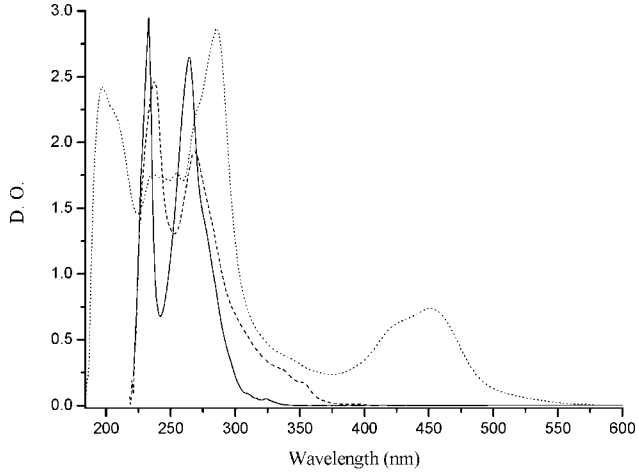

Figure 2. Absorption spectra of 1,10-phenanthroline (solid line), **1** (dotted line), and **2** (dashed line) in CH_3CN ($c = 5 \times 10^{-5}$ M).

Electrochemical properties of the electroactive ruthenium(II) complex **2** were investigated by cyclic voltammetry. Compound **2** exhibits two reversible one-electron reduction waves at $E^0_{red1} = -1.61$ V and $E^0_{red2} = -1.88$ V (vs Fc^+/Fc in CH_2Cl_2/CH_3CN 9:1) and one reversible one-electron oxidation wave at $E^0_{ox1} = +0.95$ V that could be assigned to the Ru^{II}/Ru^{III} couple (Supporting Information). These redox potentials could be compared with those of $[Ru(phen)(bpy)_2](PF_6)_2$ ($E^0_{red1} = -1.74$ V and $E^0_{red2} = -1.98$ V, $E^0_{ox1} = +0.97$ V vs Fc^+/Fc), which was prepared according to literature.[30] Such shift of reduction potentials can be assigned to the electron-withdrawing effect induced by both 2-cyanoethylsulfanyl groups.

In conclusion, we propose an efficient synthesis of a new synthetic building block in the 1,10-phenanthroline series and its corresponding ruthenium(II) complex. The interest in such systems is supported by the use of the 2-cyanoethylsulfanyl protecting group and the high efficiency of the selective sequence of deprotection−alkylation reactions of thiolate groups. This attractive thiofunctionalization in both the 5 and 6 positions offers a broad range of possibilities for an approach to new symmetrical and unsymmetrical 1,10-phenanthroline-based systems and related organometallic complexes. Moreover, the ready access to the dithiolate intermediates from building blocks **1** and **2** gives rise to two distinct coordinating sites. This opens a wide range of possibilities for an easy access to multinuclear complexes exhibiting promising electrochemical and physical properties.

Acknowledgment. This work was supported by the French National Research Agency in the frame of the program ANR PNANO entitled TTF-based Nanomat.

Supporting Information Available: Experimental details and characterization data for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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