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

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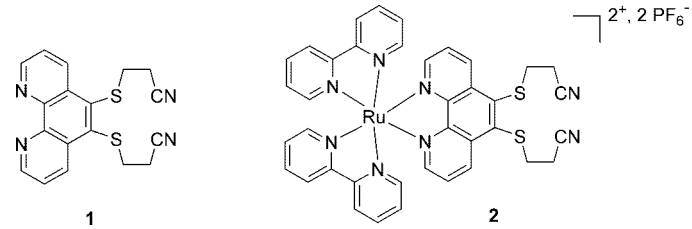
ABSTRACT



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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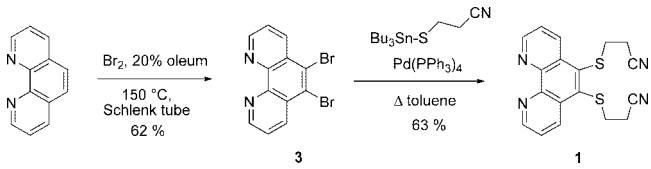
In this context, straightforward synthetic access to 1,10-phenanthroline building blocks appears of strong importance. The functionalization of the 1,10-phenanthroline ligand appears relatively limited.[11] Substitution at the 2,9-positions can be achieved using the nucleophilic addition of aryllithium[12] (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]

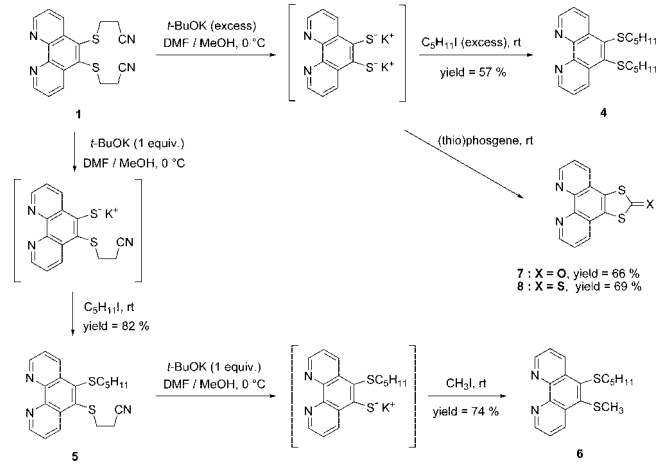
In this context, the preparation of a 1,10-phenanthroline building block allowing an easy functionalization on the 5,6-positions by reaction with electrophilic species appears complementary to these methods. To our knowledge, only the synthesis of 5,6-dibenzylsulfanyl-1,10-phenanthroline was very recently 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

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



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

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



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).

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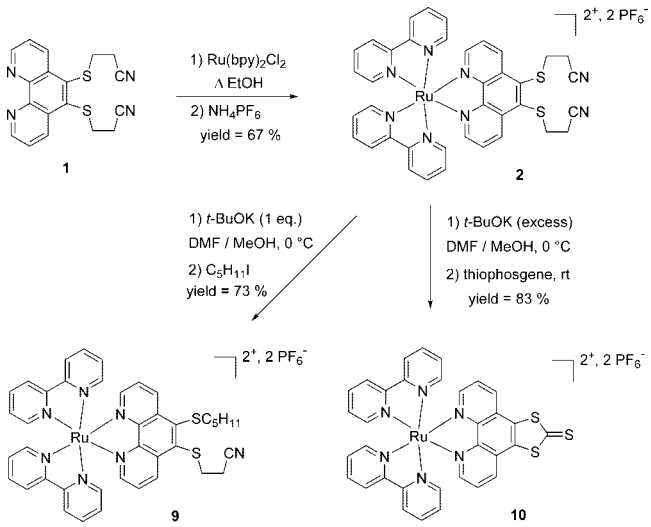
Scheme 3. Synthesis and Applications of 5,6-Bis(2-cyanoethylsulfanyl)-1,10-phenanthroline Ruthenium(II) Bipyridil Complex **2**



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

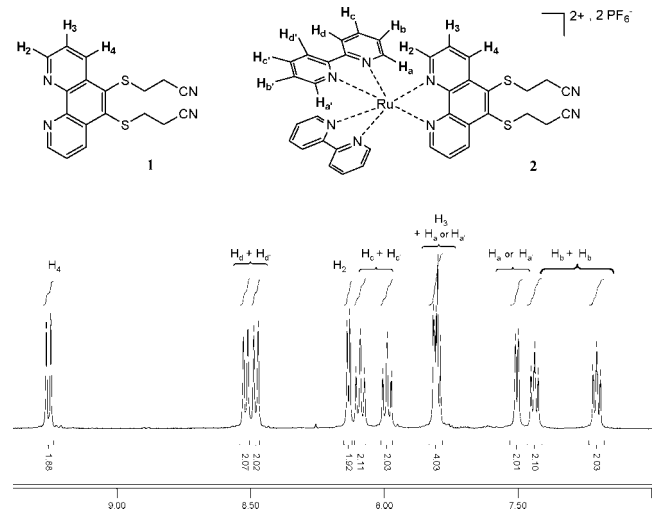


Figure 1. Aromatic part of the ^{1}H NMR spectrum of 5,6-bis(2-cyanoethylsulfanyl)-1,10-phenanthroline ruthenium(II) bipyridil complex **2**.

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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 ^{1}H 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).

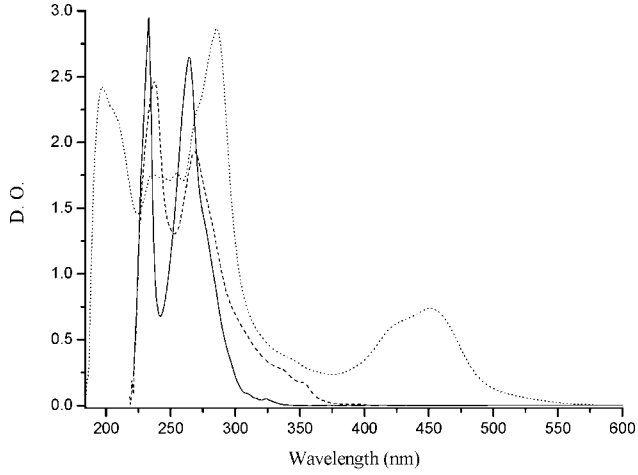

Figure 2. Absorption spectra of 1,10-phenanthroline (solid line), **1** (dotted line), and **2** (dashed line) in CH_3CN ($c = 5 \times 10^{-5}$ M).

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.

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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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