

Sulfur Bridged Multidentate Ligands Based on (Bi)pyridyl-(Bi)-1,3,4-Thiadiazolyl Conjugates

Antonino Mamo^{1*}, Andrea Pappalardo¹ and M. Teresa Clasadonte²

¹ Department of Physical and Chemical Methodologies for Engineering, Engineering Faculty, University of Catania, V.le Andrea Doria 6, I-95125 Catania, Italy. Tel.: (+39)-95-7382756, Fax: (+39)-95-33323.

² Department of Economy and Territory, Economy Faculty, University of Catania, Cso Italia 55, I-95129 Catania, Italy.

* Author to whom correspondence should be addressed; e-mail: mamo@dmfci.ing.unict.it

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Abstract: The synthesis of a series of mixed (bi)pyridyl/(bi)1,3,4-thiadiazolyl ligands, derived from the condensation of 2-mercapto-5-methylthio-1,3,4-thiadiazole or 5-mercapto-5'-methylthio-2,2'-bi-1,3,4-thiadiazole with 2,6-bis(chloromethyl)pyridine or 6,6'-bis(chloromethyl)-2,2'-bipyridine (compounds **L**₁–**L**₄), and of 2,5-dimercapto-1,3,4-thiadiazole or 5,5'-dimercapto-2,2'-di-1,3,4-thiadiazole with picolyl chloride hydrochloride or 6-chloromethyl-6'-methyl-2,2'-bipyridine (compounds **L**₅–**L**₈) in the presence of triethylamine is described. All new compounds have been characterized by FAB (+) spectrometry and NMR spectroscopy. ¹³C-NMR spectra are crucial to firmly establish the thiol structure of the title ligands.

Keywords: (Bi)pyridyl derivatives, (bi)-1,3,4-thiadiazolyl derivatives, (bi)pyridyl/(bi)-1,3,4-thiadiazolyl mixed ligands, azathio ligands.

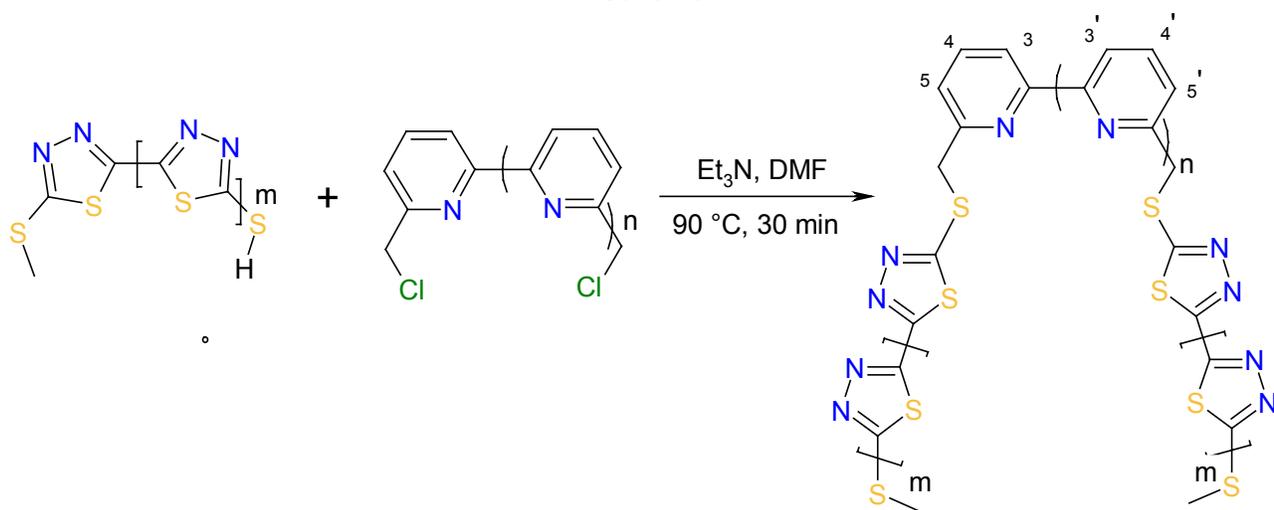
Introduction

It is well known that luminescent and redox active polypyridine-type metal complexes are playing a key role as molecular components in the development of supramolecular species capable of harvesting solar energy and transforming light information at the molecular level [1]. Most of such supramolecular species are based on ruthenium (II) and osmium (II) tris-bidentate and/or bis-terdentate (poly)pyridyl building blocks [1d, 2]. On the other hand, a few examples have been reported in the literature regarding the use of (poly)-1,3,4-thiadiazole ligands in the complexation of Ru (II) and/or Os (II) ions [3]. To the best of our knowledge, there is only one paper dealing with the preparation of Ru (II) tris-chelate complexes of thiadiazole derivatives, which show luminescence properties not only at 77 K, but even at room temperature [4]. Following our interest in the field of luminescent polypyridine ruthenium (II), osmium (II) and iridium (III) complexes [5], we now report the synthesis and characterization of eight new mixed (bi)pyridyl/(bi)-1,3,4-thiadiazolyl ligands **L**₁–**L**₈ (*vide infra*, Schemes 1 and 2) with the aim of studying the photochemical properties of their complexes with transition metals.

Results and Discussion

Pivotal intermediate 5-mercapto-5'-methylthio-2,2'-bi-1,3,4-thiadiazole (**2**), required for the synthesis of ligands **L**₂ and **L**₄ was obtained by selective methylation of 5,5'-dimercapto-2,2'-bi-1,3,4-thiadiazole (**6**) with dimethyl sulfate (1 equiv.) under basic conditions (NaOH) (Scheme 1).

Scheme 1



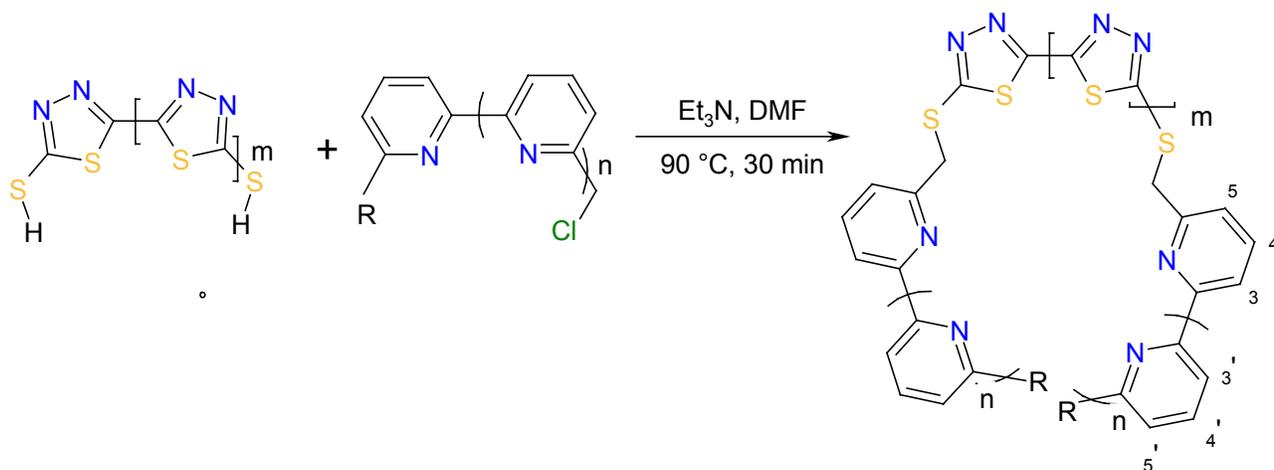
	<i>m</i>		<i>n</i>		<i>m</i>	<i>n</i>
1	0	3	0	L ₁	0	0
2	1	4	1	L ₂	1	0
				L ₃	0	1
				L ₄	1	1

The reaction produced a mixture of mono-(methylthio) derivative **2** (26%) and bis-(methylthio) derivative (30%), which were easily separated by exploiting their different solubility in the reaction medium (see Experimental). From the ^{13}C -NMR spectrum in deuterated tetrachloroethane (TCE), only the thione form of **2** ($\text{C}=\text{S}$ resonance at δ 188.7 ppm) was detected.

Reaction of 2-mercapto-5-methylthio-1,3,4-thiadiazole (**1**) with 0.5 equiv. of 2,6-bis(chloromethyl)pyridine (**3**) or 6,6'-bis(chloromethyl)-2,2'-bipyridine (**4**) in dry *N,N*-dimethylformamide (DMF) at 90°C in the presence of triethylamine (TEA, 1 equiv) afforded ligands **L**₁ and **L**₃, respectively, in high yield. Ligands **L**₂ and **L**₄ were obtained in a similar way by reacting 5-mercapto-5'-methylthio-2,2'-bi-1,3,4-thiadiazole (**2**) with **3** or **4**, respectively, in a 2 : 1 molar ratio, as shown in Scheme 1.

The ligands **L**₅–**L**₈ were synthesized using the same strategy as above, namely by condensation of 2,5-dimercapto-1,3,4-thiadiazole (**5**) or 5,5'-dimercapto-2,2'-bi-1,3,4-thiadiazole (**6**) with picolyl chloride hydrochloride (**7**) or 6-chloromethyl-6'-methyl-2,2'-bipyridine (**8**) (Scheme 2). All the compounds were characterized by elemental analysis, FAB (+) mass spectrometry, and NMR spectroscopy. The FAB (+) mass spectra of **L**₁–**L**₈ display prominent molecular ion peaks, and fragmentation patterns in accord with those described for (bi)-1,3,4-thiadiazole sulfur derivatives [6].

Scheme 2



	m		n	R
5	0	7	0	H
6	1	8	1	CH ₃

	m	n	R
L ₅	0	0	H
L ₆	1	0	H
L ₇	0	1	CH ₃
L ₈	1	1	CH ₃

Table I reports the results of a complete ^1H -NMR analysis of ligands **L**₁–**L**₈. Assignments were aided by the use of 2D homonuclear chemical shift correlated ^1H -NMR (COSY) [7]. The bipyridyl moieties of ligands **L**₃ and **L**₄ show the expected pattern for a 6,6' disubstituted 2,2'-bipyridine system, *i.e.* a doublet-triplet-doublet sequence. On the other hand, a doubling of these signals is observed when

the substituents in the 6,6'-positions of the bipyridyl moiety are different, as in **L**₆ and **L**₈. The downfield resonances of the protons in the 3,3'-positions (δ in the range 8.16–8.37 ppm, Table I) are suggestive of an *anti* disposition of the bipyridyl units [8].

Table I. ¹H-NMR parameters of ligands **L**₁–**L**₈.

Proton	L ₁	L ₂	L ₃	L ₄	L ₅	L ₆	L ₇	L ₈
3	7.34 d <i>J</i> = 8.0	7.41 d <i>J</i> = 8.0	8.31 d <i>J</i> = 7.5	8.37 d <i>J</i> = 7.5	7.41 d <i>J</i> = 8.0	7.48 d <i>J</i> = 7.5	8.16 d <i>J</i> = 8.0	8.20 d <i>J</i> = 8.0
4	7.62 t <i>J</i> = 7.5	7.67 t <i>J</i> = 7.8	7.79 dt <i>J</i> = 7.5, 1.5	7.81 t <i>J</i> = 7.5	7.65 dt <i>J</i> = 7.5, 2.0	7.67 dt <i>J</i> = 7.5, 1.0	7.76 t <i>J</i> = 8.0	7.79 t <i>J</i> = 8.0
5	7.34 d <i>J</i> = 8.0	7.41 d <i>J</i> = 8.0	7.44 d <i>J</i> = 8.0	7.49 d <i>J</i> = 7.5	7.20 t <i>J</i> = 6.0	7.22 t <i>J</i> = 7.5	7.39 d <i>J</i> = 7.5	7.45 d <i>J</i> = 8.0
6					8.54 dd <i>J</i> = 3.5, 2.0	8.57 dd <i>J</i> = 4.0, 1.0		
3'			8.31 d <i>J</i> = 7.5	8.37 d <i>J</i> = 7.5				8.37 d <i>J</i> = 7.5
4'			7.79 dt <i>J</i> = 7.5, 1.5	7.81 t <i>J</i> = 7.5			7.68 t <i>J</i> = 7.5	7.69 t <i>J</i> = 8.0
5'			7.44 d <i>J</i> = 8.0	7.49 d <i>J</i> = 7.5			7.16 d <i>J</i> = 7.5	7.17 d <i>J</i> = 7.5
CH ₂	4.57 s	4.72 s	4.69 s	4.83 s	4.58	4.72 s	4.68 s	4.83 s
CH ₃	2.73 s	2.84 s	2.73 s	2.84 s			2.61 s	2.61 s

Notes: The spectra were obtained in TCE, chemical shifts in ppm, and coupling constants in Hz. Numbering pattern as shown in Schemes 1 and 2. Abbreviations used: s = singlet, d = doublet, dd = double doublet, t = triplet, dt = double triplet.

It is important to point out, however, that these spectral data alone afforded little assistance in the structural assignment of the products of alkylation of our heterocyclic thiols (**1**, **2**, **5**, and **6**), because of their aptitude for thiol-thione tautomerism. Since ¹³C-NMR spectroscopy provides a powerful tool for distinguishing between substitution on nitrogen and/or on sulfur [9], we deemed essential the acquisition of the ¹³C-NMR spectra of **L**₁–**L**₈ to unambiguously assign their structures. To this end, we assumed the chemical shifts of the quaternary carbons in model compounds 2,5-bis(methylthio)-1,3,4-

thiadiazole ($\delta = 165.5$ ppm in CDCl_3) and 3,4-dimethyl-1,3,4-thiadiazolidine-2,5-dithione ($\delta = 180.3$ ppm in CDCl_3) as standards for substitution on sulfur or on nitrogen, respectively [10].

The ^{13}C -NMR spectra of ligands L_1 – L_8 are gathered in Table II, along with their analytical data. A scrutiny of the Table shows that the resonance(s) of the quaternary carbons of the thiadiazole ring(s) in the range 164.1 ± 6.0 ppm. These values unambiguously prove that the thiols used in this investigation (compounds **1**, **2**, **5**, and **6**) have undergone regioselective *S*-alkylation under basic conditions.

Table II. Analytical and ^{13}C -NMR Spectral Data for the Ligands L_1 – L_8 .

Lig.	Yield (%) (Cryst. Solv.)	Melting Point (°C)	Molecular Formula	%C Found (Calcd)	%H Found (Calcd)	%N Found (Calcd)	^{13}C NMR
L_1	84 (EtOH)	94–95	$\text{C}_{13}\text{H}_{13}\text{N}_5\text{S}_6$	36.13 (36.17)	3.33 (3.03)	16.04 (16.22)	167.0, 164.0, 155.6, 137.7, 122.1, 39.8, 16.7
L_2	63 (DMF)	207–212	$\text{C}_{17}\text{H}_{13}\text{N}_9\text{S}_6$	33.82 (34.04)	2.22 (2.18)	21.06 (21.02)	170.1, 168.2, 158.8, 158.1, 155.2, 137.8, 123.3, 39.7, 16.7
L_3	90 (EtOH- CHCl_3)	157–158	$\text{C}_{18}\text{H}_{16}\text{N}_6\text{S}_6$	42.83 (42.49)	3.06 (3.17)	16.74 (16.52)	166.9, 164.4, 155.2, 154.9, 137.7, 123.1, 120.0, 40.3, 16.7
L_4	71 (DMF)	257–258	$\text{C}_{22}\text{H}_{16}\text{N}_{10}\text{S}_8$	39.17 (39.03)	2.03 (2.38)	20.92 (20.69)	170.1, 168.6, 158.6, 158.2, 155.2, 154.4, 137.9, 123.2, 120.2, 40.2, 16.7
L_5	95 (MeOH- H_2O)	80–81	$\text{C}_{14}\text{H}_{12}\text{N}_4\text{S}_3$	50.91 (50.58)	3.57 (3.64)	16.94 (16.85)	164.9, 155.4, 149.5, 136.9, 123.3, 122.7, 39.9
L_6	80 (AcOEt)	163–165	$\text{C}_{26}\text{H}_{22}\text{N}_6\text{S}_3$	61.01 (60.67)	3.90 (4.31)	16.41 (16.33)	165.4, 157.9, 156.0, 154.8, 154.7, 137.6, 137.0, 123.4, 122.7, 119.9, 118.1, 40.4, 24.6
L_7	73 (Dioxane)	159–160	$\text{C}_{16}\text{H}_{12}\text{N}_6\text{S}_4$	46.52 (46.13)	2.49 (2.90)	19.74 (20.17)	168.3, 158.6, 155.0, 149.6, 136.9, 123.3, 122.8, 39.8
L_8	80 Dioxane/DMF	248–250	$\text{C}_{28}\text{H}_{22}\text{N}_8\text{S}_4$	55.98 (56.16)	3.85 (3.70)	18.92 (18.71)	168.8, 158.6, 157.9, 156.2, 154.7, 154.2, 137.7, 137.0, 123.5, 122.7, 120.0, 118.1, 40.3, 26.6

Notes: The ^{13}C -NMR spectra were obtained in TCE, chemical shifts in ppm.

Conclusions

We have synthesized and characterized a series of polydentate aza/sulfur ligands, based on the (bi)pyridine/(bi)-1,3,4-thiadiazole skeletons, that are potential chelating molecules for the complexation of metal cations such as Ru, Os, and Ir. These complexes, owing to the simultaneous presence of nitrogen and sulfur binding sites, may display new and interesting photophysical properties.

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Experimental

General

2-Mercapto-5-methylthio-1,3,4-thiadiazole (**1**) [11], 2,6-bis(chloromethyl)pyridine (**3**) [12], 6,6'-bis(chloromethyl)-2,2'-bipyridine (**4**) [13], 5,5'-dimercapto-2,2'-bi-1,3,4-thiadiazole (**6**) [14], and 6-chloromethyl-6'-methyl-2,2'-bipyridine (**8**) [13], were synthesized according to literature procedures. 2,5-Dimercapto-1,3,4-thiadiazole (**5**), picolyl chloride hydrochloride (**7**), and anhydrous solvents were purchased from Fluka, and used without further purification. All reactions were conducted under N₂ atmospheres. Melting points were determined on an Electrothermal melting point apparatus and are uncorrected. Elemental analyses were obtained commercially. Unless otherwise stated ¹H- and ¹³C-NMR spectra were performed in deuterated TCE (CDCl₂CDCl₂) with a Varian INOVA 500 instrument, using TMS as an internal standard. The ¹H- and ¹³C-NMR spectra of all compounds synthesized are collected in Tables I and II. FAB (+) MS spectra were taken on a Kratos MS 50 S double-focusing mass spectrometer equipped with a standard FAB source, using 3-nitrobenzyl alcohol as a matrix.

5-Mercapto-5'-methylthio-2,2'-bi-1,3,4-thiadiazole (**2**).

To a chilled solution of 5,5'-dimercapto-2,2'-bi-1,3,4-thiadiazole (**6**, 2.34 g, 10.0 mmol), in aqueous NaOH (0.5 N, 40 mL) was added dropwise dimethyl sulfate (1.26 g, 10 mmol). After stirring for 1 h at room temperature, the solid bis(methylthio) derivative was collected by filtration and recrystallized from MeOH (0.78 g, 30%, mp. 177-178 °C). The filtrate was adjusted to pH 4.0–4.5 by addition of hydrochloric acid, and the precipitate was collected by suction filtration, dried under vacuum and then recrystallized from MeOH to give 0.65 g (26%) of yellow needles: mp 225 °C (dec.); ¹H-NMR δ: 11.16 (bs, 1 H), 2.85 (s, 3 H); ¹³C-NMR δ 188.7, 171.1, 156.4, 151.5, 16.8; FAB (+) MS, *m/z* 249 [MH]⁺; *Anal.* Calcd. for C₅H₄N₄S₄: C, 24.18; H, 1.62; N, 22.56. Found: C, 23.96; H, 1.84; N, 22.71.

General Procedure for the Nucleophilic Displacement Reactions: Synthesis of 2,6-Bis[5-methylthio-1,3,4-thiadiazol-2-ylthio)methyl]pyridine (L₁)

A stirred mixture of 2-mercapto-5-methylthio-1,3,4-thiadiazole (0.328 g, 2 mmol), 2,6-bis(chloromethyl)pyridine (0.176 g, 1 mmol), and Et₃N (0.4 mL) in dry DMF (5 mL) was heated under stirring at 90 °C for 30 min. After cooling, the mixture was diluted with water and the precipitate was collected by filtration, washed with water, and dried. Recrystallization from EtOH provided L₁ as white elongated prisms. Yields, analytical and spectral data of L₁–L₈ are reported in Tables I and II.

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Sample availability: Available from the authors.

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