Synthesis of New Tetradentate Ligands Containing Both 2,2'-Bipyridine and 3-Pyridyl-1,2,4-triazine Moieties

Ernest Graf

Laboratoire d'Electrochimie et de Chimie Physique du Corps Solide, U.R.A. au C.N.R.S. n° 405, Universite Louis Pasteur, 4 rue Blaise Pascal, F-67000 Strasbourg, France

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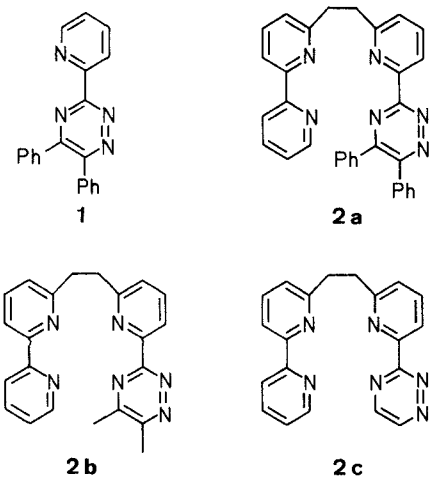
The synthesis of three new tetradentate ligands containing both 2,2'-bipyridine and 1,2,4-triazine subunits bridged by an ethyl chain is reported.

During our previous study of the 5,6-diphenyl-3-(2-pyridyl)-1,2,4-triazine (DPT) ligand **(1)**, we showed that this compound was not only able to bind iron(II)[1] through its pyridine–triazine coordination sites, but in addition, due to its triazine moiety, its iron(II) complex was electroactive.[1]

In the present study, we persued this concept of coexistence of a pH dependent electroactive centre and of coordination sites by modifying the latter. In order to enhance the binding ability of the coordinating part, we prepared compounds **2a–c** containing a bipyridine moiety as the coordination site.

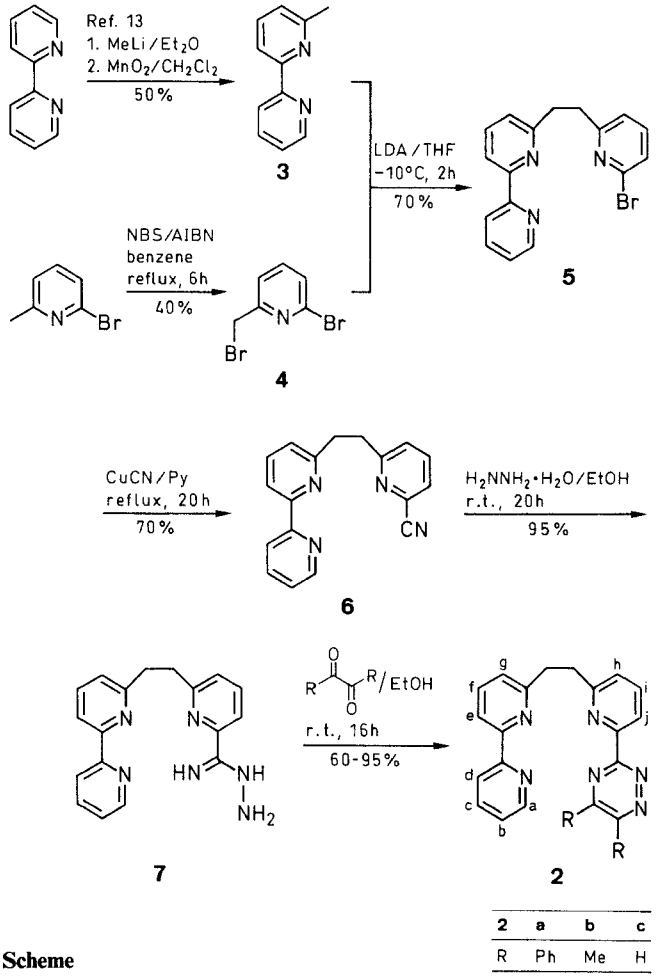


We report here the synthesis of three new ligands, **2a–c** containing both 2,2'-bipyridine and 1,2,4-triazine subunits linked by an ethyl chain.

The coordination properties of these ligands towards transition metals as well as the electrochemical behaviour of their complexes will be reported elsewhere.

Due to the pioneering synthetic work of Burstall[2] and Holm et al.[3] substituted bipyridine derivatives are now available. Further synthetic achievements leading to a variety of these compounds have been reported by other groups.[4–7] Among various controlled syntheses of polypyridine derivatives,[8–10] the coupling of two bipyridines with an ethyl chain was first reported by Elliott[11] and recently was further improved.[12]

In order to connect a 2,2'-bipyridine with a 3-pyridyl-1,2,4-triazine, we developed a new strategy (Scheme). The linker, an ethyl bridge, was introduced in two steps, leading to asymmetrical ligands **2a–c** in high yields. The key intermediate **5** was prepared by coupling the two precursors **3** and **4**. Compound **3** was obtained by reacting one equivalent of methyllithium with 2,2'-bipyridine[13] in dry diethyl ether. The reoxidation of the non-isolated adduct by manganese(IV) oxide afforded the 6-methyl-2,2'-bipyridine **(3)** in 50% yield.[14] The 2-bromo-6-bromomethylpyridine **(4)**, was obtained in two steps from 2-bromo-6-methylpyridine. The latter was prepared in 75% yield following a published procedure[15] and was subsequently brominated by *N*-bromosuccinimide (NBS) in hot benzene in the presence of 2,2'-azobisisobutyronitrile (AIBN) and irradiation ($\lambda > 320$ nm) affording **4** in 40% yield. Addition at -10 °C of one equivalent of lithium diisopropylamide to **3** in dry and degassed tetrahydrofuran[16] afforded a deep blue solution which was slowly added at -10 °C to a dry and degassed tetrahydrofuran solution of **4** leading to compound **5** which was purified by chromatography (silica gel; hexane/diethyl ether) (70% yield). Compound **5** was trans-



Scheme

formed into the nitrile derivative **6** by treatment with copper(I) cyanide[17] in 70% yield. The carboxamidrazone compound **7** was obtained in 95% yield from the cyanopyridine **6** by addition of an excess of hydrazine monohydrate to an alcoholic solution of **6**.[18] The triazines **2a–c** were then obtained in 95%, 90%, and 60% yield, respectively, by reacting stoichiometric amounts of the carboxamidrazone **7** and appropriate diketone derivatives in ethanol.

^{1}H NMR spectra were obtained on a Bruker WP 200 NMR spectrometer with TMS as internal standard. All NMR measurements were performed at 25 ± 4°C in $CDCl_3$ or CD_2Cl_2. Melting points were obtained on a Koffler block and are uncorrected. Elemental analysis were performed at the Strasbourg Division of the Microanalytical Laboratory of the C.N.R.S. 6-Methyl-2,2′-bipyridine (**3**) was prepared by slight modification of the published procedure,[13] instead of $KMnO_4$, MnO_2 (Merck N° 805958) was used for the reoxidation step. 2-Bromo-6-methylpyridine was obtained following the described procedure.[15]

2-Bromo-6-bromomethylpyridine (4):
A solution of 2-bromo-6-methylpyridine (10.1 g, 58.7 mmol), NBS (11.1 g, 62.4 mmol) and AIBN (0.1 g, 0.6 mmol) in benzene (150 mL) was refluxed for 6 h under Ar and irradiation (W lamp; 150 Watt; $\lambda > 320$ nm). After cooling and separation of succinimide by filtration the solvent was removed. The oily residue containing two compounds was purified by chromatography on silica gel. Elution with hexane/CH_2Cl_2 (70:30) afforded 2-bromo-6-dibromomethylpyridine (yield: 1.25 g, 34%) which was subsequently recrystallized in hexane; mp 83–84°C.

$C_6H_4Br_3N$	calc.	C 21.85	H 1.22	N 4.25
(329.8)	found	22.00	1.06	4.17

^{1}H NMR (200 MHz, $CHCl_3$): δ = 6.57 (s, 1 H, $CHBr_2$), 7.44 (d, 1 H, J = 7.8 Hz, H_3 pyridine), 7.66 (dd, 1 H, J_1 = 7.8 Hz, J_2 = 7.7 Hz, H_4 pyridine), 7.81 (d, 1 H, J = 7.7 Hz, H_5 pyridine).

Further elution with hexane/CH_2Cl_2 (30:70) gave the desired compound **4** (yield: 5.9 g, 40%); recrystallization from hexane; mp 138–139°C.

$C_6H_6Br_2N$	calc.	C 28.72	H 2.01	N 5.58
(250.9)	found	28.48	1.87	5.51

^{1}H NMR (200 MHz, $CHCl_3$): δ = 4.49 (s, 2 H, CH_2Br), 7.41 (d, 2 H, J = 7.5 Hz, H_3 H_6 pyridine), 7.56 (dd, 1 H, J = 7.5 Hz, H_4 pyridine).

1-(2,2′-Bipyridyl-6-yl)-2-(6-bromo-2-pyridyl)ethane (5):
The reaction vessel was carefully dried and kept under Ar during the reaction. In a three-neck flask BuLi (1.6 M, 22.5 mL) was added by syringe at r.t. to i-Pr_2NH (3.67 g, 36.2 mmol) dissolved in anhydrous and degassed THF (25 mL). This solution was cooled to −10°C and then a solution of 6-methyl-2,2′-bipyridine (**3**; 6 g, 35.2 mmol) in dry THF (30 mL) was added dropwise over a period of 40 min. The solution immediately turns blue. After further stirring at −10°C for 1 h, the solution was transferred dropwise (45 min) via cannula to a three-neck flask containing compound **4** (8.85 g, 35.2 mmol) at −10°C dissolved in THF (50 mL). The coupling reaction was easily followed by the fast decoloration of the blue solution. After the reaction was completed, the mixture was further stirred for another 10 min and then was quenched with H_2O (5 mL) and evaporated to dryness. The residue was dissolved in CH_2Cl_2 (100 mL) and extracted with H_2O (100 mL). The organic layer was dried ($MgSO_4$), filtered, and evaporated to dryness. The desired compound **5** (yield: 8 g, 70%) was obtained by chromatography (alumina, Merck activity (II, III); hexane/Et_2O); mp 60–61°C.

$C_{17}H_{14}BrN_3$	calc.	C 60.02	H 4.15	N 12.35
(340.2)	found	60.07	4.30	12.55

^{1}H NMR (200 MHz, CH_2Cl_2): δ = 3.29 (s, 4 H, CH_2), 7.15 (2 dd, 2 H, J = 8 Hz, $H_{e,8}$), 7.30 (m, 2 H, $H_{b,d}$), 7.43 (dd, 1 H, J = 7.6 Hz, H_h), 7.71 (dd, 1 H, J = 7.7 Hz, h_j), 7.82 (dd, 1 H, J = 7.7, 1.8 Hz, H_i), 8.23 (dd, 1 H, J = 7.8 Hz, H_f), 8.44 (ddd, 1 H, J = 8, 2 Hz, H_c), 8.65 (ddd, 1 H, J = 4.8, 0.9 Hz, H_a).

1-(2,2′-Bipyridyl-6-yl)-2-(6-cyano-2-pyridyl)ethane (6):
A solution of compound **5** (5 g, 14.7 mmol) in freshly distilled and degassed pyridine (20 mL) and solid CuCN (1.5 g, 16.7 mmol) was refluxed for 20 h. After a few minutes the solution turned dark brown. The solvent was evaporated and the dark brown oil was dissolved in CH_2Cl_2 (100 mL) and extracted with conc. NH_4OH (3 × 50 mL) followed by washing with distilled H_2O (2 × 50 mL). The slightly brownish organic layer was dried ($MgSO_4$), filtered, and evaporated. The brown residue was then purified by chromatography on alumina [Merck activity (II–III); elution solvent: Et_2O affording compound **6** (yield: 2.95 g, 70%); recrystallization from Et_2O/hexane; mp 88–89°C.

$C_{18}H_{14}N_4$	calc.	C 75.51	H 4.93	N 19.57
(286.3)	found	75.44	5.10	19.75

^{1}H NMR (200 MHz, CH_2Cl_2): δ = 3.36 (m, 4 H, CH_2), 7.17 (dd, 1 H, J = 8, 1 Hz, H_8), 7.30 (ddd, 1 H, J = 8, 4.8, 1 Hz, H_b), 7.39 (dd, 1 H, J = 8, 1 Hz, H_e), 7.52 (dd, 1 H, J = 8, 1 Hz, H_d), 7.70 (2 dd, 2 H, J = 8 Hz, $H_{h,j}$), 7.81 (dd, 1 H, J = 8 Hz, H_i), 8.23 (dd, 1 H, J = 8, 1 Hz, H_f), 8.41 (ddd, 1 H, J = 8, 1 Hz, H_c), 8.64 (ddd, 1 H, J = 4.8, 1 Hz, H_a).

6-[2-(2,2′-Biyridyl-6-yl)ethyl]pyridine-2-carbohydrazide Imide (7):
Compound **6** (3 g, 10.5 mmol) dissolved in degassed abs. EtOH (100 mL) was allowed to react at r.t. with $H_2NNH_2 \cdot H_2O$ (50 mL, 1 mmol) for 20 h. After addition of H_2O (100 mL), the desired compound **7** was extracted with CH_2Cl_2 (100 mL). The organic layer was dried ($MgSO_4$), filtered, and evaporated. The carboxamidrazone **7** (yield: 3.1 g, 95%) was recrystallized from toluene; mp 107–108°C.

$C_{18}H_{18}N_6$	calc.	C 67.90	H 5.70	N 26.40
(318.4)	found	68.05	5.88	26.68

^{1}H NMR (200 MHz, CH_2Cl_2): δ = 3.34 (s, 4 H, CH_2), 4.55 (br s, 2 H, NH_2), 5.23 (br s, 2 H, =NH), 7.15 (2 d, 2 H, J = 8 Hz, $H_{e,g}$), 7.30 (ddd, 1 H, J = 8, 5, 1.5 Hz, H_b), 7.57 (dd, 1 H, J = 8 Hz, H_j), 7.70 (dd, 1 H, J = 8 Hz, H_i), 7.76–7.86 (m, 2 H, $H_{d,h}$), 8.22 (dd, 1 H, J = 8 Hz, H_f), 8.45 (ddd, 1 H, J = 8, 1.5 Hz, H_c), 8.64 (ddd, 1 H, J = 5, 1.5 Hz, H_a).

Compounds 2; General Procedure:
The carboxamidrazone **7** (1 g, 3.14 mmol) dissolved in degassed abs. EtOH (75 mL) was allowed to react with three different α-diketones in slight excess (5%). The pale-yellowish solution was stirred for 16 h at r.t., then the solvent was evaporated. All three compounds **2a–c** were recrystallized from toluene or toluene/hexane mixtures.

1-(2,2′-Bipyridyl-6-yl)-2-[6-(5,6-diphenyl-1,2,4-triazin-3-yl)-2-pyridyl]ethane **(2a)**:
Recrystallized from toluene/hexane mixture; yield: 1.48 g (95%); mp 163–164°C.

$C_{32}H_{24}N_6$	calc.	C 78.03	H 4.91	N 17.06
(492.6)	found	77.75	4.90	16.97

^{1}H NMR (200 MHz, CH_2Cl_2): δ = 3.48 (m, 4 H, CH_2), 7.24–7.48 (m, 9 H, $H_{b,e,g}$, phenyl $H_{ortho,\ para}$), 7.61–7.87 (m, 7 H, $H_{d,h,j}$, phenyl H_{meta}), 8.24 (dd, 1 H, J = 8, 1 Hz, H_f), 8.48 (m, 2 H, $H_{c,i}$), 8.64 (ddd, 1 H, J = 4, 1 Hz, H_a).

1-(2,2′-Bipyridyl-6-yl)-2-[5,6-dimethyl-1,2,4-triazin-3-yl)-2-pyridyl]ethane: **(2b)**
Recrystallized from toluene: yield: 1.0 g (90%); mp 132–133°C.

$C_{22}H_{20}N_6$	calc.	C 71.72	H 5.47	N 22.81
(368.4)	found	71.95	5.48	22.91

^{1}H NMR (200 MHz, CH_2Cl_2): δ = 2.66 (s, 3 H, N=CCH_3), 2.74 (s 3 H, NN=CCH_3), 3.42 (m, 4 H, CH_2), 7.24 (dd, 1 H, J = 8, 1 Hz H_g), 7.28–7.37 (m, 2 H, $H_{b,e}$), 7.69–7.87 (m, 3 H, $H_{d,k,i}$), 8.24 (dd 1 H, J = 8, 1 Hz, H_j), 8.35 (dd, 1 H, J = 8, 1 Hz, H_f), 8.48 (ddd, 1 H J = 8, 1 Hz, H_c), 8.65 (ddd, 1 H, J = 4, 1 Hz, H_a)

1-(2,2'-Bipyridyl-6-yl)-2-[6-(1,2,4-triazin-3-yl)-2-pyridyl]ethane **(2c)**

Precipitated from toluene/hexane; yield: 0.64 g (60%); mp 165–166 °C.

$C_{20}H_{16}N_6 + 0.5$ EtOH	calc.	C 69.40	H 5.27	N 23.12
(340.4)	found	69.65	4.95	23.17

^{1}H NMR (200 MHz, CH_2Cl_2): δ = 3.42 (m, 4H, CH_2), 7.21 (dd, 1H, J = 8, 1.5 Hz, H_g), 7.30 (ddd, 1H, J = 4, 2, 1 Hz, H_b), 7.38 (dd, 1H, J = 8, 1.5 Hz, H_a), 7.51 (dd, 1H, J = 8 Hz, H_j), 7.82 (m, 2H, $H_{d,i}$), 8.23 (dd, 1H, J = 8, 2 Hz, H_h), 8.41 (dd, 1H, J = 8, 1.5 Hz, H_f), 8.46 (ddd, 1H, J = 8, 2 Hz, H_c), 8.64 (ddd, 1H, J = 4, 2, 1 Hz, H_a), 8.81 (d, 1H, J = 2.5 Hz, N=CH), 9.26 (d, 1H, J = 2.5 Hz, NN=CH).

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