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Improved synthesis of 4,4′-diamino-2,2′-bipyridine from 4,4′-dinitro-2,2′-bipyridine-*N*,*N*′-dioxide

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Abstract—A superior synthetic route to 4,4′-diamino-2,2′-bipyridine has been developed. This procedure compares favorably with existing methods, producing 4 times the yield previously reported. In addition, mild reaction conditions are utilized, allowing a considerably more efficient production, and subsequent purification, of the diamino complex.

Derivatives of 2,2′-bipyridine[1–9] have received much attention due to their potential for metal coordination to form polypyridyl metal complexes, particularly of ruthenium, which have diverse applications.

The photochemical and redox properties of these complexes can be varied through appropriate substitution on the pyridine rings. The derivatization of a 2,2′-bipyridyl ligand with electron donating/withdrawing groups in the 4,4′-positions has been a popular means of controlling the redox potential of transition metal bipyridyl complexes. The 4,4′ disubstitution pattern is desirable, not only because it is the synthetically simplest to prepare but also because substitution at these positions offers no steric complications on complexation. However, even with the prevalent use of functionalized 2,2′-bipyridines for chelation of transition metals, the available methods of synthesis are, usually, not practical and are low yielding.

Due to the electron donating character of amino groups, increasing interest has been expressed in the use of 4,4′-diamino-2,2′-bipyridine **3** as a ligand in transition metal bipyridyl complexes in both electrochemical[10–14] and photochemical studies.[10–17] Furthermore, it can be used as a building block in supramolecular assemblies,[18] as the amino moieties react readily with a variety of carbonyl complexes, allowing the bridging of metal centres[19,20] as well as extension of the ligand.

Our interest lies in the utilization of this ligand in the synthesis of low redox potential osmium and ruthenium complexes, for sensor and fuel cell applications.[21] Transition metal complexes containing diamino substituted bipyridine ligands have previously been used as electrochemical probes for DNA detection[12,22] and as electron transfer mediators for glucose oxidase.[23] Metal complexes are sometimes difficult to use as electrochemical probes for DNA hybridization due to their high redox potentials. This can result in the destruction of the complementary DNA immobilized on the electrode surface (adenine and guanine oxidation).[24,25] However, such complexes can be modified by the introduction of an electron donating ligand, such as **3**, to shift the complex redox potential to lower (more negative) potentials.

To the best of our knowledge only one report exists detailing the synthesis of **3**.[26] This complicated and poorly yielding (18–20%) procedure involves the reduction of 4,4′-dinitro-2,2′-bipyridine-*N*,*N*′-dioxide using iron powder and glacial acetic acid. Although the reduction takes place in 70 min, the extraction and purification of the complex from the resulting mixture proved to be a long and tedious procedure.

In this report we describe an improved, easy, two-step synthesis of **3** (Scheme 1), in which the yield exceeds 4-fold than that previously reported.[26] The first step involves the nitration of 2,2′-bipyridine-*N*,*N*′-dioxide **1**,

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Keywords: diamino; substituted bipyridine; electron donor; reduction.

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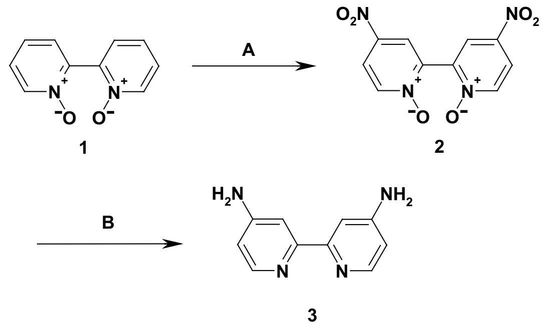

Scheme 1. Reagents and conditions: (A) concd sulfuric acid/fuming nitric acid 2.25:1 (95–100 °C), 20 h; (B) ethanol, Pd/C (10%), hydrazine hydrate, 15 h.

using concentrated sulfuric acid and fuming nitric acid, to produce 4,4′-dinitro-2,2′-bipyridine-*N*,*N*′-dioxide **2** in 86% yield. This is followed by the reduction of **2**, catalyzed by 10% Pd/C and hydrazine hydrate, to form **3** in an improved overall yield for the two-step process of 73%.

In addition to the overall synthesis of the target ligand **3**, we report relatively high yields of **2** compared to previous reports (86% vs 54%).[27] This is significant in itself, as this compound is an important precursor, not only in the preparation of **3**, but also in the synthesis of several widely used 2,2′-bipyridine derivatives:[10,26] 4,4′-[X]$_2$-2,2′-bipyridine, X = Cl, Br, OMe, OEt, OPh and NEt$_2$.

The dinitro compound **2** was synthesized, by nitration of **1** with a combination of sulfuric acid and nitric acid (2.25:1), as follows: 7.2 mL (0.135 mol) of concentrated sulfuric acid was added to 1.5 g (8 mmol) of **1** (Aldrich). The mixture was first cooled in ice, before addition of 2.5 mL (0.06 mol) of fuming nitric acid (**CAUTION**). The resulting solution was held at reflux (95–100 °C) for 20 h before cooling to room temperature. The acidic mixture was then poured onto ice (−40 °C), prepared by the addition of an excessive amount of liquid nitrogen onto 40 mL of water with constant stirring. Initially, the solution became green with liberation of N_2O_4 fumes. After continued stirring, a bright yellow precipitate formed, to which a further measure of liquid nitrogen was added. The solution was subsequently filtered and the yellow precipitate collected. The solid was washed successively with 3 × 25 mL of water and allowed to air dry. Yield: 1.92 g of yellow powder[†] (6.9 mmol, 86%).

The reduction of **2** was carried out via a similar procedure to that first reported by Bodige and MacDonnell,[28] for the synthesis of 5,6-diamino-1,10-phenanthroline. The synthesis of **3** was carried out as follows: a mixture of 1.11 g (4 mmol) of **2** and 1.0 g Pd/C (10%) in 120 mL of ethanol was purged with N_2 gas. The suspension was then heated to reflux under nitrogen and, after the complex was completely dissolved, 8.6 mL (0.276 mol) of hydrazine hydrate in 30 mL ethanol was added dropwise over a period of 1 h. The resulting solution was held at reflux for 15 h. When completed, the mixture was immediately filtered hot, through a bed of Celite, and the pad washed with 4 × 30 mL of boiling ethanol. After removal of the solvent, the yellow precipitate was ground in 80 mL of water and left at 2 °C overnight. The white solid that separated was vacuum filtered, washed with cold water and dried at 50 °C. Yield: 0.63 g of white powder[‡] (3.4 mmol, 85%).

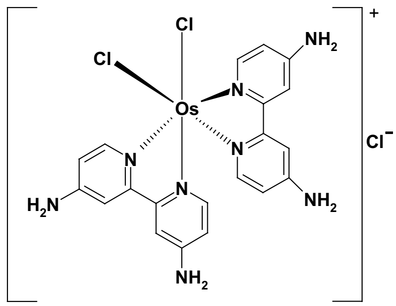

Figure 1. Bis-[Os-(4,4′-diamino-2,2′-bipyridine)Cl$_2$]Cl.

The coordination of **3** with ammonium hexachloroosmate ($(NH_4)_2OsCl_6$), to form bis-[Os-(4,4′-diamino-2,2′-bipyridine)Cl$_2$]Cl **4** (Fig. 1), was achieved as previously reported.[21] This report contained no electrochemical data for the complex.

From cyclic voltammetry in phosphate buffer solutions of **4** drop coated on glassy carbon electrodes, we observed one pair of well defined peaks ($E^{0'} = -570$ mV vs Ag/AgCl) (Fig. 2A, current is normalized to maximum current observed in the voltammogram of each complex to allow comparison). The effect of the electron donating character of the amino groups, on the bipyridine ligand, can be clearly seen when the cyclic voltammogram is compared to that of bis-[Os-(2,2′-bipyridine)Cl$_2$]Cl[29] (Fig. 2B), which displays an $E^{0'}$ of −40 mV (vs Ag/AgCl). Therefore, the amino groups have a significant effect on the redox potential, resulting in a shift of 530 mV in the negative direction.

In addition, the electron donating character of the amino groups compares well with other electron donors, such as methyl and methoxy groups,[30] which shift the redox potential by −125 and −260 mV, respectively, when compared to bis-[Os-(2,2′-bipyridine)Cl$_2$]Cl.

In conclusion, the use of Pd/C (10%) and hydrazine hydrate, as a reducing combination, provides an easy

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[†] Selected data for **2**: IR: 1510 (NO_2), 1340 (NO_2), 1290 (N–O) cm^{-1}. ^{1}H NMR (DMSO)-d_6: δ 8.68 (d, 2H, J_{HH} = 3.42 Hz, $H^{3,3'}$), δ 8.58 (d, 2H, J_{HH} = 7.32 Hz, $H^{6,6'}$), δ 8.36 (dd, 2H, J_{HH} = 2.92, 2.93 Hz, $H^{5,5'}$) ppm. Calcd for $C_{10}H_6N_4O_6 \cdot 0.25\ H_2O$: C, 42.51; H, 2.13; N, 19.83. Found: C, 42.08; H, 2.21; N, 19.88.

[‡] Selected data for **3**: IR: 3450 (NH_2), 3141 (NH), 1635 (NH) cm^{-1}. ^{1}H NMR (DMSO)-d_6: δ 8.01 (d, 2H, J_{HH} = 4.88 Hz, $H^{6,6''}$), δ 7.52 (s, 2H, $H^{3,3'}$), δ 6.43 (d, 2H, J_{HH} = 3.90 Hz, $H^{5,5'}$), δ 6.02 (s, 4H, NH_2) ppm. Calcd for $C_{10}H_{10}N_4$: C, 64.50; H, 5.41; N, 30.09. Found: C, 63.85; H, 5.44; N, 29.57.

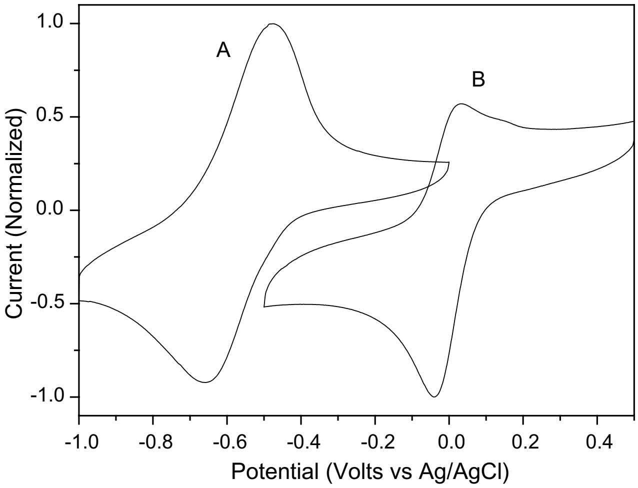

Figure 2. Cyclic voltammograms of bis-[Os-(4,4′-diamino-2,2′-bipyridine)Cl_2]Cl, A, and bis-[Os-(2,2′-bipyridine)Cl_2]Cl, B, adsorbed on glassy carbon electrodes, in 0.1 M phosphate buffer, scan rate 100 mV/s.

and more efficient synthetic route (85% yield) to the desired ligand. 4,4′-Diamino-2,2′-bipyridine can be readily coordinated to form bis[22] and tris[10] transition metal complexes, for which potential applications are currently been studied.

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