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Short Communication

Template synthesis of a ferrocene–metallocyclam conjugate

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Abstract

Arylsulfonamides act as efficient locking fragments in the Ni^{II} template cyclization of open-chain tetramines, in the presence of formaldehyde, to give cyclam-like azamacrocycles. In particular, if ferrocenesulfonamide is used, a ferrocene–metallocyclam conjugate is obtained, which releases two electrons according to two distinct and consecutive one-electron steps (Fc/Fc^+ and Ni^{II}/Ni^{III}).

Introduction

1,4,8,11-Tetraazacyclotetradecane (cyclam) forms very stable transition metal complexes from both a thermodynamic and kinetic viewpoint [1]. Moreover, it promotes the redox activity of the encircled metal centre, in particular favouring the access to unusually high oxidation states (Ni^{III}, Cu^{III}, Ag^{II}, Ag^{III}) [2]. Cyclam can be conveniently prepared through the Ni^{II} template reaction between the open-chain tetramine 3.2.3-tet and glyoxal, followed by hydrogenation of the C=N double bonds which form in the Schiff base condensation [3]. The $[Ni^{II}(cyclam)]^{2+}$ complex, which is obtained in high yield, can be demetallated in a boiling cyanide solution to give the free ligand. Then, the uncomplexed ligand can be protected in all but one of its secondary amine nitrogen atoms and reacted with appropriate fragments, to give a functionalized macrocycle [4].

We describe here a convenient template synthesis in which a cyclam-like system already carrying the wanted functionalization is prepared in a one-pot reaction. Through this novel procedure, a ferrocene–metallocyclam conjugate is obtained, whose redox properties have been characterized through cyclic voltammetry experiments.

Experimental

UV–Vis spectra were measured on a Hewlett-Packard 8452A diode array spectrophotometer or on a Varian Cary 2300 spectrophotometer. Electrochemical experiments were performed as previously described [5]. 1,9-Diamino-3,7-diazanonane (2.3.2-tet) was prepared according to the literature method [3].

Synthesis of macrocyclic complexes

*[3-(4'-Toluenesulfonyl)-1,3,5,8,12-pentaazacyclotetradecane]copper(II) nitrate, [**2a**$(NO_3)_2$]*

$Cu(NO_3)_2 \cdot 3H_2O$ (10 mmol) was dissolved in ethanol (40 cm^3) in a round-bottom flask equipped with reflux condenser, thermometer and dropping funnel. A solution of 2.3.2-tet (10 mmol) in ethanol (20 cm^3) was added dropwise to the magnetically stirred solution of copper(II) nitrate. The resulting violet suspension was warmed to 50 °C and 4-toluenesulfonamide (10 mmol, in 30 cm^3 of ethanol), triethylamine (1.5 cm^3, in one portion) and 40% aqueous formaldehyde (5 cm^3, in several portions during the reaction) were added to the violet solution through the dropping funnel. Heating and magnetic stirring were continued for 5 days. The silky violet precipitate which had formed was filtered through a sintered glass funnel, washed with cold ethanol and acetone, and dried *in vacuo*. Yield 41%. *Anal.* Found: C, 35.15; H, 5.47; N, 17.91. Calc. for $C_{16}H_{29}CuN_7O_8S$: C, 35.40; H, 5.51; N, 18.05%.

*[3-Ferrocenesulfonyl-1,3,5,8,12-pentaazacyclotetradecane]copper(II) nitrate, [**3a**$(NO_3)_2$]*

The synthesis was performed through the same procedure and by using the same amount of reagents as for **2a**. The locking fragment, ferrocenesulfonamide, was dissolved in 150 cm^3 of ethanol. Yield 43%. *Anal.* Found: C, 35.83; H, 4.96; N, 15.37. Calc. for $C_{19}H_{31}N_7O_8SCuFe$; C, 35.84; H, 4.90; N, 15.39%.

*[3-(4'-Toluenesulfonyl)-1,3,5,8,12-pentaazacyclotetradecane]nickel(II) perchlorate (**2b**$(ClO_4)_2$]*

An ethanolic solution (25 cm^3) of 2.3.2-tet (10 mmol) was slowly added under magnetic stirring to $NiCl_2 \cdot 6H_2O$

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(10 mmol in 50 cm^3 of ethanol) in a round-bottom flask (equipped as described for the synthesis of **2a**). The resulting blue solution was heated at 60 °C, then 4-toluenesulfonamide (10 mmol, in 50 cm^3 of ethanol), triethylamine (1.5 cm^3) and 40% aqueous formaldehyde (10 cm^3, in several portions) were added. After 2 days, a pink–violet precipitate was isolated by filtration, dissolved in ethanol and treated with a few drops of 70% aqueous $HClO_4$. The product was recovered as an orange crystalline precipitate, which is insoluble in water. Yield 24%. *Anal.* Found: C, 30.88; H, 4.74; N, 11.09. Calc. for $C_{16}H_{29}N_5O_{10}SCl_2Ni$: C, 30.65; H, 4.66; N, 11.16%.

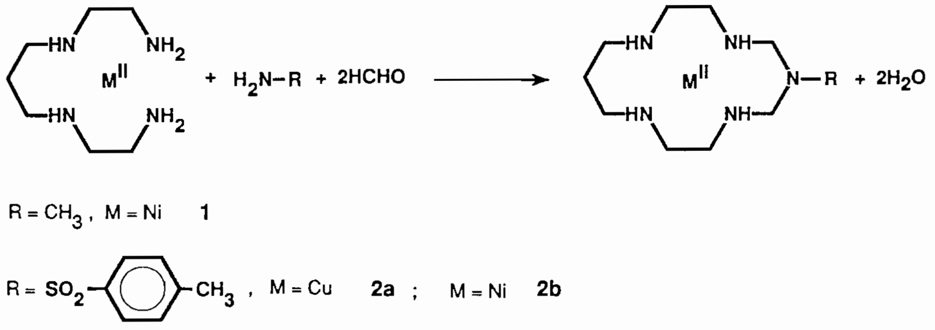
[3-Ferrocenesulfonyl-1,3,5,8,12-pentaazacyclotetradecane]nickel(II) perchlorate, [3b(ClO$_4$)$_2$]

The synthesis was performed as described for **2b**, but after 5 days no precipitate had formed in the flask. Then, the yellow solution was treated, in a nitrogen atmosphere, with 10 cm^3 of 70% aqueous perchloric acid. A yellow precipitate rapidly formed, which was recovered by a fast filtration and washed twice with cold water. Yield 27%. *Anal.* Found: C, 32.09; H, 4.56; N, 10.06. Calc. for $C_{19}H_{31}N_5O_{10}SCl_2FeNi$: C, 32.29; H, 4.41; N, 9.90%. In the electronic spectrum, the absorption band pertinent to the ferrocene fragment (λ_{max} 418 nm, $\epsilon = 320$ dm^3 mol^{-3} cm^{-1}) obscures those expected for the Ni^{II} macrocyclic chromophore. A shoulder at 480 nm (pertinent to low-spin Ni^{II}) is observed.

Results and discussion

The primary amine group acts as an efficient locking fragment in the Ni^{II} template synthesis of poly-azamacrocycles [6]. A typical reaction is shown in Scheme 1. In particular, the Ni^{II} assisted condensation of the open-chain tetramine 1,9-diamino-3,7-diazanonane (2.3.2-tet) with formaldehyde and methylamine gives the metal complex of the 14-membered penta-azamacrocycle **1**, azacyclam [7]. The X-ray investigation shows that in the low-spin Ni^{II} complex **1**, which is obtained in good yield as its perchlorate salt, only the four secondary amine nitrogen atoms are coordinated to the metal centre [7]. The tertiary amine nitrogen atom is not involved in the coordination and plays a merely structural role. Thus, the $[Ni^{II}(azacyclam)]^{2+}$ complex presents very similar features to the corresponding $[Ni^{II}(cyclam)]^{2+}$ complex. In particular, it is especially resistant to the demetallation, persisting in strongly acidic aqueous solution, and undergoes a reversible one-electron oxidation to give a stable Ni^{III} complex.

We have now found that also the $-NH_2$ group of arylsulfonamides is an effective locking fragment in the template synthesis of azacyclam ligands and that the Cu^{II} ion behaves as well as Ni^{II} as a templating agent. For instance, on reacting equivalent amounts of Cu^{II}, 2.3.2-tet, 4-toluenesulfonamide with excess formaldehyde, in ethanol, the complex **2a** was obtained, as the silky violet nitrate salt, in more than 40% yield. The occurrence of the polyamine cyclization was confirmed by the fact that complex **2a** displayed the typical macrocyclic inertness towards demetallation, persisting intact in a 1 mol dm^{-3} HCl solution for one week and more, as monitored through the intensity of the d–d band centred at 526 nm. The corresponding low-spin Ni^{II} complex, **2b**, was obtained through a similar procedure, as the yellow diamagnetic perchlorate salt. It dissolves in acetonitrile to give a blue solution, whose d–d spectrum displays absorption bands pertinent to a pseudo-octahedral high-spin chromophore (326 nm, $\epsilon = 25$ dm^3 mol^{-1} cm^{-1}; 670 nm, $\epsilon = 5$ dm^3 mol^{-1} cm^{-1}) and to a planar low-spin chromophore (484 nm, $\epsilon = 16$ dm^3 mol^{-1} cm^{-1}). Co-existence of the high-spin and low-spin forms in polar solvents is well documented for Ni^{II} complexes with cyclic and non-cyclic tetramines [8]. The $[Ni^{II}L]^{2+}$ complex in the same solution, made 0.1 mol dm^{-3} in Bu_4NClO_4, at 25 °C, undergoes a reversible one-electron oxidation process to the Ni^{III} species, as shown by voltammetric investigations, using a platinum microsphere as a working electrode. The



Scheme 1.

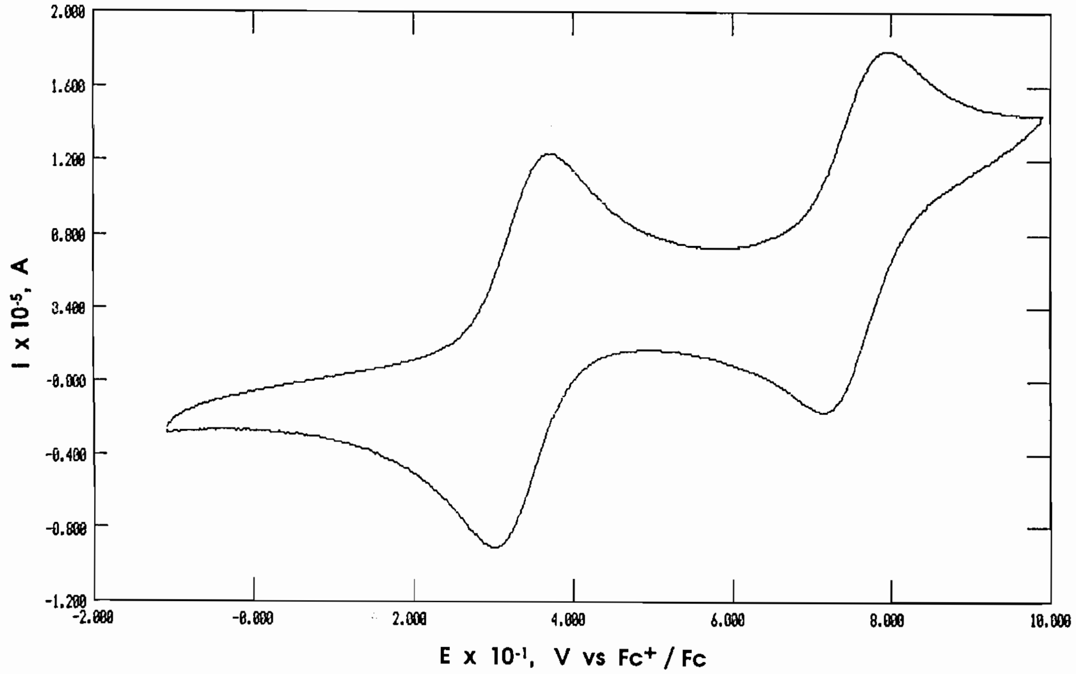
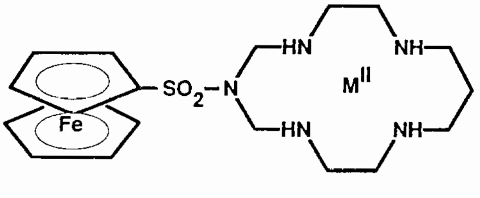


Fig. 1. Cyclic voltammetry profile of a MeCN solution 10^{-3} mol dm^{-3} in **3b** and 0.1 mol dm^{-3} in Bu_4NClO_4. Working electrode: platinum microsphere; potential scan rate: 100 mV s^{-1}. The less anodic wave corresponds to the oxidation of the ferrocene subunit, the more anodic peak corresponds to the oxidation of the metallocyclam subunit (Ni^{II}/Ni^{III}).

half-wave potential for the Ni^{II}/Ni^{III} redox change of **2b**, is 0.78 V versus Fc^+/Fc. Further experiments have shown that any kind of arylsulfonamide derivative gives an analogous template macrocyclization, opening a novel route to the synthesis of functionalized cyclam-like macrocycles. In particular, as any aromatic ring can be easily sulfonated (and the sulfonic group can be easily transformed in its amide), it derives that any subunit can be appended to the metallocyclam framework, provided it contains an aromatic cycle or heterocycle.



M = Cu 3a ; M = Ni 3b

An interesting application of this general procedure involves a particular arylsulfonamide fragment: ferrocenesulfonamide. Template reactions of ferrocenesulfonamide, carried out in the same conditions as for **2a** and **2b**, produced two novel heterodimetallic systems, Cu–Fe and Ni–Fe (**3a** and **3b**). In particular, the **3b** derivative is expected to display distinctive redox activity, as it couples the most classical redox agents of macrocyclic chemistry (the Ni–cyclam subunit, active through the Ni^{II}/Ni^{III} change) [2] and of organometallic chemistry (ferrocene, active through the Fc/Fc^+ change) [9].

Figure 1 displays the cyclic voltammetry profile obtained with an MeCN solution 0.1 mol dm^{-3} in Bu_4NClO_4, containing **3b**. The profile presents two reversible one-electron waves, separated by 430 mV. The more anodic peak has an $E_{1/2}$ value (0.80 V versus Fc^+/Fc) slightly more positive than that observed with the mononuclear Ni^{II} complex **2b** under the same conditions and it is thus assigned to the Ni^{II}/Ni^{III} redox change taking place in the azacyclam subunit. Therefore, the less anodic peak has to be assigned to the Fc/Fc^+ oxidation process, taking place in the organometallic moiety of **3b**. It should be noted that the potential associated to the reversible oxidation of the ferrocene subunit of **3b** (0.37 V versus Fc^+/Fc) is 70 mV more positive than that observed for the oxidation of ferrocenesulfonamide ($E_{1/2}$ values versus Fc^+/Fc are displayed in the potential diagram in Fig. 2).

This excess potential should reflect the extra electrical work to be spent in order to generate a positive charge on the ferrocene subunit of **3b** in the presence of a proximate dipositive cation (Ni^{II}). On the contrary, very small or no electrostatic repulsive effects are observed in the oxidation process involving the azacyclam fragment of **3b**, whose $E_{1/2}$ potential is only slightly more

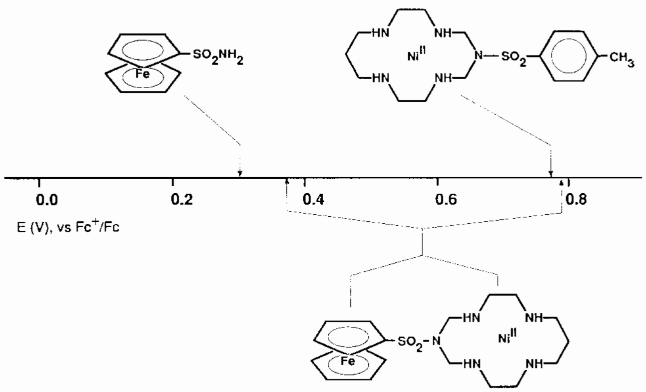


Fig. 2. Half-wave potentials (V vs. Fc$^+$/Fc, in an MeCN solution 0.1 mol dm^{-3} in Bu_4NClO_4, at 25 °C) associated to the oxidation behaviour of the heterodimetallic system **3b** and related compounds.

positive than that observed for the oxidation of the reference system **2b** (see Fig. 2). In this connection, it should be considered that the charge increase of the redox active metal centre takes place under a much more moderate repulsive field, i.e. that exerted by the adjacent monopositive ferrocenium moiety.

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