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Functional dyes: bipyridines and bipyrimidine based boradiazaindacene

Gilles Ulrich* and Raymond Ziessel*

Laboratoire de Chimie Moléculaire, Ecole de Chimie, Polymères, Matériaux (ECPM), Université Louis Pasteur (ULP), 25 rue Becquerel, 67087 Strasbourg Cedex 02, France

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Abstract—The synthesis of molecules bearing pyridine, 2,2′-bipyridine or 2,2′-bipyrimidine donor units appended with one or two highly luminescent indacene fragments was undertaken by using two distinct pathways. The first used direct condensation of krytopyrrole with the corresponding aldehydes. The second, and more universal is based on a Pd cross-coupling reaction between an iodo functionalized BODIPY and the corresponding stable ethynyl derivatives. All compounds are strongly luminescent in solution with quantum yields as high as 70%. Interlocking of two 6,6′-BODIPY substituted bipyridines around a single copper(I) center is observed by proton NMR and cyclic voltammetry. These synthetic routes have made a variety of functionalized dyes available for studies of their optical properties in the presence of incoming cations, of their coordination chemistry and as light emitting solid state materials.

The boradiazaindacene family (BODIPY) of fluorescent dyes has recently received considerable attention by scientists, due to their peculiar properties such as high extinction coefficients, high quantum yields of the singlet emitter and high stability compared to other green dyes such as fluorescein.[1] The association of this cyanine type of fluorophore with a tertiary amine or azacrown ether induces an inhibition of the fluorescence.[2] This luminescence can be recovered after complexation of a substrate at the nitrogen atom, by perturbation of a possible photoinduced electron transfer mechanism. Furthermore, when two BODIPY fragments are connected to the 4,4′-positions of a 2,2′-bipyridine (bipy)[3] or to the 4′-position of a 2,2′:6′,2″-terpyridine (terpy),[4] the luminescence is effectively quenched by various incoming cations. This very interesting process could also be visually observed when the terpy dye was embedded into polymeric matrices and the cations sprayed through a shadow mask on the polymer film. Interestingly, simultaneous luminescence quenching and a pronounced red shift of the color are observed. This so-called writing process is reversible by means of an adequate competitor of zinc cations.[4] This opens the way to the development of sensitive and selective fluorescent chemio-dosimeters. An efficient association of this dye with a selective complexing pocket could allow chemists to obtain very efficient ON/OFF sensors by analogy with previously reported molecules.[5]

We here present the synthesis and complexation properties of pyridine, bipyridine and bipyrimidine based BODIPY-dyes, either directly connected to the chelating platform or via an acetylene–phenyl linkage.

There are two common ways to build a boradiazaindacene core: (i) starting either from an aldehyde[6] or (ii) from an acyl chloride.[7] In the first case, the condensation of the pyrrole is catalyzed by protons affording a dipyrromethane intermediate, which is subsequently oxidized to dipyrromethene by DDQ. This unstable moiety is readily used to complex boron under basic conditions using boron trifluoride etherate. In the second case, the condensation of the pyrrole directly affords the hydrochloride salt of the dipyrromethene. This salt can be isolated or used directly for the production of BODIPY using an excess of base in the presence of the boron precursor. We found the sequential one-pot synthesis, from the carbonyl group to the boron complex, more convenient and reliable.[8]

The condensation of 1 equiv of 4-formylpyridine or 5-formyl-5′-methyl-2,2′-bipyridine[9] (0.3 g scale) with 2 equiv of kryptopyrrole (3-ethyl-2,4-dimethylpyrrole) in

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* Corresponding authors. Tel./fax: +33-390-242689; e-mail addresses: ziessel@chimie.u-strasbg.fr; gulrich@chimie.u-strasng.fr

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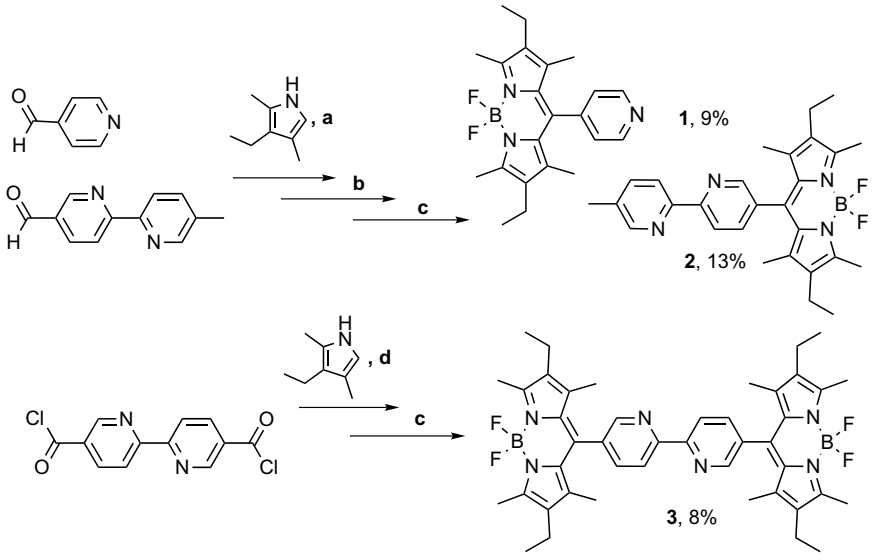


Scheme 1. Reagents and conditions: (a) CH_2Cl_2, *p*-TsOH, rt; (b) DDQ, 4 h, rt; (c) TEA, $BF_3{\cdot}Et_2O$, CH_2Cl_2, rt; (d) CH_2Cl_2, rt.

the presence of a catalytic amount of *p*-toluenesulfonic acid, in dichloromethane, during 2 days at rt, followed by the addition of 1 equiv of DDQ, and the subsequent addition (4 h later) of 4 equiv of TEA and 6 equiv of $BF_3{\cdot}Et_2O$, afforded the corresponding boradiazaindacene dyes **1**[†] and **2**, in overall yields of 9% and 13%, respectively (Scheme 1). The bis-functionalized bipyridine analogue **3** was prepared starting from the corresponding acyl chloride (1 equiv),[10] which was condensed with the pyrrole (4 equiv) in dichloromethane at rt, for three days. The dipyrromethene intermediate thus obtained was deprotonated in the same pot with triethylamine and reacted with boron trifluoride etherate. The low yields obtained by direct condensation seems to be rather dependent on the structure of the oligopyridine as we noticed in our work on terpy derivatives.[4]

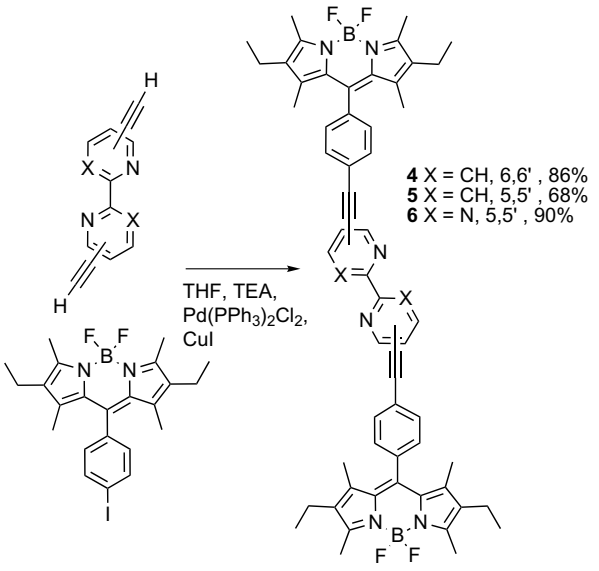
In an effort to prepare additional oligopyridine frameworks bearing BODIPY dyes in a more practical way and also with a more extended π-conjugated connector on various positions, we decided to couple acetylenic oligopyridines to an activated: 4-iodo-phenyl-bodipy dye.[11]

By means of Sonogashira couplings, it was possible to obtain compounds **4**[‡]–**6**, in good yields (70–90%), starting from the corresponding stable acetylenic derivatives (1 equiv, 0.100 g scale) such as: 6,6′-diethynyl-2,2′-bipyridine,[12] 5,5′-diethynyl-2,2′-bipyridine[12] and 5,5′-diethynyl-2,2′-bipyrimidine[13]; and 4-iodo-phenyl-bodipy (2.2 equiv) in the presence of a catalytic amount of $Pd(PPh_3)_2Cl_2$ (12 mol %) and cuprous iodide (20 mol %), in degassed THF containing an excess of diisopropylamine (Scheme 2). The reaction was found to be very fast when the reaction mixture was sonicated.

All these compounds exhibited a strong green fluorescence, which can be attributed to a transition from the singlet excited state of the boradiazaindacene to the ground state.[14] The strong visible absorption (at 527–529 nm) with a high molar extinction coefficient ($\varepsilon = 60{,}000$–$80{,}000\ M^{-1}\,cm^{-1}$ per dye unit) is likely to be due to a S_0–S_1 transition. The weak Stokes' shift (ca. $600\ cm^{-1}$), the relatively high quantum yield (50–70%) and the short lifetimes are in keeping with literature data (Table 1).[7,11]

[†] 4,4-Difluoro-8-(4′-pyridinyl)-1,3,5,7-tetramethyl-2,6-diethyl-4-bora-3a,4a-diaza-s-indacene: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.99$ (t, 6H, $^3J = 7.6$ Hz), 1.32 (s, 6H), 2.31 (q, 4H, $^3J = 7.6$ Hz), 2.55 (s, 6H), 7.31 (dd, 2H, $^3J = 4.3$ Hz, $^4J = 1.5$ Hz), 8.78 (dd, 2H, $^3J = 4.5$ Hz, $^4J = 1.7$ Hz). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): $\delta = 12.30$ (CH_3), 12.97 (CH_3), 14.95 (CH_3), 17.45 (CH_2), 124.09 (CH), 130.12 (Cq), 133.80 (Cq), 136.56 (Cq), 138.22 (Cq), 144.82 (Cq), 150.95 (CH), 155.15 (Cq). ^{11}B NMR (128.4 MHz, $CDCl_3$): 3.79 (t, $^1J_{B-F} = 32.8$ Hz). UV–vis (CH_2Cl_2, 23 °C): λ_{max} (ε, $M^{-1}cm^{-1}$) = 235 (14,800), 382 (6300), 501 (sh, 21,000), 528 (59,000). IR (KBr): 1638 (s, $\nu_{C=N}$), 1414, 1118 (m, $\nu_{B=F}$), cm^{-1}. MS (FAB$^+$, *m*NBA): *m*/*z* (%) = 382.2(30) [M+H$^+$], 381.2 (100) [M], 362.3 (20) [M−F]$^+$. Anal. Calcd for $C_{22}H_{26}BF_2N_3$: C, 69.30; H, 6.87; N, 11.02; Found C, 69.10; H, 6.61; N, 10.82.

[‡] 6,6′-{bis-ethynylphenyl-4″-[4′,4′-Difluororo-8′-(1′,3′,5′,7′-tetramethyl-2′,6′-diethyl-4′-bora-3′a,4′a-diaza-s-indacene)]}-2,2′-bipyridine 86%. ^{1}H NMR (300.1 MHz, $CDCl_3$): $\delta = 0.99$ (t, 12H, $^3J = 7.5$ Hz), 1.33 (s, 12H), 2.31 (q, 8H, $^3J = 7.5$ Hz), 2.54 (s, 12H), 7.55 (AB, 8H, $J_{AB} = 8.3$ Hz, $\nu_0\delta = 129.7$ Hz), 7.62 (dd, 2H, $^3J = 7.7$ Hz, $^4J = 1.1$ Hz), 7.87 (t, 2H, $^3J = 7.8$ Hz), 8.52 (dd, 2H, $^3J = 8.5$ Hz, $^4J = 1.0$ Hz). $^{13}C\{^1H\}$ Dept NMR (75.4 MHz, $CDCl_3$): $\delta = 11.9$ (CH_3), 12.5 (CH_3), 15.6 (CH_3), 17.0 (CH_2), 88.7, 90.3, 121.4, 123.4, 128.0, 129.1, 130.9, 133.1, 133.4, 137.1, 137.6, 138.6, 139.4, 142.9, 154.5, 156.4. ^{11}B NMR (128.4 MHz, $CDCl_3$): 3.86 (t, $J_{B-F} = 32.86$ Hz). IR (KBr): 3435, 2922, 1647 (br, $\nu_{C=N}$), 1577, 1122 (w, $\nu_{B=F}$), cm^{-1}. UV–vis (CH_2Cl_2, 23 °C): λ_{max} (ε, $M^{-1}cm^{-1}$) = 287 (60,000), 315 (52,400), 499 (sh, 53,400), 527 (160,000). MS (FAB$^+$, *m*NBA): *m*/*z* (%) = 960.4 (100) [M]$^+$, 922.2 (49) [M−2F]$^+$. Anal. Calcd for $C_{60}H_{58}B_2F_4N_6$: C, 75.01; H, 6.08; N, 8.75; Found C, 74.73; H, 5.90; N, 8.56.



Scheme 2. Reagents and conditions: (a) $Pd(PPh_3)_2Cl_2$, CuI, THF, $(i\text{Pr})_2NH$.

One of the targets of this research program is to complex the chelating part of novel molecules with cations and transition metals in order to modulate the steady state emission and also to prepare transition metal complexes displaying new optical properties and bipolar character to permit the formation of both stable cation and anion radicals. In order to test the reactivity, complexation abilities and stability of these BODIPY grafted ligands, we decided to build a tetrahedral diamagnetic copper(I) complex of ligand **4**. Two equivalents of **4** in CH_2Cl_2 were allowed to react with 1 equiv of $Cu[CH_3CN]_4ClO_4$[16] in anaerobic conditions. Immediately after mixing, the solution rapidly turned violet and the mononuclear complex **7**[§] could be isolated in almost quantitative yield (Scheme 3).

This complex exhibits an ^1H NMR spectrum typical of a fully interlocked copper(I) complex (Fig. 1). The two ligands are magnetically equivalent due to twofold symmetry. Strong shielding of the phenyl AB system is observed, due to its position in the shielding cone of the bipyridine. In contrast, the complexation induced an upfield shift of the pyridine protons, compared to the free bipyridine owing to the involvement of the ligand in copper coordination and to the *trans–cis* conformation change of the nitrogen lone pairs.

Table 1. Spectroscopic[a] data for the compounds at 298 K

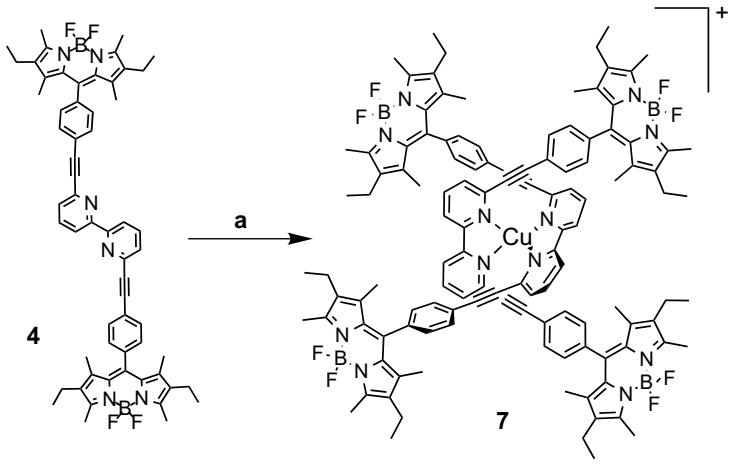
Compd	λ_{abs}/nm	ε (10^3 $M^{-1}\,cm^{-1}$)	λ_{em}/nm	Stokes shift (cm^{-1})	Φ_f[b]	τ_f/ns
1	528	59	547	657	0.50	3.6
2	529	83	546	588	0.69	3.7
3	528	141	547	657	0.51	3.7
4	527	160	544	592	0.64	4.1
5	527	195	544	592	0.70	3.7
6	527	140	546	660	0.62	3.6

[a] Determined in dichloromethane solution.
[b] In dichloromethane solution, ca. 5×10^{-7} M. Using Rhodamine 6G as reference $\Phi = 0.76$ in water, $\lambda_{exc} = 488$ nm.[15] All Φ_f values are corrected for changes in refractive indexes.

The complex exhibits a strong absorption ($320{,}000\ M^{-1}\,cm^{-1}$) at 525 nm, equivalent to the absorption of two ligands. The band associated to the metal-to-ligand-charge-transfer-state (MLCT) could be observed at ca. 460 nm, which is in agreement with literature data.[17] Absorption, fluorescence and excitation spectra of the copper(I) complex are similar to the free ligand, with a measured quantum yield of 60%.

From preliminary cyclic voltammetry measurements carried out in degassed dichloromethane using tetrabutylammonium hexafluorophosphate as supporting electrolyte we can conclude that the free ligand **4** and its copper(I) complex possess the desired bipolar character, expected from the design, generating stable cation and anion radicals (Fig. 2). Briefly, both free ligand and copper complex showed reversible redox properties, exhibiting one and two anodic waves, respectively and a single cathodic wave. The half-wave oxidation and reduction potentials for the free ligand **4** were at +1.00 V ($\Delta E_p = 60$ mV) and −1.34 V ($\Delta E_p = 80$ mV) versus SSCE, giving a formal HOMO/LUMO gap of 2.34 eV. Both reversible processes are monoelectronic as confirmed by coulommetric data. Interestingly, in the copper complex the oxidation of BODIPY to $BODIPY^{+\cdot}$ is more difficult by 40 mV due to an electrostatic effect generated by the reversible oxidation of Cu(I) to Cu(II) at +0.89 V ($\Delta E_p = 60$ mV). Furthermore, due to the charge effect induced by the presence of the Cu^+ cation the reduction of BODIPY fragments to $BODIPY^{-\cdot}$ is facilitated by 130 mV versus the free ligand. Clearly, the oxidation and reduction of the four BODIPY subunits (four electron process) in the interlocked copper complex occur at the same potential showing the absence of any electronic interaction, whereas the oxidation of copper is mono-electronic and in the expected range for such tetrahedral complexes[18] (see Fig. 2). Finally, when the scan was repeated in the same electrochemical

[§] Bis-[6,6′-{bis-ethynylphenyl-4″-[4′,4′-difluororo-8′-(1′,3′,5′,7′-tetramethyl-2′,6′-diethyl-4′-bora-3′a,4′a-diaza-s-indacene)]}-2,2′-bipyridine] copper(I) perchlorate. To a solution of **4** (0.053 g, 0.055 mmol) in DCM/acetonitrile (1:1, 20 mL) was added $Cu[CH_3CN]_4ClO_4$ (0.009 g, 0.027 mmol). The deep red-violet solution was heated at 50 °C during one day, and the solvent removed. The complex (0.053 g, 98%) was recrystallized from an acetone/benzene 1/1, v/v mixture. ^1H NMR (300.1 MHz, $CDCl_3$): $\delta = 1.04$ (t, 24H, $^3J = 7.4$ Hz), 1.36 (s, 24H), 2.42 (q, 16H, $^3J = 7.4$ Hz), 2.54 (s, 24H), 7.25 (AB, 16H, $J_{AB} = 8.2$ Hz, $v_0\delta = 70.6$ Hz), 8.15 (d, 4H, $^3J = 7.7$ Hz), 8.40 (t, 4H, $^3J = 7.2$ Hz), 8.71 (d, 4H, $^3J = 7.9$ Hz). $^{13}C\{^1H\}$ Dept NMR (75.4 MHz, $CDCl_3$): $\delta = 12.3$ (CH_3), 12.6 (CH_3), 15.0 (CH_3), 17.5 (CH_2), 88.8, 92.9, 122.3, 123.1 (CH), 129.8 (CH), 130.8 (CH), 131.0, 132.9 (CH), 133.9, 138.1, 138.9, 139.9 (CH), 142.2, 152.8, 154.9. ^{11}B NMR (128.4 MHz, $CDCl_3$): 3.73 (t, $J_{B-F} = 32.26$ Hz). IR (KBr): 3435, 2964, 2928, 1540 (s), 1476, 1193 (s), 1082 cm^{-1}. UV–vis (CH_2Cl_2, 23 °C): λ_{max} (ε, $M^{-1}\,cm^{-1}$) = 462 (sh, 19,300), 493 (sh, 116,000), 525 (320,000). MS (FAB$^+$, *m*NBA): m/z (%) = 1984.2 (100) $[M]^+$. Anal. Calcd for $C_{120}H_{116}B_4F_8N_{12}CuClO_4$: C, 69.14; H, 5.61; N, 8.06; Found C, 68.85; H, 5.41; N, 7.81.



Scheme 3. Reagents and conditions: (a) $Cu[CH_3CN]_4ClO_4$, CH_3CN, CH_2Cl_2.

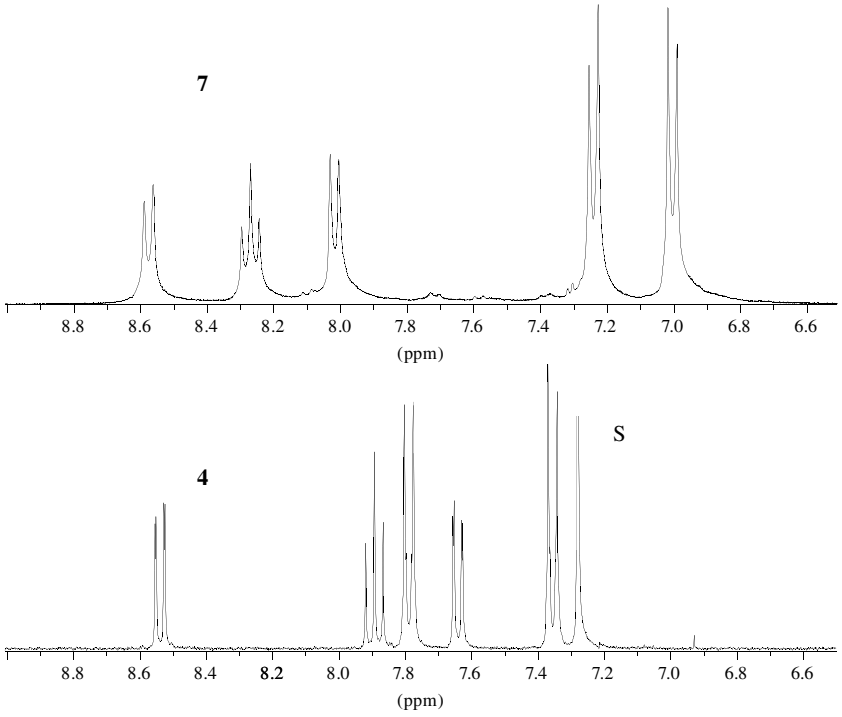


Figure 1. ^1H NMR spectra of ligand **4** and the corresponding Cu(I) complex **7** (aromatic part). S for $CDCl_3$.

window −2.0 to +1.6 V no additional waves could be detected and the traces remained superimposable proving the good stability of the radical anion and cation in both ligand and complex.

A plausible reductive photoinduced electron transfer from the copper(I) center to the BODIPY ($\Delta G_0 = 200$ mV) could be calculated from the potentials measured. However, luminescence quenching could not be observed probably due to the large number of BODIPY subunits.

In situ complexation of Cu^+ is feasible and similar electrochemical behavior is observed. However, progressive implementations of a solution of the free ligand **4** with Zn^{2+} or Fe^{2+} salts do not show any significant perturbation of the cyclic voltammograms, in keeping with the absence of complex formation. This is an interesting set of experiments allowing the amperometric speciation of Cu salts versus other transition metals. Further work along these lines is currently in progress.

In summary, a novel class of high-performance green emitting molecular materials with the desired bipolar radical character has been created. Direct construction of BODIPY grafted pyridine or bipyridine scaffolds could be produced with modest yields, while Sonogashira protocols provide larger conjugated molecules in fair yields. The present account presents a new guideline for the molecular design of strongly emitting molecules

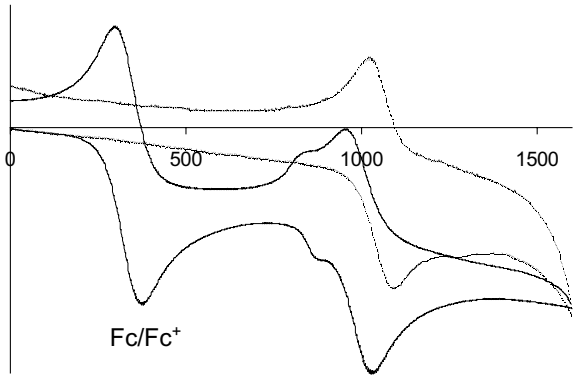


Figure 2. Cyclic voltammetry of ligand **4** (dotted line) and the corresponding Cu(I) complex **7** (full line). Potentials were standardized using ferrocene Fc/Fc^+ as internal reference and converted to SSCE assuming that E $Fc/Fc^+ = +0.38$ V versus SSCE.

in solution and in the solid state, paving the way for the future development of novel light emitting materials for various applications such as chemio-dosimeters and light emitting diodes.

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