ORGANOMETALLICS

Article

pubs.acs.org/Organometallics

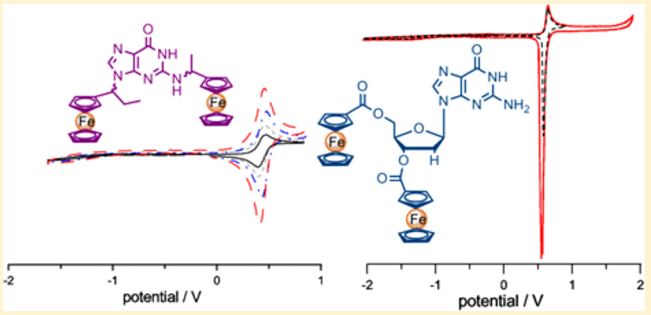
New Approaches toward Ferrocene−Guanine Conjugates: Synthesis and Electrochemical Behavior

Matteo Iurlo,* Luca Mengozzi, Stefania Rapino, Massimo Marcaccio, Rosaria C. Perone, Stefano Masiero,* Piergiorgio Cozzi,* and Francesco Paolucci*

Alma Mater Studiorum-Università di Bologna and INSTM, Unit of Bologna, Dipartimento di Chimica "Giacomo Ciamician", via Selmi, 2, 40126 Bologna, Italy

Supporting Information

ABSTRACT: Different substituted ferrocene−guanine conjugates were prepared, and their electrochemical behavior was investigated. A new approach for the introduction of ferrocene in guanine's 9-position through a quite effective S_N1-type reaction was disclosed. The electrochemical behavior of the various derivatives can be used as standard for the quantification and analysis of DNA strands.



INTRODUCTION

The field of bioorganometallic chemistry is growing rapidly, networking classical organometallic chemistry to biology, medicine, and molecular biotechnology. In this perspective, the chemical stability and electroactive behavior of ferrocene has been extensively used for its conjugation to a diverse array of bioactive molecules.[1] However, ferrocene conjugation to nucleobases, nucleosides, and nucleic acids is a relatively young domain in comparison to the studies with amino acids and peptides. As nucleobases offer the possibility of a network in terms of hydrogen bonding and supramolecular assembly,[2] the application of hierarchical structures of ferrocene−nucleobase conjugates may offer the possibility to establish mutual recognition and patterns on various supports. In this regard, as nucleobases can self-associate with the help of Watson−Crick and Hoogsteen hydrogen bonds, the possibility of arranging ferrocene around nucleobase templates has been reported.[3] Self-association motifs of ferrocene-linked mono-(nucleobase) conjugates with a single-carbon methylene spacer have been reported by Houlton's group.[4] They have prepared ferrocenyl derivatives of thymine, cytosine, and uracil and of N2-acetylguanine and 2-amino-6-chloropurine. The synthesis and crystallographic studies of a ferrocenyl conjugate of adenine, where the hydrogen-bonding interactions promote and stabilize nucleobase homotetrad formation, has been reported by Verma.[5] In this article, 3-bromopropionic acid chloride was used for ferrocene acylation, which upon base-catalyzed alkylation resulted in the formation of a modified ferrocenylated-adenine hybrid. This ferrocenylated-adenine hybrid molecule was then used by Verma and Bianco[6] in a redox-active ferrocene assembled on gold surfaces through hydrogen-bonding interactions and a uracil-terminated organothiol monolayer. A ferrocene−bis(thymine) derivative was reported by Ganesh.[7] In addition, as guanosine and its derivatives have favorable properties such as its peculiar sequence of H-bond donor or acceptor groups, it can self-assemble into ordered structures, such as G-quartets, which have potential for the development of molecular electronic devices.[8] In order to improve the self-assembly ability, significant efforts have been focused on the synthesis of modified guanosines. However, only a limited number of reports on modified guanosine derivatives obtained by Stille and Sonogashira coupling have appeared.[9] In extension to the interest in redox-active modified simple nucleobases, gene diagnosis and many DNA sensing methods require potent DNA detecting systems. These modern synthetic systems rely upon electrochemical techniques:[10] a wide variety of electrochemical DNA detecting techniques have been reported by using electrochemically intercalating molecules[11] or DNA labeling with electrochemically active reagents.[12] Rapid and direct electrochemical DNA detection has been achieved using a DNA probe-immobilized electrode where the peak current was proportional to the amount of the target DNA. This allowed electrochemical gene expression analysis with a detection limit of ca. 50 fmol.[13] In this context, a derivative of guanine has been used for a novel on/off electronic nanoswitch based on the conformational change of DNA sequence possessing a single guanine (G)-rich strand, labeled with redox-active ferrocene molecules serving as the signaling species.[14]

Special Issue: Organometallic Electrochemistry

Received: March 18, 2014

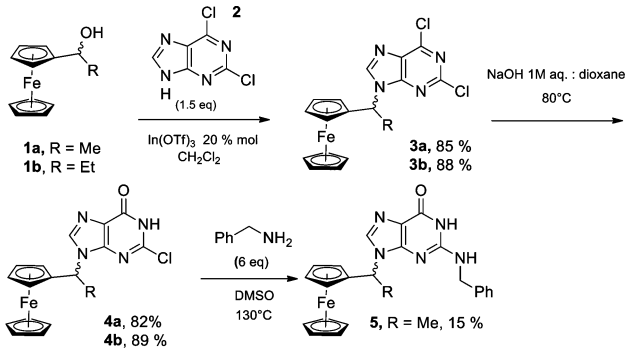
dx.doi.org/10.1021/om5002809 | *Organometallics* XXXX, XXX, XXX−XXX

In these regard, electrochemical studies on a singly modified nucleobase can be used as a standard for evaluating and developing new efficient methods for the electrochemical quantification of nucleotides and nucleosides. Such fundamental studies can clarify the nature and identity of species formed during the direct modification of DNA with specifically designed reagents.[15] To this goal, we have investigated the preparation of several guanine−ferrocene conjugates, by using specific reactions developed for this purpose, and have fully characterized the new guanine−ferrocene molecules from an electrochemical point of view. Our studies have introduced new ferrocene conjugates and, more importantly, a facile and selective method for the introduction of ferrocene residues in nucleobases based on S_N1 type reactions, which can be further exploited. In addition, the comprehensive electrochemical characterization of such species provides a standard for the selection of the best labels for the development of biosensing devices and protocols for the electrochemical detection of DNA.

RESULTS AND DISCUSSION

The reaction of purine bases with alkylating agents yields 3-, 7-, or 9-alkyl-substituted derivatives,[16] and the ratio of these derivatives depends on the nature of the alkylating agent and on the reaction conditions. Zhilina reported the reaction of ferrocenylethanol with adenine that occurs in position 9, in a biphasic reaction mixture (CH_2Cl_2−H_2O) in the presence of HBF_4.[17] In a previous article, we were able to react enantioenriched ferrocene alcohols under S_N1-type conditions with different nucleophiles, with the reaction occurring with retention of stereochemistry.[18] In particular we have used catalytic amounts of In(III) salts for the reaction with nucleophiles. As the preceding report suggested the possibility of an S_N1-type reaction with chiral and achiral ferrocene alcohols, we investigated the direct substitution of guanine. The reaction of ferrocenylethanol (**1b**) with guanine was investigated in different solvents and under various conditions in the presence of indium salts. Also, different additives, Brønsted and Lewis acids, were added to the reaction mixture. As guanine is insoluble in organic solvents, the reactions were carried out "on water". The temperatures investigated were between room temperature and 80 °C. In all cases, no traces of product were detected. The corresponding potassium salt of guanine is easily prepared by the treatment of guanine with KOH, and the isolated potassium salt was used in the reaction with stable carbenium ion. We were able to detect the reaction of guanine at the 9-nitrogen atom by using a carbenium ion obtained from *p*-NMe_2-benzhydrol, stable under aqueous conditions. However, the limited solubility of ferrocene derivatives did not allow the reaction under aqueous conditions. The direct S_N1 reaction of guanine was still considered by the use of suitable precursors that were more soluble in organic solvents. Monochloro- and dichloropurines are extensively used as precursors of nucleobases. The direct modification of nucleobases by nucleophilic aromatic substitution and successive hydrolysis allows in many cases the synthesis of the desired derivatives.[19] The chloro derivatives **2** and **8** were reacted with **1a** in the presence of a catalytic amount of In$(OTf)_3$. While **8** was insoluble in many of the solvents tested, **2** smoothly reacted with ferrocene **1a**, affording the desired compound **3a** in moderate yield. The hydrolysis of **3a** into **4a** occurred by following the standard procedure in the literature.[19] However, the synthesis of 9-ferrocenylguanine was attempted under various conditions, using ammonia or ammonia equivalents (Scheme 1). In addition, Buchwald−Hartwig methodologies

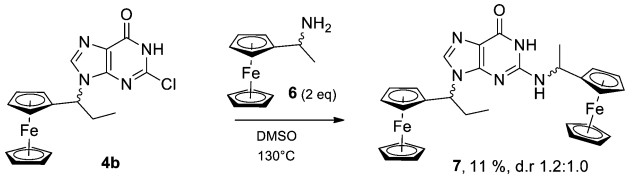
Scheme 1. Synthesis of 5



were briefly considered, but no results were obtained.[20] Under quite harsh conditions the nucleophilic displacement of the Cl group was observed for different amines.

By the direct reaction of the racemic aminoferrocene **6** with racemic **4b**, compound **7**, containing two ferrocene molecules, was prepared (Scheme 2). **7** contains two stereogenic centers

Scheme 2. Synthesis of 7



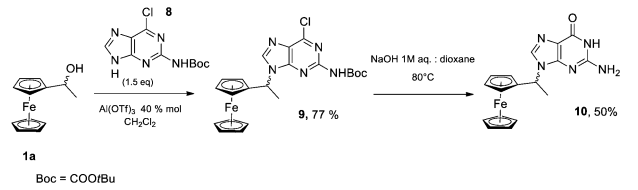
and was obtained as a inseparable mixture of diastereoisomers (ratio close to 1:1) in quite low yields. However, the direct reaction of amine with 2-chloroguanine is difficult and in order to introduce amino group at the 2-position, stronger nucleophilic compounds are often used.[21] The new compound **7** has a peculiar and quite interesting electrochemistry (see below).

In order to prepare the 9-alkylated ferrocenylguanine, a simple and effective strategy was designed. The 2-Boc chloro purine **8** (Boc = COOtBu)[22] was employed in the In(III) reaction with **1a**, but in this case partial deprotection of the Boc group occurred, giving a mixture of compounds. We found that Al$(OTf)_3$ was a suitable Lewis acid for this transformation, which allowed the preparation of the desired compound by the use of optically enriched ferrocenylethanol, without the deprotection of Boc.

The lower Lewis acidity of Al$(OTf)_3$[23] allowed the direct introduction of ferrocenylethanol at the 9-position of guanine. The direct functionalization of the 9-position of guanine by S_N1 chemistry is suggested by our study. The introduction of different groups with S_N1-type chemistry would be possible by the direct reaction of 2-Boc chloropurine with other carbenium ions generated from alcohols in the presence of Lewis acids.[24] Pleasantly, we found out that the hydrolysis of **9** with 1 N NaOH in aqueous dioxane gave not only the hydrolysis of chlorine to the desired oxo substituent but also the deprotection of Boc to the desired **10**, without any need of an acid treatment (Scheme 3). The electrochemistry of **10** was investigated in detail. When the nucleophilic 9-N atom is protected, as in the triacetyl guanosine derivative **11**, the

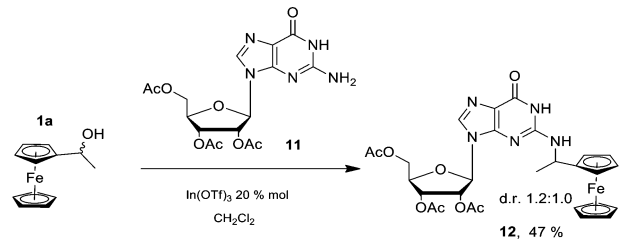
dx.doi.org/10.1021/om5002809 | *Organometallics* XXXX, XXX, XXX−XXX

Scheme 3. Synthesis of 10



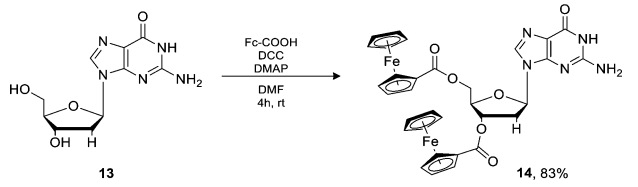
indium-promoted nucleophilic addition of ferrocenyl alcohol **1a** takes place with the available free amino group at position 2 (Scheme 4). As racemic **1a** was used for the reaction, an inseparable mixture of diastereoisomers (1.2:1) was obtained.

Scheme 4. Synthesis of 12



2′-Deoxyguanosine derivatives were also prepared. The synthesis of bis-ferrocenoyl derivative **14** was achieved by direct esterification of commercial **13** with ferrocenecarboxylic acid (Fc-COOH) in the presence of dicyclohexylcarbodiimide (DCC) as the condensing agent and 4-dimethylaminopyridine (DMAP) as the catalyst (Scheme 5). When this method is

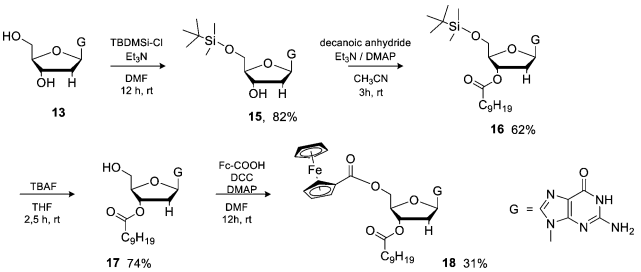
Scheme 5. Synthesis of 14



used, the protection of the exocyclic amino group on the nucleobase **13** is unnecessary. On the other hand, the use of mixed anhydrides, obtained from ferrocenecarboxylic acid, as the acylating agent proved in this case unsuccessful.

The analogous but more lipophilic monoferrocenoyl derivative **18** (Scheme 6) was obtained by selective protection of the 5′-hydroxy group (**15**), followed by esterification of the 3′-alcoholic function with decanoic anhydride (**16**). Again, the protection of the exocyclic amino function could be avoided. Subsequent desilylation with tetrabutylammonium fluoride

Scheme 6. Synthesis of 18



(TBAF) to form **17** and its direct esterification with ferrocenecarboxylic acid under the conditions mentioned above for **14** afforded the target compound **18**.

All of the electrochemistry experiments were performed under strictly aprotic conditions (DCM and DMSO), using tetrabutylammonium hexafluorophosphate (TBAHFP) as supporting electrolyte. The dynamics of the electrochemical behavior of **5**, **7**, **12**, **14**, and **18** were investigated using cyclic voltammetry (CV). At 298 K and ν = 0.5 V s^{-1}, the voltammogram of **5** in DCM displays one reversible oxidation peak at $E_{1/2}$ = +0.49 V. This oxidation is attributed to the reversible oxidation of the ferrocenyl group (Figure 1).

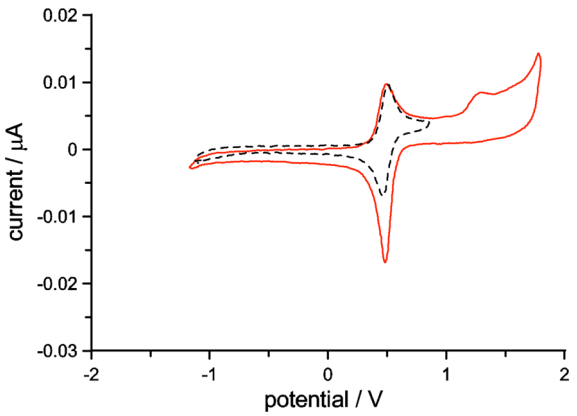


Figure 1. Cyclic voltammetric curves of compound **5** (0.8 mM) in 0.05 M TBAHFP/DCM solution, recorded with two different scan reversal potentials: T = 298 K; ν = 0.5 V s^{-1}; working electrode Pt disk (d = 125 μm). Potentials are referenced to the SCE.

At more positive potentials an irreversible peak appears. The inclusion in the potential scan of such a peak, associated with the guanine-centered oxidation, brings about a significant increase of the ferrocenyl cation centered reduction current at ~0.5 V, typical of processes involving adsorbed species. Such a behavior was tentatively attributed to the high charge of the species generated in the anodic scan that, in the present low-dielectric medium, would precipitate reversibly onto the electrode surface. In line with this hypothesis, a second scan carried out under the conditions of Figure 1 (not shown) displays an anodic pattern comparable to that of the first scan, indicating that, upon its neutralization during the cathodic scan, the precipitate is redissolved. Also in line with such a mechanistic hypothesis is the voltammetric behavior of **7**: i.e., a variant of **5** in which the benzylic moiety is replaced with a second ferrocenyl group. The bielectronic reversible peak observed at $E_{1/2}$ = +0.43 V (Figure 2) is due to the two ferrocene groups and, since it does not present any splitting, the ferrocenyl groups are electronically independent. Also in this case, an intense adsorption peak is observed when the full oxidation of the molecule (i.e., also including the guanine-centered oxidation) is carried out. However, a scan-rate-dependent CV experiment carried out in the potential region of the ferrocene oxidation (Figure 3) clearly evidenced that adsorption does take place, in the present species, also following the ferrocene oxidation. Note the typical triangular shape of peaks as the scan rate increases, the small peak separation, and the linear dependence of peak current on scan rate (inset in Figure 3).

dx.doi.org/10.1021/om5002809 | Organometallics XXXX, XXX, XXX–XXX

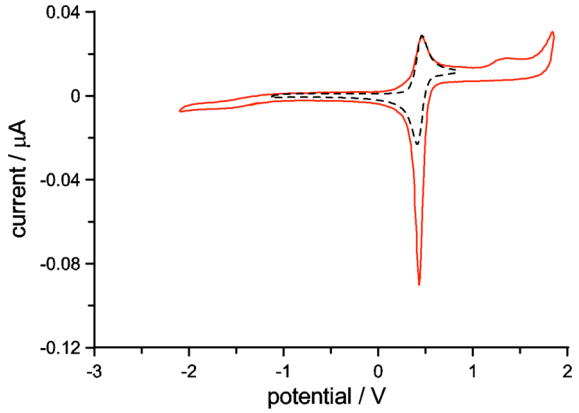


Figure 2. Cyclic voltammetric curves of compound **7** (0.8 mM) in 0.05 M TBAHFP/DCM solution: T = 298 K; v = 0.5 V s^{-1}, recorded with two different scan reversal potentials; working electrode Pt disk (d = 125 mm). Potentials are referenced to the SCE.

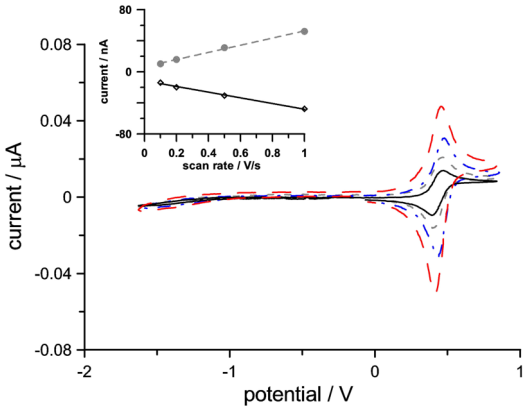


Figure 3. Cyclic voltammetric curves of compound **7** (0.8 mM) in 0.05 M TBAHFP/DCM solution: T = 298 K; v = 0.1 (solid line), 0.2 (short dashed line), 0.5 (dash-dotted line), 1 V s^{-1} (long dashed line); working electrode Pt disk (d = 125 μm) The insetgives peak currents as a function of scan rate. Potentials are referenced to the SCE.

In contrast with the above straightforward interpretation of the observed CV behavior was the cyclic voltammetric curve of Figure 4, relative to the guanosine ferrocenyl derivative **12**. The

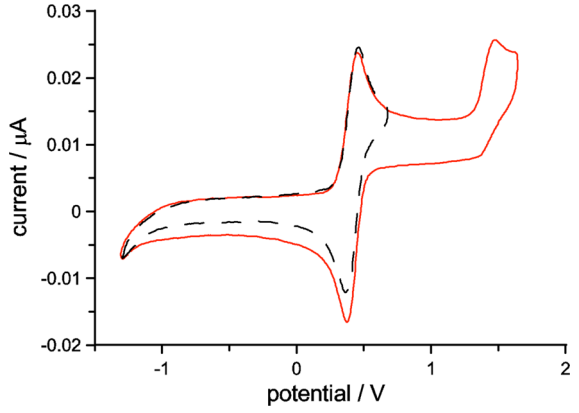


Figure 4. Cyclic voltammetric curves of compound **12** (0.8 mM) in 0.05 M TBAHFP/DCM solution: T = 298 K; v = 0.5 V s^{-1}, recorded with two different scan reversal potentials; working electrode Pt disk (d = 125 μm). Potentials are referenced to the SCE.

curve shows again the ferrocenyl oxidation process at +0.41 V and a peak at +1.41 V due to the guanosine moiety; however, no evidence of adsorption of the oxidized species is observed in this case. The presence of the sugar moiety, imparting an increased solubility to the charged species and thus preventing its precipitation, may in fact explain the observed behavior. However, in view of the known ability of guanosine and its derivatives to self-assemble into ordered structures, such as G-quartets or ribbons,[25] a possible steric effect associated with the position of the ferrocenyl group with respect to the guanine moiety and its role in the H-bonding ability of the guanine moieties cannot be ruled out.

To further investigate such an issue, compound **7**, previously investigated in DCM (Figure 2), was also investigated in DMSO, a solvent known for its ability to disrupt the H-bond network in proteins, DNA, and artificial supramolecular systems alike.[26] Interestingly, although not totally unexpectedly, in such a solvent the CV curve (Figure 5) displays no strong evidence

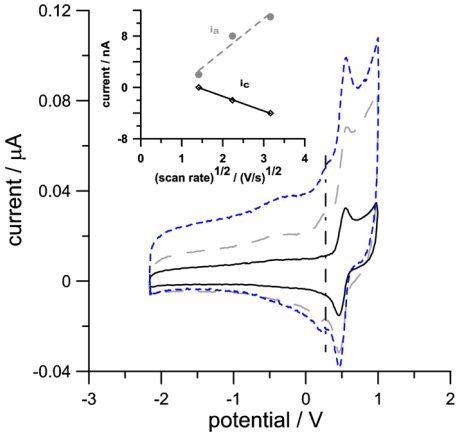


Figure 5. Cyclic voltammetric curves of compound **7** in 0.05 M TBAHFP/DMSO solution; T = 298 K; v = 0.2 (solid line), 0.5 (long dashed line), 10 V s^{-1} (short dashed line); working electrode Pt disk (d = 125 μm). The inset gives the scan rate dependence of the shoulder indicated by the dash-dotted line on the CV curves. Potentials are referenced to the SCE.

of adsorption at any rate. The scan-rate-dependent investigation evidenced in fact the typical diffusion-controlled two-electron reversible peak associated with ferrocene oxidation. The presence of a secondary species in solution, responsible for the reversible shoulder located at ~0.25 V, was also observed (dash-dotted vertical line in Figure 5). Such a low intensity peak is only observed at relatively high scan rates with a linear dependence on the square root of scan rate (see inset in Figure 5), thus excluding that it may be associated with an adsorbed species. A possible explanation of the observed behavior, that is in line with the known self-assembly behavior of guanosine, is that **7** may form, under the conditions of Figure 5, aggregates that are dynamically linked to the monomer (prevalent species).

The bis-ferrocenyl species **14**, in which the two ferrocenes are both located on the sugar moiety, was then investigated. The CV curve (Figure 6) displays in this case huge adsorption spikes that are observed after the full oxidation of the species (i.e., also including oxidation of the guanine unit) but also immediately after the two-electron oxidation of the two equivalent ferrocenes.

dx.doi.org/10.1021/om5002809 | *Organometallics* XXXX, XXX, XXX–XXX

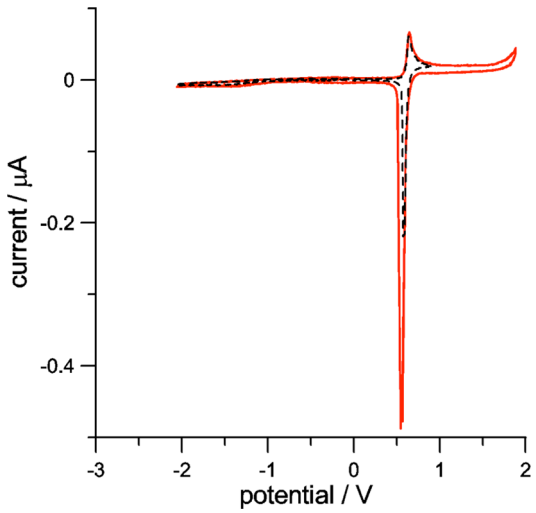


Figure 6. Cyclic voltammetric curves of compound **14** (0.8 mM) in 0.05 M TBAHFP/DCM solution: T = 298 K; ν = 0.5 V s^{-1}, recorded with two different scan reversal potentials; working electrode Pt disk (d = 125 μm). Potentials are referenced to the SCE.

Such a process is largely shifted to more positive potentials than for the previous species, as a consequence of the electron-withdrawing effect of the carboxylate substituents. However, the relative position of the two ferrocenes with respect to the guanine is assumed to be responsible for the different behaviors with respect to the previous bis-ferrocene **7**, since in this case the self-recognition of guanines and their aggregation via H bonding should be much less disturbed by the ferrocene moieties. Finally, the monoferrocene **18**, which also carries a long lipophilic chain on the sugar moiety, displayed a much more diffusion controlled reversible behavior likely associated with the increased solubility of the monomers and aggregates (Figure 7).

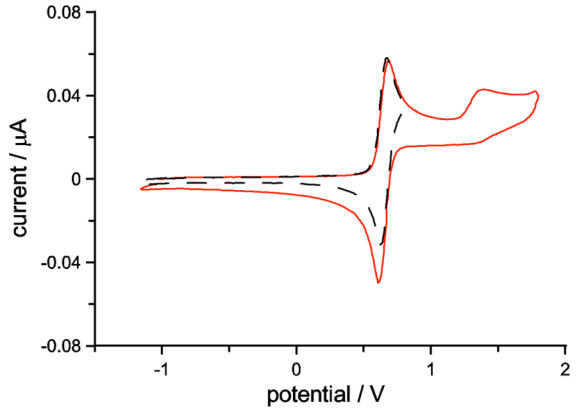


Figure 7. Cyclic voltammetric curves of compound **18** (0.8 mM) in 0.05 M TBAHFP/DCM solution: T = 298 K; ν = 0.5 V s^{-1}, recorded with two different scan reversal potentials; working electrode Pt disk (d = 125 μm). Potentials are referenced to SCE.

All potentials relative to oxidation of the ferrocene moieties in the investigated species are gathered in Table 1.

As already anticipated above, the potentials for the ferrocene-based oxidation in **14** and **18** are significantly higher than those in compounds **5** and **7**, an expected effect of the electron-withdrawing carboxyl linker groups.

Table 1. Electrochemical Properties[a]

	$E_{1/2}$ (V)	
compound	DMSO	DCM
5	0.53	0.49
7	0.51*	0.43*
12	0.48	0.41
14	0.75*	0.61*
18	0.73	0.65

[a] $E_{1/2}$ values for all investigated species in DMSO/TBAHFP and DCM/TBAHFP solutions. Working electrode: Pt disk (d = 125 μm), T = 298 K. Potentials are referenced to the SCE. The potentials marked with asterisks are associated with two-electron oxidations.

CONCLUSION

In conclusion, we have described the straightforward synthesis of new ferrocene guanine conjugates and we have reported their complete electrochemical characterization by cyclic voltammetry under ultradry conditions. The investigation highlighted a rather intriguing behavior where self-aggregation of the guanine derivatives, driven by H-bonding, and solubility effects associated with the increased charge induced electrochemically, bring about the formation of adsorbed layers onto the electrode surface. Such layers may be reversibly redissolved by reducing the oxidized ferrocenyl/guanine moieties, a process that takes place on the time scale of the CV experiments. Further studies about the ability of these compounds to form ordered supramolecular structures on solid supports are in progress in our laboratories and will be reported in due time.

EXPERIMENTAL SECTION

General Considerations. All reactions requiring anhydrous conditions were carried out in oven-dried glassware under a dry argon atmosphere. Macherey-Nagel Polygram silica gel plates (layer 0.20 mm) were used for TLC analyses. Column chromatography was performed on Geduran silica gel 60 (40−63 μm). Purification by preparative thin-layer chromatography was done on Merck TLC silica gel 60 F_{254}. Reagents and solvents, including dry solvents, were purchased from Aldrich or Alfa Aesar.

Instrumentation. NMR spectra were recorded on Varian (Inova 600 MHz, Mercury plus 400 MHz, Mercury 300 MHz, Gemini 200) spectrometers. Mass spectra were measured on an ESI spectrometer. LC-electrospray ionization mass spectra (ESI-MS) were obtained with an Agilent Technologies MSD1100 single-quadrupole mass spectrometer. Melting points were recorded on a Stuart SMP3 Scientific Melting Point Apparatus and were not corrected.

Chemical shifts are reported in ppm from TMS with the solvent resonance as the internal standard (deuterochloroform: δ 7.27 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, bs = broad signal, m = multiplet), coupling constants (Hz). Mass data are reported as m/z (relative intensity).

Electrochemistry. All materials were reagent grade chemicals. The supporting electrolyte tetrabutylammonium hexafluorophosphate (TBAHFP, from Fluka) was used as received. Ultradry dimethyl sulfoxide (DMSO) and dichloromethane (DCM) was chosen as solvents. The commercial solvents (DMSO, purum from Sigma-Aldrich; DCM, purum from Sigma-Aldrich) were first treated with basic alumina (from MP Biomedicals) in a flask for at least 48 h. Afterward, the solvent was distilled trap-to-trap into an especially designed Schlenk, containing activated 3 Å molecular sieves. It was stored in the same Schlenk, protected from light and kept under vacuum prior to use. The cell, containing the supporting electrolyte and the electroactive compound, was dried under vacuum at 370 K for at least 48 h. Afterward the solvent was distilled by a trap-to-trap procedure into the electrochemical cell just before performing the

dx.doi.org/10.1021/om5002809 | Organometallics XXXX, XXX, XXX−XXX

electrochemical experiment. The pressure measured in the electrochemical cell prior to performing the trap-to-trap distillation of the solvent was typically around 1×10^{-5} mbar.

The one-compartment electrochemical cell was of airtight design, with high-vacuum glass stopcocks fitted with either Teflon or Viton O-rings, to prevent contamination by grease. The connections to the high-vacuum line and to the Schlenk flask containing the solvent were made by spherical joints fitted with Viton O-rings. Also, the working electrode consisted of a Pt-disk ultramicroelectrode (with diameter of 125 μm), sealed in glass. The counter electrode consisted of a platinum spiral, and the quasi-reference electrode was a silver spiral. The quasi-reference electrode drift was negligible for the time required by a single experiment. Both the counter and reference electrodes were separated from the working electrode by 0.5 cm. Further details about the electrochemical cell are described elsewhere.[27] Potentials were measured with the decamethylferrocene standard and are always referenced to the SCE, which was also used as an internal standard for checking the electrochemical reversibility of a redox couple. Voltammograms were recorded with a homemade fast potentiostat controlled by an AMEL Model 568 function generator. Data acquisition was performed by a Nicolet Model 3091 digital oscilloscope interfaced to a PC.

9-(1′-Ferrocenylethyl)-2-*N*-benzylguanine (5). In a Schlenk tube under a nitrogen atmosphere were placed 9-(1′-ferrocenylethyl)-2-chloro-6-oxopurine (**4a**; 0.15 mmol, 58 mg), DMSO (500 μL), and benzylamine (0.9 mmol, 100 μL). The solution was stirred at 150 °C for 6 h until complete conversion was observed by TLC. Ethyl acetate (10 mL) was added, and an orange precipitate was formed. The solid was filtered and washed with DCM until a white solid was left: the yellow DCM solution was concentrated to give pure **5** as a yellow solid: yield 0.022 mmol, 10.3 mg, 15%; ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ 10.42−10.72 (bs, 1H), 7.75 (s, 1H), 7.37−7.46 (m, 4H), 7.29−7.35 (m, 1H), 6.91 (t, J = 4.8 Hz, 1H), 5.38 (q, J = 7.1 Hz, 1H), 4.51−4.66 m, 2H), 4.33−4.38 (m, 1H), 4.12−4.18 (bs, 6H), 4.09−4.12 (m, 1H), 4.06−4.08 (m, 1H), 1.82 (d, J = 7.1 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6, 25 °C) δ 157.2, 152.5, 150.5, 139.9, 136.0, 128.8 (2C), 127.8 (2C), 127.4, 117.1, 90.0, 69.0 (5C), 68.3, 67.9, 67.8, 67.7, 49.3, 44.5, 20.4; ESI-MS: m/z 454.1 $[M + H]^+$, 476.0 $[M + Na]^+$, 907.1 $[2M + H]^+$, 1835.4 $[4M + Na]^+$; decomposition at 190 °C. Anal. Calcd for $C_{24}H_{23}FeN_5O$: C, 63.59; H, 5.11; N, 15.45. Found: C, 63.69.; H, 5.19; N, 15.41.

2-*N*-(1″-Ferrocenylethyl)-9-(1′-ferrocenylpropyl)guanine (7). In a Schlenk tube under a nitrogen atmosphere were placed 9-(1′-ferrocenylpropyl)-2-chloro-6-oxopurine (**4b**; 0.75 mmol, 299 mg), DMSO (2.3 mL), and 1′-ferrocenylethylamine (**6**; 1.5 mmol, 346 mg). The solution was stirred at 150 °C for 11 h. The crude mixture was directly purified by column chromatography (eluting mixture 90/10/2 DCM/MeOH/NH_3) to give pure **7** as an orange solid in a 1.2/1.0 diastereomeric ratio determined by ^{1}H NMR (δ_{major} 7.85; δ_{minor} 7.83): yield 0.08 mmol, 42.0 mg, 11%; ^{1}H NMR (600 MHz, DMSO-d_6, 25 °C) δ_{major} 10.61 (s, 1H), 7.85 (s, 1H), 6.22 (d, J = 8.2 Hz, 1H), 5.14 (dd, J_1 = 11.0 Hz, J_2 = 4.3 Hz, 1H), 4.88−4.95 (m, 1H), 4.35−4.38 (m, 1H), 4.25−4.27 (m, 1H), 4.19−4.24 (m, 7H), 4.14−4.18 (m, 3H), 4.11−4.14 (m, 1H), 4.07 (s, 5H), 2.25−2.32 (m, 1H), 2.13−2.21 (m, 1H), 1.51 (d, J = 6.7 Hz, 3H), 0.76 (q, J = 9.0 Hz, 3H), δ_{minor} 10.57 (s, 1H), 7.83 (s, 1H), 6.21 (d, J = 8.2 Hz, 1H), 5.14 (dd, J_1 = 11.0 Hz, J_2 = 4.3 Hz, 1H), 4.88−4.95 (m, 1H), 4.35−4.38 (m, 1H), 4.28−4.30 (m, 1H), 4.19−4.24 (m, 8H), 4.14−4.18 (m, 2H), 4.11−4.14 (m, 1H), 4.06 (s, 5H), 2.25−2.32 (m, 1H), 2.13−2.21 (m, 1H), 1.49 (d, J = 6.7 Hz, 3H), 0.76 (q, J = 9.0 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6, 25 °C) δ_{major} 156.8, 151.2, 150.6, 136.3, 116.4, 91.5, 89.4, 68.4 (5C), 68.3 (5C), 67.6, 67.5, 67.3, 67.2, 67.0, 66.73, 66.70, 65.6, 55.3, 44.6, 27.5, 21.0, 11.1, δ_{minor} 156.8, 151.2, 150.6, 136.4, 116.3, 91.5, 89.6, 68.4 (5C), 68.3 (5C), 67.7, 67.5, 67.3, 67.2 (2C), 66.74, 66.6, 65.6, 55.1, 44.5, 27.5, 20.9, 11.1; ESI-MS: m/z 590.2 $[M + H]^+$, 612.3 $[M + Na]^+$; decomposition at 180 °C. Anal. Calcd for $C_{30}H_{31}Fe_2N_5O$: C, 61.14; H, 5.30; N, 11.88. Found: C, 61.22; H, 5.39; N, 11.79.

9-(1′-Ferrocenylethyl)guanine (10). In a Schlenk tube were placed 9-(1′-ferrocenylethyl)-2-*N*-Boc-6-chloropurine (**9**; 0.17 mmol, 80 mg), dioxane (1.5 mL), and 1 M aqueous NaOH (0.8 mmol, 800 μL). The solution was stirred at 80 °C for 8 h until complete conversion was observed by TLC. The dioxane was evaporated under reduced pressure, then aqueous saturated NH_4Cl was added until the pH was neutral. The aqueous mixture was extracted with DCM (5 mL × 3), and the collected organic layers were concentrated under reduced pressure. **10** was obtained as an orange solid after chromatographic purification (ethyl acetate until the byproduct was eluted, then 90/10/2 DCM/MeOH/NH_3): yield 0.084 mmol, 30.6 mg, 50%; ^{1}H NMR (400 MHz, DMSO-d_6, 25 °C) δ 10.56 (s, 1H), 7.70 (s, 1H), 6.48 (s, 2H), 5.36 (q, J = 7.1 Hz, 1H), 4.37−4.39 (m, 1H), 4.23−4.25 (m, 1H), 4.21−4.23 (m, 1H), 4.18−4.21 (bs, 6H), 1.82 (d, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6, 25 °C) δ 157.3, 153.9, 150.9, 136.3, 117.2, 90.5, 69.6 (5C), 69.0, 68.5, 68.2, 67.4, 49.5, 21.7; ESI-MS m/z 363.0 $[M]^+$, 364.1 $[M + H]^+$, 727.0 $[2M + H]^+$; decomposition at 230 °C. Anal. Calcd for $C_{17}H_{17}FeN_5O_6$: C, 56.22; H, 4.72; N, 19.28. Found: C, 56.30; H, 4.80; N, 19.14.

9-(1″-Ferrocenylethyl)-2′,3′,5′-tri-*O*-acetylguanosine (12). To a solution of 1-ferrocenylethanol (**1a**; 0.3 mmol, 69 mg) in DCM (2 mL) were added 2′,3′,5′-tri-*O*-acetylguanosine (**11**; 0.2 mmol, 82 mg) and $In(OTf)_3$ (0.04 mmol, 132 μL of a solution 0.3 M in CH_3CN). The mixture was stirred for 48 h at room temperature. Then the reaction was quenched with water (2 mL). The organic phase was separated, and the aqueous phase was extracted with DCM (3 mL × 2). The collected organic layers were concentrated under reduced pressure and purified by preparative TLC on silica (95/5 DCM/MeOH as eluting mixture) to give **12** as a yellow solid in a 1.1/1.0 (diastereomeric ratio determined by ^{1}H NMR: δ_{major} 5.67; δ_{minor} 5.62): yield 0.93 mmol, 58 mg, 47%; ^{1}H NMR (400 MHz, DMSO-d_6, 25 °C) δ_{major} 10.76 (s, 1H), 7.91 (s, 1H), 6.39 (d, J = 8.0 Hz, 1H), 6.11 (d, J = 4.0 Hz, 1H), 6.04 (dd, J_1 = J_2 = 6.0 Hz, 1H), 5.67 (dd, J_1 = J_2 = 6.0 Hz, 1H), 4.88−5.00 (m, 1H), 4.31−4.46 (m, 3H), 4.25 (s, 5H), 4.18−4.28 (m, 4H), 2.14 (s, 3H), 2.12 (s, 3H), 2.03 (s, 3H), 1.51 (d, J = 6.3 Hz, 3H), δ_{minor} 10.76 (s, 1H), 7.92 (s, 1H), 6.40 (d, J = 8.0 Hz, 1H), 6.11 (d, J = 4.0 Hz, 1H), 6.03 (dd, J_1 = J_2 = 6.0 Hz, 1H), 5.62 (dd, J_1 = J_2 = 6.0 Hz, 1H), 4.88−5.00 (m, 1H), 4.31−4.46 (m, 3H), 4.26 (s, 5H), 4.18−4.28 (m, 4H), 2.13 (s, 3H), 2.10 (s, 3H), 2.01 (s, 3H), 1.52 (d, J = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6, 25 °C) δ_{major} 169.86, 169.23, 169.18, 156.5, 151.69, 150.0, 137.0, 117.3, 91.1, 86.1, 78.4, 71.8, 69.7, 68.31 (5C), 67.5, 67.1, 66.4, 65.5, 62.9, 44.8, 20.9, 20.3, 20.17, 20.12, δ_{minor} 169.83, 169.28, 169.20, 156.5, 151.73, 150.1, 136.9 117.4, 91.2, 86.4, 78.5, 71.8, 69.7, 68.28 (5C), 67.5, 67.2, 66.5, 65.6, 62.8, 44.7, 21.1, 20.3, 20.19, 20.15; ESI-MS m/z 621.0 $[M]^+$, 622.2 $[M + H]^+$, 1243.1 $[2M + H]^+$; decomposition at 200 °C. Anal. Calcd for $C_{28}H_{31}FeN_5O_8$: C, 54.12; H, 5.03; N, 11.27. Found: C, 54.17; H, 5.11; N, 11.24.

2′-Deoxy-3′,5′-*O*-diferrocenoylguanosine (14). Ferrocenecarboxylic acid (194 mg, 0.84 mmol) and 2′-deoxyguanosine hydrate (**13**; 100 mg, 0.35 mmol) were dried over P_2O_5 in vacuo for 2 h at 60 °C. Ferrocenecarboxylic acid was dissolved in DMF (8 mL), DCC (294 mg, 1.43 mmol) was added, and the resulting solution was stirred under an argon atmosphere. After 30 min 2′-deoxyguanosine and DMAP (43 mg, 0.35 mmol) were added and the resulting solution was stirred for 4 h. The solvent was removed under reduced pressure, the crude product was dissolved in dichloromethane, and the solution was extracted with saturated $NaHCO_3$. The organic layer was dried over $MgSO_4$, and the residue was applied to a silica gel column packed with dichloromethane and eluted with a gradient of methanol in dichloromethane. The final product was eluted with a mixture of dichloromethane and methanol (95/5) and was obtained as a yellow solid: yield 214 mg, 83%; ^{1}H NMR (DMSO-d_6) δ 10.67 (bs, 1H, N^1H), 8.01 (s, 1H, H^8), 6.48 (bs, 2H, NH_2), 6.30 (dd, J = 7.2 Hz, J = 6.0 Hz, 1H, $H^{1'}$), 5,57 (m, J = 6.0 Hz, 1H, $H^{3'}$), 4,84 (bs, 2H, cp), 4.77 (bs, 2H, cp), 4.56 (bs, 2H, cp), 4.51 (bs, 2H, cp), 4.49 (m, 1H, $H^{5'}$), 4.42 (m, 2H, $H^{4'}$, $H^{5'}$), 4.30 (s, 5H, cp), 4.21 (s, 5H, cp), 3.08 (m, J = 14.4 Hz, J = 7.2 Hz, J = 6.0 Hz, 1H, $H^{2'}$), 2.63 (dd, J = 14.4 Hz, J = 6.0 Hz, 1H, $H^{2'}$); ^{13}C NMR (DMSO-d_6) δ 170.94 (FcCO), 170.70 (FcCO), 157.14 (C^6), 154.19 (C^2), 151.51 (C^4), 135.59 (C^8), 117.40 (C^5), 83.36 ($C^{1'}$), 82.07 ($C^{4'}$), 74.61 ($C^{3'}$), 72.18 (CH_{cp}), 72.01 (CH_{cp}), 70.59 (C_{cp}), 70.47 (C_{cp}), 70.40 (CH_{cp}), 70.35 (CH_{cp}), 70.18 (CH_{cp}), 70.07 (CH_{cp}), 64.03 ($C^{5'}$), 36.32 ($C^{2'}$); ESI-MS (positive

dx.doi.org/10.1021/om5002809 | Organometallics XXXX, XXX, XXX−XXX

mode, MeOH solution, *m/z*) 692.3 $[M + H]^+$, 714.2 $[M + Na]^+$. Anal. Calcd for $C_{32}H_{29}Fe_2N_5O_6$: C, 55.60; H, 4.23; N, 10.13. Found: C, 55.77; H, 4.22; N, 10.14.

2′-Deoxy-3′-*O*-decanoyl-5′-*O*-ferrocenoylguanosine (18). Ferrocenecarboxylic acid (135 mg, 0.58 mmol) and 2′-deoxy-3′-*O*-decanoylguanosine **17** (178 mg, 0.42 mmol) were dried over P_2O_5 in vacuo for 2 h at 60 °C. Ferrocenecarboxylic acid was dissolved in DMF (10 mL), DCC (207 mg, 1.00 mmol) was added, and the resulting solution was stirred under an argon atmosphere. After 30 min 2′-deoxy-3′-*O*-decanoylguanosine and DMAP (43 mg, 0.35 mmol) were added and the solution was stirred for 4 h. The solvent was then removed under reduced pressure, the crude product was dissolved in dichloromethane, and the solution was extracted with saturated $NaHCO_3$. The organic layer was dried over $MgSO_4$. The reaction mixture was applied to a silica gel column packed in dichloromethane and eluted with a gradient of methanol in dichloromethane. The final product was eluted with a mixture of dichloromethane and methanol (94/6), giving the product as a pale yellow solid: yield 83 mg, 31%; ^{1}H NMR (DMSO-d_6) δ 10.66 (bs, 1H, N^{1}H), 7.96 (s, 1H, H^8), 6.48 (bs, 2H, NH_2), 6.18 (dd, J = 9.0 Hz, J = 6.0 Hz, 1H, H$^{1'}$), 5.42 (m, J = 6.0 Hz, 1H, H$^{3'}$), 4.75 (bs, 2H, cp), 4.50 (bs, 2H, cp), 4.43 (dd, J = 11.4 Hz, J = 6.0 Hz, 1H, H$^{5'}$), 4.33 (dd, J = 11.4 Hz, J = 5.0 Hz, 1H, H$^{5'}$), 4.29 (m, 1H, H$^{4'}$), 4.19 (s, 5H, cp), 2.98 (m, 1H, H$^{2'}$), 2.51 (m, 1H, H$^{2'}$), 2.38 (t, J = 7.2 Hz, 2H, $COCH_2$), 1.56 (quint, J = 7.2 Hz, 2H, $COCH_2CH_2$), 1.24 (m, 12H, CH_2), 0.84 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (DMSO-d_6) δ 172.99 (CH_2CO), 170.91 (FcCO), 157.14 (C6), 154.23 (C2), 151.53 (C^4), 135.51 (C^8), 117.33 (C^5), 83.25 (C$^{1'}$), 82.04 (C$^{4'}$), 74.72 (C$^{3'}$), 72.02 (CH_{cp}), 70.58 (C_{cp}), 70.27 (CH_{cp}), 70.07 (CH_{cp}), 63.94 (C$^{5'}$), 36.25 (C$^{2'}$), 33.90 (CH_2CO), 31.72 (CH_2), 29.30 (CH_2), 29.16 (CH_2), 29.09 (CH_2), 28.87 (CH_2), 24.77 (CH_2), 22.54 (CH_2), 14.41 (CH_3); ESI-MS (positive mode, MeOH solution, *m/z*) 634.5 $[M + H]^+$, 657.2 $[M + Na]^+$. Anal. Calcd for $C_{31}H_{39}FeN_5O_6$: C, 58.77; H, 6.21; N, 11.05. Found: C, 58.92; H, 6.19; N, 11.06.

■ ASSOCIATED CONTENT

Supporting Information

Text and figures giving syntheses and NMR spectra for **3a−18** and cyclic voltammograms for select compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail for M.I.: matteo.iurlo@unibo.it.
*E-mail for S.M.: stefano.masiero@unibo.it.
*E-mail for P.C.: piergiorgio.cozzi@unibo.it.
*E-mail for F.P.: francesco.paolucci@unibo.it.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The TEC FP7 ICT-MolArNet project (318516) is fully acknowledged for the financial support of this research. Partial support from the PRIN (Rome) and University of Bologna is also acknowledged.

■ REFERENCES

(1) (a) Sloop, F. V.; Brown, G. M.; Sachleben, R. A.; Garrity, M. L.; Elbert, J. E.; Jacobson, K. B. *New J. Chem.* **1994**, *18*, 317−326. (b) Takenaka, S.; Uto, Y.; Kondo, H.; Ihara, T.; Takagi, M. *Anal. Biochem.* **1994**, *218*, 436−443. (c) Ihara, T.; Maruo, Y.; Takenaka, S.; Takagi, M. *Nucleic Acids Res.* **1996**, *24*, 4273−4281. (d) Uto, Y.; Kondo, H.; Abe, M.; Suzuki, T.; Takenaka, S. *Anal. Biochem.* **1997**, *250*, 122−124. (e) Ihara, T.; Maruo, Y.; Takenaka, S.; Takagi, M. *Nucleic Acids Res.* **1996**, *24*, 4273−4281. (f) Uto, Y.; Kondo, H.; Abe, M.; Suzuki, T.; Takenaka, S. *Anal. Biochem.* **1997**, *250*, 122−124.

(2) (a) Sivakova, S.; Rowan, S. J. *Chem. Soc. Rev.* **2005**, *34*, 9−21. (b) Davis, J. T. *Angew. Chem., Int. Ed.* **2004**, *43*, 668−698. (c) Krishnan-Ghosh, Y.; Liu, D.; Balasubramanian, S. *J. Am. Chem. Soc.* **2004**, *126*, 11009−11016.

(3) (a) van Staveren, D. R.; Metzler-Nolte, N. *Chem. Rev.* **2004**, *104*, 5931−5985. (b) Patwa, A. N.; Gupta, S.; Gonnade, R. G.; Kumar, V. A.; Bhadbhade, M. M.; Ganesh, K. N. *J. Org. Chem.* **2008**, *73*, 1508−1515. (c) Hocek, M.; Štěpnička, P.; Ludvík, J.; Císařová, I.; Votruba, I.; Řeha, D.; Hobza, P. *Chem. Eur. J.* **2004**, *10*, 2058−2066.

(4) Houlton, A.; Isaac, C. J.; Gibson, A. E.; Horrocks, B. R.; Clegg, W.; Elsegood, M. R. J. *J. Chem. Soc., Dalton Trans.* **1999**, 3229−3234.

(5) Kumar, J.; Purohit, C. S.; Verma, S. *Chem. Commun.* **2008**, 2526−2528.

(6) Fabre, B.; Ababou-Girard, S.; Singh, P.; Kumar, J.; Verma, S.; Bianco, A. *Electrochem. Commun.* **2010**, *12*, 831−834.

(7) Patwa, A. N.; Gupta, S.; Gonnade, R. G.; Kumar, V. A.; Bhadbhade, M. M.; Ganesh, K. N. *J. Org. Chem.* **2008**, *73*, 1508−1515.

(8) Maruccio, G.; Visconti, P.; Arima, V.; D'Amico, S.; Biasco, A.; D'Amone, E.; Cingolani, R.; Rinaldi, R.; Masiero, S.; Giorgi, T.; Gottarelli, G. *Nano Lett.* **2003**, *3*, 479−483.

(9) (a) Coutouli-Argyropoulou, E.; Tsitabani, M.; Petrantonaki, Ge.; Terzis, A.; Raptopoulou, C. *Org. Biomol. Chem.* **2003**, *1*, 1382−1388. (b) Anne, A.; Blanc, B.; Moiroux, J. *Bioconjugate Chem.* **2001**, *12*, 396−405. (c) Song, H.; Kraatz, H.-B. *Inorg. Chim. Acta* **2009**, *362*, 1355−1368.

(10) (a) Wang, J.; Cai, X.; Wang, J.; Jonsson, C. *Anal. Chem.* **1995**, *67*, 4065−4070. (b) Ihara, T.; Maruo, Y.; Takenaka, S.; Takagi, M. *Nucleic Acids Res.* **1996**, *24*, 4273−4280. (c) Korri-Youssoufi, H.; Garnier, F.; Srivastava, P.; Godillot, P.; Yassar, A. *J. Am. Chem. Soc.* **1997**, *119*, 7388−7389.

(11) (a) Boon, E. M.; Ceres, D. M.; Drummond, T. G.; Hill, M. G.; Barton, J. K. *Nat. Biotechnol.* **2000**, *18*, 1096−1100. (b) Yamashita, K.; Takagi, M.; Kondo, H.; Takenaka, S. *Anal. Biochem.* **2002**, *306*, 188−196. (c) Yamashita, K.; Takagi, A.; Takagi, M.; Kondo, H.; Ikeda, Y.; Takenaka, S. *Bioconjugate Chem.* **2002**, *13*, 1193−1199. (d) Wakai, J.; Takagi, A.; Nakayama, M.; Miya, T.; Miyahara, T.; Iwanaga, T.; Takenaka, S.; Ikeda, Y.; Amano, M. *Nucleic Acids Res.* **2004**, *32*, e141.

(12) (a) Brazill, S. A.; Kuhr, W. G. *Anal. Chem.* **2002**, *74*, 3421−3428. (b) Fan, C.; Plaxco, K. W.; Heeger, A. J. *Proc. Natl. Acad. Sci. U.S.A.* **2003**, *100*, 9134−9137. (c) Wang, J.; Li, J.; Baca, A. J.; Hu, J.; Zhou, F.; Yan, W.; Pang, D. W. *Anal. Chem.* **2003**, *75*, 3941−3945. (d) Wang, J.; Li, J.; Baca, A. J.; Hu, J.; Zhou, F.; Yan, W.; Pang, D. W. *Anal. Chem.* **2003**, *75*, 3941−3945. (e) Thorp, H. H. *Trends Biotechnol.* **2003**, *21*, 522−524.

(13) Mukumoto, K.; Nojimab, T.; Takenaka, S. *Tetrahedron* **2005**, *61*, 11705−11715.

(14) Wu, Z.-S.; Chen, C.-R.; Shen, G.-L.; Yu, R.-Q. *Biomaterials* **2008**, *29*, 2689−2696.

(15) Singh, P.; Ménard-Moyon, C.; Kumar, J.; Fabre, B.; Verma, S.; Bianco, A. *Carbon* **2012**, *50*, 3170−3177.

(16) Breugst, M.; Bautista, F. C.; Mayr, H. *Chem. Eur. J.* **2012**, *18*, 127−137 and references therein.

(17) (a) Zhilina, Z. V.; Gumenyuk, V. V.; Nekrasov, Y. S.; Babin, V. N.; Snegur, L. V.; Starikova, Z. A.; Yanovsky, A. L. *Russ. Chem. Bull.* **1998**, 1781−1784. See also: (b) Snegura, L. V.; Nekrasova, Y. S.; Sergeevab, N. S.; Zhilinaa, Z. V.; Gumenyuka, V. V.; Starikovaa, Z. A.; Simenela, A. A.; Morozovab, N. B.; Sviridganomet. Covab, I. K.; Babina, V. N. *Appl. Organomet. Chem.* **2008**, *22*, 139−147.

(18) (a) Vicennati, P.; Cozzi, P. G. *Eur. J. Org. Chem.* **2007**, 2248−2253. (b) Cozzi, P. G.; Zoli, L. *Green Chem.* **2007**, *9*, 1292−1295. (c) Arima, V.; Iurlo, M.; Zoli, L.; Kumar, S.; Piacenza, M.; Della Sala, F.; Matino, F.; Maruccio, G.; Rinaldi, R.; Paolucci, F.; Marcaccio, M.; Cozzi, P. G.; Bramanti, A. P. *Nanoscale* **2012**, *4*, 813−823.

(19) Dee Nord, L.; Dalley, K. N.; McKernan, P. A.; Robins, R. K. *J. Med. Chem.* **1987**, *30*, 1044−1054.

(20) Boyle, G. A.; Edlin, C. D.; Li, Y.; Liotta, D. C.; Morgans, G. L.; Musonda, C. C. *Org. Biomol. Chem.* **2012**, *10*, 1870−1876.

(21) Xu, Y.; Ikeda, R.; Sugiyama, I. *J. Am. Chem. Soc.* **2003**, *125*, 13519−13524.

(22) Fletcher, S.; Shahania, V. M.; Loughb, A. J.; Gunning, P. T. *Tetrahedron* **2010**, *66*, 4621−4632.
(23) du Plessis, M. *Synlett* **2013**, *24*, 2329−2330.
(24) Emer, E.; Sinisi, R.; Capdevila, M. G.; Petruzziello, D.; De Vincentiis, F.; Cozzi, P. G. *Eur. J. Org. Chem.* **2011**, 647−666.
(25) (a) Lena, S.; Masiero, S.; Pieraccini, S.; Spada, G. P. *Chem. Eur. J.* **2009**, *15*, 7792−7806. (b) Masiero, S.; Pieraccini, S.; Spada, G. P. The self-assembly of lipophilic guanosine derivatives. In *Molecular Self-Assembly: Advances and Applications*; Li, A. D., Ed.; Pan Stanford: Singapore, 2012; pp 93−122.
(26) Scarel, F.; Valenti, G.; Gaikwad, G.; Marcaccio, M.; Paolucci, F.; Mateo-Alonso, A. *Chem. Eur. J.* **2012**, *18*, 14063−14068.
(27) Marcaccio, M.; Paolucci, F.; Paradisi, C.; Carano, M.; Roffia, S.; Fontanesi, C.; Yellowlees, L. J.; Serroni, S.; Campagna, S.; Balzani, V. *J. Electroanal. Chem.* **2002**, *532*, 99−112.