Available online at www.sciencedirect.com
SCIENCE DIRECT
Journal of Organometallic Chemistry 691 (2006) 3909–3918
Journal of Organometallic Chemistry
www.elsevier.com/locate/jorganchem

Synthesis, structural characterization and electrochemical study of 1,1′-ferrocenylene labeled amino acids

Evdoxia Coutouli-Argyropoulou [a,*], Christos Sideris [a], George Kokkinidis [b]

[a] Laboratory of Organic Chemistry, Department of Chemistry, Aristotle University of Thessaloniki, Thessaloniki 54 124, Greece
[b] Laboratory of Physical Chemistry, Department of Chemistry, Aristotle University of Thessaloniki, Thessaloniki 54 124, Greece

Received 7 April 2006; received in revised form 23 May 2006; accepted 23 May 2006
Available online 7 June 2006

Abstract

Unsymmetrical 1,1′-disubstituted ferrocenes bearing an amino acid moiety and a conjugated electron density controlling substituent were synthesized conveniently starting from 1,1′-ferrocenedicarbaldehyde. The novel ferrocene amino acid derivatives were completely characterized from their MS, ^{1}H NMR and ^{13}C NMR spectra. Their electrochemical behavior was studied by cyclic voltammetry. Their formal redox potentials E_f were slightly influenced by the nature of the amino acid and mainly by the kind of the ethenyl substituent. Furthermore all the (*Z*)-isomers exhibited a slight anodic shift compared with the corresponding (*E*)-isomers.

Keywords: Amino acids; Usymmetrical disubstituted ferrocenes; Schiff bases; Wittig reactions; Biosensors

1. Introduction

Since its discovery in the early 1950s [1], ferrocene has attracted the attention of the scientists worldwide because of its numerous applications in chemical sensing, in asymmetric catalysis and in material science [2]. Due to their stability, convenient synthetic chemistry and tunable redox properties ferrocene and its derivatives are among the best candidates for the electroanalytical determination of biological analytes. As a result several methods have been developed for the attachment of ferrocene moiety to fundamental biomolecules as purine and pyrimidine bases, nucleic acids, amino acids and peptides [3–8]. Ferrocene-peptide bioconjugates are able to respond to the structural changes that will take place upon substrate binding to the peptide portion of the molecule [6]. Furthermore the ferrocene moiety can act as template to generate supramolecular assemblies with various degrees of inter and intramolecular bonding [7].

Thus conjugates of ferrocene with amino acids or peptides are of special interest and numerous *C*- and *N*-ferrocenyl substituted a-amino acids have been described [5–8]. In most cases monosubstituted or symmetrically 1,1′-disubstituted derivatives are referred. However, the synthesis of unsymmetrically 1,1′-disubstituted ferrocene amino acids can lead to improved multifunctional systems for both purposes of labeling and molecular recognition modeling [8]. Thus a different substituent at the other cyclopentadiene ring can induce an intermolecular interaction or a change in the electrochemical parameters. Applying ferrocene derivatives with different electrochemical parameters a four "color" DNA sequencing system has been successfully developed [9].

In connection with our former studies on ferrocenes and ferrocene labeling of organic biomolecules [10] we report in this paper the synthesis, the structural characterization and the electrochemical study of 1,1′-disubstituted ferrocenes bearing an amino acid moiety and a conjugated alkenyl substituent which can act as chromophore.

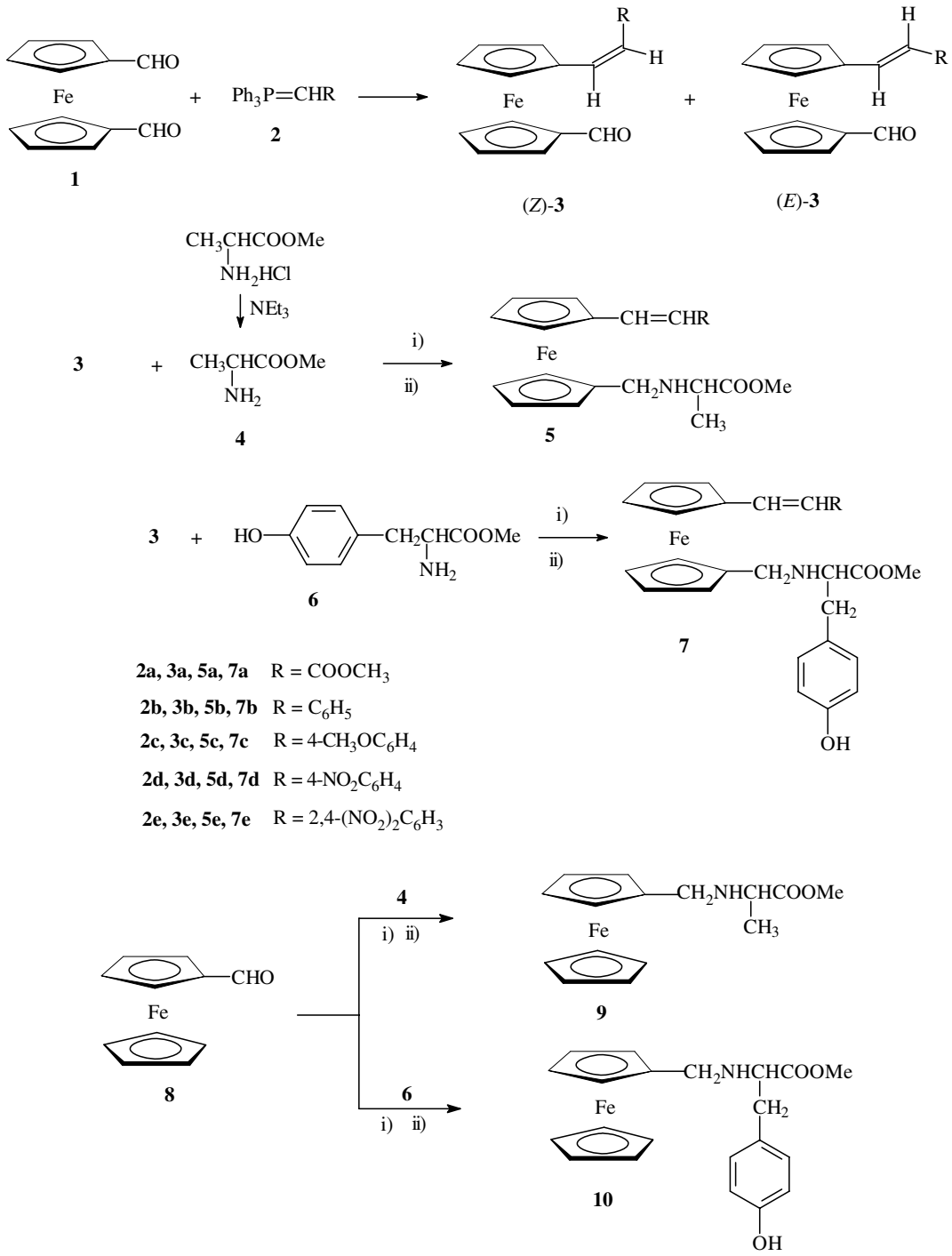
2. Results and discussion

The synthesis of the targeted compounds was made according to Scheme 1. 1,1′-Ferrocenedicarbaldehyde (**1**)

* Corresponding author. Tel.: +302310997733; fax: +302310997679.
E-mail address: evd@chem.auth.gr (E. Coutouli-Argyropoulou).

0022-328X/$ - see front matter © 2006 Elsevier B.V. All rights reserved.
doi:10.1016/j.jorganchem.2006.05.045

which was prepared directly from ferrocene by the previously described procedure [11] was used as starting material. Partial Wittig olefination of **1** with ylides **2** resulted alkenes **3**. The formation of bis adducts was avoided by using the aldehyde in excess (2:1). The ylides **2** were prepared by dehydrohalogenation of the corresponding phosphonium salts. The reactions with the stabilized ylides (**2a**, **2e**) were carried out after the isolation of the ylide in dichloromethane or benzene solution. In the reactions with the semistabilized ylides **2b**, **2c** and **2d** the formation of the ylide was made in situ under biphasic conditions in dichloromethane/aqueous NaOH solution or in benzene by butyllithium. The biphasic conditions proved to be better and gave exclusively mono adducts whereas in benzene substantial amounts of bis adducts were also formed. It should be mentioned that for the synthesis of analogous formylethenylferrocenes more complicated procedures including protection and deprotection steps of the formyl group have been referred [12]. Under the applied procedure these steps were avoided and the yields were satisfactory ranging



Scheme 1. Reagents and conditions: (i) CH_2Cl_2, MS 4 Å, r.t., 24 h; (ii) $NaBH_4$, 0 °C, 30 min.

between 50% and 90%. In all cases both (*Z*)- and (*E*)-stereoisomers were formed which were separated by column chromatography. The unreacted aldehyde **1** was also obtained from the column and introduced in the reaction circle again. The reaction conditions, the yields of the reactions and the ratio of (*Z*)- and (*E*)-isomers are given in Table 1.

The observed stereoselectivity of the Wittig reactions is in accordance with the known behavior of phosphorus ylides [13]. It is known that Wittig reactions of aldehydes with stabilized ylides as **2a**, **2e** lead stereoselectively to the preferential formation of (*E*)-alkenes, whereas reactions with semi-stabilized ylides as **2b**, **2c**, **2d** afford mixtures of (*Z*)-alkenes and (*E*)-alkenes. Furthermore we have previously found a slight increase in the proportion of (*E*)-isomer in the reactions of semi-stabilized ylides under biphasic conditions compared to that in organic media [13c]. This behavior is also observed in the reactions of the ylide **2c**.

The synthesis of the amino acid derivatives was accomplished by condensation of **3** with the amino acid esters **4** and **6** and subsequent reduction of the intermediate Schiff bases with $NaBH_4$. In all cases the amino derivatives were used in a slight excess and the condensation reaction was monitored by TLC until the disappearance of **3**. The intermediate Schiff bases were not isolated although their formation was evidenced from the TLC and confirmed by ^1H NMR in some cases. In the reduction step the use of $NaBH_4$ in equimolecular ratio permitted the preservation of all the other reductable groups as $COOCH_3$, NO_2. The expected derivatives **5** and **7** were obtained in satisfactory yields 50–93%. Following the same procedure and starting from ferrocene carboxaldehyde **8** the monosubstituted derivatives **9** and **10** were also prepared for comparison purposes.

The structure assignment of compounds **3**, **5** and **7** was made on the basis of their spectral data. In the mass spectra they give peaks corresponding to the molecular ion and in the ^1H NMR and ^{13}C NMR give the expected chemical shifts. The distinction between (*E*)- and (*Z*)-isomers was easily made in all cases on the basis of the olefinic protons coupling constant value ranging between 11.6–12.2 Hz for (*Z*)-isomers and 15.5–16.1 Hz for (*E*)-isomers. Compounds **3** exhibit four broad singlets at the range 4.03–4.84 corresponding to the *o*- and *m*-protons of the two cyclopentadiene rings. The more characteristic chemical shift is that of the *o*- to the formyl group protons which appears at the higher δ value 4.60–4.84 depending on the kind of the substituent. In the carbon NMR spectra there are also four peaks for the CH cyclopentadienyl carbons ranging between 69.7 and 74.5 and two peaks for the quaternary cyclopentadienyl carbons in the range 79.6–85.7. The most characteristic peak is also the most downfield shift of the carbons *o*- to the formyl group which appears in a narrow range 74.2–74.5. In compounds **5** and **7** all the chemical shifts in both the ^1H NMR and ^{13}C NMR are upfield shifted compared to that of compounds **3** due to the transformation of the electron withdrawing formyl group. Thus all the proton shifts appear in the range 4.06–4.50 and the carbon chemical shifts in the range 67.0–71.4. Also the presence of the chiral carbon center in the amino acid generates two non chemical equivalent diastereotopic sides of the molecule and both protons and carbons of the cyclopentadiene rings give more than four peaks as in the case of compounds **3**. The $FcCH_2$ hydrogens being also diastereotopic give different chemical shifts which in compounds **7** appear as two characteristic doublets in the range 3.26–3.47 with a large geminal coupling constant (12.8–13.3 Hz). Alanine derivatives give an easily distinguishable chemical shift for the NH proton in the range 1.75–2.02 ppm. Regarding tyrosine derivatives the chemical shifts of the labile NH and OH could not be assigned. This is probably due to a dynamic exchange between them resulting in large broadening. It should also be noted, that the chemical shifts of both the ferrocene and the olefinic moieties are almost invariant with respect to the amino acid substitution although two amino acids with considerable different electronic and neighboring group effects have been used.

Table 1
Reaction conditions, yields and ratio of the (*Z*)/(*E*)-isomers of the reactions of ylides **2** with aldehyde **1**

Product	Reaction conditions	Yield %	Ratio of (*Z*)/(*E*)
3a	CH_2Cl_2, r.t., 24 h	90	1/20
3b	In situ, $NaOH/CH_2Cl_2$, r.t., 24 h	84	2/1
3c	In situ, BuLi, THF, −78 °C	82	2/1
3c	In situ, $NaOH/CH_2Cl_2$, r.t., 24 h	70	1/2
3d	In situ, $NaOH/CH_2Cl_2$, r.t., 24 h	50	1.5 /1
3e	C_6H_6, 80 °C, 24 h	55	1/4

The electrochemical behavior of the prepared ferrocene derivatives was studied by cyclic voltammetry in CH_2Cl_2 solutions (0.001 M) containing Et_4NClO_4 (0.05 M) as supporting electrolyte at 27 °C. The measurements were made with five different potential scan rates in the region of 50–300 mV s^{-1}. In all cases quasi-reversible one-electron voltammograms were obtained. The i_p^C/i_p^A was almost equal to unity and the differences between the anodic and cathodic peak potentials ($\Delta E_p = E_p^A - E_p^C$) were in the range 140–250 mV depending on the potential scan rate. The cyclic voltammograms had a symmetrical shape and the mean value of the peak potentials $(E_p^A + E_p^C)/2$ was almost constant independently of the potential scan rate. Therefore, this value may be considered as the formal redox potential, E_f, for each compound. Calculated E_f potentials are given in Table 2.

As it is expected the replacement of the strong electron-withdrawing formyl group by the amino acid moiety causes a significant cathodic shift of about 200 mV for both the amino acids studied. A small differentiation of E_f values ranging between 10 and 30 mV is also observed between the two kinds of the amino acids. Thus, in all cases the E_f of tyrosine derivatives exhibits a cathodic shift compared to that of the corresponding alanine derivative.

Table 2
Formal redox potentials (E_f) of compounds **3**, **5**, **7**

Compound	E_f (V)	Compound	E_f (V)	Compound	E_f (V)
(*E*)-**3a**	1.10	(*E*)-**5a**	0.83	(*E*)-**7a**	0.81
(*Z*)-**3b**	1.02	(*Z*)-**5b**	0.74	(*Z*)-**7b**	0.73
(*E*)-**3b**	0.99	(*E*)-**5b**	0.73	(*E*)-**7b**	0.72
(*Z*)-**3c**	0.99	(*Z*)-**5c**	0.71	(*Z*)-**7c**	0.69
(*E*)-**3c**	0.96	(*E*)-**5c**	0.70	(*E*)-**7c**	0.68
(*Z*)-**3d**	1.06	(*Z*)-**5d**	0.79	(*Z*)-**7d**	0.76
(*E*)-**3d**	1.02	(*E*)-**5d**	0.77	(*E*)-**7d**	0.74
(*E*)-**3e**	1.08	(*E*)-**5a**	0.80	(*E*)-**7a**	0.78
8	0.99	**9**	0.73	**10**	0.70

Small shifts of 10 mV between different amino acids have been also observed in monosubstituted ferrocene amino acid conjugates and they have been considered too small to be analytically useful for the discrimination or different amino acids [5d]. However, in the disubstituted derivatives studied the potential changes caused by the conjugated alkenyl substituent are significantly larger covering a range of 130 mV for each kind of amino acid. Thus as expected for ferrocene derivatives [14] the value of E_f depends on the electron-donor or electron acceptor properties of the substituent the largest differences observed between the 4-methoxyphenyl (**3c**, **5c**, **7c**) and carboxymethyl (**3a**, **5a**, **7a**) derivatives. A remarkable and rather unexpected feature observed in all the arylethenyl derivatives studied, is that the (*Z*)-isomers exhibit an anodic shift of 10–30 mV in comparison to the corresponding (*E*)-isomers. This behavior cannot be rationalized on the basis of the conjugative effects of the substituents especially for electron acceptors as nitro substituent which are expected to be more effective in the less hindered planar conformation of (*E*)-isomers. A possible explanation is a through space interaction between the metal center and the aromatic ring which is possible in the (*Z*)-isomers as depicted in Fig. 1.

In conclusion, unsymmetrical 1,1′-disubstituted ferrocenes bearing an amino acid moiety and a conjugated ethenyl substituent were synthesized in good yields starting from 1,1′-ferrocenedicarbaldehyde by simple procedures avoiding intermediate protection and deprotection stages. The obtained derivatives showed the typical one electron reversible electrochemical behavior of the ferrocene moiety. The redox potential is slightly influenced by the kind of the amino acid and largely by the ethenyl substituent giving rise in a range of 130 mV for the formal redox potentials. By applying the described procedures further manipulation of the substituents can lead to compounds with larger electrochemical differentiation proper for analytical as well as other purposes.

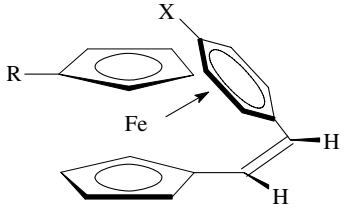


Fig. 1. Possible aromatic ring-metal interaction in (*Z*)-isomers.

3. Experimental

3.1. Materials and equipment

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. The IR spectra were obtained with a Perkin–Elmer Model 297 spectrometer. ^{1}H NMR spectra were recorded on a Bruker 300 AM spectrometer at 300 MHz and ^{13}C NMR spectra on the same spectrometer at 75.7 MHz, in deuteriochloroform solutions and are quoted relative to tetramethylsilane as internal standard. Mass spectra were determined on a VG-250 spectrometer with ionization energy maintained at 70 eV. High resolution mass spectra (HRESI) were obtained with a 7 T APEX II spectrometer. Microanalyses were performed on a Perkin–Ermer Model 2400-II analyser. Column chromatography was carried out on Merck Kieselgel (particle size 0.063–0.200).

The electrochemical experiments were performed in a three-electrode compartment cell. The working electrode was a Au rotating-disc electrode (EDI-Au from Tacussel), 2 mm in diameter. Before each experiment the electrode was activated by applying a continuous sweep ($v = 1$ V s^{-1}) between the potentials of hydrogen and just before oxygen evolution in 0.2 M $HClO_4$ until the cyclic voltammogram (at 0.1 V s^{-1}) obtained the known shape for Au. An aqueous $Hg|Hg_2SO_4|Na_2SO_4$ (sat) electrode (MSE), connected to the working electrode compartment by a Luggin capillary and a Pt sheet served as the reference and the counter electrode, respectively. The solutions were thoroughly deoxygenated by purging the cell system with ultrapure nitrogen. Electrode potentials are given on the standard hydrogen electrode (SHE) scale. The electronic set-up consisted of a Tacussel bipotentiostat (Bi/Pad), a function generator from Bank Electronics (VSG 72) and an HP 7046BX-Y_1, Y_2 recorder.

Ferrocenedicarbaldehyde (**1**) was prepared directly from ferrocene by the previously described procedure [11]. The ylides **2a** and **2e**, benzylltriphenylphosphonium chloride 4-methoxybenzylltriphenylphosphonium chloride and 4-nitrobenzylltriphenylphosphonium chloride, precursors of the ylides **2b**, **2c** and **2d**, respectively, were prepared according to previously reported procedures [12,15–18].

3.2. Wittig olefinations of 1,1′-ferrocenedicarbaldehyde (*1*)

The reaction of **1** with the stabilized ylide **2a** has been described by us elsewhere [10c]. For the reaction of **1** with **2e** a solution aldehyde **1** (2 mmoles) and the ylide **2e** (1 mmole) in dry benzene (10 ml) was heated to reflux for 24 h. Then the solvent was evaporated and the residue was chromatographed on a silica gel column with hexane–ethyl acetate (8:1) as the eluent.

The reactions with the semistabilized ylides **2b**, **2c** and **2d** were done according to the following procedures:

(I) Benzyltriphenylphosphonium chloride or 4-methoxybenzyltriphenylphosphonium chloride or 4-nitrobenzylltriphenylphosphonium chloride (1 mmole) and aldehyde **1** (2 mmoles) were dissolved in methylene chloride (5 ml) and the solution was stirred with an aqueous 10% NaOH solution (5 ml) at room temperature for 24 h. The two layers were separated and the aqueous layer was extracted with methylene chloride. The combined organic layers were extracted once with water, dried over sodium sulfate and concentrated. The residue was chromatographed on a silica gel column with hexane–ethyl acetate (10:1) as the eluent. In all cases it was possible to isolate from the column fractions with separated pure (*E*)- and (*Z*)-isomers with a small amount as mixture.

(II) To a stirred suspension of 4-methoxybenzyltriphenylphosphonium chloride (420 mg, 1 mmole) in dry benzene (5 ml) was added butyllithium (0.9 ml of 1.6 M solution in hexane, 1.5 mmoles) under argon atmosphere at −78 °C. The rapid change in the color was indicative of the ylide formation. After that, aldehyde **1** (484 mg, 2 mmoles) was added and the mixture was stirred for 4 h. Then the reaction mixture was diluted with water and extracted with ether. The organic layer was dried over sodium sulfate and concentrated. The residue was treated as in procedure I.

*3.2.1. 1-Formyl-1′-[(Z)-2-phenylethenyl]ferrocene [(Z)-**3b**]*

This compound was obtained as a red-brown oil in 56% yield; IR (neat, cm^{-1}): 1660 (CHO); ^1H NMR δ: 4.23 (s, 4H, Fc–H), 4.52 (s, 2H, Fc–H), 4.70 (s, 2H, Fc–H), 6.19 (d, $J = 11.9$ Hz, 1H, CH=CH), 6.55 (d, $J = 11.9$ Hz, 1H, CH=CH), 7.26 (m, 5H, Ph–H), 9.86 (s, 1H, CHO);^{13}C NMR δ: 70.0, 70.6, 70.7, 74.4, 80.0 and 83.6 (C–Fc), 126.2, 127, 128.2, 128.6, 129.4 and 137.7 (CH=CH and C–Ph), 193.4 (CHO); HRESIMS for $C_{19}H_{16}FeO$ $(M+H)^+$: calc., 317.0629; found, 317.0623. Anal. Calc. for $C_{19}H_{16}FeO$: C, 72.18; H, 5.10. Found: C, 72.11; H, 5.16%.

*3.2.2. 1-Formyl-1′-[(E)-2-phenylethenyl]ferrocene [(E)-**3b**]*

This compound was obtained as a red-brown oil in 28% yield; IR (neat, cm^{-1}): 1660 (C=O, CHO); ^1H NMR δ: 4.37 (s, 2H, Fc–H), 4.56 (s, 4H, Fc–H), 4.75 (s, 2H, Fc–H), 6.75 (s, 2H, CH=CH), 7.25–7.45 (m, 5H, Ph–H), 9.86 (s, 1H, CHO). ^{13}C NMR ($CDCl_3$) δ: 68.1, 70.4, 70.6, 74.4, 79.8 and 85.4 (C–Fc), 124.8, 126.0, 127.4, 128.1, 128.7 and 137.3 (CH=CH and C–Ph), 193.7 (CHO). MS, *m*/*z* (RI%): 316 (80, M^+). Anal. Calc. for $C_{19}H_{16}FeO$: C, 72.18; H, 5.10. Found: C, 72.21; H, 5.28%.

*3.2.3. 1-Formyl-1′-[(Z)-2-(4-methoxyphenyl)ethenyl] ferrocene [(Z)-**3c**]*

This compound was obtained as a red-brown oil in 55% yield; IR (neat, cm^{-1}): 1655 (C=O, CHO); ^1H NMR δ: 3.69 (s, 3H, OCH_3), 4.13 (br s, 2H, Fc–H), 4.17 (br s, 2H, Fc–H), 4.41 (br s, 2H, Fc–H), 4.60 (br s, 2H, Fc–H), 6.00 (d, $J = 12.2$ Hz, 1H, CH=CH), 6.38 (d, $J = 12.2$ Hz, 1H, CH=CH), 6.71 (d, $J = 8.7$ Hz, 2H, Ar–H), 7.11 (d, $J = 8.7$ Hz, 2H, Ar–H), 9.76 (s, 1H, CHO); ^{13}C NMR δ: 55.0 (OCH_3) 69.7, 70.5, 74.3, 79.8 and 83.9 (C–Fc), 113.4, 124.7, 128.8, 129.7 and 158.4 (CH=CH and C–Ar), 193.3 (CHO); MS, *m*/*z* (RI%): 346 (100, M^+). Anal. Calc. for $C_{20}H_{18}FeO_2$: C, 69.39; H, 5.24. Found: C, 69.16; H, 4.94%.

*3.2.4. 1-Formyl-1′-[(E)-2-(4-methoxyphenyl)ethenyl]ferrocene [(E)-**3c**]*

This compound was obtained as a red brown oil in 27% yield; IR (neat, cm^{-1}): 1655 (C=O, CHO); ^1H NMR δ: 3.71 (s, 3H, OCH_3), 4.24 (br s, 2H, Fc–H), 4.44 (m, 4H, Fc–H), 4.65 (br s, 2H, Fc–H), 6.50 (d, $J = 16.1$ Hz, 1H, CH=CH), 6.61 (d, $J = 16.1$ Hz, 1H, CH=CH), 6.79 (d, $J = 9.0$ Hz, 2H, Ar–H), 7.28 (d, $J = 9$ Hz, 2H, Ar–H), 9.80 (s, 1H, CHO); ^{13}C NMR δ: 55.2 (OCH_3) 67.8, 70.1, 70.4, 74.2, 79.6 and 85.7 (C–Fc), 114.1, 122.4, 127.1, 127.6, 130.0 and 159.0 (CH=CH and C–Ar), 193.7 (CHO); MS, *m*/*z* (RI%): 346 (100, M^+). Anal. Calc. for $C_{20}H_{18}FeO_2$: C, 69.39; H, 5.24. Found: C, 69.08; H, 5.06%.

*3.2.5. 1-Formyl-1′-[(Z)-2-(4-nitrophenyl)ethenyl]ferrocene [(Z)-**3d**]*

This compound was obtained as a dark-red oil in 30% yield; IR (neat, cm^{-1}): 1655 (C=O, CHO); ^1H NMR δ: 4.23 (br s, 2H, Fc–H), 4.31 (br s, 2H, Fc–H), 4.54 (br s, 2H, Fc–H), 4.73 (br s, 2H, Fc–H), 6.38 (d, $J = 11.6$ Hz, 1H, CH=CH), 6.54 (d, $J = 11.6$ Hz, 1H, CH=CH), 7.44 (d, $J = 8.7$ Hz, 2H, Ar–H), 8.13 (d, $J = 8.7$ Hz, 2H, Ar–H), 9.86 (s, 1H, CHO); ^{13}C NMR δ: 70.63, 70.72, 70.84, 74.31 80.21 and 82.4 (C–Fc), 123.6, 126.4, 126.8, 129.5, 129.8 and 144.6 (CH=CH and C–Ar), 193.2 (CHO); MS, *m*/*z* (RI%): 361 (100, M^+). Anal. Calc. for $C_{19}H_{15}FeNO_3$: C, 63.18; H, 4.19; N, 3.88. Found: C, 62.97; H, 4.05; N, 3.67%.

*3.2.6. 1-Formyl-1′-[(E)-2-(4-nitrophenyl)ethenyl]ferrocene [(E)-**3d**]*

This compound was obtained as a dark-red solid m.p. 163–165 °C, in 20% yield; IR (Nujol, cm^{-1}): 1655 (C=O, CHO); ^1H NMR δ: 4.45 (br s, 2H, Fc–H), 4.61 (m, 4H, Fc–H), 4.79 (br s, 2H, Fc–H), 6.75 (d, $J = 16.1$ Hz, 1H, CH=CH), 6.95 (d, $J = 16.1$ Hz, 1H, CH=CH), 7.55 (d, $J = 8.7$ Hz, 2H, Ar–H), 8.18 (d, $J = 8.7$ Hz, 2H, Ar–H), 9.89 (s, 1H, CHO); ^{13}C NMR δ: 68.71, 70.84, 71.20, 74.28, 80.03 and 83.6 (C–Fc), 123.6, 124.3, 125.7, 126.4, 130.6 and 143.8 (CH=CH and C–Ar), 193.5 (CHO); MS, *m*/*z* (RI%): 361 (93, M^+). Anal. Calc. for $C_{19}H_{15}FeNO_3$:

C, 63.18; H, 4.19; N, 3.88. Found: C, 63.11; H, 4.05; N, 3.64%.

3.2.7. 1-Formyl-1′-[(Z)-2-(2,4-dinitrophenyl)ethenyl]-ferrocene [(Z)-3e]

This compound was obtained as a dark-violet solid m.p. 102–104 °C, in 11% yield; IR (Nujol, cm^{-1}): 1665 (C=O, CHO); ^1H NMR δ: 4.03 (br s, 2H, Fc–H), 4.30 (br s, 2H, Fc–H), 4.53 (br s, 2H, Fc–H), 4.73 (br s, 2H, Fc–H), 6.52 (d, $J = 11.6$ Hz, 1H, CH=CH), 6.74 (d, $J = 11.6$ Hz, 1H, CH=CH), 7.60 (d, $J = 8.7$ Hz, 1H, Ar–H), 8.31 (d, $J = 8.7$ Hz, 1H, Ar–H), 8.92 (s, 1H, Ar–H), 9.87 (s, 1H, CHO); ^{13}C NMR δ: 70.53, 70.86, 71.1, 74.5, 80.1 and 80.7 (C–Fc), 120.3, 122.2, 126.9, 131.1, 133.6, 140.0, 146.6 and 148.0 (CH=CH and C–Ar), 193.3 (CHO); MS, *m/z* (RI%): 406 (90%, M^+). Anal. Calc. for $C_{19}H_{14}FeN_2O_5$: C, 56.18; H, 3.47; N, 6.90. Found: C, 56.14; H, 3.56; N, 7.18%.

3.2.8. 1-Formyl-1′-[(E)-2-(2,4-dinitrophenyl)ethenyl]-ferrocene [(E)-3e]

This compound was obtained as a dark-violet solid m.p. 200–202 °C, in 44% yield; IR (Nujol, cm^{-1}): 1665 (C=O, CHO);^1H NMR δ: 4.50 (br s, 2H, Fc–H), 4.61 (br s, 2H, Fc–H), 4.69 (br s, 2H, Fc–H), 4.84 (br s, 2H, Fc–H), 6.98 (d, $J = 15.5$ Hz, 1H, CH=CH), 7.23 (d, $J = 15.5$ Hz, 1H, CH=CH), 7.96 (d, $J = 8.6$ Hz, 1H Ar–H), 8.41 (d, $J = 8.6$ Hz, 1H, Ar–H), 8.80 (s, 1H, Ar–H), 9.91 (s, 1H, CHO); ^{13}C NMR δ: 69.3, 71.1, 71.9, 74.4, 80.2 and 82.5 (C–Fc), 120.5, 120.8, 127.2, 128.8, 136.3, 138.7, 145.9 and 146.7 (CH=CH and C-Ar), 193.7 (CHO); MS, *m/z* (RI%): 406 (93%, M^+). Anal. Calc. for $C_{19}H_{14}FeN_2O_5$: C, 56.18; H, 3.47; N, 6.90. Found: C, 56.55; H, 3.52; N, 6.59%.

3.3. General procedure for the Schiff base formation and reduction reactions

The aldehyde **3** or **8** (0.5 mmol) was dissolved in dry CH_2Cl_2 (5 ml) and to this solution there were added a small quantity of molecular sieves 4 Å and the amino acid ester **4** or **6** (0.6 mmol). In the case of **4** it was formed in situ from its hydrochloride salt by addition of a equimolecular amount of NEt_3. The reaction mixture was stirred at room temperature for 24 h and after that the consumption of the aldehyde was checked by ^1H NMR. Then the molecular sieves were removed by filtration and the solvent was evaporated. The residue was redissolved in methanol (5 ml), cooled to °C and treated with $NaBH_4$ (0.6 mmol). After stirring for 30 min at 0 °C saturated aqueous $NaHCO_3$ (10 ml) was added and the mixture was extracted with CH_2Cl_2 (3×10 ml). The combined organic phases were dried over Na_2SO_4 and after evaporation of the solvent the residue was chromatographed on a silica gel column with hexane:ethyl acetate (2.5:1) as eluent.

3.3.1. N-(1′-[(E)-2-(methoxycarbonyl)ethenyl]-1-ferrocenemethyl)-L-alanine methyl ester [(E)-5a]

This compound was obtained as a red-brown oil in 55% yield; IR (neat, cm^{-1}): 3330 (N–H), 1680–1725 (C=O, $COOCH_3$); ^1H NMR δ: 1.30 (d, $J = 6.4$ Hz, 3H, CH_3), 1.91 (br s, 1H, NH), 3.31–3.42 (m, 3H, FcCH_2NHC*H*), 3.74 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 4.11–4.19 (m, 4H, Fc–H), 4.39–4.47 (m, 4H, Fc–H), 6.03 (d, $J = 15.8$ Hz, 1H, CH=CH), 7.53 (d, $J = 15.8$ Hz, 1H, CH=CH); ^{13}C NMR δ: 19.0 (CH_3), 46.4 (FcCH_2), 51.3 (OCH_3), 51.7 (OCH_3), 56.1 (NHCH), 68.9, 69.1, 69.5, 69.9, 71.3, 78.9 and 87.5 (C–Fc), 114.6 and 145.5 (CH=CH), 167.4 (CO), 175.9 (CO). MS, *m/z* (RI%): 385 (54%, M^+). Anal. Calc. for $C_{19}H_{23}FeNO_4$: C, 59.24; H, 6.02; N, 3.64. Found: C, 59.30; H, 5.98; N, 3.70%.

3.3.2. N-(1′-[(Z)-2-phenylethenyl]-1-ferrocenemethyl)-L-alanine methyl ester [(Z)-5b]

This compound was obtained as a red-brown oil in 62% yield; IR (neat, cm^{-1}): 3310 (N–H), 1720 (C=O, $COOCH_3$); ^1H NMR δ: 1.27 (d, $J = 7.1$ Hz, 3H, CH_3), 2.02 (br s, 1H, NH), 3.32–3.44 (m, 3H, FcCH_2NHC*H*), 3.69 (s, 3H, OCH_3), 4.02–4.11 (m, 8H, Fc–H), 6.26 (d, $J = 11.9$ Hz, 1H, CH=CH), 6.44 (d, $J = 11.9$ Hz, 1H, CH=CH), 7.19–7.30 (m, 5H, Ph–H); ^{13}C NMR δ: 18.9 (CH_3), 46.5 (FcCH_2), 51.6 (OCH_3), 55.9 (NHCH), 68.9, 69.0, 69.1, 69.2, 69.6, 69.8, 81.6 and 86.5 (C–Fc), 126.5, 127.4, 127.7, 127.9, 128.6 and 138.0 (CH=CH and C–Ph), 175.9 (CO); MS, *m/z* (RI%): 403 (100%, M^+). Anal. Calc. for $C_{23}H_{25}FeNO_2$: C, 68.50; H, 6.25; N, 3.47. Found: C, 68.21; H, 6.30; N, 3.50%.

3.3.3. N-(1′-[(E)-2-phenylethenyl]-1-ferrocenemethyl)-L-alanine methyl ester [(E)-5b]

This compound was obtained as a red-brown oil in 52% yield; IR (neat, cm^{-1}): 3310 (N–H), 1720 (C=O, $COOCH_3$); ^1H NMR δ: 1.23 (d, $J = 7.1$ Hz, 3H, CH_3), 1.88 (br s, 1H, NH), 3.31–3.46 (m, 3H, FcCH_2NHC*H*), 3.67 (s, 3H, OCH_3), 4.08–4.26 (m, 4H, Fc–H), 4.27 (br s, 2H, Fc), 4.43 (br s, 2H, Fc), 6.70 (d, $J = 16.3$ Hz, 1H, CH=CH), 6.83 (d, $J = 16.3$ Hz, 1H, CH=CH), 7.19–7.29 (m, 5H, Ph–H); ^{13}C NMR δ: 19.0 (CH_3), 46.7 (FcCH_2), 51.6 (OCH_3), 56.0 (NHCH), 67.2, 67.3, 69.0, 69.1, 69.5, 69.6, 83.6 and 86.9 (C–Fc), 125.7, 126.3, 126.5, 126.8, 128.6 and 137.8 (CH=CH and C–Ph), 176.1 (CO); MS, *m/z* (RI%): 403 (100%, M^+). Anal. Calc. for $C_{23}H_{25}FeNO_2$: C, 68.50; H, 6.25; N, 3.47. Found: C, 68.35; H, 6.32; N, 3.33%.

3.3.4. N-(1′-[(Z)-2(4-methoxyphenyl)ethenyl]-1-ferrocenemethyl)-L-alanine methyl ester [(Z)-5c]

This compound was obtained as a red-brown oil in 86% yield; IR (neat, cm^{-1}): 3305 (N–H), 1720 (C=O, $COOCH_3$); ^1H NMR δ: 1.27 (m, 3H, CH_3), 1.99 (br s, 1H, NH), 3.31–3.48 (m, 3H, FcCH_2NHC*H*), 3.71 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 4.00–4.20 (m, 8H, Fc–H), 6.19 (d, $J = 12.2$ Hz, 1H, CH=CH), 6.39 (d, $J = 12.2$ Hz,

1H, CH=CH), 6.81 (d, $J = 9.0$ Hz, 2H, Ar–H), 7.25 (d, $J = 9.0$ Hz, 2H, Ar–H); ^{13}C NMR δ: 18.9 (CH_3), 46.6 (Fc*C*H_2), 51.7 (OCH_3), 55.2 (OCH_3), 56.0 (NHCH), 68.9, 69.1, 69.2, 69.4, 69.7, 69.8, 82.1 and 86.4 (C–Fc), 113.4, 126.4, 127.2, 129.9, 130.5, 158.3 (CH=CH and C–Ar), 176.0 (CO); MS, *m*/*z* (RI%): 433 (37%, M^+). Anal. Calc. for $C_{24}H_{27}FeNO_3$: C, 66.52; H, 6.28; N, 3.23. Found: C, 66.22; H, 5.99; N, 3.29%.

3.3.5. N-(1′-[(E)-2(4-methoxyphenyl)ethenyl]-1-ferrocenemethyl)-L-alanine methyl ester [(E)-**5c**]

This compound was obtained as a red-brown oil in 73% yield; IR (neat, cm^{-1}): 3305 (N–H), 1720 (C=O, $COOCH_3$); ^{1}H NMR δ: 1.26 (m, 3H, CH_3), 1.75 (br s, 1H, NH), 3.31–3.48 (m, 3H, FcCH_2NHC*H*), 3.68 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 4.00–4.20 (m, 8H, Fc–H), 6.69 (s, 2H, CH=CH), 6.82 (d, $J = 8.4$ Hz, 2H, Ar–H), 7.35 (d, $J = 9.0$ Hz, 2H, Ar–H); ^{13}C NMR δ: 19.0 (CH_3), 46.8 (Fc*C*H_2), 51.7 (OCH_3), 55.3 (OCH_3), 56.1 (NHCH), 67.0, 67.1, 68.8, 68.9, 69.1, 69.2, 69.5, 69.8, 84.1 and 86.8 (C–Fc), 114.1, 124.1, 125.9, 126.9, 127.2, 130.5, 158.7 (CH=CH and C–Ar), 176.1 (CO); MS, *m*/*z* (RI%): 433 (50%, M^+). Anal. Calc. for $C_{24}H_{27}FeNO_3$: C, 66.52; H, 6.28; N, 3.23. Found: C, 66.25; H, 6.48; N, 3.19%.

3.3.6. N-(1′-[(Z)-2(4-nitrophenyl)ethenyl]-1-ferrocenemethyl)-L-alanine methyl ester [(Z)-**5d**]

This compound was obtained as a dark-red oil in 50% yield; IR (neat, cm^{-1}): 3300 (N–H), 1720 (C=O, $COOCH_3$); ^{1}H NMR δ: 1.24 (d, $J = 7.1$ Hz, 3H, CH_3), 1.87 (br s, 1H, NH), 3.27–3.39 (m, 3H, FcCH_2NHC*H*), 3.67 (s, 3H, OCH_3), 4.03–4.10 (m, 6H, Fc–H), 4.18 (t, $J = 1.9$ Hz, 2H, Fc–H), 6.38 (d, $J = 11.9$ Hz, 1H, CH=CH), 6.45 (d, $J = 11.9$ Hz, 1H, CH=CH), 7.43 (d, $J = 8.7$ Hz, 2H, Ar–H), 8.07 (d, $J = 8.7$ Hz, 2H, Ar–H); ^{13}C NMR δ: 18.9 (CH_3), 46.4 (Fc*C*H_2), 51.6 (OCH_3), 55.9 (NHCH), 69.0, 69.2, 69.3, 69.4, 69.7, 69.9, 80.3 and 87.0 (C–Fc), 123.3, 124.7, 129.3, 131.7, 145.0 and 146.0 (CH=CH and C–Ar), 175.8 (CO); MS, *m*/*z* (RI%): 448 (39%, M^+). Anal. Calc. for $C_{23}H_{24}FeN_2O_4$: C, 61.62; H, 5.40; N, 6.25. Found: C, 61.47; H, 5.48; N, 6.27%.

3.3.7. N-(1′-[(E)-2(4-nitrophenyl)ethenyl]-1-ferrocenemethyl)-L-alanine methyl ester [(E)-**5d**]

This compound was obtained as a dark-red oil in 53% yield; IR (neat, cm^{-1}): 3300 (N–H), 1720 (C=O, $COOCH_3$); ^{1}H NMR δ: 1.23 (d, $J = 6.4$ Hz, 3H, CH_3), 1.84 (br s, 1H, NH), 3.32–3.45 (m, 3H, FcCH_2NHC*H*), 3.69 (s, 3H, OCH_3), 4.11–4.21 (m, 4H, Fc–H), 4.37 (br s, 2H, Fc–H), 4.50 (br s, 2H, Fc–H), 6.73 (d, $J = 16.7$ Hz, 1H, CH=CH), 7.06 (d, $J = 16.7$ Hz, 1H, CH=CH), 7.51 (d, $J = 8.7$ Hz, 2H, Ar–H), 8.16 (d, $J = 8.7$ Hz, 2H, Ar–H); ^{13}C NMR δ: 19.1 (CH_3), 46.7 (Fc*C*H_2), 51.7 (OCH_3), 56.1 (NHCH), 67.9, 68.0, 69.1, 69.2, 69.3, 69.5, 70.5, 82.0 and 87.5 (C–Fc), 123.6, 124.2, 125.9, 132.6, 144.3 and 146.0 (CH=CH and C–Ar), 176.1 (CO); MS, *m*/*z* (RI%): 448 (62%, M^+). Anal. Calc. for $C_{23}H_{24}FeN_2O_4$: C, 61.62; H, 5.40; N, 6.25. Found: C, 61.37; H, 5.44; N, 5.97%.

3.3.8. N-(1′-[(E)-2(2,4-dinitrophenyl)ethenyl]-1-ferrocenemethyl)-L-alanine methyl ester [(E)-**5e**]

This compound was obtained as a red oil in 55% yield; IR (neat, cm^{-1}): 3300 (N–H), 1720 (C=O, $COOCH_3$); ^{1}H NMR δ: 1.19 (d, $J = 6.4$ Hz, 3H, CH_3), 1.84 (br s, 1H, NH), 3.28–3.40 (m, 3H, FcCH_2NHC*H*), 3.64 (s, 3H, OCH_3), 4.11–4.21 (m, 4H, Fc–H), 4.39 (br s, 2H, Fc–H), 4.49 (br s, 2H, Fc–H), 7.11 (s, 2H, CH=CH), 7.84 (d, $J = 8.7$ Hz, 1H, Ar–H), 8.28 (d, $J = 8.7$ Hz, 1H, Ar–H), 8.69 (s, 1H, Ar–H); ^{13}C NMR δ: 19.0 (CH_3), 46.5 (Fc*C*H_2), 51.7 (OCH_3), 55.9 (NHCH), 68.6, 68.7, 69.4, 69.5, 69.6, 70.1, 71.4, 81.0 and 87.6 (C–Fc), 118.0, 120.9, 126.7, 127.9 138.6, 138.9 145.1 and 146.3 (CH=CH and C–Ar), 175.9 (CO); MS, *m*/*z* (RI%): 493 (59%, M^+). Anal. Calc. for $C_{23}H_{23}FeN_3O_6$: C, 56.00; H, 4.70; N, 8.52. Found: C, 55.94; H, 4.90; N, 8.31%.

3.3.9. N-(1′-[(E)-2-(methoxycarbonyl)ethenyl]-1-ferrocenemethyl)-L-tyrosine methyl ester [(E)-**7a**]

This compound was obtained as an orange solid m.p. 108–110 °C, in 93% yield; IR (Nujol, cm^{-1}): 3280–3400 (N–H, O–H), 1680-1725 (C=O, $COOCH_3$); ^{1}H NMR δ: 2.90 (m, 2H, ArCH_2), 3.26 (d, $J = 12.9$ Hz, 1H, FcCH_2), 3.38 (d, $J = 12.9$ Hz, 1H, FcCH_2), 3.54 (t, $J = 6.8$ Hz, 1H, NHC*H*), 3.66 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 4.04–4.09 (m, 4H, Fc–H), 4.29–4.37 (m, 4H, Fc–H), 5.99 (d, $J = 15.7$ Hz, 1H, CH=CH), 6.73 (d, $J = 8.4$ Hz, 2H, Ar–H), 6.99 (d, $J = 8.4$ Hz, 2H, Ar–H), 7.51(d, $J = 15.7$ Hz, 1H, CH=CH); ^{13}C NMR δ: 38.6 (Ar*C*H_2), 46.5 (Fc*C*H_2), 51.5 (OCH_3), 51.7 (OCH_3), 62.2 (NHCH), 68.9, 69.1, 69.3, 69.6, 69.8, 71.5, 78.7 and 87.2 (C–Fc), 114.4, 115.6, 128.2, 130.3, 146.0 $\kappa\alpha\iota$ 155.3 (CH=CH and C–Ar), 167.9 and 174.8 (CO); MS, *m*/*z* (RI%): 493 (13%, M^+). Anal. Calc. for $C_{25}H_{27}FeNO_5$: C, 62.91; H, 5.70; N, 2.93. Found: C, 62.87; H, 5.47; N, 2.70%.

3.3.10. N-(1′-[(Z)-2-phenylethenyl]-1-ferrocenemethyl)-L-tyrosine methyl ester [(Z)-**7b**]

This compound was obtained as a red-brown oil, in 78% yield; IR (neat, cm^{-1}): 3280–3400 (N–H, O–H), 1725 (C=O, $COOCH_3$); ^{1}H NMR δ: 2.87 (d, $J = 6.4$ Hz, 2H, ArCH_2), 3.31 (d, $J = 12.9$ Hz, 1H, FcCH_2), 3.47 (d, $J = 12.9$ Hz, 1H, FcCH_2), 3.53 (t, $J = 6.4$ Hz, 1H, NHC*H*), 3.63 (s, 3H, OCH_3), 4.01–4.03 (m, 8H, Fc–H), 6.21 (d, $J = 12.2$ Hz, 1H, CH=CH), 6.42 (d, $J = 12.2$ Hz, 1H, CH=CH), 6.67 (d, $J = 8.4$ Hz, 2H, Ar–H), 6.97 (d, $J = 8.4$ Hz, 2H, Ar–H), 7.19–7.29 (m, 5H, Ph–H); ^{13}C NMR δ: 38.7 (Ar*C*H_2), 46.8 (Fc*C*H_2), 51.7 (OCH_3), 62.4 (NHCH), 69.1, 69.3, 69.6, 69.9 and 86.4 (C–Fc), 115.4, 126.7, 127.5, 127.8, 128.1, 128.7, 128.8, 130.3, 138.3 and 154.7 (CH=CH, C–Ph and C–Ar), 174.9 (CO); MS, *m*/*z* (RI%): 495 (15%, M^+). Anal. Calc. for $C_{29}H_{29}FeNO_3$: C, 70.31; H, 5.90; N, 2.83. Found: C, 70.05; H, 6.04; N, 2.75%.

3.3.11. N-(1′-[(E)-2-phenylethenyl]-1-ferrocenemethyl)-L-tyrosine methyl ester [(E)-7b]

This compound was obtained as a red-brown oil in 75% yield; IR (neat, cm^{-1}): 3280–3400 (N–H, O–H), 1725 (C=O, $COOCH_3$); ^1H NMR δ: 2.88 (d, $J = 6.4$ Hz, 2H, $ArCH_2$), 3.38 (d, $J = 12.7$ Hz, 1H, $FcCH_2$), 3.49 (d, $J = 12.7$ Hz, 1H, $FcCH_2$), 3.54 (t, $J = 6.4$ Hz, 1H, NHCH), 3.61 (s, 3H, OCH_3), 4.01–4.16 (m, 5H, Fc–H), 4.19 (t, $J = 1.6$ Hz, 1H, Fc–H), 4.35–4.39 (m, 2H, Fc–H), 6.67 (d, $J = 8.4$ Hz, 2H, Ar–H), 6.70 ($J = 16.2$ Hz, 1H, CH=CH), 6.79 (d, $J = 16.2$ Hz, 1H, CH=CH), 6.96 (d, $J = 8.4$ Hz, 2H, Ar–H), 7.19–7.33 (m, 3H, Ph–H), 7.42 (d, $J = 7.0$ Hz, 2H, Ph–H); ^{13}C NMR δ: 38.3 ($ArCH_2$), 46.9 ($FcCH_2$), 51.7 (OCH_3), 61.1 (NHCH), 67.3, 67.4, 69.1, 69.3, 69.4, 69.5, 69.8, 69.9 83.7 and 85.5 (C–Fc), 115.5, 125.8, 126.4, 126.9, 128.5, 128.7, 130.3, 137.8 and 154.7 (CH=CH, C–Ph and C–Ar), 174.2 (CO); MS, *m/z* (RI%): 495 (15%, M^+). Anal. Calc. for $C_{29}H_{29}FeNO_3$: C, 70.31; H, 5.90; N, 2.83. Found: C, 70.11; H, 6.03; N, 2.60%.

3.3.12. N-(1′-[(Z)-2(4-methoxyphenyl)ethenyl]-1-ferrocenemethyl)-L-tyrosine methyl ester [(Z)-7c]

This compound was obtained as a red-brown oil in 76% yield; IR (neat, cm^{-1}): 3280–3400 (N–H, O–H), 1725 (C=O, $COOCH_3$); ^1H NMR δ: 2.88 (d, $J = 6.5$ Hz, 2H, $ArCH_2$), 3.30 (d, $J = 13.4$ Hz, 1H, $FcCH_2$), 3.42 (d, $J = 13.4$ Hz, 1H, $FcCH_2$), 3.53 (t, $J = 6.5$ Hz, 1H, NHCH), 3.65 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 4.02 and 4.09 (m, 8H, Fc–H), 6.15 (d, $J = 12.2$ Hz, 1H, CH=CH), 6.37 (d, $J = 12.2$ Hz, 1H, CH=CH), 6.68 (d, $J = 8.3$ Hz, 2H, Ar–H), 6.81 (d, $J = 9$ Hz, 2H, Ar–H), 7.00 (d, $J = 8.3$ Hz, 2H, Ar–H), 7.24 (d, $J = 9$ Hz, 2H, Ar–H); ^{13}C NMR δ: 38.5 ($ArCH_2$), 46.8 ($FcCH_2$), 51.6 (OCH_3), 55.3 (OCH_3), 62.4 (NHCH), 67.0, 67.1, 69.1, 69.3, 69.7, 84.2 and 86.3 (C–Fc), 114.1, 115.4, 124.1, 125.9, 126.9, 129.9, 130.2, 130.7, 154.9 and 158.7 (CH=CH and C–Ar), 174.9 (CO); HRESIMS for $C_{30}H_{31}FeNO_4$ $(M+H)^+$: Calc., 526.1681; found, 526.1675.

3.3.13. N-(1′-[(E)-2(4-methoxyphenyl)ethenyl]-1-ferrocenemethyl)-L-tyrosine methyl ester [(E)-7c]

This compound was obtained as a red-brown oil in 70% yield; IR (neat, cm^{-1}): 3280–3400 (N–H, O–H), 1725 (C=O, $COOCH_3$); ^1H NMR δ: 2.84 (d, $J = 6.7$ Hz, 2H, $ArCH_2$), 3.34 (d, $J = 12.8$ Hz, 1H, $FcCH_2$), 3.45 (d, $J = 12.8$ Hz, 1H, $FcCH_2$), 3.52 (t, $J = 6.4$ Hz, 1H, NHCH), 3.60 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 3.99–4.19 (m, 6H, Fc–H), 4.33 (d, $J = 4.2$ Hz, 2H, Fc–H), 6.62 (s, 2H, 1H, CH=CH), 6.67 (d, $J = 7.9$ Hz, 2H, Ar–H), 6.85 (d, $J = 8.6$ Hz, 2H, Ar–H), 6.93 (d, $J = 7.9$ Hz, 2H, Ar–H), 7.34 (d, $J = 8.6$ Hz, 2H, Ar–H); ^{13}C NMR δ: 38.7 ($ArCH_2$), 46.7 ($FcCH_2$), 51.6 (OCH_3), 55.3 (OCH_3), 62.4 (NHCH), 68.2, 69.1, 69.2, 69.3, 69.5, 69.7, 69.8, 82.0 and 86.5 (C–Fc), 113.5, 115.3, 126.5, 127.2, 129.1, 130.0, 130.3, 130.6, 154.6 and 158.3 (CH=CH and C–Ar), 174.9 (CO); HRESIMS for $C_{30}H_{31}FeNO_4$ $(M+H)^+$: calc., 526.1681; found, 526.1675. Anal. Calc. for $C_{30}H_{31}FeNO_4$: C, 68.58; H, 5.95; N, 2.67. Found: C, 68.41; H, 6.18; N, 2.82%.

3.3.14. N-(1′-[(Z)-2(4-nitrophenyl)ethenyl]-1-ferrocenemethyl)-L-tyrosine methyl ester [(Z)-7d]

This compound was obtained as a dark-red glassy oil in 91% yield; IR (Nujol, cm^{-1}): 3250–3400 (N–H, O–H), 1715 (C=O, $COOCH_3$); ^1H NMR δ: 2.87 (d, $J = 6.4$, 2H, $ArCH_2$), 3.31 (d, $J = 12.9$ Hz, 1H, $FcCH_2$), 3.42 (d, $J = 12.9$ Hz, 1H, $FcCH_2$), 3.53 (t, $J = 6.4$ Hz, 1H, NHCH), 3.64 (s, 3H, OCH_3), 4.01–4.12 (m, 8H, Fc–H), 6.39 (s, 2H, CH=CH), 6.66 (d, $J = 7.4$ Hz, 2H, Ar–H), 6.94 (d, $J = 7.4$ Hz, 2H, Ar–H), 7.43 (d, $J = 8.4$ Hz, 2H, Ar–H), 8.09 (d, $J = 8.4$ Hz, 2H, Ar–H); ^{13}C NMR δ: 38.5 ($ArCH_2$), 46.6 ($FcCH_2$), 51.7 (OCH_3), 62.1 (NHCH), 69.2, 69.4, 69.8, 69.9, 70.0, 80.4 and 86.3 (C–Fc), 115.5, 123.4, 124.8, 128.0, 129.3, 130.2, 131.7, 145.1, 146.1 and 155.1 (CH=CH and C–Ar), 174.7 (CO); HRESIMS for $C_{29}H_{28}FeN_2O_5$ $(M+H)^+$: calc., 541.1426; found, 541.1420. Anal. Calc. for $C_{29}H_{28}FeN_2O_5$: C, 64.46; H, 5.22; N, 5.18. Found: C, 64.17; H, 5.47; N, 5.14%.

3.3.15. N-(1′-[(E)-2(4-nitrophenyl)ethenyl]-1-ferrocenemethyl)-L-tyrosine methyl ester [(E)-7d]

This compound was obtained as a dark-red solid m.p. 76–78 °C, in 93% yield; IR (Nujol, cm^{-1}): 3250–3400 (N–H, O–H), 1710 (C=O, $COOCH_3$);^1H NMR δ: 2.84 (d, $J = 6.4$, 2H, $ArCH_2$), 3.31 (d, $J = 12.9$ Hz, 1H, $FcCH_2$), 3.43 (d, $J = 12.9$ Hz, 1H, $FcCH_2$), 3.51 (t, $J = 6.4$ Hz, 1H, NHCH), 3.62 (s, 3H, OCH_3), 4.08–4.42 (m, 8H, Fc–H), 6.65 (d, $J = 8.4$ Hz, 2H, Ar–H), 6.69 (d, $J = 16.1$ Hz, 1H, CH=CH), 6.93 (d, $J = 8.4$ Hz, 2H, Ar–H), 7.01 (d, $J = 16.1$ Hz, 1H, CH=CH), 7.49 (d, $J = 8.4$ Hz, 2H, Ar–H), 8.14 (d, $J = 8.4$ Hz, 2H, Ar–H); ^{13}C NMR δ: 38.5 ($ArCH_2$), 46.6 ($FcCH_2$), 51.7 (OCH_3), 62.1 (NHCH), 67.8, 67.9, 69.3, 69.9, 70.4, 82.0 and 86.7 (C–Fc), 115.5, 123.6, 124.1, 125.9, 128.1, 130.2, 132.5, 144.3, 145.9 and 155.0 (CH=CH and C–Ar), 174.8 (CO); HRESIMS for $C_{29}H_{28}FeN_2O_5$ $(M+H)^+$: calc., 541.1426; found, 541.1415. Anal. Calc. for $C_{29}H_{28}FeN_2O_5$: C, 64.46; H, 5.22; N, 5.18. Found: C, 64.42; H, 5.43; N, 5.01%.

3.3.16. N-(1′-[(E)-2(2,4-dinitrophenyl)ethenyl]-1-ferrocenemethyl)-L-tyrosine methyl ester [(E)-7e]

This compound was obtained as a dark-violet solid m.p. 48–50 °C, in 68% yield; IR (Nujol, cm^{-1}): 3250–3400 (N–H, O–H), 1715 (C=O, $COOCH_3$); ^1H NMR δ: 2.87 (d, $J = 5.8$, 2H, $ArCH_2$), 3.29 (d, $J = 12.8$ Hz, 1H, $FcCH_2$), 3.43 (d, $J = 12.8$ Hz, 1H, $FcCH_2$), 3.52 (t, $J = 5.8$ Hz, 1H, NHCH), 3.66 (s, 3H, OCH_3), 4.13–4.17 (m, 4H, Fc–H), 4.38–4.49 (m, 4H, Fc–H), 6.73 (d, $J = 6.9$ Hz, 2H, Ar–H), 7.01 (d, $J = 6.9$ Hz, 2H, Ar–H), 7.11 (s, 2H, CH=CH), 7.87 (d, $J = 7.2$ Hz, IH, Ar–H), 8.33 (d, $J = 7.2$ Hz, 1H, Ar–H), 8.76 (s, 1H, Ar–H); ^{13}C NMR δ: 38.7 ($ArCH_2$), 46.6 ($FcCH_2$), 51.7 (OCH_3), 62.3 (NHCH),

68.6, 68.8, 69.3, 69.5, 70.0, 71.4, 81.0 and 88.0 (C–Fc), 115.3, 118.1, 120.9, 126.8, 128.0, 129.1, 130.4, 138.7, 138.9, 145.2, 146.4 and 154.6 (CH=CH and C–Ar), 174.9 (CO); HRESIMS for $C_{29}H_{27}FeN_3O_7$ $(M+H)^+$: calc., 586.1277; found, 586.1267.

3.3.17. N-ferrocenemethyl-L-alanine methyl ester (**9**)

This compound was obtained as a red-brown oil in 53% yield; IR (neat, cm^{-1}): 3310 (N–H), 1720 (C=O, $COOCH_3$);^{1}H NMR δ: 1.29 (d, $J = 7.1$ Hz, 3H, CH_3), 1.96 (br s, 1H, NH), 3.37–3.49 (m, 3H, $FcCH_2NHCH$), 3.71 (s, 3H, OCH_3), 4.08–4.20 (m, 9H, Fc–H); ^{13}C NMR δ: 18.9 (CH_3), 46.7 ($FcCH_2$), 51.5 (OCH_3), 55.8 (NHCH), 67.5, 67.7, 68.2 and 86.1 (C–Fc), 175.9 (CO); MS, *m*/*z* (RI%): 301 (87%, M^+). Anal. Calc. for $C_{15}H_{19}FeNO_2$: C, 59.82; H, 6.36; N, 4.65. Found: C, 59.71; H, 6.56; N, 4.42%.

3.3.18. N-ferrocenemethyl-L-tyrosine methyl ester (**10**)

This compound was obtained as an orange solid m.p. 108–110 °C, in 74% yield; IR (Nujol, cm^{-1}): 3260–3400 (N–H, O–H), 1710 (C=O, $COOCH_3$); ^{1}H NMR δ: 2.92 (s, 2H, $ArCH_2$), 3.36–3.81 (m, 6H, $FcCH_2NHCH$ and OCH_3), 4.05–4.35 (m, 9H, Fc–H), 6.69 (d, $J = 6.4$ Hz, 2H, Ar–H), 6.98 (d, $J = 6.4$ Hz, 2H, Ar–H); ^{13}C NMR δ: 38.5 ($ArCH_2$), 47.0 ($FcCH_2$), 51.7 (OCH_3), 62.2 (NHCH), 67.8, 67.9, 68.4 and 85.7 (C–Fc), 115.6, 128.1, 130.2 and 155.0 (C–Ar), 174.8 (CO); MS, *m*/*z* (RI%): 393 (60%, M^+). Anal. Calc. for $C_{21}H_{23}FeNO_3$: C, 64.14; H, 5.89; N, 3.56. Found: C, 63.97; H, 5.61; N, 3.27%.

References

[1] (a) T.J. Kealy, P.L. Pauson, Nature 168 (1951) 1039;
(b) G. Wilkinson, M. Rosenblum, M.C. Whiting, R.B. Woodward, J. Am. Chem. Soc. 74 (1952) 2125.

[2] A. Togni, T. Hayashi (Eds.), Ferrocenes, VCH, Weinheim, 1995.

[3] (a) D.R. van Staveren, N. Metzler-Nolte, Chem. Rev. 104 (2004) 5931;
(b) H.-B. Kraatz, J. Inorg. Organomet. 15 (2005) 83.

[4] (a) T. Ihara, Y. Maruo, S. Takenaka, M. Takagi, Nucleic Acids Res. 24 (1996) 4273;
(b) R.C. Mucic, M.K. Herrlein, C.A. Mirkin, R.L. Letsinger, Chem. Commun. (1996) 555;
(c) Y. Uto, H. Konto, M. Abe, T. Suzuki, S. Takenaka, Anal. Biochem. 250 (1997) 122;
(d) E. Bucci, L. De Napoli, G. Di Fabio, A. Messere, D. Montesarchio, A. Romanelli, G. Piccialli, M. Varra, Tetrahedron 55 (1999) 14435;
(e) C.J. Yu, H. Yowanto, Y. Wan, T.J. Meade, Y. Chong, M. Strong, L.H. Donilon, J.F. Kayyem, M. Gozin, G.F. Blackburn, J. Am. Chem. Soc. 122 (2000) 6767;
(f) A.E. Beilstein, M.W. Grinstaff, Chem. Commun. (2000) 509;
(g) C.J. Yu, H. Wang, Y. Wan, H. Yowanto, J.C. Kim, L.H. Donilon, C. Tao, M. Strong, Y. Chong, J. Org. Chem. 66 (2001) 2937;
(h) A. Anne, B. Blanc, J. Moiroux, Bioconjugate Chem. 12 (2001) 396;
(i) A.E. Beilstein, M.W. Grinstaff, J. Organomet. Chem. 637–639 (2001) 398;
(j) C.J. Yu, Y. Wan, H. Yowanto, J. Lie, C. Tao, M.D. James, C.L. Tan, G.F. Blackburn, T.J. Meade, J. Am. Chem. Soc. 123 (2001) 11155;
(k) M. Chahma, J.S. Lee, H.-B. Kraatz, J. Organomet. Chem. 648 (2002) 81;
(l) A.R. Pike, L.C. Ryder, B.R. Horrocks, W. Clegg, M.R.J. Elsegood, B.A. Connnolly, A. Houlton, Chem. Eur. J. 8 (2002) 2891;
(m) W.A. Wlassoff, G.C. King, Nucleic Acids Res. 30 (2002) 58;
(n) A.E. Navarro, N. Spinelli, C. Moustrou, C. Chaix, B. Mandrand, H. Brisset, Nucleic Acids Res. 32 (2004) 5310;
(o) C. Baldoni, P. Cerea, C. Giannini, E. Licandro, C. Rigamonti, S. Maiorana, Synlett 13 (2005) 1984.

[5] (a) R.L. Cox, T.W. Schneider, M.D. Koppand, Anal. Chim. Acta 262 (1992) 145;
(b) K. Severin, R. Bergs, W. Beck, Angew. Chem., Int. Ed. 37 (1998) 1634;
(c) O. Brosch, T. Weyhermüller, N. Metzler-Nolte, Inorg. Chem. 38 (1999) 5308;
(d) A. Hess, O. Brosch, T. Weyhermüller, N. Metzler-Nolte, J. Organomet. Chem. 589 (1999) 75;
(e) A. Hess, N. Metzler-Nolte, Chem. Commun. (1999) 885;
(f) O. Brosch, T. Weyhermüller, N. Metzler-Nolte, Eur. J. Inorg. Chem. (2000) 323;
(g) A. Hess, J. Sehnert, T. Weyhermüller, N. Metzler-Nolte, Inorg. Chem. 39 (2000) 5437;
(h) J. Sehnert, A. Hess, N. Metzler-Nolte, J. Organomet. Chem. 637–639 (2001) 349;
(i) H. Dialer, K. Polborn, W. Ponikwar, K. Sünkel, W. Beck, Chem. Eur. J. 8 (2002) 691;
(j) D. Savage, G. Malone, J.F. Gallanger, Y. Ida, P.T.M. Kenny, J. Organomet. Chem. 690 (2005) 383;
(k) F.E. Appoh, T.C. Sutherland, H.-B. Kraatz, J. Organomet. Chem. 690 (2005) 1209;
(l) Á. Kuik, R. Skoda-Földes, J. Balogh, L. Kollár, J. Organomet. Chem. 690 (2005) 3237;
(m) D. Savage, N. Neary, G. Malone, S.R. Alley, J.F. Gallanger, P.T.M. Kenny, Inorg. Chem. Commun. 8 (2005) 429;
(n) U. Hoffmanns, N. Metzler-Nolte, Bioconjugate Chem. 17 (2006) 204.

[6] (a) H.-B. Kraatz, J. Lusztyk, G.D. Enright, Inorg. Chem. 36 (1997) 2400;
(b) H.-B. Kraatz, D.M. Leek, A. Houmam, G.D. Enright, J. Lusztyk, D.D.M. Wayner, J. Organomet. Chem. 589 (1999) 38;
(c) H.-B. Kraatz, M. Galka, Met. Ions Biol. Syst. 38 (2001) 385.

[7] (a) T. Moriuchi, A. Nomoto, K. Yoshida, T. Hirao, Organometallics 20 (2001) 1008;
(b) T. Moriuchi, K. Yoshida, T. Hirao, J. Organomet. Chem. 637–639 (2001) 75;
(c) T. Moriuchi, A. Nomoto, K. Yoshida, A. Ogawa, T. Hirao, J. Am. Chem. Soc. 123 (2001) 68;
(d) I. Bediako-Amoa, R. Silenova, H.-B. Kraatz, Chem. Commun. (2002) 2430;
(e) H.S. Mandal, H.-B. Kraatz, J. Organomet. Chem. 674 (2003) 32;
(f) T. Moriuchi, T. Nagai, T. Hirao, Org. Lett. 8 (2006) 31.

[8] (a) Y. Xu, H.-B. Kraatz, Tetrahedron Lett 42 (2001) 2601;
(b) L. Barišić, W. Rapić, V. Kovac, Croat. Chem. Acta 75 (2002) 199;
(c) L. Barišić, W. Rapić, H. Pritzkow, G. Pavlović, I. Nemet, J. Organomet. Chem. 682 (2003) 131.

[9] S.A. Brazill, P.H. Kim, W.G. Kuhr, Anal. Chem. 73 (2001) 4882.

[10] (a) E. Coutouli-Argyropoulou, A. Kelaidopoulou, C. Sideris, G. Kokkinidis, J. Electoanal. Chem. 477 (1999) 130;
(b) E. Coutouli-Argyropoulou, I. Sabbas, S. Konarski, J. Heterocyclic Chem. 37 (2000) 1055;
(c) N.G. Argyropoulos, E. Coutouli-Argyropoulou, J. Organomet. Chem. 654 (2002) 117;
(d) E. Coutouli-Argyropoulou, M. Tsitabani, G. Petrantonakis, A. Terzis, C. Paptopoulou, Org. Biomol. Chem. 1 (2003) 1382.

[11] G.G.A. Balavoine, G. Doisneau, T. Fillebeen-Khan, J. Organomet. Chem. 412 (1991) 381.

[12] J.-G. Rodríguez, S. Pleite, J. Organomet. Chem. 637–639 (2001) 230.
[13] (a) B.R. Maryanoff, A.B. Reitz, Chem. Rev. 89 (1989) 863;
(b) A. Johnson, Ylides and Imines of Phosphorus, John Wiley & Sons, New York, 1993;
(c) E. Coutouli-Argyropoulou, C. Zachariadou, J. Heterocyclic Chem. 42 (2005) 1135.
[14] (a) M.E.N.P.R.A. Silva, A.J.L. Pombeiro, J.J. Fraústo da Silva, R. Herrmann, N. Deus, T.J. Castilco, M.F.C.G. Silva, J. Organomet. Chem. 421 (1991) 75;
(b) M.E.N.P.R.A. Silva, A.J. Pombeiro, J.J. Fraústo da Silva, R. Herrmann, N. Deus, R.E. Bozak, J. Organomet. Chem. 480 (1994) 81.
[15] M. Grayson, P. Tarpey Keough, J. Am. Chem. Soc. 82 (1960) 3919.
[16] R. Ketcham, D. Jambotkar, L. Martinelli, J. Org. Chem. 27 (1962) 4666.
[17] A.W. Johnson, V.L. Kyllingstad, J. Org. Chem. 31 (1966) 334.
[18] O.I. Kolodiazhnyl, Phosphorus Ylides. Chemistry and Application in Organic Synthesis, John Wiley & Sons, Inc., New York, 1999.