A Two-Step Palladium-Catalyzed Coupling Scheme for the Synthesis of Ferrocene-Labeled Amino Acids

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This work describes a Pd-catalyzed coupling of ferrocene alkyne derivatives to iodo amino acids. Ferrocene carboxylic acid propargyl amides were easily obtained in high yield. The crystal structures of the propargyl amine derivative **3** and the 1,1-diethylpropargylamine derivative **4** have been determined by X-ray diffraction. Pd-catalyzed coupling to ***p***-iodoanilide amino acids gave the corresponding ferrocene-labeled amino acid derivatives, which were easily purified by diethyl ether extraction in the case of the 1,1-diethyl derivatives **8**. The coupling reaction did not require anhydrous solvents and tolerated a variety of functional groups present in peptides such as alcohols (**8a**, Ser), thioethers (**8b**, Met), disulfide bonds (cystine, **12**) esters (as in the *N*-labeled Leu derivative **10**) and of course amides. A minor by-product of the coupling reaction, namely the homo-dimer bis(ferrocene carboxylic acid propargylamide) **9**, was identified in the crude reaction mixtures by mass spectrometry and independently synthesized by oxidative coupling (Glaser and Eglington) of **3**. All new compounds were completely characterized spectroscopically, including ^{15}N- and 2D NMR spectroscopy, Mössbauer spectroscopy and electrochemistry. This work introduces a versatile procedure for a selective functionalization of amino acids with organometallics at the *C-terminus* which is expected to be of general applicability to peptide chemistry.

Introduction

We are exploring new ways of covalently linking organometallic compounds to biomolecules.[1−5] In these conjugates, the organometallic moiety serves as a sensitive probe for the detection of the biomolecule, e. g. electrochemically[6−8] or by IR spectroscopy.[9−18] The key issue in any of these assays is *chemoselectivity*:[12,18] No doubt is to remain about the number of attached organometallics nor their site of attachment to the biomolecule − which may even be, for example, a large enzyme[10,11,13] or peptide hormone like secretin.[19] Also, the reaction should be mild enough to comply with the possibly sensitive organometallic compounds and the variety of functional groups present in a peptide. We[1] and others[20,21] have suggested the use of a Pd-catalyzed two-step coupling reaction for this purpose. In the first step, an anchoring group is incorporated into the peptide. Secondly, a suitably-functionalized organometallic compound is reacted with that anchoring group to form the covalent link to the peptide. The prerequisite of this concept is that the anchoring group is left untouched under standard peptide chemistry conditions and vice versa the reaction that links the organometallic to the peptide may not affect any functionality present in the peptide other than the anchoring group. In compliance with this prerequisite, our group has recently reported the synthesis of alkynyl amino acids for the coupling with organometallic halides and demonstrated the viability of our approach by selectively labeling the *N*- and *C*-protected tripeptide Boc-Phe-Glu-Met-OMe at the C_γ of Glu with a ferrocene derivative.[1] However, derivatizing a peptide with alkynyl groups is not feasable in solid-state synthesis of peptides as the alkyne may not withstand the concentrated HF frequently used to cleave the peptide from the support. In an effort to circumvent this problem, this work reports the synthesis of alkynyl ferrocene derivatives and their Pd-catalyzed coupling to iodobenzene amino acids with different functional groups. Iodinated aromatic compounds were previously used as radio-labels for amino acids[22] and monoclonal antibodies[23] and as such were successfully employed in solid support peptide synthesis.[24] In this study, alternatively-functionalized amino acids were chosen as model compounds for peptides and ferrocene was selected owing to its potential in electrochemical detection.[3,8,25−31]

Results and Discussion

Synthesis

Ferrocene carboxylic acid chloride **2**, which was prepared in situ by heating ferrocene carboxylic acid **1** at reflux with oxalic acid chloride, reacts with propargyl amine and 1,1-diethylpropargyl amine to give the ferrocene amido alkynes **3** and **4** in >90% yield (Scheme 1). Both derivatives are orange, crystalline solids and their solid-state structures were determined by X-ray diffraction (vide infra).

In these preparations, ferrocene carboxylic acid anhydride was frequently found as a by-product. To avoid the formation of this anhydride, we explored other means of activating the organometallic acid. Kraatz et al. prepared ferrocene amino acids by activation of **1** with hydroxybenzotriazole and dicyclohexylcarbodiimide in >70% yield.[32] In our hands, however, yields for this coupling were usually much lower. Isobutyl chloroformate/*N*-methyl-

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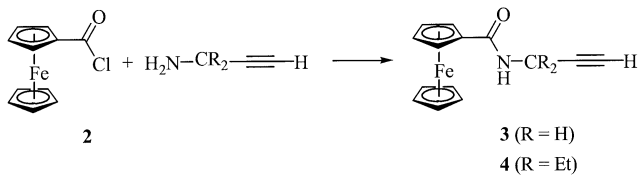
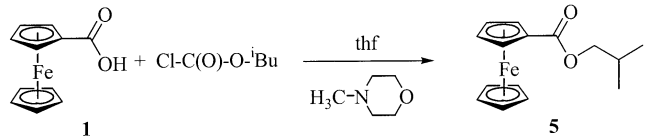


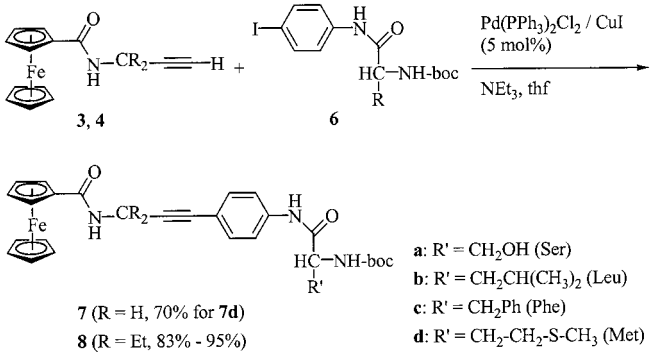
Scheme 1

morpholine in THF is an alternative well-established reagent for peptide coupling reactions in solution.[33] According to Scheme 2, ferrocene carboxylic acid isobutyl ester **5** could be prepared in 95% yield. However, 14 h of reflux were necessary to obtain **3** from **5** and propargyl amine. Unlike amino acids, which react with amines within minutes under comparable conditions,[34] ferrocene carboxylic acid is not easily activated by the most common reagents.



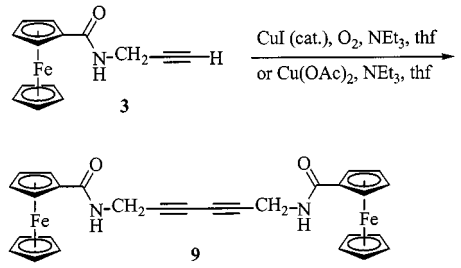
Scheme 2

Reaction of organometallic alkynes **3** and **4** with iodoarene amino acid derivatives **6** gave the desired ferrocene-labeled amino acids **7** and **8** in very good yield (Sonogashira coupling,[35–37] Scheme 3). By extracting the crude reaction products with diethyl ether, the diethyl derivatives **8** could be obtained as analytically pure solids. Owing to their reduced solubility, the simpler propargyl amine derivatives **7** were more difficult to separate from impurities. In fact, only the methionine derivative **7d** could be obtained analytically pure after extensive washing.



Scheme 3

The inability to obtain pure coupling products **7** prompted us to carry out a careful product analysis. Electron spray ionization mass spectrometry (ESI-MS) revealed the presence (< 5%) of an iron-containing by-product with m/z = 532. In addition, the ^{1}H-NMR spectrum of the crude reaction mixture contained a number of Cp signals, a signal for one amide proton and a further signal which was not assigned. Since we suspected that oxidative homo-coupling of **3** might have occurred, we set out to synthesize the dimer **9** by air oxidation of **3** with a catalytic amount of CuI (Glaser coupling,[38] 32% yield) or stoichiometric amounts of $Cu(OAc)_2$ under Ar (Eglington coupling,[38] 38% yield, Scheme 4). The bis-ferrocene-diyne **9** is an orange-coloured solid, which is stable both as a solid and in solution for prolonged periods of time.



Scheme 4

Characterization

Solid-State Structures of 3 and 4

Crystals of suitable quality for an X-ray structure analysis were obtained for the two alkynyl–ferrocene derivatives **3** and **4**. Both compounds crystallize in the orthorhombic space group *Pbca* with very similar unit cells and packing in the crystal lattice (see Table 1, Experimental Section). ORTEP plots of the molecular structures are shown in Figures 1 and 2, repectively. The amide groups are almost parallel to the plane of the neighbouring cyclopentadienyl ring (9° angle between amide and Cp least squares planes for **3** and 15.5° for **4**). The tilt of both cyclopentadienyl rings is 1.8° (**3**) and 2.5° (**4**) away from an eclipsed conformation (mean value of H/C–C–C–H dihedral angles) and the rings are almost parallel as shown by the centroid–Fe–centroid angle (179° and 177.8° for **3** and **4**, respectively). All these parameters compare well to related compounds.[32,39,40] Unlike ferrocene carboxylic acid, which forms dimers in the solid state,[40,41] both **3** and **4** form hydrogen bridges with their nearest neighbours through the amide bonds in the crystal lattice. By arranging in a "head-to-tail" fashion, the molecules form one-dimensional zigzag chains (Figure 3).

Spectroscopy and Discussion

The Sonogashira coupling has recently gained some attention for the synthesis of organometallic alkynes[42,43] and polymers.[44,45] Beck et al. have used *p*-ethynylphenylalanine, which is a potent inhibitor of tryptophan hydroxylase,[46] in Pd-catalyzed alkyne coupling reactions to obtain a variety of novel phenylalanine derivatives.[47–49] NMR spectroscopy provides an excellent handle to establish the constitution of all new compounds. The alkyne pro-

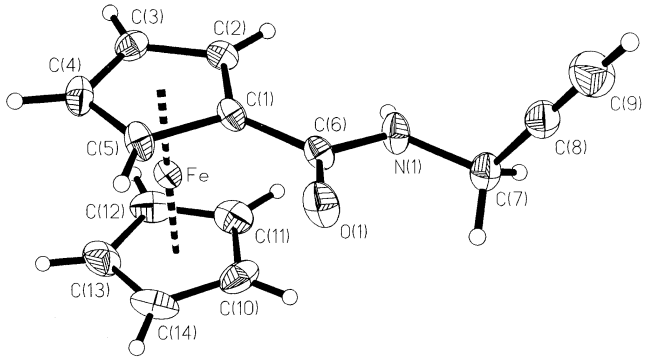


Figure 1. ORTEP drawing of **3**, indicating the numbering scheme. Selected bond lengths [Å] and angles eg.]: Fe−C_{Cp} (av.) 2.038, Fe−Cp(centroid) 1.647 and 1.647 (unsubstituted Cp), C(1)−C(6) 1.476(4), C(6)−O(1) 1.233(3), C(6)−N(1) 1.338(3), C(8)−C(9) 1.164(5), O(1)−C(6)−N(1) 121.2(3), N(1)−C(7)−C(8) 114.1(3)

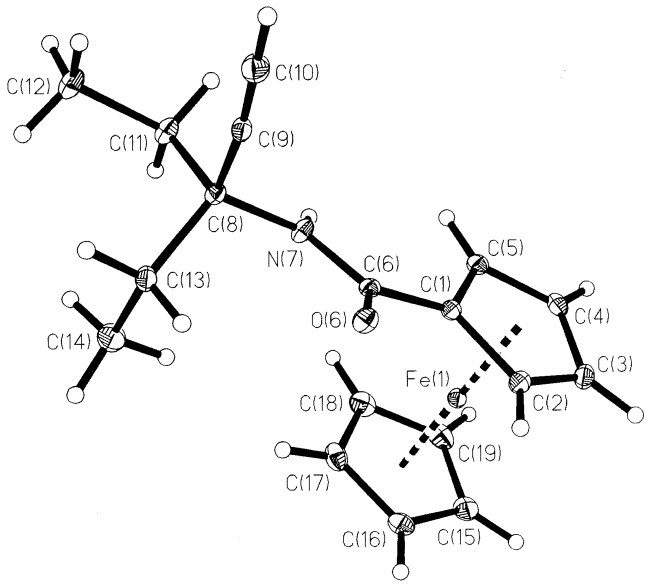


Figure 2. ORTEP drawing of **4**, indicating the numbering scheme. Selected bond lengths [Å] and angles eg.]: Fe−C_{Cp} (av.) 2.050, Fe−Cp(centroid) 1.652 and 1.653 (unsubstituted Cp), C(1)−C(6) 1.489(3), C(6)−O(6) 1.239(2), C(6)−N(7) 1.351(3), C(9)−C(10) 1.190(3), O(6)−C(6)−N(7) 122.3(2), N(7)−C(8)−C(9) 110.3(2)

ton in **3** and **4** is readily detected at ca. δ = 2.3 as a singlet (**4**) or a triplet with $^4J_{HH}$ = 2.6 Hz due to coupling with the methylene protons (**3**). The success of the Pd-catalyzed coupling can be immediately established by ^{1}H-NMR spectroscopy, especially by the disappearance of this signal of the terminal alkyne. In an earlier report on ferrocene carboxylic acid amides of amino acids,[32] two signals were observed for the *ortho* protons of the substituted Cp ring owing to the presence of a chiral centre. Even at 500 MHz, we were unable to detect more than one signal for these *ortho* protons, probably because of the large distance between the Cp ring and the chiral centre. From molecular modelling (Sybyl force field[50]) of the alanine derivative **7e** (R = H, R′ = CH_3), it follows that the C≡C triple bond, an aromatic ring and two amide groups enforce a minimum distance of >10 Å between the iron centre and the chiral

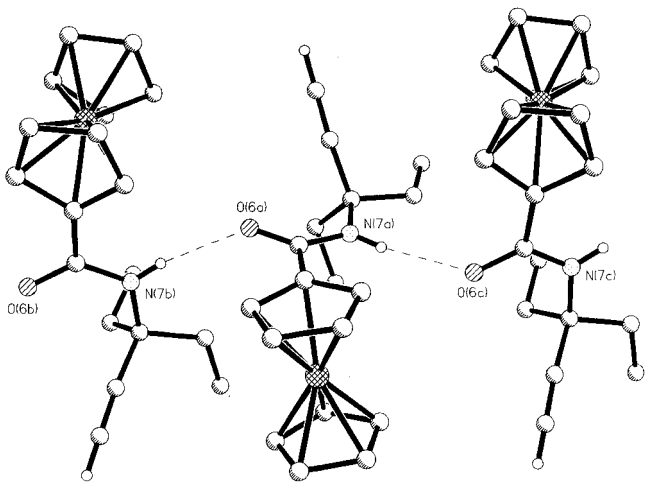


Figure 3. Part of the solid-state structure of **4**, showing the head-to-tail orientation of neighbouring molecules by means of hydrogen bridges. Distance N(7b)−O(6a) 2.998 Å

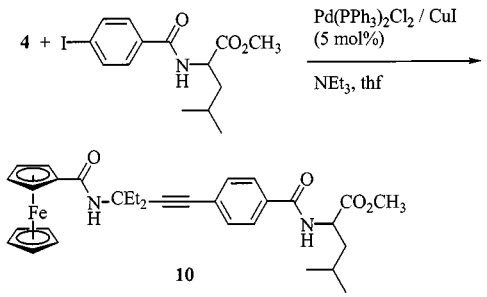
carbon atom C_α. There are also characteristic signals in the ^{13}C-NMR spectra of conjugates **7** and **8**, in particular for the two carbon atoms between which the new bond is formed. The alkyne carbon atom shifts downfield by about 13 ppm, whereas the signal of the aryl carbon atom, having been shielded by the iodine centre in **6** (ca. 87 ppm), is found at ca. 119 ppm in **7** and **8**. The alkyne ^{13}C-NMR signals for the diyne **9** are observed remarkably upfield (δ = 65.5 for the internal carbon atoms and δ = 76.7). These values are about 6 and 10 ppm higher than in a related phenylacetylene-chromium-tricarbonyl dimer[42] or in (ethynylcyclobutadiene)-cyclopentadienyl-cobalt dimer by Bunz and co-workers.[51] Since the NMR signals for all amide protons are readily detectable in aprotic solvents we used 2D indirect detection ^{1}H-^{15}N NMR spectroscopy to detect the ^{15}N-NMR signals of all nitrogen atoms in the new compounds. There are indeed characteristic ranges for ^{15}N-NMR shifts which will facilitate the identification of related coupling products in the future, namely δ_N = −275 for **7** and δ_N = −260 for **8**. The N_{Boc} signal is generally observed at δ_N = −290 and the anilide nitrogen atom at δ_N = −250.[52,53] All these chemical shifts are fairly insensitive to solvent changes, which indicates that intermolecular hydrogen bonds are broken up in solution for **7** and **8**. This notion is further substantiated by IR spectroscopy.

In the IR spectra of **3**, **4**, **7** and **8**, the C≡C stretching frequency is often too weak to be detected. It is, however, usually the strongest band in the RAMAN spectra. Upon substitution of the terminal proton, its frequency shifts by more than 100 cm^{-1} from 2121 cm^{-1} (**3**) and 2105 cm^{-1} (**4**) to about 2230 cm^{-1} (see Experimental Section). It is possible to distinguish between propargylamine compounds **7** and their 1,1-diethyl derivatives **8** on the basis of their RAMAN spectra alone since there is a difference of about 10 cm^{-1} in the respective stretching frequencies of the C≡C bond (ca. 2230 cm^{-1} in **8** and 2240 cm^{-1} in **7**), quite comparable to compounds **3** and **4**. Unfortunately, we were unable to obtain single crystals of the ferrocene amino acid

conjugates **7** or **8**. However, the IR spectrum of **7d** sheds some light on structural differences between the solid-state and solutions of **7** and **8**.[54,55] A broad band well below 3400 cm^{-1} for **7d** in a KBr pellet is indicative of hydrogen bonding involving the amide groups. These hydrogen bonds will govern the packing of molecules in the solid state[56] as described for **3** and **4**. In contrast, there is only one sharp amide band observed at 3428 cm^{-1} in CH_2Cl_2 solution, clearly showing that all hydrogen bonds are broken up even in aprotic solvents.[57]

Electrochemical detection − where applicable − is a useful tool in chromatography (HPLC-ECD) and the use of ferrocene derivatives in peptide chemistry has been explored by the group of Eckert.[6,7] Their approach of using activated acids of ferrocene derivatives was hampered by low yields in the coupling reactions or by precursors which were difficult to prepare. Using the methodology outlined in this work, we can easily prepare electrochemically active amino acid derivatives in high yield. To demonstrate the feasibility of ECD, compounds **7** and **8** were investigated electrochemically. Both groups of compounds show a reversible wave in the cyclic voltammogram (CV) at +173 mV (**7**) and between +187 and +197 mV (**8**) vs. ferrocene/ferrocenium. Similar values have previously been observed for ferrocene carboxylic acid amides.[32] A second, irreversible wave in the CV of **8d** is attributed to oxidation of the sulfur atom.

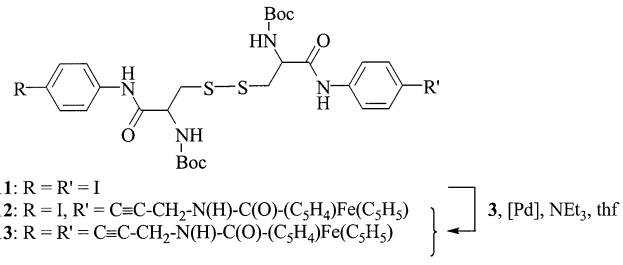
Compounds **7** and **8** demonstrate a general principle for the functionalization of the *C-terminus* of amino acids, which has not been achieved before. Naturally, this two-step procedure can also be applied to the labeling of the *N-terminus* of amino acids as shown in Scheme 5.



Scheme 5

An excess of *p*-iodobenzoic acid chloride is reacted with leucine methyl ester and subsequently coupled to **4** under Pd catalysis. The coupling product **10**, which is obtained analytically pure in 89% yield, is easily identified by its spectral features, namely the disappearance of the signal of the alkyne proton in the ^{1}H-NMR spectrum, characteristic changes in the ^{13}C-NMR spectrum as described above and a strong band at 2227 cm^{-1} in the RAMAN spectrum. Compounds **4** and **10** were also investigated by ^{57}Fe Mössbauer spectroscopy. The isomer shift (0.53 mm s^{-1} for **4** and 0.52 mm s^{-1} for **10**) and quadrupolar splitting [2.34 mm s^{-1} (**4**) and 2.32 mm s^{-1} (**10**)] are very similar to the values of ferrocene (0.53 mm s^{-1} and 2.37 mm s^{-1}).[58] This similarity indicates that attachment of an amino acid (**10**) or even functionalization of one Cp ring (**4**) has no significant influence on the field gradients of the iron nucleus. Significant deviations were observed only in compounds where the two Cp rings were no longer coplanar.[59]

Beck and co-workers have prepared a veritable number of stable Pd^{II} complexes of amino acids and peptides, in which the metal coordinates − usually in a chelating fashion − to the N, O, or S atoms of the amino acids.[5,60−65] Other authors reported the hydrolysis of amino acid esters by *ortho*-metallated Pd complexes.[66,67] In the light of their results, the success of the Pd-catalyzed coupling with amino acids is all the more surprising. A number of ubiquitous functional groups in peptide chemistry such as thio-ethers (**7d** and **8d**), alcohols (**8a**), esters (**10**), and of course amides is tolerated without notable loss of catalytic activity. Since disulfide bonds play a pivotal structural role in many enzymes,[68] and insertion reactions into disulfide bonds are well documented for Pt complexes,[69,70] the obvious question needs to be answered as to whether our coupling would work for cystine derivatives. The bis(*N*-Boc)-bis(*p*-iodo-anilined)-cystine **11** was prepared from activated *N*-protected cystine and two equivalents of *p*-iodo-aniline. Reaction with **3** under Pd-catalysis yielded the mono-ferrocene derivative **12** (Scheme 6).



Scheme 6

Using an excess of **3**, the bis-ferrocene derivative **13** could also be obtained but was impossible to purify. Regardless of the stoichiometry used, signals were detected for both **12** (*m*/*z* = 1004 for [**12** + Na]) and **13** (*m*/*z* = 1143 for [**13** + Na]) by ESI-MS in all preparations. We were able to obtain **12** in analytically pure form by liquid chromatography (HPLC). ^{1}H-NMR spectroscopy shows characteristic patterns for two AA′XX′ spin systems. In addition, the presence of eight ^{13}C NMR signals in the aromatic region is indicative of two different aromatic rings. A reversible oxidation occurs at a potential of +196 mV vs. Fc/Fc^+ for a solution of **12** in CH_2Cl_2. Controlled potential coulometry of this solution requires 89% of the charge calculated for *one* ferrocene unit. All these results taken together allow for the conclusion that the disulfide bridge in cystine derivatives does not interfere with the Pd-catalyzed alkyne coupling. Furthermore the two iodoarene rings are so far away from each other in **11** that it is impossible to control the

ratio of mono- to disubstitution during the Pd-catalyzed coupling to ferrocene derivative **3**.

Conclusion

We have demonstrated a general way of attaching amino acids to ferrocene derivatives by means of a Pd-catalyzed two-step procedure starting from the amino acid ester and ferrocene alkyne derivatives. Using this scheme, a selective labeling of the *C-terminus* of amino acids is possible.[13,21] A different approach for ferrocene functionalization of hemin was recently proposed by Ryabov et al. by means of activation of the propionic acid groups and reaction with ferrocene methylamine.[71] The disadvantage of their approach, i.e. unselective reaction of the activated acid with *any* primary amine, can only be resolved by employing different, "non-peptide" chemistry. The Pd-catalyzed Sonogashira coupling applied in this work tolerates a wide variety of functional groups often encountered in peptides and does not require dry solvents. In fact, Schmidtchen and coworkers have recently introduced water-soluble cationic phosphane ligands for Heck-type reactions in water.[72] It should be noted that the coupling reactions were usually carried out for 4 h at 80°C. Very similar yields and product purity were obtained by stirring for 24 h at room temperature, making this method suitable for the derivatization of more sensitive organometallic or biological compounds. Investigations along these lines are currently underway in our laboratory.

Experimental Section

General: All reactions were carried out in ordinary glassware and solvents without further precautions except where indicated. Chemicals were purchased from Aldrich-Sigma GmbH and Fluka AG and used as received, only enantiomerically pure L-amino acids were used. Ferrocene carboxylic acid chloride **1** was prepared by refluxing ferrocene carboxylic acid with oxalic chloride in CH_2Cl_2 for 1 h, followed by complete removal of all volatiles. The resulting red oil was handled under argon and used immediately. Iodoarene amino acids **6** were prepared from the pre-activated *N*-Boc-protected amino acids (isobutyl chloroformate and *N*-methylmorpholine) and *p*-iodoaniline in THF and recrystallized from hot heptane/THF (10:1).[73] − Melting points (uncorrected) were determined in a Tottoli apparatus (Büchi, Switzerland). − Elemental analysis were carried out by H. Kolbe, Analytisches Laboratorium, Mülheim. − IR spectra were recorded on a Perkin−Elmer System 2000 instrument as KBr disks, and additionally in CH_2Cl_2 solution where indicated. Frequencies $\tilde{\nu}$ are given in cm^{-1}. − RAMAN spectra were recorded on the same instrument as neat substances ($\tilde{\nu}$ in cm^{-1}). − UV/Vis spectra were recorded on a Perkin−Elmer Lambda 19 spectrometer, only the wavelengths of the highest-energy ferrocene transition is given in nm, ε ($dm^3mol^{-1}cm^{-1}$) in brackets. − Mass spectra were recorded by the mass spectrometry service group, Mülheim, on a MAT 8200 (Finnigan GmbH, Bremen) instrument (EI, 70 eV) or on a MAT95 (Finnigan GmbH, Bremen) instrument (ESI, CH_3OH solution, positive ion detection mode). Only characteristic fragments from EI spectra are given with relative intensities (%) in brackets. − HPLC separations were carried out on a Nucleosil-7-C_{18} column (Merck L6000 pump and Shimadzu SPD-2A UV detector operating at 260 nm), 4 mL min^{-1} flow rate with a methanol/water (5:1) mixture. − Cyclic voltammograms were obtained with a three-electrode cell and an EG&G Princeton Applied Research model 273A potentiostat. A $Ag/AgNO_3$ (0.01 mol L^{-1} in $AgNO_3$) reference electrode, a glass carbon disk working electrode of 2 mm diameter and a Pt wire counter electrode were used. CH_2Cl_2 solutions (ca. 10^{-4} mol L^{-1}) contained 0.1 mol L^{-1} Bu_4NPF_6 as supporting electrolyte. Potentials $E^{0\prime}$ were determined by square-wave voltammetry. As an internal standard, ferrocene was added in excess as a reference. − NMR spectra were recorded in $CDCl_3$ at room temp. on a Bruker ARX 250 (^1H at 250.13 MHz and ^{13}C), DRX 400 (^1H at 400.13 MHz, ^{13}C and 2D spectra) and DRX 500 (^1H at 500.13 MHz, ^{13}C, ^{15}N, 2D). ^1H and ^{13}C spectra were referenced to TMS, using the residual proton signals of the deuterated solvents (^1H) or solvent signals (^{13}C) as internal standards [$CDCl_3 \equiv 7.24$ (^1H) and 77.0 (^{13}C), DMSO ≡ 2.49 (^1H) and 39.5 (^{13}C), $CD_3OD \equiv 3.30$ (^1H) and 49.0 (^{13}C)]. Positive chemical shift values δ (in ppm) indicate a downfield shift from the standard, only the absolute values of coupling constants are given in Hz. ^{15}N spectra were referenced to the absolute frequency of 50.6969910 MHz, which was the resonance frequency of neat nitromethane under the same experimental conditions. All resonances were assigned by 2D NMR (H,H-COSY and ^1H,^{13}C-HMQC for ^1J and long-range couplings). ^{15}N chemical shifts were taken from the F1 projection of indirect detection ^1H,^{15}N-correlated 2D spectra with 1024/256 data points in F1/F2, processed after applying a matched cosine function and zero filling in both dimensions. − Mössbauer data were recorded on a spectrometer with alternating constant-accelaration and a ^{57}Co source in 6 μm Rh matrix. The minimum experimental line width was 0.24 mms^{-1} full width at half maximum. The sample temperature was maintained constant in an Oxford Instruments VARIOX cryostat. Isomer shifts are quoted relative to iron metal at 300 K.

X-ray Crystallographic Data Collection and Refinement: Transparent yellow-orange single crystals of 0.74 × 0.35 × 0.05 mm (**3**) and 0.47 × 0.20 × 0.03 mm (**4**) were sealed in glass capillaries and mounted on the diffractometer. Graphite monochromated Mo-*Kα* radiation (λ = 0.71073 Å) was used. For **3**, cell constants were obtained from a least square fit of the setting angles of 25 carefully centred reflections and intensities were collected by the usual ω/2θ scan technique and corrected for Lorentz and polarization effects. The Siemens ShelXTL software package (Siemens Analytical X-ray Instruments, Inc.) was used for solution and refinement of the structure. Neutral atom scattering factors were taken from the usual source.[74] All non-hydrogen atoms were refined anisotropically. H-atoms were placed at calculated positions and refined as riding atoms with isotropic displacement parameters. All crystallographic details are listed in Table 1. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre and allocated the deposition numbers CCDC 119109 (**3**) and CCDC 119110 (**4**). Copies of the data may be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat). +44 1223/33 60 33; E-mail: deposit@ccdc.cam.ac.uk].

Preparations: Ferrocene propargylamine derivatives **3** and **4**: Ferrocene carboxylic acid chloride was dissolved in CH_2Cl_2 (40 mL). Propargylamine [(0.36 g, 6.5 mmol) for **3**, 1,1-diethylpropargylamine (0.72 g, 6.5 mmol) in the case of **4**] and triethylamine (0.66 g, 6.5 mmol) were added at room temp. and the solution was stirred for 4 h. After removal of the triethylamine−hydrochloride the solvent was removed in vacuo. The residue was dissolved in chloro-

form, the organic phase washed three times with water and dried with Na_2SO_4. After filtration and removal of the solvent, virtually pure products were obtained which could be recrystallized to yield single crystals. **3** (1.51. g, 87%), recrystallized from warm ethyl acetate/methanol, m.p. 167°C. − ^{1}H NMR ($CDCl_3$): δ = 5.85 (br, 1 H, N*H*), 4.66 (pseudo-t, 2 H, H_{Cp}), 4.34 (pseudo-t, 2 H, H_{Cp}) 4.21 (s, 5 H, H_{Cp}), 2.25 (t, *J* = 2.6 Hz, 1 H, C≡C*H*). − ^{13}C NMR ($CDCl_3$): δ = 170.2 (*C*=O), 80.3 (*C*≡CH), 71.5 (C≡*C*H), 75.0, 70.7, 69.8, 68.2 (C_{Cp}), 29.2 (*C*H$_2$). − ^{15}N NMR ($CDCl_3$): δ = −276. − IR: ṽ (cm^{-1}) = 3281 (m), 3264 (m), 2121 (w), 1634 (s). − Raman: 2121 cm^{-1} (C≡C). CV: +187 mV. MS (EI, 70 eV): 267 (100), 213 (4), 186 (14). − $C_{14}H_{13}FeNO$ (267.11): calcd. C 63.0, H 4.9, N 5.2; found C 62.9, H 4.9, N 5.2. − **4** (1.91 g, 91%) recrystallized from methanol, m.p. 149°C. − ^{1}H NMR ($CDCl_3$): δ = 5.61 (br, 1 H, N*H*), 4.61 (pseudo-t, 2 H, H_{Cp}), 4.30 (pseudo-t, 2 H, H_{Cp}) 4.21 (s, 5 H, H_{Cp}), 2.38 (s, 1 H, C≡C*H*), 2.33−2.19 and 1.93−1.79 (mult., 2 H each, C*H*$_2$-CH$_3$), 1.03 (t, *J* = 7.4 Hz, 6 H, CH$_2$-C*H*$_3$). − ^{13}C NMR ($CDCl_3$): δ = 169.2 (*C*=O), 85.6 (*C*≡CH), 76.8 (C_{Cp}), 71.6 (C≡*C*H), 70.3, 69.7, 68.1 (C_{Cp}), 57.5 [*C*(Et)$_2$], 30.8 (*C*H$_2$), 8.8 (*C*H$_3$). − ^{15}N NMR ($CDCl_3$): δ = −263. − IR: ṽ (cm^{-1}) = 3304 (w), 3277 (m), 1631 (s). − Raman 2105. − CV: +182 mV. − MS (EI, 70 eV): 323 (100), 229 (40), 213 (32), 121 (19). − $C_{18}H_{21}FeNO$ (323.22): calcd. C 66.9, H 6.6, N 4.3; found C 67.2, H 6.5, N 4.3. − **5**: Ferrocene carboxylic acid (0.5 g, 2.17 mmol) was dissolved in THF (30 mL) at room temp. and neutralized with N-methylmorpholine (0.22 g, 2.17 mmol). Upon addition of isobutyl chloroformate (0.3 g, 2.17 mmol) a white precipitate rapidly formed. After stirring for one hour, the solution was filtered and the solvent was removed in vacuo. The residue was dissolved in chloroform, the organic phase washed three times with water and dried with Na_2SO_4. After filtration the solvent was removed to yield 0.57 g (79%) of **5. 5** can be recrystallized from *n*-pentane, m.p. 46°C. − ^{1}H NMR ($CDCl_3$): δ = 4.84 (pseudo-t, 2 H, H_{Cp}), 4.51 (pseudo-t, 2 H, H_{Cp}) 4.28 (s, 5 H, H_{Cp}), 4.08 (d, *J* = 6.6 Hz, 2 H, C*H*$_2$), 2.05 (mult., 1 H, C*H*), 0.98 (d, *J* = 6.7 Hz, 6 H, C*H*$_3$). − ^{13}C NMR ($CDCl_3$): δ = 166.5 (Fc-*C*=O), 149.9 (*C*=O), 75.4 (*C*H$_2$), 72.8, 70.9, 70.2, 67.7 (C_{Cp}), 27.7 (*C*H), 18.8 (*C*H$_3$). − IR: ṽ (cm^{-1}) = 3450 (br), 1793 (s), 1731 (s). − MS (EI, 70 eV): 330 (35), 230 (100), 213 (38), 185 (8), 138 (31). − $C_{16}H_{18}FeO_4$ (330.16): calcd. C 58.2, H 5.5; found C 58.4, H 5.5.

General Procedure for Pd Coupling Reactions: The iodoamino acid (1 mmol), bis(triphenylphosphane)palladium(II) dichloride (35 mg, 0.05 mmol), and copper(I) iodide (9.5 mg, 0.05 mmol) were dissolved at room temp. in a deoxygenated mixture of THF (40 mL) and triethylamine (10 mL). The alkyne (1 mmol), dissolved in THF (3 mL) was added dropwise at room temp. After complete addition, the reaction mixture was immediately heated at reflux under argon for 4 hours. After cooling to room temp., the dark suspension was filtered and the solvents were removed on a rotary evaporator. The resulting residue was redissolved in chloroform, the organic phase was washed three times with water and dried with Na_2SO_4. After filtration *n*-pentane was added until a light orange precipitate was formed. The precipitate was collected and dried in vacuo for several hours to yield 70−95% of light orange product. If necessary the product can be purified by redissolving the precipitate in ether, filtration and evaporation of the solvent. − **7d**, m.p. 105−108°C. − ^{1}H NMR ($CDCl_3$): δ = 8.78 (s,br, 1 H, N*H*$_{Ar}$), 7.42 (pseudo-d, 2 H, H_{Ar}), 7.29 (pseudo-d, 2 H, H_{Ar}), 6.14 (s, 1 H, N*H*-CH$_2$), 5.41 (d, *J* = 8 Hz, 1 H, N*H*$_{Boc}$), 4.72 (s, 2 H, H_{Cp}), 4.37 (mult., 1 H, C$_\alpha$*H*), 4.36 (mult., 2 H, C*H*$_2$-C≡C), 4.33 (s, 2 H, H_{Cp}), 4.20 (s, 5 H, H_{Cp}), 2.59−2.55 (mult., 2 H, C$_\gamma$*H*), 2.15−2.12 (mult., 1 H, C$_\beta$*H*), 2.07 (s, 3 H, S-C*H*$_3$), 1.99−1.96 (mult., 1 H, C$_\beta$*H*), 1.41 (s, 9 H, C(C*H*$_3$)$_3$). − ^{13}C NMR ($CDCl_3$): δ = 170.3 (*C*=O), 170.2 (C_{Fc} = O), 156.1 (C_{Boc} = O), 137.8, 132.4, 119.5, 118.3 (C_{Ar}), 85.2 (*C*≡C-CH$_2$), 82.8 (C≡*C*-CH$_2$), 80.7 [*C*(CH$_3$)$_3$], 75.1, 70.7, 69.8, 68.3, (C_{Cp}), 54.3 (C$_\alpha$), 31.2 (C$_\beta$), 30.3 (C$_\gamma$), 30.0 (C≡C-*C*H$_2$), 28.3 [C(*C*H$_3$)$_3$], 15.3 (S-*C*H$_3$). − ^{15}N NMR ($CDCl_3$): d = −291 (*N*H$_{Boc}$), −274 (*N*H), −249 (*N*H$_{Ar}$). − IR: ṽ (cm^{-1}) = 3315 (br, m), 1678 (br, m), 1636 (br, m), 1601 (m). − IR (CH_2Cl_2): 3428 (m), 1701 (s), 1660 (s), 1606 (m). − Raman: 2240 cm^{-1}. − MS (ESI): 590 (M + H), 612 (M + Na), 628 (M + K). − $C_{30}H_{35}FeN_3O_4S$ (589.54): calcd. C 61.1, H 6.0, N 7.1; found C 61.3, H 6.0, N 6.7. − **8a**, m.p. 114°C. − ^{1}H NMR ($CDCl_3$): δ = 8.89 (s, 1 H, N*H*$_{Ar}$), 7.46 (app. d, 2 H, H_{Ar}), 7.39 (app. d, 2 H, H_{Ar}), 5.70 (s, 1 H, N*H*-C(Et)$_2$), 5.65 (br, 1 H, N*H*$_{Boc}$), 4.64 (pseudo-t, 2 H, H_{Cp}), 4.31 (pseudo-t, 2 H, H_{Cp}), 4.25−4.21 (mult., 7 H, H_{Cp}, O*H*, C$_\alpha$*H*), 3.70 (mult., 1 H, C$_\beta$*H*), 3.01 (mult., 1 H, C$_\beta$*H*), 2.42−2.34 (mult., 2 H, C*H*$_2$-CH$_3$), 1.96−1.87 (mult., 2 H, C*H*$_2$-CH$_3$), 1.46 (s, 9 H, C(C*H*$_3$)$_3$), 1.12−1.06 (overlapping t, 6 H, CH$_2$-C*H*$_3$),. − ^{13}C NMR ($CDCl_3$): δ = 170.3 (*C*=O), 169.1 (C_{Fc} = O), 155.1 (C_{Boc} = O), 137.5, 132.6, 119.6, 118.8 (C_{Ar}), 90.4 [*C*≡C-C(Et)$_2$], 83.6 (C≡*C*-C(Et)$_2$), 81.1 (*C*(CH$_3$)$_3$), 76.0, 70.3, 69.7, 68.1 (C_{Cp}), 62.3 (C$_\beta$), 58.6 [C≡C-*C*(Et)$_2$], 55.9 (C$_\alpha$), 31.1 (*C*H$_2$-CH$_3$), 28.3 [C(*C*H$_3$)$_3$], 9.1 (CH$_2$-*C*H$_3$). − ^{15}N NMR ($CDCl_3$): δ = −295 (*N*H$_{Boc}$), −258 (*N*H), −252 (*N*H$_{Ar}$). − IR: ṽ (cm^{-1}) = 3235 (br, m), 1686 (m), 1643 (m). − Raman: 2227 cm^{-1}. − CV: +193 mV. − UV: 442 (400). − MS (EI, 70 eV): 601 (100), 572 (11), 501 (23), 385 (4), 229 (89), 213 (64), 185 (16). − $C_{32}H_{39}FeN_3O_5$ (601.52): calcd. C 63.9, H 6.5, N 7.0; found C 64.1, H 6.7, N 6.9. − **8b**, m.p. 100°C. − ^{1}H NMR ($CDCl_3$): δ = 7.55 (app. d, 2 H, H_{Ar}), 7.45 (s, 1 H, N*H*$_{Ar}$), 7.38 (app. d, 2 H, H_{Ar}), 6.19 (s, 1 H, N*H*-C(Et)$_2$), 4.85 (br, 1 H, N*H*$_{Boc}$), 4.76 (pseudo-t, 2 H, H_{Cp}), 4.41 (s, 2 H, H_{Cp}), 4.23 (s, 5 H, H_{Cp}), 4.00 (mult., 1 H, C$_\alpha$*H*), 2.32−2.26 (mult., 2 H, C*H*$_2$-CH$_3$), 1.84−1.80 (mult., 2 H, C*H*$_2$-CH$_3$), 1.67−1.62 (mult., 2 H, C$_\beta$*H* und C$_\gamma$*H*) 1.46−1.42 (mult., 1 H, C$_\beta$*H*), 1.42 [s, 9 H, C(C*H*$_3$)$_3$], 1.04−0.97 (overlapping t, 6 H, CH$_2$-C*H*$_3$), 0.94−0.90 (mult., 6 H, C$_\delta$*H*). − ^{13}C NMR ($CDCl_3$): δ = 171.3 (*C*=O), 168.6 (C_{Fc} = O), 155.7 (C_{Boc} = O), 138.2, 132.7, 119.2, 118.1 (C_{Ar}), 90.0 [*C*≡C-C(Et)$_2$], 83.5 [C≡*C*-C(Et)$_2$], 80.1 [*C*(CH$_3$)$_3$], 76.0, 71.0, 69.9, 68.3 (C_{Cp}), 58.6 (C≡C-*C*(Et)$_2$), 53.0 (C$_\alpha$), 40.9 (C$_\beta$), 30.3 und 30.9 (*C*H$_2$-CH$_3$), 28.3 [C(*C*H$_3$)$_3$], 24.8 (C$_\gamma$), 22.1 und 22.9 (C$_\delta$), 8.9 und 9.0 (CH$_2$-*C*H$_3$). − ^{15}N NMR ($CDCl_3$): δ = −289 (*N*H$_{Boc}$), −258 (*N*H), −254 (*N*H$_{Ar}$). − IR: ṽ (cm^{-1}) = 3421 (m), 3324 (m), 1701 (sh), 1654 (br, m). − Raman: 2228 cm^{-1}. − CV: +197 mV. − UV: 444 (400). − MS (EI, 70 eV): 627 (100), 571 (3), 553 (29), 385 (30), 213 (64), 185 (36), 129 (21). − $C_{35}H_{45}FeN_3O_4$ (627.60): calcd. C 67.0, H 7.2, N 6.7; found C 66.5, H 6.9, N 6.7. − **8c**. m.p. 194°C. − ^{1}H NMR ($CDCl_3$): δ = 7.85 (s,br, 1 H, N*H*$_{Ar}$), 7.39−7.20 (mult., 9 H, H_{Ar} and H_{Phe}) 5.70 (s, 1 H, N*H*$_{DEPA}$), 5.30 (br, 1 H, N*H*$_{Boc}$), 4.64 (pseudo-t, 2 H, H_{Cp}), 4.31 (s, 2 H, H_{Cp}), 4.40 (mult., 1 H, C$_\alpha$*H*), 4.21 (s, 5 H, H_{Cp}), 3.13 (d, *J* = 6.9 Hz, 2 H, C$_\beta$*H*), 2.43−2.35 (mult., 2 H, C*H*$_2$-CH$_3$), 1.95−1.87 (mult., 2 H, C*H*$_2$-CH$_3$), 1.40 (s, 9 H, C$_{Boc}$*H*$_3$), 1.12−1.06 (overlapping t, 6 H, CH$_2$-C*H*$_3$). − ^{13}C NMR ($CDCl_3$): δ = 169.6 (*C*=O), 169.1 (C_{Fc} = O), 155.8 (C_{Boc} = O), 137.4, 132.5, 119.5, 118.6 (C_{Ar}), 136.5, 129.3, 128.8, 127.8 (C_{Phe}), 90.6 [*C*≡C-C(Et)$_2$], 83.3 [C≡*C*-C(Et)$_2$], 80.7 [*C*(CH$_3$)$_3$], 76.0, 70.3, 69.7, 68.1 (C_{Cp}), 58.6 [*C*(Et)$_2$], 56.8 (C$_\alpha$), 38.3 (C$_\beta$), 30.3 und 31.1 (*C*H$_2$-CH$_3$), 28.2 [C(*C*H$_3$)$_3$], 9.24 and 9.11 (CH$_2$-*C*H$_3$). − ^{15}N NMR ($CDCl_3$): δ = −291 (*N*H$_{Boc}$), −262 (*N*H), −249 (*N*H$_{Ar}$). − IR: ṽ (cm^{-1}) = 3432 (br, m), 3310 (br, m), 1665 (br, s), 1601 (sh). − Raman: 2226 cm^{-1}. − MS (EI, 70 eV): 661 (100), 644 (28), 587 (53), 561 (33), 229 (85), 120 (52). − $C_{38}H_{43}FeN_3O_4$ (661.62): calcd. C 69.0, H 6.6, N 6.4; found C 68.7, H 6.5, N 6.3. − **8d**, m.p. 107°C. − ^{1}H NMR ($CDCl_3$): δ = 8.53 (s,br, 1 H, N*H*$_{Ar}$), 7.47 (app. d, 2 H, H_{Ar}), 7.38 (app. d, 2 H, H_{Ar}), 5.70 (s, 1 H, N*H*-C(Et)$_2$), 5.25 (d, *J* = 8 Hz, 1 H, N*H*$_{Boc}$), 4.63 (pseudo-t, 2 H, H_{Cp}), 4.40 (mult., 1 H, C$_\alpha$*H*), 4.30 (s, 2 H, H_{Cp}), 4.21 (s, 5 H, H_{Cp}), 2.63−2.57

(mult., 2 H, $C_\gamma H$), 2.41−2.36 (mult., 2 H, CH_2-CH_3), 2.20−2.13 (mult., 1 H, $C_\beta H$), 2.10 (s, 3 H, S-CH_3), 2.01−1.91 (mult., 3 H, $C_\beta H$ and CH_2-CH_3), 1.43 [s, 9 H, C(CH_3)$_3$], 1.10−1.06 (overlapping t, 6 H, CH_2-CH_3). − ^{13}C NMR ($CDCl_3$): δ = 170.3 (C=O), 169.1 (C_{Fc} = O), 155.9 (C_{Boc} = O), 137.8, 132.4, 119.4, 118.4 (C_{Ar}), 90.5 [C≡C-C(Et)$_2$], 82.4 [C≡C-C(Et)$_2$], 80.5 [$C(CH_3)_3$], 76.0, 70.3, 69.6, 68.0 (C_{Cp}) 58.5 [C(Et)$_2$], 54.2 (C_α), 31.3 (C_β), 31.34 und 31.01(CH_2-CH_3), 30.3 (C_γ), 28.3 [C(CH_3)$_3$], 15.3 (S-CH_3), 9.08 and 8.23 (CH_2-CH_3). − ^{15}N NMR($CDCl_3$): δ = −291 (NH_{Boc}), −262 (NH), −249 (NH_{Ar}). − IR: $\tilde{\nu}$ (cm^{-1}) = 3433 (br, m), 3316 (br, m), 1685 (br, s), 1648 (br, s). − Raman: 2229 cm^{-1}. − MS (ESI): 646 (M + H), 668 (M + Na), 684 (M + K). − $C_{34}H_{43}FeN_3O_4S$ (645.64): calcd. C 63.3, H 6.7, N 6.5; found C 62.9, H 6.7, N 6.2. − **10**, m.p. 132°C. − ^{1}H NMR ($CDCl_3$): δ = 7.72 (app. d, 2 H, H_{Ar}), 7.49 (app. d, 2 H, H_{Ar}), 6.49 (d, J = 8 Hz, 1 H, NH_{Leu}), 5.69 (s, 1 H, NH-C(Et)$_2$), 4.82 (mult., 1 H, $C_\alpha H$), 4.65 (pseudo-t, 2 H, H_{Cp}), 4.32 (s, 2 H, H_{Cp}), 4.21 (s, 5 H, H_{Cp}), 3.75 (s, 3 H, OCH_3), 2.41−2.32 (mult., 2 H, CH_2-CH_3), 2.00−1.91 (mult., 2 H, CH_2-CH_3), 1.78−1.63 (mult., 3 H, $C_\beta H_2$ and $C_\gamma H$), 1.13−1.07 (overlapping t, 6 H, CH_2-CH_3), 0.97−0.95 (overlapping t, 6 H, $C_\delta H$). − ^{13}C NMR ($CDCl_3$): δ = 173.6 (C=O), 169.1 (C_{Fc} = O), 166.3 (C_{OMe}=O), 133.2, 131.9, 127.0, 126.4 (C_{Ar}), 93.6 [C≡C-C(Et)$_2$], 82.8 [C≡C-C(Et)$_2$], 76.8, 70.3, 69.7, 68.1 (C_{Cp}), 58.2 [C(Et)$_2$], 52.4 (OCH_3), 51.2 (C_α), 41.8 (C_β), 31.0 (CH_2-CH_3), 25.0 (C_γ), 22.0 and 22.8 (C_δ), 9.0 (CH_2-CH_3). − ^{15}N NMR ($CDCl_3$): δ = −267 (NH_{Leu}), −263 (NH). − IR: $\tilde{\nu}$ (cm^{-1}) = 3313 (m), 1746 (m), 1637 (s), 1608 (w). − Raman: 2227 cm^{-1}. − CV: +197 mV. − UV: 444 (400). − MS (EI, 70 eV): 570 (100), 541 (4), 229 (34), 213 (35), 185 (9). − $C_{32}H_{38}FeN_2O_4$ (570.51): calcd. C 67.3, H 6.7, N 4.9; found C 67.5, H 6.8, N 4.8. − **9**: Compound **3** (267 mg, 1 mmol) was dissolved in methanol (30 mL). A solution of copper(II) acetate monohydrate (199.6 mg, 1 mmol) in a mixture of methanol (20 mL) and pyridine (10 mL) was added dropwise and the resulting solution was stirred at 60°C for one hour. After cooling to room temp., the solution was reduced to about one third of the initial volume and CH_2Cl_2 and water were added. The organic phase was separated, washed three times with water and dried with Na_2SO_4. After filtration, the solvent was removed on a rotary evaporator to yield 101 mg (38%) of light-orange product, m.p. 108°C. − ^{1}H NMR ($CDCl_3$): δ = 5.76 (br, 2 H, NH), 4.65 (pseudo-t, 4 H, H_{Cp}), 4.34 (pseudo-t, 4 H, H_{Cp}) 4.24−4.20 (mult., 14 H, H_{Cp} and CH_2). − ^{13}C NMR ([D$_6$]DMSO): δ = 169.0 (C=O), 76.7 (C≡C-C≡C), 75.3, 70.2, 69.3, 68.2 (C_{Cp}), 65.5 (C≡C-C≡C), 28.7 (CH_2). − IR: $\tilde{\nu}$ (cm^{-1}) = 3324 (br), 3306 (br), 1637 (s), 1533 (s). − MS (EI, 70 eV): 532 (100), 467 (19), 401 (14), 211 (15), 121 (19). − $C_{28}H_{24}Fe_2N_2O_2$ (532.20): calcd. C 63.2, H 4.6, N 5.3; found C 62.9, H 4.3, N 5.1. − **11**: Boc-protected cystine (10 mmol, 4.41 g) was dissolved in THF (100 mL) at room temp. and neutralized with *N*-methylmorpholine (2.02 g, 20 mmol). Isobutyl chloroformate (2.74 g, 20 mmol) was added and a white precipitate was rapidly formed. 4-iodoaniline (4.38 g, 20 mmol) was added and the solution was allowed to stir for one hour. The *N*-methylmorpholine hydrochloride was removed by filtration and the solvent was removed on a rotary evaporator. The resulting residue was redissolved in ether, the organic phase was washed three times with water and dried with Na_2SO_4. After filtration the solvent was removed to yield 7.1 g (84%) of **11**. **11** can be recrystallized from hot chloroform, m.p. 218°C. − ^{1}H NMR ([D$_6$]DMSO): δ = 10.14 (s, 2 H, NH), 7.61 and 7.42 (app. d, 4 H each, H_{Ar}), 7.20 (d, 2 H, $N_{Boc}H$, J = 7.6), 4.32 (mult., 2 H, $C_\alpha H$) 3.14 and 2.94 (mult., 2 H each, $C_\beta H_2$), 1.36 (s, 18 H, C(CH_3)$_3$). − ^{13}C NMR ([D$_6$]DMSO): δ = 169.3 (C=O), 155.2 (C_{Boc} = O), 138.5, 137.3, 121.7, 87.0 (C_{Phe}), 78.4 (C (CH_3)$_3$), 54.5 (C_α) 40.1 (C_β), 28.1 [C(CH_3)$_3$]. − ^{15}N NMR ([D$_6$]DMSO): δ = −290 (N_{Boc}), −249 (N_{Ar}). − IR: $\tilde{\nu}$ (cm^{-1}) = 3341 (m), 1685 (m), 1670 (s). − MS (EI, 70 eV): 842 (< 1%), 422 (9), 366 (32), 219 (46), 57 (88), 41 (100). − $C_{28}H_{36}I_2N_4O_6S_2$ (842.55): calcd. C 39.9, H 4.3, N 6.7; found C 40.0, H 4.4, N 6.6. − **12**, purified by HPLC: ^{1}H NMR ($CDCl_3$): δ = 9.32 (br, 2 H, NH_{Ar}), 7.61−7.54 (mult., 4 H, H_{Ar}), 7.38−7.36 (mult., 4 H, H_{Ar}), 5.84 (br, 1 H, NH-CH_2), 5.61 (br, 2 H, NH_{Boc}), 4.92 (mult., 2 H, $C_\alpha H$), 4.68 (pseudo-t, 2 H, H_{Cp}), 4.37−4.34 (mult., 4 H, H_{Cp} and CH_2), 4.21 (s, 5 H, H_{Cp}), 3.09−2.96 (mult., 4 H, $C_\beta H_2$), 1.45 [s, 18 H, C(CH_3)$_3$]. − ^{13}C NMR ($CDCl_3$): δ = 169.8 (C_{Fc} = O), 168.5 (C_{Cys}=O), 156.1 (C_{Boc} = O), 137.8, 137.2, 132.2, 122.6, 119.6, 120.4, 118.7, 85.3 (C_{Ar}), 88.2 (C≡C-CH_2), 82.8 (C≡C-CH_2), 80.5 [$C(CH_3)_3$], 75.1, 70.7, 69.8, 68.2 (C_{Cp}), 55.6 (C_α), 47.4 (C_β), 30.0 (CH_2), 28.4 [C(CH_3)$_3$]. − ^{15}N NMR ($CDCl_3$): δ = −292 (NH_{Boc}), −275 (NH), −250 (NH_{Ar}). − IR (CH_2Cl_2): 3420 (w), 3327 (w), 1683 (br, s), 1659 (sh). − MS (ESI, in CH_2Cl_2): 1004 [M + Na]. − $C_{42}H_{48}FeIN_5O_7S_2$ (981.76): calcd. C 51.4, H 4.9, N 7.1; found C 51.9, H 5.2, N 7.1. − **13**: Compound **13** could not be separated completely from **12**. Compounds **12** and **13** have virtually identical NMR spectra, except for the integration ratios. − MS (ESI, in CH_2Cl_2): 1043 [M + Na], 1160 [M + K].

Table 1. Crystallographic details

	3	**4**
Empirical formula	$C_{14}H_{13}FeNO$	$C_{18}H_{21}FeNO$
Formula weight	267.10	323.21
Temperature [K]	293 (2)	100 (2)
Crystal system, space group	orthorhombic, *Pbca*	orthorhombic, *Pbca*
Diffractometer used	Enraf−Nonius CAD4	Siemens SMART
Unit cell dimensions, l. s., on	25 reflections	8192 reflections
a [Å]	11.636(2)	11.844(2)
b [Å]	9.881(2)	9.962(1)
c [Å]	21.053(3)	25.770(4)
Volume [Å^3]	2420.6(7)	3040.6(8)
Z	8	8
Absorption coefficient [mm^{-1}]	1.227	0.990
Absorption correction	None	SADABS (G. Sheldrick, 1994)
θ range for data collection [°]	2.61 to 25.99	1.58 to 30.00
Reflections collected, Independent reflections	2376, 2376	28110, 4369
R_{int}	−	0.0767
Data/Restraints/ Parameters	2067/0/160	4054/0/195
Goodness-of-fit on F^2	1.050	1.039
Final R indices $[I > 2\sigma(I)]$[a]	R_1 = 0.0402, wR_2 = 0.1004	R_1 = 0.0465, wR_2 = 0.0895
R indices (all data)[a]	R_1 = 0.0701, wR_2 = 0.1137	R_1 = 0.0809, wR_2 = 0.1018
Largest diff. peak and hole [eA^{-3}]	0.656, −0.434	0.557, −0.561

[a] $R_1 = (\Sigma||F_o| - |F_c||/\Sigma|F_o|)$; $wR_2 = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma wF_o^4]^{1/2}$.

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