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Synthesis of organometallic amines and their coupling to the C-terminus of amino acids and peptides

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Abstract

This work describes the use of organometallic amines for the labelling of the C-terminus of amino acids and peptides. *N*-substituted ferrocene-methylamines **2** could be readily prepared and coupled to a variety of amino acids in good yield. The novel ferrocene amino acid derivatives **4** exist in two conformations in solution, which differ in the orientation of the tertiary amide bond and interconvert slowly in solution. For the glycine derivative **4a** the activation energy was determined to be 70.3 kJ mol^{-1} by ^{1}H-NMR spectroscopy. All new compounds were completely characterised spectroscopically including ^{15}N-NMR by indirect detection 2D ^{1}H-^{15}N-NMR. The potential difference of ca. + 50 mV between ferrocene derivatives **2** and the ferrocenyl amino acids **4** in cyclic voltammetry was used to monitor the peptide coupling reaction in situ. Also described are attempts towards the synthesis of organometallic amine derivatives of benzene chromium tricarbonyl and η-cyclopentadienyl molybdenum dicarbonyl. The solid state structures of $CpMo(CO)_2–C_2H_4–N(CO)_2C_6H_4$ **14** and $CpFeC_5H_4–CH_2–NH–CH_2$-*p*-$CH_3–C_6H_4$ **2a** (Cp: η-cyclopentadienyl) were determined by single-crystal X-ray diffraction.

Keywords: Bioorganometallic chemistry; Ferrocene derivatives; Chromium derivatives; Amino acids; Biosensors

1. Introduction

Bioorganometallic chemistry is a growing area spanning inorganic to biomedical chemistry [1–4]. In its applications it makes use of the unique spectroscopic or chemical properties of organometallic complexes for the synthesis or detection of biomolecules. For example, ferrocene has been employed as a marker for the electrochemical detection of amino acids in liquid chromatography (ECD-HPLC) [5,6] or in selective anion sensors [7]. The group of Jaouen has pioneered the use of infrared spectroscopy in immuno-assays. They have demonstrated that organometallic carbonyl compounds when covalently bound to the biological target can achieve the same sensitivity in immuno-assays as conventional radioactive markers, thus avoiding the need to handle radioactive, 'hot' material [8–16]. However, up to now this procedure is limited to special cases where an activated organometallic acid is coupled to biologically active amines. Obviously, labelling is restricted to the N-terminus of peptides, which imposes a major limitation on the solid state synthesis of labelled peptides. In this work we describe the synthesis of organometallic amines and their coupling to the C-terminus of amino acids and peptides. Electrochemical data on ferrocene derivatives underscore the potential of the new bioorganometallics for electrochemical assays. A slightly different approach to the labelling of peptides involves π-complexation of arene rings (as in tyrosine or phenylalanine) with unsaturated organometallic fragments [17–19]. Although this approach is obviously very selective, as shown for the hormone peptide secretin by Grotjahn et al. [19] it is by its very nature limited to the labelling of aromatic amino acids.

Starting from ferrocene aldehyde **1**, a variety of secondary amines **2** were synthesized. Reaction of **1** with primary amines in refluxing chloroform yields Schiff bases **3** in excellent yield [20–22]. The formation of **3** can be followed by ^{1}H-NMR spectroscopy by the disappearance of the aldehyde proton resonance at 9.9 ppm,

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and the occurrence of a new singlet at ca. 8.2 ppm for the RN=C(Fc)*H* proton. Subsequent reduction of Schiff bases **3** with sodium borohydride in methanol yields amines **2** as yellow crystalline solids [22–24]. An X-ray single-crystal structure of **2a** is shown in Fig. 1. The structure consists of discrete monomeric molecules, Fe–Cp(centroid) distances are 1.650 Å (unsubstituted Cp) and 1.643 Å as expected. The conformation of the two Cp rings is almost eclipsed, with a twist angle of 2.0° (average of H–C–C–H vectors). These structural features are similar to two other structures of ferrocenemethylamino derivatives [22,24]. In general, macrocyclic N-donor-substituted ferrocenes have recently gained considerable attention owing to their use as redox-active ion-sensors [7].

Ferrocene amine **2a** can be coupled with a variety of *N*-protected amino acids using 3-hydroxy-1,2,3-benzotriazin-4(3*H*)one (DhbtOH)/dicyclhexylcarbodiimide (DCC) in CH_2Cl_2/DMF as shown in Scheme 1. The resulting amides **4** are obtained in up to 75% yield after chromatography on silica as orange oils or solids (**4e**). The most notable feature, and at the same time unambiguous proof of their constitution, is the complex NMR spectra of amides **4** (Fig. 2). The protons on the two methylene groups appear as two singlets in the ^{1}H-NMR spectrum of **2a** (Fig. 2, top trace). In amides **4**, the carbonyl group can be *cis* or *trans* oriented with respect to the substituents on the nitrogen atoms, giving rise to two pairs of singlets as exemplified for the glycine derivative **4a** (middle trace in Fig. 2). An even more complex situation arises for all chiral amino acids. Due to the presence of a chiral centre at the C_α atom, the protons on each methylene group become diastereotopic. This causes each singlet not only to split into two further signals, but the singlets now appear as AB spin systems which in addition may partially overlap (Fig. 2, bottom trace for **4d**). This gives rise to eight signals of equal intensity.

This reasoning is supported by the C–H correlated spectrum of **4d**. Since each pair of diastereotopic hydrogen atoms must be bonded to the *same* carbon atom, but *separate* carbon resonances are expected for *cis* and *trans* isomers of **4d**, a characteristic pattern of cross peaks is expected, with each of the four carbon resonances having cross peaks to two diastereotopic hydrogen atoms (Fig. 3). At the same time, C–H correlated spectra serve to unambiguously assign the partially overlapping signals of all proton resonances between 3.5 and 5 ppm (see Fig. 2) due to the well-separated ^{13}C resonances in characteristic regions (70.5–68 ppm for the Cp–C, ca. 50 ppm for C_α of the amino acids and 49–44 ppm for the CH_2 groups).

Dynamic ^{1}H-NMR spectroscopy was used to determine the energy barrier for rotation about the amide bond in **4a**. In DMSO-d_6, coalescence was observed for all methylene singlets in the range between 40 and 100°C and the activation energy was determined to be 70.3 ± 0.5 kJ mol^{-1}. Two-dimensional exchange spectroscopy (2D-EXSY) was used to identify the interchanging methylene protons in the other amides **4**. A quantitative examination of the exchange spectra shows that both *cis* and *trans* conformers are present in solution to the same amount and hence very similar in energy [25]. In an attempt to induce a preference for one conformer in solution, amide **5** was prepared from (2-hydroxy-ethylamino)-methylferrocene **2b** by reaction with activated Boc-alanine (Scheme 2). One isomer is expected to be stabilized by an intramolecular hydrogen bond from the hydroxy group to the neighbouring amide carbonyl group, as suggested in Scheme 2. However, signals for both isomers were observed with approximately equal intensity in the ^{1}H-NMR spectrum of **5**, indicating no specific preference for either the *cis* or *trans* conformation. Infrared (IR) spectroscopy is a powerful tool for the elucidation of hydrogen bonding [26,27]. In the solid state, a strong, very broad band

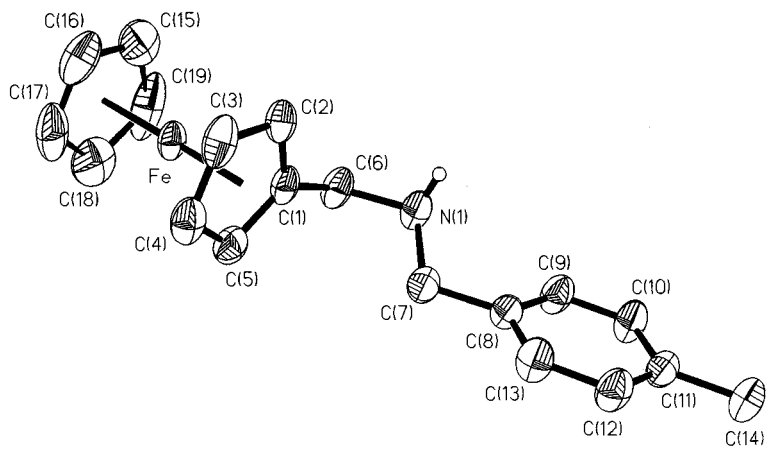
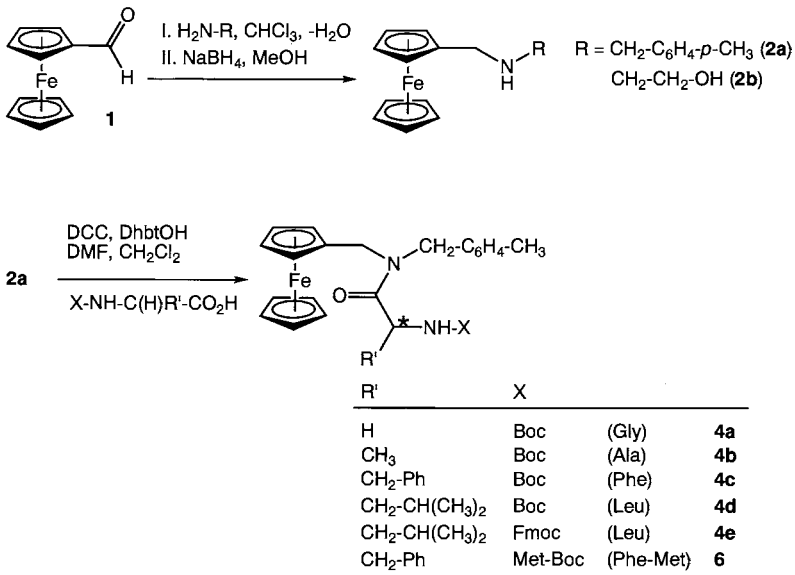


Fig. 1. ORTEP drawing of **2a**. Selected bond lengths and angles: Fe–C_{Cp} (av.) 2.030 Å, Fe–Cp(centroid) 1.643 Å and 1.650 Å (unsubstituted Cp), C(1)–C(6) 1.507(4) Å, C(1)–C(6)–N(1) 114.2(2)°, angle between planes C(1) to C(5) and C(8) to C(13) 87.8°.



Scheme 1.

around 3423 cm^{-1} is indicative of hydrogen bridges in **5**. In contrast, this band is not observed in CH_2Cl_2 solution and two sharp bands at 3618 and 3428 cm^{-1} rather point to O–H and amide N–H not engaged in any hydrogen bonding. In addition, the position of all amide carbonyl stretches remains almost unchanged in CH_2Cl_2 solution and KBr disks. It thus appears that *inter*-molecular hydrogen bonds are important for the solid state structure of **5**, but break up in solution. Janiak et al. have utilized *inter*-molecular hydrogen bonds to stabilize a variety of small water clusters [28,29], and recently stabilisation of the first Ni(0) alkyne complex was achieved via *intra*-molecular hydrogen bonds [30].

An electrochemical study was carried out on compounds **4** to see whether a recognition of the attached amino acid via a potential shift of the ferrocene/ferrocenium couple would be possible (Table 1) [31,32]. All ferrocene amino acid conjugates **4** show a reversible one-electron oxidation at ca. + 50 mV versus ferrocene/ferrocenium, comparable to the shift of + 47 mV induced by an additional methyl group on ferrocene [24,33]. Our values for the ferrocene amines **2** compare very well to values previously reported for macrocyclic amino-ferrocenes [22]. Although the exact position of the redox potential can be very accurately determined from a square-wave voltammogram, a maximum difference of 10 mV between different amino acids is at present too small to be analytically useful for the discrimination of different amino acids. There is, however, a potential change of about 50 mV between amines **2** and amides **4**, thus allowing us to follow the kinetics of the coupling reaction electrochemically.

The lipophilic ferrocene moiety was introduced into peptide chemistry by the group of Eckert to increase the solubility of the peptide in organic solvents, as exemplified for the hexapeptide $(Fem\text{-}gly)_6$. This hexapeptide was soluble in a hexane–THF mixture and chromatographic purification was facilitated [5,34,35]. The UV–vis spectra of **4** serve to underscore this second aspect with absorptions of the ferrocene moiety at 440 nm. The position of these ferrocene transitions is hardly affected by the presence of an amide bond and does not permit a discrimination of the attached amino acid in **4**.

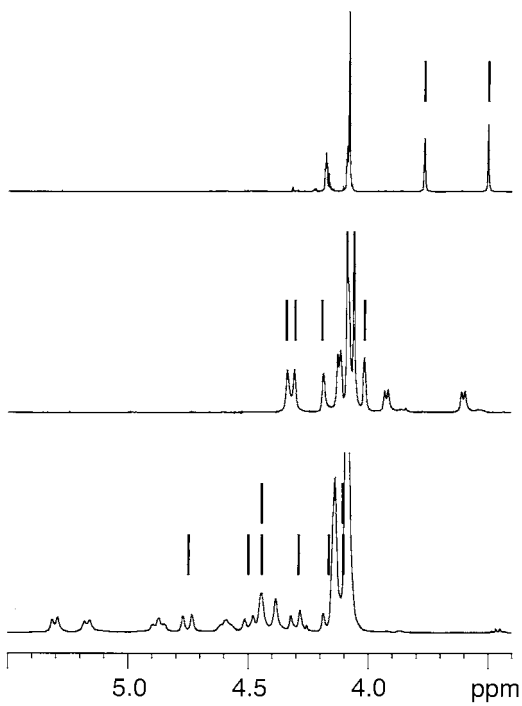


Fig. 2. ^{1}H-NMR spectra of **2a** (top trace), **4a** (middle trace) and **4d** (bottom trace) in $CDCl_3$ at room temperature. CH_2 groups discussed in the text are marked by vertical bars.

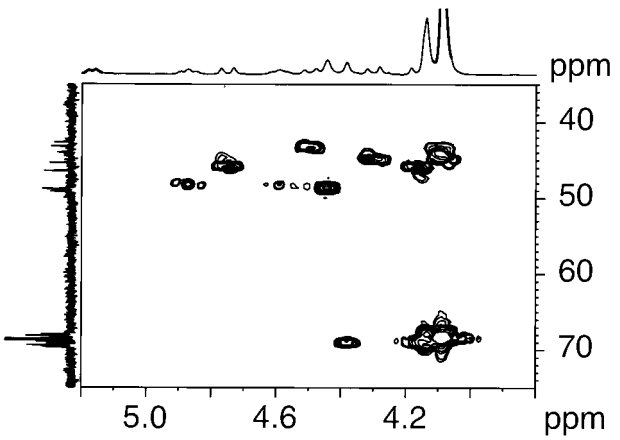


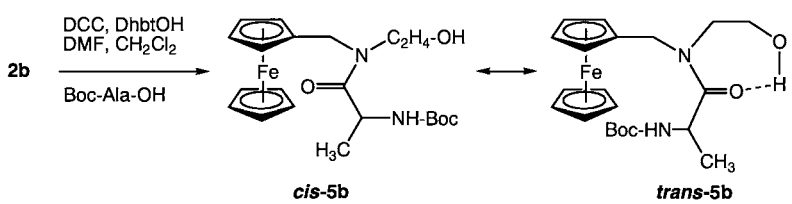
Fig. 3. Partial $^{1}H-^{13}C$-HMQC spectrum, showing H–C connectivities of the diastereotopic CH_2 groups in **10d**.

The methodology outlined before is by no means restricted to simple amino acids. We have prepared the *N*-protected methioninyl-phenylalanine (*N*-Boc-Met-Phe-OH) [36] and successfully coupled this dipeptide to ferrocenylmethylamine **2a** to yield the ferrocene-labelled dipeptide **6** in 75% yield after chromatography (Scheme 1). As in amides **4**, most signals in the NMR spectra of **6** are doubled due to the presence of two rotational isomers about the tertiary amide bond. Even the very remote signals for the thioether and the benzylic methyl group appear as two singlets with 10 and 15 Hz separation, respectively. Again, a complete signal assignment even in the crowded region around 4 ppm (overlapping Cp, C_α and CH_2 signals) is achieved by the help of EXSY- and C–H-correlated spectra (see Section 2).

We made an attempt to synthesize amino acid derivatives of benzene chromium tricarbonyl in order to extend the analytical tool-box towards IR spectroscopy. *o*-Toluidine-chromium-tricarbonyl **7** is a moderately air-stable organometallic amine. However, **7** did not react with activated amino acids using the isobutyl-chloro-formiate/*N*-methyl-morpholine or dicyclohexyl-carbodiimide (DCC)/*N*-hydroxy-succinimide methods, both of which represent standard protocols in peptide chemistry [36,37]. We suspected that the reason is a drastically decreased nucleophilicity of the amino group due to the strongly electron-withdrawing chromium-tricarbonyl group on the phenyl ring, which has been compared to a *para*-NO_2 group. Consequently, (η^6-chromium-tricarbonyl)-*p*-methyl-benzyl-amine **8** appeared to be a better synthetic target. Since the direct reaction of *p*-methyl-benzyl-amine **9** with $Cr(CO)_6$ did not lead to π-complexation, the nitrogen atom was protected with the *tert*-butoxy-carbonyl (Boc) group to yield *N*-Boc-*p*-methyl-benzylamine **10**. **10** cleanly reacted with $Cr(CO)_6$ to *N*-Boc-(η^6-chromium-tricarbonyl)-*p*-methyl-benzylamine **11** (Scheme 3). Spectroscopic data of **11** support our initial notion that the amino group should be 'electronically decoupled' from the benzene–chromium–tricarbonyl moiety. For instance, IR stretching frequencies for the A bands of the carbonyl groups are 1952 cm^{-1} for **7** and 1946 cm^{-1} for aniline–chromium–tricarbonyl, but 1974 cm^{-1} for **11** and 1971 cm^{-1} for benzene–chromium–tricarbonyl [38]. To our disappointment, amine deprotection of **11** under the usual acidic conditions (trifluoro acetic acid in CH_2Cl_2, HPF_6 or HBF_4 in Et_2O) was usually accompanied by massive decomposition of the chromium compound. A small amount of pure (η^6-chromium-tricarbonyl)-*p*-methyl-benzyl-amine **8** could finally be obtained by using 10% H_2SO_4 in dioxane. However, the yield of **8** was too low for **8** to be a useful synthon. In order to demonstrate that toluidine–chromium–tricarbonyl derivatives of amino acids are by no means inherently unstable, *N*-Boc-alanine-(toluidinyl–chromium–tricarbonyl) **12** was synthesized by refluxing a mixture of *N*-Boc-alaninyl-*o*-toluidine **13** and $Cr(CO)_6$ in Bu_2O–THF overnight and isolated as a yellow powder (**12**: $m/z = 414$ [M^+] and 386 [M^+–CO], IR: 1948, 1881 and 1851 cm^{-1}). However, this procedure lacks selectivity as *any* aromatic ring, e.g. the ones present in aromatic amino acids like phenylalanine and tryptophane, could in principle react with $Cr(CO)_6$. It is

Table 1
Electrochemical data of ferrocenes described in this work (ca. 10^{-4} mol l^{-1} solutions in CH_2Cl_2+0.1 mol l^{-1} Bu_4NPF_6 as supporting electrolyte, referenced vs. Fc/Fc^+)

Ferrocene derivative	E_p (mV)
2a	−8
2b	−2
4b	+45
4c	+49
4d	+55

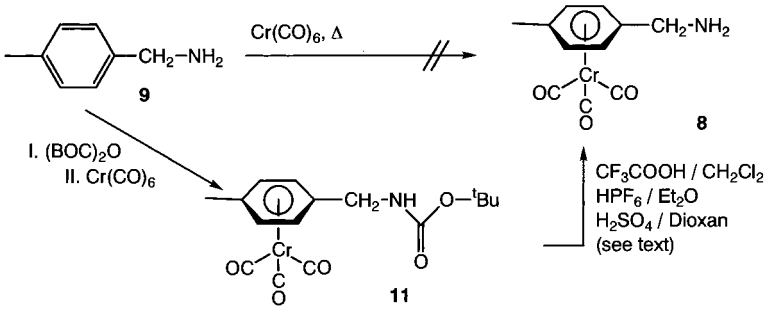


Scheme 2.

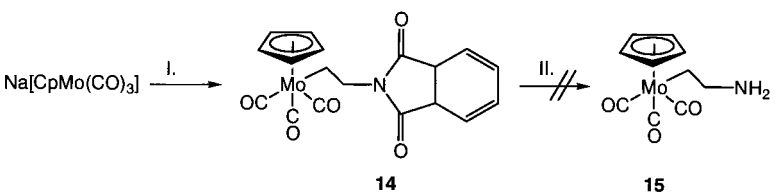
interesting to note that Sergheraert et al. reported the complexation of phenylalanine with $Cr(CO)_6$ in deaerated mixtures of THF and water [39]. Also, the harsh reaction conditions (14 h at 135°C) may be unsuitable for more sensitive peptides.

We thus turned to the synthesis of η^5-cyclopentadienyl molybdenum derivatives. Reaction of the $[CpMo(CO)_2]^-$ anion with 2-bromo-ethyl-phthalimide gave [(η-cyclopentadienyl)-molybdenum-tricarbonyl]-ethyl-phthalimide **14**, although in only 15% yield (Scheme 4). Reaction with 2-iodo-ethyl-phthalimide, on the other hand, gave no **14** at all [13,40]. For the deprotection of phthalimides, either acidic conditions or hydrazinolysis were considered to obtain [(η-cyclopentadienyl) - molybdenum - tricarbonyl] - 2 - amino - ethane **15**. While reaction with aqueous HCl led mainly to decomposition of **14**, no reaction with hydrazine in refluxing ethanol was observed even after prolonged reaction times. The molecular structure of **14** in the solid state was determined in quest for a possible reason for this unexpected behaviour on a molecular basis (Fig. 4). The complex exhibits four-legged piano stool geometry with the three carbonyl groups and the alkyl substituent serving as legs. The Mo–Cp(centroid) distance is 2.011 Å, the Mo–CH_2 distance is 2.326(3) Å and the CH_2–Mo–Cp(centroid) angle 111.5°. These values compare well with that of other $CpMo(CO)_3$-alkyl derivatives, namely $CpMo(CO)_3CH_2CH_3$ [41], $CpMo(CO)_3CH_2COOH$ [42] and $CpMo(CO)_3CH_2COO$–NS (NS = *N*-succinimidyl) [40]. The latter compound, although an activated ester, did not react with amines such as β-alanine methyl ester under conditions where the closely related activated ester $[(\eta\text{-}C_5H_4COO\text{–}NS)Mo(CO)_3CH_3]$ gave the β-alaninyl amide quite readily. Prout and co-workers reported a decreased acidity of acids $CpM(CO)_nCH_2COOH$ (M = Fe, $n = 2$ and M = Mo, $n = 3$) [42]. Both findings were explained by an interaction between the metal–carbon bonding electrons and the carbonyl π-orbitals [42,43]. We propose a related interaction as a rationale for our difficulty in deprotecting the phthalimido group in **14**.

We have introduced a versatile method for the synthesis of secondary ferrocene methyl-amino derivatives. These amines can be readily coupled to the C-terminus of amino acids and peptides using standard protocols in peptide chemistry. NMR spectroscopy gives valuable insight into the constitution and conformation of this interesting class of compounds, while IR spectroscopy highlights the importance of hydrogen bonding. Electrochemistry allows to monitor the progress of the coupling reaction in situ and provides a handle for the sensitive electrochemical detection of the peptide in less than μmol quantities. Using the fundamental insights from this work, we are currently expanding this chemistry towards chiral recognition and general use in peptide chemistry.



Scheme 3.



I. Br-CH_2-CH_2-$N(CO)_2C_6H_4$, THF, -NaBr (15 %) *but not*
I-CH_2-CH_2-$N(CO)_2C_6H_4$, THF, -NaI (0 %).
II. H_2N-NH_2, EtOH *or* HCl, H_2O

Scheme 4.

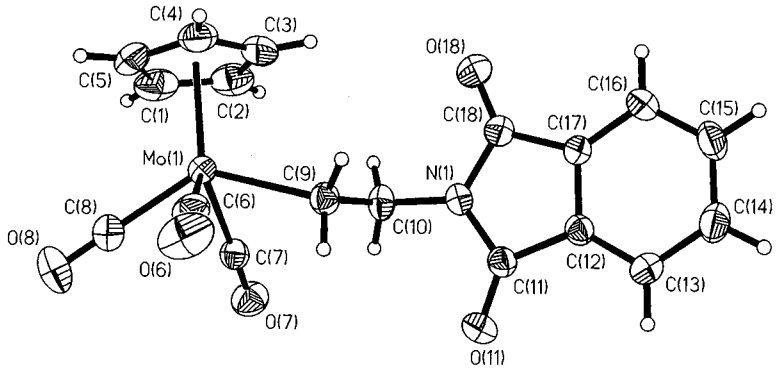


Fig. 4. ORTEP drawing of **14**. Selected bond lengths and angles: Mo(1)–C_{Cp} (av.) 2.340 Å, Mo(1)–Cp(centroid) 2.011 Å, Mo(1)–C(6) 1.985(3) Å, Mo(1)–C(7) 1.984(3) Å, Mo(1)–C(8) 1.983(4) Å, Mo(1)–C(9) 2.326(3) Å, C(9)–C(10) 1.504(4) Å, C(10)–N(1) 1.466(3) Å, Cp(centroid)–Mo(1)–C(9) 111.5°, Mo(1)–C(9)–C(10) 116.2(2)°, angle between planes C(1) to C(5) and N(1), C(11), C(12), C(17), C(18) 84.6°.

2. Experimental

All reactions were carried out in ordinary glassware and solvents without further precautions except where indicated. Chemicals were purchased from Aldrich–Sigma GmbH and used as received, only enantiomerically pure L amino acids were used. 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, additionally in CH_2Cl_2 solution where indicated. Frequencies ν are given in cm^{-1}. UV–vis spectra were recorded on a Perkin–Elmer Lambda 19 spectrometer; only the wavelength of the highest-energy ferrocene transition (benzene chromium moiety in the case of **11**) is given in nm, ε ($dm^3\ mol^{-1}\ cm^{-1}$) 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 are given with intensities (%) and possible composition in brackets. 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 was used. CH_2Cl_2 solutions (ca. 10^{-4} mol l^{-1}) contained 0.1 mol l^{-1} Bu_4NPF_6 as supporting electrolyte. As an internal standard, ferrocene was added in excess as a reference. NMR spectra were recorded at room temperature (r.t.) on 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) spectrometers. ^1H and ^{13}C spectra were referenced to TMS, using the ^{13}C signals or the residual proton signals of the deuterated solvents 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. Pairs of signals originating from *cis–trans* isomers (see text) are grouped by 'and'. ^{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 and coupling constants 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.

3. Preparations

3.1. General preparation of ferrocene-methylamine derivatives **2**

The amine and ferrocene-aldehyde were refluxed in dry $CHCl_3$ for 3 h. After evaporation of the solvent on a rotary evaporator the imine was obtained quantitatively as a yellow solid, the purity of which was checked by ^1H-NMR (see text). The imine was dissolved in dry CH_3OH and 4 equiv. of solid $NaBH_4$ were added in small portions at 0°C. After stirring for 30 min, aqueous NaOH (20 ml, 1 mol l^{-1}) was added and the organic phase extracted with $CHCl_3$ (3 × 100 ml). The combined organic phases were dried and evaporated to dryness to afford the pure ferrocene-methylamine quantitatively.

2a: m.p. 42°C (Found: C 71.0; H 6.7; N 4.5%. $C_{19}H_{21}FeN$ (319.22) requires C 71.5; H 6.6; N 4.5%); ν_{max}/cm^{-1} (CH) 3093m, 3019w, 2921m, 2854m, 2819m (KBr); $\delta_H(CDCl_3)$ 7.20 (2H, pseudo-d), 7.12 (2H,

pseudo-d), 4.17 (2H, pseudo-t, Cp), 4.09 (2H, pseudo-t, Cp), 4.08 (5H, s, Cp), 3.76 (2H, s, CH_2), 3.50 (2H, s, CH_2), 2.32 (3H, s, CH_3); $\delta_C(CDCl_3)$ 137.3 (C_{quart}), 136.4 (C_{quart}), 129.0, 128.0, 86.9 (Cp_i), 68.33, 68.28, 67.7, 53.0, 48.1, 21.1 (CH_3); m/z 319 (100, M^+), 252 (22), 226 (40); λ_{max}/nm (CH_2Cl_2) 437 (109).

2b: m.p. 79°C (Found: C 60.0; H 6.6; N 5.3%. $C_{13}H_{17}FeNO$ (259.13) requires C 60.3; H 6.6; N 5.4%); ν_{max}/cm^{-1} (CH) 3103m, 3085m, 2915m, 2898m, 2873m, 2835s (KBr); $\delta_H(CDCl_3)$ 4.15 (2H, pseudo-t, Cp), 4.11 (5H, s, Cp), 4.09 (2H, pseudo-t, Cp), 3.61 (2H, mult, CH_2), 3.51 (2H, s, CH_2), 2.78 (2H, mult, CH_2); $\delta_C(CDCl_3)$ 86.7 (Cp_i), 68.4, 68.3, 67.8 (all Cp), 60.8, 50.6, 48.5; m/z 259 (100, M^+), 199 (73); λ_{max}/nm (CH_2Cl_2) 438 (110).

3.2. General preparation of ferrocene amino acids **4**

The amino acid (1.15 equiv.), DhbtOH (1.15 equiv.) and ferrocene-methylamine **2** (1 equiv., typically ca. 1 mmol) were dissolved in 25 ml of DMF. After addition of 25 ml of CH_2Cl_2 and cooling to 0°C DCC (1.25 equiv.) was added, stirring continued for 2 h and an additional 12 h at r.t. A white precipitate of dicyclohexylurea was removed by filtration and washed twice with CH_2Cl_2. The combined organic phases were washed with saturated $NaHCO_3$ (3 × 50 ml), brine (50 ml), $KHSO_4$ (3 × 50 ml) and brine (50 ml). The organic phase is dried over $MgSO_4$ and the solvent removed on a rotary evaporator. The oily residue was chromatographed over a silica column with ether–pentane (5:1).

4a: yellow oil, 240 mg (54%, Found: C 61.6; H 6.3; N 5.57%. $C_{26}H_{32}FeN_2O_3$ (476.39) + 0.5 CH_2Cl_2 (which was difficult to remove and its presence confirmed in the ^{1}H-NMR) requires C 61.3; H 6.4; N 5.4%); ν_{max}/cm^{-1} (CO) 1713s, 1654vs (KBr), 3418w, 1709s, 1652vs (CH_2Cl_2); $\delta_H(CDCl_3)$ 7.13 (2H, mult), 7.08 and 6.97 (2H, mult), 5.6 and 5.5 (1H, br, NH), 4.51 and 4.28 (2H, s, CH_2), 4.32 and 4.06 (2H, s, CH_2), 4.14 (4H, mult, Cp), 4.08 (5H, s, Cp), 4.15 and 3.89 (2H, br, $C_\alpha H_2$), 2.32 (3H, s, CH_3), 1.45 and 1.41 (9H, s, Boc); $\delta_C(CDCl_3)$ 168.2 and 167.8 (CO), 155.8 and 155.6 (CO_{Boc}), 137.4 and 137.1, 133.7 and 132.6, 129.6, 129.3, 128.0, 126.3, 79.5 and 79.4 (**C**$(CH_3)_3$), 69.8, 69.1, 68.8, 68.7, 68.5, 68.3, 48.4 and 47.1 (CH_2), 44. 9 and 44.4 (CH_2), 42.5 and 42.3 (C_α), 28.3 (C(**C**$H_3)_3$), 21.0 (CH_3); m/z 476 (100, M^+), 420 (50, M–C_4H_8), 199 (73, Fc–CH_2^+).

4b: yellow oil, 190 mg (62%, Found: C 63.3; H 6.5; N 5.3%. $C_{27}H_{34}FeN_2O_3$ (490.4) requires C 66.1; H 7.0; N 5.7%); ν_{max}/cm^{-1} (CO) 1709s, 1642vs (KBr); $\delta_H(CDCl_3)$ 7.13 (2H, pseudo-t), 7.03 (2H, pseudo-t), 5.47 and 5.43 (1H, d, $J = 8.4$ and 7.6 Hz, NH), 4.83 and 4.57 (1H, quint., $J = 7.6$ Hz, $C_\alpha H$), 4.61 and 4.35 (1H, d, $J = 14.8$ Hz, diast. CH_2), 4.42 (1H, s, diast. CH_2), 4.39 and 4.18 (1H, d, diast. CH_2), 4.20 (1H, s, diast. CH_2) 4.22 and 4.11 (1H each, s, Cp_o), 4.14 (2H, s, Cp_m), 4.10 and 4.09 (5H, s, Cp), 2.33 (3H, s, CH_3), 1.45 and 1.39 (9H, s, Boc), 1.35 and 1.19 (3H, d, $J = 6.8$ Hz, $C_\beta H_3$); $\delta_C(CDCl_3)$ 172.9 and 172.7 (CO), 155.1 and 154.9 (CO_{Boc}), 137.4 and 137.0, 133.9 and 133.1, 129.5, 129.3, 127.8, 126.7, 82.6 and 82.3 (Cp_i) 79.5 (**C**$(CH_3)_3$), 69.6, 69.3, 69.2, 69.1, 68.7 (Cp), 68.64, 68.60 (Cp), 68.22, 68.20, 68.1, 49.0 (CH_2), 46.8, 46.4, 46.2, 45.7, 43.9 (CH_2, C_α), 28.3 (C(**C**$H_3)_3$), 21.0 (CH_3), 19.7 and 19.5 (C_β); $\delta_N(CDCl_3)$ −288; m/z 490 (100, M^+), 434 (50, M–C_4H_8), 369 (44), 199 (53, Fc–CH_2^+); λ_{max}/nm (CH_2Cl_2) 436 (105).

4c: yellow oil, 252 mg (71%, Found: C 69.8; H 6.7; N 4.8%. $C_{33}H_{38}FeN_2O_3$ (566.52) requires C 70.0; H 6.8; N 4.9%); ν_{max}/cm^{-1} (CO) 1707s, 1637vs (KBr); $\delta_H(CDCl_3)$ 7.23 (2H, mult), 7.10 (4H, mult), 6.97 (2H, mult), 6.84 (1H, d), 5.39 and 5.32 (1H, d, $J = 9.2$ and 9.3 Hz, NH), 5.03 and 4.75 (1H, app. quart, $J = 7.6$ Hz, $C_\alpha H$), 4.75 and 4.09 (1H, diast. CH_2), 4.53 and 3.85 (1H, d, $J = 13.6$ Hz and 13.2 Hz, diast. CH_2), 4.11 and 3.96 (1H, br, diast. CH_2), 3.99 and 3.46 (1H, d, $J = 7.2$ Hz, diast. CH_2) 4.22 and 3.96 (1H each, s, Cp_o), 4.08 (5H, s, Cp), 4.06 (2H, s, Cp_m), 3.02 and 2.88 (2H, mult, $C_\beta H_2$), 2.34 and 2.31 (3H, s, CH_3), 1.43 and 1.37 (9H, s, Boc); $\delta_C(CDCl_3)$ 171.6 and 171.4 (CO), 155.0 and 154.8 (CO_{Boc}), 137.2, 136.9, 136.8, 136.4, 133.7 and 133.1 (all C_{quart}), 129.5, 129.4, 129.1, 128.5, 128.4, 128.2, 126.8, 126.6, 82.0 (Cp_i) 79.5 and 79.5 (**C**$(CH_3)_3$), 70.2, 69.9, 69.5, 69.1, 68.8, 68.7 (2 Cp), 68.5, 68.2, 68.1, 51.8 (C_α), 48.9, 46.9, 45.3, 44.0 (all CH_2), 40.6 and 40.2 (C_β), 28.3 (C(**C**$H_3)_3$), 21.1 (CH_3); $\delta_N(CDCl_3)$ −290; m/z 566 (100, M^+), 510 (26, M–C_4H_8), 445 (23), 199 (29, Fc–CH_2^+); λ_{max}/nm (CH_2Cl_2) 440 (112).

4d: yellow oil, 230 mg (68%, Found: C 67.3; H 8.1; N 5.8%. $C_{30}H_{40}FeN_2O_3$ (532.50) requires C 67.7; H 7.6; N 5.3%); ν_{max}/cm^{-1} (CO) 1709s, 1642vs (KBr); $\delta_H(CDCl_3)$ 7.12 (2H, mult), 7.04 (2H, mult), 5.30 and 5.17 (1H, d, $J = 8.8$ and 8.8 Hz, NH), 4.87 and 4.59 (1H, mult, $C_\alpha H$), 4.75 and 4.11 (1H, d, J = 14.8 Hz, diast. CH_2), 4.49 and 4.08 (1H, d, $J = 14.0$ Hz, diast. CH_2), 4.44 (1H, s, diast. CH_2), 4.30 and 4.08 (1H, d, $J = 15.2$ Hz, diast. CH_2), 4.38 (1H, s, Cp_o), 4.14 and 4.09 (8H, s, Cp), 2.33 (3H, s, CH_3), 1.80 and 1.55 (1H, mult, $C_\gamma H$), 1.75 and 1.39 (2H, mult, $C_\beta H_2$), 1.45 and 1.39 (9H, s, Boc), 1.08, 0.96, 0.80, 0.75 (6H, d, $J = 6.4$ Hz, $C_\delta H_3$); $\delta_C(CDCl_3)$ 173.2 and 172.7 (CO), 155.7 and 155.4 (CO_{Boc}), 137.3 and 137.0, 134.1 and 133.3 (all C_{quart}), 129.5, 129.3, 127.9, 126.9, 82.8 and 82.1 (Cp_i), 79.4 (**C**$(CH_3)_3$), 69.6, 69.5, 69.4, 69.3, 68.9, 68.7 and 68.6 (C_5H_5), 68.3, 68.1, 68.0, 49.2 (CH_2), 48.8 (C_α), 46.5, 45.4, 44.0 (all CH_2), 43.3 and 42.7 (C_β), 28.3 (C(**C**$H_3)_3$), 24.7 and 24.5 (C_γ), 24.7, 24.5, 23.6, 23.4 (all C_δ), 21.0 (CH_3); m/z 532 (100, M^+), 476 (41, M–C_4H_8), 458 (29), 411 (34), 199 (33, Fc–CH_2^+); λ_{max}/nm (CH_2Cl_2) 437 (102).

4e: m.p. 68 °C, 400 mg (54%, Found: C 73.8; H 7.1; N 4.1%. $C_{40}H_{42}FeN_2O_3$ (654.63) requires C 73.4; H 6.5; N 4.3%); ν_{max}/cm^{-1} (CO) 3282m (br), 1714s, 1636vs (KBr), 3421m, 1720s, 1644s (CH_2Cl_2); $\delta_H(CDCl_3)$ 7.75

(2H, pseudo-d), 7.59 (2H, pseudo-t), 7.37 (2H, pseudo-t), 7.29 (2H, pseudo-d, all Fmoc), 7.12 (2H, mult), 7.05 (2H, mult), 5.63 and 5.48 (1H, d, $J = 9.2$ and 8.8 Hz, NH), 5.00 and 4.65 (1H, mult, $C_\alpha H$), 4.87 and 4.02 (1H, d, $J = 14.8$ Hz, diast. CH_2), 4.59 and 4.04 (1H, d, $J = 14.0$ Hz, diast. CH_2), 4.45 and 4.40 (1H, d, diast. CH_2), 4.42 (1H, s, Cp_o), 4.41–4.31 (2H, $CH_{2,Fmoc}$), 4.39 and 3.98 (1H, d, diast. CH_2), 4.24 and 4.20 (1H, t, CH_{Fmoc}), 4.13 and 4.09 (8H, s, Cp), 2.33 and 2.31 (3H, s, CH_3), 1.85 and 1.65 (1H, mult, $C_\gamma H$), 1.68 and 1.42 (2H, mult, $C_\beta H_2$), 1.10, 0.98, 0.81, 0.77 (6H, d, $J = 6.5$ Hz, all $C_\delta H_3$); $\delta_C(CDCl_3)$ 172.6 and 172.2 (CO), 156.3 (CO_{Fmoc}), 143.9 and 143.8, 141.3 ($C_{quart,Fmoc}$), 137.4 and 137.1, 133.9 and 133.1 (all C_{quart}), 129.6, 129.4, 128.0 (all CH_{Ph}), 127.6, 127.1, 127.0, 126.8, 125.2, 120.0 (all CH_{Fmoc}), 82.6 and 81.9 (Cp_i), 69.7, 69.4, 69.2, 69.1, 68.7, 68.6, 68.4, 68.1, 68.0, 67.0 and 66.9 ($CH_{2,Fmoc}$), 49.6 and 49.5 (C_α), 49.1 (CH_2), 47.2 (CH_{Fmoc}), 46.5, 45.4, 44.1 (all CH_2), 43.2 and 42.7 (C_β), 24.7 and 24.5 (C_γ), 23.6, 23.4, 21.6, 21.5 (all C_δ), 21.1 and 21.0 (CH_3); δ_N ($CDCl_3$) −292; m/z 654 (100, M^+), 589 (15), 432 (47), 199 (72, Fc–CH_2^+); λ_{max}/nm (CH_2Cl_2) 438 (107).

5: yellow oil (Found: C 58.8; H 7.3; N 5.9%. $C_{21}H_{30}FeN_2O_4$ (430.33) requires C 58.6; H 7.0; N 6.5%); ν_{max}/cm^{-1} 3423s, br, 1702s, 1636vs (KBr), 3618w, 3428m, 1706s, 1644s (CH_2Cl_2); $\delta_H(CDCl_3)$ 5.36 and 5.21 (1H, d, $J = 7.7$ and 7.5 Hz, NH), 4.77 and 4.66 (1H, mult, $C_\alpha H$), 4.72 and 4.04 (1H, d, $J = 14.0$ Hz, diast. CH_2), 4.39 and 4.34 (1H, d, $J = 15$ Hz, diast. CH_2), 4.20 (1H, s, diast. CH_2) 4.25 and 4.20 (1H each, s, Cp), 4.16 (1H, s, Cp), 4.15 and 4.13 (5H, s, Cp), 4.08 (1H, s, Cp), 3.74, 3.63, 3.51, 3.46, 3.34, 3.32 (4H, 6 mult, CH_2–CH_2), 3.19 and 3.02 (1H, br, OH), 1.44 and 1.40 (9H, s, Boc), 1.32 and 1.23 (3H, d, $J = 5.6$ Hz, $C_\beta H_3$); $\delta_C(CDCl_3)$ 174.4 and 173.3 (CO), 156.0 and 155.2 (CO_{Boc}), 83.2 and 80.1 (Cp_i) 79.8 (**C**$(CH_3)_3$), 69.4, 69.2, 69.09, 69.07, 69.0, 68.8, 68.7 and 68.5 (Cp), 68.4, 68.0, 61.8 and 60.5 (CH_2–OH), 49.2 and 48.7 (**C**H_2–CH_2), 48.6 and 44.8 (Fc–CH_2), 46.3 (C_α), 28.37 and 28.31 (C(**C**$H_3)_3$), 19.5 and 18.2 (C_β); $\delta_N(CDCl_3)$ −286.5 and −286.0; m/z 430 (100, M^+), 374 (52, M − C_4H_8), 231 (82), 199 (68, Fc–CH_2^+).

6: yellow solid, m.p. 70–71°C (Found: C 65.3; H 6.8; N 6.1%. $C_{38}H_{47}FeN_3O_4S$ (697.71) requires C 65.4; H 6.8; N 6.0%); ν_{max}/cm^{-1} (CO) 1712s, 1637sh, 1630vs (KBr); $\delta_H(CDCl_3)$ 7.21 (2H, mult), 7.15–7.06 (4H, mult,), 6.98 (2H, mult), 6.95 and 6.86 (1H, br, NH), 6.82 (1H, d), 5.15 and 5.11 (1H, mult, NH_{Boc}), 5.32 and 4.98 (1H, app. quart, $J = 7.5$ Hz, $C_{\alpha,Phe}H$), 4.26–4.02 (4H, 4 s, Cp), 4.07 and 4.04 (5H, s, Cp), 4.26 and 4.22 (1H, mult, $C_{\alpha,Met}H$), 4.79 and 4.01 (1H, d, $J = 14.5$ Hz, diast. CH_2), 4.58 and 3.81 (1H, d, $J = 14.1$ Hz, diast. CH_2), 4.12 and 3.91 (1H, d, diast. CH_2), 3.95 and 3.58 (1H, d, $J = 15.8$ Hz, diast. CH_2), 3.03 (1H, mult, $C_{\beta,Phe}H_2$), 2.91 (1H, mult, $C_{\beta,Phe}H_2$), 2.45 (2H, mult, $C_\gamma H_2$), 2.34 and 2.31 (3H, s, CH_3), 2.07 and 2.05 (3H, s, SCH_3), 1.98 (1H, mult, $C_{\beta,Met}H_2$), 1.84 (1H, mult, $C_{\beta,Met}H_2$), 1.43 (9H, s, Boc); $\delta_C(CDCl_3)$ 170.8, 170.6, 170.4 (all CO), 155.0 (CO_{Boc}), 137.2, 136.9, 136.8, 136.4, 133.7 and 133.1 (all C_{quart}), 129.5, 129.4, 129.1, 128.5, 128.4, 128.2, 126.8, 126.6,? 82.2 and 81.8 (Cp_i) 79.5 and 79.5 (**C**$(CH_3)_3$), 70.2, 69.9, 69.5, 69.1, 68.8, 68.7 (2 Cp), 68.5, 68.2, 68.1, 51.8 (C_α), 48.9, 46.9, 45.3, 44.0 (all CH_2), 40.6 and 40.2 (C_β), 28.3 (C(**C**$H_3)_3$), 21.1 (CH_3); $\delta_N(CDCl_3)$ −260, −293; m/z 697 (74, M^+), 641 (2, M–C_4H_8), 576 (10), 454 (28), 199 (100, Fc–CH_2^+).

10: 2.4 g (11 mmol) Di-*tert*-butyl carbonate were added to a solution of 1.21 g of *p*-methylbenzylamine (10 mmol) in dioxane. After stirring for 1 h at room temp. the solvent was removed in vacuo, the residue dissolved in $CHCl_3$, washed three times with water and dried over Na_2SO_4, and the solvent removed in vacuo. Yield 1.99 g of white **10** (90%). m.p. 69°C (Found: C 70.7; H 8.3; N 6.3%. $C_{13}H_{19}NO_2$ (221.29) requires C 70.6; H 8.7; N 6.3%); ν_{max}/cm^{-1} 3359m, 1682vs (KBr); $\delta_H(CDCl_3)$ 7.17 – 7.09 (4H, mult, H_{Ar}), 4.81 (1H, br, NH), 4.24 (2H, d, $J = 5.8$ Hz, CH_2), 2.31 (3H, s, CH_3), 1.44 (9H, s, $C(CH_3)_3$); $\delta_C(CDCl_3)$ 155.8, (CO), 136.9 (C_{quart}), 135.9 (C_{quart}), 129.2, 127.4, 79.3 (**C**$(CH_3)_3$), 44.4 (CH_2), 28.4 (C(**C**$H_3)_3$), 21.0 (CH_3); m/z 221 (4, M^+), 164 (100), 150 (55).

11: 0.5 g (2.26 mmol) of **10** were dissolved in a degassed mixture of 40 ml of $^nBu_2O$ and 5 ml of THF. $Cr(CO)_6$ (0.45 g, 2.3 mmol) was added and the solution stirred for 14 h at 145°C under argon. After cooling, the solvent was completely removed on a vacuum line, the yellow residue was dissolved in Et_2O and filtered via canula through a bed of Celite. After removal of the solvent and sublimation of excess ligand from the mixture (80°C, 10^{-2} bar) **11** is obtained as a yellow powder (0.72 g, 87%). m.p. 112°C (Found: C 54.0; H 5.5; N 3.9%. $C_{16}H_{19}CrNO_5$ (357.3) requires C 53.8; H 5.4; N 3.9%); ν_{max}/cm^{-1} 3285m, 1974vs, 1883vs, 1866vs, 1677s (KBr), 3448m, 1960vs, 1897vs, 1874vs, 1713vs (CH_2Cl_2); $\delta_H(CDCl_3)$ 5.37 (2H, pseudo-d, H_{Ar}), 5.19 (2H, pseudo-d, H_{Ar}), 4.89 (1H, br, NH), 4.01 (2H, d, $J = 6.3$ Hz, CH_2), 2.15 (3H, s, CH_3), 1.45 (9H, s, $C(CH_3)_3$); $\delta_C(CDCl_3)$ 233.1 (Cr–CO), 155.9 (CO), 108.6 (C_{quart}), 107.3 (C_{quart}), 93.2, 93.1, 80.1 (**C**$(CH_3)_3$), 42.8 (CH_2), 28.3 (C(**C**$H_3)_3$), 20.3 (CH_3); $\delta_N(CDCl_3)$ −296; m/z 357 (6, M^+), 329 (5, M – CO), 273 (44), 217 (100); λ_{max}/nm (CH_2Cl_2) 318 (5565).

8: 200 mg (0.56 mmol) of **11** were stirred in a deaerated mixture of 3 ml of H_2SO_4 and 30 ml of dioxane at 0°C. 60 ml of a $CHCl_3$–H_2O mixture (1:1) were added, the organic phase separated, dried and evaporated to dryness in vacuo to give 32 mg (0.12

mmol, 22%) of **8** as a yellow powder. ν_{max}/cm^{-1} 3389m, 1956vs, 1870vs (br) (KBr); $\delta_H(CDCl_3)$ 5.48 (2H, pseudo-d, H_{Ar}), 5.21 (2H, pseudo-d, H_{Ar}), 3.61 (2H, s, CH_2), 2.16 (3H, s, CH_3), 1.35 (2H, br, NH_2); $\delta_C(CDCl_3)$ 233.5 (Cr–CO), 111.4 (C_{quart}), 108.6 (C_{quart}), 93.3, 93.1, 44.5 (CH_2), 20.4 (CH_3); m/z 257 (23, M^+), 229 (3, M – CO), 201 (12, M–2CO), 173 (100, M–3CO).

14: NaCp (1.0 g, 10 mmol) and $Mo(CO)_6$ (2.55 g, 10 mmol) were suspended in a mixture of $^nBu_2O$ (45 ml) and THF (5 ml). The reaction mixture was heated under reflux until no more CO evolved and a yellow solution with a white precipitate had formed. After cooling to room temp. 2-bromo-*N*-ethylphthalimide was added and stirring continued for 12 h. The reaction mixture was filtered and the yellow solution evaporated to dryness in vacuo. The product was recrystalized from diethyl ether to yield 0.51 g (1.2 mmol, 12%) **14** as yellow crystals. m.p. 150–152°C; ν_{max}/cm^{-1} (CO) 2016vs, 1928vs, 1709vs (KBr); $\delta_H(CDCl_3)$ 7.80 (2H, mult), 7.68 (2H, mult), 5.42 (5H, s, Cp), 3.82 (2H, mult, NCH_2), 1.56 (2H, mult, Mo–CH_2); $\delta_C(CDCl_3)$ 226.9 (C_{Mo-CO}), 168.2 (C_{N-CO}), 133.7, 132.5 (C_{quart}), 123.1, 92.7 (C_{Cp}), 43.9, −2.6 (Mo–CH_2); m/z 421 (6, M^+), 393 (13, M–CO), 365 (21, M–2CO), 335 (65), 309 (100).

4. X-ray crystallographic data collection and refinement

Transparent colorless single crystals of $0.59 \times 0.31 \times 0.14$ mm^3 (**2a**) and $0.35 \times 0.73 \times 0.91$ mm^3 (**14**) were sealed in glass capillaries and mounted on an Enraf–Nonius CAD4 diffractometer system at ambient temperature (Table 2). Graphite monochromated Mo–K_α radiation ($\lambda = 0.71073$ Å) was used. Cell constants were obtained from a least squares fit of the setting angles of 25 carefully centred reflections. Intensities were collected by the usual $\omega/2\theta$ scan technique and corrected for Lorentz and polarization effects. No correction for absorption was considered necessary due to the relatively small absorption coefficients. The SHELXTL software package (Siemens) was used for solution and refinement of the structure. Neutral atom scattering factors were taken from the usual sources [44]. All non-hydrogen atoms were refined anisotropically. H-atoms were placed at calculated positions and refined as riding atoms with isotropic displacement parameters.

5. Supplementary information

The crystallographic data have been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition numbers CCDC116246 (**2a**) and CCDC116247 (**14**). Copies of the data may be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk).

Table 2
Crystallographic details for **2a** and **14**

	2a	**14**
Empirical formula	$C_{19}H_{21}FeN$	$C_{18}H_{13}MoNO_5$
Formula weight	319.22	419.23
Temperature (K)	293 (2)	293 (2)
Crystal system, space group	Triclinic, $P\bar{1}$	Monoclinic, $P2_1/n$
Unit cell dimensions		
a (Å)	7.340(2)	11.947(2)
b (Å)	10.539(2)	12.501(3)
c (Å)	10.854(2)	12.065(2)
α (°)	94.55(3)	90.0
β (°)	104.69(3)	111.96(3)
γ (°)	103.65(3)	90.0
Volume	780.5(3)	1671.2(6)
Z	2	4
Absorption coefficient (mm^{-1})	0.959	0.813
θ range for data collection (°)	2.59–25.00	2.44–27.45
Reflections collected, independent reflections	2984, 2749	3990, 3812
R_{int}	0.0107	0.0098
Data:restraints:parameters	2577:0:193	3806:0:226
Goodness-of-fit on F^2	1.089	1.178
Final R indices [$I>2\sigma(I)$]	$R_1 = 0.0369$ [a], $wR_2 = 0.0972$	$R_1 = 0.0327$ [a], $wR_2 = 0.0888$
R indices (all data)	$R_1 = 0.0505$, $wR_2 = 0.1044$	$R_1 = 0.0462$, $wR_2 = 0.1057$
Largest diff. peak and hole (e Å^{-3})	0.485, −0.373	0.839, −0.587

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

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References

[1] P. Köpf-Maier, H. Köpf, Chem. Rev. 89 (1987) 1137.
[2] P. Köpf-Maier, H. Köpf, Struct. Bond. 70 (1988) 105.
[3] G. Jaouen, A. Vessières, I.S. Butler, Acc. Chem. Res. 26 (1993) 361.
[4] K. Severin, R. Bergs, W. Beck; Angew. Chem. 110 (1998) 1722; Angew. Chem. Int. Ed. Engl. 37 (1998) 1634.
[5] H. Eckert, M. Koller, Z. Naturforsch. Teil B 45 (1990) 1709.
[6] H. Eckert, M. Koller, J. Liq. Chromatogr. 13 (1990) 3399.
[7] P.D. Beer, Acc. Chem. Res. 31 (1998) 71.
[8] G. Jaouen, A. Vessières, S. Top, J. Am. Chem. Soc. 107 (1985) 4778.

[9] M. Savignac, A. Sasaki, P. Potier, G. Jaouen, J. Chem. Soc. Chem. Commun. (1991) 615.
[10] M. Salmain, A. Vessières, I.S. Butler, G. Jaouen, Bioconjugate Chem. 2 (1991) 13.
[11] M. Salmain, A. Vessières, P. Brossier, I.S. Butler, G. Jaouen, J. Immun. Meth. 148 (1992) 65.
[12] M. Salmain, K.L. Malisza, S. Top, G. Jaouen, M.-C. Sénéchal-Tocquer, D. Sénéchal, B. Caro, Bioconjugate Chem. 5 (1994) 655.
[13] A. Gorfti, M. Salmain, G. Jaouen, J. Chem. Soc. Chem. Commun. (1994) 433.
[14] K.L. Malisza, S. Top, J. Vaissermann, B. Caro, M.-C. Sénéchal-Tocquer, D. Sénéchal, J.-Y. Saillard, S. Triki, S. Kahlal, J.F. Britten, M.J. McGlinchey, G. Jaouen, Organometallics 14 (1995) 5273.
[15] D. Osella, M. Ravera, M. Vincenti, M. Salmain, G. Jaouen, Organometallics 15 (1996) 3037.
[16] C.E. Anson, C.S. Creaser, O. Egyed, M.A. Fey, G.R. Stephenson, J. Chem. Soc. Chem. Commun. (1994) 39.
[17] W.S. Sheldrick, A.J. Gleichmann, J. Organomet. Chem. 470 (1994) 183.
[18] A.J. Gleichmann, J.M. Wolff, W.S. Sheldrick, J. Chem. Soc. Dalton Trans. (1995) 1549.
[19] D.B. Grotjahn, C. Joubran, D. Combs, D.C. Brune, J. Am. Chem. Soc. 120 (1998) 11814.
[20] M. Bracci, C. Ercolani, B. Floris, M. Bassetti, A. Chiesi-Villa, C. Guastini, J. Chem. Soc. Dalton Trans. (1990) 1357.
[21] D. Freiesleben, K. Polborn, C. Robl, K. Sünkel, W. Beck, Can. J. Chem. 73 (1995) 1164.
[22] J. Cano, A. Benito, R. Martínez-Máñez, J. Soto, J. Payá, F. Lloret, M. Julve, M.D. Marcos, E. Sinn, Inorg. Chim. Acta 231 (1995) 45.
[23] A.L.J. Beckwith, G.G. Vickery, J. Chem. Soc. Perkin Trans. I (1975) 1818.
[24] P.D. Beer, Z. Chen, M.G.B. Drew, A.O.M. Johnson, D.K. Smith, P. Spencer, Inorg. Chim. Acta 246 (1996) 143. The electrochemical data in this work seem to be inconsistent (190 mV difference between compounds **4** and **5**) and are difficult to compare with our data since no value for a standard is reported.
[25] C.L. Perrin, T.J. Dwyer, Chem. Rev. 90 (1990) 935.
[26] G.-B. Liang, G.P. Dado, S.H. Gellman, J. Am. Chem. Soc. 113 (1991) 3994.
[27] S.H. Gellman, G.P. Dado, G.-B. Liang, B.R. Adams, J. Am. Chem. Soc. 113 (1991) 1164.
[28] C. Janiak, T.G. Scharmann, W. Gunther, F. Girgsdies, H. Hemling, W. Hinrichs, D. Lentz, Chem. Eur. J. 1 (1995) 637.
[29] C. Janiak, T.G. Scharmann, H. Hemling, D. Lentz, J. Pickardt, Chem. Ber. 128 (1995) 235.
[30] D. Walther, A. Schmidt, T. Klettke, W. Imhof, H. Gorls, Angew. Chem. Int. Ed. Engl. 33 (1994) 1373.
[31] L. Lin, A. Berces, H.-B. Kraatz, J. Organomet. Chem. 556 (1998) 11.
[32] H.-B. Kraatz, J. Lusztyk, G.D. Enright, Inorg. Chem. 36 (1997) 2400.
[33] B. Bildstein, A. Hradsky, H. Kopacka, R. Malleier, K. Ongania, J. Organomet. Chem. 540 (1997) 127.
[34] H. Eckert, C. Seidel, Angew. Chem. 98 (1986) 168; Angew. Chem. Int. Ed. Engl. 25 (1986) 159.
[35] H. Eckert, B. Forster, C. Seidel, Z. Naturforsch. Teil B 46 (1991) 339.
[36] M. Bodanszky, A. Bodanszky, The Practice of Peptide Synthesis, Springer-Verlag, Berlin, 1984.
[37] M. Bodanszky, Principles of Peptide Synthesis, Springer-Verlag, Berlin, 1984.
[38] R.D. Fischer, Chem. Ber. 93 (1960) 165.
[39] C. Sergheraert, J.-C. Brunet, A. Tartar, J. Chem. Soc. Chem. Commun. (1982) 1417.
[40] B. El Mouatassim, H. Elamouri, J. Vaissermann, G. Jaouen, Organometallics 14 (1995) 3296.
[41] M.J. Bennett, R. Mason, Proc. Chem. Soc. (1963) 273.
[42] J.K.P. Ariyaratne, A.M. Bierrum, M.L.H. Green, M. Ishaq, C.K. Prout, J. Chem. Soc. A (1969) 1309.
[43] E.R. Burkhardt, J.J. Doney, R.G. Bergman, C.H. Heathcock, J. Am. Chem. Soc. 109 (1987) 2022.
[44] International Tables for Crystallography, Kynoch Press, Birmingham, 1974, Vol. 4.