DOI: 10.1002/ejoc.200900552

Stereoselective Synthesis of New Ferrocene-Derived Amino Acid Building Blocks

Andrea Hunold,[a] Ines Neundorf,[b] Philippe James,[a] Jörg Neudörfl,[a] and Hans-Günther Schmalz*[a]

Keywords: Metallocenes / Amino acids / Chirality / Stereochemistry / Solid-phase synthesis / Peptidomimetics

As a contribution to bioorganometallic chemistry, a dia- and enantioselective synthesis of novel carbocyclic amino acid analogues with a 1,2-ferroceno-fused cyclopentene backbone has been developed. Using two related planar-chiral intermediates, i.e. (1*S*,*E*)-ethyl-3-[2-(phenylsulfonylacetyl)-ferrocen-1-yl]acrylate, (1*S*,*E*)-ethyl-3-[2-(methoxycarbonyl)-ferrocen-1-yl]acrylate, stereoselective entries to different *t*Boc- or Fmoc-protected ferroceno-fused 1-amino-3-carboxyalkyl-2-cyclopentenes were elaborated. These compounds were then used for the preparation of metal-containing peptides by means of solid-phase peptide synthesis (SPPS).

Introduction

The first ferrocenyl amino acid was reported in 1957 when Schlögl[1] published the synthesis and characterization of different ferrocene-containing amino acid derivatives, such as ferrocenylalanine and *p*-ferrocenyl-phenylalanine. In addition, amides derived from ferrocene carboxylic acid and amino acid esters and the first *N*-ferrocenylmethyl (Fem) amino acids were described. Since then, a few dozens of papers were published concerning this type of peptidic compounds. This reflects the growing interest in the use of ferrocene derivatives in biological studies, as a consequence of their specific optical and electrochemical properties.[2] For instance, several ferrocenyl derivatives have been used as biosensors.[3] Furthermore, it was demonstrated by Jaouen and co-workers that ferrocene analogues of established cytotoxic or antibiotic drugs can lead to greatly enhanced activities or selectivities.[4] A current review covers the bioorganic chemistry of ferrocene in almost all its aspects.[5]

For the investigation of the specific biological effects of organometallic fragments on biological systems it is attractive to incorporate them as building blocks into peptide chains. While metal-containing units have been attached in the past in most cases to the termini of peptide chains (such as in compounds **1**,[6] **2**[7] and **3**, Figure 1)[8] peptidic constructs with an internal ferrocenyl unit for instance derived from 1-aminoferrocene-1′-carboxylic acid (Fca) or 1,1′-ferrocenedicarboxylic acid have also been reported.[9] Following our own interests in incorporating configurationally and conformationally well-defined ferrocenyl units into peptide chains, we considered amino acids **4** and **5** as promising building blocks for the synthesis of iron-containing peptides of type **6** (Figure 2).

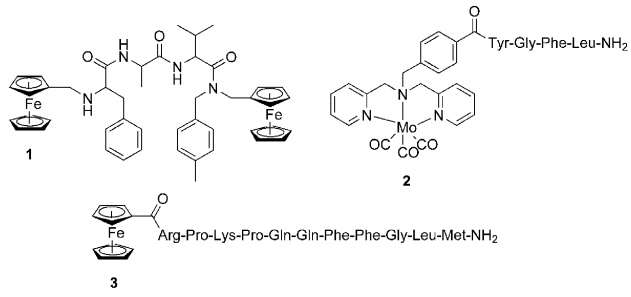


Figure 1. Examples for metal-containing peptides.

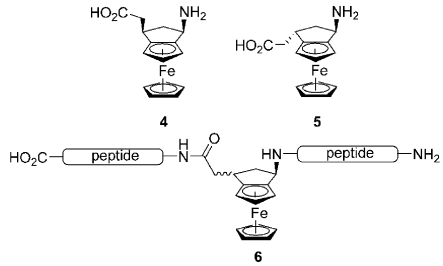


Figure 2. Target compounds of the present study: amino acids **4** and **5** as building blocks for metal-containing peptides of type **6**.

Our decision to focus on amino acids **4** and **5** was triggered by our experience in the synthesis of ferrocene-containing nucleoside analogues, such as **7** and **8**, developed in

[a] Department für Chemie, Universität zu Köln
Greinstr. 4, 50939 Cologne, Germany
Fax: +49-2214703064
E-mail: schmalz@uni-koeln.de
[b] Institut für Biochemie, Universität Leipzig,
Brüderstr. 34, 04103 Leipzig, Germany

our group. These compounds (Figure 3) were shown to exhibit significant apoptosis-inducing activity (LD_{50} = 10–20 μmol) against tumor cells.[10]

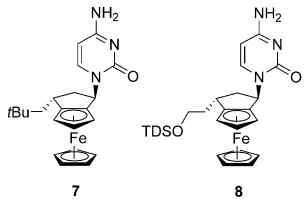
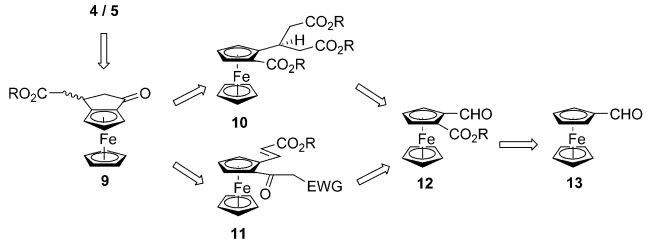


Figure 3. Iron-containing nucleoside analogues **7** and **8**.

Our synthetic plan (Scheme 1) is based on the consideration to use ketones of type **9** as precursors, which in turn could be prepared either through Dieckman condensation (via intermediate **10**) or via intramolecular Michael addition (via intermediate **11**). While the stereochemical outcome of the proposed cyclization had to be experimentally investigated, the enantioselective synthesis of the planar chiral building block **12** was considered to be achieved following the protocol of Kagan.[11]

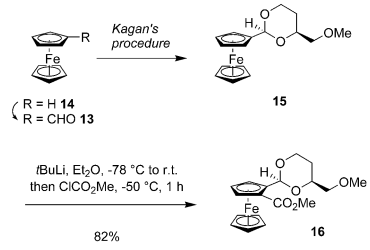


Scheme 1. Retrosynthetic analysis.

Results and Discussion

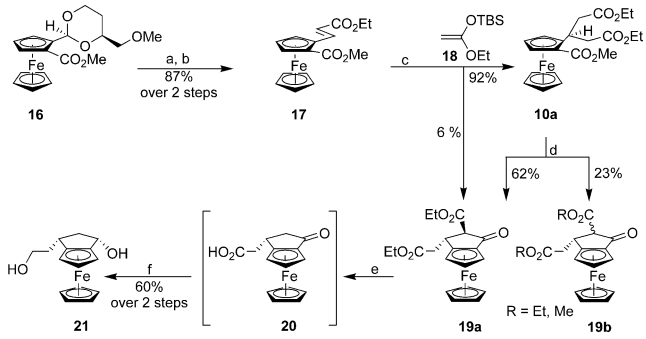
As a key intermediate for the synthesis of ferrocene-containing compounds related to **4** and **5**, we first prepared the planar chiral compound **16**, starting from ferrocenecarbaldehyde[12] (**13**) and *S*-butantriol (>99%ee)[13] as shown in Scheme 2. Following the protocol of Kagan and co-workers we converted **13** into the chiral acetal **15**, which was then functionalized through highly diastereoselective *ortho*-lithiation.[11] When the lithiated species, derived from **15** by treatment with *tert*-butyllithium in diethyl ether, was added to an excess of methyl chloroformate at –50 °C (reversed addition), the methoxycarbonylated product **16** was obtained as a virtually pure diastereomer in 82% yield. This compound was then employed in two separate synthetic schemes, which lead diastereoselectively to the epimeric target structures as described below.

The conversion of **16** into *trans*-configured amino acid building blocks (related to **5**) starts with the acidic cleavage of the chiral auxiliary group. Subsequent Horner–Wadsworth–Emmons olefination of the resulting aldehyde



Scheme 2. Diastereoselective preparation of **16**.

intermediate with triethylphosphonoacetate gave the diester **17** as a pure *E*-diastereomer (Scheme 3). This compound was analyzed by X-ray crystallography to also confirm the expected absolute configuration (Figure 4).



Scheme 3. Synthesis of diol **21**; a) *p*TosOH, H_2O, DCM, room temp., 15 h; b) NaH, THF, 0 °C, room temp., 1 h, then $(EtO)_2POCH_2CO_2Et$, THF, room temp., 30 min; c) $Al(OTf)_3$, DCM, –78 °C, 2.5 h; d) KH, THF, reflux, 1 h; e) NaOH, EtOH/H_2O, 80 °C, 15 h; f) $LiAlH_4$, THF/Et_2O (3:1), 0 °C, room temp., 15 h.

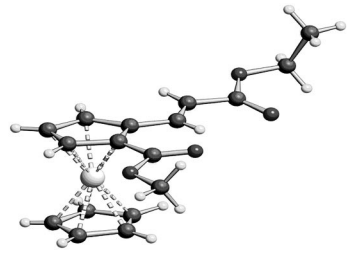


Figure 4. Structure of **17** in the crystalline state.[10,14]

Treatment of **17** with the *O*-silyl ketene acetal **18**[15] in the presence of $Al(OTf)_3$ as an (in situ generated) Lewis acid catalyst[16] resulted in the formation of **10a** in 92% isolated yield as the product of a Mukaiyama–Michael reaction.[17] In addition, 6% of the already cyclized product **19a** were obtained as a pure diastereomer. Obviously, the *O*-silylated ketene acetal, formed diastereoselectively from **17** and **18**, was able to undergo a Dieckmann-type 5-*exo*-*trig*-cyclization to give **19a** in a tandem process.

Treatment of **10a** with KH in refluxing THF resulted in a group-selective reaction, i.e. the formation of a mixture containing only products **19a/b** with an *endo*-configured acetic acid ester side chain. After chromatography separation compound **19a** was obtained in 62% yield besides 23% of a second component, which turned out to be a mono-

methyl ester arising from partial transesterification with methanol formed during the reaction. The relative configuration of the main product **19a** was determined by means of NOE experiments (Figure 5). Saponification of the mixture of diesters **19a/b**, decarboxylation (to give **20**) and reduction with $LiAlH_4$ led to one and the same product **21**. This confirmed the configuration of **19a/b** being identical with respect to the (lasting) stereocenter in *β*-position to the carbonyl group.

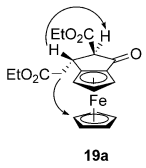
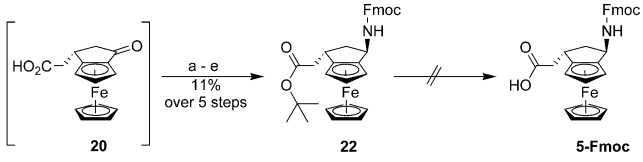


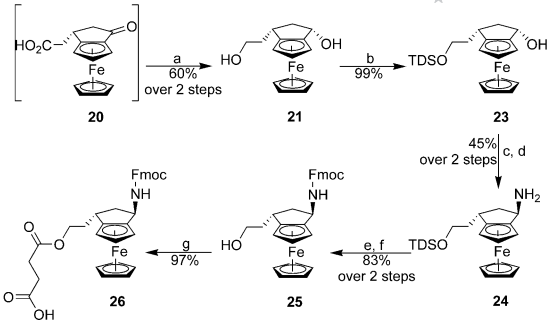
Figure 5. NOE analysis of the two diastereomers **19a** and **19b**.

During the preparation of **20**, it turned out that this carboxylic acid is very unstable (especially in solution) in contrast to the corresponding ester obtained by treatment of **20** with *tert*-butyl alcohol, DMAP and DCC. After treatment of this ester with $NaBH_4$ the resulting *endo*-alcohol was converted into the corresponding *exo*-amine through Mitsunobu reaction with $Zn(N_3)_2$ and subsequent Staudinger reduction. *N*-Protection with Fmoc-Cl led to the amino acid derivative **22**, as a stable, fully characterized compound (Scheme 4). However, all our attempts to convert **22** into the target compound **5-Fmoc** by cleavage of the *tert*-butyl ester failed due to the (surprising) inherent instability of this type of ferrocenophanes bearing an *endo*-acetic acid side chain.



Scheme 4. Attempted synthesis of the amino acid 5-Fmoc; a) *t*BuOH, DMAP, DCC, DCM, room temp., 3.5 h; b) $NaBH_4$, H_2O, EtOH, 0 °C, room temp., 15 h; c) PPh_3, $Zn(N_3)_2$·2py, toluene, DEAD, room temp, 15 h; d) PPh_3, THF, room temp., 15 h then H_2O, 8 h; e) 10% K_2CO_3 (aq.), MeCN, 0 °C, Fmoc-Cl, MeCN, room temp., 15 h.

While any further attempts to prepare compounds of type **5** thus seemed less promising, we considered the stable diol **21** as a promising intermediate for the synthesis of *trans* amino acid building blocks related to **5**, such as the Fmoc-protected amino acid **26** (Scheme 5). This compound was expected to be of improved stability as compared to **5-Fmoc** due to the larger distance between the carboxylic function and the ferrocenyl iron atom. The conversion of **20** to **26** was achieved as shown in Scheme 5. First the *endo*-diol **21** was prepared by $LiAlH_4$ reduction from the crude carboxylic acid **20** and its structure was unambiguously confirmed by means of X-ray crystallography (Figure 6).



Scheme 5. Synthesis of the amino acid building block **26** and NOE analysis of 43; a) $LiAlH_4$, THF/Et_2O (3:1), 0 °C, room temp., 15 h; b) TDS-Cl, DMAP, pyridine, room temp., 2 h; c) DIAD, THF, 0 °C, PPh3, toluene, 0 °C, 30 min then **23**, THF, $Zn(N_3)_2$, 0 °C, 2 h; d) PPh_3, THF, room temp., 8 h then H_2O, room temp., 15 h; e) TMSOTf, DCM, 0 °C, 1 h; f) Fmoc-Cl, K_2CO_3 (10% in H_2O), MeCN, 0 °C, room temp., 15 h; g) succinic acid anhydride, DMAP, DCM/pyridine, room temp., 15 h.

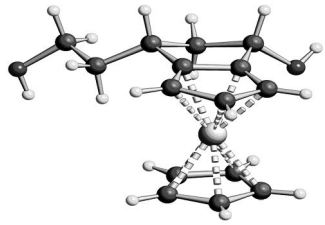
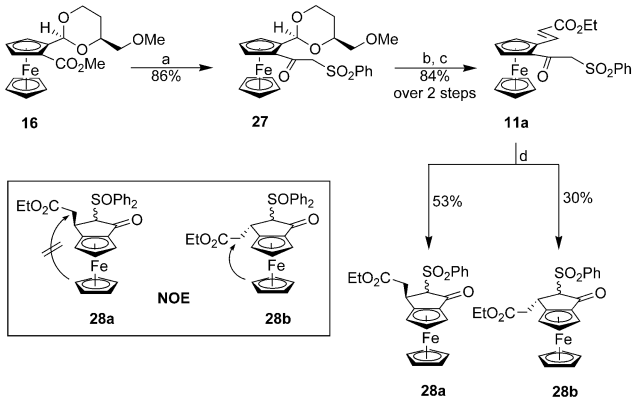


Figure 6. Structure of **21** in the crystalline state.[10,14]

After selective monoprotection of the primary alcohol function of **21** using 1.2 equiv. of chlorodimethylthexylsilane, the remaining (secondary) alcohol function of **23** was substituted by an amino group in a S_N2 process applying Mitsunobu conditions using $Zn(N_3)_2$ as nucleophile[18] and subsequent Staudinger reduction.[19] Treatment of the resulting amine **24** with TMSOTf gave the deprotected amino alcohol, which was directly converted into the Fmoc-derivative **25** under standard conditions. The configuration of compound **25** was evidenced by the fact that no NOE could be detected between the two *pseudo*-benzylic hydrogen atoms in the azide precursor. Finally, on treatment of **25** with succinic acid anhydride in the presence of DMAP the amino acid building block **26** was obtained in high yield. This compound proved to be sufficiently stable and suitable for SPPS (see below).

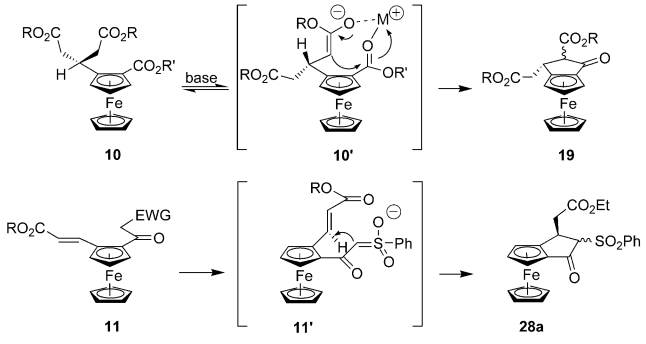
We next turned our attention towards the *cis*-configured target molecules, i.e. amino acid building blocks of type **4**. For this purpose the methyl ester **16** was first converted into the corresponding β-keto sulfone **27** by treatment with lithiated methyl phenyl sulfone (86% yield). After acidic acetal hydrolysis the crude aldehyde was subjected to a Horner–Wadsworth–Emmons olefination to afford ester **11a** (Scheme 6). On treatment of **11a** with LDA (2.0 equiv.) an intramolecular Michael addition occurred to give a cyclopentenone derivative. The two resulting diastereomers **28a** and **28b** could be easily separated by column chromatography and were isolated in a yield of 53 and 30%, respectively. The relative configuration (concerning the po-

sition of the ethyl acetate side chain) was determined by NOE experiments (Scheme 6). Only in the case of **28b** an NOE interaction between the CH_2 group of the side chain and the unsubstituted Cp-ring was observed.



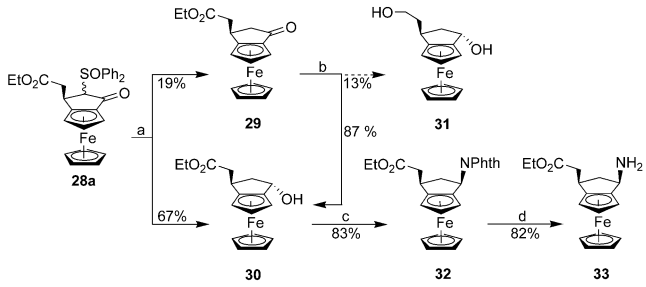
Scheme 6. Conversion of **16** into the two diastereomers **28a** and **28b**; a) $MeSO_2Ph$, *n*BuLi, THF, –78 °C, 1 h then **16**, THF, –78 °C, 15 min, room temp., 15 h; b) *p*TosOH, H_2O, DCM, room temp., 15 h; c) NaH, THF, 0 °C, room temp., 1 h then $(EtO)_2POCH_2CO_2Et$, THF, room temp., 30 min; d) LDA, THF, –78 °C to 10 °C, 15 h.

To explain the formation of the different diastereomers **19a/b** and **28a/b**, respectively, we postulate the following cyclization modes: in the first case we assume a reversible base-induced formation of diastereomeric ester enolates. As sketched in Scheme 7 we hypothesize a kinetically controlled Dieckman cyclization in which the *endo*-configured products **19a/b** result from a chelated transition state of type **10′**. In contrast, the base-induced Michael cyclization of substrate of type **11** preferentially affords the *exo*-product **28a** via a 5-*exo*-*trig* transition state **11′** involving a nucleophilic attack at the enoate side chain in an *exo*-out-of-plane conformation.



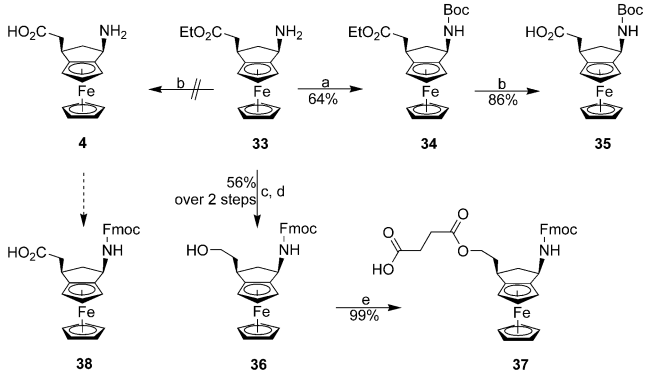
Scheme 7. Mechanistic models to rationalize the diastereoselective formation of Dieckmann products **19a/19b** and Michael product **28a**.

On treatment of the β-keto sulfone **28a** with SmI_2 (3.5 equiv.) in THF a mixture of the desulfonated ketone **29** and the corresponding alcohol **30** was formed. The *endo*-configuration of the alcohol **30** was confirmed by $NaBH_4$ reduction of **29** to give the same diastereomer (besides small amounts of the diol **31** as a side product). Reaction of **30** with phthalimide under Mitsunobu conditions afforded **32** which on hydrazinolysis gave rise to the aimed amino ester **33** with the *cis*-configuration of the substituents (Scheme 8).



Scheme 8. Synthesis of the amino ester **33**; a) SmI_2, –78 °C, **28a**, THF/MeOH (3:1), –78 °C, 1 h, room temp., 2 h; b) $NaBH_4$, EtOH, room temp. 15 h; c) phthalimide, PPh_3, THF, 0 °C, DEAD, room temp., 4 h; d) H_4N_2, EtOH, 60 °C, 2 h.

In order to provide an amino acid building block compatible with routine methods of solid-phase peptide synthesis (SPPS), we tried to prepare the Fmoc-protected amino acid **38**. However, the free amino acid **4** could not be isolated after alkaline ester hydrolysis of **33**. In contrast, when the amino ester **33** was first converted into the Boc derivative **34**, ester hydrolysis cleanly afforded the desired amino acid building block **35** (Scheme 9). In analogy to the preparation of **26** (Scheme 5), the epimeric Fmoc-protected amino acid derivative **37** was prepared from **33** by reduction with $LiAlH_4$, Fmoc protection und succinylation of the intermediate alcohol **36**. The relative (and absolute) configuration of the Boc-protected amino acid ester **34** was proved by X-ray crystal structure analysis (Figure 7).



Scheme 9. Synthesis of the *cis*-configured amino acid building blocks **35** and **37**; a) Boc_2O, DMAP, MeCN, 0 °C, room temp., 15 h; b) NaOH, $EtOH/H_2O$, 80 °C, 15 h; c) $LiAlH_4$, THF/Et_2O (3:1), 0 °C, room temp. 15 h; d) Fmoc-Cl, K_2CO_3 (10% in H_2O), MeCN, 0 °C, room temp., 15 h; e) succinic anhydride, DMAP, DCM, pyridine, room temp., 15 h.

Having succeeded in the stereoselective synthesis of the ferrocenyl amino acid building blocks **26**, **35** and **37** we turned our attention to probe their use in solid phase peptide synthesis (SPPS). For this purpose a model peptide sequence (QTAIGVGAP, position 24–32 from the human

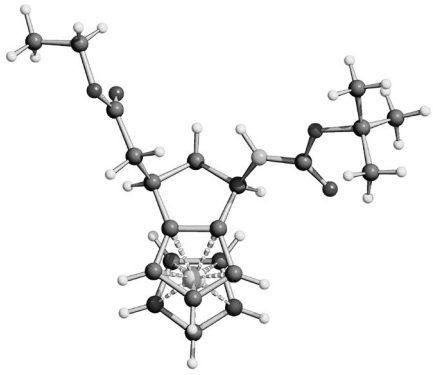
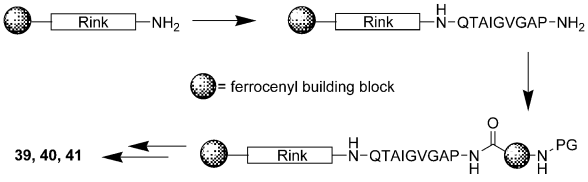


Figure 7. Structure of **34** in the crystalline state.[20]

peptide hormone calcitonin)[21] was synthesized according to the Fmoc-strategy using an automated multiple solid-phase peptide synthesizer and a Rink amide resin as solid support (Scheme 10).



Scheme 10. Solid-phase peptide synthesis.

The N-terminus of this peptide was then equipped with **26** and **37**, respectively. This was achieved in the following manner: the building block was activated by HATU and subsequently added to the peptide resin. After 2–3 h Fmoc was cleaved by addition of piperidine in DMF (30%). Both sequences were then elongated with Fmoc-Gln(Trt)-OH under activation with HOBt and DIC. After cleavage of the Fmoc group the peptides were detached from the resin using TFA in the presence of TIS as scavenger. The *trans*-building block derived product **39** was very stable and could be easily purified by preparative reverse-phase HPLC. The peptide **40** derived from the *cis*-building block **37** proved to be more labile. Nevertheless, the crude product, obtained in good yield, gave satisfactory analytical data.

Finally the *cis*-building block **35** was also empoyed to modify the model peptide N-terminally. For this purpose, **35** was activated with HATU in DMF and incubated with the peptide resin for 2 h. The product was cleaved from the resin using TFA in the presence of TIS as scavenger. HPLC and mass spectral analysis revealed the successful formation of the peptide **41** with a yield of 80%. Again due to its limited stability the final peptide was not further purified by preparative HPLC (Figure 8).

Conclusions

In summary, we have elaborated reliable and stereoselective routes of three new ferrocene-derived, *N*-protected amino acid building blocks with defined relative and absolute configuration. The syntheses require 13 to 15 steps and comprise highly diastereoselective cyclization reactions. Moreover, we have demonstrated that these compounds are suitable to be incorporated in peptide sequences by means of solid-phase peptide synthesis. We are optimistic that the results disclosed here will pave the way for the synthesis of new metal-containing peptides with interesting biological properties. This topic is under current investigation.

Experimental Section

General: Reactions were conducted in flame-dried glassware under an atmosphere of argon using freshly distilled anhydrous solvents. NMR spectra were routinely recorded at 300 MHz (^{1}H) and at 75 MHz (^{13}C) at 25 °C with a Bruker DPX 300 spectrometer. Deuterated chloroform was used as solvent unless otherwise indicated. Proton shifts are reported in ppm (δ) downfield from TMS and were determined by reference to the residual solvent peaks ($CDCl_3$: 7.24 ppm, CD_3OD: 3.31 ppm). Data are reported as follows: chemical shift (multiplicity [singlet (s), doublet (d), triplet (t), quartet

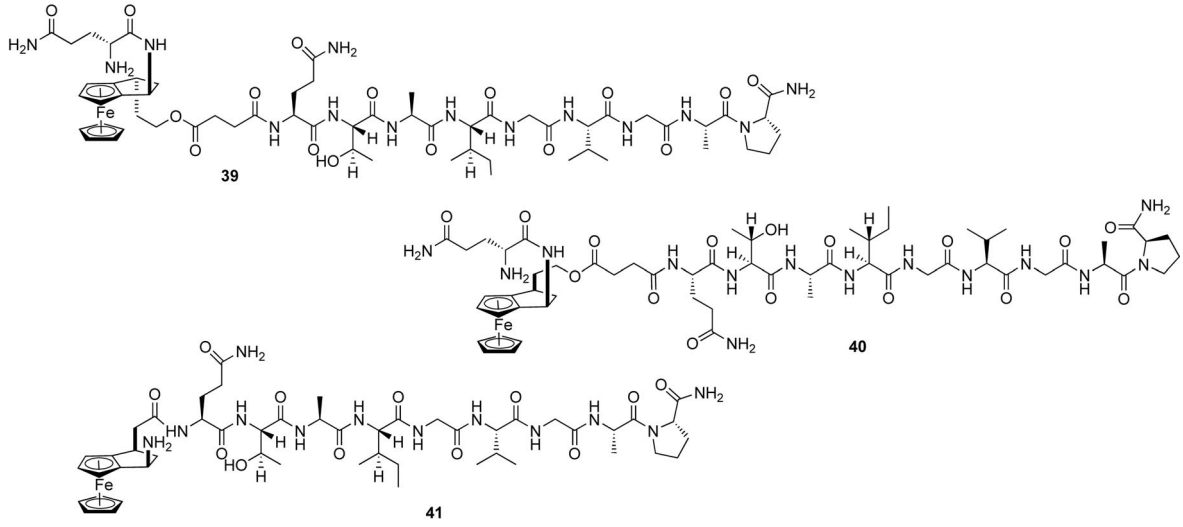


Figure 8. Peptides **39**, **40** and **41** obtained by SPPS.

(q), quintet (quint) and multiplet (m)], coupling constants [Hz], integration, assignment). ^{13}C NMR spectra were recorded using the APT sequence with complete proton decoupling. Multiplicities [C (s), CH_2 (t) or CH (d), CH_3 (q)] were deduced from these spectra. ^{13}C chemical shifts are reported in ppm (δ) relative to solvent resonance as the internal standard ($CDCl_3$: 77 ppm, CD_3OD: 49.05 ppm). Melting points were measured with a Büchi B-454 and are not corrected. Optical rotations were recorded at the given wavelengths (path length 100 mm) with a Perkin–Elmer 343 polarimeter. The concentration is given in g/100 mL. IR spectra were measured at 25 °C as ATR (attenuated total reflectance) with a Perkin–Elmer FT-IR Paragon 1000. Data are reported as follows: absorption [$\tilde{\nu}$], weak (w), middel (m), strong (s), broadened (br). Mass spectra were recorded with a Finnigan MAT Incos 50 Galaxy system and a Finnigan MAT 900. Energy and method of ionization are noted for each measurement and the intensities are given proportionally to the basic peak (100%). Flash-chromatography was done with Merck silica gel 60 (230–400 mesh).

For peptide synthesis N^{α}-Fmoc-protected amino acids, 1-hydroxybenzotriazole (HOBt) and 4-(2′,4′-dimethoxyphenyl-Fmoc-aminomethyl)phenoxy (Rink amide) resin were purchased from NovaBiochem (Läufelfingen, Switzerland). The side-chain protecting groups for the amino acids were: *tert*-butyl (*t*Bu) for Thr and trityl (Trt) for Gln. *N*,*N*′-Diisopropylcarbodiimide (DIC) was obtained from Sigma–Aldrich (Taufkirchen, Germany). Trifluoroacetic acid (TFA), *O*-(7-azabenzotriazol-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate (HATU), *N*,*N*-diisopropylethylamine (DIEA), thioanisole, *p*-thiocresole, triisopropylethylsilane (TIS), hydrazine hydrate solution and piperidine were purchased from Fluka (Taufkirchen, Germany). Acetonitrile (ACN for HPLC) was obtained from Merck (Darmstadt, Germany). Diethyl ether, dichloromethane and *N*,*N*-dimethylformamide (DMF, peptide synthesis grade) were obtained from Biosolve (Valkenswaard, Netherlands). The peptide QTAIGVGAP was synthesized according to the Fmoc/*t*Bu strategy by using an automated multiple solid-phase peptide synthesizer (Syro, MultiSynTech, Bochum, Germany) on the Rink amide resin (15 mg, resin loading 0.5 mmol g^{-1}).[21]

Synthesis of Ester 16 Through Diastereoselective *ortho*-Deprotonation/Alkylation: To a cooled solution of **15**[11] (26.57 g, 1 equiv., 84.00 mmol. $[\alpha]_D^{20}$ = –32.7 (*c* = 0.38, $CHCl_3$, ref.[11] $[\alpha]_D^{20}$ = –32.5) in dry Et_2O (400 mL) was added dropwise at –78 °C a 1.5 M solution of *t*BuLi in hexane (61.6 mL, 1.1 equiv., 92.40 mol). After 10 min the cooling bath was removed and the mixture was warmed to room temperature and stirred for 1 h. The suspension was then cannulated into another flask containing an excess of methyl chloroformate (65.0 mL, 10 equiv., 840 mmol) in Et_2O (65 mL) stirred at a temperature of –50 °C. After addition was completed, the mixture was warmed slowly to room temperature and stirring was continued for 15 h. The mixture was then quenched with water and the layers were separated. The organic layer was washed with saturated aqueous NH_4Cl, brine, dried with Na_2SO_4, filtered, and concentrated in vacuo. After flash chromatography (cyclohexane/ethyl acetate, 2:1) the desired ester **16** was obtained as a dark red oil (25.93 g, 69.3 mmol, 82%. $[\alpha]_D^{20}$ = +24.7 (*c* = 0.35, $CHCl_3$). The spectroscopic data were in accordance to those reported in the literature.[10,11]

Synthesis of Ester 17 Through Acetal Cleavage and Horner Olefination: The aldehyde **42** was obtained from **16** through acidic acetal cleavage according to Kagan's procedure.[11] Transformation of **42** into the diester **17** was achieved as follows. To a suspension of NaH (60% in mineral oil, washed with dry hexane, 1.72 mg, 1.5 equiv., 42.90 mmol) in THF (120 mL) (triethylphosphono)acetate (8.5 mL, 1.5 equiv., 42.90 mmol) was added at 0 °C and the resulting mixture was warmed to room temperature and stirred for 1 h. After this period, the aldehyde **42** (7.8 g, 1 equiv., 28.60 mmol) dissolved in THF (50 mL) was added to the mixture. The reaction mixture was stirred at room temperature for another 30 min and the reaction was quenched with saturated aqueous NH_4Cl. The layers were separated and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried with $MgSO_4$ and filtered. Evaporation of the solvents and purification by flash chromatography (cyclohexane/ethyl acetate, 3:1) afforded **17** as an auburn solid (8.51 g, 24.9 mmol, 87% yield); m.p. 84 °C. $[\alpha]_D^{20}$ = 1257.0 (*c* = 0.36, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3095 (w), 2987 (m), 2948 (m), 2902 (w), 1711 (s), 1694 (s), 1623 (s), 1449 (s), 1419 (s), 1367 (s), 1266 (s), 1216 (s), 1170 (s), 1082 (s), 1038 (s), 984 (s), 939 (m), 857 (s), 820 (s), 776 (s), 732 (m), 678 (w) cm^{-1}. ^1H NMR: δ = 1.31 (t, *J* = 7.1 Hz, 3 H, CH_3CH_2), 3.82 (s, 3 H, CH_3), 4.17 (s, 5 H, Cp), 4.20 (q, *J* = 7.1 Hz, 2 H, CH_2CH_3), 4.56 (t, *J* = 2.7 Hz, 1 H, CHCp), 4.77 (m, 1 H, CHCp), 4.97 (m, 1 H, CHCp), 6.13 (d, *J* = 16.0 Hz, 1 H, CH=CHCO$_2$Et), 8.26 (d, *J* = 16.0 Hz, 1 H, CH=CHCO$_2$Et) ppm. ^{13}C NMR: δ = 14.3 (q, CH_3CH_2), 51.7 (q, CH_3), 60.2 (t, CH_3CH_2), 69.3 (d, CHCp), 71.2 (s, CCp), 71.4 (d, Cp), 72.0 (d, CHCp), 73.6 (d, CHCp), 80.3 (s, CCp), 117.4 (d, CH=CHCO$_2$Et), 143.7 (d, CH=CHCO$_2$Et), 166.8 (s, CO$_2$Et), 171.7 (s, CO$_2$Me) ppm. MS (EI, 70 eV): *m*/*z* (%) = 343 (5) [M + 1]$^+$, 342 (30) [M]$^+$, 329 (17), 328 (96), 297 (6), 277 (3) [M – Cp]$^+$, 263 (13), 245 (12), 233 (16), 231 (67), 201 (20), 152 (23), 145 (78), 122 (60), 117 (85), 89 (100), 56 (45) [Fe]$^+$. HRMS (EI, 70 eV) calcd. for $C_{17}H_{18}FeO_4$ 342.0554; found 342.055.

Synthesis of 10a and 19a Through Mukaiyama–Michael Addition: To a solution of trifluoromethanesulfonic acid (1.3 mL, 0.57 equiv., 14.20 mmol) in CH_2Cl_2 (130 mL) was added dropwise at –78 °C a 2 M solution of $AlMe_3$ in toluene (2.49 mL, 0.20 equiv., 4.98 mmol). After 5 min at this temperature, the mixture was stirred 30 min at room temperature. The mixture was then recooled to –78 °C and the ester **17** (8.51 g, 1 equiv., 24.90 mmol) in CH_2Cl_2 (80 mL) was added dropwise, followed by the addition of the silyl enol ether **18**[15] (6.25 g, 1.24 equiv., 30.72 mmol) in CH_2Cl_2 (80 mL). The solution was stirred for 2.5 h at –78 °C and afterwards MeOH was added. After warming to 0 °C, saturated aqueous NH_4Cl was added and the layers were separated. The aqueous layer was washed with CH_2Cl_2 and the combined organic layers were washed with brine, dried with $MgSO_4$, filtered, and concentrated in vacuo. Purification by flash chromatography (cyclohexane/ethyl acetate, 3:1) afforded the addition product **10a** as an orange oil (9.88 g, 22.98 mmol, 92%) and the cyclized product **19a** as a dark red oil (554 mg, 1.4 mmol, 6%; 98% global yield). **10a**: $[\alpha]_D^{20}$ = –42.6 (*c* = 0.385, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3092 (w), 2977 (m), 2948 (m), 1731 (s), 1711 (s), 1445 (m), 1370 (m), 1340 (w), 1293 (m), 1216 (m), 1158 (s), 1090 (m), 818 (w) cm^{-1}. ^1H NMR: δ = 0.99 (t, *J* = 7.1 Hz, 3 H, CH_3CH_2), 1.17 (t, *J* = 7.1 Hz, 3 H, CH_3CH_2), 2.43 (m, 2 H, CH_2CO_2Et), 2.78 (dd, *J* = 15.3, 9.7 Hz, 1 H, CHCO$_2$Et), 2.90 (dd, *J* = 15.4, 4.1 Hz, 1 H, CHCO$_2$Et), 3.66 (s, 3 H, CH_3), 3.80 (q, *J* = 7.1 Hz, 2 H, CH_3CH_2), 3.90 (m, 1 H, CH), 4.02 (s, 5 H, Cp), 4.05 (q, *J* = 7.1 Hz, 2 H, CH_3CH_2), 4.16 (s, 2 H, CHCp), 4.65 (s, 1 H, CHCp) ppm. ^{13}C NMR: δ = 13.8 (q, CH_3CH_2), 13.9 (q, CH_3CH_2), 30.8 (d, CH), 37.9 (t, CH_2CO_2Et), 39.9 (t, CH_2CO_2Et), 51.0 (q, CH_3), 59.6 (t, CH_3CH_2), 60.1 (t, CH_3CH_2), 68.0 (s, CCp), 69.0 (d, CHCp), 69.9 (d, Cp), 70.3 (d, CHCp), 70.5 (d, CHCp), 93.5 (s, CCp), 171.3 (s, CO$_2$Et), 171.8 (s, CO$_2$Me), 172.0 (s, CO$_2$Et) ppm. MS (EI, 70 eV): *m*/*z* (%) = 431 (25) [M + 1]$^+$, 430 (100) [M]$^+$, 319 (17), 121 (24) [FeCp]$^+$. HRMS (EI, 70 eV) calcd. for $C_{21}H_{26}FeO_6$ 430.1078; found 430.108. **19a**: $[\alpha]_D^{20}$ = +309 (*c* = 0.085, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3105 (w), 2978 (w), 1731 (s), 1703 (s), 1462

(w), 1425 (w), 1369 (w), 1327 (w), 1255 (m), 1154 (m), 1106 (w), 1026 (m), 822 (w) cm^{-1}. ^1H NMR: δ = 1.23 (m, 6 H, CH_3CH$_2$), 2.82 (dd, J = 15.8, 7.7 Hz, 1 H, CHHCO$_2$Et), 2.90 (dd, J = 15.6, 6.9 Hz, 1 H, CHHCO$_2$Et), 3.66 (m, 1 H, CH), 3.73 (d, J = 6.2 Hz, 1 H, CHCO$_2$Et), 4.15 (m, 4 H, CH_2CH$_3$), 4.19 (s, 5 H, Cp), 4.41 (br. s, 1 H, CHCp), 4.55 (br. s, 1 H, CHCp), 4.64 (br. s, 1 H, CHCp) ppm. ^{13}C NMR: δ = 14.2 (q, CH$_3$CH$_2$), 34.0 (d, CH), 40.3 (t, CH$_2$CO$_2$Et), 60.9 (t, CH$_3$$CH_2$), 61.5 (t, CH$_3$$CH_2$), 61.9 (d, CHCp), 65.1 (d, CHCO$_2$Et), 66.2 (d, CHCp), 70.5 (d, Cp), 76.3 (d, CHCp), 78.9 (s, CCp), 106.5 (s, CCp), 168.9 (s, CO$_2$Et), 171.4 (s, CO$_2$Et), 199.0 (s, C=O) ppm. MS (EI, 70 eV): m/z (%) = 399 (15) [M + 1]$^+$, 398 (68) [M]$^+$, 353 (21), 352 (45), 325 (12), 324 (39), 252 (20), 121 (100) [FeCp]$^+$, 103 (36), 89 (62), 56 (58) [Fe]$^+$. HRMS (EI, 70 eV) calcd. for $C_{20}H_{22}FeO_5$ 398.0816; found 398.082

Synthesis of 19a and 19b Through Group-Selective Dieckmann Cyclization: To a mixture of KH (30% in oil, washed with dry hexane, 12.3 g, 4 equiv., 91.92 mmol) in THF (400 mL) was added the triester **10a** (9.88 g, 1 equiv., 22.98 mmol) in THF (250 mL). The reaction mixture was refluxed for 1 h. The red solution was then cooled to 0 °C and water was added slowly and then 1 N HCl. The layers were separated and the aqueous layer was washed with MTBE. The combined organic layers were washed with brine, dried with $MgSO_4$, filtered, and concentrated in vacuo. Purification by flash chromatography (cyclohexane/ethyl acetate, 3:1) gave **19a** (5.63 g, 14.1 mmol, 62%. $[\alpha]_D^{20}$ = +289 (c = 0.30) and **19b** (2.06 g, 5.2 mmol, 23%; 85% global yield), both as dark red oils. **19b**: IR (neat): $\tilde{\nu}$ = 2982 (w, br), 1732 (s), 1700 (s), 1461 (w), 1155 (m), 1462 (w), 1106 (w), 1026 (m), 827 (w), 616 (m) cm^{-1}. ^1H NMR: δ = 1.27 (t, J = 7.2 Hz, 3 H, CH$_2$CH_3), 2.92 (m, 2 H, CH), 3.78 (m, 2 H, CH_2CH$_3$), 3.77 (s, 3 H, CH_3), 4.19 (dd, J = 7.2, 2.0 Hz, 2 H, CH_2CH$_3$), 4.25 (s, 5 H, Cp), 4.47 (d, J = 2.3 Hz, 1 H, CHCp), 4.61 (t, J = 2.4 Hz, 1 H, CHCp), 4.72 (d, J = 2.5 Hz, 1 H, CHCp) ppm. ^{13}C NMR: δ = 14.19 (q, CH$_2$$CH_3$), 34.02 (d, CH), 40.31 (t, CH$_2$CO$_2$Et), 52.58 (q, CH$_3$), 60.90 (t, CH$_2$CH$_3$), 61.91 (d, CHCp), 65.09 (d, CHCO$_2$Et), 66.20 (d, CHCp), 70.46 (d, Cp), 76.21 (d, CHCp), 78.90 (s, CCp), 106.52 (s, CCp), 168.76 (s, CO$_2$Me), 171.32 (s, CO$_2$Et), 198.97 (s, C=O) ppm. MS (EI, 70 eV): m/z (%) = 398 (27) [M]$^+$, 385 (26), 384 (100), 352 (53), 324 (40), 121 (20) [FeCp]$^+$, 56 (11) [Fe]$^+$. HRMS (ESI) calcd. for $C_{20}H_{22}FeO_5$ 384.0660; found 384.066.

Synthesis of Diol 21 from 19a/19b: A mixture of the triester **19a/19b** (1.02 g, 2.55 mmol) was dissolved in ethanol (40 mL) and 1 N NaOH (40 mL) was added. The mixture was heated to 80 °C and stirred at the same temperature for 15 h. After cooling to room temperature, MTBE was added and the phases were separated. The organic layer was washed with 1 N NaOH. The combined aqueous layers were then acidified with 2 N HCl, extracted with MTBE and the new organic phase was finally washed with brine. Afterwards, Na_2SO_4 was added, the solution was filtered and concentrated in vacuo to afford the intermediate carboxylic acid. The crude carboxylic acid (760 mg, 1 equiv., 2.55 mmol) was dissolved in THF (25 mL) and the solution was cooled to 0 °C. A suspension of $LiAlH_4$ (290 mg, 3 equiv., 7.65 mmol) in Et_2O (8 mL) was then added carefully. The reaction mixture was stirred at room temperarture for 15 h and quenched by adding 1 N NaOH. It was filtered through a pad of celite, rinsed many times with CH_2Cl_2 and the filtrate was concentrated in vacuo. Purification by flash chromatography (cyclohexane/ethyl acetate, 1:1) afforded **21** as a yellow solid (436 mg, 1.52 mmol, 60% for 2 steps). An analytical sample of **21** was prepared by recrystallization from 1,2-dichloroethane; m.p. 116 °C. $[\alpha]_D^{20}$ = +16.5 (c = 0.43, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3327 (m), 3090 (w), 2922 (m), 2851 (m), 1725 (w), 1673 (w), 1447 (m), 1327 (m), 1260 (s), 1104 (s), 1079 (s), 1040 (s), 1007 (s), 997 (s), 884 (m), 804 (s), 734 (m) cm^{-1}. ^1H NMR: δ = 1.59 (br. s, 1 H, OH), 1.86 (m, 3 H, OH, CHHCH$_2$OH, CHH), 2.04 (m, 1 H, CHHCH$_2$OH), 2.44 (m, 1 H, CH), 2.73 (m, 1 H, CHH), 3.77 (t, J = 6.8 Hz, 2 H, CH$_2$CH_2OH), 3.97 (d, J = 2.0 Hz, 1 H, CHCp), 4.02 (d, J = 2.0 Hz, 1 H, CHCp), 4.13 (br. t, 1 H, CHCp), 4.28 (s, 5 H, Cp), 4.52 (q, J = 7.0 Hz, 1 H, CHOH) ppm. ^{13}C NMR: δ = 32.2 (d, CH), 38.7 (t, CH$_2$CH$_2$OH), 47.1 (t, CH$_2$), 58.9 (d, CHCp), 60.7 (d, CHCp), 61.8 (t, CH$_2$$CH_2$OH), 68.3 (d, Cp), 69.3 (d, CHOH), 70.0 (d, CHCp), 98.3 (s, CCp), 100.3 (s, CCp) ppm. MS (EI, 70 eV): m/z (%) = 313 (17) [M + 1]$^+$, 312 (91) [M]$^+$, 284 (10), 247 (23) [M – Cp]$^+$, 239 (18), 215 (24), 188 (7), 175 (9), 121 (100) [FeCp]$^+$, 103 (31), 56 (98) [Fe]$^+$.

Synthesis of 23 via Selective Mono-Protection of 21: To a solution of diol **21** (135 mg, 1 equiv., 0.47 mmol) and DMAP (12 mg, 0.2 equiv., 0.09 mmol) in pyridine (4.5 mL) was added dropwise TDSCl (112 µL, 1.2 equiv., 0.56 mmol). After 3.5 h at room temperature, 1 N HCl was added. The mixture was extracted with MTBE and the organic phase was washed with brine, dried with $MgSO_4$, filtered, and concentrated in vacuo. Purification by flash chromatography (cyclohexane/ethyl acetate, 2:1) afforded **23** as a yellow oil (200 mg, 1.46 mmol, 99%). $[\alpha]_D^{20}$ = +25.9 (c = 0.46, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3334 (s, br), 2921 (s), 1716 (w, br), 1329 (m), 1104 (s), 1039 (s), 999 (s), 816 (s), 611 (m) cm^{-1}. ^1H NMR: δ = 0.10 [s, 6 H, Si(CH_3)$_2$], 0.84 (s, 6 H, 2× CH$_3$), 0.86 (s, 3 H, CH$_3$), 0.89 (s, 3 H, CH$_3$), 1.61 [m, 1 H, CH(CH$_3$)$_2$], 1.90 (m, 3 H, CHH, CH_2CH$_2$OTDS), 2.43 (m, 1 H, CH), 2.71 (m, 1 H, CHH), 3.70 (t, J = 6.6 Hz, 2 H, CH$_2$CH_2OTDS), 3.95 (d, J = 1.9 Hz, 1 H, CHCp), 4.01 (d, J = 2.0 Hz, 1 H, CHCp), 4.12 (t, J = 1.8 Hz, 1 H, CHCp), 4.27 (s, 5 H, Cp), 4.53 (t, J = 7.3 Hz, 1 H, CHOH) ppm. ^{13}C NMR: δ = –3.33 [q, Si(CH$_3$)$_2$], 18.50 (q, CH$_3$), 20.34 (q, CH$_3$), 25.14 [s, SiC(CH$_3$)$_2$], 32.06 (d, CH), 34.16 [d, CH(CH$_3$)$_2$], 38.87 (t, CH$_2$CH$_2$OTDS), 47.08 (t, CH$_2$), 58.77 (d, CHCp), 60.72 (d, CHCp), 61.71 (t, CH$_2$$CH_2$OTDS), 68.17 (d, Cp), 69.40 (d, CHOH), 69.80 (d, CHCp), 98.24 (s, CCp), 100.75 (s, CCp) ppm. MS (EI, 70 eV): m/z (%) = 429 (32) [M + 1]$^+$, 428 (100) [M]$^+$, 410 (9), 345 (12), 250 (15), 205 (7), 138 (9), 130 (7), 85 (7), 75 (14), 59 (9). HRMS (ESI) calcd. for $C_{23}H_{36}FeO_2Si$ 428.1834; found 428.185.

Synthesis of 43 via Mitsunobu Reaction: DIAD (1.09 mL, 2 equiv., 2.73 mmol) was dissolved in THF (25 mL), cooled to 0 °C and PPh_3 (1.44 g, 2 equiv., 5.46 mmol) was added. After 30 min at the same temperature a solution of **23** (1.17 g, 1 equiv., 2.73 mmol) in THF (15 mL) and $Zn(N_3)_2$ (284 mg, 0.75 equiv., 2.05 mmol) were added. After 2 h at 0 °C the mixture was filtered through a pad of celite, rinsed several times with CH_2Cl_2 and concentrated in vacuo. Purification by flash chromatography (cyclohexane/ethyl acetate, 5:1) afforded **43** as an orange brown oil (620 mg, 1.37 mmol, 50%). $[\alpha]_D^{20}$ = –77.3 (c = 0.44, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3091 (w), 2995 (s), 2862 (s), 2091 (s), 1741 (m), 1464 (m), 1376 (m), 1248 (s), 1104 (s), 1017 (m), 998 (m), 934 (m), 874 (m), 818 (s), 774 (s), 658 (w) cm^{-1}. ^1H NMR: δ = 0.11 [s, 6 H, Si(CH_3)$_2$], 0.86 [s, 6 H, (CH_3)$_2$], 0.87 (s, 3 H, CH_3), 1.90 (s, 3H CH_3), 1.65 [m, 1 H, CH(CH$_3$)$_2$], 1.82 (m, 1 H, CHHCH$_2$OTDS), 2.00 (m, 1 H, CHHCH$_2$OTDS), 2.39 (m, 2 H, CH_2), 2.77 (m, 1 H, CH), 3.73 (m, 2 H, CH$_2$CH_2OTDS), 3.98 (d, J = 2.2 Hz, 1 H, CHCp), 4.14 (s, 5 H, Cp), 4.17 (t, J = 2.3 Hz, 1 H, CHCp), 4.22 (d, J = 2.1 Hz, 1 H, CHCp), 4.63 (d, J = 4.6 Hz, 1 H, CHN$_3$) ppm. ^{13}C NMR: δ = –3.31 [q, Si(CH$_3$)$_2$], 18.50 [q, (CH$_3$)$_2$], 20.39 [q (CH$_3$)$_2$], 25.17 [s, SiC(CH$_3$)$_2$], 32.74 (d, CH), 34.16 [d, CH(CH$_3$)$_2$], 38.36 (t, CH$_2$CH$_2$OTDS), 44.78 (t, CH$_2$), 60.83 (d, CHCp), 61.32 (d, CHCp), 61.67 (d, CHN$_3$), 61.81 (t, CH$_2$$CH_2$OTDS), 68.86 (d, Cp), 70.61 (d, CHCp), 89.65 (s,CCp), 100.57 (s, CCp) ppm. MS (EI, 70 eV): m/z (%) = 454 (3) [M + 1]$^+$, 453 (11) [M]$^+$, 412 (32) [M – N$_3$ + 1]$^+$, 411 (100) [M – N$_3$]$^+$, 251

(9), 225 (11). HRMS (ESI) calcd. for $C_{23}H_{35}FeN_3OSi$ 453.1898; found 453.190.

Synthesis of 24 via Staudinger Reduction: To a solution of **43** (183 mg, 1 equiv., 404 μmol) in THF (10 mL) PPh_3 (157 mg, 1.5 equiv., 606 μmol) was added. After 8 h H_2O (11 mL, 1.5 equiv., 606 μmol) was added and the reaction mixture was stirred for 15 h. After quenching with saturated aqueous $NaHCO_3$ the layers were separated and the aqueous layer was extracted with MTBE. The combined organic layers were concentrated in vacuo. Purification by flash chromatography (CH_2Cl_2/MeOH, 2:1 + 1% NEt_3) afforded **24** as a yellow oil (156 mg, 356 μmol, 90%). $[\alpha]_D^{20}$ = +16.1 (c = 0.35, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3600–2400 (br), 2953 (s), 2862 (m), 1556 (br., m), 1434 (m), 1389 (m), 1248 (m), 1180 (w), 1092 (s), 998 (m), 827 (s), 775 (m), 720 (s), 694 (s) cm^{-1}. ^1H NMR: δ = 0.53 [s, 6 H, Si(CH_3)$_2$], 0.79 [s, 6 H, (CH_3)$_2$] 0.81 (s, 3 H, CH_3), 0.83 (s, CH_3) 1.57 [m, 1 H, CH(CH_3)$_2$], 1.87 (m, 2 H, CH_2CH_2OTDS), 2.18 (m, 1 H, CHH), 2.36 (m, 1 H, CHH), 2.71 (m, 1 H, CH), 3.65 (m, 2 H, CH_2CH_2OTDS), 3.82 (d, J = 1.8 Hz, 1 H, CHCp), 4.04 (s, 5 H, Cp), 4.08 (br. m, 3 H, 2× CHCp, CHNH$_2$) ppm. ^{13}C NMR: δ = –3.27 [q, Si(CH_3)$_2$], 18.51 [q, (CH_3)$_2$], 20.40 [q, (CH_3)$_2$], 25.17 [s, SiC(CH_3)$_2$], 32.06 (d, CH), 34.16 [d, CH(CH_3)$_2$], 38.79 (t, CH_2CH_2OTDS), 45.39 (t, CH_2), 50.84 (d, $CHNH_2$), 60.90 (d, $CHCp$), 61.01 (d, $CHCp$), 61.95 (t, CH_2CH_2OTDS), 68.77 (d, Cp), 70.18 (d, $CHCp$), 92.79 (s, CCp), 100.13 (s, CCp) ppm. MS (EI, 70 eV): m/z (%) = 428 (30) [M + 1]$^+$, 427 (100) [M]$^+$, 410 (14), 277 (16), 250 (21), 248 (24), 201 (26), 121 (17) [FeCp]$^+$, 73 (17). HRMS (ESI) calcd. for $C_{23}H_{37}FeNOSi$ 427.1994; found 427.199.

Synthesis of 25 by TMS-OTf Deprotection and Fmoc-protection: To a solution of **24** (108 mg, 1 equiv., 253 μmol) in CH_2Cl_2 (6.25 mL) TMSOTf (294 μL, 6 equiv., 1.52 mmol) was added at 0 °C. The mixture was stirred at the same temperature for 1 h. After quenching with saturated aqueous $NaHCO_3$, the layers were separated, the aqueous layer was extracted with CH_2Cl_2 and the combined organic phases were finally washed with brine. Afterwards, Na_2SO_4 was added, the solution was filtered and concentrated in vacuo to afford the intermediate amino alcohol. The crude product (72 mg, 1 equiv., 253 μmol) was dissolved in MeCN (2.5 mL), 10% aqueous K_2CO_3 (2 mL) was added and the solution was cooled to 0 °C. A solution of Fmoc-Cl (134 mg, 2 equiv., 506 μmol) in MeCN (2 mL) was added carefully. The reaction mixture was stirred at room temperature for 15 h and quenched by adding CH_2Cl_2/H_2O. The layers were separated and the aqueous layer was extracted with CH_2Cl_2. The solution was concentrated in vacuo. Purification by flash chromatography (cyclohexane/ethyl acetate, 1:1) afforded **25** as a yellow foam (106 mg, 209 μmol, 83% for 2 steps); m.p. 82 °C. $[\alpha]_D^{20}$ = –65.0 (c = 0.36, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3417 (m, br), 2923 (m), 1695 (s), 1505 (m), 1476 (w), 1447 (s), 1330 (w), 1244 (m), 1104 (m), 1056 (m), 907 (m), 820 (w), 756 (s), 738 (s) cm^{-1}. ^1H NMR: δ = 1.91 (m, 1 H, CHH), 2.06 (m, 1 H, CHH), 2.36 (m, 1 H, CHHCH$_2$OH), 2.48 (m, 1 H, CHHCH$_2$OH), 2.72 (m, 1 H, CH), 3.79 (t, J = 5.5 Hz, 2 H, CH_2CH_2OH), 3.94 (s, 1 H, $CHCp$), 4.15 (s br, 8 H, CH_{Fmoc}, 2× CHCp, Cp), 4.76 (d, J = 5.0 Hz, 2 H, $CH_{2\ Fmoc}$), 4.80 (s, 1 H, CHNHFmoc), 7.27 (t, J = 7.3 Hz, 2 H, 2× CH_{arom}), 7.37 (t, J = 7.1 Hz, 2 H, 2× CH_{arom}), 7.54 (d, J = 7.1 Hz, 2H, 2× CH_{arom}), 7.73 (d, J = 7.3 Hz, 2 H, 2× CH_{arom}) ppm. ^{13}C NMR: δ = 32.26 (d, CH), 38.22 (t, CH_2), 45.28 (CH_2CH_2OH), 47.25 (d, CH_{Fmoc}), 51.29 (d, $CHNHFmoc$), 60.85 (d, $CHCp$), 61.31 (d, $CHCp$), 61.81 (t, CH_2CH_2OH) 66.46 (t, $CH_{2\ Fmoc}$), 69.04 (d, Cp), 70.30 (d, $CHCp$), 91.94 (s, CCp), 100.44 (s, CCp), 119.91 (d, CH_{arom}), 124.98 (d, CH_{arom}), 126.99 (d, CH_{arom}), 127.62 (d, CH_{arom}), 141.27 (s, C_{arom}), 143.92 (s, C_{arom}), 155.52 (s, C=O$_{Fmoc}$) ppm. MS (pos. ESI) m/z (%) 530 [M + Na]$^+$ (100), 507 [M]$^+$ (96), 413 (5), 269 (21), 219 (3). HRMS (ESI) calcd. for $C_{30}H_{29}FeNO_3$ 507.1497; found 507.150.

Synthesis of 26 by Esterification of 25 with Succinic Anhydride: To a solution of **25** (150 mg, 1 equiv., 296 μmol) in CH_2Cl_2 (5.4 mL) and pyridine (0.6 mL) succinic anhydride (89 mg, 3 equiv., 887 μmol) and DMAP (21 mg, 0.6 equiv., 177 μmol) were added. After strirring at room temperature for 15 h the reaction mixture was concentrated in vacuo and redissolved in EtOAc. The solution was washed with icecold 5% aqueous citric acid, dried with $MgSO_4$, filtered, and concentrated in vacuo. Purification by flash chromatography (CH_2Cl_2/MeOH, 10:1) afforded **26** as a yellow foam (175 mg, 288 μmol, 97%); m.p. 75 °C. $[\alpha]_D^{20}$ = –45.5 (c = 0.385, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3400–2800 (br), 2940 (w), 1783 (m), 1711 (s, br), 1506 (m), 1448 (m), 1330 (w), 1239 (s), 1163 (s), 1105 (m), 1004 (m), 907 (w), 821 (w), 758 (m), 740 (s) cm^{-1}. ^1H NMR: δ = 1.93 (m, 1 H, CHHCH$_2$OR), 2.08 (m, 1 H, CHHCH$_2$OR), 2.32 (m, 2 H, CH_2), 2.61 (m, 5 H, $CH_2CH_2CO_2H$, CH), 3.90 (s, 1 H, $CHCp$), 4.11 (m, 5 H, 2× $CHCp$, CH_{Fmoc}, CH_2CH_2OR), 4.12 (s, 5 H, Cp), 4.33 (m, 2 H, $CH_{2\ Fmoc}$), 4.78 (t, J = 6.0 Hz, 1 H, CHNHFmoc), 7.31 (m, 4 H, 4× CH_{arom}), 7.54 (d, J = 7.0 Hz, 2 H, 2× CH_{arom}), 7.70 (d, J = 7.0 Hz, 2 H, 2× CH_{arom}), 10.71 (br., 1 H, CO_2H) ppm. ^{13}C NMR: δ = 30.61 (t, $CH_2CH_2CO_2H$), 32.48 (d, CH), 34.17 (t, CH_2CH_2OR), 45.00 (t, CH_2), 47.20 (d, CH_{Fmoc}), 51.10 (d, $CHNHFmoc$), 60.70 (d, $CHCp$), 61.22 (d, $CHCp$), 63.07 (t, CH_2CH_2OR), 66.36 (t, $CH_{2\ Fmoc}$), 68.83 (d, Cp), 70.15 (d, $CHCp$), 92.17 (s, CCp), 99.69 (s, CCp), 119.80 (d, CH_{arom}), 124.98 (d, CH_{arom}), 126.92 (d, CH_{arom}), 127.53 (d, CH_{arom}), 141.15 (s, C_{arom}), 143.86 (s, C_{arom}), 155.52 (s, C=O$_{Fmoc}$), 173.47 (s, C=O), 177.55 (s, CO_2H) ppm. MS (pos. ESI) m/z (%) 630 [M + Na]$^+$ (100), 607 [M]$^+$ (96), 488 (42), 369 (15), 319 (25), 249 (100), 179 (16). HRMS (ESI; M+Na$^+$) calcd. for $C_{34}H_{33}FeNO_6$ 630.1560; found 630.156.

Synthesis of 27 Through Ester Condensation: Methyl phenyl sulfone (49.7 mg, 1.1 equiv., 0.29 mmol) was dissolved in THF (3 mL) and the solution was cooled to –78 °C. A 1.1 M solution of *n*BuLi in hexane (0.53 mL, 2 equiv., 0.58 mmol) was added dropwise to the mixture and the resulting intense yellow-orange solution was stirred at –78 °C for 1 h. A solution of **16** (108 mg, 1 equiv., 0.29 mmol) in THF (3 mL) was subsequently added dropwise. After 1 h the mixture was warmed to room temperature and stirred for 15 h. After quenching with a saturated aqueous NH_4Cl, the layers were separated and the aqueous layer was washed with MTBE. The organic layers were combined, dried with Na_2SO_4, filtered, and concentrated in vacuo. Purification by flash chromatography (cyclohexane/ethyl acetate, 1:1) afforded **27** as a red foam (124 mg, 0.25 mmol, 86%). $[\alpha]_D^{20}$ = +73 (c = 0.255, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2924 (w), 1662 (s), 1476 (w), 1446 (m), 1429 (m), 1373 (w), 1320 (s), 1243 (w), 1153 (s), 1099 (s), 1012 (m), 931 (w), 827 (w), 761 (m), 687 (w) cm^{-1}. ^1H NMR: δ = 1.40 (br. d, 1 H, OCH$_2CH$H), 1.75 (m, 1 H, OCH$_2$CHH), 3.24 (s, 3 H, CH_3), 3.27 (dd, J = 10.5, 4.6 Hz, 1 H, OCHCHH), 3.37 (dd, J = 10.4, 5.7 Hz, 1 H, OCHCHH), 3.88 (br. dd, 1 H, OCHHCH$_2$), 3.99 (m, 1 H, OCHCH$_2$), 4.17 (s, 5 H, Cp), 4.19 (m, 1 H, OCHHCH$_2$), 4.68 (m, 4 H, CH_2SO_2Ph, 2× $CHCp$), 4.89 (br. s, 1 H, $CHCp$), 5.82 (s, 1 H, CH), 7.49 (m, 2 H, 2× CH_{Ph}), 7.57 (m, 1 H, CH_{Ph}), 7.92 (d, J = 7.1 Hz, 2 H, 2× CH_{Ph}) ppm. ^{13}C NMR: δ = 27.76 (t, OCH$_2CH_2$), 58.97 (q, CH_3), 64.74 (t, CH_2SO_2Ph), 66.82 (t, OCH$_2CH_2$), 71.09 (d, Cp), 71.75 (d, $CHCp$), 72.08 (d, $CHCp$), 73.09 (d, $CHCp$), 75.12 (t, OCHCH_2), 75.57 (s, CCp), 75.73 (d, OCHCH$_2$), 87.61 (s, CCp), 98.65 (d, CH), 128.47 (d, CH_{Ph}), 128.96 (d, CH_{Ph}), 133.78 (d, CH_{Ph}), 139.41 (s, C_{Ph}), 191.64 (s, C=O) ppm. MS (EI, 70 eV): m/z (%) = 499 (13) [M + 1]$^+$, 498 (46) [M]$^+$, 403 (80), 359 (26), 331 (100), 239 (76), 121 (88) [FeCp]$^+$, 85 (34), 77

(55), 56 (54) $[Fe]^+$. HRMS (ESI) calcd. for $C_{24}H_{26}FeO_6S$ 498.0799; found 498.080.

Synthesis of 11a Through Acetal Cleavage and Horner Olefination: The keto sulfone **27** (15.68 g, 1 equiv., 31.5 mmol) was dissolved in a mixture of CH_2Cl_2 (200 mL) and water (100 mL) and *p*-toluenesulfonic acid monohydrate (6.4 g, 1.05 equiv., 33.1 mmol) was added. The mixture was vigorously stirred for 15 h. The layers were separated and the aqueous phase was washed with MTBE. The combined organic layers were dried with $MgSO_4$, filtered, and concentrated in vacuo. The crude aldehyde was obtained as red foam and directly converted as follows. To a suspension of NaH (60% in mineral oil, washed with dry hexane, 4.41 g, 3.5 equiv., 110.25 mmol) in THF (300 mL) triethylphosphonoacetate (22 mL, 3.5 equiv., 110.25 mmol) was added at 0 °C. The resulting mixture was warmed to room temperature and stirred for 1 h. After this period, the aldehyde (1 equiv., 31.5 mmol) dissolved in THF (70 mL) was added to the mixture. The reaction mixture was stirred at room temperature for another 30 min and the reaction was quenched with saturated aqueous NH_4Cl. The layers were separated and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried with $MgSO_4$ and filtered. Evaporation of the solvents in vacuo and subsequent purification by flash chromatography (cyclohexane/ethyl acetate, 1:1) gave **11a** as a red oil (12.34 g, 26.5 mmol, 84% over 2 steps). $[\alpha]_D^{20}$ = +880 (*c* = 0.22, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2930 (w), 1705 (s), 1458 (m), 1446 (m), 1424 (w), 1372 (w), 1306 (s), 1147 (s), 1106 (w), 1083 (m), 1037 (m), 832 (w), 744 (w), 725 (m), 686 (m) cm^{-1}. ^1H NMR: δ = 1.34 (t, *J* = 7.1 Hz, 3 H, CH_3CH$_2$), 4.22 (m, 2 H, CH$_3$CH_2), 4.27 (s, 5 H, Cp), 4.43 (d, *J* = 14.1 Hz, 1 H, C*H*HSO$_2$Ph), 4.61 (d, *J* = 14.0 Hz, 1 H, CH*H*SO$_2$Ph), 4.78 (t, *J* = 2.8 Hz, 1 H, C*H*Cp), 4.95 (s, 1 H, C*H*Cp), 5.04 (s, 1 H, C*H*Cp), 6.20 (d, *J* = 16.0 Hz, 1 H, CH=C*H*CO$_2$Et), 7.60 (t, *J* = 7.6 Hz, 2 H, 2× CH_{Ph}), 7.71 (t, *J* = 7.8 Hz, 1 H, CH_{Ph}), 7.97 (d, *J* = 7.6 Hz, 2 H, 2× CH_{Ph}), 8.18 (d, *J* = 16.0 Hz, 1 H, C*H*=CHCO$_2$Et) ppm. ^{13}C NMR: δ = 14.28 (q, *C*H$_3$CH$_2$), 60.27 (t, CH$_3$*C*H$_2$), 64.95 (t, *C*H$_2$SO$_2$Ph), 71.42 (d, *C*HCp), 71.89 (d, Cp), 73.96 (d, *C*HCp), 74.76 (d, *C*HCp), 77.42 (s, *C*Cp), 81.11 (s, *C*Cp), 118.38 (d, CH=*C*HCO$_2$Et) 128.53 (d, *C*H$_{Ph}$), 129.16 (d, *C*H$_{Ph}$), 134.09 (d, *C*H$_{Ph}$), 139.01 (s, *C*$_{Ph}$), 142.98 (d, *C*H=CHCO$_2$Et), 166.55 (s, *C*O$_2$Et), 191.76 (s, C=O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 466 (11) $[M + 1]^+$, 401 (14), 355 (6). HRMS (ESI) calcd. for $C_{23}H_{22}FeO_5S$ 466.0537; found 466.054.

Synthesis of 28a and 28b Through an Anionic 5-*exo-trig* Cyclization: To a solution of diisopropylamine (1.2 mL, 2 equiv., 8.4 mmol) in THF (73 mL) a 1.96 M solution of *n*BuLi in hexane (4.3 mL, 2 equiv., 8.4 mmol) was added dropwise at –78 °C. After 2 h at the same temperature the resulting LDA solution was added dropwise to a cooled solution of the keto sulfone **11a** (1.96 g, 1.0 equiv., 4.2 mmol) in THF (73 mL) at –78 °C. The reaction mixture was warmed up very slowly to 10 °C over 15 h. After recooling to –78 °C the reaction was quenched with EtOH and warmed to 0 °C. Saturated aqueous NH_4Cl was added slowly. The layers were separated and the organic layer was washed with brine, dried with $MgSO_4$, filtered, and concentrated in vacuo. Purification by flash chromatography (cyclohexane/ethyl acetate, 3:1) afforded the diastereomers **28a** (1.05 g, 2.24 mmol, 53%) and **28b** (0.58 g, 1.24 mmol, 30%) as a red foam (global yield 83%). **28a**: $[\alpha]_D^{20}$ = +197.6 (*c* = 0.33, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3800–3000 (m, br), 2919 (m), 2930 (m), 1699 (s), 1456 (m), 1307 (m), 1147 (s), 1082 (m), 1035 (m), 909 (w), 831 (w), 725 (m), 685 (m), 612 (w) cm^{-1}. ^1H NMR: δ = 1.22 (t, *J* = 7.1 Hz, 3 H, CH_3CH$_2$), 2.49 (dd, *J* = 15.8, 8.5 Hz, 1 H, C*H*HCO$_2$Et), 2.74 (dd, *J* = 15.8, 5.1 Hz, 1 H, CH*H*CO$_2$Et), 4.08 (m, 3 H, CH$_3$*C*H$_2$, C*H*SO$_2$Ph), 4.32 (s, 5 H, Cp), 4.42 (m, 1 H, C*H*), 4.55 (t, *J* = 2.4 Hz, 1 H, C*H*Cp), 4.57 (d, *J* = 2.5 Hz, 1 H, C*H*Cp), 4.69 (d, *J* = 2.3 Hz, 1 H, C*H*Cp), 7.61 (m, 3 H, 3× CH_{Ph}), 8.02 (d, *J* = 7.1 Hz, 2 H, 2× CH_{Ph}) ppm. ^{13}C NMR: δ = 14.04 (q, *C*H$_3$CH$_2$), 34.43 (d, *C*H), 40.14 (t, *C*H$_2$CO$_2$Et), 60.72 (t, CH$_3$*C*H$_2$), 61.92 (d, *C*HCp), 67.78 (d, *C*HCp), 71.40 (d, Cp), 76.22 (d, *C*HCp), 78.22 (d, *C*HSO$_2$Ph), 81.02 (s, *C*Cp), 101.99 (s, *C*Cp), 128.95 (d, *C*H$_{Ph}$), 129.11 (d, *C*H$_{Ph}$), 133.93 (d, *C*H$_{Ph}$), 138.93 (s, *C*$_{Ph}$) 170.63 (s, *C*O$_2$Et), 194.56 (s, *C*=O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 467 (15) $[M + 1]^+$, 466 (50) $[M]^+$, 325 (20), 324 (100), 296 (10), 121 (23) $[FeCp]^+$, 77 (17), 56 (15) $[Fe]^+$. HRMS (ESI) calcd. for $C_{23}H_{22}FeO_5S$ 466.0537; found 466.054. **28b**: $[\alpha]_D^{20}$ = +317.4 (*c* = 0.375, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3800–3000 (m, br), 2920 (m), 2930 (m), 1698 (s), 1461 (m), 1306 (m), 1146 (s), 1082 (m), 1026 (m), 910 (w), 831 (w), 723 (m), 685 (m), 611 (w) cm^{-1}. ^1H NMR: δ = 1.33 (t, *J* = 7.1 Hz, 3 H, CH_3CH$_2$), 2.91 (dd, *J* = 15.5, 10.7 Hz, 1 H, C*H*HCO$_2$Et), 3.25 (dd, *J* = 15.5, 4.6 Hz, 1 H, CH*H*CO$_2$Et), 3.90 (m, 1 H, C*H*), 4.21 (s, 5 H, Cp), 4.28 (m, 3 H, CH$_3$CH_2, C*H*SO$_2$Ph), 4.45 (d, *J* = 2.3 Hz, 1 H, C*H*Cp), 4.60 (t, *J* = 2.5 Hz, 1 H, C*H*Cp), 4.70 (d, *J* = 2.5 Hz, 1 H, C*H*Cp), 7.57 (m, 3 H, 3×), 7.92 (m, 2 H, 2× CH_{Ph}) ppm. ^{13}C NMR: δ = 14.27 (q, *C*H$_3$CH$_2$), 32.55 (d, *C*H), 41.24 (t, *C*H$_2$CO$_2$Et), 60.97 (t, CH$_3$*C*H$_2$), 62.56 (d, *C*HCp), 67.61 (d, *C*HCp), 70.63 (d, Cp), 76.77 (d, *C*HCp), 77.75 (d, *C*HSO$_2$Ph), 79.17 (s, *C*Cp), 104.70 (s, *C*Cp), 128.97 (d, *C*H$_{Ph}$), 129.58 (d, *C*H$_{Ph}$), 133.97 (d, *C*H$_{Ph}$), 138.93 (s, *C*$_{Ph}$) 170.63 (s, *C*O$_2$Et), 194.56 (s, *C*=O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 467 (8) $[M + 1]^+$, 466 (30) $[M]^+$, 325 (25), 324 (100), 296 (13), 121 (23) $[FeCp]^+$, 77 (32), 56 (15) $[Fe]^+$. HRMS (ESI) calcd. for $C_{23}H_{22}FeO_5S$ 466.0537; found 466.053.

Synthesis of 29 and 30 Through Reductive Elimination: To a vigorously stirred suspension of Sm (3.9 g, 2.0 equiv., 26 mmol) in THF (130 mL) CH_2I_2 (1.84 mL, 1.75 equiv., 22.75 mmol) was added dropwise at 0 °C. The mixture was allowed to come to room temperature and was stirred for 2.5 h. A part of the resulting 0.175 M SmI_2 solution (101.2 mL, 3.5 equiv., 17.71 mmol) was transferred into another flask and a solution of **28a** (2.36 g, 1.0 equiv., 5.06 mmol) in THF (36 mL) and MeOH (15 mL) was added at –78 °C. After 1 h at this temperature, the mixture was warmed to room temperature and stirred for 2 h before saturated aqueous K_2CO_3 was added. The aqueous phase was extracted with MTBE, the combined extracts were dried with $MgSO_4$, filtered, and concentrated in vacuo. Purification by flash chromatography (cyclohexane/ethyl acetate, 3:1) afforded **29** (313 mg, 0.96 mmol, 19%) and **30** (1.11 g, mmol, 67%) as a red foam (global yield 86%). **29**: $[\alpha]_D^{20}$ = +92.8 (*c* = 0.35, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3096 (w), 2922 (m), 1724 (s), 1695 (s), 1457 (m), 1425 (m), 1406 (m), 1371 (m), 1309 (m), 1281 (m), 1254 (m), 1178 (s), 1105 (m), 1040 (m), 824 (w), 640 (w) cm^{-1}. ^1H NMR: δ = 1.21 (t, *J* = 7.2 Hz, 3 H, CH_3CH$_2$), 2.34 (dd, *J* = 18.5, 1.7 Hz, 1 H, C*H*H), 2.42 (d, *J* = 7.7 Hz, 2 H, CH_2CO$_2$Et), 3.34 (dd, *J* = 18.5, 7.6 Hz, 2 H, CH*H*), 3.73 (m 1 H, C*H*), 4.22 (s br, 7 H, Cp, CH$_3$CH_2), 4.49 (t, *J* = 2.4 Hz, 1 H, C*H*Cp), 4.59 (s, *J* = 2.6 Hz, 1 H, C*H*Cp), 4.62 (d, *J* = 2.2 Hz, 1 H, C*H*Cp) ppm. ^{13}C NMR: δ = 14.18 (q, *C*H$_3$CH$_2$), 31.82 (d, *C*H), 42.23 (t, *C*H$_2$CO$_2$Et), 48.76 (t, *C*H$_2$), 60.57 (t, CH$_3$*C*H$_2$), 61.51 (d, *C*HCp), 67.39 (d, *C*HCp), 71.00 (d, Cp), 76.01 (d, *C*HCp), 80.00 (s, *C*Cp), 106.18 (s, *C*Cp), 171.65 (s, *C*O$_2$Et), 205.98 (s, *C*=O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 327 (23) $[M + 1]^+$, 326 (100) $[M]^+$, 298 (20), 261 (15), 296 (10), 239 (14), 224 (17), 215 (16), 121 (44) $[FeCp]^+$, 56 (23) $[Fe]^+$. HRMS (ESI) calcd. for $C_{17}H_{18}FeO_3$ 326.0605; found 326.061. **30**: $[\alpha]_D^{20}$ = +48.3 (*c* = 0.41, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3600 (m, br), 3086 (w), 2932 (m), 2850 (m), 1728 (s), 1445 (m), 1369 (s), 1247 (m), 1152 (m), 1104 (m), 1088 (m), 999 (m), 915 (w), 884 (w), 815 (m), 721 (w), 618 (w) cm^{-1}. ^1H NMR: δ = 1.22 (t, *J*

= 7.1 Hz, 3 H, CH_3CH$_2$), 1.90 (d, J = 8.8 Hz, 1 H, OH), 2.24 (m, 2 H, CH_2CO$_2$Et), 2.44 (m, 2 H, CH_2), 3.32 (q, J = 7.7 Hz, 1 H, CH), 4.00 (s br, 1 H, CHCp), 4.11 (s br, 4 H, CH$_3$CH_2, 2× CHCp), 4.20 (s, 5 H, Cp), 4.72 (q, J = 7.6 Hz, 1 H, CHOH) ppm. ^{13}C NMR: δ = 14.22 (q, CH$_3$CH$_2$), 34.21 (d, CH), 41.26 (t, CH$_2$CO$_2$Et), 46.60 (t, CH$_2$), 59.43 (d, CHCp), 60.34 (t, CH$_3$$CH_2$), 61.80 (d, CHCp), 68.74 (d), 68.84 (d, Cp), 70.45 (d, CHCp), 97.03 (s, CCp), 98.31 (s, CCp), 171.18 (s, C=O) ppm. MS (EI, 70 eV): m/z (%) = 329 (18) [M + 1]$^+$, 328 (100) [M]$^+$, 263 (51), 245 (86), 121 (23) [FeCp]$^+$, 115 (32), 103 (22), 56 (8) [Fe]$^+$. HRMS (ESI) calcd. for $C_{17}H_{20}FeO_3$ 328.0762; found 328.076.

Synthesis of 30 and 31 Through $NaBH_4$ Reduction: The ketone **29** (576 mg, 1 equiv., 1.82 mmol) was dissolved in EtOH (62 mL) and $NaBH_4$ (689 mg, 10 equiv., 18.2 mmol) was added. A few drops of water were given to the solution and the mixture was stirred for 15 h. After adding $CHCl_3$ (530 mL) and water (53 mL), the layers were separated and the organic layer was dried with $MgSO_4$. Evaporation of the solvents and purification by flash chromatography (cyclohexane/ethyl acetate, 1:1) afforded **30** (521 mg, 1.59 mmol, 87% yield. $[a]_D^{20}$ = +50.2 (c = 0.26, $CHCl_3$; see above) as yellow foam and **31** (66 mg, 0.23 mmol, 13% yield) as a yellow solid. **31**: $[a]_D^{20}$ = +24.7 (c = 0.325, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3347 (s, br), 2929 (m), 1409 (w), 1319 (w), 1104 (s), 1036 (s), 999 (s), 815 (m) cm^{-1}. ^{1}H NMR: δ = 1.44 (m, 1 H, CHHCH$_2$OH), 1.63 (m, 1 H, CHHCH$_2$OH), 2.38 (m, 2 H, CH_2), 2.93 (q, J = 7.3 Hz, 1 H, CH), 3.60 (m, 2 H, CH$_2$CH_2OH), 4.02 (s, 1 H, CHCp), 4.14 (s, 2 H, 2× CHCp), 4.21 (s, 5 H, Cp), 4.66 (t, J = 6.8 Hz, 1 H, CHOH) ppm. ^{13}C NMR: δ = 32.97 (d, CH), 39.29 (t, CH$_2$CH$_2$OH), 46.97 (t, CH$_2$), 59.43 (d, CHCp), 61.08 (t, CH$_2$$CH_2$OH), 61.81 (d, CHCp), 69.00 (d, Cp), 69.05 (d, CHOH), 70.42 (d, CHCp), 98.17 (s, CCp), 98.44 (s, CCp) ppm. MS (EI, 70 eV): m/z (%) = 287 (18) [M + 1]$^+$, 286 (100) [M]$^+$, 268 (29), 203 (93), 159 (66), 138 (32), 121 (47) [FeCp]$^+$, 117 (65), 115 (61), 103 (46), 91 (27), 77 (30), 56 (35) [Fe]$^+$. HRMS (ESI) calcd. for $C_{15}H_{18}FeO_2$ 286.0656; found 286.066.

Synthesis of 32 via Mitsunobu Reaction: To a solution of **30** (100 mg, 1 equiv., 0.3 mmol) in THF (1.5 mL), PPh_3 (99 mg, 1.25 equiv., 0.38 mmol) and phthalimide (88 mg, 2 equiv., 0.6 mmol) were added. The solution was cooled to 0 °C and DEAD (0.06 mL, 1.25 equiv., 0.38 mmol) was added dropwise. After 4 h at room temperature the solvent was removed in vacuo. Purification by flash chromatography (cyclohexane/ethyl acetate, 4:1) afforded **32** as a yellow foam (114 mg, 0.25 mmol, 83%). $[a]_D^{20}$ = –173 (c = 0.28, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3489 (w), 3087 (w), 2974 (w), 1768 (m), 1704 (s), 1609 (w), 1465 (m), 1387 (s), 1352 (s), 1328 (s), 1285 (m), 1220 (w), 1171 (s), 1104 (s), 1086 (m), 1028 (s), 909 (m), 821 (m), 752 (s), 716 (s), 666 (m) cm^{-1}. ^{1}H NMR: δ = 1.24 (t, J = 7.1 Hz, 3 H, CH_3CH$_2$), 2.17 (dt, J = 14.4, 2.6 Hz, 1 H, CH), 2.77 (m, 2 H, CH_2CO$_2$Et), 3.57 (m, 2 H, CH_2), 4.04 (m, 2 H, CH$_3$CH_2), 4.08 (s, 5 H, Cp), 4.15 (m, 3 H, 3× CHCp), 5.80 (dd, J = 9.1, 2.7 Hz, 1 H, CHPhth), 7.66 (m, 2 H, 2× CH_{arom}), 7.76 (m, 2 H, 2× CH_{arom}) ppm. ^{13}C NMR: δ = 14.29 (q, CH$_3$CH$_2$), 35.46 (d, CH), 40.59 (t, CH$_2$CO$_2$Et), 43.48 (t, CH$_2$), 49.93 (d, CHPhth), 60.23 (t, CH$_3$$CH_2$), 61.22 (d, CHCp), 61.94 (d, CHCp), 69.98 (d, Cp), 70.89 (d, CHCp), 90.51 (s, CCp), 97.75 (s, CCp), 123.11 (d, CH$_{arom}$), 131.90 (s, C_{arom}), 133.88 (d, CH$_{arom}$), 167.77 (s, C=O), 173.06 (s, CO$_2$Et) ppm. MS (EI, 70 eV): m/z (%) = 458 (31) [M + 1]$^+$, 457 (100) [M]$^+$, 391 (6), 370 (9), 317 (9), 305 (6), 245 (12), 158 (6), 130 (11), 121 (45) [FeCp]$^+$, 115 (43), 103 (26), 91 (11), 76 (14), 56 (10) [Fe]$^+$. HRMS (ESI) calcd. for $C_{25}H_{23}FeNO_4$ 457.0976; found 457.098.

Synthesis of 33 via Hydrazinolysis: To a solution of **32** (63 mg, 1 equiv., 0.14 mmol) in EtOH (3 mL) hydrazine hydrate (60% hydrazine; 0.68 mL, 100 equiv., 14 mmol) in EtOH (1 mL) was added. The solution was stirred at 60 °C for 2 h, cooled to room temperature, transferred with EtOAc and saturated aqueous $NaHCO_3$ was added. The layers were separated and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried with $MgSO_4$ and concentrated in vacuo. Purification by flash chromatography (CH_2Cl_2/MeOH, 2:1 + 1% NEt_3) afforded **33** as a yellow oil (37 mg, 0.11 mmol, 82%). $[a]_D^{20}$ = +25.2 (c = 0.395, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2932 (s, br), 1728 (s), 1573 (w), 1436 (m), 1369 (m), 1160 (m), 1103 (m), 1029 (m), 818 (m), 721 (w), 696 (w), 616 (w) cm^{-1}. ^{1}H NMR: δ = 1.23 (t, J = 7.1 Hz, 3 H, CH_3CH$_2$), 1.79 (br. s, 1 H, CHH), 2.49 (dd, J = 7.8, 2.5 Hz, 2 H, CH_2CO$_2$Et), 3.15 (m, 1 H, CHH) 3.29 (q, J = 7.8 Hz, 1 H, CH), 4.00 (s, 5 H, Cp), 4.10 (m, 5 H, CH_2CH$_3$, 3× CHCp), 4.24 (d, J = 6.8 Hz, 1 H, CHNH$_2$) ppm. ^{13}C NMR: δ = 14.26 (q, CH$_3$CH$_2$), 35.21 (d, CH), 43.10 (t, CH$_2$CO$_2$Et), 46.79 (t, CH$_2$), 51.72 (d, CHNH$_2$), 60.27 (t, CH$_3$$CH_2$), 60.64 (d, CHCp), 61.56 (d, CHCp), 69.52 (d, Cp), 70.32 (d, CHCp), 96.52 (s, CCp), 96.76 (s, CCp), 172.47 (s, CO$_2$Et) ppm. MS (EI, 70 eV): m/z (%) = 328 (20) [M + 1]$^+$, 327 (100) [M]$^+$, 217 (59), 189 (58), 187 (86), 172 (23), 131 (25), 121 (70) [FeCp]$^+$, 91 (23), 56 (47) [Fe]$^+$. HRMS (ESI) calcd. for $C_{17}H_{21}FeNO_2$ 327.0921; found 327.092.

Synthesis of 34 by Boc-Protection: A solution of **33** (150 mg, 1 equiv., 0.46 mmol) in MeCN (7.5 mL) was cooled to 0 °C, Boc_2O (0.15 mL, 1.5 equiv., 0.69 mmol) was added carefully and finally DMAP (4.9 mg, 8.5 mol-%, 0.04 mmol) was added. The reaction mixture was stirred at room temperature for 15 h and then transferred into another flask using EtOAc. The solution was concentrated in vacuo. Purification by flash chromatography (cyclohexane/ethyl acetate, 3:1) afforded **34** as a yellow solid (126 mg, 0.29 mmol, 64%); m.p. 148 °C. $[a]_D^{20}$ = –73.8 (c = 0.36, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3360 (w, br), 2975 (m), 1697 (s, br), 1503 (m), 1389 (m), 1365 (m), 1243 (m), 1163 (s), 1104 (m), 1028 (m), 912 (w), 820 (m), 729 (m), 610 (m) cm^{-1}. ^{1}H NMR: δ = 1.22 (t, 3 H, CH_3CH$_2$), 1.25 [br. s, 9 H, C(CH_3)$_3$], 1.96 (d, J = 14.0 Hz, 1 H, CHH), 2.39 (m, 2 H, CH_2CO$_2$Et), 3.19 (m, 1 H, CHH) 3.30 (q, J = 7.7 Hz, 1 H, CH), 4.02 (s br, 6 H, Cp, CHCp), 4.07 (d, J = 1.9 Hz, 1 H, CHCp), 4.12 (d, J = 7.1 Hz, 2 H, CH$_3$CH_2), 4.15 (d, J = 2.2 Hz, 1 H, CHCp), 4.65 (br., 1 H, NH), 4.81 (t br, 1 H, CHNHBoc) ppm. ^{13}C NMR: δ = 14.23 (q, CH$_3$CH$_2$), 28.38 [q, C(CH$_3$)$_3$], 34.86 (d, CH), 42.65 (t, CH$_2$CO$_2$Et), 44.51 (t, CH$_2$), 50.85 (d, CHNHBoc), 60.36 (t, CH$_3$$CH_2$), 61.61 (d, CHCp), 61.78 (d, CHCp), 69.69 (d, Cp), 70.74 (d, CHCp), 79.28 [s, C(CH$_3$)$_3$], 92.46 (s, CCp), 97.10 (s, CCp) 154.96 (s, C=O), 172.16 (s, CO$_2$Et) ppm. MS (DIP-EI, 70 eV): m/z (%) = 428 (11) [M + 1]$^+$, 427 (45) [M]$^+$, 371 (100), 263 (37), 245 (46), 217 (26), 172 (28), 121 (54) [FeCp]$^+$, 103 (22), 57 (47) [Fe + 1]$^+$. HRMS (ESI) calcd. for $C_{22}H_{29}FeNO_4$ 427.1446; found 427.145.

Synthesis of 35 by Ester Saponification: To a solution of **34** (126 mg, 0.29 mmol) in ethanol (4.5 mL) 1 N NaOH (4.5 mL) was added. The mixture was then stirred at 80 °C for 15 h. After cooling to room temperature, MTBE was added and the phases were separated. The organic layer was washed with 1 N NaOH. The combined aqueous layers were acidified with 2 N HCl (pH 2), extracted with MTBE and the new organic phase was finally washed with brine. Afterwards, $MgSO_4$ was added, the solution was filtered and concentrated in vacuo. Purification by flash chromatography (CH_2Cl_2/MeOH, 10:1) afforded the carboxylic acid **35** as a yellow foam (100 mg, 0.25 mmol, 86% yield); m.p. 60 °C. $[a]_D^{20}$ = –71.9 (c = 0.30, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3600–2800 (w, br), 2969 (m), 1697 (s, br), 1493 (m), 1391 (m), 1365 (m), 1244 (m), 1160 (s), 1104 (m), 1065 (w), 999 (w), 909 (m), 820 (m), 729 (s), 645 (w) cm^{-1}. ^{1}H NMR: δ = 1.41 [br. s, 9 H, C(CH_3)$_3$], 1.99 (d, J = 13.9 Hz, 1 H,

CHH), 2.45 (m, 2 H, CH_2CO_2H), 3.18 (m, 1 H, CHH), 3.29 (q, J = 7.8 Hz, 1 H, CH), 4.03 (s, 6 H, Cp, CHCp), 4.10 (d, J = 1.6 Hz, 1 H, CHCp), 4.16 (d, J = 1.9 Hz, 1 H, CHCp), 4.65 (br. s, CHNHBoc), 8.69 (s br, 1 H, CO_2H) ppm. ^{13}C NMR: δ = 28.39 [q, $C(CH_3)_3$], 34.59 (d, CH), 42.47 (t, CH_2CO_2H), 44.50 (t, CH_2), 50.87 (d, CHNHBoc), 61.69 (d, CHCp), 61.86 (d, CHCp), 69.70 (d, Cp), 70.79 (d, CHCp), 79.46 [s, $C(CH_3)_3$], 92.31 (s, CCp), 96.98 (s, CCp), 155.05 (s, C=O), 177.29 (s, CO_2H) ppm. MS (DIP-EI, 70 eV): m/z (%) = 400 (7) $[M + 1]^+$, 399 (32) $[M]^+$, 344 (20), 343 (100), 299 (11), 282 (13), 277 (20), 217 (37), 121 (27) $[FeCp]^+$, 59 (43), 56 (96) $[Fe]^+$. HRMS (ESI) calcd. for $C_{20}H_{25}FeNO_4$ 422.1031; found 422.104.

Synthesis of 36 by Reduction and Fmoc-Protection: The ester **33** (150 mg, 1 equiv., 0.46 mmol) was dissolved in THF (4.5 mL) and the solution was cooled to 0 °C. A suspension of $LiAlH_4$ (35.6 mg, 2 equiv., 0.92 mmol) in Et_2O (1.5 mL) was added carefully. The reaction mixture was stirred at room temperature for 15 h and quenched by adding 1 N NaOH. It was filtered through a pad of celite, rinsed many times with CH_2Cl_2 and the filtrate was concentrated in vacuo. The resulting crude alcohol (131 mg, 1 equiv., 0.46 mmol) was dissolved in MeCN (4.6 mL), 10% aqueous K_2CO_3 (3.6 mL) was added and the solution was cooled to 0 °C. A solution of Fmoc-Cl (244 mg, 2 equiv., 0.92 mmol) in MeCN (3.8 mL) was added carefully. The reaction mixture was stirred at room temperature for 15 h and quenched by adding CH_2Cl_2/H_2O. The layers were separated and the aqueous layer was extracted with CH_2Cl_2. The solution was concentrated in vacuo. Purification by flash chromatography (cyclohexane/ethyl acetate, 1:1) afforded **36** as a yellow foam (131 mg, 0.26 mmol, 56% for 2 steps); m.p. 71 °C. $[\alpha]_D^{20}$ = –44.9 (c = 0.23, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3400 (m, br), 2932 (w), 2246 (w), 1694 (s), 1495 (m), 1448 (m), 1324 (m), 1240 (m), 1103 (m), 1076 (m), 998 (m), 819 (w), 757 (m), 726 (s), 625 (m) cm^{-1}. ^{1}H NMR: δ = 1.64 (m, 2 H, CH_2CH_2OH), 2.01 (m, 1 H, CHH), 2.97 (m, 1 H, CH), 3.19 (m, 1 H, CHH), 3.63 (m, 2 H, CH_2CH_2OH), 4.09 (br. s, 8 H, Cp, 3× CHCp), 4.38 (s, 1 H, CH_{Fmoc}), 4.40 (m, 2 H, $CH_{2\ Fmoc}$), 5.13 (d, J = 6.8 Hz, 1 H, CHNHFmoc), 7.35 (m, 4 H, 4× CH_{arom}), 7.58 (m, 2 H, 2× CH_{arom}), 7.75 (m, 2 H, 2× CH_{arom}) ppm. ^{13}C NMR: δ = 34.96 (d, CH), 40.76 (t, CH_2CH_2OH), 44.56 (t, CH_2), 47.20 (d, CHNHFmoc), 51.42 (d, CH_{Fmoc}), 61.06 (t, CH_2CH_2OH), 61.58 (d, CHCp), 61.67 (d, CHCp) 66.38 (t, $CH_{2\ Fmoc}$), 69.67 (d, Cp), 70.66 (d, CHCp), 92.08 (s, CCp), 98.04 (s, CCp), 119.87 (d, CH_{arom}), 124.91 (d, CH_{arom}), 126.94 (d, CH_{arom}), 127.57 (d, CH_{arom}), 141.19 (s, C_{arom}), 143.85 (s, C_{arom}), 155.36 (s, C=O) ppm. MS (EI, 70 eV): m/z (%) = 508 (3) $[M + 1]^+$, 507 (9) $[M]^+$, 311 (11), 268 (12), 237 (7), 203 (11), 196 (17), 179 (28), 178 (56), 164 (55), 165 (100), 139 (9), 121 (39) $[FeCp]^+$, 91 (8), 56 (16) $[Fe]^+$. HRMS (ESI) calcd. for $C_{30}H_{29}FeNO_3$ 507.1497; found 507.152.

Synthesis of 37 by Esterification of 36 with Succinic Anhydride: To a solution of **36** (109 mg, 1 equiv., 0.21 mmol) in CH_2Cl_2 (3.8 mL) and pyridine (0.4 mL) were added succinic anhydride (64 mg, 3 equiv., 0.64 mmol) and DMAP (15 mg, 0.6 equiv., 0.13 mmol). After strirring at room temperature for 15 h the mixture was concentrated in vacuo and redissolved in EtOAc. The solution was washed with icecold 5% citric acid, dried with $MgSO_4$, filtered, and concentrated in vacuo. Purification by flash chromatography (CH_2Cl_2/MeOH, 10:1) afforded **37** as a yellow foam (138 mg, 0.23 mmol, 99%); m.p. 102 °C. $[\alpha]_D^{20}$ = –44.9 (c = 0.37, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3300–2900 (br), 2954 (w), 1728 (s), 1713 (s), 1512 (w), 1446 (m), 1333 (m), 1232 (s), 1165 (s), 1104 (m), 997 (m), 821 (w), 758 (m), 740 (s), 619 (m) cm^{-1}. ^{1}H NMR: δ = 1.70 (m, 2 H, CH_2CH_2OR), 1.99 (m, 1 H, CHH), 2.61 (m, 4 H, $CH_2CH_2CO_2H$), 2.91 (m, 1 H, CH), 3.17 (m, 1 H, CHH), 4.06 (m, 10 H, Cp, 3× CHCp, CH_2CH_2OR), 4.27 (m, 1 H, CH_{Fmoc}), 4.52 (m, 2 H, $CH_{2\ Fmoc}$), 4.91 (m, 1 H, CH), 7.36 (m, 4 H, 4× CH_{arom}), 7.66 (m, 2 H, 2× CH_{arom}), 7.73 (m, 2 H, 2× CH_{arom}), 9.33 (br., 1 H, CO_2H) ppm. ^{13}C NMR: δ = 29.01 (t, $CH_2CH_2CO_2H$), 35.25 (d, CH), 36.86 (t, CH_2CH_2OR), 44.86 (t, CH_2), 47.32 (d, CH_{Fmoc}), 51.54 (d, CHNHFmoc), 61.82 (d, CHCp), 62.05 (d, CHCp), 63.49 (t, CH_2CH_2OR), 66.59 (t, $CH_{2\ Fmoc}$), 68.85 (d, Cp), 70.89 (d, CHCp), 91.89 (s, CCp), 97.69 (s, CCp), 120.02 (d, CH_{arom}), 125.06 (d, CH_{arom}), 127.07 (d, CH_{arom}), 127.72 (d, CH_{arom}), 141.32 (s, C_{arom}), 143.93 (s, C_{arom}), 155.50 (s, C=O_{Fmoc}), 172.29 (s, C=O), 177.38 (s, CO_2H) ppm. MS (DIP-EI, 70 eV): m/z (%) = 607 (96) $[M]^+$, 369 (17), 368 (69), 179 (27), 178 (100), 155 (72), 121 (57) $[FeCp]^+$, 91 (16), 56 (18) $[Fe]^+$. HRMS (ESI) calcd. for $C_{34}H_{33}FeNO_6$ 607.1657; found 607.170.

Synthesis of 39: To equip the Rink-amide-bond peptide (QTAIGVGAP-NH_2) N-terminally with **26**, the pre-swollen resin was incubated with 5 equiv. of **26** in DMF, 5 equiv. of HATU and 2.5 equiv. of DIPEA for 3 h in the dark at room temperature. After cleavage of the Fmoc group with 30% piperidine in DMF for two times (20 min), Fmoc-Gln(Trt)-OH was coupled manually (again using 5 equiv. of the amino acid building block, 5 equiv. of HOBt and 5 equiv. of DIC for 3 h in the dark at room temperature). Afterwards, the Fmoc group was cleaved as described above. Finally the peptide was cleaved from the resin using a mixture of TFA/TIS/H_2O (95:2.5:2.5, v/v/v) within 3 h at room temperature, removing all acid-labile protecting groups simultaneously. Subsequently, the peptide was precipitated from ice cold diethyl ether, collected by centrifugation, washed four times and lyophilized from water/*tert*-butyl alcohol (3:1, v/v). 5.3 mg (54% yield) crude product were obtained as a grey solid. Purification of the peptide was achieved by semi-preparative RP-HPLC on a RP C-18 column (Vydac, 250 × 25 mm, 10 μm) with a gradient of 0–50% B in A (A = 0.1% TFA in water; B = 0.08% TFA in acetonitrile) over 50 min and a flow of 3 mL min^{-1}. The peptide was analyzed by MALDI-ToF/ToF (Ultraflex III TOF/TOF, Bruker Daltonics) and ESI (Agilent Technologies 1200 series, ESI Iontrap, Bruker Daltonics) mass spectrometry and by analytical RP-HPLC on a Vydac RP18-column (4.6 × 250 mm; 5 μm, 300 Å) using a linear gradient of 0–50% B in A over 30 min and a flow rate of 0.6 mL min^{-1}. MW: 1306. MALDI: 1306.6 $[M + H]^+$. ESI: 654.3 $[M + 2H]^{2+}$, 665.3 $[M + Na + H]^{2+}$.

Synthesis 40: The synthesis was carried out as described for the *trans* building block **26**. Yield of the crude product was 52%, MW = 1306. MALDI: 1306.7 $[M + H]^+$. ESI: 1307.5 $[M + H]^+$, 653.9 $[M + 2H]^{2+}$.

Synthesis of 41: The pre-swollen resin was incubated with 5 equiv. of **35** in DMF, 5 equiv. of HATU and 2.5 equiv. of DIEA for 2 h in the dark at room temperature. Then the peptide was cleaved from the resin by using a mixture of TFA/TIS/H_2O (95:2.5:2.5, v/v/v) within 3 h at room temperature, removing all acid-labile protecting groups simultaneously. Subsequently, the peptide was precipitated from ice cold diethyl ether, collected by centrifugation, washed four times and lyophilized from water/*tert*-butyl alcohol (3:1, v/v). The peptide was analyzed by MALDI-ToF/ToF (Ultraflex III TOF/TOF, Bruker Daltonics) and ESI (Agilent Technologies 1200 series, ESI Iontrap, Bruker Daltonics) mass spectrometry and by analytical RP-HPLC on a Vydac RP18-column (4.6 × 250 mm; 5 μm, 300 Å) using a linear gradient of 0–50% B in A (A = 0.1% TFA in water; B = 0.08% TFA in acetonitrile) over 30 min and a flow rate of 0.6 mL min^{-1}. MW: 1092. MALDI: 1093.6 $[M + H]^+$. ESI: 1093.5 $[M + H]^+$, 546.8 $[M + 2H]^{2+}$,1116.5 $[M + Na]^+$.

Acknowledgments

This work was supported by the Deutsche Forschungsgemeinschaft (DFG) within the Project "Biologische Funktion von Organometallverbindungen" (FOR 630). We would also like to thank Dr. Matthias Schäfer and Regina Reppich-Sacher for the mass-spectrometic measurements, Jan Hoyer for help in peptide synthesis and Chemetall for generous gifts of butyllithium.

[1] K. Schlögl, *Monatsh. Chem.* **1957**, *88*, 601–621.
[2] P. Štěpnička in *Ferrocenes: ligands, materials and biolmolecules* (Ed.: P. Štěpnička), Wiley, Chichester, **2008**.
[3] Selected publication: a) F. Real-Fernandez, A. Colson, J. Bayardon, F. Nuti, E. Peroni, R. Meunier-Prest, F. Lolli, M. Chelli, C. Darcel, S. Juge, A. M. Papini, *Pept. Sci.* **2008**, *90*, 488–495; b) K. A. Mahmoud, H.-B. Kraatz, *Chem. Eur. J.* **2007**, *13*, 5885–5895.
[4] G. Jaouen, in: *Bioorganometallics* (Ed.: G. Jaouen), Wiley-VCH, Weinheim, **2006**.
[5] D. R. van Staveren, N. Metzler-Nolte, *Chem. Rev.* **2004**, *104*, 5931–5985.
[6] a) J. Sehnert, A. Hess, N. Metzler-Nolte, *J. Organomet. Chem.* **2001**, *637–639*, 349–355; b) R. S. Herrick, R. M. Jarret, T. P. Curran, D. R. Dragoli, M. B. Flaherty, S. E. Lindyberg, R. A. Slate, L. C. Thornton, *Tetrahedron Lett.* **1996**, *37*, 5289–5292.
[7] D. R. van Staveren, N. Metzler-Nolte, *Chem. Commun.* **2002**, 1406–1407.
[8] P. Hublau, C. Sergheraert, L. Ballester, M. Dautrevaux, *Eur. J. Med. Chem.* **1983**, *18*, 131–133.
[9] For peptides derived from 1-amino-1′-carboxylic acid, see for instance: a) K. Heinze, M. Schlenker, *Eur. J. Inorg. Chem.* **2004**, 2974–2988; b) M. Č. Semenčić, L. Barišić, R. Rapić, *Tetrahedron: Asymmetry* **2007**, *18*, 2125–2128; c) C. N. Tharamani, K. A. Mahmoud, G. R. Vasanthakumar, H.-B. Kraatz, *Sens. Actuators, B* **2009**, 253–258; for peptides derived from 1,1′-ferrocenedicarboxylic acid, see for instance: d) S. Chowdhury, G. Schatte, H.-B. Kraatz, *Angew. Chem.* **2008**, *120*, 7164–7167; e) T. Hirao, *J. Organomet. Chem.* **2009**, *694*, 806–811; f) S. I. Kirin, U. Schatzscheider, S. D. Köster, D. Siebler, N. Metzler-Nolte, *Inorg. Chim. Acta* **2009**, *362*, 894–906; g) C. Drexler, M. Milne, E. Morgan, M. Jennings, H.-B. Kraatz, *Dalton Trans.* **2009**, 4370–4378; for ferrocenophane-derived amino acid building blocks, see for instance: h) S. Maricic, A. Ritzén, U. Berger, T. Frejd, *Tetrahedron* **2001**, *57*, 6523–6529; i) L. Tebben, K. Bussmann, M. Hegemann, G. Kehr, R. Fröhlich, G. Erker, *Organometallics* **2008**, *27*, 4269–4272.
[10] P. James, J. Neudörfl, M. Eissmann, P. Jesse, A. Prokop, H.-G. Schmalz, *Org. Lett.* **2006**, *8*, 2763–2766.
[11] O. Riant, O. Samuel, T. Flessner, S. Taudien, H. B. Kagan, *J. Org. Chem.* **1997**, *62*, 6733–6745.
[12] A. F. Neto, J. Miller, V. Faria de Andrade, S. Y. Fujimoto, M. Maisa de Freitas Afonso, F. C. Archanjo, V. A. Darin, M. L. Andrade e Silva, A. Donizete Lanchote Borges, G. Z. Del Ponte, *Z. Anorg. Allg. Chem.* **2002**, *628*, 209–216.
[13] S. Hanessian, A. Ugolini, D. Dubé, A. Glamyan, *Can. J. Chem.* **1984**, *62*, 2146–2147.
[14] Details for the X-ray of **17** and **21**: see Cambridge Crystallographic Data Centre, reference codes XELFAW (for **17**) and XELFEA (for **21**).
[15] Y. Kita, J. Segawa, J.-I. Haruta, H. Yasuda, Y. Tamura, *J. Chem. Soc. Perkin Trans. 1* **1982**, 1099–1104.
[16] N. Minowa, T. Mukaiyama, *Chem. Lett.* **1987**, 1719–1722.
[17] K. Saigo, M. Osaki, T. Mukaiyama, *Chem. Lett.* **1976**, 163–164.
[18] a) O. Mitsunobu, *Synthesis* **1981**, 1–28; b) M. C. Viaud, P. Rollin, *Synthesis* **1990**, 130–132.
[19] M. Vaultier, N. Knouzi, R. Carrie, *Tetrahedron Lett.* **1983**, *24*, 763–764.
[20] CCDC-729381 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
[21] B. Rist, M. Entzeroth, A. G. Beck-Sickinger, *J. Med. Chem.* **1998**, *41*, 117–123.

Received: May 18, 2009
Published Online: July 27, 2009

