# Group-4 Metallocene Cation Complexes of Oligopeptides: Reaction of $[Cp_2ZrCH_3(THF)^+BPh_4^-]$ with Boc-Protected Di- and Tripeptide Esters

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The dipeptide derivatives Boc-Gly-Val-OMe (**2**) and Boc-Ala-Val-OMe (**3**) selectively add the methylzirconocene cation **1** to the carbonyl oxygen atom of the *N*-terminal amino acid residue (κ-$C^4$=O coordination) upon treatment with $[Cp_2ZrCH_3(THF)^+BPh_4^-]$ in dichloromethane at low temperature (< 0 °C) to generate the complexes **2-I** and **3-I**, respectively. Above 0 °C methane is eliminated to give the stable chelate peptide metallocene cation complexes **2-A** and **3-A**, respectively, both featuring a combined $C^1$=O/N2/$C^4$=O coordination to the zirconium center. Complex **3-A** was characterized by X-ray diffraction. The analogous tripeptide derivatives Boc-Gly-Val-Val-OMe (**6**), Boc-Ala-Ala-Val-OMe (**7**), Boc-Ala-Val-Val-OMe (**8**), and Boc-Val-Val-Gly-OMe (**9**) all form analogous κ-$C^4$=O $Cp_2ZrCH_3^+$ cation adducts (**6–9**)-**I** under kinetic control and after subsequent loss of $CH_4$ $C^1$=O/N2/$C^4$=O chelate complexes (**6–9**)-**A** under thermodynamic control, both involving selective bonding of the organometallic cation to the terminal amino acid residue of the respective peptide derivatives. Thermolysis of the primary adduct **7-I** (> 0 °C) resulted in methane elimination and formation of a mixture of the isomers **7-B** and **7-A** (isolated in a 3:4 ratio). According to the detailed NMR analysis **7-A** shows the favored chelate coordination at the *N*-terminus involving $C^1$=O/N2/$C^4$=O bonding, whereas the cation complex **7-B** exhibits a similar chelate structure at the internal Ala moiety, characterized by $C^4$=O/N5/$C^7$=O coordination to the zirconium center. Similarly, methane liberation from **8-I** and **9-I** gave mixtures of the respective cationic chelate complex isomers **8-A/8-C** (2:3) and **9-A/9-C** (1:1), respectively. The (**8**,**9**)-**A** isomers have the zirconium ion bonded at the *N*-terminus, whereas (**8**,**9**)-**C** exhibit the $Cp_2Zr^+$ unit at the *C*-terminus of the peptide chain, involving the ester carbonyl group in forming the chelate framework ($C^7$=O/N8/$C^{10}$=O coordination). The (**6–9**)-**A** isomers are thermodynamically favored. The cation complexes **7-B**, **8-C**, **9-C** rearrange to the **A**-type isomers upon prolonged standing at temperatures > 0 °C in dichloromethane solution.

## Introduction

Principles and many details of the important interaction of metal ion systems with typical biomolecules have been recognized due to a large number of investigations in the field of bioinorganic chemistry. Bioorganometallic chemistry is a much less mature discipline.[1] It tries to combine favorably the characteristic features of typical biomolecules, such as amino acids, oligopeptides, heterocyclic nucleobases, oligonucleotides etc., with those of organometallic building blocks in order to generate e.g. new reagents for organic synthesis or precursors of novel active and selective catalyst systems, but also to study the response of the "natural" bio-related systems to interactions with rather "unnatural" organometallic metal/ligand combinations and arrangements.[2] A major problem in bioorganometallic chemistry is to find suitable conditions that allow to combine the usually rather hydrophilic biomolecules with the in part extremely hydrophobic world of many organometallic systems and to keep their mutual adducts and reaction products stable. It is very likely that many useful applications will follow once this has been achieved for a sufficient number of bioorganometallic systems.[3]

The methylzirconocene cation ($[Cp_2ZrCH_3^+]$, **1**) is a sensitive, very electrophilic organometallic fragment that has found important use in homogeneous metallocene Ziegler catalysis.[4] We have used this species as a typical model system to investigate the modes of interaction of a very reactive, extremely hydrophobic organometallic building block derived from an oxophilic transition metal from the left side of the periodic table with peptide derivatives, as typical examples of biomolecule-related substrates. This has led to the disclosure of interesting coordination behavior and subsequent reactions of this metallocene-derived reagent with such multifunctional and polar substrates. A series of typical examples is described in this article.

## Results and Discussion

As the organometallic starting material the ligand-stabilized $[Cp_2ZrCH_3(THF)^+BPh_4^-]$ methylzirconocene cation **1a** was used in this study.[4a] The coordinated tetrahydrofuran is readily exchanged for other donor ligands under very mild conditions. The cation complex **1a** was treated with a variety of *N*-*tert*-butoxycarbonyl-(i.e. Boc-)protected oligopeptide esters. Here the outcome of the reactions with two

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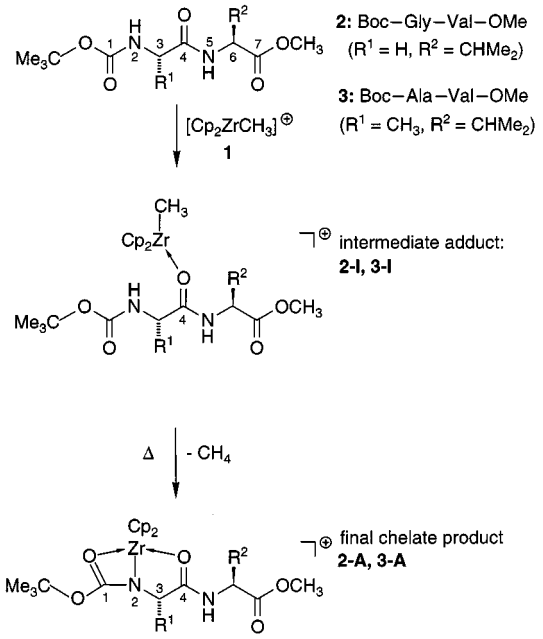



Scheme 1. Reaction of **1** with dipeptide derivatives

Table 1. Selected $^1$H-NMR chemical shifts of the [$Cp_2ZrCH_3^+$] (**1**) plus dipeptide (**2**, **3**) reaction products (atom numbering as in Scheme 1)[a]

| Compound | $CMe_3$ | 2-H[b] | 3-H | 5-H[b] | 6-H | $OCH_3$ | $ZrCH_3$ |
|---|---|---|---|---|---|---|---|
| **2** | 1.40 | 5.86 | 3.78 | 7.16 | 4.46 | 3.69 | – |
| **2-I** | 1.43 | 7.69 | 3.63 | 7.45 | 4.35 | 3.80 | 0.48 |
| **2-A** | 1.52 | – | 3.54 | 7.36 | 4.33 | 3.77 | – |
| **3** | 1.41 | 5.00 | 4.15 | 6.65 | 4.49 | 3.70 | – |
| **3-I**[c] | 1.42 | 5.30 | 3.65 | 8.60 | 3.85 | 3.78 | 0.54 |
| **3-A** | 1.56 | – | 4.39 | [d] | 4.39 | 3.83 | – |

[a] In $CD_2Cl_2$, chemical shifts in ppm, δ scale, 258 K. – [b] N-H signals, see Scheme 1. – [c] At 223 K. – [d] Not located.

selected dipeptide and a series of four tripeptide methyl esters will be described.[5]

The reaction of **1a** with the dipeptide ester Boc-Gly-Val-OMe (**2**) shall serve as an example to illustrate a typical reaction series. Upon mixing the two components in a 1:1 stoichiometry at −15°C in [$D_2$]dichloromethane an instantaneous reaction was observed by NMR to take place. THF is liberated from "Jordan's cation" ([$Cp_2ZrCH_3(THF)^+$]) and the reactive $Cp_2ZrCH_3^+$ cation takes up a dipeptide ester as a ligand. A combination of various NMR techniques (for details see the Experimental Section) has allowed for a complete spectroscopic characterization of this rapidly formed primary product as the [$Cp_2Zr(CH_3)$(Boc-Gly-Val-OMe)$^+$] coordination complex **2-I** (see Scheme 1). As it is evident from the compilation of the $^1$H- and $^{13}$C-NMR data (Tables 1 and 2), compound **2-I** still contains all the intact components of both the subunits [$Cp_2Zr$-$CH_3^+$] (**1**) and Boc-Gly-Val-OMe (**2**): The zirconium-bonded [Zr]-$CH_3$ group is still there and both NH functionalities are intact. From the $^{13}$C-NMR comparison between **2** and **2-I** (see Table 2) it is deduced that complex formation has apparently occurred by coordination of the glycine-derived amido carbonyl group to the zirconium center. The pronounced shifting of the respective O=$C^4$ $^{13}$C-NMR resonance from δ = 170.1 to δ = 179.1 strongly indicates the newly formed (Gly)amido−Zr bond as the essential structural feature of the primary [(Boc-Gly-Val-OMe)·**1**] adduct. All the other $^{13}$C-NMR resonances are essentially unaffected.

Table 2. Selected $^{13}$C-NMR data of the peptide derivatives **2**, **3**, and their reaction products with the methylzirconocene cation (atom numbering as in Scheme 1)[a]

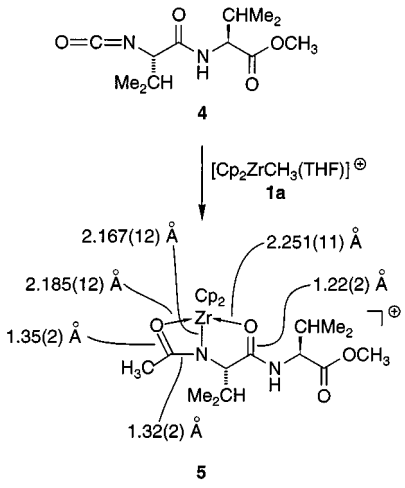
| Compound | *C*$Me_3$ | C-1 | C-3 | C-4 | C-6 | C-7 | $OCH_3$ | $ZrCH_3$ |
|---|---|---|---|---|---|---|---|---|
| **2** | 79.9 | 156.2 | 44.1 | 170.1 | 57.0 | 172.7 | 52.5 | – |
| **2-I** | 81.1 | 155.3 | 44.1 | 179.1 | 58.4 | 168.4 | 53.0 | 33.0 |
| **2-A** | 85.5 | 156.6 | 50.0 | 179.1 | 60.3 | 170.0 | 53.1 | – |
| **3**[b] | 79.7 | 155.4 | 51.8 | 172.7 | 56.9 | 172.0 | 49.8 | – |
| **3-I** | 81.6 | 155.0 | 51.8 | 182.5 | 58.8 | 168.8 | [c] | 33.4 |
| **3-A** | 86.3 | 156.5 | 57.3 | 182.2 | 60.2 | 170.3 | [c] | – |

[a] In $CD_2Cl_2$ at 258 K, chemical shifts in ppm, δ scale. – [b] In $CDCl_3$. – [c] Hidden under solvent signal.

Complex **2-I** is a reactive intermediate. At temperatures above 0°C it reacts further. Methane is formed[6] and the final product **2-A** is obtained. The stable complex **2-A** was synthesized by treatment of **1a** with Boc-Gly-Val-OMe in dichloromethane (0°C to room temperature for a few hours) on a preparative scale and isolated in 96% yield. Both the $^1$H- and the $^{13}$C-NMR spectra show that the [Zr]-$CH_3$ group is no longer present. It has been utilized for selectively abstracting the N*H* proton[6b] of the Gly part of the peptide ligand systems. Consequently, the former 2-H resonance of the peptide chain is not observed in the $^1$H-NMR spectrum of the product **2-A** (see Table 1 and Scheme 1). The pronounced shift of the amido O=$C^4$ $^{13}$C-NMR resonance to a larger δ value for **2-A** relative to the free peptide ligand **2** (Δδ = +9.0 ppm) strongly indicates the coordination of this amido group to the zirconium center.[7]

A more detailed picture of the coordination behavior of the mono-deprotonated peptide ligand to the remaining $Cp_2Zr$ unit in the cation complex **2-A** is hard to obtain from the NMR-spectroscopic analysis alone, but − as we will see later − can be derived quite confidently in a combination of the spectroscopic features with the result of an X-ray crystal structure analysis.

We had recently characterized a related (peptide)zirconocene tetraphenylborate salt by X-ray diffraction.[3b] The complex **5** was prepared by treatment of **1a** with the isocyanate **4** of the dipeptide H-Val-Val-OMe.[8] The Zr−$CH_3$ group had added to the heterocumulene to form the cationic bis-chelate complex **5**. It was shown by X-ray diffraction that the zirconium center was bonded to the *N*-terminal Val-nitrogen atom and to the oxygen atoms of both adjacent C=O groups, i.e. the *N*-acetyl carbonyl group and the C=O group of the *N*-terminal Val moiety (see Scheme 2).




Scheme 2. Formation and structural parameters of **5**

Treatment of Boc-Ala-Val-OMe (**3**) with **1a** at low temperature (−15°C) in $CD_2Cl_2$ gave the adduct **3-I** (see Scheme 1 and Tables 1 and 2). The NMR analysis also indicates the selective coordination of the $Cp_2ZrCH_3^+$ cation to the amido carbonyl group of the *N*-terminal amino acid building block (i.e. formation of $C^4{=}O{-}$[Zr] of the Ala moiety). Warming to room temperature again leads to a rapid reaction that results in (Ala)$N^2$-H deprotonation with liberation of methane and the selective formation of the cationic chelate complex **3-A**. Diffusion of pentane vapor into a solution in bromobenzene gave single crystals of **3-A** for an X-ray crystal structure analysis. This structure suffers from the presence of a small nonidentified molecule (probably water). Therefore, we will not discuss the structure in detail. But the X-ray analysis is of a sufficient quality to characterize the overall structural arrangement of **3-A** as being of the same type as **5**. Thus, complex **3-A** is again of a bis-chelate type and exhibits a metallabicyclic central framework around the zirconium center. In this, the amido carbonyl group of the *N*-terminal Ala unit strongly coordinates to the zirconium ion − this was already deduced from the strong deshielding effect[3b] in the $^{13}$C-NMR spectrum (C4 coordination shift **3** → **3-A** $\Delta\delta = +10$ ppm, see Table 2). In addition, the *N*-Boc carbonyl group also coordinates strongly to the zirconium ion (see Figure 1). This feature did not show up in the $^{13}$C-NMR analysis, which is probably due to a compensation effect (the $C^1{=}O$ bond becomes weaker upon coordination, but at the same time the C1=N2 bond becomes stronger). But a close inspection of the $^{13}$C-NMR data (see Table 2) shows that the chelate coordination (i.e. the transformation of **3-I** → **3-A**) results in a pronounced and characteristic shift of the Boc-*C*$Me_3$ $^{13}$C-NMR resonance to larger δ values ($\Delta\delta = +4.7$ ppm for **3-A**, +5.4 for **2-A**). We thus conclude, that the thermodynamically favored final products **2-A** and **3-A** are both characterized by a doubly chelating coordination of the Boc−amido unit and the internal amido moiety of the *N*-terminal amino acid building block of the dipeptide derivatives as depicted in Scheme 1. This follows from the combined NMR/X-ray analysis. This typical coordination mode does not lead to any significant shifting of the $C^1{=}O$ $^{13}$C-NMR signal, but can readily be recognized by the resulting pronounced $^{13}$C-NMR coordination shifts of the Boc-*C*$Me_3$ and the $C^4{=}O$ resonances.

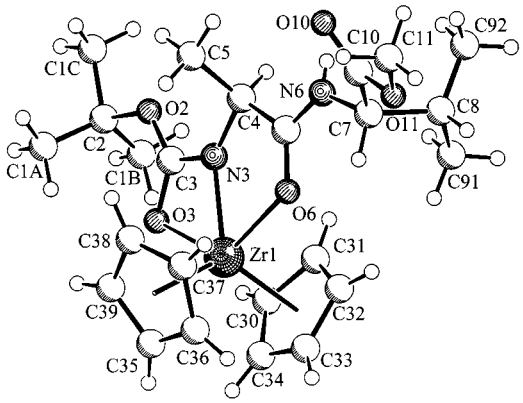
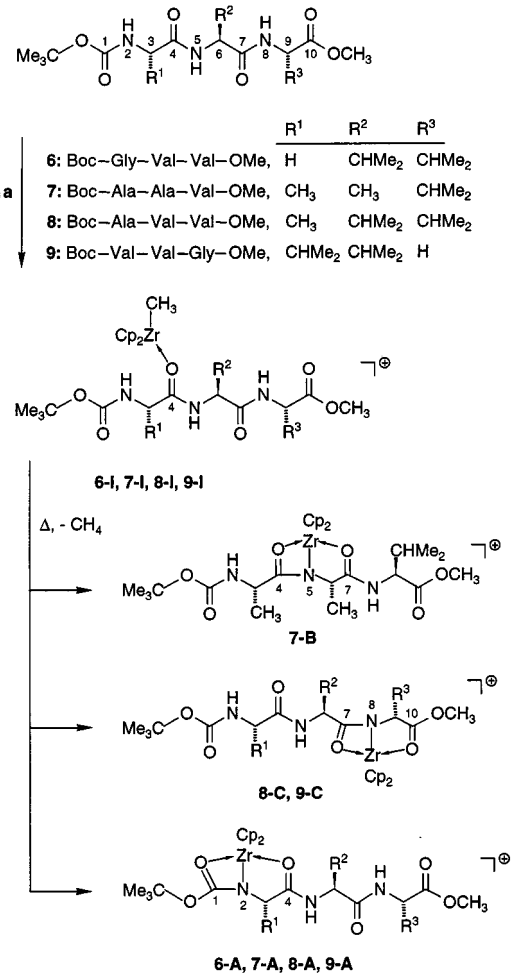



Figure 1. A view of the molecular structure of the product **3-A** (cation only, with unsystematical atom numbering scheme) as determined by X-ray diffraction

We next treated "Jordan's cation" (**1a**) with the tripeptide derivative Boc-Gly-Val-Val-OMe (**6**).[9] There is a clean and selective adduct formation observed at −15°C in [$D_2$]dichloromethane. The product contains the intact $Cp_2Zr{-}CH_3^+$ unit coordinated to the tripeptide framework. This is evident from the observation of the NMR signals of a pair of diastereotopic Cp ligands at the zirconium center and the presence of a [Zr]$-CH_3$ group. From the characteristic coordination shift of the carbonyl carbon atom C4 in the $^{13}$C-NMR spectrum ($\Delta\delta = +7.8$ ppm) attachment of the methylzirconocene cation to the $C^4{=}O$ amido carbonyl group of the *N*-terminal Gly moiety of **6** is indicated. Since there are no other significant NMR changes we must assume that the **1a** + **6** reaction has resulted in a simple adduct formation to give the cationic complex **6-I** (see Scheme 3, with $BPh_4^-$ anion).

Warming of the intermediate **6-I** above 0°C again leads to methane evolution. In this case also a single thermodynamically favored product (**6-A**) is obtained, that was also prepared and isolated on a preparative scale. The $^1$H-NMR spectrum (see Table 3) shows that the N*H* proton of the Gly section of the tripeptide has been abstracted by the [Zr]$-CH_3$ group to give methane. The adjacent amido carbonyl group ($C^4{=}O$) is involved in the chelate complex formation. This is evident by the shifting of the $^{13}$C-NMR signals of carbon atoms C4 ($\Delta\delta = +7.7$ ppm) and C3 ($\Delta\delta = +6.2$ ppm) for the **6** → **6-A** transformation. Again, we must assume that the $C^1{=}O$ amido carbonyl group adjacent to the directly bonded nitrogen atom N2 is involved and used for constructing the typical second chelate "arm" of the overall metallabicyclic framework. This is evident from the characteristic shifting of the *C*$Me_3$ $^{13}$C NMR signal of the Boc group ($\Delta\delta = +5.9$ ppm), whereas the corresponding C1 resonance remains completely unaffected from the **6** → **6-A** transformation, probably due to the typical compensation effect discussed above and in the literature.[3b] Thus, treatment of the tripeptide derivative **6** with $Cp_2ZrCH_3^+$




Scheme 3. Reactions of **1a** with tripeptide derivatives

Table 3. Selected $^1$H-NMR data of the reaction products of **1a** with the peptide derivatives **6** and **7** (atom numbering as in Scheme 3)[a]

| Compound | $CMe_3$ | 2-H[b] | 3-H | 5-H[b] | 6-H | 8-H[b] | 9-H | $OCH_3$ | $ZrCH_3$ |
|---|---|---|---|---|---|---|---|---|---|
| **6** | 1.38 | 6.14 | 3.86 | 7.84 | 4.45 | 7.72 | 4.54 | 3.68 | – |
| **6-I** | 1.43 | 7.78 | 3.71 | 6.66 | 4.16 | 6.41 | 4.46 | 3.76 | 0.50 |
| **6-A** | 1.57 | – | 4.21 | 6.78 | 4.45 | 9.13 | 4.49 | 3.78 | – |
| **7** | 1.38 | 5.80 | 4.26 | 7.53 | 4.68 | 7.59 | 4.46 | 3.69 | – |
| **7-I** | 1.44 | 5.54 | 3.78 | 8.67 | 3.82 | 9.17 | 3.93 | 3.79 | 0.54 |
| **7-B** | 1.55 | 5.26 | 3.88 | – | 4.99 | 8.31 | 4.48 | 3.82 | – |
| **7-A** | 1.54 | – | 4.41 | 8.13 | 4.33 | 6.32 | 4.49 | 3.74 | – |

[a] In $CD_2Cl_2$ at 258 K, chemical shifts in ppm, δ scale. – [b] N-H resonances.

from **1a** leads to a selective kinetically controlled adduct formation at the *N*-terminal Gly amido group followed by thermally induced methane elimination to give a single cationic metallocene/peptide chelate complex (**6-A**) where the zirconium center is bonded to the $C^1$=O, N2, and $C^4$=O groups (see Scheme 3).

The reaction between Boc-Ala-Ala-Val-OMe (**7**) with **1a** is slightly more complicated. At low temperature, the adduct [Boc-Ala-Ala-Val-OMe · $ZrCp_2CH_3^+$] (**7-I**) is formed selectively. Unfortunately, this is the only case where we

Table 4. Selected $^{13}$C-NMR data of the **1a** + **6/7** reaction products (atom numbering as given in Scheme 3)[a]

| Compound | $CMe_3$ | C-1[b] | C-3 | C-4[b] | C-6 | C-7[b] | C-9 | C-10[b] | $OCH_3$ | $ZrCH_3$ |
|---|---|---|---|---|---|---|---|---|---|---|
| **6** | 79.6 | 156.2 | 43.9 | 170.1 | 57.3 | 172.6 | 58.5 | 172.2 | 52.4 | – |
| **6-I** | 81.5 | 156.1 | 44.8 | 177.9 | 58.1 | 171.3 | 60.0 | 171.7 | 52.2 | 32.4 |
| **6-A** | 85.5 | 156.2 | 50.1 | 177.8 | 60.1 | 169.7 | 58.1 | 171.5 | 52.7 | – |
| **7** | 79.6 | 155.5 | 49.9 | 173.1 | 48.8 | 172.4 | 57.2 | 172.6 | 52.3 | – |
| **7-I** | 81.8 | 156.8 | 51.9 | [c] | 50.7 | [c] | 59.7 | 169.6 | 53.3 | 33.6 |
| **7-B** | 80.6 | 155.4 | 47.8 | 181.0 | 57.0 | 179.0 | 59.7 | 170.4 | 53.3 | – |
| **7-A** | 85.5 | 156.0 | 56.8 | 180.8 | 50.7 | 170.0 | 57.8 | 171.8 | 52.7 | – |

[a] In $CD_2Cl_2$ at 258 K, chemical shifts in ppm, δ scale. – [b] Carbonyl carbon signals. – [c] Not located.

were not able to locate two of the $^{13}$C-NMR carbonyl resonances, but from the overall spectral characteristics it is quite obvious that again the typical Zr coordination to the amide oxygen atom of the *N*-terminal amino acid residue (here: Ala) has taken place (see Tables 3 and 4).

Raising the temperature again results in consumption of the reactive intermediate **7-I** with formation of $CH_4$. However, in this case a mixture of two bis-chelate complexes is obtained. These were formed in a ratio of **7-B**/**7-A** ≈ 3:4 under the specific conditions used for their synthesis on a preparative scale (see the Experimental Section for details). Complex **7-A** exhibits the typical spectroscopic features (see Tables 3 and 4) that identifies it as an example of the *N*-terminal chelate peptide/zirconocene cation complex type. Analogously, as in the "**A**-type" cation examples discussed above, the double framework is formed by attaching the $C^1$=O/N2/$C^4$=O subunits to the central $Cp_2Zr$ moiety.

Complex **7-B** is of a similar type, only that the $C^4$=O/N5/$C^7$=O groups are here involved in the coordination to the zirconium center. The $^1$H-NMR spectra show that in this case it is the 5-H amido hydrogen atom that is lost upon thermally induced methane formation. In addition, pronounced $^{13}$C-NMR shift differences have resulted in the **7** → **7-B** transformation at the carbonyl carbon atoms C4 (Δδ = +7.7 ppm) and C7 (Δδ = +6.6 ppm) as well as the adjacent Ala-*C*HMe carbon atom C6 (Δδ = +8.2 ppm).

The *N*-terminal chelate cation complex **7-A** seems to be the thermodynamically favored product. During ca. two weeks at 0°C in $CD_2Cl_2$ the by-product **7-B** has almost completely disappeared and has been transformed into the more stable peptide–group-4 metallocene cation system **7-A**.

A similar situation was found when the peptide derivatives Boc-Ala-Val-Val-OMe (**8**) or Boc-Val-Val-Gly-OMe (**9**) were treated with **1a**. In each case a single $Cp_2ZrCH_3^+$ adduct was formed at low temperature (–15°C). Coordination at the $C^4$=O carbonyl oxygen atom of the *N*-terminal amino acid moiety was evident from the NMR analysis (see Tables 5 and 6). The thus formed primary product **8-I** eliminated methane at temperatures > 0°C to form a mixture of the new cationic chelate complex **8-C** (see Scheme 3) in addition to **8-A** (obtained in a 2:3 ratio on a preparative scale). In the case of **8-C** the $C^7$=O/N8 amido

Table 5. Selected $^1$H-NMR data of the **1a** + **8/9** reaction products (atom numbering as given in Scheme 3)[a]

| Compound | $CMe_3$ | 2-H[b] | 3-H | 5-H[b] | 6-H | 8-H[b] | 9-H | $OCH_3$ | $ZrCH_3$ |
|---|---|---|---|---|---|---|---|---|---|
| **8** | 1.38 | 6.04 | 4.40 | 7.79 | 4.52 | 7.60 | 4.47 | 3.68 | – |
| **8-I** | 1.44 | 5.29 | 4.08 | 8.36 | 4.50 | 7.62 | 4.43 | 3.71 | 0.59 |
| **8-C** | 1.54 | 5.25 | 4.00 | 8.10 | 4.51 | – | 5.12 | 3.75 | – |
| **8-A** | 1.40 | – | 4.51 | 8.64 | 4.50 | 6.42 | 4.37 | 3.82 | – |
| **9** | 1.38 | 5.62 | 3.98 | 7.23 | 4.36 | 7.62 | 3.98 | 3.67 | – |
| **9-I** | 1.44 | 5.27 | 3.97 | 6.78 | 3.78 | [c] | 3.82 | 3.79 | 0.55 |
| **9-C** | 1.55 | 5.82 | 4.17 | 7.89 | 3.77 | – | 3.84 | 3.71 | – |
| **9-A** | 1.48 | – | 4.37 | 7.46 | 3.67 | 7.59 | 3.20 | 3.74 | – |

[a] In $CD_2Cl_2$ at 258 K, chemical shifts in ppm, δ scale. – [b] N-H signals. – [c] Not observed.

Table 6. Selected $^{13}$C-NMR data of the **1a** + **8/9** reaction products (atom numbering as given in Scheme 3)[a]

| Compound | $CMe_3$ | C-1[b] | C-3 | C-4[b] | C-6 | C-7[b] | C-9 | C-10[b] | $OCH_3$ | $ZrCH_3$ |
|---|---|---|---|---|---|---|---|---|---|---|
| **8** | 79.5 | 156.6 | 49.9 | 173.3 | 57.1 | 171.9 | 58.7 | 172.5 | 52.3 | – |
| **8-I** | 82.1 | 156.7 | 53.1 | 176.3 | 59.7 | 167.4 | 60.1 | 169.7 | 52.1 | 33.8 |
| **8-C** | 80.9 | 155.9 | 46.9 | 171.5 | 59.9 | 180.8 | 66.8 | 179.8 | 57.9 | |
| **8-A** | 85.5 | 156.7 | 58.5 | 181.5 | 60.0 | 169.1 | 57.1 | 170.1 | 52.7 | – |
| **9** | 79.9 | 156.2 | 60.4 | 172.1 | 58.2 | 171.8 | 41.0 | 170.2 | 52.3 | – |
| **9-I** | 82.7 | 155.4 | 61.9 | 178.2 | 58.8 | 167.3 | 42.3 | 166.6 | 50.6 | 33.4 |
| **9-C** | 80.9 | 155.6 | 66.5 | 169.5 | 57.5 | 179.3 | 41.3 | 180.6 | 52.6 | – |
| **9-A** | 85.9 | 157.2 | 66.8 | 180.8 | 59.9 | 168.5 | 42.5 | 167.7 | 52.8 | – |

[a] In $CD_2Cl_2$ at 258 K, chemical shifts in ppm, δ scale. – [b] Carbonyl signals.

group of the *C*-terminal Val moiety and $C^{10}$=O of the terminal ester group have formed the chelate coordination to the zirconium center [$^{13}$C-NMR shift differences of the **8** → **8-C** transformation: Δδ = +8.9 ppm (C7), +7.3 (C10), +8.1 (C9)].

Similarly, the selectively formed addition product **9-I** ($C^4$=O coordinated to zirconium, see Scheme 3 and Tables 5 and 6) is transformed to a ca. 1:1 mixture of **9-C** and **9-A** upon heating (with loss of $CH_4$). Again the product **9-C** exhibits $C^7$=O/N8/$C^{10}$=O chelate coordination to zirconium [Δδ = +7.5 ppm (C7), +10.4 (C10)] whereas complex **9-A** is again characterized by the presence of the *N*-terminal $C^1$=O/N2/$C^4$=O chelate. Both the complexes **8-C** and **9-C** do not represent the most stable structures on their respective hypersurfaces. They both convert completely to their thermodynamically favored isomers **8-A** and **9-A**, respectively, upon standing for prolonged time at temperatures > 0°C.

We conclude that complexes between the electrophilic methylzirconocene cation and *N*- and *C*-protected di- and tripeptides can readily be generated. In the series investigated these are formed with a very high selectivity – in all the cases characterized here the [$Cp_2ZrCH_3^+$] attachment takes place exclusively at the amido carbonyl oxygen function of the *N*-terminal amino acid moiety, i.e. adjacent to the Boc-protective group. We assume that this position is sterically the least shielded, and that the regioselective formation of the adduct complexes (**2**, **3**, **6**–**9**)-**I** under kinetic control is probably governed by steric effects. Very stable chelate complexes (**2**, **3**, **6**–**9**)-**A** are obtained from these intermediates by thermally induced methane elimination. Overall, an analogous regiochemical preference for the *N*-terminal amino acid coordination (here with involvement of the $C^1$=O group of the Boc-protective group) is observed for this product formation under thermodynamic control. Other regioisomers (**7-B**, **8-C**, **9-C**) that have been observed on the way to these final chelate products may again be less favored because of steric interference. For this series of peptide derivative/$Cp_2ZrCH_3^+$ reactions we have shown that a group-4 metal complex fragment can rather readily and even selectively be attached to peptide frameworks. The resulting complexes are rather stable and they can be prepared on a preparative scale. This might open new ways to use peptide derivatives as stereochemically active and well-defined ligand systems in less protected early transition metal complexes that may have an interesting potential especially in asymmetric catalysis. Such developments are actively being pursued in our laboratory.

## Experimental Section

**General Remarks:** Reactions involving organometallic compounds were carried out under argon in a glove box or using Schlenk type glassware. Solvents (including deuterated solvents) were dried and distilled under argon prior to use. – NMR experiments were performed on a Varian Unity Plus 600 spectrometer at 258 K ($^1$H: 600 MHz, $^{13}$C: 150 MHz). Assignments in $^1$H- and $^{13}$C-NMR spectra were confirmed by GCOSY, 1D-TOCSY, GHSQC, and GHMBC experiments.[10] Atom numbering as given in Schemes 1 and 3. – IR spectra were acquired with a Nicolet 5 DXC Fourier transform IR spectrometer. – Melting points were obtained by differential scanning calorimetry (DSC 2010, TA Instruments), elemental analyses were determined with a Foss-Heraeus CHN-Rapid elemental analyzer. – The organometallic reagent [$Cp_2ZrCH_3(THF)^+BPh_4^-$] (**1a**),[4a] the oligopeptides and Boc-protected di- and tripeptide esters were prepared according to literature procedures.[9][11]

**General Procedures. – Preparation of Protected Dipeptide Esters (A):** A typical run was as follows: To a stirred and ice-cooled solution of the Boc-protected amino acid (20 mmol) in chloroform (30 mL) dicyclohexylcarbodiimide (4.13 g, 20 mmol) was added. After 30 min, the mixture was combined with a mixture of the amino acid methyl ester hydrochloride (20 mmol) and triethylamine (2.02 g, 2.72 mL, 20 mmol) in chloroform (30 mL). The combined phases were stirred in an ice bath for 3 h and then kept overnight; then a few drops of acetic acid were added. The mixture was stirred for 15 min and filtered. The filtrate was washed successively with water, a 10 % citric acid solution, a 5 % sodium hydrogen carbonate solution, and water. The solution was dried with magnesium sulfate; solvent was then removed in vacuo. Separation from remaining dicyclohexyl urea was achieved by solving the dipeptide ester product in ethyl acetate and filtering off the insoluble urea. The ethyl acetate was removed in vacuo to yield the analytically pure dipeptide derivative as a white solid.

**Preparation of Protected Tripeptide Esters (B):** A typical run was as follows: To an ice-cooled solution of the *C*-deprotected Boc-dipeptide (10 mmol) in chloroform (20 mL) hydroxybenztriazol

(1.54 g, 10 mmol) and dicyclohexylcarbodiimide (2.06 g, 10 mmol) were added. After 30 min, the mixture was combined with a mixture of the amino acid methyl ester hydrochloride (10 mmol) and triethylamine (1.01 g, 1.39 mL, 10 mmol) in chloroform (30 mL). The combined phases were stirred in an ice bath for 3 h and then kept overnight. A few drops of acetic acid were added. The mixture was then stirred for 15 min and filtered. The filtrate was washed successively with water, a 10% citric acid solution, a 5% sodium hydrogen carbonate solution, and water. The solution was dried with magnesium sulfate and solvent was then removed in vacuo. Separation from remaining dicyclohexyl urea was done by dissolving the dipeptide in ethyl acetate and filtering off the insoluble urea. Further purification was by chromatography on a silica-gel column using an ethyl acetate/petroleum ether/ether solvent mixture as eluent.

**Preparation of the Metal Peptide Complexes (C):** A solution of the protected dipeptide or tripeptide ester (2.0 mmol) in dichloromethane (5 mL) was combined with a solution of Jordan′s cation (2.0 mmol) in dichloromethane (10 mL) at 0 °C. The mixture was stirred for 3 h and then warmed to room temperature. The solvent was removed in vacuo, the residue washed with toluene and pentane to yield the analytically pure metal peptide complex as a white solid.

**Preparation of the Metal Peptide Complexes (NMR Experiment) (D):** A solution of the protected dipeptide or tripeptide ester (63.8 μmol) in [$D_2$]dichloromethane (0.4 mL) was combined with a solution of Jordan′s cation (63.8 μmol) in [$D_2$]dichloromethane (0.4 mL) at −15°C.

**Preparation of Boc-Gly-Val-OMe (2):** *N-tert*-Butoxycarbonylglycine (3.50 g, 20.0 mmol) and valine methyl ester hydrochloride (3.35 g, 20 mmol) were treated according to procedure A to yield the dipeptide Boc-Gly-Val-OMe (5.25 g, 91%) as an oil. − IR (KBr): $\tilde{\nu}$ = 3326 (s, NH), 2971 (m), 2932 (m), 2878 (w), 1744 (m), 1683 (s), 1664 (vs), 1525 (s), 1366 (w), 1169 (m), 864 (m), 737 (w) $cm^{-1}$. − $^1$H NMR ($CD_2Cl_2$, 599.8 MHz): δ = 7.16 (br., 1 H, 5-H), 5.86 (br., 1 H, 2-H), 4.46 (dd, $^3J$ = 9.0 Hz, $^3J$ = 5.2 Hz, 1 H, 6-H), 3.78 (m, 2 H, 3- and 3′-H), 3.69 (s, 3 H, 7-OC$H_3$), 2.17 [m, 1 H, 6-C$H$($CH_3$)$_2$], 1.40 [s, 9 H, 1-OC(C$H_3$)$_3$], 0.88 and 0.84 [2 d, 2 $^3J$ = 7.4 Hz, 2× 3 H, 6-CH(C$H_3$)$_2$]. − $^{13}$C NMR ($CD_2Cl_2$, 150.8 MHz): δ = 172.7 (C-7), 170.1 (C-4), 156.2 (C-1), 79.9 [1-O$C$($CH_3$)$_3$], 57.0 (C-6), 52.5 (7-OC$H_3$), 44.1 (C-3), 31.3 [6-$C$H($CH_3$)$_2$], 28.1 [1-OC($C$H$_3$)$_3$], 19.0 and 17.6 [6-CH($C$H$_3$)$_2$].

**Reaction of Boc-Gly-Val-OMe (2) with [$Cp_2ZrCH_3(THF)^+BPh_4^-$] (1a). − Formation of 2-I:** Boc-Gly-Val-OMe (18.4 mg, 63.8 μmol) and **1a** (40.0 mg, 63.8 μmol) were treated according to procedure D to generate **2-I**. − $^1$H NMR ($CD_2Cl_2$, 599.8 MHz): δ = 7.69 (br., 1 H, 2-H), 7.45 (br., 1 H, 5-H), 6.24 and 6.20 (2 s, 2 × 5 H, Cp- and Cp′-H), 4.35 (br., 1 H, 6-H), 3.80 (s, 3 H, 7-OC$H_3$), 3.63 (m, 2 H, 3- and 3′-H), 2.10 [m, 1 H, 6-C$H$($CH_3$)$_3$], 1.43 [s, 9 H, 1-OC(C$H_3$)$_3$], 0.87 and 0.84 [2 d, 2 $^3J$ = 6.7 Hz, 2 × 3 H, 6-CH(C$H_3$)$_2$], 0.48 (s, 1 H, Zr-C$H_3$), [$BPh_4$]$^-$: 7.45 (m, 8 H, *o*-H), 7.10 (m, 8 H, *m*-H), 6.93 (m, 4 H, *p*-H); THF: δ = 3.72 (m, 4 H, α-H), 1.81 (m, 4 H, β-H). − $^{13}$C NMR ($CD_2Cl_2$, 150.8 MHz): δ = 179.1 (C-4), 168.4 (C-7), 155.3 (C-1), 113.2 and 113.1 (Cp C and Cp′ C), 81.1 [1-O$C$($CH_3$)$_3$], 58.4 (C-6), 53.0 (7-OC$H_3$), 44.1 (C-3), 33.0 (Zr-$C$H$_3$), 31.0 [6-$C$H($CH_3$)$_2$], 27.4 [1-OC($C$H$_3$)$_3$], 18.1 and 16.8 [6-CH($C$H$_3$)$_2$]; [$BPh_4$]$^-$: δ = 163.8 (q, $^1J_{CB}$ = 49 Hz, *i-C*), 135.3 (*o*-C), 125.7 (*m*-C), 121.7 (*p*-C); THF: δ = 67.9 (α-C), 25.2 (β-C).

**Reaction of 2 with 1a. − Formation of 2-A:** Boc-Gly-Val-OMe (**2**, 0.58 g, 2.0 mmol) and **1a** (1.25 g, 2 mmol) were treated according to procedure C to yield the metal peptide complex **2-A** (1.59 g, 96 %) as a white solid; m.p. 51 °C (decomp). − $[\alpha]_D$ = −25 (*c* = 0.10, $CH_2Cl_2$). − $C_{47}H_{53}BN_2O_5Zr$ (828.0): calcd. C 68.18, H 6.45, N 3.38; found C 68.24, H 6.74, N 3.30. − IR (KBr): $\tilde{\nu}$ = 3377 (s, NH), 3045 (m), 2965 (s), 1743 (s), 1684 (s), 1591 (s), 1431 (s), 1155 (m), 797 (vs), 703 (s) $cm^{-1}$. − $^1$H NMR ($CD_2Cl_2$, 599.8 MHz): δ = 7.36 (br., 1 H, 5-H), 6.19 and 6.16 (2 s, 2 × 5 H, Cp- and Cp′-H), 4.33 (dd, $^3J$ = 8.3 Hz, $^3J$ = 5.2 Hz, 1 H, 6-H), 3.77 (s, 3 H, 7-OC$H_3$), 3.54 (m, 2 H, 3- and 3′-H), 2.17 [m, 1 H, 6-C$H$($CH_3$)$_2$], 1.52 [s, 9 H, 1-OC(C$H_3$)$_3$], 0.96 and 0.94 [2 d, 2 $^3J$ = 6.9 Hz, 2 × 3 H, 6-CH(C$H_3$)$_2$]; [$BPh_4$]$^-$: δ = 7.37 (m, 8 H, *o*-H), 7.07 (m, 8 H, *m*-H), 6.92 (m, 4 H, *p*-H). − $^{13}$C NMR ($CD_2Cl_2$, 150.8 MHz): δ = 179.1 (C-4), 170.0 (C-7), 156.6 (C-1), 115.1 and 115.0 (Cp C and Cp′ C), 85.5 [1-O$C$($CH_3$)$_3$], 60.3 (C-6), 53.1 (7-O$C$H$_3$), 50.0 (C-3), 31.0 [6-$C$H($CH_3$)$_2$], 28.7 [1-O$C$($CH_3$)$_3$], 19.1 and 18.3 [CH($C$H$_3$)$_2$]; [$BPh_4$]$^-$: δ = 164.6 (q, $^1J_{CB}$ = 49 Hz, *i-C*), 135.7 (*o*-C), 126.0 (*m*-C), 122.2 (*p*-C).

**Preparation of Boc-Ala-Val-OMe (3):** *N-tert*-Butoxycarbonylalanine (3.78 g, 20 mmol) and valine methyl ester hydrochloride (3.35 g, 20 mmol) were treated according to procedure A to yield the dipeptide **3** (5.25 g, 89 %) as a white solid; m.p. 66 °C. − $[\alpha]_D$ = −28 (*c* = 0.10, $CH_2Cl_2$). − IR (KBr): $\tilde{\nu}$ = 3318 (s, NH), 2971 (m), 2935 (m), 2878 (w), 1744 (m), 1727 (m), 1662 (vs), 1522 (s), 1366 (w), 1169 (m), 860 (m) $cm^{-1}$. − $^1$H NMR ($CD_2Cl_2$, 599.8 MHz): δ = 6.82 (d, $^3J$ = 8.8 Hz, 1 H, 5-H), 5.17 (d, $^3J$ = 7.1 Hz, 1 H, 2-H), 4.44 (dd, $^3J$ = 8.8 Hz, $^3J$ = 4.9 Hz, 1 H, 6-H), 4.13 (m, 1 H, 3-H), 3.68 (s, 3 H, 7-OC$H_3$), 2.13 [m, 1 H, 6-C$H$($CH_3$)$_2$], 1.40 [s, 9 H, 1-OC(C$H_3$)$_3$], 1.28 (d, $^3J$ = 7.1 Hz, 3 H, 3-C$H_3$), 0.87 and 0.84 [2 d, 2 $^3J$ = 6.8 Hz, 2 × 3 H, 6-CH(C$H_3$)$_2$]. − $^{13}$C NMR ($CD_2Cl_2$, 150.8 MHz): δ = 172.5 and 172.3 (C-4 and C-7), 155.3 (C-1), 79.9 [1-O$C$($CH_3$)$_3$], 56.8 (C-6), 52.3 (C-3), 50.0 (7-O$C$H$_3$), 31.2 [6-$C$H($CH_3$)$_2$], 28.0 [1-OC($C$H$_3$)$_3$], 18.8 (3-$C$H$_3$), 17.5 and 17.3 [6-CH($C$H$_3$)$_2$].

**Generation of the Intermediate Adduct 3-I:** Boc-Ala-Val-OMe (**3**, 19.3 mg, 63.8 μmol) and **1a** (40.0 mg, 63.8 μmol) were treated according to procedure D to give **3-I**. − $^1$H NMR ($CD_2Cl_2$, 599.8 MHz): δ = 7.48 (d, $^3J$ = 7.8 Hz, 1 H, 5-H), 6.32 and 6.28 (2 s, 2 × 5 H, Cp- and Cp′-H), 5.08 (br., 1 H, 2-H), 4.85 (m, 1 H, 6-H), 3.81 (s, 3 H, 7-OC$H_3$), 3.61 (m, 1 H, 3-H), 2.14 [m, 1 H, 6-C$H$($CH_3$)$_2$], 1.47 [s, 9 H, 1-OC(C$H_3$)$_3$], 1.05 (d, $^3J$ = 7.1 Hz, 1 H, 3-C$H_3$), 0.92 [pst, $^3J$ = 7.0 Hz, 2 × 3 H, 6-CH(C$H_3$)$_2$], 0.59 (s, 1 H, Zr-C$H_3$); [$BPh_4$]$^-$: δ = 7.36 (m, 8 H, *o*-H), 7.08 (m, 8 H, *m*-H), 6.93 (m, 4 H, *p*-H); THF: 3.73 (m, 4 H, α-H), 1.86 (m, 4 H, β-H). − $^{13}$C NMR ($CD_2Cl_2$, 150.8 MHz): δ = 182.9 (C-4), 168.9 (C-7), 155.4 (C-1), 113.9 and 113.8 (Cp C and Cp′ C), 82.1 [1-O$C$($CH_3$)$_3$], 59.1 (C-6), 53.5 (7-O$C$H$_3$), 52.3 (C-3), 33.9 (Zr-$C$H$_3$), 31.3 [6-$C$H($CH_3$)$_2$], 27.8 [1-OC($C$H$_3$)$_3$], 18.7 and 17.7 [6-CH($C$H$_3$)$_2$], 16.5 (3-$C$H$_3$); [$BPh_4$]$^-$: δ = 163.9 (q, $^1J_{CB}$ = 49 Hz, *i-C*), 135.9 (*o*-C), 125.9 (*m*-C), 122.0 (*p*-C); THF: δ = 67.9 (α-C), 25.6 (β-C).

**Preparation of the Chelate Product 3-A:** Boc-Ala-Val-OMe (**3**, 0.61 g, 2.0 mmol) and **1a** (1.25 g, 2 mmol) were treated according to procedure C to yield the metal peptide complex **3-A** (1.57 g, 1.9 mmol, 95 %) as a white solid; m.p. 44 °C (decomp). − $[\alpha]_D$ = −14 (*c* = 0.10, $CH_2Cl_2$). − $C_{47}H_{53}BN_2O_5Zr$ (828.0): calcd. C 68.47, H 6.58, N 3.33; found C 67.32, H 6.58, N 3.29. − IR (KBr): $\tilde{\nu}$ = 3340 (w, NH), 3055 (m), 2981 (s), 1744 (s), 1597 (s), 1551 (s), 1438 (s), 1370 (m), 1150 (s), 812 (s), 733 (s), 704 (vs) $cm^{-1}$. − $^1$H NMR ($CD_2Cl_2$, 599.8 MHz): δ = 7.88 (d, $^3J$ = 8.1 Hz, 1 H, 5-H), 6.21 and 6.20 (2 s, 2 × 5 H, Cp- and Cp′-H), 4.45 (dd, $^3J$ = 8.3 Hz, $^3J$ = 5.0 Hz, 1 H, 6-H), 4.42 (q, $^3J$ = 6.8 Hz, 1 H, 3-H), 3.82 (s, 3 H, 7-OC$H_3$), 2.25 [m, 1 H, 6-C$H$($CH_3$)$_2$], 1.55 [s, 9 H, 1-OC(C$H_3$)$_3$], 1.47 (d, $^3J$ = 6.8 Hz, 3 H, 3-C$H_3$), 1.01 and 0.96 [2 d, 2 $^3J$ = 6.9 Hz, 2 × 3 H, 6-CH(C$H_3$)$_2$]; [$BPh_4$]$^-$: δ = 7.35 (m, 8 H, *o*-

H), 7.08 (m, 8 H, *m*-H), 6.93 (m, 4 H, *p*-H). − $^{13}$C NMR ($CD_2Cl_2$, 150.8 MHz): δ = 181.7 (C-4), 170.4 (C-7), 155.9 (C-1), 114.7 and 114.6 (Cp C and Cp′ C) 85.6 [1-O*C*$(CH_3)_3$], 59.6 (C-6), 56.7 (C-3), 53.2 (7-OC$H_3$), 30.9 [6-*C*H$(CH_3)_2$], 28.4 [1-OC(*C*$H_3)_3$], 19.0 and 18.4 [6-CH(C$H_3)_2$], 17.7 (3-*C*$H_3$); $[BPh_4]^-$: δ = 163.9 (q, $^1J_{CB}$ = 49 Hz, *i*-C), 135.9 (*o*-C), 125.8 (*m*-C), 122.0 (*p*-C).

**X-ray Crystal Structure Analysis of 3-A:** Formula $C_{48}H_{55}BN_2O_5Zr \cdot 1/2\ H_2O$, $M$ = 849.97, colorless crystal, 0.60 × 0.30 × 0.20 mm, $a$ = 14.468(2), $b$ = 19.939(2), $c$ = 33.232(2) Å, $V$ = 9586.7(17) Å$^3$, $\rho_{calcd.}$ = 1.178 g cm$^{-3}$, $F$(000) = 3568 e, μ = 2.74 cm$^{-1}$, empirical absorption correction via φ scan data (0.853 ≤ $T$ ≤ 0.947), $Z$ = 8, orthorhombic, space group $P2_12_12_1$ (No. 19), λ = 0.71073 Å, $T$ = 223 K, ω scans, 8838 reflections collected (+$h$, +$k$, +$l$), [(sinθ)/λ] = 0.59 Å$^{-1}$, 8837 independent and 3416 observed reflections [$I \geq 2\ \sigma(I)$], 895 refined parameters, $R$ = 0.079, $wR^2$ = 0.204, max. residual electron density 0.71 (−0.61) e Å$^{-3}$, Flack parameter 0.05(11), Cp rings and phenyl groups refined as rigid groups, hydrogen atoms at N6 and N26 from difference Fourier, others calculated and all refined as riding atoms. Data set was collected with an Enraf Nonius MACH3 diffractometer. Programs used: data reduction MolEN, structure solution SHELXS-86, structure refinement SHELXL-97, graphics SCHAKAL-92. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-114803. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: int. code + 44-1223/336-033, E-mail: deposit@ccdc.cam.ac.uk].

**Preparation of Boc-Gly-Val-Val-OMe 6:** (*N-tert*-Butoxycarbonylglycyl)valine (2.74 g, 10.0 mmol) and valine methyl ester hydrochloride (1.68 g, 10 mmol) were treated according to procedure B to yield the tripeptide Boc-Gly-Val-Val-OMe (**6**, 2.91 g, 75 %) as a white solid; m.p. 215 °C. − $[\alpha]_D$ = −14 ($c$ = 0.10, $CH_2Cl_2$). − $C_{18}H_{33}N_3O_6$ (387.5): calcd. C 55.80, H 8.58, N 10.84; found C 55.36, H 8.60, N 10.52. − IR (KBr): ṽ = 3311 (s, NH), 2967 (m), 2936 (m), 2877 (w), 1747 (m), 1723 (m), 1648 (vs), 1545 (s), 1367 (w), 1162 (m), 864 (m), 786 (m) cm$^{-1}$. − $^1$H NMR ($CD_2Cl_2$, 599.8 MHz): δ = 7.84 (d, 1 H, $^3J$ = 8.5 Hz, 5-H), 7.72 (d, 1 H, $^3J$ = 8.6 Hz, 8-H), 6.14 (br. s, 1 H, 2-H), 4.54 (dd, $^3J$ = 8.6 Hz, $^3J$ = 5.4 Hz, 1 H, 9-H), 4.45 (dd, $^3J$ = 8.5 Hz, $^3J$ = 5.7 Hz, 1 H, 6-H), 3.86 (m, 2 H, 3- and 3′-H), 3.68 (s, 3 H, 10-OC$H_3$), 2.11 [m, 1 H, 6-C*H*$(CH_3)_2$], 1.98 [m, 1 H, 9-C*H*$(CH_3)_2$], 1.38 [s, 9 H, 1-OC(C$H_3)_3$], 0.90 and 0.88 [2 d, 2 $^3J$ = 6.8 Hz, 2 × 3 H, 9-CH(C$H_3)_2$], 0.86 and 0.83 [2 d, 2 $^3J$ = 6.8 Hz, 6 H, 6-CH(C$H_3)_2$]. − $^{13}$C NMR ($CD_2Cl_2$, 150.8 MHz): δ = 172.6 (C-7), 172.2 (C-10), 170.0 (C-4), 156.2 (C-1), 79.6 [1-O*C*$(CH_3)_3$], 58.5 (C-9), 57.3 (C-6), 52.4 (10-O*C*H$_3$), 43.9 (C-3), 31.6 [6-*C*H$(CH_3)_2$], 31.0 [9-*C*H$(CH_3)_2$], 28.3 [1-OC(*C*$H_3)_3$], 19.1 and 19.0 [9-CH(*C*$H_3)_2$], 18.6 and 17.8 [6-*C*H$(CH_3)_2$].

**Generation of the Intermediate Adduct 6-I:** Boc-Gly-Val-Val-OMe (**6**, 24.7 mg, 63.8 μmol) and **1a** (40.0 mg, 63.8 μmol) were treated according to procedure D to give **6-I**. − $^1$H NMR ($CD_2Cl_2$, 599.8 MHz): δ = 7.78 (br., 1 H, 2-H), 6.66 (br., 1 H, 5-H), 6.41 (br., 1 H, 8-H), 6.26 and 6.20 (2 s, 2 × 5 H, Cp- and Cp′-H), 4.46 (br., 1 H, 9-H), 4.16 (br., 1 H, 6-H), 3.71 (m, 2 H, 3- and 3′-H), 3.76 (s, 3 H, 10-OC$H_3$), 2.25 [m, 1 H, 9-C*H*$(CH_3)_2$], 1.98 [m, 1 H, 6-C*H*$(CH_3)_2$], 1.43 [s, 9 H, 1-OC(C$H_3)_3$], 0.99 and 0.95 [2 d, 2 $^3J$ = 7.0 Hz, 6 H, 9-CH(C$H_3)_2$], 0.89 and 0.88 [2 d, 2 $^3J$ = 7.0 Hz, 2 × 3 H, 6-CH(C$H_3)_2$], 0.50 (s, 3 H, Zr-C$H_3$); $[BPh_4]^-$: δ = 7.43 (m, 8 H, *o*-H), 7.10 (m, 8 H, *m*-H), 6.94 (m, 4 H, *p*-H); THF: 3.72 (m, 4 H, α-H), 1.85 (m, 4 H, β-H). − $^{13}$C NMR ($CD_2Cl_2$, 150.8 MHz): δ = 177.9 (C-4), 171.7 (C-10), 171.3 (C-7), 156.1 (C-1), 114.8 and 113.7 (Cp C and Cp′ C), 81.5 [1-O*C*$(CH_3)_3$], 60.0 (C-9), 58.1 (C-6), 52.2 (10-O*C*H$_3$), 44.8 (C-3), 32.4 (Zr-*C*H$_3$), 31.8 [6-*C*H$(CH_3)_2$], 30.2 [9-*C*H$(CH_3)_2$], 27.8 [1-OC(*C*$H_3)_3$], 18.9 and 18.6 [6-CH(C$H_3)_2$], 17.8 and 17.2 [9-CH(C$H_3)_2$]; $[BPh_4]^-$: δ = 163.9 (q, $^1J_{CB}$ = 49 Hz, *i*-*C*), 135.7 (*o*-C), 126.0 (*m*-C), 122.1 (*p*-C); THF: δ = 68.0 (α-C), 25.7 (β-C).

**Preparation of the Chelate Product 6-A:** Boc-Gly-Val-Val-OMe (**6**, 0.78 g, 2.0 mmol) and **1a** (1.25 g, 2 mmol) were treated according to procedure C to yield the metal peptide complex **6-A** (1.59 g, 97 %) as a white solid; m.p. 67 °C (decomp). − $[\alpha]_D$ = −59 ($c$ = 0.10, $CH_2Cl_2$). − $C_{52}H_{62}BN_3O_6Zr$ (927.1): calcd. C 67.37, H 6.74, N 4.53; found C 67.13, H 6.69, N 4.42. − IR (KBr): ṽ = 3292 (s, NH), 3269 (m), 2966 (m), 2966 (s), 2877 (w), 1743 (m), 1652 (vs), 1591 (s), 1543 (s), 1240 (s), 1159 (m), 869 (m), 789 (m) cm$^{-1}$. − $^1$H NMR ($CD_2Cl_2$, 599.8 MHz): δ = 9.13 (br., 1 H, 8-H), 6.78 (br., 1 H, 5-H), 6.25 and 6.19 (2 s, 2 × 5 H, Cp- and Cp′-H), 4.49 (dd, $^3J$ = 8.2 Hz, $^3J$ = 4.9 Hz, 1 H, 9-H), 4.45 (dd, $^3J$ = 8.8 Hz, $^3J$ = 6.0 Hz, 1 H, 6-H), 4.21 (AB, $^2J$ = 18.7 Hz, 2 H, 3- and 3′-H), 3.78 (s, 3 H, 10-OC$H_3$), 2.26 [m, 1 H, 9-C*H*$(CH_3)_2$], 2.13 [m, 1 H, 6-C*H*$(CH_3)_2$], 1.57 [s, 9 H, 1-OC(C$H_3)_3$], 1.07 and 0.99 [2 d, 2 $^3J$ = 7.0 Hz, 6 H, 6-CH(C$H_3)_2$], 1.02 and 1.00 [2 d, 2 $^3J$ = 7.0 Hz, 2 × 3 H, 9-CH(C$H_3)_2$]; $[BPh_4]^-$: δ = 7.41 (m, 8 H, *o*-H), 7.10 (m, 8 H, *m*-H), 6.96 (m, 4 H, *p*-H). − $^{13}$C NMR ($CD_2Cl_2$, 150.8 MHz): δ = 177.8 (C-4), 171.5 (C-10), 169.7 (C-7), 156.2 (C-1), 114.8 and 114.7 (Cp C and Cp′ C), 85.5 [1-O*C*$(CH_3)_3$], 60.1 (C-6), 58.1 (C-9), 52.7 (10-O*C*H$_3$), 50.1 (C-3), 32.3 [6-*C*H$(CH_3)_2$], 30.8 [9-*C*H$(CH_3)_2$], 28.4 [1-OC(*C*$H_3)_3$], 19.1 and 19.0 [6-CH(*C*$H_3)_2$], 18.0 and 17.9 [9-CH(*C*$H_3)_2$]; $[BPh_4]^-$: δ = 164.0 (q, $^1J_{CB}$ = 49 Hz, *i*-*C*), 135.8 (*o*-C), 125.8 (*m*-C), 121.9 (*p*-C).

**Preparation of Boc-Ala-Ala-Val-OMe (7):** (*N-tert*-Butoxycarbonylalanyl)alanine (2.60 g, 10.0 mmol) and valine methyl ester hydrochloride (1.68 g, 10 mmol) were treated according to procedure B to yield the tripeptide Boc-Ala-Ala-Val-OMe **7** (2.58 g, 69 %) as a white solid material; m.p. 146 °C. − $[\alpha]_D$ = −61 ($c$ = 0.10, $CH_2Cl_2$). − $C_{17}H_{31}N_3O_6$ (373.4): calcd. 54.68, H 8.37, N 11.25; found C 54.68, H 8.41, N 10.90. − IR (KBr): ṽ = 3382 (s, NH), 3308 (s, NH), 2978 (s), 2934 (m), 2878 (w), 1738 (m), 1706 (m), 1638 (vs), 1535 (s), 1347 (w), 1166 (m), 865 (m), 789 (w) cm$^{-1}$. − $^1$H NMR ($CD_2Cl_2$, 599.8 MHz): δ = 7.59 (d, $^3J$ = 8.6 Hz, 1 H, 8-H), 7.53 (d, $^3J$ = 7.2 Hz, 1 H, 5-H), 5.80 (d, $^3J$ = 7.2 Hz, 1 H, 2-H), 4.68 (m, 1 H, 6-H), 4.46 (dd, $^3J$ = 8.6 Hz, $^3J$ = 5.2 Hz, 1 H, 9-H), 4.26 (m, 1 H, 3-H), 3.69 (s, 3 H, 10-OC$H_3$), 2.11 [m, 1 H, 9-C*H*$(CH_3)_2$], 1.38 [s, 9 H, 1-OC(C$H_3)_3$], 1.31 (d, $^3J$ = 7.0 Hz, 3 H, 6-C$H_3$), 1.27 (d, $^3J$ = 7.0 Hz, 3 H, 3-C$H_3$), 0.87 and 0.84 [2 d, 2 $^3J$ = 6.8 Hz, 2 × 3 H, 9-CH(C$H_3)_2$]. − $^{13}$C NMR ($CD_2Cl_2$, 150.8 MHz): δ = 173.1 (C-4), 172.6 (C-10), 172.4 (C-7), 155.5 (C-1), 79.6 [1-O*C*$(CH_3)_3$], 57.2 (C-9), 52.3 (10-O*C*H$_3$), 49.9 (C-3), 48.8 (C-6), 31.2 [9-*C*H$(CH_3)_2$], 28.1 [1-OC(*C*$H_3)_3$], 18.9 (6-*C*H$_3$), 18.8 (3-*C*H$_3$), 18.4 and 17.7 [9-CH(*C*$H_3)_2$].

**Generation of the Intermediate Adduct 7-I:** Boc-Ala-Ala-Val-OMe (**7**, 23.8 mg, 63.8 μmol) and **1a** (40.0 mg, 63.8 μmol) were treated according to procedure D to give **7-I**. − $^1$H NMR ($CD_2Cl_2$, 599.8 MHz): δ = 9.17 (br., 1 H, 8-H), 8.67 (br., 1 H, 5-H), 6.33 and 6.30 (2 s, 2 × 5 H, Cp- and Cp′-H), 5.54 (br., 1 H, 2-H), 3.92 (br., 1 H, 9-H), 3.82 (br., 1 H, 6-H), 3.79 (s, 3 H, 10-OC$H_3$), 3.78 (br., 1 H, 3-H), 2.24 [m, 1 H, 9-C*H*$(CH_3)_2$], 1.44 [s, 9 H, 1-OC(C$H_3)_3$], 1.24 (d, $^3J$ = 6.9 Hz, 3 H, 6-C$H_3$), 1.18 (d, $^3J$ = 7.2 Hz, 3 H, 3-C$H_3$), 0.92 and 0.90 [2 d, 2 $^3J$ = 6.7 Hz, 2 × 3 H, 9-CH(C$H_3)_2$], 0.54 (s, 3 H, Zr-C$H_3$); $[BPh_4]^-$: 7.32 (m, 8 H, *o*-H), 7.07 (m, 8 H, *m*-H), 6.92 (m, 4 H, *p*-H); THF: δ = 3.71 (m, 4 H, α-H), 1.84 (m, 4 H, β-H). − $^{13}$C NMR ($CD_2Cl_2$, 150.8 MHz): δ = 169.6 (C-10), 156.8 (C-1), 113.9 and 113.8 (Cp C and Cp′ C), 81.8

[1-O*C*($CH_3$)$_3$], 59.7 (C-9), 53.3 (10-O*C*$H_3$), 51.9 (C-3), 50.7 (C-6), 33.6 (Zr-*C*$H_3$), 30.3 [9-*C*H($CH_3$)$_2$], 27.9 [1-OC(*C*$H_3$)$_3$], 19.0 (6-*C*$H_3$), 18.4 (3-*C*$H_3$), 17.1 and 16.8 [9-CH(*C*$H_3$)$_2$]; [$BPh_4$]$^-$: δ = 163.8 (q, $^1J_{CB}$ = 49 Hz, *i-C*), 135.8 (*o*-C), 126.0 (*m*-C), 122.0 (*p*-C); THF: δ = 68.0 (α-C), 25.7 (β-C). The resonance signals of C-7 and C-11 were not observed.

**Preparation of the Chelate Products 7-A/B:** Boc-Ala-Ala-Val-OMe (**7**, 0.75 g, 2.0 mmol) and **1a** (1.25 g, 2 mmol) were treated according to procedure C to yield a mixture of the two isomeric metal peptide complexes **7-A** and **7-B** (1.75 g, 96 %) in a 4:3 ratio as a white solid; m.p. 59 °C. (decomp). − $[\alpha]_D$ = −43 (*c* = 0.10, $CH_2Cl_2$). − $C_{51}H_{60}BN_3O_6Zr$ (913.1): calcd. C 67.09, H 6.62, N 4.60; found C 66.39, H 6.91, N 4.45. − IR (KBr): ṽ = 3295 (s, NH), 3054 (s), 2985 (m), 2964 (m), 1744 (m), 1690 (m), 1609 (m), 1264 (s), 1157 (m), 858 (m), 785 (m) cm$^{-1}$. − Isomer **7-A**: $^1$H NMR ($CD_2Cl_2$, 599.8 MHz): δ = 8.13 (d, $^3J$ = 5.6 Hz, 1 H, 5-H), 6.32 (br., 1 H, 8-H), 6.21 and 6.19 (2 s, 2 × 5 H, Cp- and Cp′H), 4.49 (dd, $^3J$ = 7.0 Hz, $^3J$ = 4.8 Hz, 1 H, 9-H), 4.41 (q, $^3J$ = 7.1 Hz, 1 H, 3-H), 4.33 (m, 1 H, 6-H), 3.74 (s, 3 H, 10-OC*H*$_3$), 2.20 [m, 1 H, 9-C*H*($CH_3$)$_2$], 1.54 [s, 9 H, 1-OC(C*H*$_3$)$_3$], 1.44 (d, $^3J$ = 7.1 Hz, 3 H, 3-C*H*$_3$), 1.29 (d, $^3J$ = 7.1 Hz, 3 H, 6-C*H*$_3$), 0.97 and 0.93 [2 d, 2 $^3J$ = 6.8 Hz, 2 × 3 H, 9-CH(C*H*$_3$)$_2$]; [$BPh_4$]$^-$: δ = 7.34 (m, 8 H, *o*-H), 7.07 (m, 8 H, *m*-H), 6.92 (m, 4 H, *p*-H). − $^{13}$C NMR ($CD_2Cl_2$, 150.8 MHz): δ = 180.8 (C-4), 171.8 (C-10), 170.0 (C-7), 156.0 (C-1), 114.7 and 114.6 (Cp C and Cp′ C), 85.5 [1-OC(*C*$H_3$)$_3$], 57.8 (C-9), 56.8 (C-3), 52.7 (10-O*C*$H_3$), 50.8 (C-6), 31.1 [9-*C*H($CH_3$)$_2$], 28.4 [1-OC(*C*$H_3$)$_3$], 21.0, 19.0, 18.9, 18.8, 18.5, 17.8, 17.7, and 15.8 [9-CH(*C*$H_3$)$_2$ of both isomers]; [$BPh_4$]$^-$: δ = 163.9 (q, $^1J_{CB}$ = 49 Hz, *i-C*), 135.9 (*o*-C), 125.9 (*m*-C), 121.9 (*p*-C). − Isomer **7-B**: $^1$H NMR ($CD_2Cl_2$, 599.8 MHz): δ = 8.31 (d, $^3J$ = 8.4 Hz, 1 H, 8-H), 6.24 and 6.19 (2 s, 2 × 5 H, Cp- and Cp′-H), 5.26 (d, $^3J$ = 5.5 Hz, 1 H, 2-H), 4.99 (q, $^3J$ = 7.1 Hz, 1 H, 6-H), 4.48 (dd, $^3J$ = 8.4 Hz, $^3J$ = 5.0 Hz, 1 H, 9-H), 3.88 (m, 1 H, 3-H), 3.82 (s, 3 H, 10-OC*H*$_3$), 2.29 [m, 1 H, 9-C*H*($CH_3$)$_2$], 1.55 [s, 9 H, 1-OC(C*H*$_3$)$_3$], 1.51 (d, $^3J$ = 7.1 Hz, 3 H, 6-C*H*$_3$), 1.27 (d, $^3J$ = 7.1 Hz, 3 H, 3-C*H*$_3$), 1.04 and 0.99 [2 d, 2 $^3J$ = 6.9 Hz, 2 × 3 H, 9-CH(C*H*$_3$)$_2$]; [$BPh_4$]$^-$: δ = 7.34 (m, 8 H, *o*-H), 7.07 (m, 8 H, *m*-H), 6.92 (m, 4 H, *p*-H). − $^{13}$C NMR ($CD_2Cl_2$, 150.8 MHz): δ = 181.0 (C-4), 179.0 (C-7), 170.4 (C-10), 155.4 (C-1), 115.0 and 114.8 (Cp C and Cp′ C), 80.6 [1-O*C*($CH_3$)$_3$], 59.7 (C-9), 57.0 (C-6), 53.3 (10-O*C*$H_3$), 47.8 (C-3), 30.9 [9-*C*H($CH_3$)$_2$], 28.1 [1-OC(*C*$H_3$)$_3$], 21.0, 19.0, 18.9, 18.8, 18.5, 17.8, 17.7, and 15.8 [9-CH(*C*$H_3$)$_2$ of both isomers]; [$BPh_4$]$^-$: δ = 163.9 (q, $^1J_{CB}$ = 49 Hz, *i-C*), 135.9 (*o*-C), 125.9 (*m*-C), 121.9 (*p*-C). − Upon standing at 0 °C for two weeks isomer **7-B** rearranged quantitatively to form isomer **7-A**.

**Preparation of Boc-Ala-Val-Val-OMe (8):** (*N-tert*-Butoxycarbonylalanyl)valine (2.88 g, 10.0 mmol) and valine methyl ester hydrochloride (1.68 g, 10 mmol) were treated according to procedure B to yield the tripeptide Boc-Ala-Val-Val-OMe (**8**, 2.73 g, 68 %) as a white solid; m.p. 214 °C. − $[\alpha]_D$ = −66 (*c* = 0.10, $CH_2Cl_2$). − IR (KBr): ṽ = 3325 (m, NH), 2967 (m), 2933 (m), 1745 (m), 1696 (m), 1648 (s), 1541 (s), 1169 (m), 834 (m), 711 (s) cm$^{-1}$. − $^1$H NMR ($CD_2Cl_2$, 599.8 MHz): δ = 7.79 (d, $^3J$ = 8.7 Hz, 1 H, 5-H), 7.60 (d, $^3J$ = 8.7 Hz, 1 H, 8-H), 6.04 (d, $^3J$ = 8.3 Hz, 1 H, 2-H), 4.52 (dd, $^3J$ = 8.7 Hz, $^3J$ = 5.6 Hz, 1 H, 6-H), 4.47 (pst, $^3J$ = 8.7 Hz, 1 H, 9-H), 4.40 (m, 1 H, 3-H), 3.68 (s, 3 H, 10-OC*H*$_3$), 2.13 [m, 2 H, 6-C*H*($CH_3$)$_2$], 1.99 [m, 2 H, 9-C*H*($CH_3$)$_2$], 1.38 [s, 9 H, 1-OC(C*H*$_3$)$_3$], 1.22 (d, $^3J$ = 7.0 Hz, 3 H, 3-C*H*$_3$), 0.91 and 0.89 [m, 12 H, 9-CH(C*H*$_3$)$_2$], 0.86 and 0.82 [m, 12 H, 6-CH(C*H*$_3$)$_2$]. − $^{13}$C NMR ($CD_2Cl_2$, 150.8 MHz): δ = 173.3 (C-4), 172.5 (C-10), 171.9 (C-7), 156.6 (C-1), 79.5 [1-O*C*($CH_3$)$_3$], 58.7/58.6 (C-9), 57.1/57.0 (C-6), 52.3 (10-O*C*$H_3$), 49.9 (C-3), 31.3/31.1 [6-*C*H($CH_3$)$_2$], 31.1/31.0 [9-*C*H($CH_3$)$_2$], 28.3 [1-OC(*C*$H_3$)$_3$], 19.1 and 19.0 [6-CH(*C*$H_3$)$_2$], 18.6 and 17.8 [9-CH(*C*$H_3$)$_2$], 18.5 (3-*C*$H_3$).

**Generation of the Intermediate Adduct 8-I**: Boc-Ala-Val-Val-OMe (**8**, 25.6 mg, 63.8 μmol) and **1a** (40.0 mg, 63.8 μmol) were treated according to procedure D to give **8-I**. − $^1$H NMR ($CD_2Cl_2$, 599.8 MHz): δ = 8.36 (br. s, 1 H, 5-H), 7.62 (d, $^3J$ = 7.3 Hz, 1 H, 8-H), 6.33 and 6.32 (2 s, 2 × 5 H, Cp- and Cp′-H), 5.29 (br. s, 1 H, 2-H), 4.50 (dd, $^3J$ = 8.6 Hz, $^3J$ = 4.5 Hz, 1 H, 6-H), 4.43 (m, 1 H, 9-H), 4.08 (br. s, 1 H, 3-H), 3.80 (s, 3 H, 10-OC*H*$_3$), 2.28 [m, 1 H, 9-C*H*($CH_3$)$_2$], 2.01 [m, 1 H, 6-C*H*($CH_3$)$_2$], 1.44 [s, 9 H, 1-OC(C*H*$_3$)$_3$], 1.27 (d, $^3J$ = 7.2 Hz, 3 H, 3-C*H*$_3$), 1.01 and 0.97 [2 d, 2 $^3J$ = 6.8 Hz, 2 × 3 H, 9-CH(C*H*$_3$)$_2$], 0.97 and 0.92 [2 d, 2 $^3J$ = 6.2 Hz, 2 × 3 H, 6-CH(C*H*$_3$)$_2$], 0.59 (s, 3 H, Zr-C*H*$_3$); [$BPh_4$]$^-$: δ = 7.34 (m, 8 H, *o*-H), 7.07 (m, 8 H, *m*-H), 6.92 (m, 4 H, *p*-H); THF: δ = 3.74 (m, 4 H, α-H), 1.86 (m, 4 H, β-H). − $^{13}$C NMR ($CD_2Cl_2$, 150.8 MHz): δ = 176.3 (C-4), 169.7 (C-10) 167.4 (C-7), 156.7 (C-1), 113.9 and 113.8 (Cp C and Cp′ C), 82.1 [1-O*C*($CH_3$)$_3$], 60.1 (C-9), 59.7 (C-6), 53.1 (C-3), 52.1 (10-O*C*$H_3$), 33.8 (Zr-*C*$H_3$), 33.1 [6-*C*H($CH_3$)$_2$], 32.4 [9-*C*H($CH_3$)$_2$], 27.9 [1-OC(*C*$H_3$)$_3$], 19.3 and 19.0 [6-CH(*C*$H_3$)$_2$], 18.6 and 17.1 [9-CH(*C*$H_3$)$_2$], 18.1 (3-*C*$H_3$); [$BPh_4$]$^-$: δ = 163.9 (q, $^1J_{CB}$ = 49 Hz, *i-C*), 135.9 (*o*-C), 125.9 (*m*-C), 122.0 (*p*-C); THF: δ = 67.9 (α-C), 25.7 (β-C).

**Preparation of the Chelate Products 8-A/C:** Boc-Ala-Val-Val-OMe (**8**, 0.80 g, 2.0 mmol) and **1a** (1.25 g, 2 mmol) were treated according to procedure C to yield the isomeric metal peptide complexes **8-A** and **8-C** (1.75 g, 93 %) in a ratio of 3:2 as a white solid; m.p. 56 °C (decomp). − $[\alpha]_D$ = −29 (*c* = 0.10, $CH_2Cl_2$). − $C_{53}H_{64}BN_3O_6Zr$ (941.0): calcd. C 67.64, H 6.85, N 4.46; found C 66.04, H 6.85, N 4.22. − IR (KBr): ṽ = 3296 (s, NH), 3069 (m), 2969 (s), 1743 (m), 1660 (s), 1612 (m), 1546 (s), 1433 (s), 1249 (s), 1171 (m), 806 (s), 709 (vs) cm$^{-1}$. − **Isomer 8-A:** $^1$H NMR ($CD_2Cl_2$, 599.8 MHz): δ = 8.64 (br. s, 1 H, 5-H), 6.42 (br. d, $^3J$ = 7.5 Hz, 1 H, 8-H), 6.29 and 6.10 (2 s, 2 × 5 H, Cp- and Cp′-H), 4.51 (q, $^3J$ = 5.5 Hz, 1 H, 3-H), 4.37 (m, 1 H, 9-H), 4.50 (dd, $^3J$ = 8.0 Hz, $^3J$ = 5.3 Hz, 1 H, 6-H), 3.82 (s, 3 H, 10-OC*H*$_3$), 2.31 [m, 1 H, 9-C*H*($CH_3$)$_2$], 2.21 [m, 1 H, 6-C*H*($CH_3$)$_2$], 1.40 [s, 9 H, 1-OC(C*H*$_3$)$_3$], 1.42 (d, $^3J$ = 5.5 Hz, 3 H, 3-C*H*$_3$), 1.10 and 1.09 [2 d, 2 $^3J$ = 6.9 Hz, 2 × 3 H, 9-CH(C*H*$_3$)$_2$], 1.04 and 1.03 [2 d, 2 $^3J$ = 7.0 Hz, 2 × 3 H, 6-CH(C*H*$_3$)$_2$]; [$BPh_4$]$^-$: δ = 7.34 (m, 8 H, *o*-H), 7.07 (m, 8 H, *m*-H), 6.92 (m, 4 H, *p*-H). − $^{13}$C NMR ($CD_2Cl_2$, 150.8 MHz): δ = 181.5 (C-4), 170.1 (C-10), 169.1 (C-7), 156.7 (C-1), 114.8 and 114.6 (Cp C and Cp′ C), 85.5 [1-O*C*($CH_3$)$_3$], 60.0 (C-6), 58.5 (C-3), 57.1 (C-9), 52.7 (10-O*C*$H_3$), 33.1 [6-*C*H($CH_3$)$_2$], 30.9 [9-*C*H($CH_3$)$_2$], 28.4 [1-OC(*C*$H_3$)$_3$], 19.2 (3-*C*$H_3$), 18.8 and 18.7 [6-CH(*C*$H_3$)$_2$], 18.0 and 17.8 [9-CH(*C*$H_3$)$_2$]; [$BPh_4$]$^-$: δ = 164.0 (q, $^1J_{CB}$ = 49 Hz, *i-C*), 135.8 (*o*-C), 125.9 (*m*-C), 121.9 (*p*-C). − **Isomer 8-C:** $^1$H NMR ($CD_2Cl_2$, 599.8 MHz): δ = 8.10 (d, $^3J$ = 7.5 Hz, 1 H, 5-H), 6.22 and 6.21 (2 s, 2 × 5 H, Cp- and Cp′-H), 5.25 (d, $^3J$ = 6.0 Hz, 1 H, 2-H), 5.12 (d, $^3J$ = 6.0 Hz, 1 H, 9-H), 4.48 (m, 1 H, 6-H), 4.01 (m, 1 H, 3-H), 3.76 (s, 3 H, 10-OC*H*$_3$), 2.22 [m, 1 H, 9-C*H*($CH_3$)$_2$], 2.19 [m, 1 H, 6-C*H*($CH_3$)$_2$], 1.54 [s, 9 H, 1-OC(C*H*$_3$)$_3$], 1.31 (d, $^3J$ = 7.0 Hz, 3 H, 3-C*H*$_3$), 1.08 and 1.06 [2 d, 2 $^3J$ = 6.9 Hz, 2 × 3 H, 6-CH(C*H*$_3$)$_2$], 0.97 and 0.94 [2 d, 2 $^3J$ = 6.8 Hz, 2 × 3 H, 9-CH(C*H*$_3$)$_2$]; [$BPh_4$]$^-$: δ = 7.34 (m, 8 H, *o*-H), 7.07 (m, 8 H, *m*-H), 6.92 (m, 4 H, *p*-H). − $^{13}$C NMR ($CD_2Cl_2$, 150.8 MHz): δ = 180.8 (C-7), 179.8 (C-10), 171.5 (C-4), 155.9 (C-1), 115.3 and 115.0 (Cp C and Cp′ C), 80.9 [1-O*C*($CH_3$)$_3$], 66.8 (C-9), 59.9 (C-6), 57.9 (10-O*C*$H_3$), 46.9 (C-3), 30.7 [9-*C*H($CH_3$)$_2$], 34.6 [6-*C*H($CH_3$)$_2$], 28.1 [1-OC(*C*$H_3$)$_3$], 19.0 and 18.9 [6-CH(*C*$H_3$)$_2$], 18.7 and 17.6 [9-CH(*C*$H_3$)$_2$], 17.9 (3-*C*$H_3$); [$BPh_4$]$^-$: δ = 164.0 (q, $^1J_{CB}$ = 49 Hz, *i-C*), 135.8 (*o*-C), 125.9 (*m*-C), 121.9 (*p*-C). Isomer **8-C** rearranges upon standing at 25 °C for 4 d to form isomer **8-A** quantitatively.

**Preparation of Boc-Val-Val-Gly-OMe (9):** (*N-tert*-Butoxycarbonyl-valyl)valine (3.17 g, 10.0 mmol) and glycine methyl ester hydrochloride (1.26 g, 10 mmol) were treated according to procedure B to yield the tripeptide Boc-Val-Val-Gly-OMe (**9**, 2.76 g, 74 %) as a white solid; m.p. 176°C. − $[\alpha]_D = -35$ ($c$ = 0.10, $CH_2Cl_2$). − $C_{18}H_{33}N_3O_6$ (373.5): calcd. C 55.80, H 8.58, N 10.84; found C 55.81, H 8.61, N 10.63. − IR (KBr): $\tilde{\nu}$ = 3295 (vs, NH), 2967 (s, NH), 2933 (m), 1759 (m), 1695 (s), 1640 (vs), 1554 (s), 1526 (s), 1393 (w), 1365 (w), 1209 (s), 1179 (m), 781 (s) $cm^{-1}$. − $^1H$ NMR ($CD_2Cl_2$, 599.8 MHz): δ = 7.62 (br., 1 H, 8-H), 7.23 (d, $^3J$ = 8.9 Hz, 1 H, 5-H), 5.62 (d, $^3J$ = 6.6 Hz, 1 H, 2-H), 4.36 (dd, $^3J$ = 8.9 Hz, $^3J$ = 6.8 Hz, 1 H, 6-H), 3.98 (m, 2 H, 9- and 9′-H), 3.98 (m, 1 H, 3-H), 3.67 (s, 3 H, 10-OC$H_3$), 2.15 [m, 1 H, 6-C$H$(CH$_3$)$_2$], 2.05 [dsept, $^3J$ = 6.9 Hz, $^3J$ = 6.8 Hz, 1 H, 3-C$H$(CH$_3$)$_2$], 1.38 [s, 9 H, 1-OC(C$H_3$)$_3$], 0.95−0.94, [m, 4 × 3 H, 3- and 6-CH(C$H_3$)$_2$]. − $^{13}C$ NMR ($CD_2Cl_2$, 150.8 MHz): δ = 172.1 (C-4), 171.8 (C-7), 170.2 (C-10), 156.2 (C-1), 79.9 [1-O$C$(CH$_3$)$_3$], 60.4 (C-3), 58.2 (C-6), 52.3 (10-O$C$H$_3$), 41.0 (C-9), 30.5 [3-$C$H(CH$_3$)$_2$], 30.4 [6-$C$H(CH$_3$)$_2$], 28.0 [1-OC($C$H$_3$)$_3$], 19.1 and 19.0 [6-CH($C$H$_3$)$_2$], 17.9 and 17.6 [3-CH($C$H$_3$)$_2$].

**Generation of the Intermediate Adduct 9-I**: Boc-Val-Val-Gly-OMe (**9**, 24.7 mg, 63.8 μmol) and 40.0 mg (63.8 μmol) of **1a** were treated according to procedure D to give **9-I**. − $^1H$ NMR ($CD_2Cl_2$, 599.8 MHz): δ = 6.78 (br., 1 H, 5-H), 6.30 and 6.29 (2 s, 2 × 5 H, Cp- and Cp′-H), 5.27 (br. s, 1 H, 2-H), 3.97 (dd, $^3J$ = 6.2 Hz, $^3J$ = 3.6 Hz, 1 H, 3-H), 3.82 (ABX, $^2J$ = 17.8 Hz, 2 H, 9- and 9′-H), 3.79 (s, 10-OC$H_3$), 3.78 (dd, $^3J$ = 4.4 Hz, $^3J$ = 2.5 Hz, 1 H, 3-H), 2.14 [m, 1 H, 6-C$H$(CH$_3$)$_2$], 2.04 [m, 1 H, 3-C$H$(CH$_3$)$_2$], 1.44 [s, 9 H, 1-OC(C$H_3$)$_3$], 1.05 and 1.03 [2 d, 2 $^3J$ = 7.0 Hz, 2 × 3 H, 3-CH(C$H_3$)$_2$], 0.98 and 0.97 [2 d, 2 $^3J$ = 7.2 Hz, 2 × 3 H, 6-CH(C$H_3$)$_2$], 0.55 (s, 3 H, Zr-C$H_3$); [BPh$_4$]$^-$: δ = 7.35 (m, 8 H, *o*-H), 7.07 (m, 8 H, *m*-H), 6.92 (m, 4 H, *p*-H); THF: δ = 3.70 (m, 4 H, α-H), 1.84 (m, 4 H, β-H), the 8-H resonance was not observed. − $^{13}C$ NMR ($CD_2Cl_2$, 150.8 MHz): δ = 178.2 (C-4), 167.3 (C-7), 166.6 (C-10), 155.4 (C-1), 113.8 and 113.7 (Cp C and Cp′ C), 82.7 [1-O$C$(CH$_3$)$_3$], 61.9 (C-3), 58.8 (C-6), 50.6 (10-O$C$H$_3$), 42.3 (C-9), 33.4 (Zr-$C$H$_3$), 33.1 [3-$C$H(CH$_3$)$_2$], 29.5 [6-$C$H(CH$_3$)$_2$], 27.9 [1-OC($C$H$_3$)$_3$], 19.7 and 19.1 [6-CH($C$H$_3$)$_2$], 17.7 and 15.6 [3-CH($C$H$_3$)$_2$]; [BPh$_4$]$^-$: δ = 164.0 (q, $^1J_{CB}$ = 49 Hz, *i-C*), 135.8 (*o*-C), 126.2 (*m*-C), 122.3 (*p*-C); THF: δ = 68.0 (α-C), 25.7 (β-C).

**Preparation of the Chelate Products 9-A/C:** Boc-Val-Val-Gly-OMe (**9**, 0.78 g, 2.0 mmol) and **1a** (1.25 g, 2 mmol) were treated according to procedure C to yield the two isomeric metal peptide complexes **9-A** and **9-C** (1.72 g, 93 %) in a 1:1 ratio as a white solid; m.p. 61 °C (decomp). − $[\alpha]_D = -44$ ($c$ = 0.10, $CH_2Cl_2$). − $C_{52}H_{62}N_3O_6Zr$ (927.1): calcd. C 67.37, H 6.74, N 4.53; found C 66.54; H 6.99; N 4.42. − IR (KBr): $\tilde{\nu}$ = 3293 (s, NH), 3269 (m), 2963 (m), 2934 (w), 1760 (m), 1677 (m), 1611 (s), 1544 (s), 1262 (s), 1016 (m), 799 (vs) $cm^{-1}$. − **Isomer 9-A:** $^1H$ NMR ($CD_2Cl_2$, 599.8 MHz): δ = 7.59 (br., 1 H, 8-H), 7.46 (br., 1 H, 5-H), 6.23 and 6.04 (2 s, 2 × 5 H, Cp- and Cp′-H), 4.37 (d, $^3J$ = 3.0 Hz, 1 H, 3-H), 3.74 (s, 3 H, 10-OC$H_3$), 3.67 (hidden by the THF resonance signal, 1 H, 6-H), 3.20 (ABX, $^2J$ = 17.5 Hz, 2 H, 9- and 9′-H), 2.17 [m, 1 H, 3-C$H$(CH$_3$)$_2$], 1.93 [m, 1 H, 6-C$H$(CH$_3$)$_2$], 1.48 [s, 9 H, 1-OC(C$H_3$)$_3$], 1.07−0.93 [m, 4 × 3 H, 3- and 6-CH(C$H_3$)$_2$]; [BPh$_4$]$^-$: δ = 7.37 (m, 8 H, *o*-H), 7.08 (m, 8 H, *m*-H), 6.93 (m, 4 H, *p*-H). − $^{13}C$ NMR ($CD_2Cl_2$, 150.8 MHz): δ = 180.8 (C-4), 168.5 (C-7), 167.7 (C-10), 157.2 (C-1), 115.3 and 114.9 (Cp C and Cp′ C), 85.9 [1-O$C$(CH$_3$)$_3$], 66.8 (C-3), 59.9 (C-6), 52.8 (10-O$C$H$_3$), 42.5 (C-9), 34.8 [3-$C$H(CH$_3$)$_2$], 29.3 [6-$C$H(CH$_3$)$_2$], 28.4 [1-OC($C$H$_3$)$_3$], 18.8 [6-CH($C$H$_3$)$_2$], 18.6 and 18.2 [3-CH($C$H$_3$)$_2$]; [BPh$_4$]$^-$: δ = 164.0 (q, $^1J_{CB}$ = 49 Hz, *i-C*), 135.8 (*o*-C), 126.2 (*m*-C), 122.3 (*p*-C). − **Isomer 9-C:** $^1H$ NMR ($CD_2Cl_2$, 599.8 MHz): δ = 7.89 (br., 1 H, 5-H), 6.30 and 6.17 (2 s, 2 × 5 H, Cp- and Cp′-H), 5.82 (br., 1 H, 2-H), 4.17 (dd, $^3J$ = 8.4 Hz, $^3J$ = 5.9 Hz, 1 H, 3-H), 3.84 (AB, $^2J$ = 17.0 Hz, 2 H, 9- and 9′-H), 3.77 (m, 1 H, 6-H), 3.71 (s, 3 H, 10-OC$H_3$), 2.01 [m, 1 H, 3-C$H$(CH$_3$)$_2$], 1.95 [m, 1 H, 6-C$H$(CH$_3$)$_2$], 1.55 [s, 9 H, 1-OC(C$H_3$)$_3$], 1.07−0.93 [m, 4 × 3 H, 3- and 6-CH(C$H_3$)$_2$]; [BPh$_4$]$^-$: δ = 7.37 (m, 8 H, *o*-H), 7.08 (m, 8 H, *m*-H), 6.93 (m, 4 H, *p*-H). − $^{13}C$ NMR ($CD_2Cl_2$, 150.8 MHz): δ = 180.6 (C-10), 179.3 (C-7), 169.5 (C-4), 155.6 (C-1), 114.8 and 114.4 (Cp C and Cp′ C), 80.9 [1-O$C$(CH$_3$)$_3$], 66.5 (C-6), 57.5 (C-3), 52.6 (10-O$C$H$_3$), 41.3 (C-9), 34.8 [3-$C$H(CH$_3$)$_2$], 31.6 [6-$C$H(CH$_3$)$_2$], 28.2 [1-OC($C$H$_3$)$_3$], 20.5 and 19.7 [6-CH($C$H$_3$)$_2$], 17.8 and 16.8 [3-CH($C$H$_3$)$_2$]; [BPh$_4$]$^-$: δ = 164.0 (q, $^1J_{CB}$ = 49 Hz, *i-C*), 135.8 (*o*-C), 126.2 (*m*-C), 122.3 (*p*-C). Isomer **9-C** rearranges upon standing at 0 °C for one month to form isomer **9-A** quantitatively.

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