Preparation of Amino Acid-Bridged Dicatechol Ligands for Dinuclear Titanium(IV) Complexes

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Abstract: Amino acid-bridged dicatechol ligands **2a**–**e**-H_4 were prepared by peptide coupling reactions. Under special conditions, an unusual BBr_3-promoted amide to methyl ester transformation was observed for the asparagine and glutamine side chain functions. The ligands were used in coordination studies with titanium(IV) ions in the presence of an alkali metal carbonate. Double-stranded complexes $Li_2[(\mathbf{2a}–\mathbf{e})_2(OR)_2Ti_2]$ which have alcoholate coligands (R = CH_3, C_2H_5, C_3H_5) bridging the metals were selectively formed with lithium counter cations. On the other hand, with potassium or sodium cations triple-stranded complexes $M_4[(\mathbf{2b},\mathbf{c},\mathbf{e})_3Ti_2]$ were obtained in addition to the double-stranded $M_2[(\mathbf{2b},\mathbf{c},\mathbf{e})_2(OCH_3)_2Ti_2]$ (M = Na, K).

Key words: peptide coupling, amino acid, ligands, metal complex, template effect

Introduction

Enzymes are nature's molecular machines to catalyze chemical reactions which are essential for the functioning of organisms on a molecular level. Despite their high complexity they are made from a small pool of approximately 20 amino acid building blocks. Hereby binding of substrates occurs by hydrogen bonding, electrostatic, hydrophobic/hydrophilic and charge-transfer interactions with amino acid side chains which are appropriately arranged on the surface or in cavities of the enzyme.[1] In metalloenzymes, the metal centers are not only able to support a specific folding of the peptide chains, but also might introduce an additional metal-coordination binding site for substrates or even a catalytically active center.[2]

Recently we described the preparation of the dicatechol derivatives **1**-H_4, which possess the nonpolar, hydrophobic amino acids glycine (**a**), alanine (**b**), valine (**c**), leucine (**d**) or phenylalanine (**e**) as spacers.[3] The derivatives **1** form dinuclear complexes $[(\mathbf{1})_2Ti_2(OCH_3)_2]^{2-}$ with titanium(IV) ions in the presence of an alkali metal carbonate as base in methanolic solution (Figure 1). They have some common structural features with the active centers of dinuclear metalloenzymes.[4] The amino acids form a chiral pocket in which the alkoxide coligands were fixed by coordination to the two metal centers. Triple-stranded helicate-type complexes $[(\mathbf{1})_3Ti_2]^{4-}$ could not be observed with the ligands **1**.[5,6]

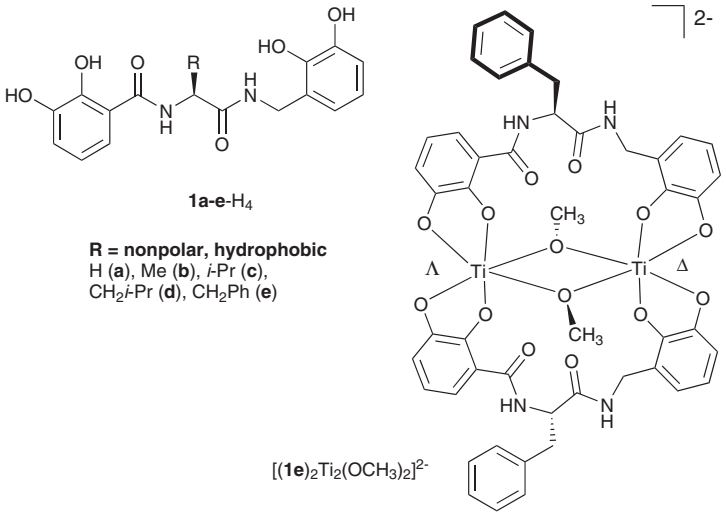

Figure 1 Amino acid-bridged dicatechol ligands **1a**–**e**-H_4 and a complex, which is formed from the phenylalanine-bridged ligand **1e**. Only the thermodynamically most favored isomer of $[(\mathbf{1e})_2Ti_2(OCH_3)_2]^{2-}$ out of seven possible isomers is shown.

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All our recent synthetic, metal coordination and structural studies were performed with nonpolar, hydrophobic amino acids as spacers of the ligands **1a**–**e**-H_4. However, to enable some additional weak secondary interactions between the amino acids and functionalized alkoxide coligands, we need to substitute the alkyl-bearing amino acids by others, which possess appropriate functionalities in the side chain.

In this study we present the synthesis of seven new amino acid-bridged dicatechol ligands **2a**–**e**-H_4, which bear polar, uncharged (amide: **2a**, **2b**; ester: **2a′**, **2b′**; phenol: **2c**), basic (imidazole: **2d**), or conformationally constrained (proline: **2e**) amino acids as spacers (Figure 2). Preliminary coordination studies which were monitored by FT-ICR MS show that the ligands **2** form dinuclear metal complexes with titanium(IV) ions and that we are able to introduce different types of alkoxides as coligands. For the first time we observed triple-stranded complexes which are formed in addition to the double-stranded ones.

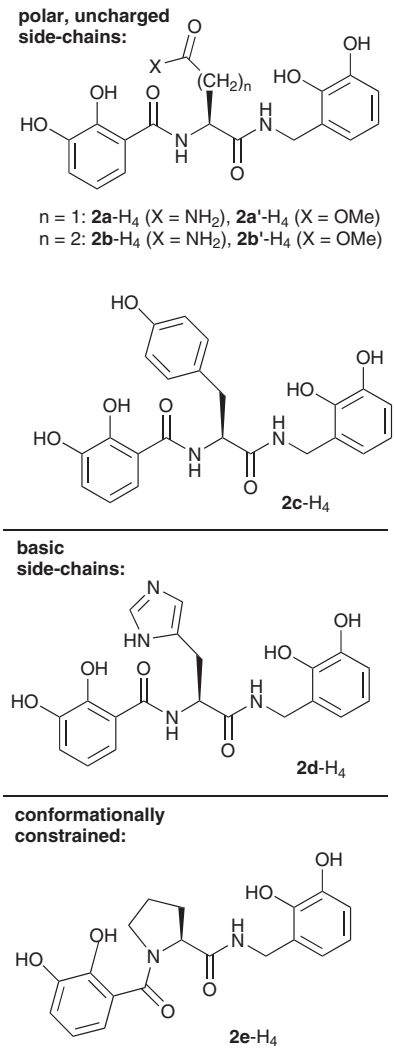


Figure 2 Ligands **2a**–**e**-H_4 described in this study, which bear polar, uncharged, or basic, or conformationally constraining amino acid side chains.

Preparation of the Amino Acid-Bridged Dicatechols 2a–e-H_4

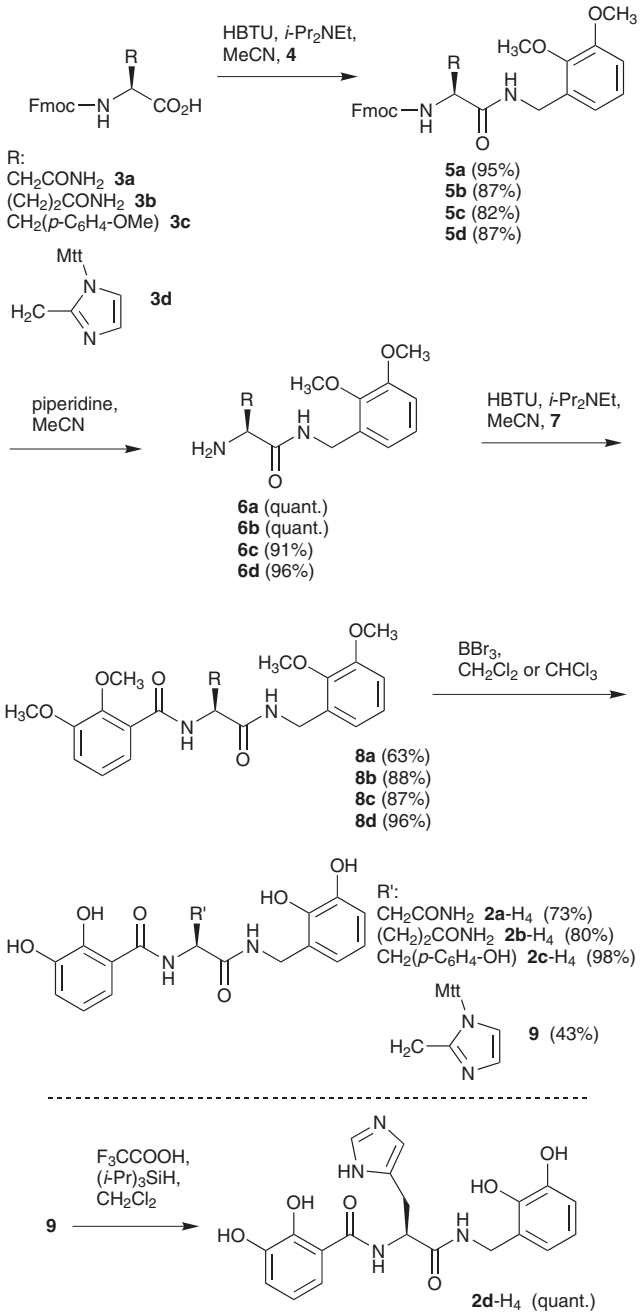
The earlier preparation of the ligands **1a**–**e**-H_4 was done by use of the unprotected amino acid. First 2,3-dimethoxybenzoic acid (**7**) and then 2,3-(dimethoxy)benzylamine (**4**) were attached. The reactions were performed in DMF/CH_2Cl_2 with DCC/NHS (dicyclohexylcarbodiimide/*N*-hydroxysuccinimide) or EDC/HOBt [ethyl(dimethylaminopropyl)carbodiimide/hydroxybenzotriazole] as coupling reagent. Following this protocol we obtained the compounds **1a–e**-H_4 with up to 10–20% racemization at the α-position of the amino acid residue.[3,6] An independent study with isoleucine as amino acid revealed that the partial epimerization takes place during the second coupling step. To suppress this epimerization, we tested several solvents and found out that, e.g. acetone leads to a full epimerization during the second amide coupling.

The epimerization can be suppressed by inverting the coupling procedure. Therefore, in our new approach we started with an *N*-Fmoc-protected amino acid **3** and attached 2,3-(dimethoxy)benzylamine (**4**) to the C-terminus.[7,8] After removal of the Fmoc group, 2,3-dimethoxybenzoic acid (**7**) was connected to the C-terminus. In preliminary studies with isoleucine derivatives it was found, that the use of HBTU/Hünig's base (*i*-Pr_2NEt)[9] as coupling reagents in acetonitrile as solvent was most appropriate for amide bond formation without epimerization at the α-carbon.

Following this strategy, we prepared the ligands **2a**–**d**-H_4 (Scheme 1). We used Fmoc-protected amino acids (Fmoc-Asn-OH: **3a**, Fmoc-Gln-OH: **3b**, Fmoc-Tyr(Me)-OH: **3c**, Fmoc-His(Mtt)-OH: **3d**) as starting materials. Hereby the tyrosine derivative **3c** bore an additional methyl group to protect the phenolic OH, while the imidazole of **3d** was protected by an Mtt (methyltrityl) group.[10] Coupling with 2,3-(dimethoxy)benzylamine (**4**) proceeded smoothly by use of HBTU/Hünig's base in acetonitrile to afford the derivatives **5a**–**d** in 82–95% yield. The Fmoc protecting group of **5** was removed by reaction with piperidine[8] in acetonitrile. The advantage of this solvent was that we could obtain pure amines by simple extraction of the reaction mixture with hot *n*-hexane. The amines **6a**–**d** remained in the acetonitrile phase and were obtained in very high yields (91%–quant.).

A second amide coupling with HBTU/Hünig's base was performed in acetonitrile to attach 2,3-dimethoxybenzoic acid (**7**) to the amines **6**. The protected ligand precursors **8a**–**d** were obtained in 63–96% yield.

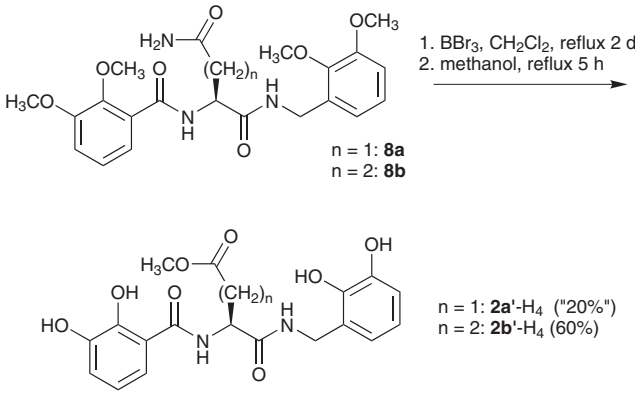
The methyl ethers of **8a**,**b** were cleaved by reaction with BBr_3[11] in chloroform to give the asparagine- (**2a**-H_4, 73%) and glutamine-bridged ligands (**2b**-H_4, 80%). However, this procedure highly depends on the reaction conditions and the work-up of the reaction mixture. Following the general procedure for methyl ether cleavage, side products **2a′**-H_4 and **2b′**-H_4 (vide infra) were observed. However, **2a**-H_4 and **2b**-H_4 were obtained by reaction with



Scheme 1 Preparation of the asparagine, glutamine, tyrosine, and histidine-bridged dicatechol ligands **2a**–**e**-H_4.

BBr_3 at 0 °C followed by work-up with ethanol instead of methanol.

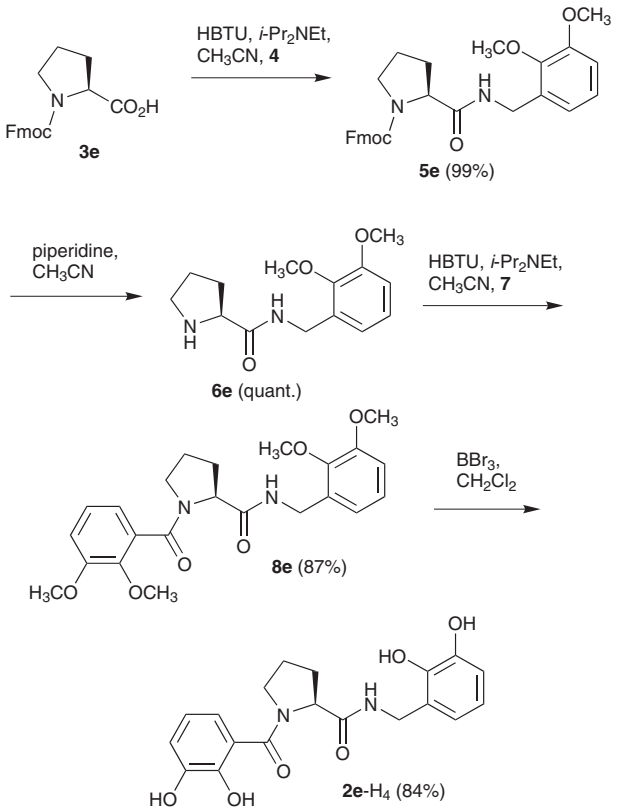
The formation of the side products could be maximized by performing the cleavage and quenching the reaction mixture at high temperatures. Hereby an amide to methyl ester transformation occurred at the side chain of the amino acid residues (Scheme 2). In case of the asparagine bridged derivative **8a**, the corresponding ester **2a′**-H_4 was observed as the minor component of a 1:4 mixture with **2a**-H_4. We were able to obtain the corresponding ester of the glutaric acid derivative **2b′**-H_4 in 60% yield in pure form.



Scheme 2 BBr_3-promoted amide to ester transformation.

The Mtt protecting group of **8d** was not affected by BBr_3. Only the methyl groups were removed and the intermediate **9** was formed in 43%. However, ligand **2d**-H_4 was finally obtained in quantitative yield by cleavage of the Mtt-group of **9** with trifluoroacetic acid and triisopropylsilane in dichloromethane[10] (Scheme 1).

Due to solubility problems, the methyl ethers of the tyrosine derivative **8c** had to be removed by reaction with BBr_3 in chloroform. Compound **2c**-H_4 was obtained in 98% yield by concomitant ether cleavage at the catechol as well as at the tyrosine moiety.

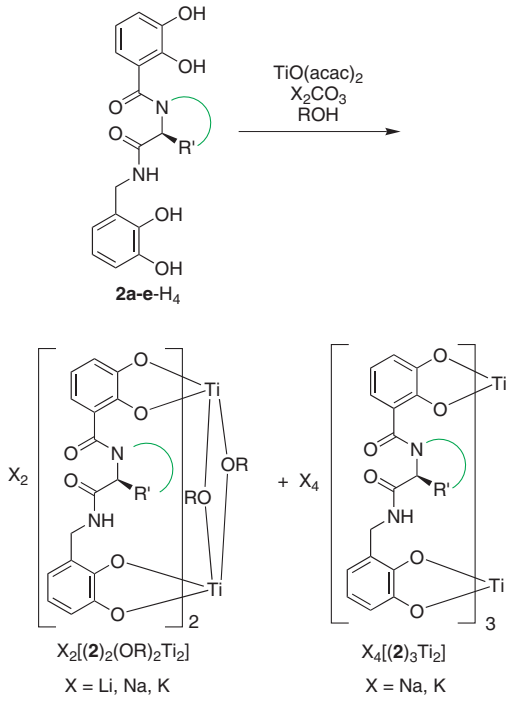


Scheme 3 Preparation of the proline-bridged ligand **2e**-H_4.

Scheme 3 shows that the sterically constrained proline-bridged ligand **2e**-H_4 was obtained as was described for the corresponding derivatives **2a**–**d**-H_4. The attachment of the amine **4** to Fmoc-protected proline **3e** proceeded in 99% yield to form **5e**. After quantitative cleavage of the Fmoc-group, the benzoic acid **7** was coupled to **6e** and the ligand precursor was obtained in 87% yield. Final ether cleavage afforded the ligand **2e**-H_4 in 84%.

Preparation of Amino Acid-Bridged Dinuclear Titanium(IV) Complexes

We investigated the coordination behavior of the ligands **2a**–**e**-H_4 with titanium(IV) ions in methanol and tested some selected examples in the presence of ethanol or allyl alcohol as solvent (Scheme 4). In most cases ^{1}H NMR spectroscopy showed complicated and broad spectra, which were due to the presence of many different species.[6] As an exceptionally well resolved spectrum the one of $Li_2[(\mathbf{2c})_2(OCH_3)_2Ti_2]$ in methanol-d_4 has to be mentioned which shows the presence of only one isomer (see Experimental section).



Scheme 4 Formation of titanium(IV) complexes of the ligands [**2a**–**e**]$^{4-}$ (only one isomer of double- and triple-stranded dinuclear complexes is indicated).

Because the NMR spectra were often not sufficiently informative, we performed extensive ESI MS studies, to find out if the complex formation was successful and what kind of species was formed. The results are listed in Table 1. Coordination studies of the ligands **2a**–**e**-H_4 with titanium(IV) ions in the presence of lithium carbonate in methanol resulted in the exclusive formation of $Li_2[(\mathbf{2a}–\mathbf{e})_2(OCH_3)_2Ti_2]$. Negative ESI MS showed the corresponding peaks for the dianions $[(\mathbf{2a}–\mathbf{e})_2(OCH_3)_2Ti_2]^{2-}$ and the monoanions $Li[(\mathbf{2a}–\mathbf{e})_2(OCH_3)_2Ti_2]^-$ with correct isotopic pattern.

Table 1 Results of Negative ESI MS Spectrometry of the Complexation Studies of Ligands **2a**–**e**-H_4 with Titanium(IV) Ions in the Presence of Alkali Metal Carbonate with Methanolate (CH_3O), Ethanolate (C_2H_5O), or Allyl Alcoholate (C_3H_5O) as Coligands

L^1/X/L^2	$X_2[(L^1)_2(L^2)_2Ti_2]$ (*m*/*z*)	$X_4[(L^1)_3Ti_2]$ (*m*/*z*)			
	$-2X^+$	$-X^+$	$-3X^+$	$-2X^+$	$-X^+$
2a/Li/CH_3O	464	935	–	–	–
2b/Li/CH_3O	478	963	–	–	–
2b/Na/CH_3O	478	979	–	–	–
2b/K/CH_3O	478	995	–	686	–
2b′/Li/CH_3O	493	993	–	–	–
2b′/Na/CH_3O	493	1009	–	–	–
2b′/K/CH_3O	493	1025	–	–	–
2c/Li/CH_3O	513	1033	–	–	–
2c/Na/CH_3O	513	1049	474	722	1467
2c/K/CH_3O	513	1065	479	738	1515
2d/Li/CH_3O	–	978	–	–	–
2e/Li/CH_3O	447	901	–	–	–
2e/Na/CH_3O	447	917	408	623	1269
2e/K/CH_3O	447	933	–	639	1317
2b/Li/C_2H_5O	492	991	–	–	–
2c/Li/C_3H_5O	539	1085	–	–	–
2e/Li/C_3H_5O	473	953	–	–	–

If sodium or potassium carbonate were used as base, the corresponding dinuclear double-stranded complexes $[(\mathbf{2b},\mathbf{c},\mathbf{e})_2(OCH_3)_2Ti_2]^{2-}$ were observed as well by ESI MS (Figure 3). However, the potassium derivatives of **2b** showed a characteristic peak for the triple-stranded $K_2[(\mathbf{2b})_3Ti_2]^{2-}$ at m/z = 686. In case of the sodium and potassium salts of the titanium complexes of **2c** and **2e** always the triple-stranded complex $[(\mathbf{2c},\mathbf{e})_3Ti_2]^{4-}$ was observed in addition to the double-stranded $[(\mathbf{2c},\mathbf{e})_2(OCH_3)_2Ti_2]^{2-}$.[12] For the glutaric ester only double-stranded complexes $[(\mathbf{2b′})_2(OCH_3)_2Ti_2]^{2-}$ are observed independent of the counter ions.

Our observations show that a specific formation of the double-stranded coordination compounds with two coligands is only guaranteed, if lithium is the counter cation. This template effect[13] by the small Li^+ cation is not understood yet, but has to be considered in the preparation of

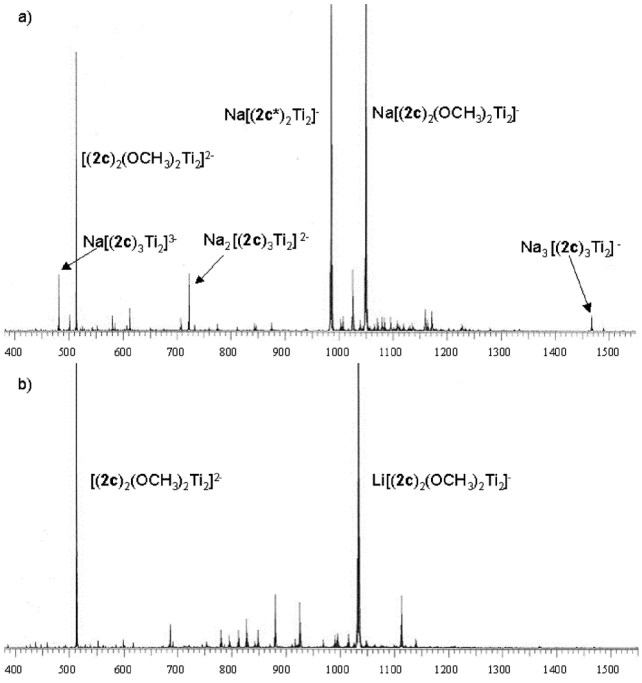


Figure 3 ESI MS spectra of $Li_2[(\mathbf{2c})_2(OCH_3)_2Ti_2]$ and of the mixture of $Na_4[(\mathbf{2c})_3Ti_2]$ and $Na_2[(\mathbf{2c})_2(OCH_3)_2Ti_2]$. In **2c*** the phenolic side group of tyrosine is deprotonated.

double-stranded complexes with coligands of the type $[(\mathbf{2})_2(OR)_2Ti_2]^{2-}$. In addition, we performed the complex formation of ligand **2b**-H_4 with titanium(IV) ions in ethanol in the presence of lithium carbonate, which smoothly produced $Li_2[(\mathbf{2b})_2(OC_2H_5)_2Ti_2]$ containing bridging ethanolate coligands.

Allyl alcoholate-bridged dinuclear titanium complexes $Li_2[(\mathbf{2c},\mathbf{e})_2(OC_3H_5)_2Ti_2]$ were obtained, if the reaction of the ligands **2c**,**e**-H_4 with titanium(IV) and lithium carbonate proceeded in allyl alcohol as solvent. Here the purification of the complex salts had to be performed in allyl alcohol to prevent an exchange of the coligands.

Conclusion

In this paper, we have presented the preparation of amino acid-bridged dicatechol ligands, which bear functional groups in the side chain. With our new procedure, the preparation proceeds smoothly with acceptable to good yields without racemization. All ligands specifically form double-stranded coordination compounds $Li_2[(\mathbf{2a}–\mathbf{e})_2(OR)_2Ti_2]$ in the presence of lithium carbonate. However, in the presence of sodium and potassium carbonate triple-stranded complexes $[(\mathbf{2b},\mathbf{c},\mathbf{e})_2(OCH_3)_2Ti_2]^{4-}$ are observed in addition. Introduction of alternative alcoholates as coligands can be achieved by use of alcohols other than methanol as solvent. In preliminary experiments we were able to introduce ethanolate as well as allyl alcoholate.

Currently, we are investigating whether more functionalized coligands can be introduced and whether we finally can perform chemical reactions in the ligand sphere of our double-stranded dinuclear coordination compounds.

^1H and ^{13}C NMR spectra were recorded on a Varian Mercury 300 or Inova 400 spectrometer. FT-IR spectra were recorded by diffuse reflection (KBr) or neat on a Bruker IFS spectrometer. Mass spectra (EI, 70 eV; FAB) were taken on a Finnigan MAT 95 or 212 mass spectrometer. FT-ICR ESI mass spectra were measured on a Bruker Bioapex II FTMS equipped with a 7 Tesla magnet. Elemental analyses were obtained with a Heraeus CHN-O-Rapid analyzer. Melting points: Büchi B-540 (uncorrected).

Coupling of Fmoc-Amino Acids 3 with 2,3-(Dimethoxy)benzylamine (4); General Procedure

To a solution of the Fmoc-protected amino acid derivative **3** (1 equiv) in MeCN (50–200 mL) were added HBTU (1.2 equiv) and diisopropylethylamine (1.1 equiv). The mixture was stirred for 20 min at r.t. and 2,3-(dimethoxy)benzylamine (**4**; 1 equiv) was added. After 18–24 h at rt., work-up was done by isolation of the precipitated product **5** by filtration and purification by washing with cold MeCN. Eventually the precipitate can be dissolved in EtOAc, and the EtOAc layer was washed successively with aq NH_4Cl, $NaHCO_3$, H_2O, and brine, dried ($MgSO_4$) and the solvent removed in vacuum (Method A). If the product did not precipitate from MeCN, the solvent was removed and purification of the residue was done as described for method A (Method B).

5a

Method A; yield: 1.49 g (95%); colorless solid; mp 200 °C.

IR (KBr): 3303, 3208, 1695, 1634, 1514, 1483, 1279, 1263 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 8.19 (t, *J* = 5.7 Hz, 1 H, NH), 7.82 (dd, *J* = 7.5, 2.7 Hz, 4 H), 7.53 (d, *J* = 7.5 Hz, 1 H), 7.42 (t, *J* = 7.1 Hz, 2 H), 6.92 (m, 3 H), 4.40 (m, 1 H), 4.29 (m, 2 H), 4.22 (m, 2 H), 3.77 (s, 3 H), 3.71 (s, 3 H), 2.43 (m, 2 H).

^{13}C NMR (130 MHz, DMSO-d_6): δ = 174.2 (C), 172.1 (C), 171.9 (C, double intensity), 152.7 (C, double intensity), 144.5 (C, double intensity), 141.4 (C), 139.7 (C), 133.2 (CH, double intensity), 128.3 (CH, double intensity), 127.8 (CH, double intensity), 124.4 (CH, double intensity), 120,7 (CH), 120.5 (CH), 112.2 (CH), 66,5 (CH_2), 60.6 (CH_3), 56.3 (CH_3), 47.3 (CH), 41.0 (CH), 40.7 (CH_2), 31.8 (CH_2).

MS (LCMS-ESI, MeOH): *m*/*z* = 504 $[M + H]^+$.

Anal. Calcd for $C_{28}H_{29}N_3O_6$: C, 66.79; H, 5.81; N, 8.34. Found: C, 66.32; H, 6.03; N, 8.29.

5b

Method A; yield: 2.44 g (87%); colorless solid; mp 194 °C.

IR (KBr): 3290, 1663, 1541, 1279, 757 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 7.90 (d, *J* = 7.4 Hz, 2 H), 7.74 (d, *J* = 7.2 Hz, 2 H), 7.53 (d, *J* = 7.5 Hz, 1 H), 7.40 (t, *J* = 7.5 Hz, 2 H), 7.31 (m, 2 H), 6.97 (m, 1 H), 6.76 (m, 1 H), 4.26 (m, 2 H), 4.21 (m, 3 H), 4.10 (t, *J* = 6.8 Hz, 1 H), 3.77 (s, 3 H), 3.69 (s, 3 H), 2.06 (m, 2 H), 1.80 (m, 2 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 174.7 (C), 174.1 (C), 156.4 (C, double intensity), 152.6 (C), 146.6 (C), 144.3 (C), 144.2 (C), 139.8 (C), 137.8 (C), 129.4 (CH, double intensity), 127.7 (CH, double intensity), 124.6 (CH, double intensity), 123.8 (CH), 121.8 (CH, double intensity), 120.5 (CH), 112.1 (CH), 66.15 (CH_2), 60.5 (CH_3), 56.1 (CH_3), 54.9 (CH), 47.1 (CH), 39.4 (CH_2), 31.5 (CH_2), 28.2 (CH_2).

MS (FAB, DMSO): *m*/*z* = 518 $[M + H]^+$.

Anal. Calcd for $C_{29}H_{31}N_3O_6$: C, 67.30; H, 6.04; N, 8.12. Found: C, 67.72; H, 6.00; N, 8.67.

5c

Method B; yield: 1.67 g (82%); colorless solid; mp 188 °C.

IR (KBr): 3420, 3299, 1693, 1644 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 7.6 Hz, 2 H), 7.60 (d, *J* = 7.4 Hz, 2 H), 7.52 (m, 2 H), 7.41 (m, 2 H), 7.32 (m, 2 H), 7.02 (d, *J* = 7.8 Hz, 2 H), 6.95 (t, *J* = 8.1 Hz, 1 H), 6.83 (t, *J* = 8.1 Hz, 1 H), 6.74 (d, *J* = 7.8 Hz, 1 H), 4.33 (m, 5 H), 4.17 (t, *J* = 6.5 Hz, 1 H), 3.83 (s, 3 H), 3.75 (s, 6 H), 2.98 (d, *J* = 6.1 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.1 (C), 170.3 (C), 158.5 (C), 155.8 (C), 152.5 (C), 147.1 (C), 143.8 (C), 143.7 (C), 141.3 (C), 131.1 (C), 130.3 (CH, double intensity), 129.4 (CH, double intensity), 128.1 (CH, double intensity), 127.7 (CH, double intensity), 127.1 (CH, double intensity), 125.6 (CH, double intensity), 124.1 (CH), 121.2 (CH, double intensity), 120.0 (C), 114.0 (CH), 112.0 (CH), 66.9 (CH_2), 60.6 (CH_3), 55.7 (CH_3), 55.2 (CH_3), 38.9 (CH_2), 37.9 (CH_2).

MS (EI): *m*/*z* = 567 $[M + H]^+$.

Anal. Calcd for $C_{34}H_{34}N_2O_6$: C, 72.07; H, 6.05; N, 4.94. Found: C, 71.87; H, 6.11; N, 5.23.

5d

Method B; yield: 2.14 g (87%); colorless solid; mp 103 °C.

IR (KBr): 3305, 3061, 2937, 1723, 1671, 1481, 1273, 1243, 742 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.74 (d, *J* = 7.4 Hz, 2 H), 7.55 (t, *J* = 8.0 Hz, 2 H), 7.36 (m, 3 H), 7.29 (m, 7 H), 7.07 (m, 6 H), 6.96 (d, *J* = 8.2 Hz, 3 H), 6.70 (m, 3 H), 6.66 (s, 1 H), 4.59 (m, 1 H), 4.51 (m, 3 H), 4.33 (d, *J* = 8.1 Hz, 2 H), 3.80 (s, 6 H), 3.02 (m, 2 H), 2.33 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.3 (C), 156.0 (C, double intensity), 153.7 (C, double intensity), 147.8 (C), 143.6 (C), 142.2 (C), 140.5 (C), 139.8 (C), 139.2 (C), 137.0 (C), 136.0 (C), 134.9 (CH, double intensity), 132.9 (CH, double intensity), 130.6 (CH, double intensity), 129.7 (CH, double intensity), 129.6 (CH, double intensity), 128.0 (CH, quadruple intensity), 127.3 (CH, quadruple intensity), 126.1 (CH, double intensity), 123.3 (CH), 122.3 (CH, double intensity), 121.2 (CH), 121.1 (CH), 120.0 (C), 113.4 (CH), 74.5 (C), 66.7 (CH_2), 60.2 (CH_3), 56.4 (CH_3), 51.3 (CH), 47.1 (CH), 46.5 (CH), 39.6 (CH_2), 29.8 (CH_2), 21.1 (CH_3).

MS (FAB, DMSO): *m*/*z* = 783 $[M + H]^+$.

Anal. Calcd for $C_{50}H_{46}N_4O_5$: C, 76.70; H, 5.92; N, 7.15. Found: C, 76.31; H, 5.79; N, 7.22.

5e

Method A; yield: 2.86 g (99%); colorless solid; mp 144 °C.

IR (KBr): 3368, 3282, 1711, 1688, 1646, 1539, 1480, 1448, 1429, 1349, 1122, 739 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 7.4 Hz, 2 H), 7.57 (m, 2 H), 7.39 (t, *J* = 7.5 Hz, 2 H), 7.30 (m, 2 H), 6.83 (m, 3 H), 4.52 (m, 1 H), 4.49 (m, 2 H), 4.44 (d, *J* = 6.2 Hz, 2 H), 3.85 (s, 3 H), 3.84 (s, 3 H), 3.73 (m, 1 H), 2.93 (m, 2 H), 2.02 (m, 2 H), 1.67 (m, 2 H).

^{13}C NMR (130 MHz, DMSO-d_6): δ = 174.8 (C), 172.3 (C), 152.9 (C), 152.3 (C, double intensity), 147.8 (C, double intensity), 143.6 (C), 140.5 (C), 130.6 (CH), 127.2 (CH, double intensity), 126.1 (CH, double intensity), 123.0 (CH, double intensity), 121.6 (CH, double intensity), 119.7 (CH), 113.3 (CH), 67.8 (CH_2), 60.2 (CH_3), 58.6 (CH), 56.5 (CH_3), 47.2 (CH), 46.9 (CH_2), 39.2 (CH_2), 28.7 (CH_2), 23.8 (CH_2).

MS (FAB, DMSO): *m*/*z* = 488 $[M + H]^+$.

Anal. Calcd for $C_{29}H_{30}N_2O_5 \cdot MeCN \cdot H_2O$: C, 68.24; H, 6.17; N, 7.70. Found: C, 68.79; H, 6.03; N, 8.26.

Removal of the Fmoc-Protecting Group from 5; General Procedure

The Fmoc-protected compounds **5** (1 equiv) were suspended in MeCN (100 mL) and piperidine (6 equiv) was added. The mixture was stirred for 24 h at r.t. The MeCN phase was extracted with hot *n*-hexane (5 × 30 mL) and the MeCN was removed in vacuum to obtain the amines **6**.

6a

Yield: 1.49 g (quant.); colorless solid; mp 137 °C (dec.).

IR (KBr): 3443, 3421, 3312, 1665, 1637, 1548, 1482, 1085, 1057, 988 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 6.98 (m, 2 H), 6.83 (m, 1 H), 4.27 (d, *J* = 5.7 Hz, 2 H), 3.79 (s, 3 H), 3.74 (s, 3 H), 3.53 (dd, *J* = 8.9, 4.1 Hz, 1 H), 2.47 (m, 1 H).

^{13}C NMR (130 MHz, DMSO-d_6): δ = 174.4 (C), 173.2 (C), 153.6 (C), 147.7 (C), 124.3 (CH), 121.4 (CH), 120.5 (C), 112.1 (CH), 60.5 (CH_3), 56.1 (CH_3), 52.1 (CH), 39.5 (CH_2), 34.2 (CH_2).

MS (EI): *m*/*z* = 282 $[M + H]^+$.

Anal. Calcd for $C_{13}H_{19}N_3O_4 \cdot 0.5H_2O$: C, 53.78; H, 6.94; N, 14.47. Found: C, 53.61; H, 6.66; N, 14.99.

6b

Yield: 860 mg (ca. 100%); colorless solid; mp 183 °C (dec.).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.05 (m, 1 H), 6.85 (d, *J* = 7.4 Hz, 2 H), 4.45 (m, 2 H), 3.85 (s, 6 H), 3.50 (t, *J* = 6.6 Hz, 1 H), 2.35 (m, 2 H), 2.01 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.2 (C), 170.4 (C), 152.6 (C), 147.1 (C), 123.8 (CH), 120.9 (C), 120.7 (CH), 112.7 (CH), 59.3 (CH_3), 56.5 (CH_3), 48.7 (CH), 39.5 (CH_2), 32.0 (CH_2), 25.7 (CH_2).

MS (EI): *m*/*z* = 296 $[M + H]^+$.

Anal. Calcd for $C_{14}H_{21}N_3O_4$: C, 56.94; H, 7.17; N, 14.23. Found: C, 57.67; H, 6.78; N, 13.89.

6c

Yield: 414 mg (91%); colorless solid; mp 128 °C.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.05 (d, *J* = 7.5 Hz, 1 H), 6.93 (m, 2 H), 6.74 (m, 4 H), 4.43 (d, *J* = 6.0 Hz, 2 H), 3.81 (s, 3 H), 3.76 (s, 3 H), 3.69 (s, 3 H), 3.56 (m, 1 H), 2.98 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.2 (C), 158.5 (C), 151.8 (C), 147.3 (C), 131.9 (C), 130.6 (C), 130.5 (CH), 129.8 (CH, double intensity), 123.2 (CH, double intensity), 114.2 (CH), 113.4 (CH), 60.8 (CH_3), 56.7 (CH_3), 55.4 (CH_3), 54.1 (CH), 39.4 (CH_2), 37.8 (CH_2).

MS (EI): *m*/*z* = 345 $[M + H]^+$.

6d

Yield: 3.33 g (96%); colorless solid; mp 73 °C.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.35 (m, 2 H), 7.32 (s, 1 H), 7.31 (m, 5 H), 7.11 (m, 5 H), 6.97 (m, 3 H), 6.83 (d, *J* = 7.9 Hz, 2 H), 6.63 (s, 1 H), 4.45 (m, 2 H), 3.85 (s, 3 H), 3.84 (s, 3 H), 3.65 (m, 1 H), 3.02 (m, 2 H), 2.35 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.2 (C), 152.6 (C), 147.1 (C), 142.5 (C), 139.4 (C, double intensity), 138.5 (C), 138.0 (CH), 137.9 (C), 134.2 (CH, double intensity), 134.1 (CH), 132.1 (CH), 132.0 (CH, double intensity), 129.6 (CH, quadruple intensity), 128.0 (CH, quadruple intensity), 124.4 (CH), 124.1 (CH), 120.0 (C), 119.5 (CH), 113.6 (CH), 75.1 (C), 60.8 (CH_3), 55.7 (CH), 55.6 (CH_3), 38.2 (CH_2), 33.0 (CH_2), 21.0 (CH_3).

MS (FAB, DMSO): *m*/*z* = 561 $[M + H]^+$.

Anal. Calcd for $C_{35}H_{36}N_4O_3$: C, 74.98; H, 6.47; N, 9.99. Found: C, 73.99; H, 6.23; N, 10.15.

6e
Yield: 543 mg (quant.); brown oil.

IR (neat): 3315, 3218, 1725, 1644, 1518, 1493, 1289 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.00 (t, *J* = 8.0 Hz, 1 H), 6.84 (d, *J* = 8.0 Hz, 2 H), 4.44 (d, *J* = 6.0 Hz, 2 H), 3.85 (s, 3 H), 3.84 (s, 3 H), 3.73 (m, 1 H), 2.02 (m, 2 H), 1.91 (m, 2 H), 1.68 (m, 2 H).

^{13}C NMR (130 MHz, $CDCl_3$): δ = 170.8 (C), 152.8 (C), 148.0 (C), 123.9 (CH), 120.9 (C), 120.5 (CH), 113.4 (CH), 60.5 (CH_3), 58.9 (CH), 56.5 (CH_3), 47.9 (CH_2), 39.7 (CH_2), 31.9 (CH_2), 26.9 (CH_2).

MS (EI): *m*/*z* = 265 $[M + H]^+$.

Anal. Calcd for $C_{14}H_{20}N_2O_3$: C, 63.37; H, 7.98; N, 10.56. Found: C, 62.99; H, 7.84; N, 11.31.

Coupling of 2,3-Dimethoxybenzoic Acid (7) with the Amines 6; General Procedure
2,3-Dimethoxybenzoic acid (**7**; 1 equiv) was dissolved in MeCN (50–100 mL) and HBTU (1.2 equiv) and diisopropylethylamine (1.1 equiv) were added. The mixture was stirred for 20 min at r.t. and the amine **6** was added. After 2 d at r.t., the precipitate was removed by filtration and washed with cold MeCN. The crude product was dissolved in EtOAc and successively washed with aq NH_4Cl, aq $NaHCO_3$, H_2O, and brine. After drying ($MgSO_4$) the EtOAc was removed by distillation to afford **8**.

8a
Yield: 1.28 g (63%); colorless solid; mp 192 °C.

IR (KBr): 3419, 3291, 3256, 2180, 1663, 1636, 1534, 1481.51, 1434, 1267, 1221, 1084 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 8.90 (br, 1 H, NH), 8.25 (t, 1 H, *J* = 6.2 Hz, NH), 7.40 (m, 1 H), 7.20 (m, 1 H), 6.95 (m, 4 H), 4.79 (dd, *J* = 8.1, 2.3 Hz, 1 H), 4.29 (d, *J* = 6.2 Hz, 2 H), 3.84 (s, 3 H), 3.80 (s, 3 H), 3.78 (s, 3 H), 3.71 (s, 3 H), 2.60 (md, *J* = 8.1 Hz, 2 H).

^{13}C NMR (130 MHz, DMSO-d_6): δ = 174.3 (C), 169.6 (C), 158.3 (C), 152.3 (C), 150.0 (C), 148.2 (C), 147.1 (C), 128.2 (C), 126.3 (CH), 124.1 (CH), 121.9 (CH), 120.4 (C), 118.3 (CH), 114.9 (CH), 61.5 (CH), 60.4 (CH_3), 56.6 (CH_3), 56.5 (CH_3), 56.1 (CH_3), 50.6 (CH), 39.4 (CH_2), 37.5 (CH_2).

MS (ESI, pos): *m*/*z* = 446 $[M + H]^+$.

Anal. Calcd for $C_{22}H_{27}N_3O_7 \cdot 1/3H_2O$: C, 58.53; H, 6.18; N, 9.31. Found: C, 58.64; H, 6.08; N, 9.95.

8b
The reaction took 4 instead of 2 d to yield 1.27 g (88%) of a colorless solid; mp 167 °C (dec.).

IR (KBr): 3299, 1662, 1626, 1539, 1429, 1355, 1332, 1172, 942, 989, 868 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.21 (t, *J* = 7.9 Hz, 2 H), 7.04 (dd, *J* = 8.0, 1.6 Hz, 1 H), 6.99 (t, *J* = 8.0 Hz, 1 H), 6.97 (m, 1 H), 6.85 (m, 1 H), 4.79 (m, 1 H), 4.52 (m, 2 H), 3.77 (s, 3 H), 3.73 (s, 3 H), 3.68 (s, 3 H), 3.67 (s, 3 H), 2.15 (m, 2 H), 1.84 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.0 (C), 171.2 (C), 165.7 (C), 152.6 (C), 152.4 (C), 147.7 (C), 146.7 (C), 131.1 (C), 125.6 (CH), 124.1 (CH), 121.8 (CH), 120.7 (CH), 120.4 (C), 115.7 (CH), 111.7 (CH), 61.3 (CH_3), 60.4 (CH_3), 55.8 (CH_3), 55.5 (CH_3), 49.1 (CH), 38.2 (CH_2), 31.3 (CH_2), 29.3 (CH_2).

MS (EI): *m*/*z* = 460 $[M + H]^+$.

Anal. Calcd for $C_{23}H_{29}N_3O_7$: C, 60.12; H, 6.36; N, 9.14. Found: C, 59.01; H, 6.33; N, 9.08.

8c
Yield: 400 mg (87%); yellow oil.

IR (KBr): 3266, 2945, 2837, 1653, 1633, 1512, 1479, 1271, 1082, 1001, 750 cm^{-1}.

^1H NMR (400 MHz, CD_3OD): δ = 7.49 (m, 2 H), 7.07 (m, 3 H), 6.94 (t, *J* = 8.0 Hz, 1 H), 6.85 (t, *J* = 8.0 Hz, 1 H), 6.73 (d, *J* = 8.0 Hz, 2 H), 6.68 (m, 1 H), 4.78 (t, *J* = 6.8 Hz, 1 H), 4.37 (m, 2 H), 3.85 (s, 3 H), 3.81 (s, 3 H), 3.74 (s, 3 H), 3.72 (s, 3 H), 3.70 (s, 3 H), 3.05 (m, 2 H).

^{13}C NMR (100 MHz, CD_3OD): δ = 171.3 (C), 165.5 (C), 158.5 (C), 155.5 (C), 152.4 (C), 147.9 (C), 146.7 (C), 131.2 (CH), 130.2 (C), 128.3 (C), 125.6 (CH), 124.2 (CH), 124.0 (CH), 121.0 (CH), 120.9 (C), 115.9 (CH), 113.8 (CH), 111.8 (CH), 61.5 (CH), 61.1 (CH_3), 60.3 (CH_3), 55.8 (CH_3), 55.5 (CH_3), 55.4 (CH_3), 55.3 (CH), 38.1 (CH_2), 37.5 (CH_2).

MS (EI): *m*/*z* = 509 $[M + H]^+$.

Anal. Calcd for $C_{28}H_{32}N_2O_7$: C, 66.13; H, 6.34; N, 5.51. Found: C, 65.65; H, 6.24; N, 5.31.

8d
Yield: 3.61 g (84%); colorless solid; mp 124 °C (dec.).

IR (KBr): 2949, 2840, 2808, 1674, 1532, 845 cm^{-1}.

^1H NMR (400 MHz, CD_3OD): δ = 8.13–6.79 (22 H_{arom}), 4.46 (m, 2 H), 3.86 (s, 3 H), 3.85 (s, 3 H), 3.84 (s, 3 H), 3.82 (s, 3 H), 3.65 (m, 1 H), 3.02 (m, 2 H), 2.15 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.8 (C), 166 (C), 152,7 (C), 146.9 (C), 146.6 (C), 144.2 (C), 142.2 (C), 140.2 (C), 139.3 (C, double intensity), 136.9 (C), 134.1 (CH, double intensity), 133.6 (CH, double intensity), 133.4 (CH, double intensity), 130.8 (CH, quadruple intensity), 127.4 (CH, quadruple intensity), 124.3 (CH), 124.1 (C), 123.8 (CH), 123.4 (CH), 120.9 (CH), 120.6 (CH), 118.5 (C), 113.7 (CH), 77.9 (C), 60.6 (CH_3), 59.9 (CH_3), 55.5 (CH_3), 55.2 (CH_3), 49.4 (CH), 38.0 (CH_2), 27.4 (CH_2), 21.7 (CH_3).

MS (FAB, DMSO): *m*/*z* = 725 $[M + H]^+$.

8e
Yield: 147 mg (87%); yellow solid; mp 146 °C (dec.).

IR (KBr): 3420, 2924, 1623, 1535, 1480, 1430, 1305, 1271, 1229, 1072, 1004, 844, 797, 751, 557 cm^{-1}.

^1H NMR (300 MHz, CD_3OD): δ = 7.16–6.75 (6 H_{arom}), 4.49 (d, *J* = 4.1 Hz, 2 H), 3.89 (s, 3 H), 3.88 (s, 3 H), 3.86 (s, 3 H), 3.85 (s, 3 H), 3.74 (m, 1 H), 2.02 (m, 2 H), 1.90 (m, 2 H), 1.67 (m, 2 H).

^{13}C NMR (130 MHz, CD_3OD): δ = 172.7 (C), 172.6 (C), 168.7 (C), 152.7 (C, double intensity), 144.8 (C), 131.5 (C), 130.9 (C), 124.6 (CH), 124.5 (CH), 120,4 (CH), 120.4 (CH), 113.8 (CH), 111.7 (CH), 60.7 (CH_3), 60.6 (CH_3), 60.2 (CH), 55.2 (CH_3), 54.6 (CH_3), 42.3 (CH_2), 26.1 (CH_2), 25.6 (CH_2), 24.2 (CH_2).

MS (EI): *m*/*z* = 429 $[M + H]^+$.

Anal. Calcd for $C_{23}H_{28}N_2O_6 \cdot 3H_2O$: C, 57.25; H, 7.10; N, 5.81. Found: C, 57.37; H, 6.99; N, 6.47.

Cleavage of the Methyl Ethers of 8; General Procedure
The protected derivatives **8** (1 equiv) were dissolved in CH_2Cl_2 (20 mL). At 0 °C, BBr_3 (6-10 equiv) was added and the resulting mixture was stirred for 24 h at r.t. MeOH (15 mL) was added and the solvents were removed in vacuum. The residue was dissolved in EtOAc and the EtOAc layer was washed with H_2O and brine. The organic phase was dried ($MgSO_4$) and the solvent was removed to obtain **2a**,**b**,**c**,**e** and **9**.

Cleavage of the Methyl Ethers 8a,b; Optimized Procedure

The derivatives **8a**,**b** (1 equiv) were dissolved in $CHCl_3$ (10 mL). At 0 °C, BBr_3 (8 eq) was added and the suspension was stirred at r.t. for 24 h. The mixture was slowly hydrolyzed with EtOH (10 mL) at 0 °C. After the solvents were removed, the residue was dissolved in EtOAc and washed with H_2O and brine. The organic phase was dried ($MgSO_4$) and the solvent was removed to obtain **2a**,**b**.

2a-H$_4$

Yield: 190 mg (73%); slightly brown solid; mp 72 °C.

IR (KBr): 3380, 2983, 1699, 1641, 1594, 1549, 1482, 1457, 1335, 1268, 1169, 743 cm^{-1}.

^1H NMR (400 MHz, CD_3OD): δ = 7.19 (d, *J* = 7.4 Hz, 1 H), 6.94 (d, *J* = 7.4 Hz, 1 H), 6.75 (m, 4 H), 4.74 (t, *J* = 3.2 Hz, 2 H), 4.68 (m, 1 H), 2.99 (m, 2 H).

^{13}C NMR (100 MHz, CD_3OD): δ = 177.0 (C), 169.5 (C), 158.4 (C), 152.4 (C), 149.3 (C), 148.3 (C), 145.9 (C), 142.8 (C), 131.1 (C), 124.8 (CH), 122.6 (CH), 119.4 (CH), 118.9 (CH), 114.6 (CH), 114.3 (CH), 51.9 (CH), 38.4 (CH_2), 35.6 (CH_2).

MS (FAB, DMSO): *m*/*z* = 390 $[M + H]^+$.

Anal. Calcd for $C_{18}H_{19}N_3O_7$: C, 55.53; H, 4.92; N, 10.79. Found: C, 55.90; H, 5.03; N, 9.93.

2a′-H$_4$

Compound **8a** (100 mg, 1 equiv) was dissolved in CH_2Cl_2 (10 mL). At r.t., BBr_3 (10 eq) was added and the mixture was refluxed for 48 h. MeOH was added to the hot mixture and refluxed for an additional 5 h. The solution was allowed to cool down and the solvents were removed in vacuum. The residue was dissolved in EtOAc and washed with H_2O and brine. The organic phase was dried ($MgSO_4$) and the solvent was removed under reduced pressure. So far it was not possible to obtain the product in pure form. ^1H NMR spectrum shows a mixture of 20% of **2a′-H$_4$** and 80% of **2a-H$_4$**.

^1H NMR (400 MHz, CD_3OD): δ = 7.23 (dd, *J* = 1.5, 7.9 Hz, 1 H), 6.98 (dd, *J* = 1.5, 7.9 Hz), 6.70 (m, 4 H), 4.77 (d, *J* = 3.5 Hz, 2H), 4.73 (m, 1 H), 3.65 (s, 3 H, 20% int), 3.15 (dd, *J* = 9.1, 17.8 Hz, 1 H), 2.93 (dd, *J* = 5.7, 17.8 Hz, 1 H).

MS (EI): *m*/*z* = 405.2 $[M + H]^+$.

2b-H$_4$

Yield: 140 mg (80%); colorless solid; mp 142 °C (dec.).

IR (KBr): 3304, 1646, 1539, 1236 cm^{-1}.

^1H NMR (400 MHz, CD_3OD): δ = 7.31 (d, *J* = 8.0 Hz, 1 H), 6.94 (d, *J* = 8.0 Hz, 1 H), 6.71 (m, 4 H), 4.61 (m, 1 H), 4.37 (m, 2 H), 2.37 (m, 2 H), 1.84 (m, 2 H).

^{13}C NMR (100 MHz, CD_3OD): δ = 176.7 (C), 173.8 (C), 169.9 (C), 148.6 (C), 148.4 (C), 145.8 (C), 145.1 (C), 124.7 (CH), 120.0 (CH), 119.2 (CH), 118.6 (CH), 118.5 (CH), 118.4 (CH), 115.4 (C), 114.3 (C), 48.0 (CH), 38.6 (CH_2), 31.5 (CH_2), 27.5 (CH_2).

MS (EI): *m*/*z* = 404 $[M + H]^+$.

Anal. Calcd for $C_{19}H_{21}N_3O_7$: C, 56.57; H, 5.25; N, 10.42. Found: C, 56.89; H, 4.91; N, 11.63.

2b′-H$_4$

Compound **8b** (250 mg, 1 equiv) was dissolved in CH_2Cl_2 (20 mL). At r.t., BBr_3 (10 eq) was added and the mixture was refluxed for 48 h. MeOH was added to the hot mixture and refluxed for an additional 5 h. The solution was allowed to cool down and the solvents are removed in vacuum. The residue was dissolved in EtOAc and washed with H_2O and brine. The organic phase was dried ($MgSO_4$), concentrated and slowly added to Et_2O. The solid was collected by filtration and the filtrate was concentrated again and dissolved in EtOAc. This procedure was repeated two more times to obtain the product as a colorless solid; yield: 150 mg (60%); white solid.

IR (KBr): 3359, 2866, 2487, 1726, 1639, 1587, 1536, 1478, 1447, 1350, 1263, 1176, 1078, 840, 783, 741 cm^{-1}.

^1H NMR (400 MHz, CD_3OD): δ = 7.20 (dd, *J* = 1.5, 8.2 Hz, 1 H), 6.86 (dd, *J* = 1.5, 8.1 Hz, 1 H), 6.59 (m, 4 H), 4.55 (t, *J* = 5.4 Hz, 1 H), 4.26 (d, *J* = 8.2 Hz, 2 H), 3.52 (s, 3 H), 2.34 (m, 1 H), 2.26 (m, 1 H), 2.11 (m, 1 H), 1.98 (m, 1 H).

^{13}C NMR (100 MHz, CD_3OD): δ = 173.6 (C), 172.5 (C), 169.5 (C), 145.7 (C) double intensity, 145.1 (C) double intensity, 143.1 (C), 124.6 (C), 119.9 (CH), 119.1 (CH), 118.4 (CH), 118.3 (CH), 118.1 (CH), 114.2 (CH), 53.0 (CH), 50.9 (CH_3), 38.7 (CH_2), 30.0 (CH_2), 27.1 (CH_2).

MS (EI): *m*/*z* = 419.1 $[M + H]^+$.

Anal. Calcd for $C_{20}H_{22}N_2O_8 \cdot H_2O$: C, 55.04; H, 5.54; N, 6.42. Found: C, 54.98; H, 5.48; N, 6.63.

2c-H$_4$

$CHCl_3$ was used as the solvent instead of CH_2Cl_2; yield: 93 mg (98%); slightly brown solid; mp 98 °C.

IR (KBr): 3347, 2944, 1636, 1515, 1332, 1261, 743 cm^{-1}.

^1H NMR (400 MHz, CD_3OD): δ = 7.26 (d, *J* = 8.5 Hz, 2 H), 7.00 (d, *J* = 8.5 Hz, 2 H), 6.94 (m, 1 H), 6.71 (m, 2 H), 6.61 (m, 2 H), 6.53 (m, 1 H), 4.77 (t, *J* = 7.2 Hz, 1 H), 4.30 (m, 2 H), 3.09 (dd, *J* = 13.9, 6.5 Hz, 1 H), 2.99 (dd, *J* = 13.9, 6.5 Hz, 1 H).

^{13}C NMR (100 MHz, CD_3OD): δ = 172.7 (C), 168.9 (C), 158.4 (C), 155.8 (C), 148.0 (C), 145.7 (C), 143.2 (C), 130.0 (CH), 127.2 (C), 126.9 (C), 125.9 (CH), 124.6 (CH), 120.9 (CH), 120.0 (C), 119.2 (CH), 118.4 (CH), 118.8 (CH), 117.7 (CH), 114.8 (CH), 114.2 (CH), 55.3 (CH), 38.5 (CH_2), 37.0 (CH_2).

MS (EI): *m*/*z* = 440 $[M + H]^+$.

Anal. Calcd for $C_{23}H_{23}N_2O_7$: C, 62.86; H, 5.28; N, 6.37. Found: C, 62.83; H, 5.12; N, 6.64.

9

Yield: 40 mg (43%); brown oil.

IR (KBr): 3402, 2948, 2838, 2806, 1671, 1585, 1462, 1433, 1030 cm^{-1}.

^1H NMR (400 MHz, CD_3OD): δ = 8.15–6.50 (22 H_{arom}), 4.72 (m, 2 H), 4.46 (m, 2 H), 3.02 (m, 1 H), 2.15 (s, 3 H).

^{13}C NMR (100 MHz, CD_3OD): δ = 174.8 (C), 166.7 (C), 152.8 (C), 152.6 (C), 146.9 (C), 146.3 (C), 142.3 (C), 142.1 (C), 137.0 (C, double intensity), 136.8 (C), 134.2 (CH, double intensity), 133.7 (CH, double intensity), 133.4 (CH, double intensity), 130.9 (CH, quadruple intensity), 127.5 (CH, quadruple intensity), 124.8 (C), 123.9 (CH, double intensity), 123.4 (CH, double intensity), 120.5 (CH, double intensity), 120.1 (C), 113.5 (CH), 112.1 (CH), 77.9 (C), 49.4 (CH), 38.4 (CH_2), 27.3 (CH_2), 21.8 (CH_3).

MS (FAB, DMSO): *m*/*z* = 669 $[M + H]^+$.

2e-H$_4$

Compound **8e** (500 mg, 1 equiv) was dissolved in CH_2Cl_2 (15 mL). At 0 °C, BBr_3 (8 equiv) was added and the mixture was stirred for 8 h at 0 °C. MeOH was slowly added to the cooled suspension. The solvents were removed in vacuum, the residue was dissolved in EtOAc and washed with H_2O and brine. The organic phase was dried ($MgSO_4$) and the solvent was removed under reduced pressure; yield: 364 mg (84%); slightly brown solid; mp 67 °C (dec.).

^1H NMR (300 MHz, CD_3OD): δ = 6.87 (dd, *J* = 8.2, 2.1 Hz, 1 H), 6.76 (m, 4 H), 6.65 (dd, *J* = 8.2, 2.1 Hz, 1 H), 4.42 (d, *J* = 6.3 Hz, 2 H), 3.72 (m, 1 H), 2.92 (m, 2 H), 2.05 (m, 2 H), 1.67 (m, 2 H).

^{13}C NMR (130 MHz, CD_3OD): δ = 175.3 (C), 162.9 (C), 151.3 (C), 150.9 (C), 148.9 (C), 146.6 (C), 125.0 (CH), 121.4 (CH), 120.4 (CH), 119.5 (CH), 114.5 (CH), 113.6 (CH), 108.9 (C), 103.8 (C), 58.3 (CH), 38.7 (CH_2), 29.4 (CH_2), 26.3 (CH_2), 25.9 (CH_2).

MS (EI): *m*/*z* = 373 $[M + H]^+$.

Anal. Calcd for $C_{19}H_{20}N_2O_6$: C, 61.28; H, 5.41; N, 7.53. Found: C, 60.99; H, 5.22; N, 7.90.

Deprotection of 9 to 2d-H_4

Compound **9** (22 mg, 0.033 mmol) was dissolved in CH_2Cl_2 (20 mL) and trifluoroacetic acid (0.2 mL) and triisopropylsilane (1 mL) were added. The mixture was stirred for 2 h at r.t. The precipitate was collected by filtration, washed with CH_2Cl_2 and dried; yield: 14 mg (ca. 100%); slightly brown solid.

^{1}H NMR (400 MHz, CD_3OD): δ = 7.46 (s, 1 H), 7.37 (d, *J* = 7.4 Hz, 2 H), 6.92 (m, 1 H), 6.76–6.69 (m, 4 H), 4.30 (m, 2 H), 3.04 (m, 1 H), 1.80 (m, 2 H).

^{13}C NMR (100 MHz, CD_3OD): δ = 174.4 (C), 160.7 (C), 152.5 (C), 151.4 (C), 147.8 (C), 145.3 (C), 134.8 (CH), 133.7 (CH, double intensity), 131.0 (C), 124.3 (CH), 199.7 (CH), 118.0 (CH), 113.2 (CH), 113.2 (CH), 104.9 (C), 101.4 (C), 48.7 (CH), 38.2 (CH_2), 29.1 (CH_2).

Dinuclear Complexes with Methoxide Coligands; General Procedure

The amino acid-bridged ligand **2**-H_4 (1 equiv, ca. 0.1 mmol), $TiO(acac)_2$ (1 equiv) and alkali metal carbonate (1 equiv) were dissolved in MeOH. The mixture was stirred for 20 h and the solvent was removed in vacuum. The residue was dissolved in MeOH and filtered over Sephadex LH20 and the orange red band was collected.

$Li_2[(2a)_2(OCH_3)_2Ti_2]$

Yield: 91%; red solid.

IR (KBr): 3425, 1707, 1633, 1592, 1525, 1451, 1356, 1255, 1022, 931, 801, 744, 664 cm^{-1}.

^{1}H NMR (300 MHz, CD_3OD): δ = 7.15–6.80 (m, 2 H), 6.30–5.95 (m, 4 H), 3.04 (m, 2 H), 5.05 (m, 1 H), 3.65 (m, 2 H).

MS (ESI): *m*/*z* = 464 $[M - 2\ Li]^{2-}$, 935 $[M - Li]^-$.

Anal. Calcd for $C_{38}H_{36}Li_2N_6O_{16}Ti_2{\cdot}5H_2O{\cdot}8CH_3OH$: C, 41.43; H, 5.82; N, 6.74. Found: C, 41.14; H, 4.85; N, 3.27.

$Li_2[(2b)_2(OCH_3)_2Ti_2]$

Yield: 91%; a red solid.

IR (KBr): 3378, 2927, 1646, 1593, 1527, 1447, 1252, 1219, 741 cm^{-1}.

^{1}H NMR (300 MHz, CD_3OD): δ = 7.12 (dd, 1 H, *J* = 8.2, 2.1 Hz, NH), 6.61 (t, *J* = 8.2 Hz, 1 H), 6.55–6.43 (m, 2 H), 6.39 (d, *J* = 5.3 Hz, 2 H), 6.30–6.20 (m, 1 H), 4.46 (d, *J* = 15.2 Hz, 2 H), 4.10 (d, *J* = 4.1 Hz, 1 H), 2.65–1.95 (br m, 4 H).

MS (ESI): *m*/*z* = 478 $[M - 2\ Li]^{2-}$, 957 $[M - 2\ Li + H]^-$, 963 $[M - Li]^-$.

Anal. Calcd for $C_{40}H_{40}Li_2N_6O_{16}Ti_2{\cdot}6H_2O{\cdot}2CH_3OH$: C, 44.15; H, 5.29; N, 7.35. Found: C, 44.13; H, 5.09; N, 6.38.

$Na_2[(2b)_2(OCH_3)_2Ti_2]$

Yield: 90%; red solid.

IR (KBr): 3408, 1724, 1651, 1591, 1527, 1447, 1361, 1251, 1219, 1027, 739, 674, 634 cm^{-1}.

^{1}H NMR (300 MHz, CD_3OD): δ = 7.25 (m, 1 H), 6.34 (t, *J* = 7.9 Hz, 1 H), 6.54 (m, 1 H), 6.42 (d, *J* = 5.0 Hz, 2 H), 6.29 (t, *J* = 5.0 Hz, 1 H), 4.87 (m, 1 H), 4.49 (d, *J* = 13.3 Hz, 1 H), 4.15 (d, *J* = 13.3 Hz, 1 H), 2.56 (m, 2 H), 2.17 (m, 2 H).

MS (ESI): *m*/*z* = $Na_2[(\mathbf{2b})_2(OCH_3)_2Ti_2]$: 478 $[M - 2\ Na]^{2-}$, 979 $[M - Na]^-$.

Anal. Calcd for $C_{40}H_{40}N_6Na_2O_{16}Ti_2{\cdot}4\ H_2O$: C, 44.71; H, 4.50; N, 7.82. Found: C, 44.98; H, 4.56; N, 5.77.

$K_2[(2b)_2(OCH_3)_2Ti_2] + K_4[(2b)_3Ti_2]$

Red solid.

IR (KBr): 3408, 1728, 1667, 1527, 1445, 1345, 1251, 1219, 1027, 845, 741, 670, 633 cm^{-1}.

^{1}H NMR (300 MHz, CD_3OD): δ = 7.60 (m, 1 H), 7.11 (m, 1 H), 6.59–6.15 (br m, 4 H), 4.41 (m, 1 H), 4.05 (d, *J* = 14.7 Hz, 1 H), 4.15 (m, 1 H), 1.91 (br m, 2 H), 1.32 (br m, 2 H).

MS (ESI): *m*/*z* = $K_2[(\mathbf{2b})_2(OCH_3)_2Ti_2]$: 478 $[M - 2\ K]^{2-}$, 995 $[M - K]^-$; $K_4[(\mathbf{2b})_3Ti_2]$: 686 $[M - 2\ K]^{2-}$.

$Li_2[(2b')_2(OCH_3)_2Ti_2]$

Yield: quant.; red solid.

IR (KBr): 3403, 1639, 1525, 1448, 1254, 1219, 1064, 853, 742, 488 cm^{-1}.

^{1}H NMR (300 MHz, CD_3OD): δ = 7.24 (dd, *J* = 1.5, 8.2 Hz, 1 H), 6.63 (t, *J* = 8.2, 1 H), 6.54 (dd, *J* = 1.5, 7.7 Hz, 2 H), 6.48 (m, 1 H), 6.42, (m, 1 H), 4.83 (m, 1 H), 4.53 (m, 1 H), 4.16 (m, 1 H), 3.75 (s, 3 H), 3.38 (s, 3 H), 2.68 (m, 2 H), 2.48 (m, 1 H), 2.12 (m, 1 H).

MS (ESI): *m*/*z* = 493 $[M - 2\ Li]^{2-}$, 993 $[M - Li]^-$.

Anal. Calcd for $C_{42}H_{42}Li_2N_4O_{18}Ti_2{\cdot}8H_2O$: C, 44.07; H, 5.11; N, 4.89. Found: C, 44.37; H, 5.06; N, 5.24.

$Na_2[(2b')_2(OCH_3)_2Ti_2]$

Yield: 54%; red solid.

IR (KBr): 3410, 3245, 1719, 1642, 1539, 1446, 1250, 1218, 1064, 851, 740, 680, 632, 485 cm^{-1}.

^{1}H NMR (300 MHz, CD_3OD): δ = 9.67 (d, 1 H, *J* = 9.4, NH), 7.25 (d, *J* = 8.2, 1 H), 6.63 (t, *J* = 7.9, 1 H), 6.53 (m, 1 H), 6.41 (d, *J* = 4.9, 2 H), 6.28 (m, 1 H), 4.62 (m, 1 H), 4.50 (d, *J* = 14.1, 1 H), 4.15 (m, 1 H), 3.75 (s, 3 H), 3.38 (s, 3 H), 2.68 (m, 2 H), 2.47 (m, 1 H), 2.10 (m, 1 H).

MS (ESI): *m*/*z* = 493 $[M - 2\ Na]^{2-}$, 1009 $[M - Na]^-$.

Anal. Calcd for $C_{42}H_{42}Na_2N_4O_{18}Ti_2{\cdot}6H_2O{\cdot}CH_3OH$: C, 44.04; H, 4.99; N, 4.78. Found: C, 43.99; H, 4.98; N, 5.31.

$K_2[(2b')_2(OCH_3)_2Ti_2]$

Yield: quant.; red solid.

IR (KBr): 3390, 3241, 1720, 1642, 1536, 1445, 1251, 1218, 1062, 851, 740, 680, 632, 484 cm^{-1}.

^{1}H NMR (300 MHz, CD_3OD): δ = 9.66 (d, 1 H, *J* = 9.4 Hz, NH), 7.24 (m, 1 H), 6.63 (m, 1 H), 6.52 (m, 1 H), 6.42 (d, *J* = 4.2 Hz, 2 H), 6.30 (m, 1 H), 4.82 (t, *J* = 4.7 Hz, 1 H), 4.17 (m, 1 H), 3.76 (s, 3 H), 3.38 (s, 3 H), 2.68 (m, 2 H), 2.48 (m, 1 H), 2.12 (m, 1 H).

MS (ESI): *m*/*z* = 493 $[M - 2\ K]^{2-}$, 1025 $[M - Li]^-$.

Anal. Calcd for $C_{42}H_{42}K_2N_4O_{18}Ti_2{\cdot}8.5H_2O$: C, 41.42; H, 4.88; N,.4.60. Found: C, 41.25; H, 4.71; N, 5.15.

$Li_2[(2c)_2(OCH_3)_2Ti_2]$

Yield: 88%; red solid.

IR (KBr): 3591, 3430, 1640, 1602, 1517, 1451, 1255, 1221, 1019, 919, 742, 521 cm^{-1}.

^{1}H NMR (300 MHz, CD_3OD): δ = 7.27 (d, *J* = 8.4 Hz, 2 H), 7.19 (m, 1 H), 6.81 (d, *J* = 8.4 Hz, 2 H), 6.61 (m, 2 H), 6.40 (d, *J* = 5.2 Hz, 2 H), 6.26 (m, 1 H), 5.01 (m, 1 H), 4.48 (d, *J* = 14.3 Hz, 1 H), 4.12 (d, *J* = 14.3 Hz, 1 H), 3.21 (m, 2 H).

MS (ESI): m/z = 513 [M – 2 Li]$^{2-}$, 1033 [M – Li]$^{-}$.

Anal. Calcd for $C_{48}H_{42}Li_2N_4O_{16}Ti_2 \cdot 6H_2O \cdot CH_3OH$: C, 49.85; H, 4.95; N, 4.75. Found: C, 49.76; H, 5.24; N, 3.17.

$Na_2[(2c)_2(OCH_3)_2Ti_2] + Na_4[(2c)_3Ti_2]$
Red solid.

IR (KBr): 3412, 1645, 1594, 1517, 1451, 1360, 1251, 1220, 1023, 741, 664, 632, 517 cm^{-1}.

^{1}H NMR (300 MHz, CD_3OD): δ = 7.14 (d, J = 8.4 Hz, 2 H), 7.05 (m, 1 H), 6.67 (d, J = 8.4 Hz, 2 H), 6.47 (m, 2 H), 6.26 (d, J = 5.2 Hz, 2 H), 6.13 (m, 1 H), 4.78 (m, 1 H), 4.34 (d, J = 14.3 Hz, 1 H), 4.09 (d, J = 14.3 Hz, 1 H), 3.05 (m, 2 H).

MS (ESI): m/z = $Na_2[(\mathbf{2c})_2(OCH_3)_2Ti_2]$: 513 [M – 2Na]$^{2-}$, 1049 [M – Na]$^{-}$; $Na_4[(\mathbf{2c})_3Ti_2]$: 474 [M – 3Na]$^{3-}$, 722 [M – 2 Na]$^{2-}$, 1467 Na_3[M – Na]$^{-}$.

$K_2[(2c)_2(OCH_3)_2Ti_2] + K_4[(2c)_3Ti_2]$
Red solid.

IR (KBr): 3424, 1636, 1554, 1447, 1252, 1221, 745 cm^{-1}.

^{1}H NMR (300 MHz, CD_3OD): δ = 7.24–6.10 (m, 10 H), 4.62 (m, 1 H), 4.23 (d, J = 14.7 Hz, 1 H), 4.11 (d, J = 14.7 Hz, 2 H), 3.01 (br m, 2 H).

MS (ESI): m/z = $K_2[(\mathbf{2c})_2(OCH_3)_2Ti_2]$: 513 [M – 2 K]$^{2-}$, 1065 [M – K]$^{-}$; $K_4[(\mathbf{2c})_3Ti_2]$: 479 [M – 3 K]$^{3-}$, 738 [M – 2 K]$^{2-}$, 1515 [M – K]$^{-}$.

$Li_2[(2d)_2(OCH_3)_2Ti_2]$
Yield: 90%; red solid.

^{1}H NMR (300 MHz, CD_3OD): δ = 7.28–7.14 (m, 3 H), 7.09 (s, 1 H), 6.58–6.30 (m, 4 H), 3.58 (br s, 2 H), 3.04 (br s, 1 H), 1.83 (br m, 2 H).

MS (ESI): m/z = 981 [M – Li]$^{-}$.

$Li_2[(2e)_2(OCH_3)_2Ti_2]$
Yield: 85%; red solid.

IR (KBr): 3386, 2928, 1592, 1527, 1446, 1254, 1223, 1026, 740 cm^{-1}.

^{1}H NMR (300 MHz, CD_3OD): δ = 6.71 (dd, J = 7.6, 1.8 Hz, 1 H), 6.56–6.30 (m, 4 H), 6.23 (dd, J = 7.6, 1.8 Hz, 1 H), 4.61 (m, 1 H), 4.61 (m, 1 H), 4.25 (m, 1 H), 2.20–1.45 (br m, 6 H).

MS (ESI): m/z = 447 [M – 2 Li]$^{2-}$, 901 [M – Li]$^{-}$.

$Na_2[(2e)_2(OCH_3)_2Ti_2] + Na_4[(2e)_3Ti_2]$
Red solid.

IR (KBr): 3392, 1589, 1528, 1445, 1357, 1253, 1222, 740, 520 cm^{-1}.

^{1}H NMR (300 MHz, CD_3OD): δ = 6.47–6.18 (br m, 6 H), 4.44 (m, 1 H), 4.37 (d, J = 14.3 Hz, 1 H), 4.12 (d, J = 14.3 Hz, 1 H), 2.15–1.32 (m, 6 H).

MS (ESI): m/z = $Na_2[(\mathbf{2e})_2(OCH_3)_2Ti_2]$: 447 [M – 2 Na]$^{2-}$, 917 [M – Na]$^{-}$; $Na_4[(\mathbf{2e})_3Ti_2]$: 408 [M – 3 Na]$^{3-}$, 623 [M – 2 Na]$^{2-}$, 1269 [M – Na]$^{-}$.

$K_2[(2e)_2(OCH_3)_2Ti_2] + K_4[(2e)_3Ti_2]$
Red solid.

IR (KBr): 3423, 1656, 1594, 1525, 1445, 1359, 1253, 1222, 1025, 740 cm^{-1}.

^{1}H NMR (300 MHz, CD_3OD): δ = 6.51–6.19 (br m, 6 H), 4.60 (m, 1 H), 4.29 (d, J = 13.4 Hz, 1 H), 4.08 (d, J = 13.4 Hz, 1 H), 2.21 (br m, 1 H), 1.83 (br m, 2 H), 1.47 (br m, 2 H).

MS (ESI): m/z = $K_2[(\mathbf{2e})_2(OCH_3)_2Ti_2]$: 447 [M – 2 K]$^{2-}$, 933 [M – K]$^{-}$; $K_4[(2e)_3Ti_2]$: 639 [M –2 K]$^{2-}$, 1317 [M – K]$^{-}$.

Ethoxide-Bridged Complex $Li_2[(2b)_2(OCH_2CH_3)_2Ti_2]$
The ethoxide-bridged complex is prepared as described for the corresponding methoxide derivative, with the exception that all procedures were performed in EtOH; yield: 90%; red solid.

IR (KBr): 3395, 2935, 1642, 1591, 1545, 1448, 1252, 1220, 1025, 1000, 744, 631, 517 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.38 (br, 1 H, NH), 7.05 (d, J = 8.2 Hz, 1 H), 6.50–6.00 (m, 5 H), 4.78 (m, 1 H), 4.52 (m, 1 H), 4.05 (m, 1 H), 3.43 (br m, 2 H), 2.30-1.75 (br m, 4 H) 1.06 (t, J = 7.1 Hz, 3 H).

MS (ESI): m/z = 492 [M – 2 Li]$^{2-}$, 991 [M – Li]$^{-}$.

Anal. Calcd for $C_{42}H_{46}N_6O_{16}Ti_2Li_2 \cdot 13H_2O \cdot 3C_2H_5OH$: C, 42.15; H, 6.26; N, 6.14. Found: C, 41.95; H, 6.31; N, 5.31.

Allyloxy-Bridged Complexes
The allyloxy-bridged complexes were prepared as described for the corresponding methoxide derivatives, with the exception that all procedures were performed in allyl alcohol.

$Li_2[(2c)_2(OCH_2CH{=}CH_2)_2Ti_2]$
Yield: 67%; a red solid.

IR (KBr): 3401, 2926, 2865, 1639, 1559, 1519, 1448, 1251, 1221, 1059, 1031, 743 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.16–6.20 (m, 10 H), 6.09–578 (m, 3 H), 5.32–4.90 (m, 2 H), 4.68 (m, 1 H), 3.95 (m, 2 H), 3.01 (br m, 2 H).

MS (ESI): m/z = 539 [M – 2 Li]$^{2-}$, 1085 [M – Li]$^{-}$.

Anal. Calcd for $C_{52}H_{46}Li_2N_4O_{16}Ti_2 \cdot 11H_2O \cdot 7(HOCH_2CH{=}CH_2)$: C, 51.66; H, 6.53; N, 3.30. Found: C, 51.76; H, 6.06; N, 2.45.

$Li_2[(2e)_2(OCH_2CH{=}CH_2)_2Ti_2]$
Yield: 93%; red solid.

IR (KBr): 3404, 1588, 1529, 1443, 1353, 1254, 1026, 740, 651 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 6.42–6.00 (m, 6 H), 5.94 (br m, 3 H), 5.19 (m, 1 H), 5.02 (m, 1 H), 4.72 (t, J = 7.2 Hz, 1 H), 4.52 (d, J = 13.3 Hz, 1 H), 4.30 (d, J = 13.3 Hz, 1 H), 3.93 (m, 2 H), 2.18–1.80 (m, 6 H).

MS (ESI): m/z = 473 [M – 2 Li]$^{2-}$, 953 [M – Li]$^{-}$.

Anal. Calcd for $C_{44}H_{44}Li_2N_4O_{14}Ti_2 \cdot 6H_2O \cdot HOCH_2CH{=}CH_2$: C, 50.01; H, 5.54; N, 4.96. Found: C, 50.15; H, 5.17; N, 4.22.

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References

(1) Fersht, A. *Structure and Mechanism in Protein Science*; W. H. Freeman: New York, **1998**.
(2) Lippard, S. J.; Berg, J. M. *Principles in Bioinorganic Chemistry*; University Science Books: Mill Valley, **1994**.
(3) Albrecht, M.; Napp, M.; Schneider, M. *Synthesis* **2001**, 468.
(4) Sträter, N.; Lipscomb, W. N.; Klabunde, T.; Krebs, B. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2024; *Angew. Chem.* **1996**, *108*, 2158.

(5) Albrecht, M.; Napp, M.; Schneider, M.; Weis, P.; Fröhlich, R. *Chem. Commun.* **2001**, 409.
(6) Albrecht, M.; Napp, M.; Schneider, M.; Weis, P.; Fröhlich, R. *Chem. Eur. J.* **2001**, *7*, 3966.
(7) Bodanszky, M.; Bodanszky, A. *The Practice of Peptide Synthesis*; Springer Verlag: Berlin, **1984**.
(8) Jones, J. *Synthese von Aminosäuren und Peptiden*; VCH: Weinheim, **1995**.
(9) (a) Li, P.; Xu, J.-C. *Chin. J. Chem.* **2000**, *18*, 456; *Chem. Abstr.* **2000**, *133*, 252669. (b) Li, P.; Xu, J.-C. *Tetrahedron* **2000**, *56*, 9949. (c) Speicher, A.; Klaus, T.; Eicher, T. *J. Prakt. Chem.* **1998**, *340*, 581.
(10) Barlos, K.; Chatzi, O.; Gatos, D.; Stavropoulos, G.; Tsegenidis, T. *Tetrahedron Lett.* **1991**, *32*, 475.
(11) McOmie, J. F. W.; West, D. E. *Org. Synth. Coll. Vol. V*; Wiley: New York, **1973**, 412.
(12) Enemark, E. J.; Stack, T. D. P. *Inorg. Chem.* **1996**, *35*, 2719.
(13) Albrecht, M. *J. Inclusion Phenom. Macrocycl. Chem.* **2000**, *36*, 127.