

# Kinetic *versus* thermodynamic control of the self-assembly of isomeric double-stranded dinuclear titanium(IV) complexes from a phenylalanine-bridged dicatechol ligand

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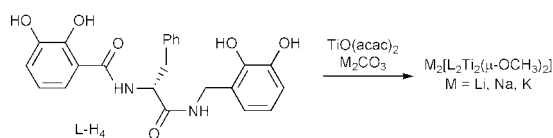
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The phenylalanine-bridged dicatechol ligand **L-H<sub>4</sub>** forms under kinetic reaction conditions a double-stranded dinuclear titanium(IV) complex  $[(L)_2Ti_2(OCH_3)_2]^{2-}$ , as a mixture of seven regio- and stereo-isomers, which in solution transforms into the thermodynamically favored major product and two minor side products.

Peptides are biopolymers which are built up from amino acid monomers. Hereby hydrogen bonding, electrostatic and steric interactions of the amino acid residues lead to the formation of  $\alpha$ -helical,  $\beta$ -sheet, turn or random coil structures.<sup>1</sup> Recently we introduced amino acids as spacers into dicatechol ligands to use the unique features of this moiety for the formation of helicates.<sup>2,3</sup>

When we perform a complexation study of the phenylalanine-bridged dicatechol ligand **L-H<sub>4</sub>** with  $[TiO(acac)_2]$  and alkali metal carbonate in methanol (15 h, r.t.), we obtain red solids (Scheme 1). Negative ESI MS in methanol (Fig. 1 shows the spectrum of the sodium salt as a representative example) reveals that only traces of a triple-stranded helicate-type



Scheme 1

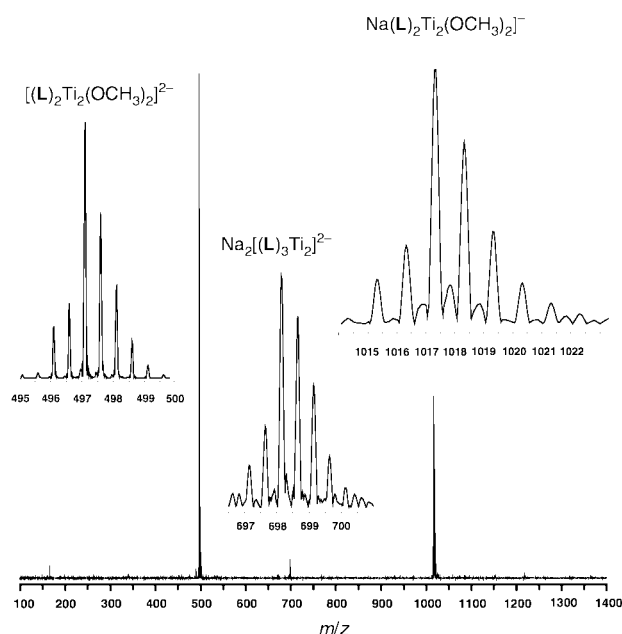


Fig. 1 Negative ESI mass spectrum (methanol) of  $Na_2[(L)_2Ti_2(OCH_3)_2]^{2-}$ .

complex  $M_4[(L)_3Ti_2]$  ( $m/z = 698$ , charge  $2-$ ,  $Na_2[(L)_3Ti_2]^{2-}$ ) are present while the major component  $M_2[(L)_2Ti_2(OCH_3)_2]$  is composed of two ligands **L**, two titanium(IV) ions and two coligands  $CH_3O^-$  {for  $M = Na$ :  $m/z = 1017$ , charge  $1-$ ,  $Na[(L)_2Ti_2(OCH_3)_2]^-$ ; and  $m/z = 497$ , charge  $2-$ ,  $Na_2[(L)_3Ti_2]^{2-}$ }. The isotopic patterns are in accordance with the proposed formulae.

Stack and coworkers already reported a similar dinuclear iron(III) complex. They were able to control the formation of double- *versus* triple-stranded complexes by the stoichiometry of the components.<sup>4</sup> With our system we could not shift the reaction towards the triple-stranded complexes  $M_4[(L)_3Ti_2]$ .

The NMR spectra of the complexes  $M_2[(L)_2Ti_2(OCH_3)_2]$  are very complicated because of the directionality<sup>5</sup> of the ligand **L** and of the stereochemistry at the complex units.<sup>6</sup> Fig. 2 shows a schematic representation of the different stereo- and regio-isomers which can be formed. The two directional ligands (N- *versus* C-terminus) can be orientated parallel or antiparallel to each other and the two complex units can be homo- or heterochiral. The isomers **I**, **II** and **IV–VII** possess a  $C_2$  axis and lead to only one set of NMR signals for the ligands, whereas **III** possesses  $C_1$  symmetry and thus would result in two sets of signals. If a  $^1H$  NMR spectrum of freshly synthesized (r.t., 15 h, methanol)  $[(L)_2Ti_2(OCH_3)_2]^{2-}$  in methanol- $d_4$  is recorded, up to eight sets of signals—all seven isomers—are observed [Fig. 3 (top), only the signals of one of the diastereotopic benzylic  $CH_2N$  protons are shown, the other signals are partly overlapping and cannot be interpreted unambiguously].

After two weeks at room temperature the spectrum gets much simpler and one major (a) and two minor species (b, c) are observed [Fig. 3 (bottom)]. From the NMR spectrum it is seen that the complexes which are present in significant amounts belong to the  $C_2$ -symmetric isomers **I**, **II** and/or **IV–VII**.

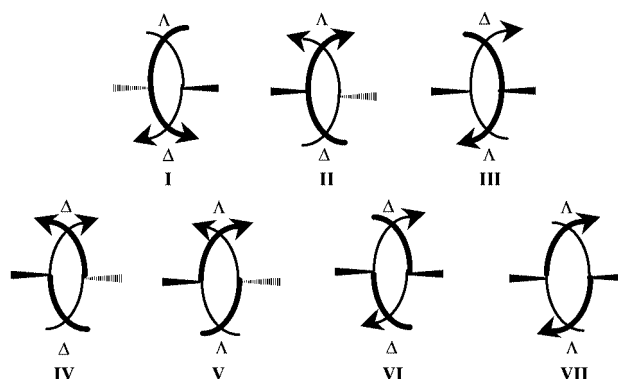
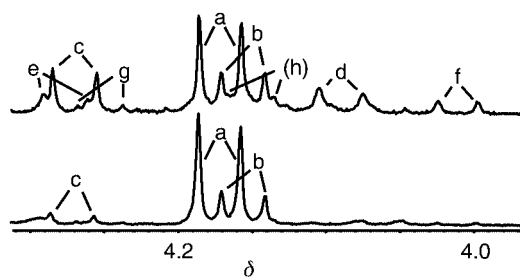


Fig. 2 Schematic representation of the possible isomers of the double-stranded complex  $[(L)_2Ti_2(OCH_3)_2]^{2-}$ . Only the two directional ligand strands **L** are shown as arrows. Additionally, the configuration at the complex units ( $\Lambda$  or  $\Delta$ ) and at the ligand are indicated. Bold lines are at front, thin lines are at the back.



**Fig. 3** Part of the  $^1\text{H}$  NMR spectrum (methanol- $d_4$ ) of  $\text{Li}_2[(\text{L})_2\text{Ti}_2(\text{OCH}_3)_2]$  (only the signal of one of the diastereotopic protons in benzylic  $[\text{NCH}_2]$ -position is shown). (Top) spectrum of a freshly prepared (r.t., 15 h, methanol) sample of  $\text{Li}_2[(\text{L})_2\text{Ti}_2(\text{OCH}_3)_2]$  showing up to eight doublets (a)–(h) ( $\rightarrow$  seven isomers) ('kinetic control'). (Bottom) spectrum after two weeks at room temperature in methanol- $d_4$  with the dominating species (a) and the minor components (b) and (c) ('thermodynamic control').

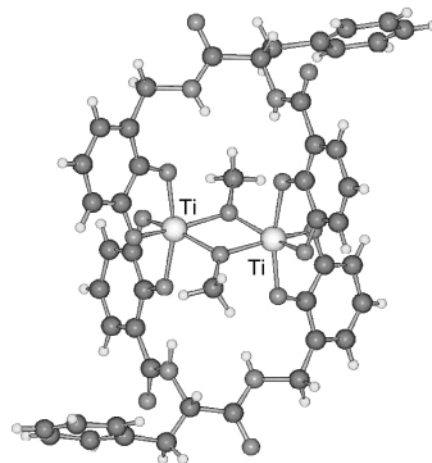
Following the optical rotation of  $[(\text{L})_2\text{Ti}_2(\text{OCH}_3)_2]^{2-}$  ( $c = 0.1$ , methanol,  $20^\circ\text{C}$ ) we observed a drop of  $[\alpha]_{\text{D}}$  from  $+70^\circ$  to about  $0^\circ$  within 18 days. Those results indicate that under kinetic control a mixture of complexes is formed which slowly transforms in solution into the thermodynamically most stable coordination compounds as the major product.<sup>7</sup> The decrease of the optical rotation gives some evidence that, initially, the helical isomers **IV–VII**, which should lead to high  $[\alpha]_{\text{D}}$  values,<sup>8</sup> are formed in significant amounts but are only minor species in the thermodynamically favored mixture. Model considerations indicate, that for the helical structures **IV–VII** the stabilizing intramolecular hydrogen bonding is disturbed.

The X-ray structure of  $\text{Li}_2[(\text{L})_2\text{Ti}_2(\text{OCH}_3)_2]$  (Fig. 4) shows a central four-membered  $[\text{Ti}(\mu\text{-OCH}_3)_2]$  unit which is bridged by two ligands **L**.<sup>†</sup> The two ligands **L** are orientated in opposite directions and are bound in a 'side-by-side' fashion to the metal centers leading to a 'meso'-relation between the two complex units. This unsymmetrical isomer **III**, which should lead to two sets of signals by NMR, cannot be detected in significant amounts in solution. Investigation of a second crystal showed the presence of the same isomer **III**.

A conformational analysis following Ramachandran's method<sup>1</sup> shows that one of the ligands adopts a conformation as found in left-handed  $\alpha$ -helical peptides ( $\Phi = 80.53^\circ$ ,  $\Psi = 30.69^\circ$ ) whereas the other one has a conformation somewhere in-between a right-handed helix and a sheet structure ( $\Phi = -115.11^\circ$ ,  $\Psi = 5.80^\circ$ ).<sup>1</sup>

Herein we presented the coordination chemistry of the phenylalanine-bridged dicatechol ligand **L** with titanium(IV) ions. ESI MS shows that the ligand **L** preferably forms double-stranded coordination compounds  $[(\text{L})_2\text{Ti}_2(\text{OR})_2]^{2-}$  and not triple-stranded helicate-type complexes  $[(\text{L})_3\text{Ti}_2]^{4-}$ . Hereby a complex mixture of isomers which is obtained under kinetic control transforms in solution within several days into the more simple 'thermodynamic' product mixture.

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**Fig. 4** SCHAKAL representation of the molecular structure of the dianion  $[(\text{L})_2\text{Ti}_2(\text{OCH}_3)_2]^{2-}$  in the crystal. Selected distances ( $\text{\AA}$ ) and angle ( $^\circ$ ) for the central four-membered ring:  $\text{Ti}(1)\cdots\text{Ti}(2)$  3.188(1);  $\text{Ti}(1)-\mu\text{-O}(1/2)$  1.996(6), 2.018(6);  $\mu\text{-O}(1)-\text{Ti}(1)-\mu\text{-O}(2)$  73.1(2). Distances ( $\text{\AA}$ ) of the intramolecular hydrogen bonds:  $\text{N}-\text{H}/\text{H}\cdots\text{O}$  0.854/2.508, 0.866/2.055, 0.780/2.229 and 1.101/1.786.

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## Notes and references

<sup>†</sup> *Crystal data* for  $\text{C}_{60}\text{H}_{74}\text{N}_8\text{O}_{20}\text{Li}_2\text{Ti}_2$ ,  $M = 1336.95$ , monoclinic, space group  $P2_1$  (no. 4),  $a = 9.404(1)$ ,  $b = 22.726(1)$ ,  $c = 15.382(1)$   $\text{\AA}$ ,  $\beta = 95.04(1)$ ,  $V = 3274.7(4)$   $\text{\AA}^3$ ,  $\mu = 3.22$   $\text{cm}^{-1}$ ,  $Z = 2$ ,  $T = 198$  K, 17559 reflections collected ( $\pm h, \pm k, \pm l$ ), 10574 independent ( $R_{\text{int}} = 0.062$ ) and 6559 observed reflections [ $I \geq 2\sigma(I)$ ],  $R = 0.068$ ,  $wR^2 = 0.121$ , Flack parameter 0.01(6).

CCDC 149452. See <http://www.rsc.org/suppdata/cc/b0/b0096571/> for crystallographic data in .cif or other electronic format.

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