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Dipicolylglycyl-phenylalanine zinc(II): a metallopeptide with a built-in conformational switch and its homochiral helical coordination polymer

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The peptide-zinc complex [(Dpg-Phe)Zn]$^{2+}$ (Dpg = *N*,*N*-dipicolylglycine; Phe = phenylalanine) reversibly forms a homochiral P-helical coordination polymer upon switching the pH from mildly basic to mildly acidic.

The controlled assembling of non-centrosymmetric metal-based supramolecular nanostructures is a matter of considerable recent interest. Possible applications in materials science, as well as the mere beauty of the designed crystal structures have stimulated many research groups to build fascinating 1-, 2-, and 3-dimensional aggregates from tailor made tectons.[1] A particularly challenging goal in the field is the design of chiral helices from coordination compounds.[2–4] Here we describe the formation of a homochiral right-handed helix from the dipeptide zinc complex fragment [(Dpg-L(*S*)-Phe-O)Zn]$^+$ (Dpg-L(*S*)-Phe-OH = *N*,*N*-dipicolylglycyl-L(*S*)-phenylalanine). The compound contains a built-in conformational switch which allows for a pH dependent reversible helix assembly–disassembly.[5] This feature is new in a chiral coordination polymer and offers promising perspectives for the design of materials *e.g.* reversible information storage or the processing of modified surfaces.

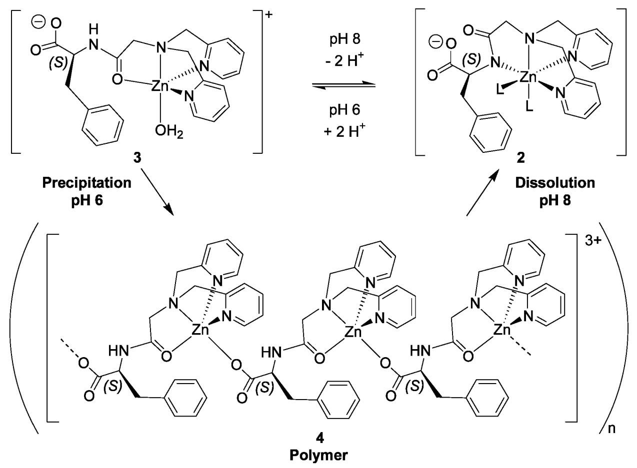
The starting material was the zinc complex [(Dpg-L(*S*)-Phe-OMe)Zn(H$_2$O)](SO$_3$CF$_3$)$_2$ (**1**) which has been described earlier.[6] The compound was treated with NaOH for several days in order to cleave its methyl ester function. NMR spectra showed that a new complex **2**† formed in which the originally O-bound amide function is presumably de-protonated and coordinates *via* its anionic nitrogen atom.[7] Unfortunately, we were not yet able to isolate and further characterize compound **2**. The complex is presumably six-coordinate with two co-ligands L which could be water or hydroxide. Formation of a binuclear species can also not be ruled out.

Scheme 1 summarizes the pH dependent coordination chemistry of the product **2**. Upon acidification of the basic solution with HCl the original carbonyl oxygen coordination was restored in the complex **3**. This was followed by spontaneous precipitation of the polymer {**4**(SO$_3$CF$_3$)}$_n$. The pH-dependent structural changes are nicely evident from the ^{1}H-NMR spectra shown in Fig. 1. At pH* = 8.8[8] we observed several remarkable features. The pyridine ligands show two distinctly different sets of signals for their CH-6 protons. The same is true for the methylene-C(O) group. Furthermore, three well resolved multiplets are seen for the side chain phenyl ring. The significant high field shift of the latter indicates the presence of π–π-stacking interactions with one of the pyridine rings.[9] This is also a likely explanation for the large difference between the two pyridine CH-6 resonances. Finally, the phenylalanine $^{\beta}$CH$_2$ group does not show the common AB pattern but rather appears as a broad singlet at *ca*. 2.95 ppm.

All these features change completely when the pH* value is adjusted to 4 with DCl. Most properties are now similar to those observed for the starting material **1** in non-polar solvents.[6,9] The only exceptions are the phenyl signals which appear as two sets of signals at around 7 ppm. In the spectrum of **1** in CDCl$_3$ these signals exhibit a distinct high field shift of the CH-4 proton resonance to *ca*. 6.5 ppm as a consequence of π–π and π–cation interactions which prevail in solution. No evidence for such interactions is observed in the spectrum of **3**. Upon switching the pH the two complexes **2** and **3** can be inter-converted several times without detectable traces of decomposition products. The spectrum of **2** is also obtained when a sample of the polymer {**4**(SO$_3$CF$_3$)}$_n$ is dissolved in basic D$_2$O/NaOD.

The crystal structure of the repetition unit in the polymeric cation $\{\mathbf{4}\}_n^{n+}$ is shown in Fig. 2. The coordination sphere around the Zn^{2+} center is distorted trigonal-bipyramidal with geometric parameters which are generally similar to those of the monomeric methylester complex **1**. Interesting is the distorted axial N151–Zn–O199 angle of *ca*. 160°. Although the carboxylate donor is clearly monodentate the weak interaction with the second oxygen atom (*d*(Zn4–O198) 3.078 Å) seems to be sufficient cause for a moderate distortion.

Three zinc complex fragments form one helix turn in $\{\mathbf{4}\}_n^{n+}$ with a pitch of 14.8 Å. Two independent {[ZnL]$^+$}$_3$ units are present in the asymmetric unit.‡ Both are right-handed and each



Scheme 1 pH-Dependent conformational changes and polymerization of [(Dpg-L(*S*)-Phe-O$^-$)Zn]$^+$ complexes.

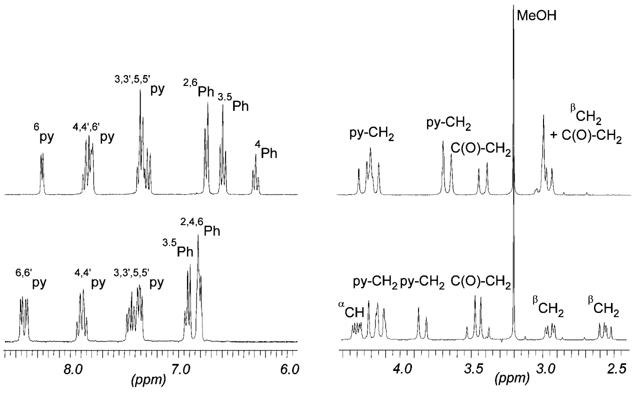


Fig. 1 ^{1}H-NMR spectra in D$_2$O obtained after cleavage of the methyl ester group in **1**; top: pH* = 8.8 (complex **2**), bottom: pH* = 4.0 (complex **3**).

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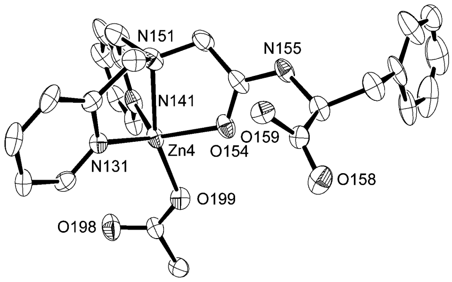

Fig. 2 ORTEP plot (30% ellipsoids) of the cationic repetition unit in $\{\mathbf{4}(SO_3CF_3)\}_n$; selected distances (Å) and angles (°): Zn4–N151 2.225(7), Zn4–N131 2.065(5), Zn4–N141 2.079(7), Zn4–O154 2.080(5), Zn4–O199 1.952(6), Zn4–O198 3.072; N151–Zn4–N131 78.8(3), N151–Zn4–N141 78.6(3), N151–Zn4–O154 76.5(2), N131–Zn4–N141 112.6(2), N131–Zn4–O154 114.1(2), N141–Zn4–O154 120.5(2), N151–Zn4–O199 160.9(2), N131–Zn4–O199 116.2(2), N141–Zn4–O199 104.3(3), O154–Zn4–O199 86.0(2).

is packed in the unit cell with an antiparallel orientation of the polymer chains. This is shown in Fig. 3 which contains a view along the [100] axis. The anions and 17 water molecules per asymmetric unit fill the open channels. It is interesting to note that even though we worked with a large excess of chloride in HCl acidic solutions only triflate ions are incorporated in either the bulk or crystalline solids formed. The bulk sample immediately obtained after acidification differs from the crystalline material only in its water content after drying under vacuum. This is evident from elemental analysis data.

The antiparallel packing of $\{\mathbf{4}\}_n^{n+}$ is an undesirable property since it results in an overall non-polar solid. However, the finding itself is interesting since it provides important insight into requirements for a parallel packing of polymer chains. Garcia-Raso *et al.*,[3] as well as Hosseini *et al.*[10] have reported examples for parallel packed coordination polymers carrying alkyl side chains. In their compounds steric interactions prevent an anti-parallel orientation. In contrast, Hong *et al.* have investigated assemblies containing L-tyrosine as the chiral building block in neutral copper(II) complexes.[4] They observed an anti-parallel non-polar packing similar to that in $\{\mathbf{4}\}_n^{n+}$. It seems that aromatic substituents result in a more rod-like topology of the helix which precludes steric interactions between neighboring chains. In our case, the cationic charge which requires the formation of anionic channels makes steric effects even less likely to play a role.

In summary, the $[(\mathrm{Dpg}\text{-L}(S)\text{-Phe})\mathrm{Zn}]^{2+}$ fragment is remarkably stable over a wide pH range. Its flexible peptidic amide bond can switch between neutral oxygen and anionic nitrogen coordination. This feature allows for controlled assembly and disassembly of the helical polymer $\{\mathbf{4}\}_n^{n+}$.

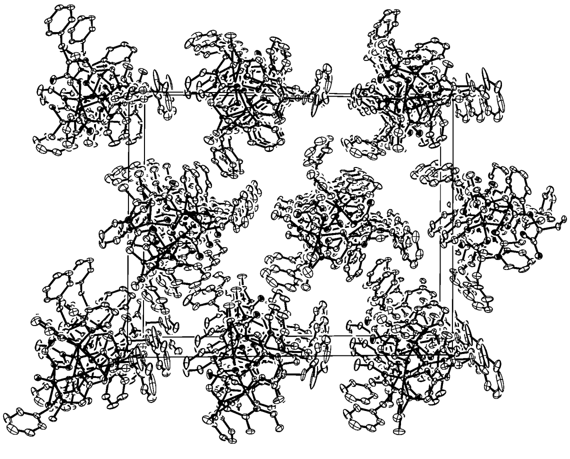

Fig. 3 Packing of the cations in the structure of $\{\mathbf{4}(CF_3SO_3)\cdot 17H_2O\}_n$.

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Notes and references

† *Synthesis*: 1.05 g (1.31 mmol) of $[(\mathrm{Dpg}\text{-L}(S)\text{-Phe-OMe})\mathrm{Zn}(H_2O)](SO_3CF_3)_2$ (**1**) were dissolved in 20 ml H_2O. The pH value was adjusted to 9.5 with 1 M NaOH. Consumption of base was monitored using a pH meter and 1 M NaOH was added several times a day until the H^+ concentration remained constant (*ca.* 3 d). Lowering the pH value to *ca.* 4 with aqueous HCl was followed by an immediate precipitation of solid $\{\mathbf{4}(CF_3SO_3)\}_n$. After 1 h the product was collected on a sintered glass filter and dried under vacuum. Crystals for an X-ray structure analysis were obtained from the supernatant solution upon standing at room temperature for several weeks.

Yield (bulk): 454.4 mg (71%); C,H,N-analysis (bulk sample) calc. (%) for $C_{24}H_{23}F_3N_4O_6SZn\cdot 1H_2O$ (M = 635.456 g mol^{-1}): C 45.33, H 3.96, N 8.81; found: C 45.56, H 4.18, N, 8.95.

^{1}H-NMR spectroscopy: A sample of **1** was dissolved in D_2O and the pH* value was adjusted to 9.0 with NaOD. Cleavage of the methyl ester function was monitored by NMR spectroscopy until complete. The pH* value was then lowered to 4.0 by addition of DCl prior to the next measurement. Repeated NMR measurements confirmed that the two complexes **2** and **3** can be inter-converted without significant decomposition by switching the pH* value between *ca.* 9 and 4.

^{1}H-NMR (**2**, pH* (D_2O/NaOD) = 9), δ(ppm) = 2.97 (m, 3H, C(O)CH$_2$, $^\beta$CH$_2$); 3.19 (s, MeOH); 3.40 (d, 1H, C(O)CH$_2$); 3.64 (d, 1H, py-CH$_2$); 4.17 (m, 3H, py-CH$_2$); 4.57 (m, 1H, $^\alpha$CH); 6.28 (m, 1H, ^{4}Ph); 6.58 (m, 2H, ^{3,5}Ph); 6. 74 (m, 2H, ^{2,6}Ph); 7.31 (m, 4H, $^{3,3',5,5'}$py); 7.83 (m, 3H, $^{4,4',6'}$py); 8.25 (d, 1H, ^{6}py).

^{1}H-NMR (**3**, pH* (D_2O/DCl) = 4), δ(ppm) = 2.55 (dd, 1H, $^\beta$CH$_2$); 2.94 (dd, 1H, $^\beta$CH$_2$); 3.19 (s, MeOH); 3.44 (m, 2H, C(O)CH$_2$); 3.83 (d, 1H, py-CH$_2$); 4.14 (m, 3H, py-CH$_2$); 4.29 (m, 1H, $^\alpha$CH); 6.80 (m, 3H, ^{2,4,6}Ph); 6. 92 (m, 2H, ^{3,5}Ph); 7.40 (m, 4H, $^{3,3',5,5'}$py); 7.89 (m, 2H, $^{4,4'}$py); 8.40 (d, 1H, ^{6}py); 8.45 (d, 1H, $^{6'}$py).

‡ *Crystal data*: asymmetric unit:$\{[C_{24}H_{23}N_4O_3Zn](SO_3CF_3)\}_6\cdot 17H_2O$; monoclinic, $P2_1$; a = 14.8038(1), b = 26.8171(1), c = 11.9026(1) Å; β = 92.039(1)°; Z = 12; V = 8689.72(8) Å^3; θ-range = 4.09–27.50°; refl. coll./unique = 38859/38859; data/restr./param. = 38859/32/2236; $R1$ [$I > 2\sigma(I)$] = 0.0820, $wR2$ = 0.2283 (all data). Due to severe disordering it was not possible to localize hydrogen atoms at the water molecules. CCDC reference number 202946. See http://www.rsc.org/suppdata/cc/b3/b303172a/ for crystallographic data in CIF or other electronic format.

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