ZINC AND COBALT(II) COMPLEXES OF TRIPODAL NITROGEN LIGANDS OF THE TRIS[2-SUBSTITUTED IMIDAZOL-4(5)-YL]-PHOSPHANE TYPE. BIOMIMETIC HYDROLYSIS OF AN ACTIVATED ESTER

Peter C. KUNZ[1,*] and Wolfgang KLÄUI[2]

Heinrich-Heine-Universität, Institut für Anorganische Chemie, Universitätsstr. 1, D-40225 Düsseldorf, Germany; e-mail: [1] peter.kunz@uni-duesseldorf.de, [2] klaeui@uni-duesseldorf.de

Received December 1, 2006
Accepted February 11, 2007

Dedicated to Dr Karel Mach on the occasion of his 70th birthday in recognition of his outstanding contributions to the area of organometallic synthesis and catalysis.

Novel tris[2-substituted imidazol-4(5)-yl]phosphane (4-TIP^R) ligands **2b** (R = Ph) and **2c** (R = tBu) were prepared as model ligands for the tris(histidine) motif found in many zinc enzymes. They readily form cobalt and zinc nitrato and chloro complexes in protic solvents. The steric requirements of the substituents R in 4(5)-position of the 4-TIP^R ligands (R = iPr (**2a**), Ph (**2b**), tBu (**2c**)) is discussed on the basis of their UV/VIS spectra. Zinc complexes of **2a** and **2c** were studied due to their ability to promote the hydrolysis of the activated ester 4-nitrophenyl pyridine-2-carboxylate (*p*Npic).

Keywords: Bioinorganic chemistry; Enzyme models; N ligands; Tripodal ligands; Water solubility; Zinc; Cobalt; Phosphines; Imidazoles; UV spectroscopy.

Zinc is found in many mono- and dinuclear metalloenzymes[1]. Carbonic anhydrase (CA) was the first identified zinc enzyme. The active site of this lyase is formed by the three histidine residues His-94, His-96 and His-119. CA is an example of an enzyme in which zinc is coordinated tetrahedrally by the tris(histidine) motif. This zinc binding motif is also found in the family of metzincins. Due to their proteolytic potential these enzymes play key roles in tumour genesis, tumour invasion, metastasis, inflammatory, rheumatoid arthritis and many other processes[2].

Since the discovery of tris(pyrazolyl)borato (Tp) ligands ("scorpionates") by Trofimenko in the early 60's, tripodal nitrogen donor ligand have attracted chemists in the organometallic and bioinorganic field. These ligands have been used since to stabilise metal complexes in catalytic reaction cycles and in the modelling of active sites in metalloenzymes[3,4]. The

Collect. Czech. Chem. Commun. 2007, Vol. 72, No. 4, pp. 492–502

doi:10.1135/cccc20070492

'Freiburg enzyme model' and related compounds by Vahrenkamp use Tp-type ligands to model the tris(histidine) motif found in many zinc-binding enzymes[5]. An inherent problem of this class of tripodal ligands is the instability of the B–N bonds to hydrolysis. Tris(imidazolyl)phosphanes seem to be suitable N ligands as models for the active site of the facial His triad in zinc-containing enzymes. The tris(imidazol-2-yl)phosphane (2-TIP) ligands usually bear alkyl and/or aryl substituents in 1- and 4- or 4- and 5-positions and show only poor solubility in protic solvents[6,7].

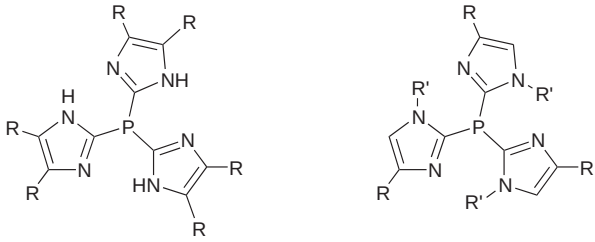


CHART 1
Tris(imidazol-2-yl)phosphanes (2-TIP^{R})

We therefore developed recently the tripodal tris(2-isopropylimidazol-4(5)-yl)phosphane ligand (Chart 1), which showed sufficient solubility in aqueous methanolic solutions and is stable towards hydrolysis[8].

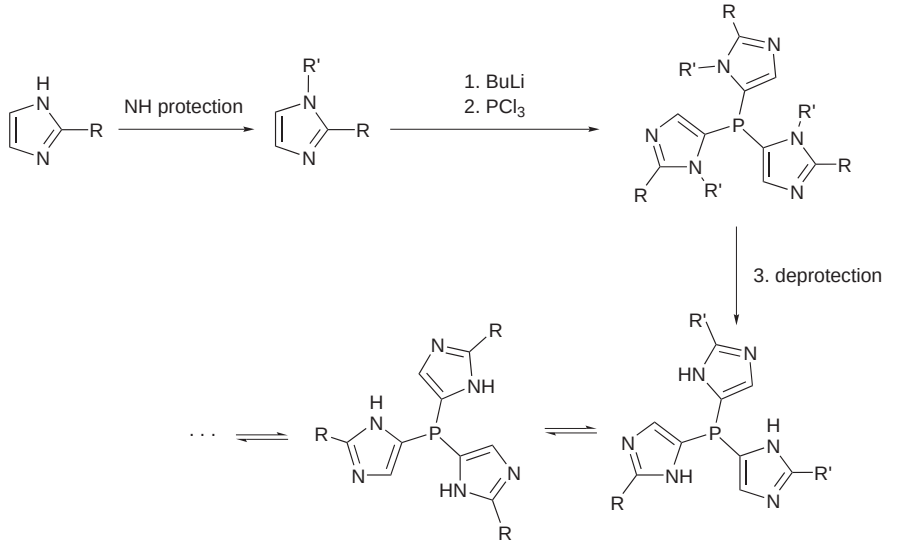
The 4-TIP^{R} (R = iPr) ligand forms octahedral as well as tetrahedral metal complexes of composition [(4-TIP^{iPr})M(X)]X, sometimes with metal-coordinated solvent molecules. The coordination geometry was shown to depend on the nature of the anion X. The substituent in 4(5)-position should also influence the coordination number and geometry. Therefore we designed ligands of the 4-TIP type with substituents R varying in bulkiness.

RESULTS AND DISCUSSION

Synthesis and Spectroscopic Characterisation

The general synthesis of ligands of the 4-TIP^{R} type is shown in Scheme 1. The easily removable diethoxymethyl group has been proven as ideal protective group for 2-isopropylimidazol[8]. Unfortunately, neither 2-phenylimidazole nor 2-*tert*-butylimidazole could be protected using this group. Both the imidazoles were protected by alkoxymethyl groups according to the procedure described by Breslow for 1-(ethoxymethyl)-2-phenylimidazole[9]. In the following step the protected imidazole is lithiated in position

5 and then treated with PCl_3 in THF at –78 °C. Tris(2-phenylimidazol-4(5)-yl)phosphane (4-TIP^{Ph}; **2b**) and tris(2-*tert*-butylimidazol-4(5)-yl)phosphane (4-TIP^{tBu}; **2c**) were isolated as colourless solids after removal of the protective group.



SCHEME 1
Synthesis of the tris[2-substituted imidazol-4(5)-yl]phosphane ligands 4-TIP^{R} (R = iPr (**2a**), Ph (**2b**), tBu (**2c**))

The ^{1}H NMR spectra of the ligands in methanol-d_4 show C_{3v} symmetry. This is explained by fast equilibria of all rotameric and tautomeric forms these ligands can adopt. The aromatic protons in **2b** give two multiplets in the region 7.6–8.2 ppm, the signal of the protons of the imidazolyl rings is found as a doublet at 8.23 ppm ($^3J_{PH}$ = 1 Hz). **2c** just shows two singlets in the ^{1}H NMR. The signal of the *tert*-butyl group shows at δ 2.30 and of the imidazolyl at δ 7.90 ppm. In the ^{31}P{^{1}H} NMR spectra, the ^{31}P signal appears around δ ≈ –80 ppm as a singlet (Table I). The FAB$^+$ mass spectra of **2b** and **2c** show the corresponding peak for the molecular ion at the expected *m/z* value, together with a characteristic fragmentation pattern.

In contrast to the in situ prepared tris[1-(diethoxymethyl)-2-isopropylimidazol-5-yl]phosphane **1a**, the protected tris[1-(alkoxymethyl)-2-substituted imidazol-5-yl]phosphanes **1b** and **1c** could be isolated and characterised. An analogous tris(imidazol-5-yl)phosphane was reported by Bell[10] as ligand for an auranofin analog.

Metal complexes were prepared in high yields by stirring the tris(imidazolyl) ligands **2b** or **2c** with the corresponding metal salts in methanol at ambient temperature. Interestingly, the Co(II) nitrato complex of **2b** was soluble in methanol whereas the corresponding Zn(II) complex **3b** precipitated after a while and could not be redissolved in methanol[11]. The ^{1}H NMR spectrum of freshly prepared **3b** shows two multiplets in the region 8.5–8.7 ppm for the phenyl protons and a doublet at δ 8.84 ppm with a $^3J_{PH}$ coupling constant of 2 Hz for the imidazolyl protons. In the zinc chloro complex of **2c**, the signal of the *tert*-butyl groups is slightly shifted downfield to δ 2.49 ppm upon coordination as is the signal of the imidazolyl protons (doublet at δ 8.43 ppm with $^3J_{PH}$ = 2 Hz). The ^{31}P{^{1}H} NMR signals of the zinc complexes **4** and **6** in methanol-d_4 are shifted to higher field (δ –106 ppm). The NMR spectra of the Co(II) complexes **3** and **5** show extensive paramagnetic broadening.

Table I
^{31}P{^{1}H} NMR chemical shifts (δ, ppm) of protected (**1**) and free (**2**) 4-TIP^R

R	**1**	**2**
iPr	**1a** not isolated	–80 (**2a**)[8]
Ph	–90 (**1b**)	–79 (**2b**)
tBu	–87 (**1c**)	–84 (**2c**)

UV/VIS Spectra of 4-TIP^R Cobalt(II) Complexes

In order to understand the solution behaviour of the zinc complexes and get an image of the species present, we analysed the UV/VIS spectra of the corresponding cobalt(II) complexes. The coordination chemistry of the 'colourless' Zn(II) is well resembled by that of Co(II), sometimes referred to as 'spectroscopic chameleon'. Because of the similar ionic radius and similar coordination chemistry, cobalt(II) has become the substitute for zinc(II) in zinc-containing enzymes (isomorphous substitution), even though detailed structural differences can occur[12].

The UV/VIS spectra of the three ligands 4-TIP^{iPr} (**2a**), 4-TIP^{Ph} (**2b**) and 4-TIP^{tBu} (**2c**) in methanol in the presence of stoichiometric amounts of cobalt(II) nitrate or chloride are shown in Fig. 1. All three chloro complexes show the characteristic absorbance in the region 550–700 nm for tetrahedrally coordinated Co(II) centres. This is in agreement with the tetrahedral

coordination environment in the solid-state structure of the complex [CoCl(4-TIP^{iPr})]Cl·MeOH·2.5H_2O (ref.[8]). The spectra of **2a** and **2b** in the presence of cobalt(II) nitrate show weak absorption in the region 450–550 nm, characteristic of octahedral coordination of the Co(II) centre. This is also in a good agreement with the solid-state structure of the cobalt(II) nitrato complex of 4-TIP^{iPr} (ref.[8]). A single crystal structure determination of the cobalt(II) nitrato complex of 4-TIP^{Ph} could not be obtained at satisfactory *R* values due to twinning of the crystals. Nevertheless, it is evident from the X-ray data, that there are two complexes in the elementary cell of **3**. One complex shows octahedral coordination of the Co(II) by the *N*,*N*′,*N*″-coordinated 4-TIP^{Ph} ligand, a didentate nitrato ligand and a coordinated methanol molecule. The other complex shows a distorted trigonal-bipyramidal coordination without a coordinated solvent molecule (Scheme 2). Interestingly, the UV/VIS spectrum of cobalt(II) nitrate in the presence of 4-TIP^{tBu} shows bands in the region of 550–670 nm with the typical habitus of a tetrahedrally coordinated Co(II) centre. This indicates a sufficient steric pressure of the *tert*-butyl groups to enforce a low coordination number (at least at equilibrium). That behaviour is known in the class of Trofimenko's scorpionate ligands, where *tert*-butyl substituents in position 3 are sometimes referred as tetrahedral enforcers[13].

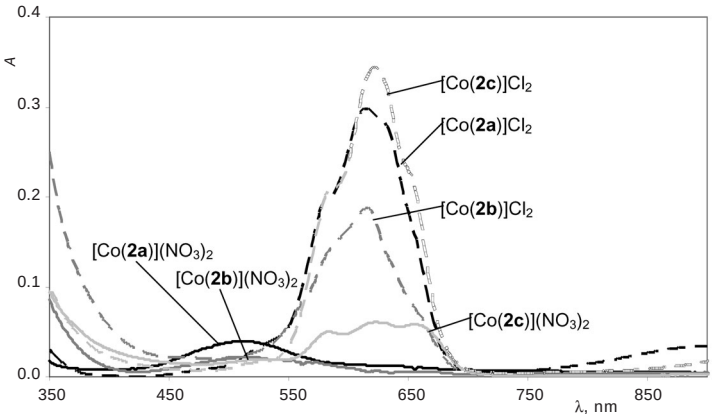
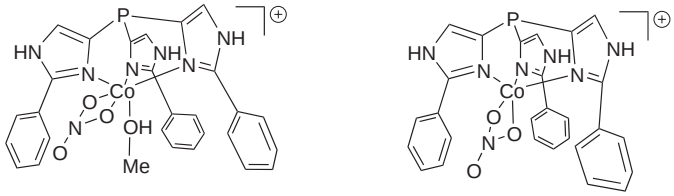


FIG. 1
UV/VIS spectra of 4-TIP^{iPr} (**2a**; black), 4-TIP^{Ph} (**2b**; medium grey) and 4-TIP^{tBu} (**2c**; light grey) in the presence of stoichiometric amounts of cobalt(II) nitrate (solid) or chloride (dashed) in methanol

Therefore, the steric nature of the substituents R in the 4(5)-positions in 4-TIP^{R} can adjust the coordination number of the bound metal. The coordination number is decreased from 6 to 4 as the steric requirement increased in the order iPr < Ph < tBu. It is likely, that by choosing the right substituents formation of a hydrophobic pocket of varying size is possible in complexes of 4-TIP^{R} type ligands.



SCHEME 2
Schematic drawing of the two complex cations found in the elementary cell of the solid **3**

Mimicking Esterase Activity

The zinc nitrato complexes of the 4-TIP^{iPr} and 4-TIP^{tBu} ligands were studied in an esterase model reaction. In addition to hydration of CO_2, the lyase carbonic anhydrase also shows some esterase activity. Thus we investigated the hydrolysis of the model compound 4-nitrophenyl pyridine-2-carboxylate (*p*Npic) in the presence of the nitrato zinc(II) complexes of **2a** and **2c** at various pH. The complexes of **2b** were not considered due to their insufficient solubility in methanol. Since picolinate, the product of hydrolysis, can coordinate to the metal, at least ten-fold excesses of complex to *p*Npic were employed to maintain pseudo-first-order conditions. The observed rate constants were the same whether an isolated complex was used or equimolar amounts of metal salt and ligand. The hydrolysis was performed in 80% ethanol/water mixtures to compare the results with those obtained by Brown on similar tris(imidazol-2-yl)phosphane systems. The observed acceleration of *p*Npic hydrolysis in the presence of **2a** or **2c** and zinc nitrate (Fig. 2) is in the range of that reported for the catalyst systems containing Zn(II) and tris(imidazol-2-yl)phosphane (**7**) or bis(4,5-diisopropylimidazol-2-yl)(imidazol-2-yl)phosphane (**8**)[6d]. Due to the structure of the 4-TIP ligands, the solubility of **2a** and **2c** allowed an increase in water content in the solvent mixture, as expected. So, the hydrolysis was repeated using 50% ethanol/water mixtures (Fig. 3). The reaction rates are very similar, with the ones for hydrolysis in the solvent containing 50% water being slightly lower.

In all cases at pH > 8.0 the rate constant drops drastically (Fig. 2) and approximates the value for the spontaneous hydrolysis. In general, this is due to the precipitation of $Zn(OH)_2$. But as no precipitate was observed, we assume the formation of soluble but inert hydroxo-bridged oligomers.

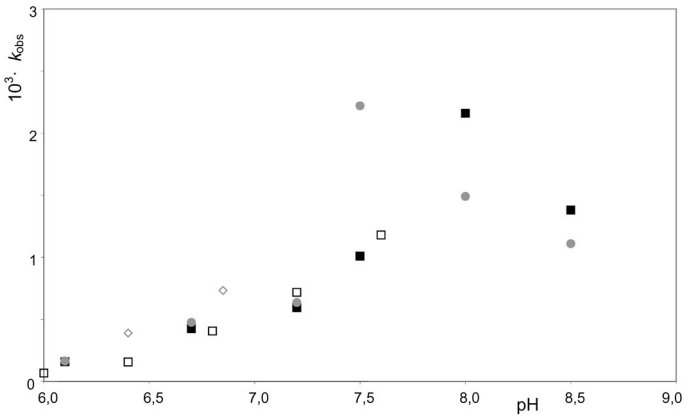


FIG. 2

Pseudo-first-order k_{cat}^{obs} values for the hydrolysis of *p*Npic by **2a** (■) and **2c** (●) in the presence of zinc(II) nitrate, compared to **7** (□) and **8** (◇) in 80% ethanol/water (c(*p*NPic) = 5×10^{-5} mol l^{-1}, c(cat.) = 5×10^{-4} mol l^{-1}, c(buffer) = 0.05 mol l^{-1}, $c(NaNO_3)$ = 0.05 mol l^{-1}, T = 20 ± 0.1 °C)

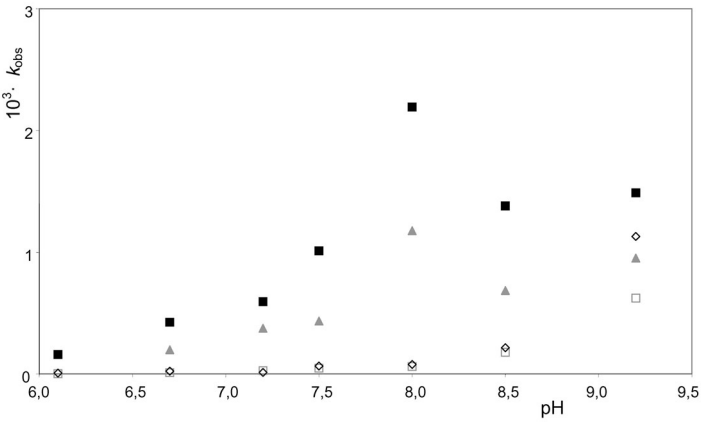


FIG. 3

Comparison of the hydrolysis of *p*Npic in 80% ethanol/water (◇ spontaneous, ■ [Zn(**2a**)]$(NO_3)_2$) and 50% ethanol/water (□ spontaneous, ▲ [Zn(**2a**)]$(NO_3)_2$)

CONCLUSION

We have synthesised two new representatives of the tris[2-substituted imidazol-4(5)-yl]phosphane ligand class: tris(2-phenylimidazol-4(5)-yl)-phosphane 4-TIP^{Ph} (**2b**) and tris(2-*tert*-butylimidazol-4(5)-yl)phosphane 4-TIP^{tBu} (**2c**). They show good solubility in protic solvents as well as in water/alcohol mixtures with the exception of the zinc(II) complex **4**. As shown by UV/VIS spectroscopy the hydrophobic cavity built by the substituents R in 4-TIP^{R} influences the coordination number and geometry around the coordinated metal ion. The coordination number of cobalt(II) is decreased from 6 to 4 as the steric requirement increased in the order iPr < Ph < tBu. The zinc(II) chloro and nitrato complexes of **2a** and **2c** show some esterase activity. The solubility of the zinc(II) complexes of **2a** allowed a decrease in the alcohol content of the reaction mixture compared with the analogous tris(imidazol-2-yl)phosphane complexes. Albeit these compounds are good structural models for active sites of tris(histidine)zinc enzymes, their catalytical activity is rather disappointing. At pH > 8 the esterase activity of the zinc(II) complexes of **2a** and **2c** drops drastically. The fate of these complexes at elevated pH is currently investigated.

EXPERIMENTAL

General

The compounds 2-*tert*-butylimidazole[14] and 1-(ethoxymethyl)-2-phenylimidazole[9] were synthesised according to published procedures. All other reagents were commercial samples and were used as received. ^{1}H and ^{31}P NMR spectra (δ, ppm; *J*, Hz) were recorded with a Bruker DRX 200 spectrometer. The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were calibrated against the proton and the carbon signals of the solvents as internal references ($CDCl_3$: δ_H 7.30 ppm and δ_C 77.0 ppm; methanol-d_4: δ_H 3.30 ppm (quintuplet) and δ_C 49.1 ppm), while the $^{31}P\{^{1}H\}$ NMR spectra were referenced to external 85% H_3PO_4. The EI mass spectra were recorded with a double focussing mass spectrometer, Varian MAT model 311 A, ionisation energy 70 eV. The FAB mass spectra were recorded with a Finnigan mass spectrometer, model MAT 8200, in an 3-nitrobenzyl alcohol (NBA) matrix. Infrared spectra were recorded with a Bruker IFS 66 FT-IR spectrometer.

Kinetic Measurements

The rate of appearance of 4-nitrophenol or 4-nitrophenolate was followed by monitoring the increase in absorbance at 320 or 405 nm depending on the pH of the buffered solution with an Analytik Jena Specord S 100 UV/VIS spectrophotometer at 20.0 ± 0.1 °C. The pH was maintained using the non-coordinating buffers 3-(*N*-morpholino)propanesulfonic acid (MOPS, pH 6.1–8.0)[15] and 2-(*N*-cyclohexylamino)ethane sulfonic acid (CHES, pH 8.5–9.2)[15], c = 0.05 mol l^{-1} and the ionic strength was $I(NaNO_3)$ = 0.05 mol l^{-1}. pH was measured using a Metrohm 744 pH meter with Metrohm pH-electrode 6.0232.100 (3 M KCl) calibrated with

standard solutions of pH 4 and 9 (Riedel–de Haën), no correction for solvent mixtures was applied. Such corrections are small and amount to a reduction from the observed readings by ~0.2 units[16]. Reactions were monitored under pseudo-first-order conditions with excess of complex, $c = 5 \times 10^{-4}$ mol l^{-1}, or equimolar ligand and zinc(II) salt. The pseudo-first-order rate constants (k_{obs}) were determined by NLLSQ fitting of the absorbance versus time traces to a standard exponential model implemented in the software Aspect Plus (*Spektralanalytische Software* **1997**, Analytik Jena). All observed rate constants were determined at least in duplicate.

Tris[1-(ethoxymethyl)-2-phenylimidazol-5-yl]phosphane (**1b**)

To a solution of 5.0 g (24 mmol) of 1-(ethoxymethyl)-2-phenylimidazole in 100 ml of absolute THF were added 17 ml (27 mmol) of 1.6 M butyllithium in hexane at –78 °C. The solution was stirred at –78 °C for 30 min and additionally at room temperature for 30 min. After cooling to –78 °C, 1.49 ml (16.7 mmol) of PCl_3 in 10 ml of absolute THF was added. The reaction mixture was kept at –78 °C for 1 h. The solvent was removed in vacuo and the residue was dissolved in 100 ml CH_2Cl_2. To the white suspension, 50 ml of concentrated aqueous ammonia were added, the organic layer separated, washed with water and dried over anhydrous $MgSO_4$. The solvent was removed in vacuo and the oily residue recrystallised from toluene (2.1 g, 50%). ^{1}H NMR (200 MHz, $CDCl_3$): 0.89 t, 9 H (J = 7, $CH_2C\mathbf{H}_3$); 3.27 q, 6 H (J = 7, $C\mathbf{H}_2CH_3$); 5.37 d, 6 H (J = 7, CH_2); 7.18 s, 3 H (H_{im}); 7.3–7.4 m, 9 H (Ph); 7.6–7.7 m, 6 H (Ph). $^{31}P\{^1H\}$ NMR (200 MHz, $CDCl_3$): –90. EI MS (70 eV, 250 °C), *m/z* (%): 634 (18) $[M]^+$. For $C_{36}H_{39}N_6O_3P$ (634.7) calculated: 68.0% C, 6.3% H, 13.2% N; found: 67.9% C, 6.1% H, 13.2% N.

Tris(2-phenylimidazol-4(5)-yl)phosphane (4-TIP^{Ph}) (**2b**)

1.28 g (2.00 mmol) of **1b** were heated to reflux in 40 ml of a 1:1 mixture of ethanol and 20% HCl for 5 h. The solution was poured into 100 ml of 1 M KOH solution, the precipitate was filtered and dried in vacuo. Yield 0.81 g (88%) of white powder. ^{1}H NMR (200 MHz, methanol-d_4): 7.6–7.8 m, 9 H (Ph); 8.1–8.2 m, 6 H (Ph); 8.23 d, 3 H (J_{PH} = 1, H_{im}). $^{31}P\{^1H\}$ NMR (200 MHz, methanol-d_4): –79. FAB^+ MS (NBA-matrix), *m/z* (%): 460 (39) $[M]^+$. For $C_{27}H_{21}N_6P{\cdot}3HCl{\cdot}6H_2O$ (460.5) calculated: 47.8% C, 5.4% H, 12.4% N; found: 47.6% C, 5.1% H, 12.2% N.

2-*tert*-Butyl-1-(methoxymethyl)imidazole

A mixture of 12.4 g (100 mmol) of *tert*-butylimidazole and 2.4 g (100 mmol) of NaH was stirred in THF till gas evolution ceased. 0.8 g (0.1 mol) of chloromethyl methyl ether in THF were added dropwise and the reaction mixture was stirred overnight, filtered and the solvent removed in vacuo. Distillation (46 °C, 2.0×10^{-2} mbar) yielded 33 g (71%) of the product as a colourless oil. ^{1}H NMR (200 MHz, $CDCl_3$): 1.35 s, 9 H ($C(CH_3)_3$); 3.23 s, 3 H (OCH_3); 5.23 s, 2 H (CH_2); 6.80 d, 1 H (H_{im}); 6.82 d, 1 H (H_{im}).

Tris[2-*tert*-butylimidazol-5-yl-1-(methoxymethyl)]phosphane (**1c**)

To a solution of 4.0 g (24 mmol) of 2-*tert*-butyl-1-(methoxymethyl)imidazole in 100 ml of absolute THF were added 17 ml (27 mmol) of 1.6 M butyllithium in hexane at –78 °C. The

solution was stirred at –78 °C for 30 min and additionally at room temperature for 30 min. After cooling to –78 °C, 1.49 ml (16.7 mmol) of PCl_3 in 10 ml of absolute THF were added. The reaction mixture was kept at –78 °C for 1 h. The solvent was removed in vacuo and the residue was dissolved in 100 ml of CH_2Cl_2. To the white suspension, 50 ml of concentrated ammonia were added, the organic layer was separated, washed with water and dried over anhydrous $MgSO_4$. The solvent was removed in vacuo and the oily residue redissolved in 100 ml of hexane. The product (2.0 g, 47%) crystallised after a few days. ^{1}H NMR (200 MHz, $CDCl_3$): 1.42 s, 27 H ($C(CH_3)_3$); 3.15 s, 9 H (OCH_3); 5.36 d, 6 H ($^4J_{PH}$ = 2, CH_2); 6.79 s, 3 H (H_{im}). $^{31}P\{^1H\}$ NMR (200 MHz, methanol-d_4): –87. EI MS (70 eV, 250 °C), *m/z* (%): 532 (7) $[M]^+$.

Tris(2-*tert*-butylimidazol-4(5)-yl)phosphane (4-TIP^{tBu}) (**2c**)

1.03 g (1.93 mmol) of **1c** were heated to reflux in 40 ml of a 1:1 mixture of ethanol and 20% HCl for 5 h. The solution was poured into 100 ml of 1 M KOH solution, the precipitate was filtered and dried in vacuo. Yield 0.65 g (84%) of white powder. ^{1}H NMR (200 MHz, methanol-d_4): 2.30 s, 27 H ($C(CH_3)_3$); 7.90 s, 3 H (H_{im}). $^{31}P\{^1H\}$ NMR (200 MHz, methanol-d_4): –84. FAB$^+$ MS (NBA), *m/z* (%): 401 (55) $[M]^+$, 277 (100) $[M - im^{tBu}]^+$.

$[Co(MeOH)(NO_3)(4\text{-}TIP^{Ph})]NO_3$ (**3**)

A methanolic solution of 0.23 g (50 mmol) of **2b** and 0.15 g (50 mmol) $Co(NO_3)_2 \cdot 6H_2O$ was stirred for 2 h and then layered with diethyl ether. The product (0.23 g, 85%) was obtained as violet crystals. FAB$^+$ MS (NBA-matrix), *m/z* (%): 581 (100) $[Co(NO_3)(4\text{-}TIP^{Ph})]^+$, 534 (9) $[Co(4\text{-}TIP^{Ph}) - H]^+$. For $C_{27}H_{21}CoN_8O_6P \cdot 2MeOH$ (707.5) calculated: 49.2% C, 4.1% H, 15.9% N; found: 49.3% C, 3.9% H, 15.8% N.

$[Zn(4\text{-}TIP^{Ph})](NO_3)_2$ (**4**)

A methanolic solution of 0.23 g (50 mmol) of **2b** and 148 mg (50.0 μmol) $Zn(NO_3)_2 \cdot 6H_2O$ was stirred for 2 h. During this time a white precipitate was formed. The suspension was stirred for additional 2 h, filtered and the white solid was dried in vacuo. Yield 0.27 g (81%). ^{1}H NMR (200 MHz, methanol-d_4): 8.5 m, 9 H (Ph); 8.7 m, 6 H (Ph); 8.84 d, 3 H (J_{PH} = 2, H_{im}). $^{31}P\{^1H\}$ NMR (200 MHz, methanol-d_4): –106. For $C_{27}H_{21}N_8O_6PZn \cdot MeOH$ (681.9) calculated: 49.3% C, 3.7% H, 16.4% N; found: 49.3% C, 3.4% H, 16.1% N.

$[Co(4\text{-}TIP^{tBu})]Cl_2$ (**5**)

A methanolic solution of 0.22 g (50 mmol) of **2c** and 65 mg (50 mmol) $CoCl_2$ was stirred for 2 h and layered with diethyl ether. The product (0.20 g, 70%) was obtained as deep blue crystals. FAB$^+$ MS (NBA), *m/z* (%): 494 (100) $[CoCl(4\text{-}TIP^{tBu})]^+$. For $C_{22}H_{37}Cl_2CoN_6OP$ (562.4) calculated: 47.0% C, 6.6% H, 14.9% N; found: 46.3% C, 6.7% H, 14.6% N.

$[Zn(4\text{-}TIP^{tBu})]Cl_2$ (**6**)

A methanolic solution of 0.20 g (50 mmol) of **2c** and 68 mg (50 mmol) $ZnCl_2$ was stirred for 2 h and layered with diethyl ether. The product (0.11 g, 40%) was obtained as colourless crystals. ^{1}H NMR (200 MHz, methanol-d_4): 2.49 s, 27 H ($C(CH_3)_3$); 8.43 d, 3 H (J_{PH} = 2, H_{im}).

$^{31}P\{^{1}H\}$ NMR (200 MHz, methanol-d_4): –106. FAB^+ MS (NBA), *m/z* (%): 499 (100) $[ZnCl(4\text{-}TIP^{tBu})]^+$. For $C_{22}H_{37}Cl_2N_6OPZn$ (562.4) calculated: 46.5% C, 6.6% H, 14.8% N; found: 46.7% C, 7.0% H, 12.7% N.

We thank the Deutsche Forschungsgemeinschaft (DFG) and the Fonds der Chemischen Industrie for financial support.

REFERENCES AND NOTES

1. a) Kaim W., Schwederski B.: *Bioanorganische Chemie*, 3rd ed. B. G. Teubner, Stuttgart 2004; b) Bertini I., Sigel A., Sigel H. (Eds): *Handbook on Metalloproteins*. Marcel Dekker, New York 2001.
2. Burzlaff N. in: *Concepts and Models in Bioinorganic Chemistry* (H.-B. Kraatz and N. Metzler-Nolte, Eds), Chap. 17; and references therein. Wiley-VCH, Weinheim 2006.
3. Trofimenko S.: *Scorpionates – The Coordination Chemistry of Polypyrazolylborate Ligands*; and references therein. Imperial College Press, London 1999.
4. a) Parkin G.: *Chem. Rev.* **2004**, *104*, 699; b) Parkin G.: *J. Chem. Soc., Chem. Commun.* **2000**, 1971.
5. a) Ibrahim M., Perez Olmo C., Tekeste T., Seebacher J., He G., Calvo M. A. J., Boehmerle K., Steinfeld G., Brombacher H., Vahrenkamp H.: *Inorg. Chem.* **2006**, *45*, 7493; b) Perez Olmo C., Boehmerle K., Steinfeld G., Vahrenkamp H.: *Eur. J. Inorg. Chem.* **2006**, 3869; c) Vahrenkamp H.: *Acc. Chem. Res.* **1999**, *32*, 589.
6. a) Kimblin C., Allen W. E., Parkin G.: *J. Chem. Soc., Chem. Commun.* **1995**, 1813; b) Kimblin C., Murphy V. J., Parkin G.: *J. Chem. Soc., Chem. Commun.* **1996**, 235; c) Kimblin C., Bridgewater B. M., Churchill D. G., Parkin G.: *J. Chem. Soc., Dalton Trans.* **2000**, 2191; d) Kimblin C., Murphy V. J., Hascall T., Bridgewater B. M., Bonanno J. B., Parkin G.: *Inorg. Chem.* **2000**, *39*, 967; e) Kläui W., Piefer C., Rheinwald G., Lang H.: *Eur. J. Inorg. Chem.* **2000**, 1549.
7. a) Huguet J., Brown R. S.: *J. Am. Chem. Soc.* **1980**, *102*, 7571; b) Read R. J., James M. N. G.: *J. Am. Chem. Soc.* **1981**, *103*, 6947; c) Brown R. S., Curtis N. J., Huguet J.: *J. Am. Chem. Soc.* **1981**, *103*, 6953; d) Brown R. S., Salmon D., Curtis N. J., Kusuma S.: *J. Am. Chem. Soc.* **1982**, *104*, 3188; e) Brown R. S., Zamkani M., Cocho J. L.: *J. Am. Chem. Soc.* **1984**, *106*, 5222; f) Ball R. G., Brown R. S., Cocho J. L.: *Inorg. Chem.* **1984**, *23*, 2315.
8. Kunz P. C., Reiss G. J., Frank W., Kläui W.: *Eur. J. Inorg. Chem.* **2003**, 3945.
9. Breslow R., Hunt J. T., Smiley R., Tarnowski T.: *J. Am. Chem. Soc.* **1983**, *105*, 5337.
10. Bell R. A., Lock C. J. L., Scholten C., Valliant J. F.: *Inorg. Chim. Acta* **1998**, 137.
11. The poor solubility of the zinc complex of **2b** is not understood, especially as the solubility of the corresponding Co(II) complex is good. We have not been able to recrystallise **4**.
12. Kremer-Aach A., Kläui W., Bell R., Strerath A., Wunderlich H., Mootz D.: *Inorg. Chem.* **1997**, *36*, 1552.
13. Trofimenko S., Calabrese J. C., Thompson J. S.: *Inorg. Chem.* **1987**, *26*, 1507.
14. Akiyama M., Hara Y., Tanabe M.: *J. Chem. Soc., Perkin Trans. 2* **1978**, 288.
15. Yu Q., Kandegedara A., Xu Y., Rorabacher D. B.: *Anal. Biochem.* **1997**, *253*, 50.
16. Bates R. G., Paabo M., Robinson R. A.: *J. Phys. Chem.* **1963**, *67*, 1833.