Monoanionic *N,N,O*-Scorpionate Ligands and their Iron(II) and Zinc(II) Complexes: Models for Mononuclear Active Sites of Non-Heme Iron Oxidases and Zinc Enzymes

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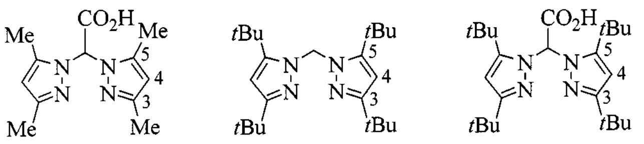
The chemical behavior of two bis(3,5-dialkylpyrazol-1-yl)acetic acids and their coordination properties towards $ZnCl_2$ and $FeCl_2$ was studied. Reaction of bis(3,5-dimethylpyrazol-1-yl)acetic acid (bdmpza) (**1**) with $ZnCl_2$ and $FeCl_2$ gave the 2:1 complexes [$(bdmpza)_2Zn$] (**4**) and [$(bdmpza)_2Fe$] (**5**). Crystal structures of both complexes were obtained. In contrast, the sterically more hindered ligand bis(3,5-di-*tert*-butylpyrazol-1-yl)acetic acid (bdtbpza) (**3**) coordinates only once to zinc(II) resulting in the complex [(bdtbpza)ZnCl] (**6**). This provides a structural model complex for the active sites of zinc enzymes such as thermolysin or carboxypeptidase. The good agreement with these active sites was demonstrated by a crystal structure of **6**. To the best of our knowledge, this is the first report of zinc complexes with a monoanionic *N,N,O*-tridentate ligand using a carboxylate *O*-donor. Substitution of benzylthiolate for the chloride ligand **6** yielded [(bdtbpza)Zn(SCH_2Ph)] (**8**) indicating that the bulky *tert*-butyl groups do not prevent access to the zinc atom. Reaction of bdtbpza (**3**) with $FeCl_2$ led to [(bdtbpza)FeCl] (**7**), which might serve as a structural model complex for the active sites of mononuclear non-heme iron oxidases and oxygenases such as IPNS, DAOCS or CAS.

Introduction

In recent years, there has been a significant progress in the structural characterization of mononuclear non-heme iron enzymes involved in dioxygen activation.[1] The facial motif of the three metal binding amino acids histidine, histidine and aspertate or glutamate is thought to be essential in many of these enzymes.[2] This has caused a growing interest in model complexes for the active sites of these enzymes. The so called facial 2-His-1-carboxylate triad, a term introduced by Que Jr.,[2] is found, for example, in enzymes such as tyrosine hydroxylase (TyrH),[3] 2,3-dihydroxy-biphenyl 1,2-dioxygenase (extradiol catechol dioxygenase) (BphC),[4] isopenicillin N synthase (IPNS)[5−7] or α-keto-glutarate-dependent enzymes such as deacetoxycephalosporine C synthase (DAOCS)[8] and clavaminic acid synthase (CAS).[9]

Due to the lack of suitable monoanionic *N,N,O* ligands that mimic this facial triad, model complexes with *N,N,N* tripod ligands were used to study these enzymatic reactions. The work of Que, Kitajima or Moro-oka often focused on tris(pyrazol-1-yl)borate (Tp) and tris(2-pyridylmethyl)amine (TPA) ligands.[10]

Furthermore, zinc complexes with such *N,N,O* ligands could serve as models for the active site of several zinc enzymes, binding the metal with two histidines and one glutamate. Examples are carboxypeptidase A and thermolysin.[11] Bioinorganic experiments with zinc complexes by Vahrenkamp, Moro-oka and Parkin are again often based on *N,N,N* ligands such as Tp and TPA.[12] Parkin accessed *N,N,O* model complexes indirectly by insertion of formaldehyde or carbon dioxide into a borohydride bond of zinc bis(pyrazol-1-yl)hydroborate complexes.[13,14] Recently, Carrano published the scorpionate ligand (3-*tert*-butyl-2-hydroxy-5-methylphenyl)-bis(3,5-dimethylpyrazol-1-yl)-methane to generate model complexes of zinc enzymes.[15,16] Instead of a carboxylate *O*-donor, this ligand contains a phenolate *O*-donor. Last year Otero et al. introduced for the first time with bis(3,5-dimethylpyrazol-1-yl)acetate (bdmpza, **1**) (Figure 1) and the resulting niobium complex [$NbCl_2$(bdmpza)(PhCCMe)], a scorpionate ligand with a carboxylate and two pyrazole donor groups.[17]



bdmpza (1) **bdtbpzm (2)** **bdtbpza (3)**

Figure 1. Bispyrazol-1-yl ligands

Herein we report on model complexes of zinc and iron with the scorpionate ligand bis(3,5-dimethylpyrazol-1-yl)acetate (bdmpza, **1**) and the new, sterically more hindered bis(3,5-di-*tert*-butylpyrazol-1-yl)acetate (bdtbpza, **3**).

Results

In our quest to find suitable *N,N,O* ligands as models for the active sites of the facial 2-His-1-carboxylate triad in iron- and zinc-containing enzymes, scorpionate ligands like bis(3,5-dimethylpyrazol-1-yl)acetate (bdmpza, **1**) seemed to be suitable as a mimic for this facial triad.

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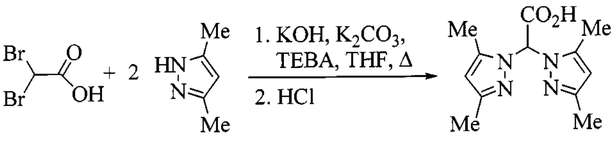
In addition to the multistep ligand synthesis published by Otero et al., we found a simple one-step synthesis for bdmpza (**1**) starting from commercially available reagents [Equation (1)].



(1)

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Treatment of dibromoacetic acid with two equivalents of 3,5-dimethylpyrazole and an excess of potassium hydroxide, potassium carbonate and a small portion of phase-transfer catalyst gave bdmpza (**1**) in reasonable yield. Unreacted 3,5-dimethylpyrazole could be recycled by extraction with diethyl ether at neutral pH value. The ^1H and ^{13}C NMR spectra exhibit resonances similar to those reported by Otero et al. for 0.25 [$\{Li(H_2O)(bdmpza)\}_4$].[17] Compound **1** is slightly soluble in water. In D_2O a resonance $\delta(^1H) = 14.02$ was detected that disappeared after 30 minutes and was assigned to the carboxylate proton.

Reaction of bdmpza (**1**) with the biologically relevant metals iron and zinc afforded the 2:1 complexes **4** and **5**. The double coordination of bdmpza to the metals demonstrated too small a steric hindrance of the ligand bdmpza (**1**). Even equimolar amounts of bdmpza (**1**), base and water-free $ZnCl_2$ or $FeCl_2$ yielded only coordination compounds with two scorpionate ligands bound to the metals. The target compounds [(bdmpza)ZnCl] and [(bdmpza)FeCl] could not be detected. The formation of small amounts of them should be detectable by MS from the typical isotopic fingerprint of the chlorine atom.

The infrared spectra of both complexes [$(bdmpza)_2Zn$] (**4**) and [$(bdmpza)_2Fe$] (**5**) show an intense $\nu_{as}(CO_2^-)$ absorption at 1659 cm^{-1} and medium intensity bands at 1558 cm^{-1} due to $\nu(C{=}N)$. These values fit those reported for the niobium complex [$NbCl_2(bdmpza)(PhCCMe)$].[17] Complex **4** was characterized spectroscopically. Due to four equivalent pyrazolyl rings, only one set of resonances was detected for these rings. For the paramagnetic complex **5** a ^1H NMR spectrum was recorded that shows four single signals at $\delta(^1H) = 1.2$, 7.0, 14.4 and 55.7. These resonances were assigned to H^4 of the pyrazolyl groups, the two methyl groups and the proton at the bridging carbon atom, respectively.

The iron compound **5** is stable and can be handled in solution for short periods of time in air. Attempts to exchange one of the bdmpza ligands in **5** with a thiolate ligand have not been successful. X-ray structure determinations of the complexes [$(bdmpza)_2Zn$] (**4**) and [$(bdmpza)_2Fe$] (**5**) finally confirmed their identity (Figure 2 and 3). Selected distances and angles are summarized in Table 1.

The coordination spheres around the zinc and iron atoms are almost octahedral with the scorpionate "clamp" causing a deviation of 4−6° from the 90° angle. The good correspondence of both structures in distances and angles emphasizes the similarity of zinc(II) and iron(II) according to their coordination reactions.

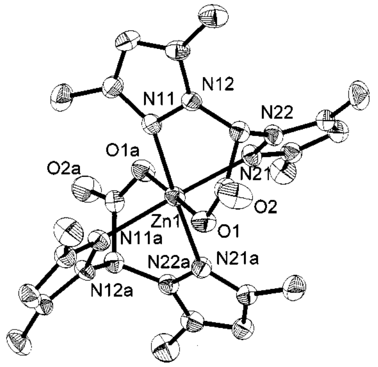


Figure 2. Molecular structure of [$(bdmpza)_2Zn$] (**4**); thermal ellipsoids are drawn at the 50% probability level

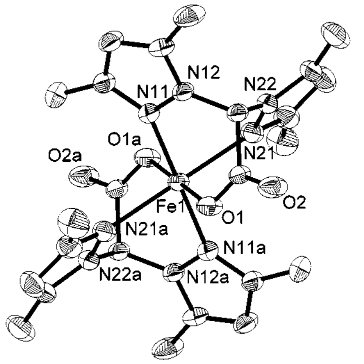


Figure 3. Molecular structure of [$(bdmpza)_2Fe$] (**5**); thermal ellipsoids are drawn at the 50% probability level

Table 1. Selected distances and angles of complexes 4 and 5

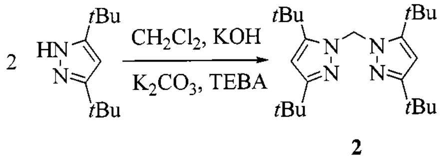
Distance [Å]	4	5	Angle [°]	4	5
M−N(11)	2.178(3)	2.169(3)	N(11)−M−N(21)	84.23(12)	84.05(10)
M−N(21)	2.180(3)	2.212(3)	O(1)−M−N(11)	84.42(11)	84.35(10)
M−O(1)	2.119(3)	2.080(3)	O(1)−M−N(21)	86.12(10)	86.36(11)

The chemical workup of iron(II) compounds under anaerobic conditions is much more difficult than with zinc complexes, and the NMR analyses are restricted to paramagnetic ^1H NMR spectroscopy because of the high-spin character. Therefore, the chemical similarity is useful to test possible synthetic routes firstly with zinc(II) and to later transfer this knowledge to reactions with iron(II). One might say that the zinc(II) serves as a "Trojan Horse".

The former studies of Moro-oka et al. with model complexes of the trispyrazolylborate ligands $Tp^{tBu,iPr}$ und $Tp^{iPr}{}_2$ have already shown that sterically more hindered pyrazoles can prevent the Tp ligands from coordinating twice to the metal.[10b] We therefore tried to prevent double coordination by introducing substituents R larger than the methyl group at the pyrazole rings.

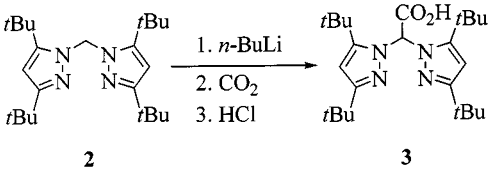
In analogy to the synthesis of bis(3,5-dimethylpyrazol-1-yl)methane,[18] 3,5-*tert*-butylpyrazole reacted with dichloromethane, base and phase-transfer catalyst to give bis(3,5-*tert*-butylpyrazol-1-yl)methane (bdtbpzm) (**2**). 5-*tert*-Butyl-

3-methylpyrazole proved to be unsuitable for this reaction because three inseparable isomers were obtained in the bis(pyrazol-1-yl)methane formation. Therefore, we used a pyrazole with two identical substituents, R, in positions 3 and 5 [Equation (2)].



(2)

As in the synthesis of bdmpza by Otero et al., the scorpionate ligand bis(3,5-di-*tert*-butylpyrazol-1-yl)acetate (bdtbpza) (**3**) could be synthesized from bis(3,5-*tert*-butylpyrazol-1-yl)methane (bdtbpzm) (**2**) by deprotonation with *n*-butyllithium and subsequent addition of carbon dioxide [(Equation (3)].



(3)

The spectroscopic properties of bdtbpza (**3**) are very similar to bdmpza (**1**), with two high-field signals in the ^1H NMR spectrum that are due to the *tert*-butyl groups. Compound **3** was also characterized by an X-ray structure determination (Figure 4 and Table 2).

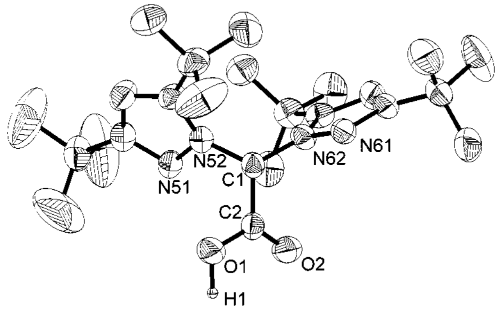


Figure 4. Molecular structure of the bdtbpza ligand (**3**); thermal ellipsoids are drawn at the 50% probability level

Table 2. Selected distances and angles of ligand **3**

Distance [Å]	3	Angle [°]	3
C(1)−C(2)	1.523(7)	O(1)−C(2)−O(2)	124.6(5)
C(2)−O(1)	1.334(5)	C(2)−C(1)−N(52)	112.5(4)
C(2)−O(2)	1.212(6)	C(2)−C(1)−N(62)	112.1(4)
C(1)−N(52)	1.448(7)	N(52)−C(1)−N(62)	116.0(4)
C(1)−N(62)	1.511(6)		

As in the previous reaction with bdmpza (**1**) the ligand bdtbpza (**3**) was treated with base and water-free $ZnCl_2$ or $FeCl_2$. Fortunately, bdtbpza (**3**) coordinates only once to zinc(II) and iron(II), so that compounds [(bdtbpza)ZnCl] (**6**) and [(bdtbpza)FeCl] (**7**) could be isolated, characterized and tested according to their chemical reactivity.

Both complexes display $\nu_{as}(CO_2^-)$ absorptions around 1680 cm^{-1}. The conformation of the complex [(bdtbpza)ZnCl] (**6**) could be confirmed by X-ray structure determination (Figure 5). Selected distances and angles are summarized in Table 3.

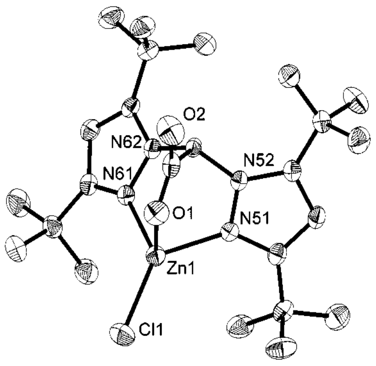


Figure 5. Molecular structure of [(bdtbpza)ZnCl] (**6**); thermal ellipsoids are drawn at the 50% probability level

Table 3. Selected distances and angles of complex **6**

Distance [Å]	6	Angle [°]	6
Zn−N(51)	2.067(3)	N(51)−Zn−N(61)	87.55(8)
Zn−N(61)	2.053(2)	O(1)−Zn−N(51)	93.85(9)
Zn−O(1)	1.990(2)	O(1)−Zn−N(61)	93.21(9)
Zn−Cl(1)	2.170(2)	N(51)−Zn−Cl(1)	130.62(7)
		N(61)−Zn−Cl(1)	127.18(7)
		O(1)−Zn−Cl(1)	114.64(7)

Compared with the structures of **4** and **5**, the angle O−Zn−N in **6** is widened by 8−9°. As expected, the distance Zn−Cl and the angles O−Zn−N and N−Zn−N are in good agreement with those in the structure of [η^3-(HCO_2)$Bp^{tBu,iPr}$]ZnCl published by Parkin.[14] Similar to this structure, the tetrahedral coordination at zinc is distorted, causing the zinc atom to stack only 0.45 Å out of the N(51)−N(61)−Cl(1) plane. Parkin observed a Zn−O distance of 2.065(4) Å. In **6** the equivalent distance is significantly shorter [1.990(2) Å], due to the fact that one of the donor groups is a carboxylate.

[(Bdtbpza)FeCl] (**7**), in contrast to [$(bdmpza)_2Fe$] (**5**), is not stable to air or moisture: it has to be handled under an atmosphere of argon or nitrogen. Although a dimer [$(bdtbpza)FeCl]_2$ cannot be ruled out completely by our data, an [M^+] peak for [(bdtbpza)FeCl] (**7**) can be detected by MS. This indicates that the product [(bdtbpza)FeCl] (**7**) might be isostructural to [(bdtbpza)ZnCl] (**6**). A final answer to this question has to be postponed until a structure determination of **7** is available.

[(Bdtbpza)ZnCl] (**6**) can be treated with benzylthiol and base to yield the benzylthiolate complex [(bdtbpza)-$ZnSCH_2Ph$] (**8**). This reaction is quantitative but it proved to be difficult to remove excess thiol. The spectroscopic properties of **8** are nearly the same as those of **6**, apart from

Table 4. Comparison of Zn−N and Zn−O distances in thermolysin and carboxypeptidase with [(bdmpza)$_2$Zn] (**4**) and [(bdtbpza)ZnCl] (**6**)

	Thermolysin [19]	Carboxypeptidase [20]	[(bdmpza)$_2$Zn]	[(bdtbpza)ZnCl]
d(Zn−N)/Å	2.08, 1.9	2.2	2.178(3)	2.067(3)
d(Zn−N)/Å	2.10, 2.0	2.2	2.180(3)	2.053(2)
d(Zn−O)/Å	2.08, 1.9	2.2	2.119(3)	1.990(2)

additional ^{1}H and ^{13}C NMR spectroscopic signals due to the benzylthiolate ligand. Particularly characteristic for this thiolate ligand is a single resonance at $\delta(^1H) = 3.93$, assigned to the methylene group. A $\nu_{as}(CO_2^-)$ absorption was found at 1677 cm^{-1} in the IR spectrum.

Discussion

The aim of the experiments was to create new structural model complexes for mononuclear non-heme iron oxidases and zinc enzymes. As shown in Table 4 and 5, the distances of the M−N and M−O bonds in [(bdmpza)$_2$Zn] (**4**) and [(bdmpza)$_2$Fe] (**5**) are in good agreement with those of the active sites of thermolysin,[19] carboxypeptidase,[20] IPNS,[5−7] DAOCS[8] and CAS.[9]

Table 5. Comparison of Fe−N and Fe−O distances in IPNS and DAOCS with [(bdmpza)$_2$Fe] (**5**)

	IPNS [6][7]	DAOCS [8]	CAS [9]	[(bdmpza)$_2$Fe]
d(Fe−N)/Å	2.19, 2.09	2.2	2.15, 2.14, 2.25	2.169(3)
d(Fe−N)/Å	2.20, 2.24	2.2	2.12, 2.12, 2.28	2.212(3)
d(Fe−O)/Å	2.06, 2.09	2.2	2.06, 2.07, 2.16	2.080(3)

These data already show that sterically more hindered derivatives of bispyrazolyl acetate should be suitable ligands for model complexes. By using the new ligand bdtbpza (**3**) we implemented this steric hindrance.

With [(bdtbpza)ZnCl] (**6**) a tetrahedral zinc complex with a monoanionic *N,N,O*-tridentate ligand using a carboxylate *O*-donor was synthesized for the first time. A comparison of the X-ray structure determination of **6** with the coordination environment of the enzymes, according to the distances Zn−N and Zn−O (Table 4) indicates their significance as structural models for these active sites. [(Bdtbpza)ZnCl] (**6**) might be the best structural analogue for the enzymes thermolysin and carboxypeptidase.

For future biomimetic studies, a coordination of possible enzymatic substrates to the bdmpza model complexes is essential. In the case of model complexes for the active site of thermolysin or carboxypeptidase, this could be a small peptide. For models of IPNS or α-ketoglutarate-dependent enzymes as CAS or DAOCS, this might be a thiolate or α-ketoglutarate or even a dioxygen. The reactivity of **6** towards an exchange of the chloro ligand by a thiolate clearly shows the potential of the chloro complexes **6** and **7** in the synthesis of zinc(II) and iron(II) model complexes. Therefore, our future work will focus on the synthesis of model complexes for non-heme iron enzymes activating dioxygen, such as IPNS, as well as their chemical reactivity.

As shown recently by Moro-oka et al., the steric hindrance of a Tp^{tBu,iPr} ligand might prevent access of substrates to the metal of the complexes.[10c] Thus, the model complex [Tp^{tBu,iPr}Fe^{II}(O$_2$CMe)] shows no affinity to O_2, in contrast to the sterically less-hindered [Tp$^{iPr}{}_2$Fe^{II}(O$_2$CMe)] complex. We propose that this affinity to dioxygen, essential for our further experiments with iron complexes, might be guaranteed by the much smaller carboxylate donor groups in future model complexes [(bdtbpza)FeR].

Conclusions

Two bis(3,5-dialkylpyrazol-1-yl)acetic acids **1** and **3** were introduced as new ligands for synthetic structural analogues of zinc or non-heme iron enzymes. The steric hindrance of bis(3,5-dimethylpyrazol-1-yl)acetic acid is too small, causing the ligand to coordinate twice to zinc(II) or iron(II). With bis(3,5-di-*tert*-butylpyrazol-1-yl)acetic acid the steric hindrance of this new *N,N,O* ligand was improved. The structural model complexes of zinc(II) and iron(II) obtained mimic the so called facial 2-His-1-carboxylate triad; this is especially important in mononuclear non-heme iron enzymes. We are sure that the obtained model complexes represent a good starting point to investigate the reactivity of such enzymes, especially with respect to dioxygen activation.

Experimental Section

All experiments involving iron(II) were carried out in Schlenk tubes under an atmosphere of argon using suitable purified solvents. Microcrystalline precipitates were separated by centrifugation with a Hettich Rotina 46 R Schlenk tube centrifuge. − IR: Biorad FTS 60, CaF$_2$ cuvets (0.5 mL). − ^{1}H NMR and ^{13}C NMR: Bruker WM 250, Bruker AC 250, JEOL GX 400, δ values relative to TMS; in some cases the ^{13}C NMR spectroscopic signals of quaternary carbon atoms were to weak to be detected. − EI-MS and FAB MS: modified Finnigan MAT 312. − Elemental analyses: Analytical Laboratory of the Fachbereich Chemie. − A modified Siemens P4 diffractometer was used for X-ray structure determinations.

3,5-Dimethylpyrazole, 2,2,6,6-tetramethyl-3,5-heptandione, dibromoacetic acid and ZnCl$_2$ were used as purchased. Water-free FeCl$_2$ was synthesized from FeCl$_3$.[21] 3,5-Di-*tert*-butylpyrazole was obtained by standard literature methods from 2,2,6,6-tetramethyl-3,5-heptandione and hydrazine hydroxide.[22]

Ligand Syntheses

Synthesis of Bis(3,5-dimethylpyrazol-1-yl)acetic Acid (bdmpza) (1): Dibromoacetic acid (5.45 g, 25.00 mmol), 3,5-dimethylpyrazole

(4.81 g, 50.00 mmol), KOH (5.05 g, 90.00 mmol), K_2CO_3 (12.44 g, 90.00 mmol) and benzyltriethylammonium chloride (1.00 g), serving as phase-transfer catalyst, were dissolved in tetrahydrofuran (100 mL) and heated under reflux for 5 to 6 hours. The solvent was removed in vacuo, the residue dissolved in water (100 mL) and acidified to a pH value of 7 with half-concentrated HCl. To remove excess pyrazole, the solution was extracted with diethyl ether (2 × 150 mL). The water phase was further acidified to a pH value of 1 and extracted again with diethyl ether (5 × 150 mL). To improve the extraction of the water-soluble bdmpza **1** tetrahydrofuran can be added. The organic layer was dried (Na_2SO_4) and the solvent was removed in vacuo. The residue was recrystallized from acetone yielding bdmpza (1) as colorless microcrystalline needles and dried in vacuo over SICAPENT©. In an analogous reaction of dichloroacetic acid chloride with three equivalents of 3,5-dimethylpyrazole, bdmpza (**1**) can be obtained in a slightly lower yield. Yield 2.79 g (45%); m.p. 171 °C (dec.). − ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 2.20$ (s, 6 H, CH_3), 2.24 (s, 6 H, CH_3), 5.90 (s, 2 H, H_{pz}), 6.76 (s, 1 H, CH). − ^{1}H NMR (D_2O, 250 MHz): $\delta = 2.09$ (s, 6 H, CH_3), 2.18 (s, 6 H, CH_3), 5.99 (s, 2 H, H_{pz}), 6.79 (s, 1 H, CH), 14.03 (s, CO_2H). − ^{13}C NMR ($CDCl_3$, 62.5 MHz): $\delta = 11.0$ (CH_3), 13.3 (CH_3), 69.9 (CH), 107.8 (C_{pz}), 141.7 (C_{pz}), 148.9 (C_{pz}), 165.1 (CO_2H). − EI MS (70 eV, 170 °C): *m/z* (%) = 248 (6) [M^+], 204 (20) [$M^+ - CO_2$], 109 (100) [$M^+ - CO_2 - C_5H_7N_2$], 96 (50) [$C_5H_8N_2$]. − IR (THF): $\tilde{\nu} = 1758$ cm^{-1} (CO_2H), 1563 (C=N). − $C_{12}H_{16}N_4O_2$ (248.28): calcd. C 58.05, H 6.50, N 22.57; found C 58.38, H 6.54, N 22.09.

Synthesis of Bis(3,5-di-*tert*-butylpyrazol-1-yl)methane (bdtbpzm) (2): 3,5-Di-*tert*-butylpyrazole (3.00 g, 16.64 mmol), KOH (3.60 g, 64.16 mmol), K_2CO_3 (9.00 g, 65.12 mmol) and benzyltriethylammonium chloride (0.5 g) were dissolved in dichloromethane (100 mL) and heated under reflux for 5 hours. Salts were removed by filtration and the filtrate was concentrated in vacuo to dryness. The white residue was dissolved in water and extracted with pentane (2 × 150 mL). The organic layer was dried ($MgSO_4$) and the solvent removed in vacuo. The white residue was recrystallized from pentane to give bdtbpzm (**2**) as a white powder, which was dried in vacuo. Yield 2.40 g (77%), m.p. 132 °C. − ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 1.21$ (s, 18 H, CH_3), 1.25 (s, 18 H, CH_3), 5.90 (s, 2 H, CH_2), 6.52 (s, 2 H, H_{pz}). − ^{13}C NMR ($CDCl_3$, 62.5 MHz): $\delta = 29.8$ (CH_3), 30.4 (CH_3), 31.9 (C-*t*Bu), 66.7 (CH_2), 101.9 (C_{pz}), 153.0 (C_{pz}), 159.1 (C_{pz}). − EI MS (70 eV, 125 °C): *m/z* (%) = 372 (10) [M^+], 315 (1) [$M^+ - C_4H_9$], 193 (100) [$M^+ - C_{11}H_{19}N_2$], 57 (18) [C_4H_9]. − IR (THF): $\tilde{\nu} = 1542$ cm^{-1} (C=N). − $C_{23}H_{40}N_4$ (372.60): calcd. C 74.14, H 10.82, N 15.04; found C 74.12, H 10.79, N 14.90.

Synthesis of Bis(3,5-di-*tert*-butylpyrazol-1-yl)acetic Acid (bdtbpza) (3): A solution of bis(3,5-di-*tert*-butylpyrazol-1-yl)methane (bdtbpzm) (**2**) (2.30 g, 6.17 mmol) in tetrahydrofuran (50 mL) was treated with *n*BuLi (≈1.6 M solution in hexane, 4 mL, 6.40 mmol) at −70 °C. The solution is allowed to warm to −45 °C during a period of 4 h and finally poured onto 200 g of crushed dry ice. After reaching room temperature, the solvent was removed in vacuo and the white residue dissolved in water (100 mL). The aqueous solution was acidified with half concentrated HCl to a pH value of 1 and extracted with diethyl ether (3 × 100 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo to give a honey-like yellow oil. The product crystallized within two days when stored at room temperature under air. The white crystalline substance was washed with pentane to remove unchanged bis(3,5-di-*tert*-butylpyrazol-1-yl)methane (bdtbpzm) (**2**), which gave bdtbpza (**3**) as a colorless powder. Upon recrystallization from acetone, cubic crystals suitable for an X-ray structure determination were obtained. Yield 2.25 g (88%), m.p. 92 °C. − ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 1.21$ (s, 18 H, CH_3), 1.24 (s, 18 H, CH_3), 6.01 (s, 2 H, H_{pz}), 7.27 (s, 1 H, CH). − ^{13}C NMR ($CDCl_3$, 62.5 MHz): $\delta = 30.0$ (CH_3), 30.1 (CH_3), 31.9 (C-*t*Bu), 32.2 (C-*t*Bu), 72.7 (CH), 103.1 (C_{pz}), 154.0 (C_{pz}), 159.6 (C_{pz}), 166.2 (CO_2H). − EI MS (70 eV, 145 °C): *m/z* (%) = 372 (8) [$M^+ - CO_2$], 315 (1) [$M^+ - CO_2 - C_4H_9$], 193 (100) [$M^+ - C_{11}H_{19}N_2 - CO_2$], 57 (20) [$C_4H_9$]. − IR (THF): $\tilde{\nu} = 1767$ cm^{-1} (CO_2H), 1542 (C=N). − $C_{24}H_{40}N_4O_2 \cdot 0.5\ C_4H_{10}O$ (453.67): calcd. C 68.84, H 10.00, N 12.35; found C 68.48, H 9.76, N 12.36.

Synthesis of Model Compounds

Synthesis of [(bdmpza)$_2$Zn] (4): A solution of bdmpza ligand (**1**) (500 mg, 2.01 mmol) in MeOH (20 mL) was deprotonated with the subsequent addition of NaOH (80 mg, 2.01 mmol). A solution of $ZnCl_2$ (137 mg, 1.01 mmol) in MeOH (10 mL) was then added. The initially clear solution was stirred at room temperature for 1 h. The white precipitate that formed was separated by centrifugation, washed with MeOH (15 mL) and dried in vacuo to afford **4** as a white powder. Colorless prism-like crystals suitable for an X-ray structure determination were obtained by recrystallization from MeOH/H_2O (20:1) at 4 °C. Treatment of bdmpza (**1**) with equimolar amounts of NaOH and $ZnCl_2$ yielded the identical compound. Yield 517 mg (92%), m.p. 280−300 °C (dec.). − ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 1.97$ (s, 12 H, CH_3), 2.45 (s, 12 H, CH_3), 5.87 (s, 4 H, H_{pz}), 6.57 (s, 2 H, CH). − ^{13}C NMR ($CDCl_3$, 62.5 MHz): $\delta = 10.9$ (CH_3), 12.7 (CH_3), 67.1 (CH), 106.7 (C_{pz}), 139.7 (C_{pz}), 150.2 (C_{pz}), 166.3 (CO_2^-). − FAB MS (NBOH-matrix): *m/z* (%) = 873 (10) [2 M − bdmpza], 559 (20) [MH^+], 419 (40) [$MH^+ - CO_2 - C_5H_7N_2$], 375 (20) [$MH^+ - 2\ CO_2 - C_5H_7N_2$], 361 (20) [$MH^+ - 2\ CO_2 - (C_5H_7N_2)CH_2$], 203 (60) [$(C_5H_7N_2)_2CH^+$], 109 (100) [$(C_5H_7N_2)CH_2^+$], 95 (75) [$C_5H_7N_2$]. − IR ($CH_2Cl_2$): $\tilde{\nu} = 1659$ cm^{-1} (CO_2^-), 1558 (C=N). − $C_{24}H_{30}N_8O_4Zn$ (559.93): calcd. C 51.48, H 5.40, N 20.01; found C 51.23, H 5.36, N 19.25 or C 51.21, H 5.66, N 20.09.

Synthesis of [(bdmpza)$_2$Fe] (5): A solution of bdmpza ligand (**1**) (500 mg, 2.01 mmol) in MeOH (15 mL) was deprotonated with the subsequent addition of NaOH (80 mg, 2.01 mmol). A solution of water-free $FeCl_2$ (128 mg, 1.01 mmol) in MeOH (10 mL) was then added. The initially clear solution was stirred at room temperature for 2 h. The tan to white precipitate that formed was separated by centrifugation, washed with MeOH (15 mL) and dried in vacuo to yield **5** as a colorless crystal powder. Recrystallization from acetonitrile/dichloromethane (1:1) yielded greenish prism-like crystals suitable for an X-ray structure determination. [(Bdmpza)$_2$Fe] (**5**) was also obtained by treatment of bdmpza (**1**) with equimolar amounts of potassium *tert*-butoxide and $FeCl_2$ in dichloromethane. Yield 512 mg (92%), m.p. 305−315 °C (dec.). − ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta = 1.2$ (s, 2 H, CH), 7.0 (s, 12 H, CH_3), 14.4 (s, 12 H, CH_3), 55.7 (s, 4 H, H_{pz}). − EI MS (70 eV, 340 °C): *m/z* (%) = 550 (8) [M^+], 398 (35) [$M^+ - CO_2 - (C_5H_7N_2)CH_2$], 204 (30) [$(C_5H_7N_2)_2CH_2^+$], 109 (78) [$(C_5H_7N_2)CH_2^+$], 96 (40) [$C_5H_8N_2$]. − IR ($CH_2Cl_2$): $\tilde{\nu} = 1659$ cm^{-1} (CO_2^-), 1558 (C=N). − $C_{24}H_{30}FeN_8O_4$ (550.40): calcd. C 52.35, H 5.50, N 20.36; found C 52.26, H 5.42, N 19.52.

Synthesis of [(bdtbpza)ZnCl] (6): To a solution of bis(3,5-di-*tert*-butylpyrazol-1-yl)acetic acid (bdtbpza) (**3**) (1.00 g, 2.40 mmol) in acetonitrile (30 mL) was added $ZnCl_2$ (380 mg, 2.79 mmol) and the solution stirred vigorously at ambient temperature. After 5 min potassium *tert*-butoxide (268 mg, 2.39 mmol) was added. Within 1 min a white precipitate was formed. After 2 h the solvent was removed in vacuo. The residue was dissolved in dichloromethane (25 mL) and salts were separated by centrifugation. Dichloromethane was removed in vacuo, the residue washed with diethyl ether (2 × 10 mL) and dried in vacuo to afford [(bdtbpza)ZnCl] (**6**) as a white crystal powder. Recrystallization from acetone at room temperature yielded prism-like colorless crystals within 5 days that were suitable for an X-ray structure determination. Yield 1.06 g (86%), m.p. 239 °C. − ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 1.44 (s, 18 H, CH_3), 1.56 (s, 18 H, CH_3), 6.16 (s, 2 H, H_{pz}), 7.42 (s, 1 H, CH). − ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ = 30.2 (CH_3), 31.2 (CH_3), 32.2 (C-*t*Bu), 32.6 (C-*t*Bu), 72.3 (CH), 103.8 (C_{pz}), 156.4 (C_{pz}), 164.4 (C_{pz}), 165.3 (CO_2^-). − EI MS (70 eV, 240 °C): *m*/*z* (%) = 514 (1) [M^+], 470 (12) [$M^+ - CO_2$], 413 (100) [$M^+ - CO_2 - C_4H_9$], 279 (21) [$M^+ - CH_2 - C_{11}H_{19}N_2 - CO_2$], 193 (7) [$M^+ - Zn - Cl - C_{11}H_{19}N_2 - CO_2$], 57 (54) [$C_4H_9$]. − IR ($CH_2Cl_2$): $\tilde{\nu}$ = 1681 cm^{-1} (CO_2^-), 1547 (C=N). − $C_{24}H_{39}ClN_4O_2Zn$ (516.43): calcd. C 55.82, H 7.61, N 10.85; found C 55.52, H 7.72, N 10.70.

Synthesis of [(bdtbpza)ZnSCH$_2$Ph] (8): A solution of [(bdtbpza)ZnCl] (**6**) (500 mg, 0.97 mmol) in acetonitrile (20 mL) was treated at ambient temperature with benzylthiol (158 mg, 2.79 mmol) and potassium *tert*-butoxide (109 mg, 0.97 mmol). After 3 h the solvent was evaporated, the residue dissolved in dichloromethane (25 mL) and salts removed by centrifugation. The solution was concentrated to dryness in vacuo and the residue was washed with pentane to yield [(bdtbpza)ZnSCH$_2$Ph] (**8**) as a colorless powder. Yield 550 mg (91%), m.p. 88 °C. − ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 1.38 (s, 18 H, CH_3), 1.56 (s, 18 H, CH_3), 3.93 (s, 2 H, SCH_2), 6.13 (s, 2 H, H_{pz}), 7.10−7.39 (m, 5 H, Ph), 7.42 (s, 1 H, CH). − ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ = 29.7 (SCH_2), 30.3 (CH_3), 31.2 (CH_3), 32.2 (C-*t*Bu), 32.5 (C-*t*Bu), 72.2 (CH), 103.6 (C_{pz}), 125.6 (CPh), 128.1 (CPh), 128.5 (CPh), 144.6 (CPh), 155.9 (C_{pz}), 164.0 (C_{pz}), 166.0 (CO_2^-). − EI MS (70 eV, 300 °C): *m*/*z* (%) = 602 (7) [M^+], 557 (2) [$M^+ - CO_2$], 501 (75) [$M^+ - CO_2 - C_4H_9$], 366 (20) [$M^+ - CH_2 - C_{11}H_{19}N_2 - CO_2$], 244 (20) [$Zn + C_{11}H_{19}N_2$], 194 (100) [$C_{11}H_{20}N_2 + CH_2$], 91 (90) [$C_7H_7$], 57 (30) [$C_4H_9$]. − IR ($CH_2Cl_2$): $\tilde{\nu}$ = 1677 cm^{-1} (CO_2^-), 1543 (C=N). − $C_{31}H_{46}N_4O_2SZn$ (604.17): calcd. C 61.63, H 7.67, N 9.27; found C 61.33, H 7.56, N 8.53.

Synthesis of [(bdtbpza)FeCl] (7): To a solution of bis(3,5-di-*tert*-butylpyrazol-1-yl)acetic acid (bdtbpza) (**3**) (500 mg, 1.20 mmol) in acetonitrile (20 mL) was added water-free $FeCl_2$ (150 mg, 1.18 mmol) and the reaction mixture stirred at ambient temperature for 10 min. Potassium *tert*-butoxide (135 mg, 1.20 mmol) was added and stirred for 3 h. The solvent was evaporated and the residue was dissolved in dichloromethane (25 mL). Salts were removed by centrifugation and the solution concentrated to dryness in vacuo. The residue was washed with diethyl ether (2 × 10 mL) and dried in vacuo to afford [(bdmpza)FeCl] (**7**) as a colorless powder. Yield 520 mg (87%), m.p. 203 °C (dec.). − ^{1}H NMR ($CDCl_3$, 250 MHz): δ = −21.4 (s, 18 H, CH_3), 3.2 (s, 2 H, H_{pz}), 11.3 (s, 18 H, CH_3). − EI MS (70 eV, 280 °C): *m*/*z* (%) = 506 (4) [M^+], 462 (11) [$M^+ - CO_2$], 405 (100) [$M^+ - CO_2 - C_4H_9$], 271 (12) [$M^+ - CH_2 - C_{11}H_{19}N_2 - CO_2$], 57 (44) [$C_4H_9$]. − IR ($CH_2Cl_2$): $\tilde{\nu}$ = 1684 cm^{-1} (CO_2^-). − $C_{24}H_{39}ClFeN_4O_2$ (506.90): calcd. C 56.87, H 7.75, N 11.05; found C 56.57, H 7.86, N 10.91.

X-ray Structure Determinations: Single crystals of **3**, **4**, **5** and **6** were sealed in glass capillaries at room temperature. A modified Siemens P4-Diffractometer was used for data collection (Wyckhoff technique, graphite monochromator, Mo-K_α radiation, λ = 0.71073 Å, scan rate 4−30°min^{-1} in ω). Compound **4** was measured at room

Table 6. Structure determination details of compounds **3**, **4**, **5** and **6**

	3	**4**	**5**	**6**
Empirical formula	$C_{24}H_{40}N_4O_2 \cdot 0.5\ Et_2O$	$C_{12}H_{15}N_4O_2Zn_{0.5} \cdot 1.5\ H_2O$	$C_{12}H_{15}Fe_{0.5}N_4O_2 \cdot 0.5\ CH_2Cl_2$	$C_{24}H_{39}ClN_4O_2Zn$
Formula weight	453.66	305.98	317.67	516.41
Crystal color/Habit	colorless prism	colorless prism	green prism	colorless column
Crystal system	tetragonal	monoclinic C	monoclinic C	monoclinic P
Space group	$P4_2/n$	$C2/c$	$C2/c$	$P2_1/n$
a [Å]	19.773(24)	16.228(15)	8.003(3)	10.586(7)
b [Å]	19.773(24)	13.421(12)	18.700(7)	16.170(9)
c [Å]	14.863(17)	14.050(14)	20.147(11)	16.255(9)
α [°]	90.00	90.00	90.00	90.00
β [°]	90.00	108.28(5)	98.62(6)	107.96(7)
γ [°]	90.00	90.00	90.00	90.00
V [Å^3]	5810.9(119)	2905.5(47)	2981.0(23)	2647.0(27)
θ [°]	2.00−23.00	2.01−26.99	2.18−27.00	2.04−27.01
h	−1 to 21	−20 to 20	−10 to 10	−1 to 12
k	−1 to 21	−11 to 17	−23 to 23	−20 to 1
l	−1 to 16	−17 to 17	−24 to 25	−20 to 20
F(000)	1992	1288	1320	1096
Z	8	8	8	4
μ(Mo-K_α) [mm^{-1}]	0.067	0.901	0.730	1.055
Crystal size [mm]	0.55 × 0.5 × 0.5	0.35 × 0.3 × 0.3	0.55 × 0.5 × 0.5	0.55 × 0.55 × 0.6
D_c [gcm^{-1}]	1.037	1.399	1.416	1.296
T [K]	241(2)	293(2)	243(2)	241(2)
Reflections collected	4234	4623	6434	6423
Independent reflections	3159	3176	3179	5134
Obs. reflections (>2σ*I*)	1764	2182	2725	4165
Parameter	301	204	186	289
Restraints	0	3	0	0
Wt. parameter a	0.0907	0.0494	0.1231	0.0388
Wt. parameter b	3.5702	1.6697	6.7913	1.4264
R_1 (obs.)	0.0755	0.0477	0.0623	0.0352
R_2 (overall)	0.1432	0.0865	0.0710	0.0492
wR_1 (obs.)	0.1796	0.0999	0.1927	0.0849
wR_2 (overall)	0.2225	0.1232	0.2062	0.0937
Diff. peak/hole [e/Å^3]	0.227/−0.161	0.429/−0.298	0.535/−1.100	0.267/−0.458

temperature and the others at −30 °C. Structures were solved using direct methods {Siemens SHELXS-93 (VMS)[23]} and refined with full-matrix least-squares against F^2 {Siemens SHELXL-96 (VMS)[24]}. A weighting scheme was applied in the last steps of the refinement with $w = 1/[\sigma^2(F_o^2) + (aP)^2 + bP]$ and $P = [2F_c^2 + \mathrm{Max}(F_o^2,0)]/3$. Hydrogen atoms were included in their calculated positions and refined in a riding model.

The metal atoms in structures of **4** and **5** are in special positions, causing the asymmetric unit to be filled by only half a molecule. Compound **4** crystallized as a solvate with 1.5 water molecules, one of which interacts with the carboxylate group. In the asymmetric unit of structure **5**, half a molecule of dichloromethane was found and refined in a special position.

Compound **3** crystallized with half a molecule of diethyl ether in the asymmetric unit in a special position. The proton of the carboxylic acid was found. The poor *R*-factors of compound **3** are caused by a weak diffraction of the crystal. So the θ-range of the measurement was only up to 23° causing a low reflection/parameter ratio. Nevertheless, anisotropic refinement was applied to all non-hydrogen atoms.

All details and parameters of the measurements are summarized in Table 6. Structure pictures were prepared with the program Diamond 2.1c.[25] Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-145052 (**4**), CCDC-145053 (**5**), CCDC-145054 (**6**) and CCDC-145055 (**3**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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