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"Inhibition" of the Enzyme Model $Tp^{Ph,Me}Zn$–OH by Diketo Compounds

Teame Tekeste[a] and Heinrich Vahrenkamp*[a]

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In order to gain a structural understanding of zinc enzyme inhibition, the model complex $Tp^{Ph,Me}Zn$–OH was treated with various diketo compounds. α-Keto carboxylic acids were attached to the zinc ion as anionic O,O-chelate ligands, of which benzoylformate was oxidatively decarboxylated in air to form the benzoate complex. Two functionalized β-diketones did not use their functionality in forming the β-diketonate complexes. Of the α-diketones, 2,3-pentanedione formed the α-keto enolate complex, while 1-phenyl-1,2-propanedione underwent oxidative C–C coupling resulting in a red dinuclear bis(α-keto enolato) complex. Of the diaryl-α-diketones, benzil did not react, but pyridil underwent hydrolytic cleavage to pyridine-2-carbaldehyde and picolinate, of which the latter was bound to the zinc ion as an N,O-chelate ligand.

Introduction

The inhibition of zinc enzymes is an active field of drug research, as it may be relevant for the treatment of such diseases as arthritis, high blood pressure, multiple sclerosis, and even cancer.[1,2] Studies towards this end can benefit from the fact that not only are a large number of zinc enzymes known, but many of them have been fully characterized by structure determinations.[3,4] Thus, there is an excellent basis for target-oriented drug design for zinc-enzyme-related diseases.

Despite this, development in this field is still mostly a matter of trial and error, and the number of zinc-specific inhibitor types is still relatively small.[2,5,6] The oldest of them, which have been successful in various fields, are the sulfonamides.[5] The best investigated are the hydroxamates.[2] They are attractive because the hydroxamate function is a very good zinc-binding group, but until now none of them has made it through all clinical tests, which is due in part to their unsuitability for oral administration as well as their potential chronic toxicity.[1,2,7]

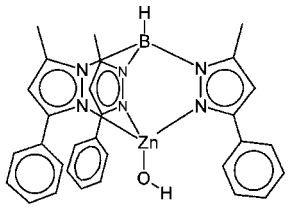
It is therefore attractive to investigate inhibitors with other zinc-binding groups.[1,2] Studies of this kind have been reported for carboxylates,[8] β-keto enolates,[2,5] and some thiolate-containing chelators.[2,9] Considering the state of the art in the coordination chemistry of zinc and the large number of well-established zinc-binding functions, one must say that amazingly little of the knowledge accumulated has reached the field of drug design.

[a] Institut für Anorganische und Analytische Chemie der Universität Freiburg,
Albertstr. 21, 79104 Freiburg, Germany
Fax: +49-761-203-6001
E-mail: vahrenka@uni-freiburg.de

We have tackled this subject sporadically. After some basic studies of zinc complexes of drug substances,[10–14] we used our enzyme models, the TpZn–OH complexes, to study the interactions between zinc and pharmaceutically relevant substrates.[15–19] From these studies we found a striking structural similarity between the geometries at the zinc centers of the enzyme and the model complex in the hydroxamate-bound state,[20] and this enabled our mechanistic proposal for the zinc-enzyme-catalyzed hydrolysis of esters and peptides.[21,22]

Until recently, none of our investigations in this field was focused on a systematic survey of zinc-binding groups against a background of enzyme inhibition. Yet, one of our enzyme models, the $Tp^{Ph,Me}Zn$–OH complex, was used by Cohen et al. for studies of this kind, addressing the interactions between zinc and hydroxamates, pyridinones, chelating Schiff bases, and various kinds of bidentate thiolates.[23–27] This provided quite a diverse structural chemistry and some important aspects of the stability of enzyme model inhibitor complexes.

Independent of Cohen's work, we also started a systematic study scanning potentially bidentate zinc-binding groups and using the same enzyme model $Tp^{Ph,Me}Zn$–OH (**1**). Fortunately, so far the parallel work in both groups (with one exception, complex **11**, see below) has not produced any overlap. After some variations of the theme of hydroxamates and oximates,[28] we turned to zinc-binding groups that should be expected to bind through oxygen atoms only and which should be good chelators. This paper describes our results with such ligands containing two carbonyl functions: α-keto carboxylates, β-diketonates, α-diketones, and ligands derived from them.



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Results and Discussion

α-Keto Carboxylic Acids

After the hydroxamic acids, the carboxylic acids are the second most investigated group of zinc enzyme inhibitors.[1] However, at physiological pH the carboxylate function binds 100–2000 times less efficiently to the zinc centers than the hydroxamate function.[1,29] It therefore seems suitable to enhance the carboxylates' binding capacity by introducing additional donor functions that make the carboxylate function part of a bidentate chelating ligand. With this in mind we applied pyruvic acid, benzoylformic acid, and oxamidic acid as inhibitor models.

The reaction between pyruvic acid and **1** was quantitative and yielded the pyruvate complex **2**. As expected, the pyruvato ligand in **2** is bound in a bidentate fashion, forming a five-membered chelate ring. This was already evident from the ^{1}H NMR spectrum, in which the pyruvate's methyl resonance experienced a high-field shift of 1 ppm upon coordination, indicating that it was embedded between the Tp's phenyl rings. This was confirmed by the structure determination (see Figure 1).

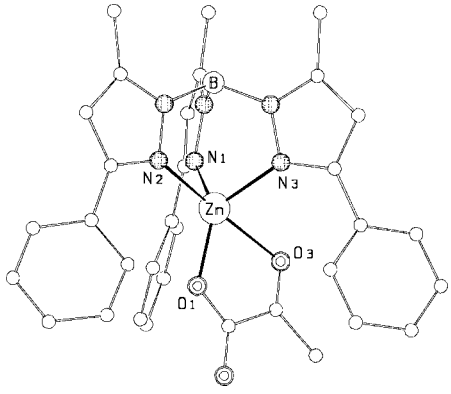
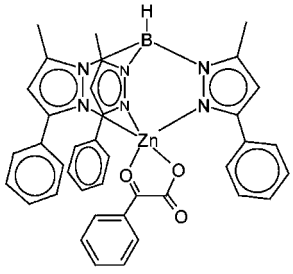


Figure 1. Molecular structure of complex **2**. Selected bond lengths [Å] and angles [°]: Zn–N1 2.020(3), Zn–N2 2.138(3), Zn–N3 2.017(3), Zn–O1 1.901(3), Zn–O3 2.397(3); O3–Zn–O1 75.6(1), O3–Zn–N1 89.7(1), O3–Zn–N3 87.7(1), O3–Zn–N2 177.5(1).

The major zinc–pyruvate interaction lies in the Zn–O bond to the carboxylate oxygen atom, which is 0.5 Å shorter than the other Zn–O bond. In part, this lengthening of the Zn–O3 bond can be ascribed to the fact that it represents the axis of a trigonal bipyramid around the zinc ion, with the Zn–N2 bond, which has also been lengthened, as the other axis. According to the Holmes definition,[30] the complex is 75% trigonal-bipyramidal and 25% square-pyramidal. Thereby **2** is one of the best examples of trigonal-bipyramidal coordination in TpZn complexes.[21]

We are not aware of any other zinc complexes of α-keto carboxylato ligands. There is, however, an iron–pyruvate complex of the $Tp^{Ph,Ph}$ ligand, the geometry of which is very similar to that of **2**.[31]

The reactions of **1** with benzoylformic acid and oxamidic acid proceeded equally straightforwardly and yielded complexes **3** and **4**. Their spectroscopic data indicate that their α-keto carboxylate functions are bound to the zinc ion in a chelating fashion, like in **2**. The main pieces of evidence are again the ^{1}H NMR resonances of the phenyl group in **3** and one of the NH_2 hydrogen atoms in **4**, which have experienced significant high-field shifts. There is a second NH signal for **4**, 2 ppm down-field from the first one. We take this as an indication that this second hydrogen atom is involved in an N–H···O hydrogen bond, as indicated in the formula drawing. Support for our structural assignments comes from two structurally characterized related complexes: a TpFe complex of benzoylformate[31] and an aqua–zinc complex of oxamidate.[32]



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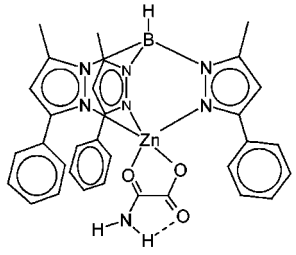

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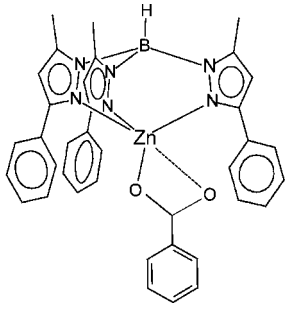
When solutions of **3** were exposed to air they turned yellow. ^{1}H NMR spectroscopy indicated that **3** was consumed and replaced by another complex. Rigorous stirring in dichloromethane completed this process within hours and led to the isolation of the benzoate complex **5** in good yields. Complex **5** was identified by a structure determination (see Exp. Sect.), which is not discussed here as it revealed no unusual features.



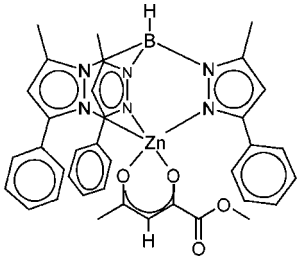
5

The conversion of **3** to **5** is an oxidative decarboxylation, a very typical reaction of α-keto carboxylic acids, which in organic chemistry is performed in the presence of Fe^{II} and

in biology by Fe-containing enzymes.[33] It is not known whether zinc enzymes catalyze such a reaction. The model complex $Tp^{Ph,Ph}$Fe–benzoylformate, a close relative of **3**, was found, however, to undergo the same reaction with concomitant hydroxylation of one of the Tp's phenyl groups.[31]

β-Diketones

Until now the reactions of TpZn complexes with β-diketones have yielded, without exception, the expected TpZn–β-diketonate complexes with the classical six-membered chelate rings.[20,21,34,35] In the present work we tried to find out whether additional functionality on the β-diketones changes this picture. For this purpose we chose methyl 2,4-dioxopentanoate, which is prone to ester cleavage by $Tp^{Ph,Me}$Zn–OH, and 2-acetylcyclohexanone, which has an unusually low pK_a of the acidic CH function. Both diketones, however, behaved conventionally toward **1**, producing complexes **6** and **7** in good yields.



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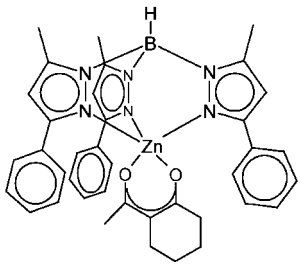


7

Both complexes were identified by structure determinations, the results of which are summarized in Table 1. In both cases the geometry around the zinc ion is square-pyramidal to a very high degree (96 and 93%, respectively, according to Holmes' definition[30]). In both cases the uniformity of the Zn–O bond lengths demonstrates the symmetrical attachment of the β-diketonates, despite their unsymmetrical nature. This, together with the high stability of the complexes, qualifies the β-diketones as particularly reliable chelators for zinc ions, which deserve intensified use in enzyme inhibitor studies.

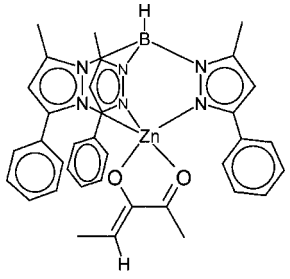
Table 1. Structural details of **6** and **7**.

	6	**7**
Zn–O1	2.005(4)	1.988(5)
Zn–O2	2.039(4)	2.000(4)
Zn–N1	2.088(4)	2.133(6)
Zn–N2	2.137(5)	2.123(6)
Zn–N3	2.088(5)	2.079(5)
O1–Zn–N1	155.6(2)	158.2(2)
O2–Zn–N2	155.8(2)	155.6(2)
N3–Zn–O1	108.1(2)	106.3(2)
N3–Zn–O2	110.5(2)	111.0(2)
N3–Zn–N1	95.2(2)	94.9(2)
N3–Zn–N2	93.7(2)	93.0(2)

Aliphatic α-Diketones

Unlike the β-diketones, the α-diketones cannot form resonance-stabilized anions after deprotonation, and their reactive anionic four-electron three-center enolate systems are not favorable as ligands. Accordingly, there seem to be no zinc–α-keto enolate complexes so far. Nevertheless, the attachment of both oxygen atoms of an α-keto enolate should lead to a complex with a favorable five-membered chelate ring. With this in mind we tested diacetyl, 2,3-pentanedione, and 1-phenyl-1,2-propanedione.

Diacetyl did not react with **1**. However, in boiling methanol, **1** and 2,3-pentanedione underwent the desired elimination of water and formation of the chelate complex **8**. Complex **8** could easily be identified by its ^{1}H NMR spectrum (see Exp. Sect.), and its constitution was confirmed by a structure determination (see Figure 2).



8

The enolate ligand in **8** is bound in a reasonably symmetrical five-membered chelate ring. Like in **2**, the Zn–O bond to the formally anionic oxygen atom is considerably shorter than the other one. The geometry at the zinc center is halfway between trigonal-bipyramidal and square-pyramidal (52% according to the Holmes definition[30]). In the trigonal bipyramid N2 and O2 would be the axial donor atoms, and in the square pyramid N1 would be at the apex.

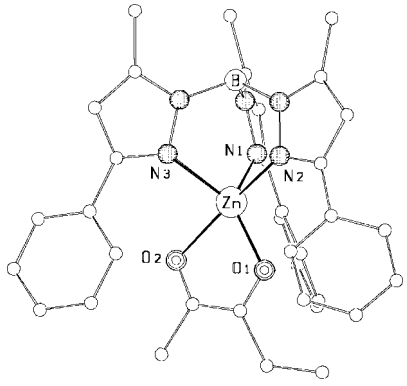
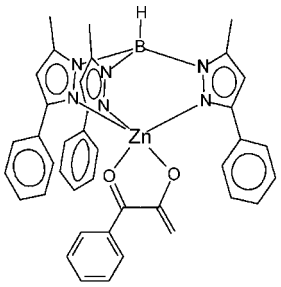


Figure 2. Molecular structure of complex **8**. Selected bond lengths [Å] and angles [°]: Zn–N1 2.067(4), Zn–N2 2.138(4), Zn–N3 2.064(4), Zn–O1 1.900(4), Zn–O2 2.255(4); N2–Zn–O2 169.0(1), N3–Zn–O1 141.7(2).

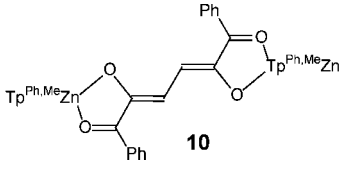
The course of the reaction between **1** and 1-phenyl-1,2-propanedione allows the assumption that its initial product is complex **9**, which is analogous to **8**. However, **9** could not be isolated, being consumed quickly by two consecutive reactions.



9

The reaction mixture turned red even in the absence of air. In the presence of air the color quickly became red-purple. Only after this could the two reaction products be isolated by fractional crystallization. One of them is the benzoate complex **5**. Its formation requires the oxidative cleavage of **9** with release of ketene, which is probably oxidized at the same time.

The second product is the red dinuclear complex **10**. Its formation can also be described as an oxidation of **9**: removal of one hydrogen atom from the vinyl group leaves a radical, the natural fate of which is dimerization leading to **10**. Although organic chemistry knows many radical dimerizations, we are not aware of an oxidative one that compares with this. Like in the formation of **5** from **4**, zinc seems to have a role here that is normally reserved for the redox-active metals.



10

The identification of **10** came from a structure determination (see Figure 3). In **10**, which is centrosymmetrical, the ligand environment of the zinc ions and its geometry is practically identical to that in **8**: in both complexes the zinc ions are attached to vinyl-substituted α-diketonato ligands. The interesting part of **10** is the conjugated system of four (*E*)-oriented double bonds (2 C=C and 2 C=O). Its eight atoms are coplanar to a good approximation (maximum deviation 0.18 Å), and the conjugation along the chain is obvious from the slight shortening of the single bonds. This delocalization is also the reason for the intense color of the complex.

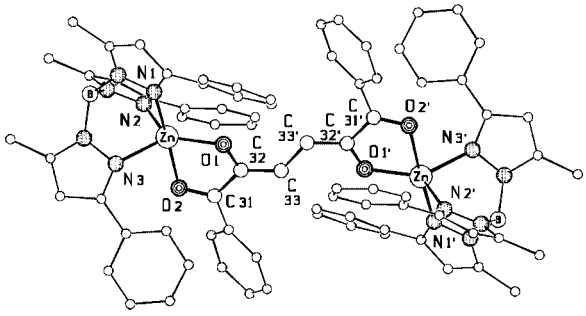
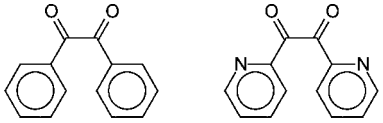


Figure 3. Molecular structure of the centrosymmetrical complex **10**. Selected bond lengths [Å]: Zn–O1 1.934(2), Zn–O2 2.281(3), Zn–N1 2.159(3), Zn–N2 2.078(3), Zn–N3 2.057(3), O1–C32 1.301(4), O2–C31 1.241(4), C31–C32 1.481(4), C32–C33 1.382(4), C33–C33′ 1.421(4).

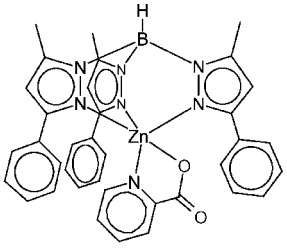
Aromatic α-Diketones

Unlike the aliphatic α-diketones, benzil and pyridil cannot form enolates. If they react at all with a TpZn–OH complex, they can either function as uncharged donor ligands or suffer nucleophilic attack by the strong Zn–OH nucleophiles. It turned out that the former does not happen, but the latter is the case.



benzil pyridil

There was no reaction between **1** and benzil. Complex **1** and pyridil did react in dichloromethane at room temperature. The isolated product of this reaction was the picolinato complex **11**, which was obtained previously directly from **1** and picolinic acid.[9] The second product, pyridine-2-carbaldehyde, was identified by ^{1}H NMR spectroscopy in the reaction solution. Thus, the course of the reaction is the unusual hydrolysis of pyridil at its central C–C bond, during which the oxygen atom of the Zn–OH function ends up in the picolinate while the hydrogen atom becomes the aldehydic hydrogen atom of the pyridinecarbaldehyde. Again we are not aware that there is precedence for such a hydrolytic reaction, and again it must be assumed that initial coordination of the substrate to the zinc ion (this time through the pyridyl nitrogen atom) is an essential part of its mechanism.



11

The favorable attachment of the picolinato ligand to the zinc ion by a five-membered chelate ring was confirmed by a structure determination (see Figure 4). The coordination geometry of the zinc ion is very close to trigonal-bipyramidal (73% according to the Holmes definition[30]) with the pyridine nitrogen atom and one Tp nitrogen atom on the axis. All atoms of the picolinato ligand are coplanar (strongest deviation 0.12 Å), and the short Zn–O bond indicates a quite strong zinc–picolinate interaction. Considering this, it is somewhat surprising that **11** is the first TpZn chelate complex of this kind, particularly as it is known that the complex $[Tp^{Cum,Me}Zn\text{-}Py]^+$ exists,[36] which demonstrates the strength of the TpZn–pyridine interaction by being a rare example of the cationic TpZn–X complexes.

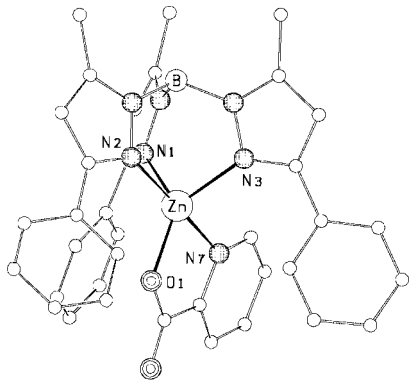


Figure 4. Molecular structure of complex **11**. Selected bond lengths [Å] and angles [°]: Zn–N1 2.051(3), Zn–N2 2.226(3), Zn–N3 2.052(3), Zn–N7 2.193(3), Zn–O1 1.966(3); N2–Zn–N7 177.5(1).

Conclusions

A general rule for zinc complexes of 3,5-substituted Tp ligands is that the Tp ligand is a "tetrahedral enforcer", that is, four-coordinate TpZn–X complexes are preferred. This paper, however, has shown again that with suitable chelating ligands this rule is broken and very stable TpZn(X,Y) complexes are obtained. In the present case the chelators were mostly bidentate O,O donors forming five-membered chelate rings.

In the context of zinc enzyme inhibition the new complexes give further support to the hypothesis that the enzyme–inhibitor complexes are transition-state analogs, as the transition state of a zinc-enzyme-catalyzed hydrolysis has the zinc ion in a fivefold coordination with a geometry halfway between trigonal-bipyramidal and square-pyramidal.[22] As we have shown here and before,[21] the TpZn complexes of O,O chelators are very variable in their geometry, covering almost the whole range of geometries for ZnL_5 systems.

Of the chelate ligands employed here, the α-keto carboxylates and the α-diketo enolates have not been used before in zinc chemistry. Their stable TpZn complexes, and the even more stable TpZn complexes of the β-diketonates and the picolinate, indicate that it should be worthwhile studying compounds with these donor groups more thoroughly as potential inhibitors for zinc enzymes. It is altogether surprising how few donor functions have been employed in such studies so far.[1,2]

An unexpected, but welcome, byproduct of these investigations were the three substrate cleavage reactions. Both the two oxidative ones leading to **5** and **10** and the hydrolytic one leading to **11** are unprecedented in zinc chemistry, and one can only guess about their mechanisms. They please the zinc chemist by demonstrating once again that the "boring element" is not so boring after all.

Experimental Section

General: For general working and measuring procedures see ref.[37] Complex **1** was prepared as described.[38] Organic reagents were obtained commercially. All IR spectra were recorded from KBr pellets. All ^{1}H NMR spectra were obtained from $CDCl_3$ solutions. The resonances of the $Tp^{Ph,Me}$ ligands in all complexes were observed at practically identical positions: δ = 2.5 [s, 9 H, Me(pz)], 6.2 [s, 3 H, H(pz)], 7.2–7.4 [m, 9 H, Ph(3,4,5)], 7.5–7.7 [m, 6 H, Ph(2,6)] ppm. Hence, only the ^{1}H NMR resonances of the co-ligands are reported here.

Complex 2: A solution of pyruvic acid (24 mg, 0.35 mmol) in methanol (5 mL) was added to a solution of **1** (200 mg, 0.35 mmol) in dichloromethane (20 mL). After stirring for 3 h, all volatiles were removed in vacuo. Crystallization by slow concentration from dichloromethane/methanol yielded **2** (199 mg, 81%) as colorless crystals, m.p. 186 °C. $C_{33}H_{31}BN_6O_3Zn$ (653.86): calcd. C 62.34, H 4.91, N 13.22; found C 62.10, H 5.02, N 13.22. IR (KBr): $\tilde{\nu}$ = 2552 m (BH), 1701 s, 1687 s (CO) cm^{-1}. ^{1}H NMR: δ = 1.33 (s, 3 H, CH_3) ppm.

Complex 3: A solution of benzoylformic acid (80 mg, 0.53 mmol) in methanol (20 mL) was added to a solution of **1** (300 mg, 0.53 mmol) in dichloromethane (20 mL). After stirring for 3 h, the volume of the solution was reduced to one half in vacuo. The resulting colorless precipitate was filtered off and washed with methanol (5 mL). Crystallization by slow concentration from dichloromethane/methanol yielded **3** (314 mg, 85%) as colorless crystals, m.p. 190 °C. $C_{38}H_{33}BN_6O_3Zn$ (697.92): calcd. C 65.40, H 4.77, N 12.04; found C 65.23, H 4.85, N 11.94. IR (KBr): $\tilde{\nu}$ = 2539 m (BH), 1676 vs, 1645 s (CO) cm^{-1}. ^{1}H NMR: δ = 7.01–7.18 [m, 12 H, Ph(Tp) and Ph], 7.42–7.53 [m, 8 H, Ph(Tp) and Ph] ppm.

Complex 4: As for **3**, from oxamidic acid (31 mg, 0.35 mmol) and **1** (200 mg, 0.35 mmol). Yield: **4** (161 mg, 72%) as colorless crystals, m.p. 210 °C. $C_{32}H_{30}BN_7O_3Zn$ (636.84): calcd. C 60.35, H 4.75, N 15.40; found C 59.51, H 4.84, N 15.18. IR (KBr): $\tilde{\nu}$ = 2544 m (BH), 1666 vs (CO) cm^{-1}. ^{1}H NMR: δ = 4.45 (s, 1 H, NH), 6.51 (s, 1 H, NH) ppm.

Complex 5: A solution of **4** (100 mg, 0.14 mmol) in dichloromethane (20 mL) was stirred in an open flask for 2 h. The solvent was removed in vacuo and the residue crystallized by slow concentration from dichloromethane/methanol, yielding **5** (59 mg, 62%) as yellowish crystals, m.p. 224 °C. $C_{37}H_{33}BN_6O_2Zn$ (669.91): calcd. C 65.46, H 5.05, N 12.38; found C 65.36, H 5.06, N 12.37. IR (KBr): $\tilde{\nu}$ = 2541 m (BH), 1615 s, 1438 s (CO) cm^{-1}. ^{1}H NMR: δ = 7.12–7.25 [m, 12 H, Ph(Tp) and Ph], 7.61–7.67 [m, 8 H, Ph(Tp) and Ph] ppm.

Complex 6: As for **2**, from methyl 2,3-dioxopentanoate (39 mg, 0.27 mmol) and **1** (150 mg, 0.27 mmol). Yield: **6** (155 mg, 83%) as colorless crystals, m.p. 187 °C. $C_{36}H_{35}BN_6O_4Zn$ (691.88): calcd. C 62.49, H 5.10, N 12.15; found C 62.19, H 5.39, N 12.03. IR (KBr): $\tilde{\nu}$ = 2540 m (BH), 1743 s, 1617 s (CO) cm^{-1}. ^{1}H NMR: δ = 1.09 (s, 3 H, CH_3), 3.38 (s, 3 H, OCH_3), 4.75 (s, 1 H, CH) ppm.

Complex 7: As for **3**, from 2-acetylcyclohexanone (49 mg, 0.35 mmol) and **1** (200 mg, 0.35 mmol). Yield: **7** (161 mg, 67%) as colorless crystals, m.p. 191 °C. $C_{38}H_{39}BN_6O_2Zn{\cdot}CH_2Cl_2$ (687.97 + 84.93): calcd. C 60.61, H 5.35, N 10.87; found C 60.89, H 5.49, N 11.09. IR (KBr): $\tilde{\nu}$ = 2541 m (BH), 1593 vs (CO) cm^{-1}. ^{1}H NMR: δ = 1.11 (s, 3 H, CH_3CO), 1.14–2.07 (m, 8 H, cyclohexyl), 5.29 (s, 2 H, CH_2Cl_2) ppm.

Complex 8: A solution of 2,3-pentanedione (44 mg, 46 μL, 0.44 mmol) in methanol (10 mL) was added to a suspension of **1** (250 mg, 0.44 mmol) in methanol (30 mL). After refluxing for 4 h, all volatiles were removed in vacuo. Crystallization by slow concentration from dichloromethane/methanol yielded **8** (225 mg, 79%) as yellow crystals, m.p. 172 °C. $C_{35}H_{35}BN_6O_2Zn$ (647.90): calcd. C 64.88, H 5.44, N 12.97; found C 64.29, H 5.51, N 12.85. IR (KBr):

Table 2. Crystallographic details.

	2	**5**	**6**	**7**	**8**	**10**	**11**
Empirical formula	$C_{33}H_{31}BN_6O_3Zn$	$C_{37}H_{33}BN_6O_2Zn$	$C_{36}H_{35}BN_6O_4Zn$	$C_{39}H_{41}BN_6O_2Zn\cdot CH_2Cl_2$	$C_{35}H_{35}BN_6O_2Zn$	$C_{39}H_{34}BN_6O_2Zn\cdot 2.5CH_2Cl_2$	$C_{36}H_{32}BN_7O_2Zn\cdot CH_3OH$
Formula mass	635.85	669.91	691.88	772.90	647.98	907.27	702.94
Crystal size [mm]	0.35×0.12×0.12	0.32×0.17×0.09	0.14×0.12×0.03	0.24×0.14×0.05	0.32×0.22×0.18	0.5×0.4×0.4	0.30×0.18×0.10
Space group	$P2_1/n$	$P2_1/c$	$P\bar{1}$	$P\bar{1}$	$P2_1/c$	$P\bar{1}$	$P2_1/n$
Z	4	4	2	2	4	2	4
a [Å]	10.209(2)	10.085(2)	9.941(1)	11.604(13)	14.824(9)	13.019(5)	15.537(2)
b [Å]	15.936(3)	23.410(3)	12.870(2)	11.803(13)	13.215(8)	13.715(5)	12.636(2)
c [Å]	18.995(4)	13.800(1)	13.877(2)	16.342(18)	16.998(10)	13.897(5)	17.607(3)
α [°]	90	90	101.062(2)	72.146(18)	90	106.341(7)	90
β [°]	93.393(4)	99.904(3)	100.023(2)	78.961(19)	105.09(1)	99.543(7)	93.361(3)
γ [°]	90	90	92.213(2)	60.974(16)	90	112.945(6)	90
V [Å^3]	3085(1)	3209(1)	1711.0(4)	1860(16)	3215(3)	2083(1)	3451(1)
$\rho_{calcd.}$ [g cm^{-3}]	1.37	1.39	1.34	1.38	1.34	1.45	1.34
μ(Mo-K_α) [mm^{-1}]	0.84	0.81	0.77	0.85	0.81	0.95	0.76
h	–13 to 14	–13 to 13	–12 to 12	–15 to 15	–20 to 19	–16 to 17	–21 to 14
k	–13 to 21	–31 to 31	–16 to 17	–15 to 15	–17 to 17	–18 to 18	–16 to 17
l	–22 to 26	–18 to 18	–18 to 17	–21 to 22	–22 to 22	–18 to 18	–21 to 22
Measured reflections	20403	28772	25879	16869	28147	18701	21303
Independent reflections	8437	7797	7996	8729	7819	9689	8241
Observed reflections [$I > 2\sigma(I)$]	3482	4079	4574	1527	3513	6755	4051
Parameters	401	428	1089	464	410	508	447
Refined reflections	8437	7797	7996	8729	7819	9689	8241
R_1 (observed reflections)	0.054	0.052	0.076	0.065	0.071	0.059	0.056
wR_2 (all reflections)	0.161	0.151	0.179	0.126	0.204	0.178	0.165
Residual electron density [e Å^{-3}]	+0.6/–0.5	+0.5/–0.7	+0.7/–0.8	+0.4/–0.7	+0.6/–0.7	+1.2/–1.9	+0.9/–0.8

$\tilde{\nu}$ = 2541 m (BH), 1635 vs (CO) cm^{-1}. ^{1}H NMR: δ = 1.11 (s, 3 H, CH_3CO), 1.83 (d, J = 7.0 Hz, 3 H, CH_3), 5.27 (q, J = 7.0 Hz, 1 H, CH) pm.

Complex 10: A solution of 1-phenyl-1,2-propanedione (52 mg, 47 μL, 0.35 mmol) in methanol (20 mL) was added to a solution of **1** (200 mg, 0.35 mmol) in dichloromethane (20 mL). After stirring in an open flask for 6 h, all volatiles were removed in vacuo. The residue was dissolved in a mixture of methanol (10 mL) and dichloromethane (5 mL) and subjected to slow concentration until most of the dichloromethane was evaporated. The resulting precipitate, which was filtered off, washed with methanol (3 mL), and dried in vacuo, consisted of **10** (78 mg, 32%) as a red powder, m.p. 230 °C. $C_{78}H_{68}B_2N_{12}O_4Zn_2\cdot 1.5CH_2Cl_2$ (1389.88 + 127.40): calcd. C 62.93, H 4.72, N 11.08; found C 62.52, H 4.62, N 11.15. IR (KBr): $\tilde{\nu}$ = 2541 m (BH), 1613 vs (CO) cm^{-1}. ^{1}H NMR: δ = 5.29 (s, 3 H, CH_2Cl_2), 6.73 (s, 2 H, CH) ppm.

Complex 11: A solution of pyridil (74 mg, 0.35 mmol) in dichloromethane (10 mL) was added to a solution of **1** (200 mg, 0.35 mmol) in dichloromethane (10 mL). After stirring for 3 h, the mixture was filtered and the filtrate treated dropwise with methanol until a precipitate started forming. After stirring for another 30 min, the precipitate was filtered off and washed with methanol (5 mL). Recrystallization from hot methanol yielded **11** (132 mg, 56%) as yellow crystals, m.p. 226 °C. $C_{36}H_{32}BN_7O_2Zn\cdot CH_3OH$ (670.90 + 32.04): calcd. C 63.82, H 4.99, N 14.27; found C 63.21, H 4.75, N 13.97. IR (KBr): $\tilde{\nu}$ = 2539 m (BH), 1665 m and 1646 vs (CO and Py) cm^{-1}. ^{1}H NMR: δ = 3.48 (s, 3 H, CH_3OH), 6.49 [t, J = 7.0 Hz, 1 H, Py(4)], 6.96 [d, J = 7.0 Hz, 1 H, Py(3)], 7.23 [t, J = 7.0 Hz, 1 H, Py(5)], 7.62 [d, J = 6.9 Hz, 1 H, Py(6)] ppm.

Structure Determinations: Crystals of **10** were obtained by recrystallization from dichloromethane. All other crystals were obtained as described above. Diffraction data were recorded at 240 K with a Bruker Smart CCD diffractometer with Mo-K_α radiation and subjected to empirical absorption corrections (program SADABS). The structures were solved with direct methods and refined anisotropically with the SHELX program suite.[39] Drawings were produced with SCHAKAL.[40] Table 2 lists the crystallographic data. CCDC-614607 (for **2**), -614608 (for **5**), -614609 (for **6**), -614610 (for **7**), -614611 (for **8**), -614612 (for **10**), and -614613 (for **11**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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