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Reactions of Pyrazolylborate–Zinc–Hydroxide Complexes Related to β-Lactamase Activity

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Simple β-lactams and their hydrolysis products, the β-amino acids, react with Tp*Zn–OH under deprotonation. The latter become semibidentate carboxylate ligands with a NH···O hydrogen bond, and the former become N-bound β-lactamide ligands. Likewise the antibiotic derivatives 6-aminopenicillanic acid and 7-aminocephalosporanic acid are incorporated as carboxylate ligands. β-Lactams bearing nitrophenyl or acyl substituents at the nitrogen atoms are opened hydrolytically by Tp*Zn–OH, and the resulting N-substituted β-amino acids are attached to zinc by their carboxylate functions. Only with trifluoroacetyl as the N-substituent does the hydrolytic cleavage occur at the external amide bond, yielding the free β-lactam and Tp*Zn–trifluoroacetate. The kinetic investigation of the opening reactions has shown them to be of second order like all other Tp*Zn–OH-induced hydrolytic cleavages, thereby supporting the four-center mechanism for the monozinc β-lactamases.

Introduction

The β-lactamases belong to a new class of enzymes resulting from the evolutionary process that is making bacteria resistant against penicillin and cephalosporin derivatives.[1] They act by opening the β-lactam rings of these antibiotics. Many of them are metalloenzymes containing one or two zinc ions in their active centers. In the simplest case one zinc ion is fixed to the protein by three histidine residues and bears an aqua ligand which is deprotonated at physiological pH,[2] and this binding motif is also present in all dizinc β-lactamases.[3] Thus the β-lactamases represent the classical $(N_3)Zn-OH$ nucleophile which is the hydrolytically active ingredient in so many zinc enzymes including carbonic anhydrase and the large group of the matrix metalloproteases.[3]

The high medicinal relevance has stimulated many studies on the structure and activity of the metallo-β-lactamases as well as on the function of the zinc ions and their amino acid environment.[1,3,4] The essence of these studies in terms of the metal content is that one zinc ion is necessary for the catalytic activity while the other can provide additional substrate activation. If one breaks down this complex biochemical scenario to the processes actually occurring at the metal center[3,5] this means that we are again faced with the hydrolytic function of $(N_3)Zn-OH_2$ or $(N_3)Zn-OH$ complexes.

We, together with G. Parkin, have provided the first mononuclear example of such a $(N_3)Zn-OH$ complex in the form of $Tp^{tBu,Me}Zn-OH$[6] ($Tp^{tBu,Me}$ is hydrotris(3-*tert*-butyl-5-methylpyrazolyl)borate) and subsequently applied Tp*Zn−OH complexes (Tp* denotes 3- and 5-substituted pyrazolylborates) for various hydrolytic reactions.[7] During these studies it was found that the Tp*Zn−OH nucleophiles are not strong enough to cleave amide or peptide bonds. The amide bonds in β-lactams, however, are more reactive due to the ring tension, and they can be activated further by placing appropriate substituents on the β-lactams. We were therefore optimistic that with the right choice of reagents β-lactam hydrolysis by Tp*Zn−OH complexes would be achieved.

A few bioinorganic chemistry papers dealing with this subject have already appeared. Beyond the basic observation that divalent and trivalent metal ions promote the opening of the lactam ring, they involve the use of mono- and dizinc complexes of polydentate ligands in the hydrolysis of penicillin-derived β-lactams.[8−11] Kinetic and mechanistic data

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(1) Page, M. I.; Laws, A. P. *J. Chem. Soc., Chem. Commun.* **1998**, 1609.
(2) Bounaga, S.; Laws, A. P.; Galleni, M.; Page, M. I. *Biochem. J.* **1998**, *331*, 703.
(3) Parkin, G. *Chem. Rev.* **2004**, *104*, 699.
(4) De Seny, D.; Prosperi-Meys, C.; Bebrone, C.; Rossolini, G. M.; Page, M. I.; Noel, P.; Frere, M.; Galleni, M. *Biochem. J.* **2002**, *363*, 687 and references therein.
(5) Kaim, W.; Schwederski, B. *Bioinorganic Chemistry*, 2nd ed.; Teubner: Stuttgart, Germany, 1995.
(6) Alsfasser, R.; Trofimenko, S.; Looney, A.; Parkin, G.; Vahrenkamp, H. *Inorg. Chem.* **1991**, *30*, 4098.
(7) Vahrenkamp, H. *Acc. Chem. Res.* **1999**, *32*, 589.

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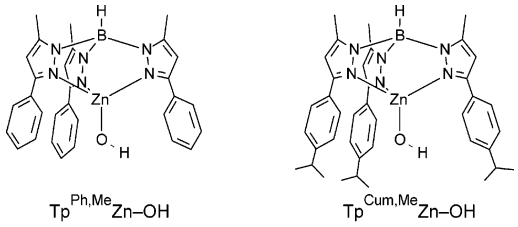
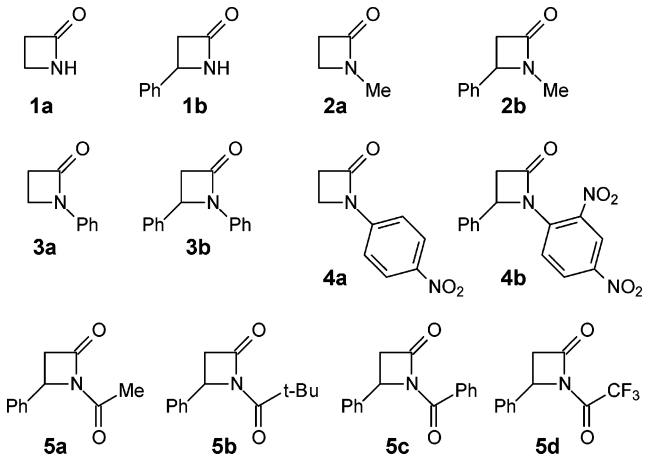
were obtained for one mononuclear and one dinuclear model complex,[8,10] and theoretical calculations were performed for a mononuclear situation modeled after the enzyme.[11] Considering this early stage of development of the field, it seemed worthwhile to us to make some contributions by Tp*Zn−OH chemistry. For this purpose we used complexes **A** and **B**. This paper describes our results.



Results and Discussion

β-Amino Acids and β-Lactams. β-Amino acids are the hydrolysis products of the β-lactams, and as such, they should be bound to zinc as carboxylates after Tp*Zn−OH-induced β-lactam cleavage. We therefore used three of them, β-alanine, 3-methyl-β-alanine, and 3-phenyl-β-alanine for reference purposes.

Among the lactams, we started with the basic species β-propiolactam (**1a**) and 4-phenyl-β-propiolactam (**1b**). Blocking of their NH function was done by methyl groups in *N*-methyl-β-propiolactam (**2a**) and *N*-methyl-4-phenyl-β-propiolactam (**2b**). A slight activation of the lactams' peptide bonds was expected in *N*-phenyl-β-propiolactam (**3a**) and *N*-phenyl-4-phenyl-β-propiolactam (**3b**). Nitrophenyl substituents were used for a stronger activation in *N*-*p*-nitrophenyl-4-phenyl-β-propiolactam (**4a**) and *N*-2,4-dinitrophenyl-4-phenyl-β-propiolactam (**4b**). Finally, activating acyl groups were applied in *N*-acetyl- (**5a**), *N*-*tert*-butyryl- (**5b**), *N*-benzoyl- (**5c**), and *N*-(trifluoroacetyl)-4-phenyl-β-propiolactam (**5d**).



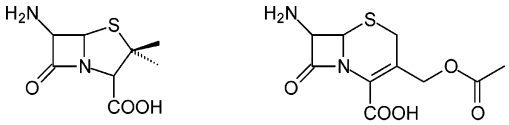
To obtain a measure of their C−N activation, the structures of **4a**,**b** were determined. Details are given in the Supporting Information. Table 1 lists the relevant bond lengths in comparison to those of reference compounds. It is evident that upon attachment of electron-withdrawing substituents

Table 1. Bond Lengths (Å) in β-lactams and Amides

	C−N	C=O
amides (av)[13]	1.32	1.24
β-propiolactam[14]	1.333(2)	1.226(1)
4a	1.376(2)	1.208(2)
4b	1.385(2)	1.200(2)

at the nitrogen atom the amide C−N bond gets longer and the amide C−O bond gets shorter. The resulting weakening of the C−N bond reflects the diminished amide resonance. Comparably weak C−N bonds are observed in β-lactams with *N*-bromophenyl substituents.[12] In line with this the C=O stretching frequency rises from amides (1600−1680 cm^{-1})[13] to β-propiolactam (1727 cm^{-1}) and further to **4a** (1755 cm^{-1}) and **4b** (1785 cm^{-1}).

Two natural derivatives of penicillin and cephalosporin were included in this investigation, the deacylated forms 6-aminopenicillanic acid (**6**) and 7-aminocephalosporanic acid (**7**) which both are amino acids.



β-Amino Acid Complexes. These complexes were prepared for reference purposes and for the purpose of finding out whether β-amino acids would be analogous to α-amino acids in acting as O,N-chelators toward zinc in the Tp*Zn environment.[15] Both Tp*Zn−OH complexes reacted smoothly with the three amino acids producing complexes **8a**−**c** and **9a**−**c** in good yields.

H_2N-CHR-CH_2-COO-Zn$Tp^{Ph,Me}$ **8**

H_2N-CHR-CH_2-COO-Zn$Tp^{Cum,Me}$ **9**

a: R = H, **b**: R = CH_3, **c**: R = C_6H_5

The IR and ^1H NMR data of complexes **8** and **9** clearly distinguish them from the corresponding α-amino acid complexes.[15] The carboxylate CO stretching bands in the 1600−1620 cm^{-1} range are in the typical region for complexes of simple carboxylates[16,17] but 40−50 cm^{-1} higher than those of the α-amino acid complexes.[15] The ^1H NMR spectra show well-resolved sets of doublets and triplets for the protons of the CHR−CH_2 units indicating that the amino acid ligands are fixed rather rigidly in similar positions.

(8) Koike, T.; Takamura, M.; Kimura, E. *J. Am. Chem. Soc.* **1994**, *116*, 8443.
(9) Ogawa, K.; Nakata, K.; Ichikawa, K. *Chem. Lett*. **1998**, 797.
(10) Kaminskaia, N. V.; Spingler, B.; Lippard, S. J. *J. Am. Chem. Soc.* **2000**, *122*, 6411.
(11) Diaz, N.; Suarez, D.; Merz, K. M. *J. Am. Chem. Soc.* **2001**, *123*, 9867. Diaz, N.; Scordo, T. L.; Suarez, D.; Mendez, R.; Martin-Villacorta, J. *New J. Chem.* **2004**, 15.
(12) Fujiwara, H.; Varley, R. L.; van der Veen, J. M. *J. Chem. Soc., Perkin Trans. 2* **1977**, 547.
(13) Barton, D., Ollis, W. D., Eds. *Comprehensive Organic Chemistry*; Pergamon Press: Oxford, U.K., 1979; Vol. 2, p 990.
(14) Yang, Q. C.; Seiler, P.; Dunitz, J. D. *Acta Crystallogr., Sect. C* **1987**, *43*, 565.
(15) Rombach, M.; Gelinsky, M.; Vahrenkamp, H. *Inorg. Chim. Acta* **2002**, *334*, 25.
(16) Darensbourg, D. J.; Holtcamp, M. W.; Khandelwal, R.; Klausmeyer, K. K.; Reibenspies, J. H. *Inorg. Chem.* **1995**, *34*, 2389.
(17) Ruf, M.; Vahrenkamp, H. *Chem. Ber*. **1996**, *129*, 1025.

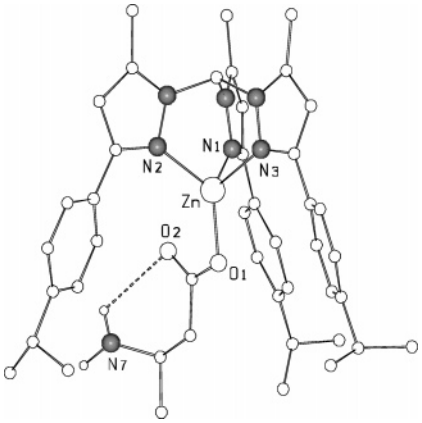
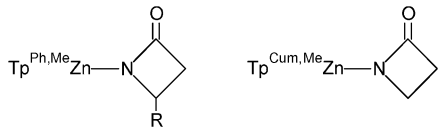


Figure 1. Molecular structure of **9b**. Relevant bond lengths (Å): Zn−N1 2.024(5), Zn−N2 2.026(5), Zn−N3 2.093(5), Zn−O1 1.923(4), Zn···O2 2.610(5), N7···O2 2.895(5).

While this did not rule out chelation by Zn−N coordination, it could be interpreted more easily by a NH···O hydrogen bond as the origin of rigidity. This was confirmed by the structure determination of **9b**; see Figure 1.

To a first approximation **9b** contains a monodentate carboxylate ligand. Yet the elongation of the Zn−N3 bond and the Zn···O2 distance of 2.61 Å indicate a weak Zn−O2 interaction which corresponds with the fact that N3 and O2 lie on the axial positions of a presumed trigonal bipyramid around zinc. Thus, the carboxylate ligand can be termed semibidentate, just like the ones in Tp^{Ph}Zn−benzylate,[16] Tp^{Ph}-Zn−2-aminobenzoate,[18] $Tp^{Ph,Me}$Zn−GlyPheBoc,[15] and $Tp^{Cum,Me}$Zn-2-hydroxypropionate.[17] The rigidity of the amino acid ligand is further established by the expected N−H···O hydrogen bond, which due to the N7···O2 distance of 2.90 Å is of moderate strength. The amino acid residue fits well into the pocket provided by the three cumenyl substituents, thereby confirming that lactam hydrolysis leading to such a zinc−β-amino acid complex should owe part of its driving force to product stabilization.

Complexes of Intact β-Lactams. All nonactivated β-lactams **1**−**3** were treated with the hydroxide complexes **A** and **B**. The NH-containing lactams **1a**,**b** did react with **A**. But the products, which according to previous observations[17] were expected to be β-amino acid complexes, were identified by structure determinations as the lactamide complexes **10a**,**b**. The related lactamide complex **11a**, derived from **B** and **1a**, had already been obtained by us from $Tp^{Cum,Me}$Zn−OMe and **1a**.[19] We had previously assigned the product of the reaction between **B** and **1a** as the β-amino acid complex **9a**,[17] which would be in accord with the spectra and analytical data. However, the present findings have rendered this assignment incorrect.



10a: R = H, **10b**: R = Ph **11a**: R = H

The structure of **10a** is depicted in Figure 2 (for the similar structure of **10b**, see Supporting Information), and the

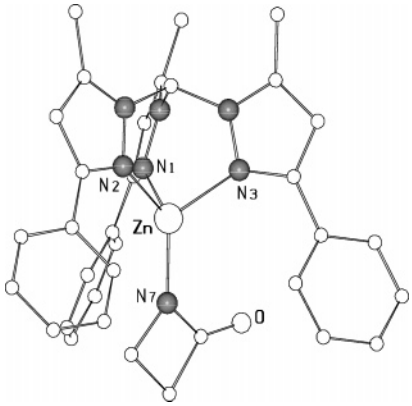


Figure 2. Molecular structure of **10a**.

Table 2. Relevant Bond Distances (Å) and Angles (deg) in **10a**,**b**

	10a	**10b**
Zn−N	1.903(2)	1.907(3)
Zn···O	3.310(3)	3.429(4)
N−C(CO)	1.351(3)	1.351(4)
N−C(CHR)	1.480(3)	1.503(4)
C−O	1.219(3)	1.225(4)
Zn−N−C(CO)	125.1(2)	130.0(2)
Zn−N−C(CHR)	141.1(2)	136.6(2)

relevant bonding details are given in Table 2. The β-lactamides act as monodentate ligands, the Zn···O separations being beyond the bonding range. The Zn−N bonds are rather short; cf. the average Zn−N(pyrazolylborate) bond lengths of 2.05 Å. With about 1.90 Å they are at the lower end of the range of bonds between zinc and anionic N-heterocycles,[19] and they can be compared with the Zn−O bond lengths in Tp*Zn−hydroxides and −alkoxides.

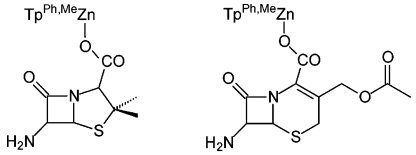
The β-lactam rings are planar within less than 0.01 Å, and the planes contain the zinc and oxygen atoms. Compared to free β-propiolactam (see Table 1) their shape is almost unchanged, the C−N bond being slightly longer and the C−O bond being barely shorter. This means that the negative charge of the lactam and its binding to zinc do not influence the amount of single bond and double bond character in the NCO array which represents the amide resonance in β-propiolactam. In contrast to this, however, the CO vibration bands, which for the free lactams are in the 1750 cm^{-1} range,[21] are lowered to 1693−1699 cm^{-1} in complexes **10** and **11**. This feature is also the major spectroscopic property distinguishing the β-lactamide complexes from the β-amino acid complexes (**10a** vs **8a** and **10b** vs **8c**), which exhibit their carboxylate bands in the 1610−1620 cm^{-1} range.

To avoid deprotonation and to direct the Tp*Zn−OH reactions to lactam ring opening, the N-methylated derivatives of **1a**,**b**, namely **2a**,**b** were applied. But even under forcing reaction conditions and in polar solvents they did not undergo reactions with **A**. The same was the case with the N-

(18) Kremer-Aach, A.; Kläui, W.; Bell, R.; Strerath, A.; Wunderlich, H.; Mootz, D. *Inorg. Chem.* **1997**, *36*, 1552.
(19) Brombacher, H.; Vahrenkamp, H. *Inorg. Chem.* **2004**, *43*, 6054.
(20) Brombacher, H.; Vahrenkamp, H. *Inorg. Chem.* **2004**, *43*, 6042.
(21) Birkhofer, L.; Schramm, J. *Liebigs Ann. Chem.* **1975**, 2195.

phenylated lactams **3a**,**b**. This means that the mild activation of the amide bonds due to the *N*-phenyl resonance is not sufficient.

In the antibiotic derivatives **6** and **7** the electron-withdrawing carboxylic acid functions could be envisaged to act as activators for amide bond cleavage in their β-lactam rings. But at the same time they are good ligating units for the Tp*Zn moieties. Reactions of $Tp^{Ph,Me}Zn-OH$ (**A**) with **6** and **7** proved the preference for zinc−carboxylate formation. Complexes **12** and **13** resulted in good yields under very mild conditions.



12 **13**

The structural assignment of **12** and **13** rests in their spectra. The ^{1}H NMR spectra show the presence of the intact units **6** and **7**. The IR spectra show the amide bands around 1770 cm^{-1}, the carboxylate bands around 1630 cm^{-1}, and in addition the ester band of **13** at 1740 cm^{-1}. The presence of the uncharged β-lactam ring in **12** and **13** induced us to try to open it by reaction with another 1 equiv of **A**. Yet there was no reaction at room temperature, and upon boiling of the sample in toluene, unidentified decomposition products resulted.

Lactam Ring Opening. The activation by electron-withdrawing N-substituents in the β-lactams **4** and **5** was strong enough to make them susceptible to nucleophilic attack by Tp*Zn−OH and subsequent ring opening. Reactions between the nitrophenyl-substituted lactams **4a**,**b** and the zinc complexes **A** and **B** proceeded in boiling toluene, and the β-amino acid complexes **14a**,**b** and **15b** were isolated in good yields. Lactam **4b** reacted about 50 times faster than lactam **4a**.

p-NO_2-C_6H_4-NH-CH_2-CH_2-COO-$Tp^{Ph,Me}$

14a

2,4-$(NO_2)_2$-C_6H_3-NH-CHPh-CH_2-COO-$Tp^{R,Me}$

14b: R = Ph, **15b**: R = Cum

Complexes **14** and **15** were identified by their spectra. The IR spectra show the NH band near 3300 cm^{-1} and the carboxylate band near 1600 cm^{-1}, and they lack the lactam band near 1750 cm^{-1}. The ^{1}H NMR spectra display the NH resonance, and all other resonances are shifted considerably with respect to their position for the free lactams.

Complex **14a** was subjected to a structure determination; see Figure 3. The attachment of the amino acid to zinc conforms with that in complex **9b**; i.e., the carboxylate unit is semi-bidentate. Bond lengths and angles in the TpZn moiety as well as in the amino acid are normal. The major difference between **9b** and **14a** consists of the hydrogen-bonding pattern. While it is intramolecular in **9b**, it is intermolecular in **14a** in such a way that the amino acid chains of two neighboring complex molecules are aligned

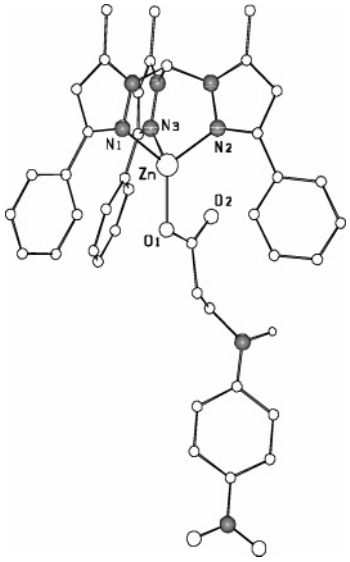


Figure 3. Molecular structure of **14a**. Relevant bond lengths (Å): Zn−N1 2.082(2), Zn−N2 2.036(2), Zn−N3 2.024(2), Zn−O1 1.935(2), Zn···O2 2.584(2), N8···O2′ 2.929(3).

in a quasi-parallel fashion across a center of symmetry and their ends are linked by N−H···O bonds, generating a 12-membered $(OCCCNH)_2$ ring.

The reactivity of the N-acylated β-lactams **5a**−**c** toward $Tp^{Ph,Me}Zn-OH$ (**A**) was intermediate between that of **4a** and **4b**. Within a few hours in boiling toluene they were converted to the amino acid complexes **16a**−**c**.

RCO-NH-CHPh-CH_2-COO-Zn$Tp^{Ph,Me}$

16a: R = Me, **16b**: R = t-Bu, **16c**: R = Ph

The spectroscopic data showed that complexes **16** are relatives of **14** and **15**. The amide IR band of the free lactams **5** near 1790 cm^{-1} has disappeared and is replaced by the carboxylate band between 1600 and 1640 cm^{-1}, while the amide band of the exocyclic acyl group near 1690 cm^{-1} is shifted by only ca. 25 cm^{-1} to lower wavenumbers in the complexes. Characteristic shifts of the ^{1}H NMR signals correspond to those in complexes **14** and **15**. Hence, there should be no doubt about the identity of **16a**−**c**. Relatively weak and low-wavenumber IR bands for the NH function indicate that there are also N−H···O hydrogen bonds, which however cannot be located in the absence of a structure determination.

The presence of two *N*-acyl functions in the lactams **5** implies the possibility of hydrolytic cleavage of the external N−COR bonds. It turned out that this takes place for the most strongly electron-withdrawing COR unit, the trifluoroacetyl function in **5d**. The reaction between **A** and **5d** at room temperature took only a few minutes to produce the free lactam **1b** and the known complex $Tp^{Ph,Me}Zn-OCOCF_3$.[17] The easiest way to follow this reaction was by ^{19}F NMR, the spectra showing only the signals for **5d** at 75.8 ppm and for the trifluoroacetate complex at 75.3 ppm.

Kinetic Investigation. The course of reaction of both **A** and **B** with the β-lactam **4b** was followed by ^{1}H NMR. The Tp*Zn−OH complexes were treated under pseudo-first-order conditions with a 5- to 9-fold excess of **4b** at 40 °C in $CDCl_3$.

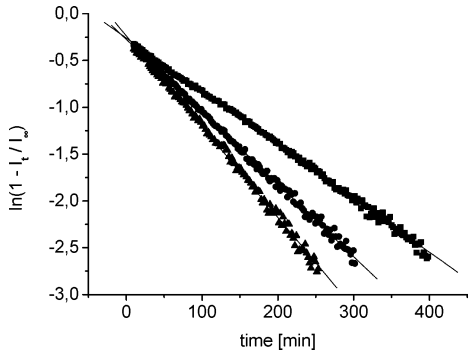


Figure 4. Logarithmic plot of the intensity of the benzylic proton ^{1}H NMR signal in **14b** for the cleavage of **4b** by **A**.

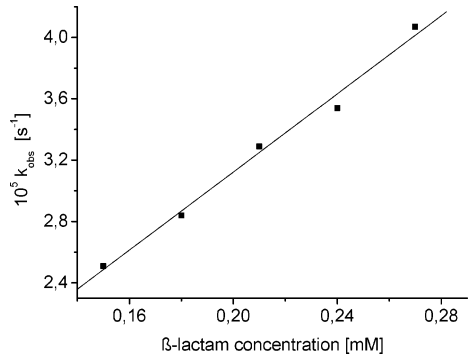


Figure 5. Plot of the k_{obs} values for the cleavage of **4b** by **B** against five concentrations of the lactam.

The intensities of the signals for the benzylic proton in the products **14b** and **15b** were recorded as a function of time. Pseudo-first-order rate constants were obtained according to $\ln(1 - I_t/I_\infty) = -k_{obs}t$. The resulting k_{obs} values, plotted against the lactam concentration, define a regression line, the slope of which is the second-order rate constant. The quality of the measurements, expressed by correlation coefficients around 0.995, can be judged from Figures 4 and 5. It should be noted that the plot of Figure 5 has an intercept at 0.5×10^{-5} s^{-1}, indicating that there is some independent lactam hydrolysis which is zero order in lactam concentration. This, however, does not affect the calculation of k''.

The two second-order rate constants k'' obtained are 0.57 M^{-1} s^{-1} for **A** and 0.13 M^{-1} s^{-1} for **B**. The fact that the phenyl-substituted Tp*Zn−OH complex **A** reacts about four times faster than the cumenyl-sunstituted **B** is in agreement with the more hindered access to the Zn−OH center in the latter. The scarcity of investigations on zinc complex induced β-lactam hydrolyses makes it difficult to compare our kinetic data with reported ones. The only study reporting a second-order rate constant for a related reaction system is that by Kimura using a zinc−cyclen complex.[8] The reported k'' value for the hydrolysis of benzylpenicillin in water (4×10^{-2} M^{-1} s^{-1}) is about 1 order of magnitude smaller than the k'' values observed here, which (taking into account the strongly accelerating influence of the water solvent) reflects the significantly reduced reactivity of benzylpenicillin in comparison to **4b**.

On the other side, the second-order rate constants observed here can be compared with those for other hydrolytic reactions induced by Tp*Zn−OH complexes. Thus, the cleavages of tris(*p*-nitrophenyl) phosphate by **A** and **B** are characterized by k'' values of 1.55 and 0.45 M^{-1} s^{-1}, respectively, and the cleavage of *p*-nitrophenyl acetate by **B** has yielded a k'' of 0.35×10^{-2} M^{-1} s^{-1}.[22] In all cases the strong activation by nitrophenyl substituents is necessary to enable hydrolysis, in accord with the hidden nature of the Zn−OH nucleophile in the Tp* ligand pocket and the completely nonpolar reaction environment. When one wants to compare phosphate, ester, and lactam hydrolysis by Tp*Zn−OH, one should use a k'' for the mononitrophenyl-substituted **4a** which could not be determined here but which can be estimated (see above) to be close to 2 orders of magnitude smaller than that for **4b**. If taken as such, it is in the same range as that for the cleavage of *p*-nitrophenyl actate. Then the sequence of reactivities (phosphate ≫ ester ≈ β-lactam) corresponds to that which has classically been established for group transfers from these species.[13]

Conclusions

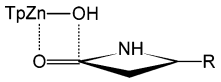
As observed before it was found in this work too that the available zinc−hydroxide complexes are not potent enough as nucleophiles to effect ring opening of simple, nonactivated β-lactams. When the lactams contain a NH function, though, they are deprotonated by Tp*Zn−OH and attached to zinc as the novel β-lactamide ligands. By using the hydrolysis products of the β-lactams, the β-amino acids, as such, it could be shown that they make stable Tp*Zn complexes in which the shape of the carboxylate-bound amino acid ligands is fixed by NH···CO hydrogen bonds. Likewise the β-lactam antibiotic derivatives 6-aminopenicillanic acid and 7-aminocephalosporanic acid are attached to the Tp*Zn moieties as carboxylates.

To have the lactams cleaved by Tp*Zn−OH they must be activated by N-bound nitrophenyl or acyl substituents. The products of ring opening end up as zinc-bound β-amino acid ligands, which can easily be identified by their characteristic spectral features. As a rule the *N*-acyl activated β-lactams undergo hydrolytic cleavage only at the lactam acyl function. Only in case of *N*-trifluoroacetyl activation is the exocyclic acetyl function cleaved yielding the free lactam and a zinc−trifluoroacetate complex.

The kinetic investigation of the Tp*Zn−OH-induced ring opening reaction has shown it to be a clean second-order process whose rate depends noticeably on the accessibility of the Zn−OH function inside the Tp* ligand pocket. This is in agreement with the generally accepted four-center mechanism for Zn−OH-induced hydrolytic reactions and our specific formulation of it for Tp*Zn systems.[7,22] For the specific case of β-lactams the essential intermediate should look like the one depicted below. The relevant conclusion from this is that β-lactam hydrolysis, like all other zinc enzyme catalyzed hydrolytic processes, needs only one zinc ion. This finding complements similar observations from biochemical[1,3] as well as from model complex studies.[8,10] The fact that several such enzymes, specifically the metallo-

(22) Rombach, M.; Maurer, C.; Weis, K.; Keller, E.; Vahrenkamp, H. *Chem.−Eur. J.* **1999**, *5*, 1013.

β-lactamases, contain two zinc ions in the active center is not contradictory to this, as various supporting functions for the second zinc ion can be envisaged.



Experimental Section

General Data. All experimental techniques and the standard IR and NMR equipment were as described previously.[23] The Tp*Zn−OH complexes were prepared as described.[24,25] The lactams **1b**,[26] **2a**,[27] **2b**,[27] **3a**,[28] **3b**,[29] **4a**,[28] **5a**,[29] **5b**,[29] and **5c**[29] were prepared by following the literature procedures. Lactams **4b** and **5d** had not been described yet. All other organic reagents were purchased from Merck and Aldrich. The IR, ^{1}H NMR, and ^{13}C NMR spectral data for the $Tp^{Ph,Me}$ and $Tp^{Cum,Me}$ ligands in the new complexes vary only negligibly between themselves and the reference compounds.[15,17,19,20,24,25] Therefore, only the data for the coligands X in the Tp*Zn−X complexes are reported here.

Lactam 4b. A solution of **1b** (1.00 g, 6.79 mmol), 2,4-dinitroiodobenzene (2.00 g, 6.79 mmol), and K_2CO_3 (939 mg, 6.79 mmol) in anhydrous dioxane (120 mL) was treated with 20 mg (0.11 mmol) of CuI and heated to 80 °C for 3d. After being cooled to room temperature, the mixture was filtered and the filtrate evaporated to dryness. The residue was dissolved in 30 mL of ethyl acetate and the product precipitated by slow addition of 60 mL of cyclohexane. The precipitate was dissolved in 10 mL of dichloromethane and filtered through a 1 cm layer of silica gel, and 30 mL of a 2:1 mixture of cyclohexane and ethyl acetate was added. Slow evaporation in an open flask yielded 750 mg (35%) of **4b** as yellow crystals, mp 143 °C. IR (KBr; cm^{-1}): 1785 vs (CO), 1388 vs (NO). ^{1}H NMR ($CDCl_3$): δ 3.21 (dd, J = 15.9 and 3.3 Hz, 1H), 3.70 (dd, J = 15.9 and 6.0 Hz, 1H), 5.34 (dd, J = 3.3 and 6.0 Hz, 1H), 7.35 (s, 5H, Ph), 7.96 (d, J = 9.0 Hz, 1H, C_6H_3), 8.35 (dd, J = 9.0 and 2.5 Hz, 1H, C_6H_3), 8.60 (d, J = 2.5 Hz, 1H, C_6H_3). Anal. Calcd for $C_{15}H_{11}N_3O_5$ (M_r = 313.27): C, 57.51; H, 3.54; N, 13.41. Found: C, 57.37; H, 3.45; N, 13.33.

Lactam 5d. A solution of **1b** (300 mg, 2.04 mmol) in anhydrous dichloromethane was treated dropwise with stirring first with 453 mg (630 μL, 4.48 mmol) of triethylamine and then upon cooling with ice with a solution of 471 mg (312 μL, 2.24 mmol) of trifluoroacetic anhydride in 5 mL of dichloromethane. After the solution was stirred for 15 h without renewing the ice, a solution of 2 g of NH_4Cl in 15 mL of water was added, and the mixture was shaken and extracted with three times 20 mL of dichloromethane. The combined extracts were dried over Na_2SO_4. After filtration the filtrate was evaporated to dryness. The remaining colorless oil was chromatographed with dichloromethane over a 5 × 20 cm silica gel column (R_f = 0.62). The resulting colorless oil had a purity of 95% according to ^{1}H NMR. The yield was 267 mg (54%). ^{1}H NMR ($CDCl_3$): δ 3.17 (dd, J = 17.0 and 3.9 Hz, 1H), 3.68 (dd, J = 17.0 and 7.0 Hz, 1H), 5.16 (dd, J = 7.0 and 3.9 Hz, 1H), 7.38 (m, 5H, Ph). ^{19}F NMR ($CDCl_3$): δ −75.84.

Complex 8a. A solution of **A** (200 mg, 0.35 mmol) in dichloromethane (20 mL) was added to a suspension of β-alanine (50 mg, 0.56 mmol) in methanol (20 mL). After the mixture was stirred for 15 h and filtered, the solvent was removed in vacuo. The raw product was purified three times by dissolving in dichloromethane and precipitating with *n*-heptane. A 142 mg (62%) amount of **8a** remained as a colorless powder, mp 124 °C. IR (KBr; cm^{-1}): 2545 w (BH), 1611 s (CO). ^{1}H NMR ($CDCl_3$): δ 1.53 (br, 4H, H_2O + NH_2), 1.82 (t, J = 5.9 Hz, 2H, CH_2), 2.41 (t, J = 5.9 Hz, 2H, CH_2). Anal. Calcd for $C_{33}H_{34}BN_7O_2Zn\cdot H_2O$ (M_r = 636.88 + 18.02): C, 60.52; H, 5.54; N, 14.97. Found: C, 60.45; H, 5.71; N, 14.72.

Complex 8b. This was synthesized like **8a** from **A** (300 mg, 0.53 mmol) and D,L-3-methyl-β-alanine (66 mg, 0.64 mmol). Purification by dissolution in dichloromethane and slow addition of *n*-heptane yielded 254 mg (78%) of **8b** as a colorless powder, mp 169 °C. IR (KBr; cm^{-1}): 2553 w (BH), 1598 s (CO). ^{1}H NMR ($CDCl_3$): δ 0.81 (d, J = 6.5 Hz, 3H, CH3), 1.52 (br, 2H, NH_2), 1.58 (dd, J = 16.7 and 9.4 Hz, 1H, CH), 1.81 (dd, J = 16.7 and 3.1 Hz, 1H, CH), 2.62 (m, 1H, CH). Anal. Calcd for $C_{34}H_{36}BN_7O_2Zn$ (M_r = 650.91): C, 62.74; H, 5.57; N, 15.06. Found: C, 62.64; H, 5.62; N, 14.93.

Complex 8c. This was synthesized like **8a** from **A** (200 mg, 0.35 mmol) and D,L-3-phenyl-β-alanine (66 mg, 0.40 mmol). Purification by slow evaporation of a acetonitrile/dichloromethane solution yielded 204 mg (82%) of **8c** as a colorless powder, mp 168 °C. IR (KBr; cm^{-1}): 2543 m (BH), 1616 s (CO). ^{1}H NMR ($CDCl_3$): δ 1.50 (br, 2H, NH_2), 2.03 (m, 2H, CH_2), 3.64 (dd, J = 9.7 and 3.4 Hz, 1H, CH), 7.21 (m, 5H, Ph). Anal. Calcd for $C_{39}H_{38}BN_7O_2Zn$ (M_r = 712.98): C, 65.70; H, 5.37; N, 13.75. Found: C, 65.55; H, 5.67; N, 14.58.

Complex 9a. This was synthesized like **8a** from **B** (200 mg, 0.29 mmol) and β-alanine (28.5 mg, 0.32 mmol). Purification by dissolution in dichloromethane and slow addition of *n*-heptane yielded 150 mg (67%) of **9a** as a colorless powder, mp 198 °C. IR (KBr; cm^{-1}): 2533 w (BH), 1612 m (CO). ^{1}H NMR ($CDCl_3$): δ 1.59 (br, 2H, NH_2), 1.82 (t, J = 5.8 Hz, 2H, CH_2), 2.44 (t, J = 5.8 Hz, 2H, CH_2). Anal. Calcd for $C_{42}H_{52}BN_7O_2Zn$ (M_r = 763.12): C, 66.11; H, 6.87; N, 12.85. Found: C, 65.47; H, 6.99; N, 12.52.

Complex 9b. This was synthesized like **8a** from **B** (200 mg, 0.29 mmol) and D,L-3-methyl-β-alanine (33 mg, 0.32 mmol). Purification by slow evaporation from a solution in dichloromethane and *n*-heptane yielded 160 mg (71%) of **9b** as a colorless crystals, mp 197 °C. IR (KBr; cm^{-1}): 2550 m (BH), 1618 s (CO). ^{1}H NMR ($CDCl_3$): δ 0.83 (d, J = 6.5 Hz, 3H, CH_3), 1.58 (dd, J = 16.1 and 9.3 Hz, 1H, CH), 1.82 (dd, J = 16.1 and 3.4 Hz, 1H, CH), 2.68 (m, 1H, CH). Anal. Calcd for $C_{43}H_{54}BN_7O_2Zn$ (M_r = 777.15): C, 66.46; H, 7.00; N, 12.62. Found: C, 66.19; H, 7.11; N, 12.45.

Complex 9c. This was synthesized like **8a** from **B** (200 mg, 0.29 mmol) and D,L-3-phenyl-β-alanine (53 mg, 0.32 mmol). Purification by slow evaporation from a solution in dichloromethane and *n*-heptane yielded 182 mg (75%) of **9c** as a colorless crystals, mp 207 °C. IR (KBr; cm[1]): 2542 m (BH), 1612 s (CO). ^{1}H NMR ($CDCl_3$): δ 1.51 (br, 2H, NH_2), 2.01 (m, 2H, CH_2), 3.82 (dd, J = 8.8 and 4.5 Hz, 1H, CH), 7.23 (m, 11H, therein C_6H_5).

Complex 10a. A solution of **1a** (50 mg, 0.71 mmol) in dichloromethane (10 mL) was added dropwise with stirring to a solution of **A** (400 mg, 0.71 mmol) in dichloromethane (20 mL). After the solution was stirred for 2 h, the solvent was removed in vacuo. Crystallization from acetonitrile yielded 337 mg (73%) of **10a** as a colorless crystals, mp 212 °C. IR (KBr; cm^{-1}): 2538 m (BH), 1693 vs (CO). ^{1}H NMR ($CDCl_3$): δ 1.86 (t, J = 4.1 Hz, 5H, CH_2), 2.00 (s, 3H, CH_3CN), 2.32 (t, J = 4.1 Hz, 2H, CH_2).

(23) Förster, M.; Burth, R.; Powell, A. K.; Eiche, T.; Vahrenkamp, H. *Chem. Ber.* **1993**, *126*, 2643.
(24) Ruf, M.; Burth, R.; Weis, K.; Vahrenkamp, H. *Chem. Ber.* **1996**, *129*, 1251.
(25) Ruf, M.; Vahrenkamp, H. *Inorg. Chem.* **1996**, *35*, 6571.
(26) Graf, R. *Liebigs Ann. Chem.* **1963**, *661*, 111.
(27) Yamawaki, J.; Ando, T.; Hanafusa, T. *Chem. Lett.* **1981**, 1143.
(28) Takahata, H.; Ohnishi, Y.; Jamazaki, T. *Heterocycles* **1980**, *14*, 467.
(29) Bergmann, H. J.; Otto, H. H. *Arch. Pharm. (Weinheim, Ger.)* **1986**, *319*, 635.

Table 3. Crystallographic Data

	4a	4b	9b	10a	10b	14a
formula	$C_{15}H_{12}N_2O_3$	$C_{15}H_{11}N_3O_5$	$C_{43}H_{54}BN_7O_2Zn$	$C_{33}H_{32}BN_7OZn{\cdot}CH_3CN$	$C_{39}H_{36}BN_7OZn{\cdot}CH_3CN$	$C_{39}H_{34}BN_8O_4Zn$
MW	268.27	313.27	777.15	659.91	736.01	757.95
space group	$P2_1/n$	$P2_1/c$	$P2_1/c$	$P\bar{1}$	$P2_1/n$	$P\bar{1}$
Z	4	4	4	2	4	2
a (Å)	6.092(1)	10.364(2)	8.946(5)	11.759(1)	11.818(1)	8.401(2)
b (Å)	19.191(3)	10.198(2)	22.526(12)	11.963(1)	16.134(1)	12.294(3)
c (Å)	11.121(2)	13.386(2)	21.761(11)	13.543(1)	19.442(1)	18.272(4)
α (deg)	90	90	90	71.861(2)	90	102.644(4)
β (deg)	95.130(3)	92.835(4)	110.30(2)	75.386(2)	93.135(1)	93.796(4)
γ (deg)	90	90	90	67.943(2)	90	98.556(4)
V (Å^3)	1294.9(4)	1413.0(4)	4113(4)	1658.0(2)	3701.5(4)	1811.3(7)
d(calcd) (g cm^{-3})	1.38	1.47	1.26	1.32	1.32	1.39
μ(Mo Kα) (mm^1)	0.10	0.11	0.64	0.78	0.71	0.73
R1 (obsd reflcns)	0.042	0.041	0.075	0.041	0.054	0.037
wR2 (all reflcns)	0.100	0.107	0.284	0.109	0.171	0.124

Anal. Calcd for $C_{33}H_{32}BN_7OZn{\cdot}CH_3CN$ (M_r = 618.86 + 41.05): C, 63.70; H, 5.35; N, 16.98. Found: C, 63.60; H, 5.37; N, 16.64.

Complex 10b. This was synthesized like **10a** from **A** (141 mg, 0.25 mmol) and **1b** (37 mg, 0.25 mmol). Yield: 120 mg (65%) of **10b** as a colorless crystals, mp 238 °C. IR (KBr; cm^{-1}): 2561 w (BH), 1699 vs (CO). ^{1}H NMR ($CDCl_3$): δ 1.96 (s, 3H, CH_3CN), 2.08 (m, 1H, CH), 2.86 (m, 1H, CH), 3.79 (br., 1H, CH), 6.10 (m, 2H, C_6H_5), 6.73 (m, 2H, C_6H_5), 6.84 (m, 1H, C_6H_5). Anal. Calcd for $C_{39}H_{36}BN_7OZn{\cdot}CH_3CN$ (M_r = 694.96 + 41.05): C, 66.91; H, 5.34; N, 15.22. Found: C, 66.46; H, 5.44; N, 14.78.

Complex 12. 6-Aminopenicillanic acid (97 mg, 0.45 mmol) was added to a solution of **A** (196 mg, 0.35 mmol) in dichloromethane (40 mL). After the solution was stirred for 5 h, the solvent was removed in vacuo and the residue dissolved in 3 mL of dichloromethane. Slow addition of 25 mL of a *n*-heptane/diethyl ether (4:1) mixture precipitated 226 mg (85%) of **12** as a colorless powder, mp 170 °C. IR (KBr; cm^{-1}): 2547 m (BH), 1768 vs (CO), 1638 s (CO). ^{1}H NMR ($CDCl_3$): δ 0.84 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 3.77 (s, 1H, CH), 4.34 (d, J = 4.1 Hz, 1H, CH), 5.12 (d, J = 4.1 Hz, 1H, CH). Anal. Calcd for $C_{38}H_{39}BN_8O_3SZn$ (M_r = 764.04): C, 59.74; H, 5.14; N, 14.67; S, 4.20. Found: C, 59.47; H, 5.60; N, 14.79; S, 3.86.

Complex 13. This was synthesized like **12** from **A** (200 mg, 0.35 mmol) and 7-aminocephalosporanic acid (106 mg, 0.39 mmol). Yield: 197 mg (68%) of **13** as a light brown powder, mp 130 °C. IR (KBr; cm^{-1}): 2552 w (BH), 1779 s (CO), 1740 s (CO), 1616 m (CO). ^{1}H NMR ($CDCl_3$): δ 1.93 (s, 3H, CH_3), 3.12 (d, J = 17.7 Hz, 1H, CH), 3.30 (d, J = 17.7 Hz, 1H, CH), 4.11 (d, J = 13.9 Hz, 1H, CH), 4.27 (d, J = 13.9 Hz, 1H, CH), 4.50−4.90 (m, 2H, CHCH). Anal. Calcd for $C_{40}H_{39}BN_8O_5SZn$ (M_r = 820.07): C, 58.59; H, 4.79; N, 13.66; S, 3.91. Found: C, 58.39; H, 5.22; N, 13.30; S, 4.20.

Complex 14a. A solution of **A** (200 mg, 0.35 mmol) and **4a** (67 mg, 0.35 mmol) in toluene (40 mL) was refluxed for **6d**. Then the solvent was removed in vacuo. Crystallization from acetonitrile yielded 178 mg (67%) of **14a** as yellow crystals, mp 218 °C. IR (KBr; cm^{-1}): 3319 m (NH), 2541 m (BH), 1593 s (CO), 1303 vs (NO). ^{1}H NMR ($CDCl_3$): δ 2.02 (t, J = 5.9 Hz, 2H, CH_2), 2.88 (m, 2H, CH_2), 5.03 (m, 1H, NH), 6.17 (d, J = 9.3 Hz, 2H, C_6H_4), 8.01 (d, J = 9.3 Hz, 2H, C_6H_4). Anal. Calcd for $C_{39}H_{37}BN_8O_4Zn$ (M_r = 757.97): C, 61.80; H, 4.92; N, 14.78. Found: C, 61.46; H, 5.14; N, 14.87.

Complex 14b. This was synthesized like **14a** from **A** (200 mg, 0.35 mmol) and **4b** (111 mg, 0.35 mmol) in 20 mL of toluene for 3 h. Yield: 209 mg (68%) of **14b** as a yellow powder, mp 120 °C. IR (KBr; cm^{-1}): 3294 w (NH), 2549 m (BH), 1618 vs (CO), 1333 vs (NO). ^{1}H NMR ($CDCl_3$): δ 2.32 (d, J = 6.0 Hz, 2H, CH_2), 4.56 (m, 1H, CH), 6.51 (d, J = 9.7 Hz, 1H, C_6H_3), 7.95 (dd, J = 9.7 and 2.8 Hz, 1H, C_6H_3), 9.04 (d, J = 2.8 Hz, 1H, C_6H_3), 9.13 (d, br., J = 6.5 Hz, 1H, NH). Anal. Calcd for $C_{45}H_{40}BN_9O_6Zn$ (M_r = 879.07): C, 61.48; H, 4.59; N, 14.34. Found: C, 60.88; H, 4.94; N, 14.53.

Complex 15b. This was synthesized like **14a** from **B** (150 mg, 0.22 mmol) and **4b** (68 mg, 0.22 mmol) in 20 mL of toluene for 10 h. Yield: 141 mg (64%) of **15b** as a yellow powder, mp 221 °C. IR (KBr; cm^{-1}): 3312 w (NH), 2548 w (BH), 1617 vs (CO), 1335 vs (NO). ^{1}H NMR ($CDCl_3$): δ 2.26 (d, J = 5.3 Hz, 2H, CH_2), 4.68 (m, 1H, CH), 6.62 (d, J = 9.5 Hz, 1H, C_6H_3), 7.95 (dd, J = 9.5 and 2.8 Hz, 1H, C_6H_3), 9.13 (d, J = 2.8 Hz, 1H, C_6H_3), 9.13 (d, J = 2.8 Hz, 1H, C_6H_3), 9.75 (d, br, J = 6.8 Hz, 1H, NH). Anal. Calcd for $C_{54}H_{58}BN_9O_6Zn$ (M_r = 1005.31): C, 64.52; H, 5.81; N, 12.54. Found: C, 64.38; H, 6.23; N, 12.41.

Complex 16a. A solution of **A** (100 mg, 0.18 mmol) and **5a** (34 mg, 0.18 mmol) in toluene (25 mL) was refluxed for 24 h. The solvent was removed in vacuo and the residue dissolved in 5 mL of dichloromethane. *n*-Heptane was added in such an amount as to barely avoid a precipitation. Then the mixture was left to evaporate, yielding a precipitate of 77 mg (56%) of **16a**, mp 202 °C. IR (KBr; cm^{-1}): 2544 m (BH), 1674 vs (CO), 1605 s (CO). ^{1}H NMR ($CDCl_3$): δ 1.58 (s, br, 2H, H_2O), 1.64 (s, 3H, CH_3), 2.20 (dd, J = 17.1 and 5.5 Hz, 1H, CH), 2.35 (dd, J = 17.1 and 4.9 Hz, 1H, CH), 4.93 (m, 1H, CH), 6.97 (d, br, J = 7.5 Hz, 1H, NH). Anal. Calcd for $C_{41}H_{40}BN_7O_3Zn{\cdot}H_2O$ (M_r = 755.01 + 18.02): C, 63.70; H, 5.48; N, 12.68. Found: C, 64.26; H, 5.38; N, 12.84.

Complex 16b. This was synthesized like **16a** from **A** (200 mg, 0.35 mmol) and **5b** (82 mg, 0.35 mmol). Yield: 177 mg (62%) of **16b** as a colorless powder, mp 212 °C. IR (KBr; cm^{-1}): 2557 m (BH), 1664 s (CO), 1603 m (CO). ^{1}H NMR ($CDCl_3$; cm^{-1}): 0.85 (s, 9H, t-Bu), 1.54 (s, 2H, H2O), 2.13 (dd, J = 16.8 and 5.5 Hz, 1H, CH), 2.40 (dd, J = 16.8 and 4.5 Hz, 1H, CH), 5.02 (m, 1H, CH). Anal. Calcd for $C_{44}H_{46}BN_7O_3Zn{\cdot}H_2O$ (M_r = 797.09 + 18.02): C, 64.84; H, 5.94; N, 12.03. Found: C, 65.23; H, 5.83; N, 11.85.

Complex 16c. This was synthesized like **16a** from **A** (200 mg, 0.35 mmol) and **5c** (89 mg, 0.35 mmol). Yield: 230 mg (78%) of **16c** as a colorless powder, mp 204 °C. IR (KBr; cm^{-1}): 2548 m (BH), 1659 s (CO), 1639 m (CO). ^{1}H NMR ($CDCl_3$): δ 2.27 (dd, J = 16.9 and 5.8 Hz, 1H, CH), 2.45 (dd, J = 16.9 and 3.9 Hz, 1H, CH), 5.25 (m, 1H, CH), 8.15 (d, br., J = 8.8 Hz, 1H, NH). Anal. Calcd for $C_{46}H_{42}BN_7O_3Zn$ (M_r = 817.08): C, 67.62; H, 5.18; N, 12.00. Found: C, 67.28; H, 5.58; N, 11.56.

Reaction of A with 5d. In an NMR tube 5.4 mg (0.02 mmol) of **5d** and 8.8 mg (0.015 mmol) of **A** were dissolved in 600 μL of $CDCl_3$. After 15 min the ^{1}H NMR signals of the starting materials

had been replaced by those of $Tp^{Ph,Me}Zn-OCOCF_3$[17] and **1b**, and in the ^{19}F NMR spectrum the resonance for **5d** at 75.78 ppm had been replaced by that for $Tp^{Ph,Me}Zn-OCOCF_3$ at 75.29 ppm.

Kinetic Measurements. Stock solutions were prepared of **A**, **B**, and **4b** in $CDCl_3$ (99.8%). All reagents and the cavity of the NMR spectrometer were thermostated to 314 K before the measurements. The reagents were combined immediately prior to the measurements. The concentrations of **A** or **B** were adjusted to 0.030 M for all measurements and to 0.15, 0.18, 0.21, 0.24, and 0.27 M for **4b**, respectively. The intensity of the ^1H NMR resonance for the benzylic proton of **14b** (during the reaction with **A**) and the intensity of the ^1H NMR resonance for the pyrazolyl-CH proton of **15b** (during the reaction with **B**) were recorded automatically every 30 s and stored for digital data processing. Each kinetic run was repeated once to ensure reproducibility. The averaged data were used for the calculations. The resulting kobs values for the given concentrations of **4b** were 0.95×10^{-4}, 1.08×10^{-4}, 1.29×10^{-4}, 1.45×10^{-4}, and 1.62×10^{-4} s^{-1} for the reaction with **A** and 2.51×10^{-5}, 2.84×10^{-5}, 3.29×10^{-5}, 3.54×10^{-5}, and 4.07×10^{-5} s^{-1} for the reaction with **B**.

Structure Determinations. Crystals resulting from the workup procedures (see above) were used for the structure determinations. Data sets were obtained at 240 K with a Bruker AXS Smart CCD diffractometer with Mo Kα radiation and subjected to empirical absorption corrections (SADABS). The structures were solved with direct methods and refined anisotropically using the SHELX program suite.[30] Hydrogen atoms were included with fixed distances and isotropic temperature factors 1.2 times those of their attached atoms. Parameters were refined against F^2. Drawings were produced with SCHAKAL.[31] Table 3 lists the crystallographic details.

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Supporting Information Available: Fully labeled ORTEP plots and X-ray crystallographic files in CIF format for the six structure determinations. This material is available free of charge via the Internet at http://pubs.acs.org.

IC050220J

(30) Sheldrick, G. M. *SHELX, program package of the Bruker AXS Smart CCD diffractometer*, version 5.1; Bruker: Madison, WI, 2002.
(31) Keller, E. *SCHAKAL for Windows*; Universität Freiburg: Freiburg, Germany, 2001.