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Zinc–Thiolate Complexes of the Bis(pyrazolyl)(thioimidazolyl)hydroborate Tripods for the Modeling of Thiolate Alkylating Enzymes

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The new tripod ligands bis(pyrazolyl)(3-*tert*-butyl-2-thioimidazol-1-yl)hydroborate (**L^1**) and bis(pyrazolyl)(3-isopropyl-2-thioimidazol-1-yl)hydroborate (**L^2**), together with zinc nitrate or zinc chloride and the corresponding thiolates, have yielded a total of 17 zinc–thiolate complexes. These comprise aliphatic as well as aromatic thiolates and a cysteine derivative. Structure determinations have confirmed the tetrahedral ZnN_2S_2 coordination in the complexes. Upon reaction with methyl iodide, the species **L^1**·Zn–SR are slowly converted to **L^1**·Zn–I and the free thioethers CH_3SR. A kinetic analysis has shown these alkylations to be about 1 order of magnitude slower than those of the tris(pyrazolyl)borate complexes $Tp^{Ph,Me}$Zn–SR. Alkylations with trimethyl phosphate were found to proceed very slowly even in DMSO at 80 °C.

Introduction

The major purpose of zinc in the active centers of enzymes is the catalysis of hydrolytic reactions.[1,2] For this purpose, zinc is attached to the protein backbone preferentially by nitrogen (histidine) donors and less prominently by oxygen (aspartate, glutamate) donors. Until quite recently, the major exception to this rule consisted in the alcohol dehydrogenase enzymes,[3] in the prominent ones of which zinc is bound in an electron-rich protein environment dominated by sulfur (cysteinate) donors. Now, there has emerged another class of zinc enzymes with a sulfur-rich environment of the metal, the thiolate-alkylating ones,[4] the most prominent one of which is cobalamin-independent methionine synthase.[5]

The modeling of all these enzymes by coordination compounds has profited a great deal from the development of tripodal donor ligands, particularly the pyrazolylborates and related ones. These have enabled the construction of viable structural and functional models of the hydrolytic enzymes and of alcohol dehydrogenase.[4] The modeling of the thiolate-alkylating enzymes is still in an early state. Zinc−thiolate complexes of simple bidentate[6,7] and tridentate chelators[8,9] as well as tripods with N_3,[10] N_2O,[11,12] N_2S,[12] NS_2,[13] and S_3 donor sets[14] have been prepared and subjected to alkylation reactions by ourselves and our competitors. Whenever kinetic studies were performed during these investigations, they supported the notion that the alkylation takes place at the zinc-bound and not at the free thiolates.

This Paper, which is the second in a four-part series on the alkylation of tripod-zinc−thiolate complexes, is meant to provide further information for a systematic investigation of these reactions. We wish to evaluate the influence of the donor set of the tripod (N_3, N_2S, NS_2, S_3) on the reactivity of the thiolates, thereby hoping to gain an understanding of why nature prefers a sulfur-rich ligand environment of the metal (notably NS_2) for zinc-catalyzed thiolate alkylations. A systematic investigation of this kind requires that the four

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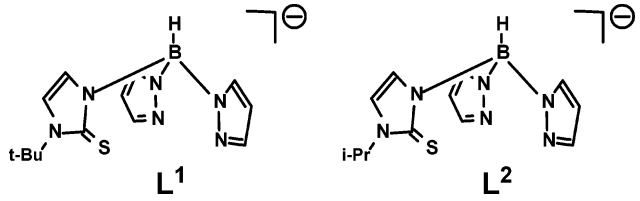
tripods used are true members of a homogeneous series. Such a series is now available in the form of the tris(donor)-hydroborate ligands ranging from Trofimenko's tris(pyrazolyl) borates[15] to Reglinski's tris(thioimidazolyl)borates.[16] Of the two mixed members, the (pyrazolyl)bis(thioimidazolyl)hydroborates were provided by Parkin[17] and ourselves.[18] Very recently, we have now found a way to synthesize the missing member of the series, the bis(pyrazolyl)-(thioimidazolyl)hydroborates.[19]

We had started our model studies on the alkylation of zinc−thiolate complexes with the tris(pyrazolyl)borates.[10] This Paper reports our findings for the $(N_2S)Zn-SR$ species derived from the bis(pyrazolyl)(thioimidazolyl)borates. The two N_2S donor ligands used were $\mathbf{L^1}$ and $\mathbf{L^2}$.[19]



Results and Discussion

Preparations. Ligands $\mathbf{L^1}$ and $\mathbf{L^2}$, which are obtained as their potassium salts,[19] could be used as such. In $\mathbf{L^2}$, however, the difficulties in isolating K$\mathbf{L^2}$ made it preferable to convert the reaction solution containing K$\mathbf{L^2}$ directly to $\mathbf{L^2}$·ZnCl with $ZnCl_2$ and use the chloride complex as the starting material. The syntheses of the thiolate complexes **1** and **2** were straightforward. Either methanol solution of K**L** was first treated with zinc nitrate and then with the deprotonated-thiols, or complexes **L**·ZnCl were treated directly with the deprotonated thiols in methanol. Compounds **1** and **2,** which form colorless crystals (except for the yellow *p*-nitrothiophenolates), were isolated in medium yields.

$\mathbf{L^1}$·Zn−SR (**1a**−**j**)	$\mathbf{L^2}$·Zn−SR (**2c**−**i**)
a: R = C_2H_5	**f**: R = C_6H_4-*p*-CH_3
b: R = CH_2CF_3	**g**: R = C_6H_4-*p*-Cl
c: R = $CH_2C_6H_5$	**h**: R = C_6H_4-*p*-NO_2
d: R = $CH_2C_6H_4$-*p*-Cl	**i**: R = C_6F_5
e: R = C_6H_5	**j**: $CH_2-CH(NHAc)(COOEt)$

Complexes **1** and **2** represent the whole range of substituents R from aliphatic (**a**, **b**) to benzylic (**c**, **d**) and aromatic (**e**−**h**) to pentafluorophenyl (**i**). To demonstrate biorelevance, doubly protected cysteine was incorporated as a thiolate in complex **1j**. There was no obvious difference in the thermal or oxidative stability between the complexes. Complex **2g** and its structure have already been described in the paper introducing ligands $\mathbf{L^1}$ and $\mathbf{L^2}$.[19]

Structures. The structures of **1a**, **1f**, **1g**, **1h**, **2f**, and **2g** were determined. Those of **1a** and **2f** are displayed here. Details for the others are given in the Supporting Information.

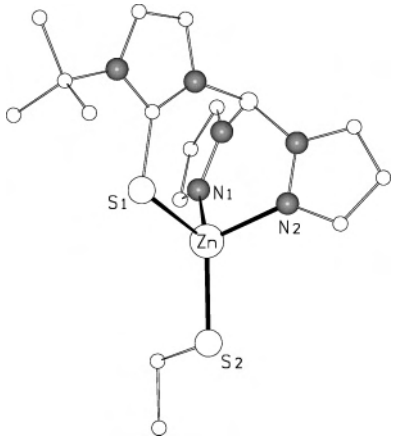


Figure 1. Molecular structure of $\mathbf{L^1}$·Zn−SEt (**1a**).

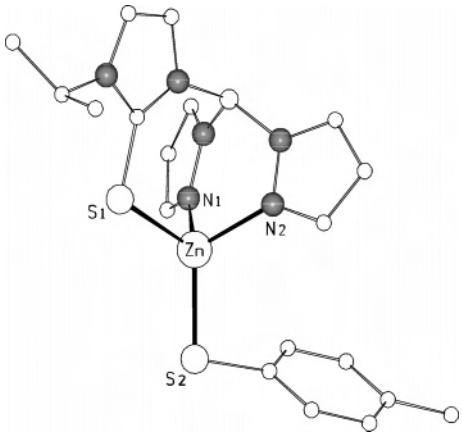


Figure 2. Molecular structure of $\mathbf{L^2}$·Zn−$SC_6H_4CH_3$ (**2f**).

As Table 1 shows, there is a remarkable similarity between all six structures. Particularly, the comparable bond lengths vary not more than 0.02 Å. Among the bond angles, the S−Zn−S angles show the widest spread, which may reflect packing interactions as well as repulsive interactions between the thiolate groups and one of the pyrazolyl groups of the tripod ligand. The Zn−N and Zn−S (thioimidazolyl) bond lengths are characteristic, as observed for tris(pyrazolyl)-borate[20] and tris(thioimidazolyl)borate zinc complexes,[21] respectively. The Zn−S (thiolate) bonds are characteristically shorter than the Zn−S (thioimidazolyl) bonds. It had been hoped that their variation might reflect differences in the zinc−thiolate interactions and hence in thiolate reactivity, for example, between electron-rich SC_2H_5 and electron-poor $SC_6H_4NO_2$. Yet, the spread of only 0.01 Å does not allow a discussion here.

Methylations. Complexes **1a**, **1c**, **1e**, **1f**, **1h**, and **1i** were chosen for methylations with methyl iodide. The reactions proceeded according to eq 1 and were quantitative (except for **1h**) according to ^{1}H NMR. Both the iodide complex $\mathbf{L^1}$·ZnI and the thioethers **3** were isolated. Only the reactions of the alkanethiolate complexes **1a** and **1c** were reasonably fast at room temperature, coming to completion within a day. The benzenethiolate complexes **1e** and **1f** needed about 5

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Table 1. Bond Distances (Å) and Angles (deg) at Zinc in the Thiolate Complexes

	1a	1f	1g	1h	2f	2g[19]
Zn−N1	2.017(5)	2.011(2)	2.013(2)	2.002(5)	2.011(3)	2.017(2)
Zn−N2	2.027(5)	2.020(2)	2.024(2)	2.015(5)	2.020(3)	2.025(2)
Zn−S1	2.349(3)	2.330(1)	2.316(1)	2.303(2)	2.316(1)	2.310(1)
Zn−S2	2.228(3)	2.233(1)	2.238(1)	2.235(2)	2.228(1)	2.240(1)
N1−Zn−N2	95.2(2)	91.37(8)	93.01(8)	94.4(2)	93.3(1)	92.85(7)
N1−Zn−S1	102.2(1)	101.25(7)	105.84(6)	105.0(2)	103.2(1)	102.68(5)
N1−Zn−S2	120.0(2)	127.24(7)	123.87(6)	104.9(2)	117.9(1)	117.54(5)
N2−Zn−S1	98.5(1)	106.86(7)	101.71(6)	103.1(2)	102.1(1)	103.70(5)
N2−Zn−S2	114.2(1)	119.03(7)	121.11(6)	128.5(2)	118.7(1)	118.31(6)
S1−Zn−S2	121.8(1)	108.31(3)	108.33(3)	116.6(1)	117.8(1)	117.87(3)

days to react, and the pentafluorothiophenolate complex **1i** needed 2 weeks. The *p*-nitrothiophenolate complex **1h** was the slowest to react. Even after refluxing a chloroform solution of **1h** and CH_3I for 10 days, it still contained the starting materials in addition to the products $\mathbf{L^1}$·ZnI and **3h**.

$$\underset{\mathbf{1}}{\mathbf{L^1}\cdot Zn-SR} + CH_3I \rightarrow \underset{\mathbf{3}}{\mathbf{L^1}\cdot ZnI} + CH_3SR \qquad (1)$$

1 and **3**	**a**	**c**	**e**	**f**	**h**	**i**
R	C_2H_5	$CH_2C_6H_5$	C_6H_5	$C_6H_4CH_3$	$C_6H_4NO_2$	C_6F_5

The alkylating agent methyl iodide chosen for these reactions is an inappropriate substitute for the biological agent methyltetrahydrofolate,[4,5] which is a methylammonium compound. Yet, so far, methylammonium salts were found not to be reactive enough for the methylation of zinc-bound thiolates.[10] However, trimethyl phosphate as a substitute for the organophosphate alkylating agents in the Ada repair process[22] could be applied for such alkylations.[4,7,9] We therefore employed it for reactions with **1e** and **1f**. No conversion was observed in chloroform, even at reflux. As found before,[7,9,23] the very polar solvent DMSO and elevated temperatures were necessary to induce reactions according to eq 2. Still, even after 3 weeks at 80 °C, the reactions were only about half complete, and the product complex $\mathbf{L^1}$·Zn−$OPO(OMe)_2$ as well as the thioethers **3** could only be identified by NMR.

$$\underset{\mathbf{1}}{\mathbf{L^1}\cdot Zn-SR} + PO(OMe)_3 \rightarrow \underset{\mathbf{3}}{\mathbf{L^1}\cdot Zn-OPO(OMe)_2} + CH_3SR \qquad (2)$$

e, R = C_6H_5; **f**, R = $C_6H_4CH_3$.

Kinetics. The methylation of the benzylthiolate complex **1c** was chosen for the kinetic analysis, first because the reaction occurs in a time frame which is convenient for NMR monitoring, and second because the resulting data could be compared with those obtained by us for the analogous tris(pyrazolyl)borate complex $Tp^{Ph,Me}Zn-SCH_2C_6H_5$.[10] **1c** was treated under pseudo-first-order conditions with an 8- to 18-fold excess of CH_3I in $CDCl_3$ at 300 K. The intensities of two sets of ^1H NMR signals were recorded for five $t_{1/2}$ intervals; see Figure 3. This way, two data sets were available to obtain the pseudo-first-order rate constants according to $\ln(I_t - I_0) = \ln(I_\infty - I_0) - k_{obs}t$.

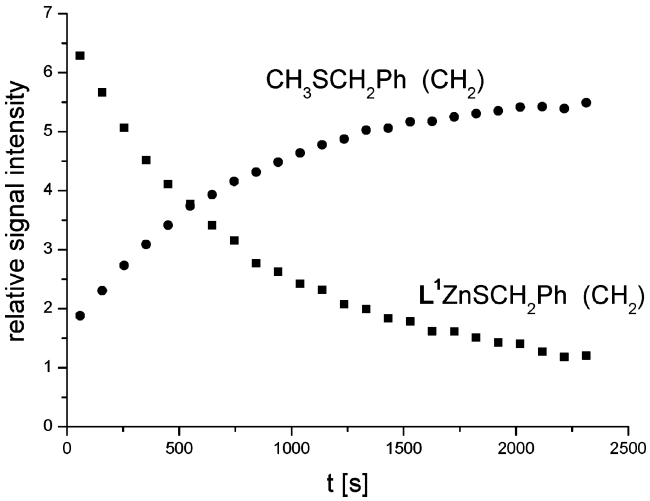

Figure 3. Intensities of selected ^1H NMR signals of **1c** and $CH_3SCH_2C_6H_5$ in $CDCl_3$ at 300 K for starting concentrations of 0.014 M for **1c** and 0.14 M for CH_3I.

The log plots for six different excess concentrations of CH_3I are linear with correlation coefficients >0.995 (see Supporting Information). The resulting k_{obs} values, plotted against the CH_3I concentration (see Supporting Information), define a regression line which passes through the origin with a correlation coefficient of 0.994. The second-order rate constant, obtained according to $k_{obs} = k''[CH_3I]$, resulted as $k'' = 6.5 \times 10^{-3}\ M^{-1}\ s^{-1}$.

As observed by us before,[10] the clean second-order reaction and its occurrence in a nonpolar medium can best be explained by an intramolecular nature of the alkylation process. In contrast, the polar medium and the forcing conditions needed for the alkylations by trimethyl phosphate indicate that these reactions require the dissociation of the thiolate from zinc prior to the alkylation. Thus, the methylations of the $(N_2S)Zn-SR$ model complexes by methyl iodide are mechanistically equivalent to the alkylations of the zinc-bound substrates in the enzyme.[4,5]

The rate constant observed here ($6.5 \times 10^{-3}\ M^{-1}\ s^{-1}$) is about 3 times smaller than that for the analogous methylation of $Tp^{Ph,Me}Zn-SCH_2C_6H_5$ ($1.8 \times 10^{-2}\ M^{-1}\ s^{-1}$).[10] A qualitative comparison of the methylations of $Tp^{Ph,Me}Zn-SR$[10] and $\mathbf{L^1}$·Zn−SR complexes and a semiquantitative one for the pair $Tp^{Ph,Me}Zn-SPh$/$\mathbf{L^1}$·Zn−SPh have confirmed this by observing that the $\mathbf{L^1}$·Zn−SR complexes on the whole react about

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1 order of magnitude slower than the $Tp^{Ph,Me}Zn-SR$ complexes. This is a puzzling observation. In a first approximation, one would have expected that the $(N_2S)Zn-SR$ species derived from $\mathbf{L^1}$ would be more electron-rich than the $(N_3)Zn-SR$ species derived from $Tp^{Ph,Me}$ and hence possess more nucleophilic SR ligands, in accordance with the experienced electron richness of the tris(thioimidazolyl)-borate−zinc complexes[21] and in accordance with nature's choice of a sulfur-rich protein environment of zinc in the thiolate-alkylating enzymes. Furthermore, the smaller steric hindrance at the Zn−SR moieties in complexes **1** compared to that in the investigated tris(pyrazolyl)borate−zinc thiolates[10] would also make one expect that the latter react more slowly than the former. At the moment, the available data do not allow a satisfying explanation of the observed phenomenon. This is one of the reasons why we are investigating other $\mathbf{L}\cdot Zn-SR$ complexes with (NS_2) and (S_3) donor sets and varying steric demands of the tripodal ligands **L**.

Conclusions

The new bis(pyrazolyl)(thioimidazolyl)hydroborate ligands $\mathbf{L^1}$ and $\mathbf{L^2}$ have enabled a further step in our systematic investigation on the modeling of biological thiolate alkylations by zinc enzymes. The imitation of the metal's protein environment by tripodal donor ligands could be extended from the ZnN_3 environment in the pyrazolylborates to the ZnN_2S environment in $\mathbf{L^1}$ and $\mathbf{L^2}$. An extension of this series to $ZnNS_2$ and ZnS_3 environments suggests itself.

The mechanistic investigation of the methylation reactions has provided further support for the notion that in the model complexes just like in the enzymes the thiolates are alkylated in the zinc-bound state. The reaction rates, however, are still far lower than those in the enzymes. Surprisingly, for the $\mathbf{L^1}\cdot Zn$ thiolates they are even lower than for the less bioanalogous TpZn thiolates. This clearly indicates that we are still far from a reasonable understanding of the factors governing the efficiency of the alkylation process, not to speak of performing it catalytically. Thus, while the mechanistic principles seem to be clear now, the performance of the model complexes requires further efforts.

Experimental Section

General Data. All experimental techniques and standard IR and NMR equipment were as described previously.[24] Starting materials were obtained from Merck. $K\mathbf{L^1}$, $\mathbf{L^1}\cdot ZnCl$, and $\mathbf{L^2}\cdot ZnCl$[19] as well as HCys(OEt)(NAc)[25] were prepared according to the published procedures.

Preparation of the Thiolate complexes. Method A. A 0.5 M stock solution of $NaOCH_3$ was prepared by dissolving 1.15 g (0.05 mmol) of clean sodium in 100 mL of methanol. A solution of 0.3−0.5 mmol of the thiol in 40 mL of methanol was deprotonated with an equimolar amount of the $NaOCH_3$ solution.

To a solution of 0.3−0.5 mmol of $K\mathbf{L^1}$ in 50 mL of methanol were slowly added with stirring first an equimolar amount of $Zn(NO_3)_2\cdot 4H_2O$ in 40 mL of methanol and then the freshly prepared thiolate solution. After stirring for 15 h, the solvent was removed in vacuo and replaced by 30 mL of chloroform. After filtration, the solvent was pumped off again and the residue was crystallized from methanol.

Method B. The freshly prepared thiolate solution (see Method A) was slowly dropped with stirring into a solution containing an equimolar amount of $\mathbf{L}\cdot ZnCl$. After stirring for 1 day, the solvent was removed in vacuo and replaced by 30 mL of chloroform. After filtration, the solvent was pumped off again and the residue was crystallized from methanol.

1a. Method B, 0.216 g (0.54 mmol) of $K\mathbf{L^1}$, 0.033 g (0.54 mmol) of C_2H_5SH. Yield 0.101 g (39%), colorless crystals, mp 176 °C. ν(BH) 2490 cm^{-1}. ^1H NMR ($CDCl_3$) 1.40 [t, $J = 7.3$ Hz, 3H, CH_3], 1.67 [s, 9H, t-Bu], 2.73 [q, $J = 7.3$ Hz, 2H, CH_2], 6.27 [t, $J = 2.2$ Hz, 2H, Pz-H], 6.89 [d, $J = 2.3$ Hz, 1H, Im-H], 6.95 [d, $J = 2.2$ Hz, 1H, Im-H], 7.67 [d, $J = 2.1$ Hz, 2H, Pz-H], 7.76 [d, $J = 1.8$ Hz, 2H, Pz-H]. Anal. Calcd for $C_{15}H_{23}BN_6S_2Zn$ ($M_r = 481.69$): C, 42.12; H, 5.42; N, 19.65; S, 14.99. Found: C, 42.34; H, 5.43; N, 19.39; S, 15.19.

1b. Method A, 0.077 g (0.29 mmol) of $Zn(NO_3)_2\cdot 4H_2O$, 0.100 g (0.29 mmol) of $K\mathbf{L^1}$, 0.034 g (0.29 mmol) of CF_3CH_2SH. Yield 0.046 g (33%), colorless crystals, mp 157 °C. ν(BH) 2488 cm^{-1}. ^1H NMR ($CDCl_3$) 1.70 [s, 9H, t-Bu], 3.25 [q, $J = 10.1$ Hz, 2H, CH_2], 6.31 [t, $J = 2.2$ Hz, 2H, Pz-H], 6.92 [d, $J = 2.3$ Hz, 1H, Im-H], 6.97 [d, $J = 2.3$ Hz, 1H, Im-H], 7.70 [d, $J = 2.2$ Hz, 2H, Pz-H], 7.77 [d, $J = 1.9$ Hz, 2H, Pz-H]. ^{19}F NMR ($CDCl_3$) − 68.7. Anal. Calcd for $C_{15}H_{20}BF_3N_6S_2Zn$ ($M_r = 481.69$): C, 37.40; H, 4.18; N, 17.45; S, 13.31. Found: C, 37.56; H, 3.79; N, 17.56; S, 13.32.

1c. Method A, 0.118 g (0.45 mmol) of $Zn(NO_3)_2\cdot 4H_2O$, 0.153 g (0.45 mmol) of $K\mathbf{L^1}$, 0.056 g (0.45 mmol) of $C_6H_5CH_2SH$. Yield 0.119 g (54%), colorless crystals, mp 146 °C. ν(BH) 2461 cm^{-1}. ^1H NMR ($CDCl_3$) 1.65 [s, 9H, t-Bu], 3.84 [s, 2H, CH_2], 6.16 [t, $J = 2.1$ Hz, 2H, Pz-H], 6.82 [d, $J = 2.2$ Hz, 1H, Im-H], 6.86 [d, $J = 2.4$ Hz, 1H, Im-H], 7.05−7.41 [m, 7H, Ar, Pz-H], 7.57 [d, $J = 2.4$ Hz, 2H, Pz-H]. Anal. Calcd for $C_{20}H_{25}BN_6S_2Zn$ ($M_r = 489.79$): C, 49.05; H, 5.14; N, 17.16; S, 13.09. Found: C, 48.49; H, 5.26; N, 17.23; S, 12.56.

1d. Method A, 0.115 g (0.44 mmol) of $Zn(NO_3)_2\cdot 4H_2O$, 0.150 g (0.44 mmol) of $K\mathbf{L^1}$, 0.070 g (0.44 mmol) of p-Cl−$C_6H_4CH_2$-SH, yield 0.058 g (25%), colorless powder, mp 118 °C. ν(BH) 2464 cm^{-1}. ^1H NMR ($CDCl_3$) 1.70 [s, 9H, t-Bu], 3.87 [s, 2H, CH_2], 6.27 [t, $J = 2.1$ Hz, 2H, Pz-H], 6.91 [d, $J = 2.2$ Hz, 1H, Im-H], 6.94 [d, $J = 2.1$ Hz, 1H, Im-H], 7.18 [d, $J = 7.6$ Hz, 2H, C_6H_4], 7.39 [d, $J = 8.3$ Hz, 2H, C_6H_4], 7.52 [s, br, 2H, Pz-H], 7.66 [d, $J = 2.2$ Hz, 2H, Pz-H]. Anal. Calcd for $C_{20}H_{24}BClN_6S_2Zn$ ($M_r = 524.24$): C, 45.82; H, 4.61; N, 16.03; S, 12.23. Found: C, 45.73; H, 4.65; N, 15.90; S, 12.11.

1e. Method A, 0.077 g (0.29 mmol) of $Zn(NO_3)_2\cdot 4H_2O$, 0.100 g (0.29 mmol) of $K\mathbf{L^1}$, 0.032 g (0.29 mmol) of C_6H_5SH, yield 0.059 g (43%), colorless crystals, mp 196 °C. ν(BH) 2494 cm^{-1}. ^1H NMR ($CDCl_3$) 1.61 [s, 9H, t-Bu], 6.16 [t, $J = 2.2$ Hz, 2H, Pz-H], 6.82−7.03 [m, 5H, Ph-H, Im-H], 7.39 [d, $J = 1.8$ Hz, 2H, Pz-H], 7.50 [d, $J = 6.8$ Hz, 2H, Ph-H], 7.59 [d, $J = 2.2$ Hz, 2H, Pz-H]. Anal. Calcd for $C_{19}H_{23}BN_6S_2Zn$ ($M_r = 475.76$): C, 47.97; H, 4.87; N, 17.66; S, 13.48. Found: C, 47.93; H, 4.90; N, 17.38; S, 13.39.

1f. Method B, 0.127 g (0.32 mmol) of $\mathbf{L^1}\cdot ZnCl$, 0.039 g (0.32 mmol) of p-CH_3−C_6H_4SH, yield 0.070 g (45%), colorless crystals, mp 183 °C. ν(BH) 2469 cm^{-1}. ^1H NMR ($CDCl_3$) 1.60 [s, 9H, t-Bu], 2.16 [s, 3H, CH_3], 6.15 [t, $J = 2.2$ Hz, 2H, Pz-H], 6.79−6.88 [m, 4H, Ph-H, Im-H], 7.36−7.39 [m, 4H, Ph-H, Pz-H], 7.58 [d, $J = 2.1$ Hz, 2H, Pz-H]. Anal. Calcd for $C_{20}H_{25}BN_6S_2Zn$ ($M_r =$

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489.79): C, 49.05; H, 5.14; N, 17.16; S, 13.09. Found: C, 48.86; H, 5.22; N, 17.39; S, 12.96.

1g. Method A, 0.077 g (0.29 mmol) of $Zn(NO_3)_2 \cdot 4H_2O$, 0.100 g (0.29 mmol) of K**L**^{1}, 0.043 g (0.29 mmol) of *p*-Cl−C_6H_4SH, yield 0.062 g (42%), colorless crystals, mp 195 °C. ν(BH) 2492 cm^{-1}. ^{1}H NMR ($CDCl_3$) 1.63 [s, 9H, t-Bu], 6.20 [t, J = 2.2 Hz, 2H, Pz-H], 6.84−6.99 [m, 4H, Pz-H, Im-H], 7.37−7.44 [m, 4H, C_6H_4], 7.61 [d, J = 2.0 Hz, 2H, Pz-H]. Anal. Calcd for $C_{19}H_{22}BClN_6S_2Zn$ (M_r = 510.21): C, 44.73; H, 4.35; N, 16.47; S, 12.57. Found: C, 44.69; H, 4.30; N, 16.27; S, 12.55.

1h. Method A, 0.077 g (0.29 mmol) of $Zn(NO_3)_2 \cdot 4H_2O$, 0.100 g (0.29 mmol) of K**L**^{1}, 0.045 g (0.29 mmol) of *p*-NO_2−C_6H_4SH, yield 0.079 g (52%), yellow crystals, mp 132 °C. ν(BH) 2470 cm^{-1}. ^{1}H NMR ($CDCl_3$) 1.65 [s, 9H, t-Bu], 6.25 [t, J = 2.2 Hz, 2H, Pz-H], 6.88 [d, J = 2.2 Hz, 1H, Im-H], 6.92 [d, J = 2.4 Hz, 1H, Im-H], 7.50−7.57 [m, 4H, Ph-H, Pz-H], 7.65 [d, J = 2.2 Hz, 2H, Pz-H], 7.81−7.88 [m, 2H, Ph-H]. Anal. Calcd for $C_{19}H_{22}BN_7O_2S_2Zn$ (M_r = 520.76): C, 43.82; H, 4.26; N, 18.83; S, 12.32. Found: C, 43.67; H, 4.39; N, 18.94; S, 12.14.

1i. Method A, 0.081 g (0.31 mmol) of $Zn(NO_3)_2 \cdot 4H_2O$, 0.105 g (0.31 mmol) of K**L**^{1}, 0.062 g (0.31 mmol) of C_6F_5SH, yield 0.096 g (55%), colorless crystals, mp 159 °C. ν(BH) 2498 cm^{-1}. ^{1}H NMR ($CDCl_3$) 1.67 [s, 9H, t-Bu], 6.32 [t, J = 2.1 Hz, 2H, Pz-H], 6.92 [d, J = 2.2 Hz, 1H, Im-H], 6.97 [d, J = 2.2 Hz, 1H, Im-H], 7.70 [s, br, 4H, Pz-H]. ^{19}F NMR ($CDCl_3$) −164.9 [s, 2F], −163.4 [s, 1F], −133.5 [s, 2F]. Anal. Calcd for $C_{19}H_{18}BF_5N_6S_2Zn$ (M_r = 565.71): C, 40.34; H, 3.21; N, 14.86; S, 11.34. Found: C, 40.26; H, 3.21; N, 15.10; S, 11.28.

1j. Method A, 0.155 g (0.059 mmol) of $Zn(NO_3)_2 \cdot 4H_2O$, 0.200 g (0.59 mmol) of K**L**^{1}, 0.112 g (0.59 mmol) of HCys(OEt)(NAc), yield 0.210 g (65%), colorless crystals, mp 74 °C. ν(BH) 2475 cm^{-1}. ^{1}H NMR ($CDCl_3$) 1.10−1.30 [m, 3H, CH_3], 1.64 [s, 9H, t-Bu], 1.74 [s, 3H, CH_3], 2.92−3.24 [m, 2H, CH_2], 4.05−4.23 [m, 2H, CH_2], 4.76−4.84 [m, 1H, CH], 6.26 [t, J = 2.1 Hz, 2H, Pz-H], 6.86 [d, J = 2.2 Hz, 1H, Im-H], 6.90 [d, J = 2.2 Hz, 1H, Im-H], 7.63 [d, J = 2.4 Hz, 2H, Pz-H], 7.74 [d, J = 4.4 Hz, 2H, Pz-H]. Anal. Calcd for $C_{20}H_{30}BN_7O_3S_2Zn$ (M_r = 556.84): C, 43.14; H, 5.43; N, 17.61; S, 11.52. Found: C, 43.23; H, 5.48; N, 17.61; S, 10.53.

2c. Method B, 0.150 g (0.39 mmol) of **L**$^{2\cdot}$ZnCl, 0.048 g (0.39 mmol) of $C_6H_5CH_2SH$, yield 0.137 g (74%), colorless crystals, mp 134 °C. ν(BH) 2488 cm^{-1}. ^{1}H NMR ($CDCl_3$) 1.33 [d, J = 6.8 Hz, 6H, CH_3], 3.91 [s, 2H, CH_2], 4.90 [sept, J = 6.7 Hz, 1H, CH], 6.25 [t, J = 2.0 Hz, 2H, Pz-H], 6.78 [d, J = 2.2 Hz, 1H, Im-H], 7.00 [d, J = 2.0 Hz, 1H, Im-H], 7.13−7.30 [m, 5H, Ph-H], 7.44−7.49 [m, 2H, Pz-H], 7.66 [d, J = 2.2 Hz, 2H, Pz-H]. Anal. Calcd for $C_{19}H_{23}BN_6S_2Zn$ (M_r = 475.76): C, 47.97; H, 4.87; N, 17.66; S, 13.48. Found: C, 47.87; H, 4.97; N, 17.34; S, 13.42.

2d. Method B, 0.150 g (0.39 mmol) of **L**$^{2\cdot}$ZnCl, 0.061 g (0.39 mmol) of *p*-Cl−$C_6H_4CH_2SH$, yield 0.133 g (68%), colorless crystals, mp 57 °C. ν(BH) 2480 cm^{-1}. ^{1}H NMR ($CDCl_3$) 1.33 [d, J = 6.8 Hz, 6H, CH_3], 3.86 [s, 2H, CH_2], 4.87 [sept, J = 6.7 Hz, 1H, CH], 6.28 [t, J = 2.1 Hz, 2H, Pz-H], 6.79 [d, J = 2.2 Hz, 1H, Im-H], 7.01 [d, J = 2.1 Hz, 1H, Im-H], 7.17−7.22 [m, 2H, Ph-H], 7.37 [d, J = 8.4 Hz, 2H, Ph-H], 7.52 [s, br, 2H, Pz-H], 7.67 [d, J = 2.0 Hz, 2H, Pz-H]. Anal. Calcd for $C_{19}H_{22}BClN_6S_2Zn$ (M_r = 510.21): C, 44.73; H, 4.35; N, 16.47; S, 12.57. Found: C, 44.77; H, 4.42; N, 16.68; S, 12.49.

2e. Method B, 0.150 g (0.39 mmol) of **L**$^{2\cdot}$ZnCl, 0.043 g (0.39 mmol) of C_6H_5SH, yield 0.089 g (50%), colorless crystals, mp 174 °C. ν(BH) 2491 cm^{-1}. ^{1}H NMR ($CDCl_3$) 1.32 [d, J = 6.7 Hz, 6H, CH_3], 4.88 [sept, J = 6.8 Hz, 1H, CH], 6.29 [s, br, 2H, Pz-H], 6.80 [d, J = 2.1 Hz, 1H, Im-H], 6.99−7.09 [m, 4H, Ph-H, Im-H], 7.42−7.59 [m, 4H, Ph-H, Pz-H], 7.69 [d, J = 2.1 Hz, 2H, Pz-H]. Anal. Calcd for $C_{18}H_{21}BN_6S_2Zn$ (M_r = 461.74): C, 46.82; H, 4.58; N, 18.20; S, 13.89. Found: C, 46.69; H, 4.62; N, 18.03; S, 13.82.

2f. Method B, 0.150 g (0.39 mmol) of **L**$^{2\cdot}$ZnCl, 0.048 g (0.39 mmol) of *p*-CH_3−C_6H_4SH, yield 0.108 g (61%), colorless crystals, mp 136 °C. ν(BH) 2493 cm^{-1}. ^{1}H NMR ($CDCl_3$) 1.30 [d, J = 6.7 Hz, 6H, CH_3], 2.25 [s, 3H, CH_3], 4.87 [sept, J = 6.7 Hz, 1H, CH], 6.25 [t, J = 2.2 Hz, 2H, Pz-H], 6.79 [d, J = 2.2 Hz, 1H, Im-H], 6.91 [d, J = 7.9 Hz, 2H, C_6H_4], 7.02 [d, J = 2.1 Hz, 1H, Im-H], 7.43−7.48 [m, 2H, C_6H_4], 7.54 [d, J = 1.4 Hz, 2H, Pz-H], 7.67 [d, J = 2.3 Hz, 2H, Pz-H]. Anal. Calcd for $C_{19}H_{23}BN_6S_2Zn$ (M_r = 475.76): C, 47.97; H, 4.87; N, 17.66; S, 13.48. Found: C, 47.65; H, 4.89; N, 17.52; S, 13.33.

2h. Method B, 0.150 g (0.39 mmol) of **L**$^{2\cdot}$ZnCl, 0.060 g (0.39 mmol) of *p*-NO_2−C_6H_4SH, yield 0.060 g (31%), yellow crystals, mp 81°C. ν(BH) 2482 cm^{-1}. ^{1}H NMR ($CDCl_3$) 1.33 [d, J = 6.7 Hz, 6H, CH_3], 4.86 [sept, J = 6.7 Hz, 1H, CH], 6.32 [t, J = 2.2 Hz, 2H, Pz-H], 6.84 [d, J = 2.2 Hz, 1H, Im-H], 7.06 [d, J = 2.1 Hz, 1H, Im-H], 7.57−7.63 [m, 4H, Ph-H, Pz-H], 7.73 [d, J = 2.2 Hz, 2H, Pz-H], 7.89−7.95 [m, 2H, C_6H_4]. Anal. Calcd for $C_{18}H_{20}BN_7O_2S_2Zn$ (M_r = 506.73): C, 42.66; H, 3.98; N, 19.35; S, 12.66. Found: C, 42.53; H, 4.00; N, 19.24; S, 12.65.

2i. Method B, 0.150 g (0.39 mmol) of **L**$^{2\cdot}$ZnCl, 0.077 g (0.39 mmol) of C_6F_5SH, yield 0.093 g (43%), colorless crystals, mp 166 °C. ν(BH) 2483 cm^{-1}. ^{1}H NMR ($CDCl_3$) 1.30 [d, J = 6.7 Hz, 6H, CH_3], 4.80 [sept, J = 6.7 Hz, 1H, CH], 6.34 [t, J = 2.2 Hz, 2H, Pz-H], 6.80 [d, J = 2.1 Hz, 1H, Im-H], 7.02 [d, J = 2.0 Hz, 1H, Im-H], 7.70 [d, J = 2.2 Hz, 2H, Pz-H], 7.76 [d, J = 1.4 Hz, 2H, Pz-H]. ^{19}F NMR ($CDCl_3$) −164.7 [s, 2F], −163.2 [s, 1F], −133.6 [s, 2F]. Anal. Calcd for $C_{18}H_{16}BF_5N_6S_2Zn$ (M_r = 551.69): C, 39.19; H, 2.92; N, 15.23; S, 11.65. Found: C, 39.29; H, 2.88; N, 15.21; S, 11.53.

Reactions with Methyl Iodide. Methyl iodide was applied as a 1 M solution in chloroform. 0.1−0.2 mmol of the thiolate complex was dissolved in 10 mL of chloroform and treated with the 5-fold molar amount of the methyl iodide solution. Reactions were followed by ^{1}H NMR and were quantitative (except for **1h**) and produced the resulting thioethers quantitatively. After 1d (**1a**, **1c**), 5d (**1e**, **1f**), or 15d (**1i**), or after refluxing for 10d (**1h**), the solvent was removed in vacuo. The residue was washed with two 5-mL portions of diethyl ether and then dried in vacuo. In **1h**, the remaining solid was a mixture of **1h** and **L**$^{1\cdot}$ZnI. In **1a**, **1c**, **1e**, **1f**, and **1i**, pure **L**$^{1\cdot}$ZnI remained. ν(BH) 2476 cm^{-1}. ^{1}H NMR ($CDCl_3$) 1.64 [s, 9H, t-Bu], 6.25 [t, J = 2.2 Hz, 2H, Pz-H], 6.86 [d, J = 2.3 Hz, 1H, Im-H], 6.91 [d, J = 2.3 Hz, 1H, Im-H], 7.64 [d, J = 2.2 Hz, 2H, Pz-H], 7.74 [d, J = 1.9 Hz, 2H, Pz-H]. Anal. Calcd for $C_{13}H_{18}BIN_6SZn$ (M_r = 493.50): C, 31.64; H, 3.68; N, 17.03; S, 6.50. Found: C, 31.72; H, 3.67; N, 17.45; S, 6.38.

The resulting methylthioethers **3** were detected by ^{1}H NMR in the reaction solutions and were then contained in the diethyl ether extracts. Except for the volatile **3a**, they remained in the residues left after pumping away the solvent from these extracts. These residues containing part of the product **L**$^{1\cdot}$ZnI were dissolved in $CDCl_3$ for ^{1}H NMR identification of the thioethers.

From **1a** (0.090 g, 0.21 mmol) resulted 0.077 g (74%) of **L**$^{1\cdot}$ZnI. ^{1}H NMR of $CH_3SC_2H_5$ (**3a**): 1.26 [t, J = 7.4 Hz, 3H, CH_3], 2.11 [s, 3H, SCH_3], 2.51 [q, J = 7.3 Hz, 2H, SCH_2].

From **1c** (0.122 g, 0.25 mmol) resulted 0.085 g (69%) of **L**$^{1\cdot}$ZnI. ^{1}H NMR of $CH_3SCH_2C_6H_5$ (**3c**): 1.99 [s, 3H, SCH_3], 3.68 [s, 2H, CH_2], 7.25−7.30 [m, 5H, Ph].

From **1e** (0.100 g, 0.21 mmol) resulted 0.068 g (66%) of **L**$^{1\cdot}$ZnI. ^{1}H NMR of $CH_3SC_6H_5$ (**3e**): 2.48 [s, 3H, CH_3], 7.10−7.31 [m, 5H, Ph].

Table 2. Crystallographic Data

	1a	1f	1g	1h	2f
formula	$C_{15}H_{23}BN_6S_2Zn$	$C_{20}H_{25}BN_6S_2Zn$	$C_{19}H_{22}BClN_6S_2Zn$	$C_{19}H_{22}BN_7O_2S_2Zn$	$C_{19}H_{23}BN_6S_2Zn$
MW	427.74	489.76	510.18	520.74	475.73
space group	$P2_1/c$	$P2_12_12_1$	$P2_1/n$	$P2_1/n$	$C2/c$
Z	4	4	4	12	8
a (Å)	10.100(2)	9.392(4)	10.103(2)	14.662(3)	21.345(4)
b (Å)	13.802(3)	12.838(5)	23.398(4)	20.193(3)	8.667(2)
c (Å)	14.714(3)	19.134(8)	10.135(2)	23.852(4)	24.500(5)
α (deg)	90	90	90	90	90
β (deg)	103.45(3)	90	103.74(3)	91.75(4)	98.93(4)
γ (deg)	90	90	90	90	90
V (Å^3)	1994(3)	2307(2)	2327.3(7)	7058(2)	4478(1)
d (calcd) [g cm^{-3}]	1.43	1.41	1.46	1.47	1.41
μ (MoKα) [mm^{-1}]	1.45	1.27	1.37	1.25	1.30
R1 (obs. reflns)	0.047	0.033	0.041	0.059	0.047
WR2 (all reflns)	0.086	0.078	0.090	0.213	0.118

From **1f** (0.065 g, 0.13 mmol) resulted 0.028 g (44%) of **L$^{1\cdot}$**ZnI. ^{1}H NMR of $CH_3SC_6H_4CH_3$ (**3f**): 2.23 [s, 3H, CH_3], 2.37 [s, 3H, SCH_3], 7.01 [d, J = 8.0 Hz, 2H, Ph], 7.11 [d, J = 8.2 Hz, 2H, Ph].

From **1h** (0.100 g, 0.19 mmol) resulted 0.064 g of a yellowish mixture of **L$^{1\cdot}$**ZnI and **1h**. ^{1}H NMR of $CH_3SC_6H_4NO_2$ (**3h**): 2.56 [s, 3H, SCH_3], 7.29 [d, J = 6.9 Hz, 2H, Ph], 8.14 [d, J = 7.0 Hz, 2H, Ph].

From **1i** (0.100 g, 0.18 mmol) resulted 0.071 g (80%) of **L$^{1\cdot}$**ZnI. ^{1}H NMR of $CH_3SC_6F_5$ (**3i**): 2.47 [s, 3H, SCH_3].

Reactions with Trimethyl Phosphate. Ca. 0.2 mmol of the thiolate complex in 15 mL of DMSO and a 10-fold excess of trimethyl phosphate were heated to 80 °C for 3 weeks. Then, the solvent was removed by distillation in vacuo. The residue was washed twice with 5-mL portions of diethyl ether and dried in vacuo. Impure **L$^{1\cdot}$**Zn−$OPO(OMe)_2$ remained as a sticky substance which could not be freed from the remaining complex **1e** or **1f** by crystallization and was only identified by ^{1}H NMR in $CDCl_3$: 1.76 [s, 9H, t-Bu], 4.01 [s, 6H, OMe], 6.42 [s, br, 2H, Pz-H], 7.33 [s, br, 2H, Im-H], 7.77 [s, br, 2H, Pz-H], 7.89 [s, br, 2H, Pz-H].

From **1e** (0.085 g, 0.18 mmol) and $PO(OMe)_3$ (0.252 g, 1.80 mmol) resulted 0.035 g of a 1:1 mixture of **1e** and **L$^{1\cdot}$**Zn−$OPO(OMe)_2$.

From **1f** (0.099 g, 0.20 mmol) and $PO(OMe)_3$ (0.283 g, 2.00 mmol) resulted 0.054 g of a 1:1.4 mixture of **1f** and **L$^{1\cdot}$**Zn$OPO(OMe)_2$.

Kinetic Measurements. The standard solutions of complex **1c** and methyl iodide in $CDCl_3$ (99.8%) were kept in the dark. All reagents and the cavity of the NMR spectrometer were thermostated to 300.0 K before the measurements. The reagents were combined immediately prior to the measurements. The concentrations of the reagents were adjusted to 0.014 M for **1c** for all six measurements and to 0.11, 0.14, 0.16, 0.19, 0.22, and 0.25 M for CH_3I, respectively. The intensities of the ^{1}H NMR resonances of the SCH_2 protons of **1c** and the thioether were recorded automatically every 30 s and were stored for digital data processing. Each kinetic run was repeated once to ensure reproducibility. The averaged data were used for the calculations. The resulting k_{obs} values for 0.11, 0.14, 0.16, 0.19, 0.22, and 0.25 M CH_3I were 4.9, 7.3, 8.9, 10.1, 11.7, and 14.3·10^{-4} sec^{-1}, respectively.

Structure Determinations. Crystals were obtained by slow evaporation of saturated methanol solutions. Data sets were obtained at 240 K with a Bruker AXS Smart CCD diffractometer and were subjected to empirical absorption corrections (SADABS). The structures were solved with direct methods and refined anisotropically using the SHELX program suite.[26] 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.[27] Table 2 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 five structure determinations and two plots for the kinetic analyses. This material is available free of charge via the Internet at http://pubs.acs.org.

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