observed for adducts with cadmium(II) and other metal ions; however, it is possible that the arrangement of platinum(II) ions among the 20 cysteine residues in the equilibrium product at room temperature is heterogeneous.[33]

Platinum(II) is also different from the other metal ions studied in its strong preference for a square-planar stereochemistry. On the basis of the similar elongated Stokes' radii of Pt_7MT and Cd_7MT (1.8 and 1.6 nm, respectively) and other evidence, we suggested a two-domain structure for Pt_7MT with three platinum(II) ions in both the α and β domains with a seventh platinum(II) bound to the N-terminal methionine and further proposed a hypothetical $Pt_3(cys)_9^{3-}$ β cluster containing square-planar platinum(II) centers.[17] The results of the present study are consistent with the presence of platinum clusters in Pt_7MT, but no evidence for a specific Pt–cysteine connectivity has been found. The DTNB assays, which show two reactive thiols in Pt_7MT (Figure 2), do suggest the possibility of $Pt_3(cys)_9^{3-}$ clusters in both domains with two uncoordinated cysteines in the 11-cysteine α domain.

Acknowledgment. The Plasmall was purchased with a Biomedical Research Support grant funded by the National Institutes of Health and administered by the Division of Sponsored Research, University of Florida. Partial support of this project was provided by a Milheim Foundation grant and the Division of Sponsored Research, University of Florida. D.E.R. is an A. P. Sloan Foundation Research Fellow, 1988–1990. We thank Joanne Lopez for her expert technical assistance.

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[33] It was hoped that ^1H NMR spectroscopy would yield evidence for possible homogeneity of the Pt_7MT derivative. The ^1H NMR spectrum of Pt_7MT is similar to the spectrum of native MT in its gross features, but individual resonances of the amino acids could not be resolved at 300 MHz under conditions that gave well-resolved spectra for Cd_7MT (Bongers, J. Ph.D. Dissertation, University of Florida, 1989). The broad, weak ^1H NMR signal may be a consequence of heterogeneity of the platinum clusters in the sample, unusual relaxation properties of Pt_7MT, or other unknown factors.

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Ferric Ion Sequestering Agents. 23. Synthesis of Tris(hydroxypyridinethione) Ligands and Their Ferric Complexes; X-ray Structure Analysis of *N*,*N*′,*N*″-Tris((1,2-didehydro-1-hydroxy-2-thioxopyrid-6-yl)carbonyl)-2,2′,2″-triaminotriethylaminato)iron(III)[1]

Kamal Abu-Dari and Kenneth N. Raymond*

Received May 7, 1990

Hexadentate thiohydroxamate ligands derived from 2-mercaptopyridine-6-carboxylic acid 1-oxide and triamines have been prepared by reaction of the amines with the active amide produced from the carboxylic acid and 1,1′-carbonyldiimidazole in DMF. The triamides isolated are *N*,*N*′,*N*″-tris((1,2-didehydro-1-hydroxy-2-thioxopyrid-6-yl)carbonyl)-2,2′,2″-triaminotriethylamine, *N*,*N*′,*N*″-tris((1,2-didehydro-1-hydroxy-2-thioxopyrid-6-yl)carbonyl)-1,-5,10-triazadecane, and 1,3,5-tris((*N*-methyl-*N*-((1,2-didehydro-1-hydroxy-2-thioxopyrid-6-yl)carbonyl)amino)methyl)benzene. These ligands have been characterized by their elemental analyses and IR and NMR spectra, and the ferric complexes have also been prepared and characterized. The structure of the complex *N*,*N*′,*N*″-tris((1,2-didehydro-1-hydroxy-2-thioxopyrid-6-yl)carbonyl)-2,2′,2″-triaminotriethylaminato)iron(III)·$0.5CHCl_3$ has been determined by single-crystal automated-counter X-ray diffraction. The complex crystallizes in the triclinic space group $P\bar{1}$ with $z = 4$, $a = 11.073$ (1) Å, $b = 13.858$ (1) Å, $c = 22.401$ (2) Å, $\alpha = 70.216$ (8)°, $\beta = 71.847$ (8)°, $\gamma = 68.104$ (8)°. Two crystallographically independent molecules of the ferric complex and one disordered chloroform molecule are in the asymmetric unit. Full-matrix least-squares refinement using 6000 reflections with $F_o^2 > 3\sigma(F_o)^2$, with all non-hydrogen atoms given anisotropic temperature factors, converged to $R = 0.040$ and $R_w = 0.058$. The coordination polyhedron around the ferric ion is intermediate between octahedral and trigonal-prismatic geometries and is similar to that of the ferric complex of 1-hydroxy-2(1*H*)-pyridinone.

Introduction

As part of a program devoted to the synthesis and characterization of ligands that might be useful in the metal chelation therapy of iron overload,[2] we have taken a biomimetic approach to the synthesis of ferric ion specific sequestering agents based on the siderophores (low molecular weight sequestering agents produced by microorganisms to enable them to solubilize and uptake essential ferric ion in a physiological environment).[3-6] Two major functional groups found in siderophores are hydroxamic acids, as in ferrichromes[7] and ferrioxamines,[8] and catechol, as in enterobactin[9] (see Figure 1). Less common functional groups found in siderophores are hydroxypyridinone[10,11] and thiohydroxamic acid (in *N*-(methylthio)formohydroxamic acid).[12,13] Most siderophores contain three bidentate ligating subunits in order to accommodate the preferred hexacoordinate geometry of ferric ion.[3]

We previously reported the synthesis of iron sequestering agents having three bidentate ligating subunits; the subunits in these ligands were catecholate,[14-20] hydroxamate,[1] or hydroxypyridionone.[21] We also have prepared and determined the structures of ferric complexes with simple catecholate,[22] thiohydroxamate,[23] and hydroxypyridinonate[2] ligands, as well as the

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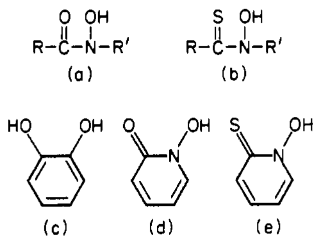


Figure 1. Some bidentate chelating ligands that can be used for iron(III) sequestering agents.

ferric complex of a hexadentate catecholate-based ligand with three ligating subunits.[20]

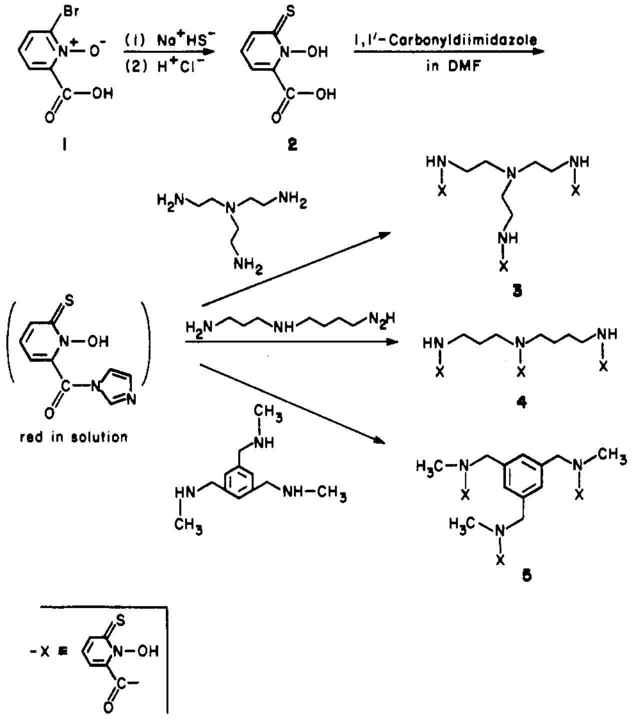
Of the siderophore ligands or their analogues, enterobactin has the highest stability constant and hence highest affinity for Fe^{3+} above neutral pH.[3] However, the effectiveness at low pH of tricatechol enterobactin and enterobactin analogues is limited by their weak acidity and required loss of six protons on binding iron(III). Hydroxypyridinones and hydroxypyridinethiones are stronger acids than catechol and hydroxamic acids, and since they are monoprotic acids, hexadentate ligands formed from three of these units only need to lose three protons to form six-coordinate bidentate complexes, which makes them competitive for iron(III) at pH 7 with similar catechol ligands despite the much lower formation constants of the iron complexes. Indeed, the simple bidentate hydroxypyridinones, 1,2-Hopo, 3,2-Hopo, and 3,4-Hopo (where *x,y*-Hopo is *x*-hydroxy-*y*(1*H*)-pyridinone), bind iron more completely than either catechol or acetohydroxamic acid at pH 7.[24]

In this paper, we report the synthesis of iron sequestering agents containing three hydroxypyridinethione ligating groups. We also report the synthesis of the ferric complexes of these ligands and the X-ray structural characterization of *N,N′,N″*-tris((1,2-didehydro-1-hydroxy-2-thioxopyrid-6-yl)carbonyl)-2,2′,2″-triaminotriethylaminato))iron(III). Little coordination chemistry has been reported for hydroxypyridinethione ligands. The structures of zinc,[25] thorium,[26] and uranyl[27] complexes of 1-hydroxy-2(1*H*)-pyridinethione have been determined, but no d transition-metal coordination chemistry has yet appeared.

Experimental Section

Analytical grade ferric nitrate nonahydrate (Mallinckrodt) was used for the synthesis of the ferric complexes. Dimethylformamide was dried over alumina and distilled over molecular sieves. Tris(2-aminoethyl)amine (Aldrich), spermidine (Ames Laboratories), 2,6-dibromopyridine (Aldrich), and 1,1′-carbonyldiimidazole (Aldrich) were used without further purification. The 1,3,5-tris[(methylamino)methyl]benzene was a generous gift of Dr. A. R. Bulls and was prepared according to the literature procedure;[17] 2-bromopyridine-6-carboxylic acid 1-oxide (**1**) was obtained by the oxidation of 2-bromopyridine-6-carboxylic acid as described earlier.[24] The ion exchange resin used in the purifications was Bio-Rad AG50-W-X2 (50–100 mesh). Lab grade solvents and reagents were used throughout the synthesis without further purification. NMR spectra were collected on a custom-built 200-MHz FT spectrometer. Infrared spectra were obtained by using a Nicolet 5/DX FT spectrometer. Visible–UV spectra were recorded on a Hewlett-Packard 8450A UV/VIS spectrometer. Melting points were taken in open capillaries with a Büchi apparatus and are uncorrected. Elemental analyses were performed by the Analytical Laboratory, University of California, Berkeley, CA.

Scheme I



Ligand Syntheses. 2-Mercaptopyridine-6-carboxylic Acid 1-Oxide (2) (Scheme I). 2-Bromopyridine-6-carboxylic acid 1-oxide (6.1 g, 0.028 mmol) was dissolved in a 100-mL aqueous solution of Na$_2$S·9H$_2$O (6.72 g, 0.028 mmol) by heating to dissolve the acid, and a solution of NaHS (0.028 mmol, prepared from Na$_2$S and HCl) in 100 mL of water was added. The combined solution (pH 10–11) was heated at 90–95 °C for 6 h, then cooled to room temperature, and acidified with HCl to pH = 2–2.5. The resultant yellow solution was concentrated under vacuum to 50 mL, and the yellow precipitate that formed was removed by filtration. This crude product was dissolved in water, and fractions of the solution were eluted from an ion exchange column in the acidic form using a methanol/H$_2$O solvent mixture. The fractions giving a blue-green color with ferric nitrate solution were collected, and most of the solvent was removed under reduced pressure. The resultant crystalline solid was removed by filtration, washed with a small volume of cold water, and dried in vacuum over P$_2$O$_5$. [An alternative method is to add HCl to the hot reaction mixture to pH < 1, reduce this volume under vacuum, and remove the crude product by filtration; the latter is then recrystallized from hot aqueous solution.] Yield: 70–80% (the product changes crystalline form at 140 °C and melts sharply at 192 °C). Anal. Calcd (Found) for C$_6$H$_5$NO$_3$S: C, 42.10 (42.18); H, 2.94 (2.97); N, 8.18 (8.05); S, 18.73 (18.64).

***N,N′,N″*-Tris((1,2-didehydro-1-hydroxy-2-thioxopyrid-6-yl)carbonyl)-2,2′,2″-triaminotriethylamine (3).** Compound **2** (1.71 g, 10.0 mmol) was dissolved in 20 mL of DMF. A solution of 1,1′-carbonyldiimidazole (1.62 g, 10.0 mmol) in 20 mL of DMF was added under N$_2$; the color changed immediately from yellow to red with the evolution of carbon dioxide. The solution was stirred under N$_2$ for 15 min, and a solution of 2,2′,2″-triaminotriethylamine (0.487 g, 3.33 mmol) in 20 mL of DMF was added; the color changed gradually to yellowish green. The solution was stirred overnight under N$_2$. Most of the DMF was removed under reduced pressure, and 100 mL of water was added, forming a clear solution. The solution was acidified with HCl (3 M) to pH ≅ 4.5, and the precipitate that formed was collected by filtration, washed with cold water, and dried in vacuum over P$_2$O$_5$. The filtrate was extracted twice with 200 mL of chloroform, the combined organic phase had the solvent removed under reduced pressure, and the residue was again dissolved in 3 mL of DMF. Addition of 20 mL of cold water resulted in additional precipitate, which was removed by filtration and dried in vacuum over

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P_2O_5. The combined products were dissolved in 5 mL of DMF, 30 mL of cold water was added, and the yellowish green product was collected by filtration, washed with a small volume of cold water, and dried in vacuum over P_2O_5: yield, 1.83 g (91%); mp, 175–178 °C (dec). Anal. Calcd (Found) for $C_{24}H_{27}N_7O_6S_3$: C, 47.59 (47.63); H, 4.49 (4.47); N, 16.19 (15.64); S, 15.88 (15.60).

***N*,*N*′,*N*″-Tris((1,2-didehydro-1-hydroxy-2-thioxopyrid-6-yl)carbonyl)-1,5,10-triazadecane (4).** To compound **2** (1.71 g, 10.0 mmol) in 20 mL of DMF was added a solution of 1,1′-carbonyldiimidazole (1.62, 10.0 mmol) in 20 mL of DMF under N_2. The red solution was stirred for 15 min, and a solution of spermidine (0.48 g, 3.3 mmol) in 20 mL of DMF was added, after which the color changed gradually from red to light green. The reaction mixture was stirred under N_2 overnight, after which most of the DMF was removed under reduced pressure, 100 mL of H_2O was added, and the mixture was acidified with HCl to pH ≅ 1–2. The gummy precipitate was extracted twice with 200 mL of chloroform, and the extract was dried over Na_2SO_4. The solvent was removed under reduced pressure, and the gummy residue was triturated with hexane and then with diethyl ether to produce a yellowish green powder. The solid product was removed by filtration, washed with ether, and dried in vacuum over P_2O_5: yield, 1.87 g (93%); mp, 110–115 °C (dec). Anal. Calcd (Found) for $C_{25}H_{28}N_6O_6S_3$: C, 49.65 (49.75); H, 4.47 (4.96); N, 13.90 (14.20); S, 15.91 (16.10).

1,3,5-Tris((*N*-methyl-*N*-((1,2-didehydro-1-hydroxy-2-thioxopyrid-6-yl)carbonyl)amino)methyl)benzene (5). Compound **2** (1.71 g, 10.0 mmol) was dissolved in 20 mL of DMF. A solution of 1-1′-carbonyldiimidazole (1.62 g, 10.0 mmol) in 20 mL of DMF was added under N_2. The resulting red solution was stirred for 15 min, and a solution of 1,3,5-tris[(methylamino)methyl]benzene trihydrochloride (0.8 g, 2.56 mmol) and triethylamine (3 mL) in 20 mL of DMF was added. The resulting yellowish green solution was stirred overnight. Most of the DMF was distilled under reduced pressure, 100 mL of H_2O was added, and the solution was acidified with HCl (pH ≅ 1–2). The resulting precipitate was removed by filtration, washed with water, and dried in vacuum over P_2O_5. The product was purified by dissolution in 3 mL of DMF and reprecipitated with water: yield, 1.26 g (70%); mp, 163–166 °C (dec). Anal. Calcd (Found) for $C_{30}H_{30}N_6O_6S_3$: C, 54.08 (53.85); H, 4.54 (4.42); N, 12.60 (12.35); S, 14.42 (14.52).

(*N*,*N*′,*N*″-Tris((1,2-didehydro-1-hydroxy-2-thioxopyrid-6-yl)carbonyl)-2,2′,2″-triaminotriethylaminato)iron(III) (6). A solution of compound **3** (0.48 g, 0.79 mmol) in chloroform (100 mL) was added to an aqueous solution of ferric nitrate nonahydrate (0.32 g, 0.79 mmol) in 100 mL of water in a separatory funnel. The mixture was shaken for 5 min, a solution of Na_2CO_3 (~3.0 g) in 50 mL of water was added, and the mixture was shaken vigorously for 5 min. The highly colored chloroform layer was separated and washed with water. The solvent was removed under reduced pressure. The resultant solid residue was redissolved in chloroform, the solution was filtered, acetone was added, and the solution was allowed to evaporate slowly to yield dark blue-violet crystals. The crystals contain half chloroform molecule per iron complex; analytical results vary, depending on the degree of dryness. For air-dried crystals, mp 243 °C (sharp), vis spectrum λ_{max}, nm (log ϵ): 512 (3.51), 600 (3.62). Anal. Calcd (Found) for $Fe(C_{24}H_{24}N_7O_6S_3)\cdot0.50\ CHCl_3$: C, 40.97 (41.68); H, 3.44 (3.55); N, 13.65 (13.53); S, 13.39 (13.37).

(*N*,*N*′,*N*″-Tris((1,2-didehydro-1-hydroxy-2-thioxopyrid-6-yl)carbonyl)-1,5,10-triazadecanato)iron(III) (7). A solution of ferric nitrate nonahydrate (0.32 g, 0.79 mmol) in 10 mL of DMF was added to a solution of compound **4** (0.48 g, 0.79 mmol) in 10 mL of DMF. The resulting dark violet solution was stirred for 20 min and then transferred to a separatory funnel. Chloroform (200 mL) and then water (200 mL) were added, and the mixture was shaken for 10 min. The chloroform layer was separated and washed with water, and the volume was reduced under vacuum. Diethyl ether was added, and the resulting precipitate was washed with ether and dried in vacuum over P_2O_5: mp, decomposes slowly at >210 °C. Vis spectrum λ_{max}, nm (log ϵ): 516 (3.470), 596 (3.523). Anal. Calcd (Found) for $Fe(C_{25}H_{25}N_6O_6S_3)\cdot0.5(C_2H_5)_2O$: C, 46.69 (46.20); H, 4.35 (4.42); N, 12.09 (12.03); S, 13.85 (13.18). Crystallization from $CHCl_3$ acetone afforded a crystalline product. Anal. Calcd (Found) for $Fe(C_{25}H_{25}N_6O_6S_3)$: C, 45.59 (45.41); H, 3.83 (4.08); N, 12.76 (12.25).

(1,3,5-Tris((*N*-methyl-*N*-((1,2-didehydro-1-hydroxy-2-thioxopyridin-6-yl)carbonyl)amino)methyl)benzenato)iron(III) (8). This compound was prepared from ferric nitrate and compound **5** by a procedure similar to that used to prepare **7**. The chloroform was removed under reduced pressure, and the glassy hygroscopic residue was collected: mp, decomposes at >260 °C. Vis spectrum λ_{max}, nm (log ϵ): 504 (sh) (3.49), 562 (3.60). Anal. Calcd (Found) for $Fe(C_{30}H_{27}N_6O_6S_3)\cdot2H_2O$: C, 47.68 (47.71); H, 4.14 (3.68); N, 11.12 (10.69); S, 12.87 (11.87).

Table I. Summary of Crystallographic Data and Parameters for Compounds **6**[a,b]

formula	$2[Fe(C_{24}H_{24}N_7O_6S_3)]\cdot CHCl_3$
fw	1436.40
space group	$P\bar{1}$
cell constants[c]	
a, Å	11.073 (1)
b, Å	13.858 (1)
c, Å	22.401 (2)
α, deg	70.216 (8)
β, deg	71.847
γ, deg	68.104 (8)
V, Å^3	2932.8 (5)
Z	4
d_{calc}, g/cm^3	1.63
d_{obsd},[d] g/cm^3	1.61
crystal size, mm	0.05 × 0.15 × 0.20
radiation	Mo Kα (λ = 0.70926 Å)
reflecns measd	$\pm h$, $\pm k$, $+l$
scan method	ω
scan range 2θ, deg	3–40
no. of unique data	7973
no. of unique data, $F_o^2 > 3\sigma(F_o)^2$	6000
no. of params refined	791
R	0.040
R_w	0.058
GOF	2.20
p factor	0.04
abs coeff, μ(Mo Kα), cm^{-1}	7.87
transm factor range, %	86.92–99.83

[a] Unit cell parameters and their esd's are from a least-squares fit to the setting of 24 reflections with 2θ near 30°. [b] In this and all subsequent tables the esd's of all parameters are given in parentheses. [c] Measured at *t* = −117 °C. [d] Measured by flotation in acetone/dibromoethene.

X-ray Crystallography. Well-shaped dark violet crystals of compound **6** were obtained from chloroform/acetone solution by slow evaporation. Satisfactory single crystals were attached with epoxy cement to a glass fiber. The crystal data and the lack of any systematic absences imply the triclinic space groups $P1$ or $P\bar{1}$; the latter was confirmed by the final structure (Table I). Routine alignment procedures and cell determination[28] were followed to collect a unique set of intensity data ($\pm h$, $\pm k$, $+l$) at −117 °C on an Enraf-Nonius CAD-4 automatic diffractometer, using monochromated Mo Kα radiation.[28] The 7974 raw data were converted to structure factor amplitudes and esd's by correction for scan speed, background, and Lorentz and polarization effects.[28,29] Inspection of the list of intensity standards showed 6% maximum decay, and hence a correction was applied. Absorption correction was made by the use of ψ-scan data.[30] Cell volume, density measurement, and analytical data indicate the presence of four ferric complexes per unit cell, plus two chloroform molecules. The structure was solved by direct methods (MULTAN)[28] followed by standard full-matrix least-squares and difference Fourier procedures. Inspection of the difference Fourier map showed the chloroform molecule is disordered; it was refined in two positions, with 0.85 and 0.15 occupancies, and only the atoms with 0.85 occupancy were refined anisotropically. The pyridine hydrogens and most other hydrogen atoms were located from the difference Fourier map. The pyridine hydrogens were introduced as fixed atoms (C–H distance = 0.95 Å, bisecting the C–C–C angle), and the methylene and amide hydrogens were introduced as fixed atoms in their ideal positions (C–H distance = 0.95 Å, N–H distance = 0.87 Å); the hydrogen temperature factors were fixed as 1.10 times the temperature factor of the non-hydrogen atom attached to that hydrogen. Full-matrix least-squares refinement with 791 variables, using the 6000 reflections with $F_o^2 > 3\sigma(F_o)^2$ led to convergence with R = 0.040, R_w = 0.058, and an error in an observation of unit weight of 2.20.[31] The three highest peaks in the final difference Fourier

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(28) For details regarding data collection, data reduction, data processing, scattering factor tables, and the program ORTEP, please refer to: Eigenbrot, C. W., Jr.; Raymond, K. N. *Inorg. Chem.* **1982**, *21*, 2653.

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(30) Reflections used for the azimuthal scans were located near χ = 90°, and the intensities were measured at 10° increments of rotation of the crystal about the diffraction vector.

(31) The function minimized in refinement is $\sum w(F_o - F_c)^2$, where F_o and F_c are the absolute values of the observed and calculated structure factors, respectively, and the weight w is $4F_o^2/\sigma^2(F_o)$. The error indices R and R_w and the standard deviation of an observation of unit weight are defined in ref 28.

map [0.82, 0.73, and 0.50 e/Å^3] are within 1.2 Å of the chlorine atoms; other peaks are less than 0.36 e/Å^3. The positional and thermal parameters of the non-hydrogen atoms are listed in Table II, those of hydrogen atoms are listed in Table S1 (supplementary material). Values of general temperature factor expressions (B's), root-mean-square amplitudes of vibrations, and F_o and F_c are listed in supplementary material Tables S2, S3, and S4, respectively.[32]

A complete list of bond lengths and angles is in Table S5 (supplementary material).

Results and Discussion

Synthesis of Compounds. The preparation of 2-mercaptopyridine-6-carboxylic acid 1-oxide (**2**) proceeds smoothly from 2-bromopyridine-6-carboxylic acid 1-oxide and NaHS in aqueous solution, followed by acidification and isolation of the desired product (Scheme I). Although Na_2S can be used for the synthesis of 2-mercaptopyridine 1-oxide from 2-bromopyridine 1-oxide,[33] the use of Na_2S with 2-bromopyridine-6-carboxylic acid 1-oxide led only to the production of the pyridinone derivative. The use of thiourea to replace the bromine atom by sulfur, which was used for the synthesis of 2-mercaptopyridine 1-oxide derivatives,[34] did not produce the desired compound.

Tris((1,2-didehydro-1-hydroxy-2-thioxopyrid-6-yl)carbonyl amides (as well as the mono, di, and tetra amide derivatives)[35] were obtained by the reaction of the carboxylic acid with 1,1′-carbonyldiimidazole in dry DMF to produce the active amide intermediate, which reacts readily with primary and secondary amines to form the corresponding amides (Scheme I). This reaction of the active amide with primary monoamines is fast, as indicated by the change in color from red (the active amide intermediate) to yellowish green (amide). However, the reaction with more hindered polyamines and secondary amines is slower, but is normally complete overnight. The yield per amide bond is usually above 97%, which is higher than the yield obtained for the pyridinone derivatives with use of phosgene in THF.[21] Furthermore, unreacted amines, other reaction products such as imidazole, and unreacted acids (**2**) are all soluble in dilute HCl solution, which enables the production of the amides in pure form.

The isolated polyamides in general are pale yellow to greenish in color, are very soluble in DMF and chloroform, have low solubility in weakly acid water (except compound **6**, which dissolves in acidic solution), and are soluble in neutral or dilute basic aqueous solution (pH > 6). The infrared spectrum of compound **2** shows a strong band at 2500 cm^{-1}, which is assigned to the S–H stretching frequency, indicating that compound **2** exists in the thiol form in the solid state. No such band was observed in the IR spectra of 1-hydroxypyridinethione and the polyamide compounds in the region 1700–2900 cm^{-1}, which indicate they exist in the thione form in the solid state. In addition to the amide C=O stretching frequency at about 1600 cm^{-1}, there are four strong bands at about 1600, 1575, 1490, and 1435 cm^{-1} in the IR spectra of the polyamide ligands, corresponding to ring stretching frequencies. These bands appear in the same region in the IR spectrum of 1-hydroxy-2-pyridinethione.[36] The C=S stretching frequency appears in the region 1110–1120 cm^{-1} in the spectra of the polyamide compounds and at 1135 cm^{-1} in the spectrum of 1-hydroxy-2-pyridinethione. This band appears at 1041 cm^{-1} in the IR spectrum of **2**, reflecting the C–S single-bond character of this derivative. The most distinctive feature in the NMR spectra of the polyamide compounds is the presence of two doublets at δ 6.9 and 7.6 and a triplet at δ 7.3, corresponding to the three protons of the 1-hydroxy-2-pyridinethione ring. These are further split into multiplets in the spectra of some of the polyamides due to their lack of symmetry.

Tris(1-hydroxy-2-pyridinethione) ligands **3**, **4**, and **5** form monomeric ferric complexes that are quite soluble in organic solvents such as chloroform and DMF. In most cases, the isolated ferric complexes contain solvent molecules of crystallization. The visible spectra are generally similar and are also similar to the spectra of ferric complexes with simple thiohydroxamic acids, showing two maxima in the regions 600 and 500 nm.

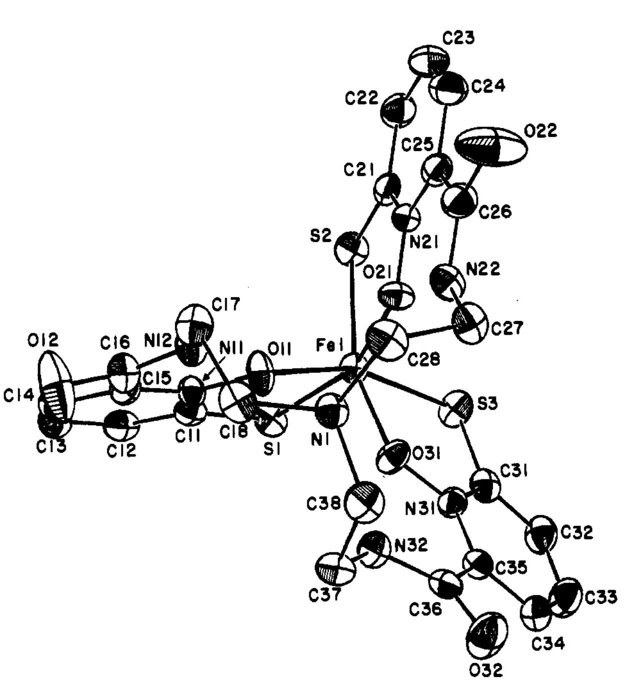

Figure 2. Perspective view of iron complex 1 of compound **6** with the numbering scheme of the non-hydrogen atoms. The non-hydrogen atoms are drawn at 50% probability contours of the thermal motion. Hydrogen atoms are not included for simplicity.

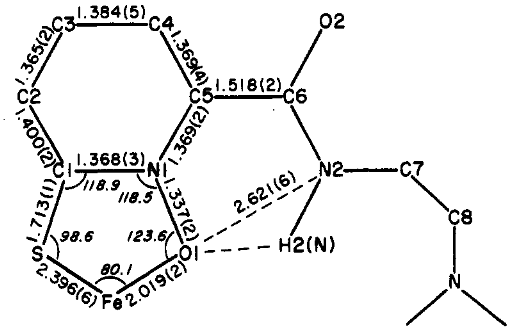

Figure 3. Numbering scheme for all atoms in both iron complex molecules of compound **6**. Averages of key bond lengths and angles (and standard deviations of the mean, from the averaging) are shown.

X-ray Crystallography. The crystal structure of the ferric complex **6** consists of discrete molecules of the complex and chloroform with no unusual intermolecular contacts. Figure 2 shows a perspective view of one of the two similar but distinct ferric complexes of **6** in the asymmetric unit. The numbering scheme for both complexes is shown in Figure 3. The numbers given to the hydrogen atoms are those of the non-hydrogen atoms to which hydrogens are attached. Average values of the most significant distances and angles (averages between the six different thiohydroxamate groups of the two different iron atoms) are in Figure 3. Bond lengths and angles within the 1-hydroxy-2-pyridinethione are in general similar to those reported for the thorium,[26] uranyl,[27] and zinc[25] complexes of 1-hydroxy-2-pyridinethione. The C–S bond length of ~1.71 Å is in good agreement with C–S bond distances in metal thiohydroxamate complexes[23] and is shorter than the C–S bond length of 1.74 Å reported for the thiohydroximato chromic complex,[37] indicating some C–S double-bond character in the polyamides. The Fe–S

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[32] Please see the statement at the end of this paper regarding supplementary material.

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Table II. Positional Parameters and Their Estimated Standard Deviations for Non-Hydrogen Atoms for Compound **6**^{a}

atom	x	y	z	B, Å^2	atom	x	y	z	B, Å^2
Fe1	0.43092 (5)	0.19127 (4)	0.62480 (3)	1.91 (1)	C24	0.6103 (5)	−0.0257 (3)	0.8426 (2)	3.1 (1)
Fe2	0.21950 (5)	0.44520 (4)	0.15818 (3)	2.25 (1)	C25	0.5976 (4)	0.0649 (3)	0.7922 (2)	2.3 (1)
S1	0.3978 (1)	0.17098 (8)	0.52998 (5)	2.43 (3)	C26	0.6580 (4)	0.1484 (3)	0.7907 (2)	2.6 (1)
S2	0.4106 (1)	0.01543 (8)	0.68626 (5)	2.59 (3)	C27	0.7031 (4)	0.3197 (3)	0.7384 (2)	2.3 (1)
S3	0.1999 (1)	0.27457 (8)	0.66066 (5)	2.76 (3)	C28	0.8326 (4)	0.3137 (3)	0.6887 (2)	2.5 (1)
S4	0.1879 (1)	0.63343 (9)	0.12496 (6)	3.05 (3)	C31	0.2018 (4)	0.4045 (3)	0.6401 (2)	2.3 (1)
S5	0.4391 (1)	0.40284 (9)	0.09136 (6)	3.16 (3)	C32	0.0862 (4)	0.4919 (3)	0.6467 (2)	3.0 (1)
S6	0.2997 (1)	0.42221 (8)	0.25167 (5)	2.90 (3)	C33	0.0946 (4)	0.5939 (4)	0.6306 (2)	3.3 (1)
O11	0.6180 (3)	0.1711 (2)	0.5708 (1)	2.62 (7)	C34	0.2191 (4)	0.6098 (3)	0.6108 (2)	2.9 (1)
O12	0.9962 (3)	0.1426 (3)	0.4675 (2)	5.3 (1)	C35	0.3331 (4)	0.5253 (3)	0.6042 (2)	2.2 (1)
O21	0.5183 (2)	0.1634 (2)	0.6980 (1)	2.14 (6)	C36	0.4645 (4)	0.5495 (3)	0.5838 (2)	2.3 (1)
O22	0.7090 (3)	0.1297 (3)	0.8363 (2)	5.75 (9)	C37	0.7020 (4)	0.5004 (3)	0.5419 (2)	2.5 (1)
O31	0.4322 (2)	0.3442 (2)	0.6068 (1)	2.35 (7)	C38	0.7727 (4)	0.4626 (3)	0.5978 (2)	2.5 (1)
O32	0.4616 (3)	0.6374 (2)	0.5867 (2)	4.14 (9)	C41	0.0194 (4)	0.6762 (3)	0.1521 (2)	2.9 (1)
O41	0.0197 (3)	0.4977 (2)	0.1848 (1)	2.88 (8)	C42	−0.0547 (6)	0.7836 (4)	0.1470 (2)	4.6 (2)
O42	−0.3829 (4)	0.5840 (3)	0.2469 (2)	7.3 (1)	C43	−0.1902 (6)	0.8124 (4)	0.1672 (3)	5.8 (2)
O51	0.1817 (3)	0.4067 (2)	0.0877 (1)	2.87 (8)	C44	−0.2536 (5)	0.7350 (4)	0.1925 (2)	4.5 (2)
O52	0.0825 (4)	0.3151 (4)	−0.0397 (2)	7.5 (1)	C45	−0.1847 (4)	0.6295 (3)	0.1980 (2)	3.0 (1)
O61	0.1955 (3)	0.3010 (2)	0.2105 (1)	2.67 (7)	C46	−0.2638 (4)	0.5499 (4)	0.2257 (2)	3.7 (1)
O62	0.1222 (3)	0.0158 (2)	0.3070 (2)	4.44 (9)	C47	−0.2776 (5)	0.3678 (4)	0.2535 (2)	4.4 (1)
N1	0.8142 (3)	0.3449 (2)	0.6216 (1)	1.99 (8)	C48	−0.2916 (4)	0.3320 (4)	0.2001 (2)	4.0 (1)
N2	−0.1627 (3)	0.2701 (3)	0.1685 (2)	2.79 (9)	C51	0.4023 (4)	0.3702 (3)	0.0331 (2)	2.8 (1)
N11	0.6557 (3)	0.1434 (2)	0.5146 (1)	2.00 (8)	C52	0.4989 (5)	0.3386 (4)	−0.0198 (2)	4.2 (1)
N12	0.8638 (3)	0.1619 (3)	0.5631 (2)	2.40 (8)	C53	0.4649 (6)	0.3089 (4)	−0.0627 (3)	5.2 (2)
N21	0.5347 (3)	0.0743 (2)	0.7458 (1)	1.80 (8)	C54	0.3357 (5)	0.3093 (4)	−0.0546 (2)	4.3 (1)
N22	0.6491 (3)	0.2359 (2)	0.7429 (2)	2.23 (8)	C55	0.2406 (5)	0.3416 (3)	−0.0037 (2)	3.0 (1)
N31	0.3219 (3)	0.4256 (2)	0.6166 (1)	2.01 (8)	C56	0.1003 (5)	0.3430 (4)	0.0017 (2)	3.6 (1)
N32	0.5756 (3)	0.4781 (2)	0.5625 (2)	2.30 (8)	C57	−0.1334 (5)	0.3785 (4)	0.0551 (2)	3.6 (1)
N41	−0.0485 (3)	0.6015 (3)	0.1784 (2)	2.50 (9)	C58	−0.1635 (4)	0.2780 (3)	0.1017 (2)	3.0 (1)
N42	−0.2043 (4)	0.4466 (3)	0.2278 (2)	3.5 (1)	C61	0.2737 (4)	0.3012 (3)	0.2955 (2)	2.4 (1)
N51	0.2762 (3)	0.3718 (3)	0.0389 (2)	2.49 (9)	C62	0.2995 (4)	0.2501 (3)	0.3576 (2)	2.8 (1)
N52	0.0030 (4)	0.3756 (3)	0.0485 (2)	3.2 (1)	C63	0.2737 (4)	0.1550 (4)	0.3909 (2)	3.2 (1)
N61	0.2195 (3)	0.2534 (2)	0.2701 (2)	2.19 (8)	C64	0.2209 (4)	0.1086 (3)	0.3624 (2)	2.8 (1)
N62	0.0857 (4)	0.1574 (3)	0.2218 (2)	3.3 (1)	C65	0.1925 (4)	0.1581 (3)	0.3027 (2)	2.1 (1)
C11	0.5613 (4)	0.1351 (3)	0.4907 (2)	2.1 (1)	C66	0.1293 (4)	0.1052 (3)	0.2761 (2)	2.8 (1)
C12	0.6049 (4)	0.1003 (3)	0.4335 (2)	2.6 (1)	C67	0.0252 (5)	0.1090 (3)	0.1938 (2)	4.1 (1)
C13	0.7360 (4)	0.0765 (3)	0.4034 (2)	2.9 (1)	C68	−0.1238 (5)	0.1577 (4)	0.2054 (2)	3.9 (1)
C14	0.8266 (4)	0.0904 (3)	0.4274 (2)	2.6 (1)	C1 (CHCl$_3$)	0.2444 (8)	0.9442 (6)	1.0231 (4)	7.1 (3)^{b}
C15	0.7872 (4)	0.1244 (3)	0.4838 (2)	2.2 (1)	Cl1	0.2459 (2)	0.8822 (2)	0.9672 (1)	7.98 (7)^{b}
C16	0.8906 (4)	0.1443 (3)	0.5058 (2)	2.6 (1)	Cl2	0.0915 (3)	0.0351 (2)	0.0398 (1)	13.8 (1)^{b}
C17	0.9620 (4)	0.1801 (3)	0.5856 (2)	2.5 (1)	Cl3	0.3680 (3)	1.0054 (2)	0.9928 (1)	15.8 (1)^{b}
C18	0.9373 (4)	0.2978 (3)	0.5781 (2)	2.4 (1)	C1 (CHCl$_3$)	0.206 (4)	0.023 (3)	0.972 (2)	6 (1)^{*c}
C21	0.4851 (4)	−0.0038 (3)	0.7475 (2)	2.2 (1)	Cl4	0.195 (1)	−1.028 (1)	0.0591 (6)	7.5 (3)^{*c}
C22	0.4994 (4)	−0.0961 (3)	0.7992 (2)	3.0 (1)	Cl5	0.347 (1)	0.049 (1)	0.9293 (6)	8.1 (3)^{*c}
C23	0.5593 (5)	−0.1062 (3)	0.8465 (2)	3.4 (1)	Cl6	0.158 (1)	0.951 (1)	0.9397 (7)	8.9 (4)^{*c}

^{a}Starred values indicate atoms were included with isotropic thermal parameters. The thermal parameter given for anisotropically refined atoms is the isotropic equivalent thermal parameter defined as: $4/3[a^2\beta_{11} + b^2\beta_{22} + c^2\beta_{33} + ab(\cos\gamma)\beta_{12} + ac(\cos\beta)\beta_{13} + bc(\cos\alpha)\beta_{23}]$, where a, b, and c are real cell parameters and β_{ij} are anisotropic betas. ^{b}Occupancy = 0.85. ^{c}Occupancy = 0.15.

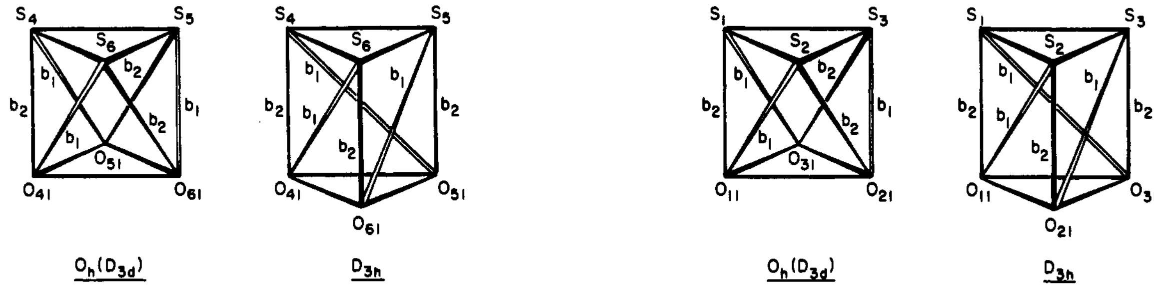

Figure 4. Six-atom family shape characteristics defining parameters used in Table III: left, for iron complex 1 (see text); right, for iron complex 2.

bond length is in good agreement with that in the ferric thiohydroxamato complex,[23] and the Fe–O bond length is also similar to those in ferric thiohydroxamato[23] and ferric 1-oxo-2-pyridinonato.[24]

One difference between this structure and that of the simple ferric thiohydroxamate complex characterized earlier is the hydrogen bonding between the amide N–H proton and the thiohydroxamate oxygen atom. The average N–O hydrogen bond distance is 2.62 Å, indicative of a very strong interaction. This is similar to the same kind of interaction seen recently in the macrocyclic terephthalamide catechol complex of Fe(III),[20] and this interaction locks the ferric ion, thiohydroxamate group, and attached amide group into one coplanar unit, as can be seen in Figure 2.

The average measured trigonal twist angle θ (60° for an idealized-octahedral geometry and 0° for trigonal-prismatic geometry) for the ferric complex **6** is ~36°, which is slightly less than that observed for tris(*N*-(methylthio)benzohydroxamato)iron(III) [42.9°][23] but similar to that observed for tris(1-hydroxy-2-pyridinonato)iron(III) [36.6°].[24] This puts the geometry between octahedral and trigonal prismatic and implies there is little strain imposed by the geometry of the ligand itself. A different approach of describing the variation from octahedral to trigonal-prismatic geometries is by using the dihedral angle

Table III. Ideal and Observed Dihedral Angles (deg) for Compound **6**

structure	δ at b_1	δ at b_2	remaining δ
ideal octahedron	70.5, 70.5 70.5	70.5, 70.5 70.5	70.5, 70.5, 70.5 70.5, 70.5, 70.5
ideal trigonal prism	0, 0, 0	120, 120 120	90, 90, 90 90, 90, 90
iron complex-1[a]	45.8, 46.2 45.8	88.5, 88.6 89.0	67.7, 67.9, 68.0 80.2, 80.9, 81.8
iron complex-2[a]	47.8, 48.3 48.9	86.6, 87.2 87.6	66.4, 67.4, 68.1 80.4, 80.7, 81.1

[a] See Figure 4 in this paper and ref 39.

between trigonal faces sharing common edges of the polyhedron.[38,39] The idealized-octahedral and trigonal-prismatic versus observed dihedral angles for the two iron complex molecules are given in Table III and are graphically presented in Figure 4. It is clear from both presentations that the twist angle and dihedral angle treatments are in good agreement in defining the coordination polyhedra of the ferric complex molecules as intermediate in the D_{3d}-D_{3h} reaction path.

In conclusion, hexadentate amide ligands derived from 2-mercaptopyridine-6-carboxylic acid 1-oxide and triamines have been prepared and characterized. The ferric complexes of these ligands also have been isolated and characterized. The structure of the ferric complex of the *N,N′,N″*-trris((1,2-didehydro-1-hydroxy-2-thioxopyrid-6-yl)carbonyl)-2,2′,2″-triaminotriethylamine shows a coordination polyhedron similar to that of the ferric complex of 1-hydroxy-2(1*H*)-pyridinone. This establishes that there is no significant strain in the complex structure caused by the amine backbone, which make this ligand geometry suitable for iron binding.

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Supplementary Material Available: Listings of positional and thermal parameters of hydrogen atoms (Table S1), general temperature factor expressions (*B*'s) (Table S2), root-mean-square amplitudes of vibration (Table S3), and complete bond lengths and angles (Table S5) (13 pages); a table of observed and calculated structure factors (Table S4) (45 pages). Ordering information is given on any current masthead page.

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Boron Derivatives of 3-Ferrocenylpyrazole

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3-Ferrocenylpyrazole (=Hpz*) has been prepared and was converted to the salt Kpz* and the complex $[(\pi\text{-}CH_2CCH_3CH_2)Pd(pz^*)]_2$. In many respects Hpz* reacts with boron compounds in a manner similar to the unsubstituted parent pyrazole. Thus, the pyrazaboles $R_2B(\mu\text{-}pz^*)_2BR_2$ (R = H, C_2H_5); the adducts $(CH_3)_2HN\cdot B(pz^*)(C_2H_5)_2$, $(CH_3)_2HN\cdot B(pz^*)(C_8H_{14})$ (where $C_8H_{14}BH$ = 9-borabicyclo[3.3.1]nonane), $Hpz^*\cdot B(pz^*)(C_8H_{14})$, and $(CH_3)_2HN\cdot B(pz^*)_3$; the salts $Tl[(pz^*)_2BH_2]$, $K[(pz^*)_2B(C_2H_5)_2]$, and $M[(pz^*)_2B(C_8H_{14})]$ (M = Na, K); and the complexes $(C_2H_5)_2(\mu\text{-}pz^*)_2Pd(\pi\text{-}CH_2CHCH_2)$ and $(C_8H_{14})B(\mu\text{-}pz^*)_2Pd(\pi\text{-}CH_2CHCH_2)$ have been prepared and characterized. On the other hand, the relative lability of the ferrocenyl unit of Hpz* prevents some reactions that are possible with other pyrazoles, e.g., formation of $K[HB(pz^*)_3]$ or $K[B(pz^*)_4]$ from Hpz* and KBH_4 or the halogenation at the boron sites of $H_2B(\mu\text{-}pz^*)_2BH_2$.

Introduction

There are many compounds known in which the two adjacent nitrogen atoms of pyrazolyl moieties bridge a boron and a metal atom (M) to give the structural arrangement $B(\mu\text{-}pz)_nM$ (Hpz = pyrazole; n = 1–3).[1] In contrast, no materials are known in which a boron atom is bonded to a metal via the dinitrogen unit and simultaneously to a different metal via one nitrogen and the carbon framework of the same pyrazolyl group. The synthesis and characterization of such species derived from 3-ferrocenylpyrazole were the ultimate goal of the present study.

Experimental Section

Elemental analyses were performed by the Schwarzkopf Microanalytical Laboratory, Woodside, NY. Melting points (uncorrected) were determined on a Mel-Temp block.

NMR spectra were recorded for solutions in $CDCl_3$ (unless otherwise noted) on a Varian VXR-400 (^{11}B and high resolution) or GEMINI-200 (^1H, ^{13}C) instrument. Chemical shift data are given in ppm with positive values indicating downfeld shifts from the reference (internal $(CH_3)_4Si$ for ^1H and ^{13}C NMR spectroscopy, external $(C_2H_5)_2O\cdot BF_3$ for ^{11}B NMR spectroscopy); s = singlet, d = doublet, t = triplet, q = quartet, p = quintuplet, h = septet, m = unresolved multiplet, and an asterisk denotes a broad signal. Coupling constants J are given in hertz. ^{13}C NMR spectra were generally recorded in the proton-decoupled mode. Electron impact (EI) mass spectral data (70 eV unless otherwise noted) were obtained on a VG ZAB-2F spectrometer under standard operating conditions. Data are listed to m/z 30 for 5% or greater relative abundances (in parentheses) only.

All nonreferenced reagents were obtained from Aldrich Chemical Co., Milwaukee, WI, and used as received.

3-Ferrocenylpyrazole (=Hpz*). To 54 g (1 mol) of dry sodium methoxide slurried in 1 L of toluene was added with stirring a solution of 228 g (1 mol) of acetylferrocene and a large excess of ethyl formate in toluene. An exothermic controlled reaction occurred, a red solution formed, and finally an orange-brown precipitate was obtained. The latter was collected and dissolved in methanol, and the resulting mixture was reacted with an aqueous solution of 68.5 g (1 mol) of hydrazine monohydrochloride. The product was extracted with methylene chloride, and the latter solvent was evaporated to leave a red tar. This material was refluxed for 1 h with 25 g (0.5 mol) of hydrazine hydrate in methanol (or ethanol). The dark reddish solution was poured slowly and with stirring into about 1 L of cold water. An oil formed, which soon solidified. The solid was collected, washed with water, and then dissolved in ca. 200 mL of methylene chloride. The solution was filtered through a short alumina column, and the orange filtrate was concentrated until crystals started appearing. After transfer to a smaller vessel, methylene chloride was driven off and, on cooling, 130 g (61%) of crystalline orange product, mp 148–149 °C, was obtained. Anal. Calcd for $C_{13}H_{12}FeN_2$

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