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# Thioether ligation in Co(III) complexes with carboxamido nitrogens as donors: implications on the coordination structure of the cobalt site in nitrile hydratase

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#### Abstract

In order to determine the role of the sulfur donors around the Co(III) site of the enzyme nitrile hydratase, we have synthesized a designed ligand PyPSMeH<sub>2</sub> (Hs are dissociable carboxamide hydrogens) with carboxamido nitrogens and thioether sulfur donors. Although Co(III) complexes with bound thioether groups have previously been synthesized with other ligands, attempts to synthesize such a species with PyPSMe<sup>2-</sup> have failed. The only complex isolated is the bis complex (Et<sub>4</sub>N)[Co(PyPSMe)<sub>2</sub>] (1) in which the potentially pentadentate PyPSMe<sup>2-</sup> ligand acts as tridentate and all four thioether sulfurs remain as pendant groups. In 1, one of the four carboxamido groups is *O*-bonded. Methylation of the analogous (Et<sub>4</sub>N)[Co<sub>2</sub>(PyPS)<sub>2</sub>] with iodomethane affords (Et<sub>4</sub>N)[Co<sub>2</sub>(PyPS(SMe))<sub>2</sub>] (2), the only Co(III) complex with weakly bound thioether groups. The dimeric complex 2 contains two bridging thiolato sulfurs and each Co(III) center has one bound thioether sulfur in its coordination sphere. These two terminal thioether groups of 2 are replaced easily by other ligands like pyridine. Reaction of CN<sup>-</sup> with 2 affords the dicyano complex (Et<sub>4</sub>N)<sub>2</sub>[Co(PyPS(SMe)(CN)<sub>2</sub>] (3) with pendant thioether group. Collectively, these results indicate that Co(III) centers with coordinated carboxamido nitrogen(s) exhibit very low affinity toward thioether sulfur. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Thioether ligation; Carboxamido nitrogens; Nitrile hydratase

### 1. Introduction

The enzyme nitrile hydratase (NHase), involved in the assimilation of organic nitriles by various microorganisms, contains either a low-spin Fe(III) or Co(III) metal center at its active site and catalyzes the conversion of a variety of nitrile substrates to the corresponding amides [1-5]. Recent crystallographic studies of two *Rhodococcus* NHases have revealed a single low-spin Fe(III) metal center coordinated to two deprotonated carboxamido nitrogens and three Cys–S centers [6] two of which are modified to Cys-sulfenic and -sulfinic groups [7]. The thiolates are ligated in a fac arrangement around the Fe(III) center in the enzyme with the unmodified thiolate positioned *trans* to the active site. The post-translational oxidation of the Cys–S centers has recently been shown to be essential for the activity of the Fe-containing enzyme [8] although their specific function is not understood at this time. The unprecedented coordination sphere around the Fe(III) center is thought to play a crucial role in the catalytic activity of the NHases. To date, no crystallographic study has been reported for a Co-containing NHase. High sequence homologies at the active sites of Fe–NHase and Co–NHase and spectroscopic evidences, however, suggest that the coordination structure of the Co(III) center in Co–NHase is very similar to that of Fe(III) in Fe–NHase [9,10]. The mechanism by which NHases hydrolyze nitriles is elusive at this time.

Recently we reported the first functional model of the Co(III) site of Co–NHase which catalyzes the hydration of acetonitrile to acetamide under mild conditions

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[11]. The functional model complex contains a Co(III) metal center ligated to a pentacoordinate ligand,  $PyPSH_4$ , which contains two deprotonated peptide nitrogens, two thiolates and a pyridine nitrogen.

In order to investigate the importance of the thiolato sulfur groups in the reactivity of our model complex, we have now synthesized the ligand PyPSMeH<sub>2</sub> (the two dissociable carboxamido protons are denoted by H<sub>2</sub>) which is identical to PyPSH<sub>4</sub> except for the two thiolates being replaced with methyl thioether groups. A close scrutiny of the literature reveals that no Co(III) complex containing thioether and carboxamido groups has been reported so far and hence the reactivity of such a species is unknown. Since the spectroscopic parameters of Co(III) complexes with thiolato and thioether sulfurs are often very similar [12,13], one expects that the reactivity of such complexes could be similar.



In this paper, we report that the reaction of  $PyPSMe^{2-}$  (deprotonated  $PyPSMeH_2$ ) with Co(III) affords the bis complex  $(Et_4N)[Co(PyPSMe)_2]$  (1) with four pendant thioether moieties. In addition, attempts to synthesize a Co(III) complex with bound thioether sulfur via the reaction of iodomethane with the previously reported model complex  $(Et_4N)_2[Co(PyPS)(CN)]$  have so far afforded no characterizable Co(III) species. The only Co(III) complex with bound thioether sulfurs that we have isolated so far is the dimeric species  $[Co_2(PyPS(SMe))_2]$  (2), which is obtained in the reaction of iodomethane with the previously reported dimeric complex  $(Et_4N)_2[Co_2(PyPS)_2]$ . However, we have also noted that the ligated thioether groups in 2 can be displaced easily by weak nucleophiles including



pyridine and 1-methylimidazole and the reaction of **2** with  $CN^-$  affords the dicyano complex  $(Et_4N)_2$ -[Co(PyPS(SMe))(CN)<sub>2</sub>] (**3**) with pendant thioether group. Therefore the results indicate that thioether groups are not good ligands for Co(III) when additional carboxamido groups are present in the coordination sphere. And finally, we report that none of the Co(III) complexes with thioether groups (bound or unbound) promote hydrolysis of nitriles.

# 2. Experimental

#### 2.1. Materials

2,6-Pyridinedicarbonyl dichloride, 2-(methylthio)aniline, sodium hydride, triethylamine, iodomethane and tetraethylammonium cyanide were purchased from Aldrich Chemical Co. and used without further purification. [Co(NH<sub>3</sub>)<sub>5</sub>Cl]Cl<sub>2</sub> was synthesized by following the published procedure [14]. All manipulations were carried out using standard Schlenk techniques except otherwise noted and the solvents were dried and distilled before use.

## 2.2. Physical measurements

Infrared spectra were obtained with a Perkin–Elmer 1600 FTIR spectrophotometer. Absorption spectra were measured on a Perkin–Elmer Lambda 9 spectrophotometer. <sup>1</sup>H NMR spectra were recorded either on a Varian Unity Plus 500 running Solaris 2.6/VNMR 6.1B or a Bruker 250 MHz spectrometer with a Tec-Mag workstation upgrade.

#### 2.3. Preparation of compounds

The ligand PyPSH<sub>4</sub>, and the two complexes reported,  $(Et_4N)_2[Co_2(PyPS)_2]$  and  $(Et_4N)_2[Co(PyPS)CN]$ , were synthesized by following published procedures [11,15].

#### 2.3.1. Preparation of PyPSMeH<sub>2</sub>

A batch of 205 mg (1.03 mmol) of 2,6-pyridinedicarbonyl dichloride was dissolved in 20 ml of chloroform with 8 ml of Et<sub>3</sub>N. To this solution, 1.27 ml (10.12 mmol) of 2-(methylthio)aniline was added and the solution was stirred for 2 days. The solvent was then removed by rotary evaporation and the yellow–green solid was washed two times with 30 ml of THF. The solid was then extracted into 50 ml of chloroform and layered with 20 ml of Et<sub>2</sub>O and kept at -28 °C for 24 h. The light yellow crystalline material thus obtained was collected and dried under high vacuum for 10 h. Yield: 0.95 g (46%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 250 MHz, 25 °C,  $\delta$  from TMS): 2.40 (s, 3H, SMe), 7.18 (t, 1H), 7.36 (t, 1H), 8.17 (t, 1H), 8.35 (d, 1H), 8.53 (d, 2H) 10.58 (s, 1H). Selected IR bands: (KBr pellet, cm<sup>-1</sup>)  $(v_{C=O})$  1684.

#### 2.3.2. Synthesis of $(Et_4N)[Co(PyPSMe)_2]$ (1)

A batch of 300 mg (0.74 mmol) of PyPSMeH<sub>2</sub> was dissolved in 10 ml of dimethylformamide (DMF) and 37 mg (1.55 mmol) of NaH was added. The solution was stirred for 10 min. Next, a batch of 185 mg (0.74 mmol) of  $[Co(NH_3)_5Cl]Cl_2$  was added and the solution was heated at 60 °C for 1.5 h. A batch of 245 mg (1.47 mmol) of (Et<sub>4</sub>N)Cl was then added to the orange solution and the DMF was removed by vacuum distillation. The solid thus obtained was dissolved in 15 ml of acetonitrile and filtered. Acetone was slowly diffused into this solution and the brown-orange crystals collected after 48 h. Yield: 330 mg (45%). <sup>1</sup>H NMR (DMSO-d<sub>6</sub>, 250 MHz, 25 °C,  $\delta$  from TMS): 1.15 (t, Et<sub>4</sub>N), 1.55 (s, 3H,SMe), 1.60 (s, 3H, SMe), 3.20 (q, Et<sub>4</sub>N), 2.06 (s, 6H, SMe) 6.87 (m, 15H), 7.40 (m, 1H), 7.95 (m, 4H), 8.09 (d, 1H), 8.22 (t, 1H). Selected IR bands: (KBr pellet, cm<sup>-1</sup>) ( $v_{C=O}$ ) 1618, 1590. Electronic absorption spectrum:  $\lambda_{max}$  (nm) ( $\epsilon$ , M<sup>-1</sup> cm<sup>-1</sup>) (acetonitrile): 690 (95), 475 sh (2550), 405 (4600).

#### 2.3.3. Synthesis of $[Co_2(PyPS(SMe))_2]$ (2)

A batch of 218 mg (0.19 mmol) of  $(Et_4N)_2[Co_2-(PyPS)_2]$  was dissolved in 15 ml of acetonitrile. To this solution, an aliquot of 480 µl (7.71 mmol) of iodomethane was added carefully and the solution was stirred for 2 h after which a dark brown microcrystalline solid began to form. The stirring was stopped and the mixture was allowed to stand for an additional 2 h. The microcrystalline solid thus obtained was collected and washed two times with 5 ml of acetonitrile and dried under high vacuum for 5 h. Yield: 130 mg (75%). <sup>1</sup>H NMR (DMSO-d<sub>6</sub>, 500 MHz, 25 °C,  $\delta$  from



Fig. 1. Thermal ellipsoid plot (50% probability level) of the anion of 1 showing the numbering scheme. Hydrogen atoms are omitted for the sake of clarity.

TMS):1.20 (s, 3H), 5.48 (d, 1H), 6.52 (t, 1H), 7.13 (t, 1H), 7.24 (t, 1H), 7.47 (d, 1H), 7.55 (d, 1H), 7.63 (t, 1H), 8.06 (d, 1H), 8.17 (d, 1H), 8.45 (t, 1H), 8.57 (d, 1H). Selected IR bands: (KBr pellet, cm<sup>-1</sup>) 1623 ( $\nu_{C=O}$ ). Electronic absorption spectrum:  $\lambda_{max}$  (nm) ( $\varepsilon$ , M<sup>-1</sup> cm<sup>-1</sup>) (DMF): 575 (2400), 430 (5410), 372 sh (6250).

#### 2.3.4. Synthesis of $(Et_4N)_2[Co(PyPS(SMe))(CN)_2]$ (3)

A batch of 105 mg (0.116 mmol) of **2** was suspended in 10 ml of acetonitrile and the mixture was stirred for 10 min. Next, a batch of 106 mg (0.680 mmol) of (Et<sub>4</sub>N)CN was added. After 2 h, the mixture became homogeneous and a deep red-orange color developed. The solution was filtered to remove any unreacted **2**. Et<sub>2</sub>O was allowed to slowly diffuse into this solution. Large orange blocks were collected after 24 h. Yield: 70 mg (70%). <sup>1</sup>H NMR (DMSO-d<sub>6</sub>, 500 MHz, 25 °C,  $\delta$ from TMS): 1.13 (t, Et<sub>4</sub>N), 2.24 (s, 3H), 3.16 (q, Et<sub>4</sub>N), 6.50 (m, 2H), 6.76 (d, 1H), 6.96 (m, 3H), 7.15 (d, 1H), 7.55 (d, 1H), 7.74 (t, 1H), 8.11 (t, 1H), 8.69 (d, 1H). Selected IR bands: (KBr pellet, cm<sup>-1</sup>) ( $v_{C=N}$ ) 2114, ( $v_{C=O}$ ) 1597. Electronic absorption spectrum:  $\lambda_{max}$  (nm) ( $\varepsilon$ , M<sup>-1</sup> cm<sup>-1</sup>) (DMF): 475 (1920), 345 (5600).

# 2.4. X-ray data collection and structure solution and refinement

Light brown parallelepipeds of  $(Et_4N)[Co(PyPSMe)_2]$ (1), suitable for X-ray analysis, were obtained by slow diffusion of acetone into a solution of 1 in acetonitrile. Black parallelepipeds of  $[Co_2(PvPS(SMe))_2]$  (2) were obtained by slow diffusion of acetone into an acetonitrile solution of 2. Red plates of (Et<sub>4</sub>N)<sub>2</sub>[Co(PyPS- $(SMe))(CN)_2$  (3) were obtained by slow diffusion of  $Et_2O$  into a solution of **3** in acetonitrile. Diffraction data for complexes 1-3 were collected on a Bruker SMART 1000 diffractometer. All structures were solved by direct methods (SHELXS-97). The data were corrected for absorption effects [16]. In the structure of 1, one pendant arm containing C36-C42 is disordered. This fact has been omitted in Fig. 1 for sake of clarity. Machine parameters, crystal data, and data collection parameters are summarized in Table 1. Selected bond distances and bond angles are listed in Table 2. The three sets of crystallographic data have been submitted as supporting information.

#### 3. Results and discussion

The potentially pentadentate ligand  $PyPSMe^{2-}$  only affords the bis complex  $(Et_4N)[Co(PyPSMe)_2]$  (1) even with a metal-ligand ratio of 1:1. Reactions of  $PyPSMe^{2-}$  and  $[Co(NH)_5Cl]Cl_2$  in DMF always result in the formation of the bis complex 1 in which the Table 1

Empirical formula	$(Et_4N)_2[Co(PyPSMe)_2 \cdot acetone C_{52}H_{60}CoN_7O_5S_4$	$[Co_2(PyPS(SMe))_2]$ ·1.5 acetone·0.5MeCN $C_{45}$ · $SH_{28}$ · $SCo2N_6$ · $SO_5$ · $SS_4$	$(Et_4N)_2[Co(PS(SMe))(CN)_2]$ ·MeCN C <sub>40</sub> H <sub>57</sub> CoN <sub>8</sub> O <sub>2</sub> S <sub>2</sub>
Molecular weight	1062.25	1010.43	804.99
Crystal color, habit	light brown parallelpiped	black parallelpiped	red plate
Temperature (K)	90(2)	90(2)	130(2)
Crystal system	monoclinic	triclinic	triclinic
Space group	$P2_1/c$	$P\overline{1}$	$P\overline{1}$
Unit cell dimensions			
a (Å)	13.4541(5)	12.1152(4)	11.141(3)
b (Å)	27.2013(11)	13.5131(5)	12.666(4)
<i>c</i> (Å)	14.9702(6)	14.1852(5)	15.098(5)
α (°)	90	84.9540(10)	106.96(2)
β (°)	111.3830(10)	79.8880(10)	94.16(2)
γ (°)	90	71.4810(10)	98.56(2)
$V(\mathbf{A}^3)$	5101.5(3)	2166.57(13)	1999.9(11)
Ζ	4	2	2
$D_{\rm calc} ({\rm g}{\rm cm}^{-3})$	1.383	1.549	1.337
Absorption coefficient ( $\mu$ ) (mm <sup>-1</sup> )	0.555	1.016	0.579
Goodness-of-fit on $F^{2 a}$	1.143	1.050	1.010
R <sub>1</sub> <sup>b</sup> (%)	5.36	3.86	4.07
R <sub>w2</sub> ° (%)	12.00	8.53	9.72

Summary of crystal data and intensity collection and structure refinement parameters for  $(Et_4N)_2[Co(PyPSMe)_2]$ ·acetone (1·acetone),  $[Co_2(PyPS(SMe))_2]$ ·1.5 acetone·0.5 MeCN (2·1.5 acetone·0.5 MeCN) and  $(Et_4N)_2[Co(PyPS(SMe))(CN)_2]$ ·MeCN (3·MeCN)

<sup>a</sup> Goodnss-of-fit =  $[\Sigma[w(F_o^2 - F_c^2)^2]/M - N]^{1/2}$  (M = number of reflections, N = number of parameters refined).

<sup>b</sup> 
$$R_1 = \Sigma ||F_0| - |F_c|| / \Sigma |F_0|.$$

<sup>c</sup> 
$$Rw_2 = [\Sigma[w(F_o^2 - F_c^2)^2] / \Sigma[w(F_o^2)^2]]^{1/2}$$

thioether moieties are not involved in coordination. All attempts to isolate a Co(III) complex with bound thioether group(s) with  $PyPSMe^{2-}$  have so far been unsuccessful. This is somewhat surprising since many Co(III) complexes with bound thioether (SR) groups have been synthesized directly from cobalt salts and ligands containing SR groups [17–20].

Both the availability of the monomeric model complex  $(Et_4N)_2[Co(PyPS)(CN)]$  in this research group and the reports on conversion of thiolato complexes to thioether species by the use of alkyl halides [12,13,21] prompted us to try to prepare  $(Et_4N)_2[Co(PyPSMe)-(CN)]$  via the reaction of  $(Et_4N)_2[Co(PyPS)(CN)]$  with iodomethane. All attempts in this direction resulted in orange solutions from which only insoluble and intractable orange residues have been obtained. As the last option, we subjected the dimeric complex  $(Et_4N)_2[Co_2(PyPS)_2]$  to react with iodomethane in acetonitrile.



This reaction afforded a new dimeric species namely,  $[Co_2(PyPS(SMe))_2]$  (2) in which only the terminal thio-

lates are converted into thioether groups. The higher basicity of the terminal thiolato sulfurs compared to that of the bridging ones is clearly responsible for this selected methylation leading to 2. Such behavior has been observed in thiolato-bridged nickel complexes [22,23]. The conversion of the thiolato sulfurs to thioether moieties results in a loss of charge and the neutral complex 2 precipitates out of the reaction mixture. This allows for isolation of 2 as a pure compound and in high yield.

Since our original intention was to synthesize a monomeric Co(III) complex with bound thioethers, we decided to split the thiolato bridge of 2 with the aid of  $CN^{-}$ . Such reaction had yielded  $(Et_4N)_2[Co(PyPS)-$ (CN)] from (Et<sub>4</sub>N)<sub>2</sub>[Co<sub>2</sub>(PyPS)<sub>2</sub>] before. Reaction of  $CN^{-}$  does split the thiolato bridge in 2. However, only complex 3 can be isolated from a reaction mixture containing 2 and 2 equiv. of (Et<sub>4</sub>N)CN. In this reaction, approximately half of the starting dimer 2 is converted into 3 while the remaining half stays unreacted. When one uses 4 equiv. of  $(Et_4N)CN$  in this reaction, complex 3 is isolated as the only product and in high yield. Since reaction of CN<sup>-</sup> with 2 in MeCN in the presence of air slowly oxidizes the thiolato sulfur to S-bound sulfenate (S=O) group, anaerobic conditions are required for isolation of complex 3 in pure form. Collectively, all these results indicate that in no case one obtains a monomeric Co(III) complex with carboxamido nitrogens and bound thioether group. This in turn suggests that a thioether group is not a good donor for Co(III)

Table 2 Selected bond distances (Å) and bond angles (°)

(Et <sub>4</sub> N)[Co(PyPSMe)	)₂]·acetone				
Bond distances					
Co(1) - N(5)	1.8408(16)	N(1)-C(7)	1.431(3)		
Co(1) - N(2)	1.8529(16)	S(3)-C(23)	1.763(2)		
Co(1) - N(6)	1.9508(19)	O(3)–C(29)	1.305(2)		
Co(1)–O(3)	1.958(14)	O(4)–C(35)	1.235(3)		
Co(1)-N(1)	1.9608(17)	N(4)-C(29)	1.306(3)		
Co(1)-N(3)	1.9617(17)	N(4)-C(28)	1.407(3)		
S(1)-C(2)	1.770(3)	N(6)-C(35)	1.354(3)		
S(1)-C(1)	1.781(3)	N(6)-C(36)	1.457(4)		
S(2)-C(21)	1.809(2)	S(4A)-C(42A)	1.804(5)		
O(1)-C(8)	1.235(3)t	S(4B) - C(42B)	1.796(6)		
O(2)–C(14)	1.241(2)				
Bond angles					
$N(5) = C_0(1) = N(2)$	177 98(7)	C(2)=S(1)=C(1)	102 72(13)		
N(5) = Co(1) = N(6)	83 03(8)	C(20) = S(2) = C(21)	102.72(13) 101.09(11)		
$N(2) C_0(1) N(6)$	07.17(7)	C(14) N(2) C(15)	101.00(11) 120.22(17)		
N(2) = CO(1) = N(0) N(5) = Co(1) = O(2)	97.17(7)	C(14) = N(3) = C(13)	120.33(17) 102.20(12)		
N(3) = Co(1) = O(3) $N(2) = C_2(1) = O(3)$	02.74(7) 07.08(6)	C(23) = S(3) = C(22)	102.20(12)		
N(2) - Co(1) - O(3)	97.08(6)	O(3) = C(29) = N(4)	129.23(18)		
N(6)-Co(1)-O(3)	165.74(7)	O(3) - C(29) - C(30)	113.43(17)		
O(3)-Co(1)-N(3)	88.97(7)	C(41A) - S(4A) - C(42A)	102.2(2)		
N(1)-Co(1)-N(3)	164.11(7)	C(41B) - S(4B) - C(42B)	103.7(2)		
$[Co_2(PyPS(SMe))_2]$ ·1.5acetone·0.5MeCN					
Bond distances					
Co(1) - N(2)	1.8516(17)	Co(2)-S(2)	2.2797(6)		
Co(1) - N(3)	1.9181(16)	Co(2)-S(4)	2.2821(5)		
Co(1)-N(1)	1.9401(16)	S(1)-C(1)	1.787(2)		
Co(1)–S(2)	2.2229(6)	S(1)-C(39)	1.805(2)		
Co(1)-S(3)	2.2640(6)	O(1)–C(7)	1.235(2)		
Co(1) - S(1)	2.2828(6)	N(3)-C(13)	1.360(3)		
Co(2)–S(3)	2.2270(5)	N(3)-C(14)	1.403(3)		
Bond angles					
N(2)-Co(1)-N(3)	83.18(7)	S(2)-Co(1)-S(3)	84.20(2)		
N(2)-Co(1)-N(1)	82.43(7)	S(2)-Co(1)-S(1)	86.16(2)		
N(3)-Co(1)-N(1)	164.62(7)	N(4)-Co(2)-N(6)	163.77(7)		
N(2)-Co(1)-S(2)	169.01(5)	N(4) - Co(1) - S(2)	170.31(4)		
N(3)=Co(1)=S(2)	89.06(5)	$S(3)=C_0(2)=S(2)$	83 74(2)		
N(2) = Co(1) = S(3)	88.97(5)	S(3) = Co(2) = S(4)	83 16(2)		
N(2) Co(1) S(3) N(3) Co(1) S(3)	96.69(5)	C(39) S(1) Co(1)	107.86(8)		
N(3) = CO(1) = S(3)	90.09(3)	C(39)=S(1)=CO(1)	107.00(0)		
$(Et_4N)_2[Co(PyPS(SMe))(CN)_2]$ ·MeCN Bond distances					
$C_0(1) = N(2)$	1 859(2)	S(1) = C(1)	1 800(3)		
$C_0(1) - C(21)$	1.039(2) 1.912(3)	S(1) - C(2)	1.000(3) 1.775(3)		
$C_0(1) C(21)$	1.912(3) 1.925(2)	O(1) C(2)	1.779(3)		
$C_{0}(1) = C(22)$	1.925(2)	O(1) = C(8)	1.236(3)		
$C_{0}(1) = N(3)$	1.920(3)	N(1) = C(3)	1.344(3)		
Co(1) - N(1)	1.973(2)	N(4) = C(22)	1.149(3)		
Co(1) - S(2)	2.2555(10)	N(5)-C(21)	1.144(4)		
Bond angles					
N(2)-Co(1)-C(21)	92.24(10)	N(2)-Co(1)-S(2)	171.10(6)		
N(2)-Co(1)-C(22)	89.14(9)	C(21)-Co(1)-S(2)	89.99(8)		
C(21)-Co(1)-C(22)	178.57(11)	C(22)-Co(1)-S(2)	88.71(7)		
N(2)-Co(1)-N(3)	82.76(9)	N(3)-Co(1)-S(2)	88.65(7)		
C(21)-Co(1)-N(3)	89.20(10)	N(1)-Co(1)-S(2)	107.48(6)		
C(22)-Co(1)-N(3)	91.33(9)	C(2)-S(1)-C(1)	100.07(14)		
N(2)-Co(1)-N(1)	81.16(8)	N(5)-C(21)-Co(1)	176.8(3)		
C(22)-Co(1)-N(1)	90.06(9)	N(4)-C(22)-Co(1)	177.7(2)		
N(3)-Co(1)-N(1)	163 84(8)	(,) =(==) ==(()	(=)		

centers when hard ligands such as carboxamido nitrogens are present in the coordination sphere. Further support for this notion comes from the fact that reaction of **2** with ligands like *N*-methylimidazole (*N*-MeIm) or pyridine (py) affords a dimeric species (still thiolato bridged) in which the thioether groups are replaced by *N*-MeIm or py. These dimeric species have been identified by NMR spectroscopy.

#### 3.1. Structure of complexes

# 3.1.1. Structure of $(Et_4N)_2[Co(PyPSMe)_2]$ ·acetone (1·acetone)

The asymmetric structure of the bis complex  $[Co(Py-PSMe)_2]^2$  is shown in Fig. 1. The coordination geometry around cobalt is pseudo-octahedral with distortions arising from the bite angle of the 2,6-pyridinedicarboxamide units. Interestingly, this complex contains both *N*-bound and *O*-bound carboxamido group presumably to relieve steric crowding between the pendant aryl thioether groups and the ligand backbone. In **1**, the Co-N<sub>pep</sub> bond and average Co-N<sub>py</sub> distances are 1.9578(19) and 1.8469(16) Å, respectively. The Co-O<sub>pep</sub> bond length is 1.958(14) Å. These values are well within the range of such distances in Co(III) complexes containing bound carboxamido-N and pyridine-N donors [24].

# 3.1.2. Structure of $[Co_2(PyPS(SMe))_2]$ ·1.5 acetone·0.5MeCN (2·1.5 acetone·0.5MeCN)

The dimeric structure of complex 2, shown in Fig. 2, is very similar to the structure of  $(Et_4N)_2[Co_2(PyPS)_2]$ reported by this group previously [11]. Methylation of  $(Et_4N)_2[Co_2(PyPS)_2]$ results in  $(Et_4N)_2[Co_2(PyPS$ which the  $(SMe))_2$ in pentadentate ligand  $PyPS(SMe)^{2}$ occupies five coordination positions around each Co(III) center. The thiolato S donor of each ligand bridges the two cobalt centers and completes the pseudo-octahedral geometry around the metal sites. In 2, the average Co-S<sub>bridging</sub> bond distance is 2.2622(6) A which is identical to the average  $Co-S_{bridging}$  bond distance for  $(Et_4N)_2[Co_2(PyPS)_2]$ (2.2623(15) Å). The average Co-S<sub>Me</sub> bond distance is 2.2825(1) Å which is within the range of previously reported Co(III)-thioether bond lengths [21,25,26]. The remaining metric parameters of 2 (Table 2) are similar to that of (Et<sub>4</sub>N)<sub>2</sub>[Co<sub>2</sub>(PyPS)<sub>2</sub>] and other Co(III) complexes with bound pyridine and carboxamido nitrogens [24,27].

### 3.1.3. Structure of

# $(NEt_4)_2[Co(PyPS(SMe))(CN)_2]$ ·MeCN (3·MeCN)

The structure of the anion of **3** is shown in Fig. 3. The two cyanide ligands are *trans* to each other with an average Co–C bond length of 1.9188(3) Å. The Co–N<sub>py</sub> and average Co–N<sub>pep</sub> bond distances of **3** (1.859(2) and 1.9497(3) Å, respectively) are very similar to the corresponding distances noted in **1**, **2**, and other related complexes [24,27–29].



Fig. 2. Thermal ellipsoid plot (50% probability level) of 2 showing the numbering scheme. Hydrogen atoms are omitted for the sake of clarity.



Fig. 3. Thermal ellipsoid plot (50% probability level) of the anion of **3** showing the numbering scheme. Hydrogen atoms are omitted for the sake of clarity.

#### 3.2. Properties

The conversion of bound thiolate to thioether group in Co(III) complexes is reported to impart little change on the electronic configuration and hence Co(III) complexes containing bound thioether moieties exhibit intense ligand-to-metal charge transfer (LMCT) bands much like the corresponding thiolato complexes. For example, Deutsch and coworkers found that conversion of the bound thiolato sulfurs of  $[(en)_2Co(SCH_2-CH_2NH_2)]^{2+}$  to methyl-thioether (SMe) group results in a 2-nm blue shift in the LMCT band [26]. Likewise, complex **2** exhibits a strong LMCT band at 430 nm in acetonitrile which is very similar to the LMCT band of  $(Et_4N)_2[Co_2(PyPS)_2]$  (427 nm in acetonitrile). The thiolate/thioether species **2** also displays a comparatively weak absorption at 570 nm.

The Co(III)–SR bonds in known thioether complexes are quite stable and resistant to ligand substitution [13,17,26]. In contrast, the bound thioether groups in 2 are replaced easily by ligands like py and N-MeIm. These ligand substitution reactions can be monitored by <sup>1</sup>H NMR spectroscopy. Thus addition of 5 equiv. of N-MeIm to a solution of 2 in DMSO results in deligation of the SMe group (1.19 ppm peak of bound SMe shifts to 1.89 ppm) and binding of N-MeIm at that site. The resulting complex, however, remains dimeric (thiolato bridge intact) as indicated by other peaks of the ligands including the characteristic one at  $\sim 5.4$  ppm. The thiolato-bridge of 2 is split only when one uses  $CN^{-}$  as the incoming ligand. Reaction of 2 with  $CN^{-}$ affords the monomeric dicyano complex (Et<sub>4</sub>N)<sub>2</sub>- $[Co(PyPS(SMe))(CN)_2]$  (3) with pendant thioether group (SMe peak at 2.24 ppm) within 2 h at room temperature. Since analogous reaction of CN- with  $(Et_4N)_2[Co_2(PyPS)_2]$  does not bring about scission of any Co(III)-S bond even after 24 h, it is evident that Co-SR bonds are considerably weakened when additional carboxamido groups are present in the coordination sphere.

The position of the SMe peak in the <sup>1</sup>H NMR spectra of the present complexes provides helpful insight regarding their structures. This peak appears at 2.43 ppm in the spectrum of free PyPSMeH<sub>2</sub> in DMSO $d_6$  and shifts upfield when ligated to Co(III) (1.19 ppm in 2). In complex 3, the pendant SMe group exhibits a resonance at 2.24 ppm which is similar to that noted for the free ligand. In the case of complex 1, the unbound thioether groups are inequivalent and exhibit three resonances at 1.59 (3H) and 1.54 (3H) and 2.06 ppm (6H) in DMSO- $d_6$ . Close examination of the crystal structure (Fig. 1) reveals that two of the four SMe groups have significant interaction with the  $\pi$ -cloud of the phenyl rings on the ligand frames. We assign the peaks at 1.59 and 1.54 ppm to these two SMe groups. The remaining two pendant SMe groups have little interaction with the ligand backbone and hence are assigned to the resonance at 2.06 ppm (similar to the SMe group of free PyPSMeH<sub>2</sub>).

Although  $(Et_4N)_2[Co(PyPS)(CN)]$  promotes significant hydrolysis of acetonitrile in aqueous buffer (pH 9.5) at 50 °C [11], complex **3** shows no such activity under similar conditions. Indeed, none of the present complexes initiate any hydrolysis of nitriles. This finding indicates that presence of thiolato sulfur(s) could be a requirement for the model complexes to promote hydrolysis of nitriles.

#### 4. Conclusions

Although several Co(III) complexes with coordinated thioether (SR) groups have been reported, the results of

the present work now indicates that the thioether (SR) group is not a good ligand for Co(III) when carboxamido nitrogens are present. The only complex with carboxamido-N and thioether-S donors that we have been able to isolate is **2**. The Co–S(R) bond in this complex is, however, weak and is substituted readily by other ligands. Collectively, the results suggest that simultaneous coordination of carboxamide group and methionine residues to Co(III) center in metalloenzymes is unlikely. The choice of cysteine (instead of methionine) sulfurs as donors for the Co(III) site in nitrile hydratase could be related to this finding.

#### 5. Supplementary material

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC Nos. 167308–167310 for complexes **1–3** respectively. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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