Zinc, Cobalt, and Cadmium Thiolate Complexes: Models for the Zinc(*S*-cys)$_2$(his)$_2$ Centre in Transcription Factor IIIA (cys = cysteine; his = histidine)

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$[M(SR)_2(1\text{-methylimidazole})_2]$ complexes of Zn^{II}, Co^{II}, and Cd^{II} have been synthesized and characterized as models for the postulated metal centre in the nucleic acid binding protein, transcription factor IIIA.

In the last year, a new and intriguing role has been suggested for zinc in nucleic acid-binding proteins which are involved in gene transcription.[1] Transcription factor IIIA (TFIIIA) is a 40-K protein which activates the transcription of the 5S RNA genes of the toad *Xenopus laevis* by binding to a 50 nucleotide region of the gene. Analysis of the amino-acid sequence of TFIIIA revealed that it contains nine repetitive units of *ca.* 30 amino-acids with each unit containing two cysteine (cys) and two histidine (his) residues. Since TFIIIA contains 7—11 zinc ions, it has been suggested that $[Zn(S\text{-cys})_2(\text{his})_2]$ co-ordination in each of these nine domains play a structural role in creating nine binding fingers which enable the protein to bind to DNA. We report the synthesis, structure, and spectroscopic properties of a series of zinc, cobalt, and cadmium complexes which reproduces the $[M(SR)_2(\text{imid})_2]$ (Himid = imidazole) units of this protein.

The reaction of $M(SR)_2$ (M = Zn, Co, Cd; SR = $S\text{-}2,4,6\text{-Pr}^i{}_3C_6H_2$, $S\text{-}2,3,5,6\text{-Me}_4C_6H$)† with two equivalents of 1-methylimidazole or pyridine in MeCN gives $[M(SR)_2(L_2)]$ in high yield. The crystal structures of two representative complexes, $[Cd(S\text{-}2,4,6\text{-Pr}^i{}_3C_6H_2)_2(1\text{-Me-imid})_2]$ (**1**) (Figure 1) and $[Co(S\text{-}2,4,6\text{-Pr}^i{}_3C_6H_2)_2(\text{pyridine})_2]$ (**2**) (Figure 2) were determined to establish their formulation and co-ordination geometries.‡

The CdS_2N_2 core in (**1**) is significantly distorted from tetrahedral symmetry with the S–Cd–S angle of 126.3(1)° and the N–Cd–N angle of 93.7(3)°. The Cd–S distance [2.46(1) Å] is considerably shorter than the distance in $[Cd(SPh)_4]^{2-}$ [2.54(1) Å] but equal to the $Cd\text{–}S_{\text{term}}$ distances in $[Cd_4(SPh)_{10}]^{2-}$ and $[Cd_2(SEt)_6]^{2-}$;[2] the average Cd–N distance in (**1**) is 2.28(1) Å. The structure of (**2**) is similar, with Co–S and Co–N distances of 2.26(1) and 2.04(1) Å. Beside reproducing the postulated co-ordination of the metal centre in TFIIIA, these complexes also have similar donor sets to the imidazole inhibited catalytic centre of liver alcohol dehydrogenase.[3]

$[Co(S\text{-}2,4,6\text{-Pr}^i{}_3C_6H_2)_2(1\text{-Me-imid})_2]$ is characterized by a paramagnetically shifted ^1H n.m.r. spectrum with chemical shifts for the imidazole ligands at δ 45.7 (2H), 2- or 4-H; 48.0 (2H), 2- or 4-H; 41.7 (2H), 5-H; 6.7 (6H), $-CH_3$ and the thiolate ligands at δ 6.11 (24H), $2,6\text{-CH}(CH_3)_2$; 2.24 (12H), $4\text{-CH}(CH_3)_2$; 21.0 (2H), $4\text{-}CH(CH_3)_2$; 29.1 (4H), *m*-H; $2,6\text{-}CH(CH_3)_2$ not observed. The electronic spectrum (MeCN) of $[Co(S\text{-}2,4,6\text{-Pr}^i{}_3C_6H_2)_2(1\text{-Me-imid})_2]$ shows intense transitions at 375sh nm (ε 5050 $dm^3\ mol^{-1}\ cm^{-1}$), 336 (8420), 292sh (6930) which are characteristic of S-to-Co^{II} charge transfer, and ligand field transitions at 1535 nm (109), 1255 (118), 1000 (110), 694 (762), 655 (784), 570sh (348). The position and the intensity of these ligand field bands are consistent with a distorted tetrahedral co-ordination about the

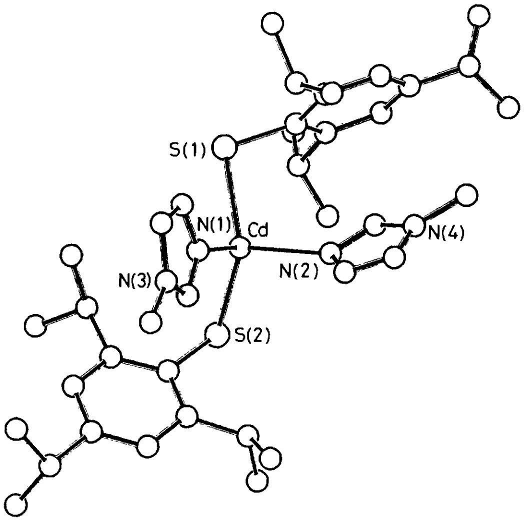

Figure 1. A ROTOCHEM view of $[Cd(S\text{-}2,4,6\text{-Pr}^i{}_3C_6H_2)_2(1\text{-Me-imid})_2]$ (**1**). Bond distances (Å): Cd–S(1) 2.474(2); Cd–S(2) 2.451(2); Cd–N(1) 2.270(7); Cd–N(2) 2.291(7). Bond angles (°): S(1)–Cd–S(2) 126.3(1); S(1)–Cd–N(1) 103.8(2); S(1)–Cd–N(2) 107.0(2); S(2)–Cd–N(1) 111.0(2); S(2)–Cd–N(2) 109.9(2); N(1)–Cd–N(2) 93.7(3).

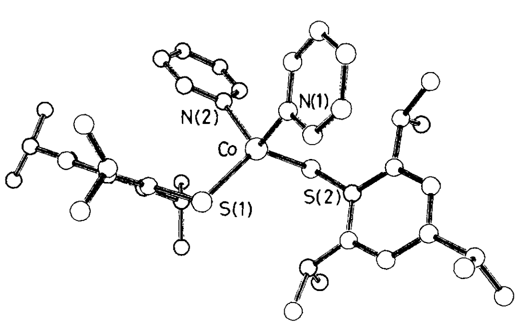

Figure 2. A ROTOCHEM view of $[Co(S\text{-}2,4,6\text{-Pr}^i{}_3C_6H_2)_2(py)_2]$ (**2**). Bond distances (Å): Co–S(1) 2.272(3); Co–S(2) 2.253(3); Co–N(1) 2.035(11); Co–N(2) 2.041(9). Bond angles (°): S(1)–Co–S(2) 123.4(2); S(1)–Co–N(1) 109.0(3); S(1)–Co–N(2) 108.7(3); S(2)–Co–N(1) 106.5(3); S(2)–Co–N(2) 104.0(3); N(1)–Co–N(2) 103.5(4).

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† $[S\text{-}2,4,6\text{-Pr}^i{}_3C_6H_2]$ = 2,4,6-tri-isopropylbenzenethiolate; $[S\text{-}2,3,5,6\text{-Me}_4C_6H]$ = 2,3,5,6-tetramethylbenzenethiolate.

‡ *Crystal data:* Compound (**1**), $C_{38}H_{58}CdN_4S_2$, M = 747.4, monoclinic, space group $P2_1/c$, a = 16.542(7), b = 15.898(6), c = 16.364(10) Å, β = 108.94(13)°, U = 4070(13) Å^3, Z = 4. $R(R_w)$ = 0.046(0.055) for 2445 unique reflections with $I > 3\sigma(I)$. Compound (**2**), $C_{40}H_{56}CoN_2S_2$, M = 688, orthorhombic, space group $Pbn2_1$, a = 15.517(8), b = 27.398(8), c = 9.374(5) Å, U = 3985(5) Å^3, Z = 4. $R(R_w)$ = 0.057(0.068) for 1332 unique data with $I > 3\sigma I$. Data collection was performed at room temperature using Mo radiation on a CAD4 diffractometer. Heavy-atom and Fourier methods were used to solve the structures. The positions of the hydrogen atoms were calculated and were included in the structure factor calculations but were not refined. For (**1**), all non-hydrogen atoms were refined anisotropically; for (**2**), anisotropic refinement was limited to the metal, the ligand donor atoms, and adjacent carbon atoms.

Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Data Centre. See Notice to Authors, Issue No. 1.

Co^{II} centre.[4] The zinc and cadmium complexes have ^1H n.m.r. spectra consistent with their solid-state structure; the ^{113}Cd n.m.r. resonance for $[Cd(S\text{-}2,4,6\text{-}Pr^i_3C_6H_2)_2(1\text{-}Me\text{-}imid)_2]$ in $CHCl_3$ occurs at 457 p.p.m. [0.1 M $Cd(ClO_4)_2$ reference].

When derivatives of TFIIIA with the spectroscopic probe metals cobalt and cadmium are available, comparison of their spectroscopic properties with those of the model compounds should prove useful.

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References

1 J. M. Berg, *Science*, 1986, **232**, 485; J. Miller, A. D. McLachlan, and A. Klug, *EMBO J.*, 1985, **4**, 1609; L. Fairall, D. Rhodes, and A. Klug, *J. Mol. Biol.*, 1986, **192**, 577; G. P. Diakun, L. Fairall, and A. Klug, *Nature*, 1986, **324**, 698.

2 D. Swenson, N. C. Baenziger, and D. Coucouvanis, *J. Am. Chem. Soc.*, 1978, **100**, 1932; K. S. Hagen and R. H. Holm, *Inorg. Chem.*, 1983, **22**, 3171; A. D. Watson, Ch. Pulla Rao, J. R. Dorfman, and R. H. Holm, *Inorg. Chem.*, 1985, **24**, 2820.

3 H. Eklund, J.-P. Samama, and L. Wallén, *Biochemistry*, 1982, **21**, 4858.

4 A. B. P. Lever, 'Inorganic Electronic Spectroscopy,' Elsevier, Amsterdam, 1984, pp. 480—505.