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Mononuclear and dinuclear model hydrolases of nickel and cobalt

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Abstract

Reaction between the dinuclear model hydrolases $[M_2(\mu-OAc)_2(OAc)_2(\mu+H_2O)(tmen)_2]$; M = Ni (1); M = Co (2) and trimethylsilyltrifluoromethanesulphonate (TMS-OTf) under identical reaction conditions gives the mononuclear complex $[Ni(OAc) (H_2O)_2(tmen)][OTf] \cdot H_2O$ (3) in the case of nickel and the dinuclear complex $[Co_2(\mu-OAc)_2(\mu+H_2O)_2(tmen)_2][OTf]_2$ (4) in the case of cobalt.

Reaction of (3) with urea gives the previously reported $[Ni(OAc)(urea)_2(tmen)][OTf]$ (5), whereas (4) gives $[Co_2(OAc)_3(urea)(tmen)_2][OTf]$ (6) previously obtained by direct reaction of (2) with urea. Both (3) and (4) react with monohydroxamic acids (RHA) to give the dihydroxamate bridged dinuclear complexes $[M_2(\mu-OAc)(\mu-RA)_2(tmen)_2][OTf]$; M = Ni (7); M = Co (8) previously obtained by the reaction of (1) and (2) with RHA, illustrating the greater ability of hydroxamic acids to stabilize dinuclear complexes over that of urea by means of their bridging mode, and offering a possible explanation for the inhibiting effect of hydroxamic acids by means of their displacing bridging urea in a possible intermediate invoked in the action of urease. © 2005 Elsevier B.V. All rights reserved.

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1. Introduction

Dinuclear metallohydrolases are an important group of metalloenzymes, which catalyse the hydrolysis of a range of peptide and phosphate ester bonds and include the amidohydrolases, amidinohydrolases and peptide hydrolases [1]. A common structural feature of these metallohydrolases is a dinuclear metal active site featuring Zn(II), Ni(II), Co(II) and Mn(II) and carboxylate bridges which occur, respectively, in leucine aminopeptidase (LAP) [2], urease [3], methionine aminopeptidase (MAP) [4] and arginase [5].

The inhibition of metalloenzymes by hydroxamic acids is important because of therapeutic applications. Generally, the inhibition involves chelation of a mononuclear zinc centre by the hydroxamate function (RCONR'OH) [6] but in the case of urease the structure of the acetohydroxamate-inhibited Cys³¹⁹Ala variant of KAU shows the deprotonated hydroxyl oxygen of the hydroxamic acid bridging the two nickel centres with the carbonyl oxygen bridging one nickel centre only [7]. This unusual mode of bonding by a hydroxamate bridging two metal centres was modelled first in the

Abbreviations: OAc, CH_3COO^- ; tmen, N,N,N',N'-tetramethylethylenediamine; OTf (triflate), $CF_3SO_3^-$; AHA, acetohydroxamic acid; AA, acetohydroxamate anion; BHA, benzohydroxamic acid; BA, benzohydroxamate anion; NPhAHA, *N*-phenylacetohydroxamic acid; NPhAA, *N*-phenylacetohydroxamate anion.

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complex [Ni₂(H₂shi)(Hshi)(pyr)₄(OAc)], where Hshi is deprotonated salicylhydroxamic acid, prepared by selfassembly [8]. Subsequently, it was shown that the structural model hydrolases [M₂(μ -OAc)₂(OAc)₂(H₂O) (tmen)₂] (M = Mn, Co, Ni) react rapidly with a range of hydroxamic acids (e.g., AHA) to give hydroxamatebridged dinuclear complexes such as [M₂(μ -OAc) (μ -AA)₂(tmen)₂] [OTf] [9], in which the hydroxamate hydroxyl is deprotonated and the oxygen then bridges the two metal centres whilst the carbonyl oxygen bonds to one metal centre only, thereby modelling the structure observed in the acetohydroxamate-inhibited Cys³¹⁹Ala variant of KAU [7].

In this paper, we report the synthesis and structural characterization of two new hydrolase model complexes:

 $[Ni(OAc)(H_2O)_2(tmen)][OTf] \cdot H_2O$ (3) and $[Co_2(\mu - OAc)_2(\mu - H_2O)_2(tmen)_2][OTf]_2$ (4) and their reactions with urea and selected monohydroxamic acids (RHA: R = Me and Ph).

2. Results and discussion

2.1. Nickel complexes

The mononuclear nickel complex (3) is formed on treatment of the dinuclear complex $[Ni_2(\mu-OAc)_2 (OAc)_2(H_2O)(tmen)_2]$ (1) with trimethylsilyltrifluoromethanesulphonate (TMS-OTf) in dichloromethane when a rapid change in colour from green to yellow–green occurs (Scheme 1).

Extraction in acetonitrile and diffusion of diethylether gave crystals suitable for X-ray crystallography



 $\mathbf{R} = \mathbf{M}\mathbf{e} \text{ or } \mathbf{P}\mathbf{h}; \mathbf{R}' = \mathbf{H} \text{ or } \mathbf{P}\mathbf{h}$

further characterized by microanalysis, infrared and UV/vis spectra (Supplementary Material I).

2.2. Crystal structure of $[Ni(OAc)(H_2O)_2(tmen)][OTf]$ · $H_2O(3)$

Crystals suitable for X-ray analysis were obtained directly from the above preparative methods. Data were collected using a Siemens SMART CCD area-detector diffractometer. A full hemisphere of reciprocal space was scanned by a combination of three sets of exposures; each set has a different ϕ angle for the crystal and each exposure of 10 s covered 0.3° in ω . The crystal to detector distance was 5.01 cm. Crystal decay was monitored by repeating the initial frames at the end of the data collection and analysing the duplicate reflection; a multiscan absorption correction was applied using SADABS [10]. The structures were solved by direct methods using SHELXTL-PC [11] and refined by full-matrix least-squares on F^2 for all data using SHELXTL 97. The water protons were located in the difference fourier map and their positional parameters were allowed to refine freely. Their isotropic temperature factors were fixed at 150% of the equivalent temperature factor of the oxygen atom to which they are attached. All other hydrogens were added at calculated positions and refined using a riding model [12]. The temperature factors were fixed at 120% (150% for methyl hydrogens) of the equivalent temperature factor of the atom to which the hydrogen is attached. Anisotropic temperature factors were used for all non-H atoms.

The structure of (3) shown in Fig. 1 confirms that (3) is a mononuclear nickel (II) complex in which the nickel (II) atom is surrounded by an N_2O_4 core consisting of one chelating acetate, two cis water ligands and one tmen ligand. Crystallographic data and selected bond lengths and angles are given in Table 1 and Fig. 1, respectively. Lattice water is hydrogen bonded as shown also in Fig. 1.

2.3. Spectroscopic studies of $[Ni(OAc)(H_2O)_2(tmen)]$ $[OTf] \cdot H_2O(3)$

2.3.1. UV/visible spectrum

The electronic spectrum of (3), measured in methanol, is typical of a distorted octahedral environment about a Ni(II) centre with three bands at (1079, 653, 391) nm being assigned to the three spin-allowed transitions ${}^{3}A_{2g}(F) \rightarrow {}^{3}T_{2g}(F)$, ${}^{3}A_{2g}(F) \rightarrow {}^{3}T_{1g}(F)$, ${}^{3}A_{2g}(F) \rightarrow {}^{3}T_{2g}(P)$ for an octahedral d⁸ ion.

2.3.2. Infrared spectra

The infrared spectrum of (3) in KBr, dichloromethane and methanol showed a peak in the region $1540-1553 \text{ cm}^{-1}$ indicating partial dissociation of the bidentate acetate.



Fig. 1. The molecular structure of $[Ni(OAc)(H_2O)_2(tmen)][OTf] \cdot H_2O$ (3). Selected bond lengths (Å) and angles (°): Ni–O3, 2.063(3); Ni1–N1, 2.099(4); Ni1–O1, 2.120(3); Ni–O4, 2.079; Ni1–O2, 2.116(3); Ni1–N2, 2.128(4); O3–Ni1–O4, 89.54(14); O4–Ni1–N1, 90.95(16); O4–Ni1–N2, 175.97(15); O4–Ni1–O2, 90.77(15); O4–Ni1–O1, 86.48(14); N1–Ni1–N2, 85.34(16); O3–Ni1–N2, 89.38(15); O3–Ni1–N1, 97.78(15); O2–Ni1–O1, 61.66(13).

2.4. Reactions of (3) with urea and monohydroxamic acids

2.4.1. Urea reactions

Complex (3) reacts readily with urea in methanol followed by removal of solvent and recrystallization from acetone to give $[Ni(OAc)(urea)_2(tmen)][OTf]$ (5) (Scheme 1) previously reported by the direct reaction of the dinuclear (1) with urea in addition to the dinuclear $[Ni_2(\mu-OAc)_3(urea)(tmen)_2][OTf]$, [13]. Satisfactory microanalysis was obtained for (5).

2.5. Reactions of (3) with monohydroxamic acids

Treatment of complex (3) with acetohydroxamic acid, AHA, in methanol at room temperature gave rapid formation of the dihydroxamate bridged dinuclear complex $[Ni_2(\mu-OAc)(\mu-AA)_2(tmen)_2][OTf]$ (7a) (Scheme 1) previously obtained by direct reaction of the dinuclear model hydrolase $[Ni_2(\mu-OAc)_2(OAc)_2(H_2O)(tmen)_2]$ (1) with AHA [9]. Similar products, $[Ni_2(\mu-OAc)(\mu-BA)_2$ $(tmen)_2][OTf]$ (7b) and $[Ni_2(\mu-OAc)(\mu-NPhA)_2(tmen)_2]$ [OTf] (7c) were obtained by analogous reactions of complex (3) with benzohydroxamic acid (BHA) and *N*-phenylacetohydroxamic acid (NPhAHA). In all cases, satisfactory microanalysis was obtained for (7a)–(7c)

Table 1 Crystal data and structure refinement for (3) and (4)

	(3)	(4)
Empirical formula	$C_9H_{25}F_3N_2O_8SNi$	$C_{18}H_{42}N_4O_{12}F_6S_2Co_2$
Formula weight	437.08	802.54
Crystal system	triclinic	monoclinic
Space group	$P\bar{1}$ (#2)	<i>C</i> 2/ <i>m</i> (#12)
a (Å)	9.2378(5)	19.388(2)
b (Å)	10.5436(9)	8.9782(10)
c (Å)	10.6841(9)	10.0216(11)
α (°)	84.622(3)	90
β (°)	64.631(3)	102.123(2)
γ (°)	88.780(4)	90
$V(A^{3})$	935.93(12)	1705.6(3)
$T(\mathbf{K})$	180(2)	293(2)
Z	2	2
$\rho_{\rm calc} ({\rm Mg/m^3})$	1.551	1.563
Crystal size (mm ³)	$0.26 \times 0.12 \times 0.10$	$0.95 \times 0.40 \times 0.15$
$\mu (\mathrm{mm}^{-1})$	1.213	1.184
hkl ranges	-8,11; -12,10; -12,12	-25,25; -11,11; -12,13
Reflections collected	4909	7265
Independent reflections	$3395 [R_{int} = 0.0291]$	$2115 [R_{int} = 0.0231]$
Max. and min. transmission	0.8883 and 0.7434	0.8424 and 0.3993
$R(F)[I > 2\sigma(I)] \ (\%)$	6.18	4.71
$R_w(F^2)$ (all data) (%)	17.4	13.27
Goodness-of-fit on F^2	1.066	1.053
Largest peak and hole (e/Å ³)	1.423 and -0.784	0.861 and -0.385
M–M distance (Å)		3.130(3)

 $[Ni(OAc)(H_2O)_2(tmen)][OTf] \cdot H_2O (3); [Co_2(\mu-OAc)_2(\mu-H_2O)_2(tmen)_2][OTf]_2 (4).$

and infrared and UV/vis spectra were in good agreement with previously reported data [9] (Supplementary Material II).

2.6. Cobalt complexes

In contrast to the isolation and characterization of the mononuclear nickel complex, $[Ni(OAc)(H_2O)_2]$ (tmen)[OTf]·H₂O (3) formed by the reaction of the dinuclear nickel complex $[Ni_2(\mu-OAc)_2(OAc)_2(H_2O)]$ $(tmen)_2$ (1) with TMS-OTf, reaction of the analogous cobalt complex $[Co_2(\mu-OAc)_2(OAc)_2(H_2O)(tmen)_2]$ (2) with TMS-OTf in methanol gave pink crystals of the dinuclear, diaqua bridged cobalt (II) complex, [Co2- $(\mu$ -OAc)₂ $(\mu$ -H₂O)₂ $(tmen)_2$ [OTf]₂ (4) (Scheme 2). Removal of solvent, extraction with acetonitrile and diffusion of diethylether gave crystals suitable for X-ray crystallography. Crystal data were collected using a Bruker SMART APEX CCD area detector diffractometer. A full sphere of the reciprocal space was scanned by ϕ - ω scans. Semi-empirical absorption correction based on redundant reflections was performed by the program SADABS [10]. The structure was solved by direct methods using shelxs-97 [14] and refined by full-matrix leastsquares on F^2 for all data using SHELXTL-97 [12]. Disordered hydrogens were added at calculated positions and refined using a riding model. Their isotropic temperature factors were fixed to 1.2 (1.5 for methyl hydrogens) times the equivalent isotropic displacement parameters of the carbon atom the H-atom is attached to. The water proton was located in the difference fourier map and allowed to refine freely with an isotropic temperature factor. Anisotropic temperature factors were used for all non-hydrogen atoms. Satisfactory microanalysis was also obtained.





The structure of the dicobalt model hydrolase (4) is shown in Fig. 2 together with selected bond lengths and angles confirming formation of a dinuclear cobalt complex with two bridging water molecules, two bridging acetates and two tmen capping ligands. Crystallographic data are given in Table 1. Comparison of the structures of the two dinuclear cobalt complexes (2) and (4) reveals that there is hydrogen bonding of the bridging water molecules with the monodentate carboxylate free oxygens in (2) and with an oxygen of the counter ion triflate in (4).

The respective H-bond distances are $O(9) \cdots O$ (free) of 2.557(4) Å in (2) and $O(1) \cdots O(OTf)$ of 2.711(3) Å in (4).

The Co–Co distance in (4) 3.130(3) Å compared with 3.597(1) Å in (2) is presumably due to the presence of an extra bridging water molecule in the former complex.

2.7. Spectroscopic studies of $[Co_2(\mu-OAc)_2(\mu-H_2O)_2(tmen)_2][OTf]_2$ (4)

2.7.1. UV/visible spectrum

The electronic spectrum of (4) in methanol is typical of a distorted octahedral Co(II) complex and very close to that of complex (2) with two broad bands at 519 and 1095 nm assigned to the spin-allowed transitions (Supplementary Material III).

2.7.2. Infrared spectrum

The infrared spectrum of $[Co_2(\mu-OAc)_2(\mu-H_2O)_2(t-men)_2][OTf]_2$ (4) in KBr showed a different pattern to that of (2) in the carboxylate region. Thus (4) and (2) showed carboxylate vibrations of $\nu(CO)$ at 1578 and 1630 cm⁻¹ assigned to bidentate bridging acetates and the carboxylate stretching vibration of acetate in (4) is lower than that in (2) because of the presence of the second aqua bridge and absence of the monodentate acetate in (4) (Supplementary Material III).

Depending upon the particular carboxylate ligand and metal ion in these dinuclear complexes, two broad bands, often accompanied by a shoulder, are observed in the region $2000-2400 \text{ cm}^{-1}$ assigned to the bridging water. This enormous lowering compared to free water is ascribed to very strong hydrogen-bond formation with the monodentate coordinating carboxylato group. Thus, the complexes (2) and (4) show weak broad peaks at (2024–2088), (2), in the presence of monodentate acetates and weak sharp peaks (1998–2070) cm⁻¹, (4), in the absence of monodentate acetates, assigned to the bridging water. These two water peaks are diagnostic in assigning (2) and (4) as dinuclear complexes.

In methanol (4) gives a single carboxylate peak at 1563 cm^{-1} assigned to the monodentate acetate group indicating dissociation of the dinuclear system.



Fig. 2. The molecular structure of [Co₂(μ-OAc)₂(μ-H₂O)₂(tmen)₂][OTf]₂ (**4**). Selected bond lengths (Å) and angles (°): Co–Co#2, 3.130(3); Co–O(3), 1.995(2); Co–O(2), 2.018(2); Co–N, 2.167(2); Co–N#1, 2.167(2); Co–O(1)#2, 2.281(19); Co–O(1), 2.281(19); O(1)–Co#2, 2.281(19); Co#2–O(1)–Co, 86.63(9); O(3)–Co–O(2), 154.16(10); O(3)–Co–N, 99.74(8); O(2)–Co–N, 99.42(8); N–Co–N#1, 83.77(13); O(3)–Co–O(1), 81.04(5); O(2)–Co–O(1), 81.31(5); N–Co–O(1), 91.43(8).

2.7.3. Reaction of (4) with urea

Reaction of (4) with urea in methanol occurred rapidly with formation of $[Co_2(\mu-OAc)_3(urea)(tmen)_2][OTf]$ (6) (Scheme 2). Removal of the solvent, extraction with acetone and vapour diffusion gave pink crystals of (6) suitable for X-ray crystallography. The structure thereby obtained was identical with that obtained previously as were microanalysis, IR and UV/vis spectra (Supplementary Material III). The product obtained from (4) is thus identical with that reported previously by the reaction of the dinuclear monobridged aqua complex (2) with urea [15].

2.8. Reactions of (4) with monohydroxamic acids

Treatment of (4) with AHA in methanol at room temperature gave rapid formation of the dihydroxamate

bridged dinuclear complex $[Co_2(\mu-OAc)(\mu-AA)_2(tmen)_2]$ [OTf] (**8a**) (Scheme 2) previously obtained upon treatment of the dinuclear model hydrolase $[Co_2(\mu-OA-c)_2(OAc)_2(H_2O)(tmen)_2]$ (**2**) with AHA [15]. A similar product $[Co_2(\mu-OAc)(\mu-BA)_2(tmen)_2]$ [OTf] (**8b**) was obtained by analogous reaction of complex **4** with BHA. In all cases satisfactory microanalyses were obtained for complexes (**8a**) and (**8b**).

Infrared and UV/vis spectra were in good agreement with previously reported data [15] (Supplementary Material IV).

3. Conclusions

The dinuclear model hydrolases, $[M_2(\mu-OAc)_2(OAc)_2(H_2O)(tmen)_2]$, M = Co (2); Ni (1) react under identical

conditions with TMS triflate to give in one case the mononuclear nickel diaqua complex $[Ni(OAc)(H_2O)_2 (tmen)][OTf] \cdot H_2O$ (3) and in contrast in the second case the dinuclear diaqua complex $[Co_2(\mu-OAc)_2(\mu-H_2O)_2 (tmen)_2][OTf]_2$ (4).

Complex (3) reacts with urea to retain its monouclear structure and forms $[Ni(OAc)(urea)_2(tmen)][OTf]$ (5) whereas with monohydroxamic acids (e.g., AHA) it forms the dihydroxamate bridged dinuclear $[Ni_2$ $(\mu$ -OAc) $(\mu$ -AA)_2(tmen)_2][OTf], previously prepared by direct reaction of AHA and (1) [9], illustrating the greater ability of hydroxamic acids to stabilize dinuclear complexes over that of urea by means of their bridging bonding mode which leads to a possible explanation for the inhibiting effect of hydroxamic acids by means of displacing a bridging urea molecule in a possible intermediate invoked in the action of urease [16].

However, the dinuclear cobalt complex $[Co_2(\mu-OAc)_2(\mu-H_2O)_2(tmen)_2][OTf]_2$ (4) reacts with both urea and hydroxamic acids to form $[Co_2(\mu-OAc)_3(urea)(tmen)_2]$ [OTf] (6) and $[Co_2(\mu-OAc)(\mu-AA)_2(tmen)_2][OTf]$ (8a), respectively, both previously prepared by direct reaction of (2) with urea and hydroxamic acid [15].

Tables of electronic and infrared spectra are available in the Supplementary Material.

4. Experimental

4.1. Materials

Reagent and solvents were used as obtained from commercial sources, without further purification unless otherwise stated. Methanol, dichloromethane and diethylether were dried by standard procedures. Nickel (II) acetate tetrahydrate (98%) and urea (99.5%), N,N,N',N'-tetramethylethylenediamine (98%), TMS-OTf (99%) and hydroxylamine hydrochloride (99%) were purchased from Aldrich Chemical Co. Ltd., London.

4.2. Instrumentation

Elemental analyses were performed by the Micro Analytical Laboratory, Chemical Services Unit, University College Dublin. Infrared spectra were recorded in the solid state 1–2% KBr (potassium bromide) discs and solution in a calcium fluoride cell, path length 0.1 mm using a Perkin–Elmer FT-IR Paragon 1000 Spectrometer. UV/vis spectra were recorded on ATI Unicam UV/visible Spectrometer.

4.3. Preparation of $[Ni(OAc)(H_2O)_2(tmen)][OTf]$ · $H_2O(3)$

The reaction was carried out under oxygen-free dry nitrogen.

Complex $[Ni_2(OAc)_4(H_2O)(tmen)_2]$ (1) (1.818 g, 3.0 mmol) was reacted with 3 mmol of TMS-OTf (0.54 ml) in 15 ml of dichloromethane and stirred for 1 h. Removal of solvent gave an oil which was dissolved in acetonitrile. Vapour diffusion of diethylether into the solution resulted in a bluish/green crystals of $[Ni(OA-c)(H_2O)_2(tmen)][OTf] \cdot H_2O$ (3). Yield: 0.49 g (37%). *Anal.* Calc. for C₉H₂₅F₃N₂O₈SNi: C, 24.73; H, 5.76; N, 6.40. Found: C, 24.80; H, 5.71; N, 6.28%. FT-IR data (KBr, cm⁻¹) major peak 1540.

4.4. Preparation of $[Ni(OAc)(urea)_2(tmen)][OTf](5)$

The reaction was carried out under oxygen-free dry nitrogen.

0.437 g (1 mmol) of [Ni(OAc)(H₂O)₂(tmen)][OTf]·H₂O (3) was reacted with 0.376 g (1.5 mmol) of urea in 10 ml dried methanol. Filtration and removal of solvent gave a solid residue. Crystallization from acetone gave (5).

Anal. Calc. for $C_{11}H_{27}F_3N_6O_7SNi$: C, 26.3; H, 5.45; N, 16.80. Found: C, 26.5; H, 5.55; N, 16.90%. FT-IR data (KBr, cm⁻¹) major peaks 1548, 1675.

5. Preparation of hydroxamate dinuclear tmen complexes from the mononuclear [Ni(OAc)(H₂O)₂(tmen)][OTf]· H₂O (3)

5.1. Preparation of the dibridged acetohydroxamate dinickel complex [Ni₂(OAc)(AA)₂(tmen)₂][OTf] (7a)

Under nitrogen, 0.136 g (0.311 mmol) of compound [Ni(OAc)(H₂O)₂(tmen)][OTf]·H₂O (**3**) was dissolved in 3 ml of dry methanol. A solution of acetohydroxamic acid 0.023 g (0.311 mmol) in 2 ml of dried methanol was added and the mixture stirred for 30 min. After filtering, solvent was removed under vacuum to give an oil, which was dissolved in acetonitrile. Vapour diffusion of diethylether into the solution gave bluish/green crystals of (**7a**). Yield: 0.123 g (54.6%). *Anal.* Calc. for $C_{19}H_{43}F_3N_6O_9SNi_2$: C, 31.52; H, 6.26; N, 11.61. Found: C, 31.14; H, 6.09; N, 11.31%. FT-IR data (KBr, cm⁻¹) major peaks 1632, 1596.

5.2. Preparation of the dibridged benzohydroxamate dinickel complex $[Ni_2(OAc)(BA)_2(tmen)_2][OTf] \cdot H_2O(7b)$

Under nitrogen, 0.874 g (2 mmol) of compound [Ni $(OAc)(H_2O)_2(tmen)$][OTf]·H₂O (3) was dissolved in 15 ml of methanol. A solution of BHA 0.274 g (2 mmol) in 5 ml of methanol was added and the mixture stirred for 30 min. After filtering, solvent was removed under vacuum to give an oil, which was

dissolved in acetonitrile. Vapour diffusion of diethylether into the solution gave bluish/green crystals of (**7b**). Yield: 0.862 g (50.8%). *Anal.* Calc. for $C_{29}H_{49}$ - $F_3N_6O_{10}SNi_2$: C, 41.07; H, 5.82; N, 9.91. Found: C, 41.19; H, 5.56; N, 9.80%. FT-IR data (KBr, cm⁻¹) major peaks 1623, 1583.

5.3. Preparation of the dibridged N-phenylacetohydroxamate dinickel complex $[Ni_2(OAc)(NPhAA)_2(tmen)_2]$ $[OTf] \cdot 2H_2O(7c)$

Under nitrogen, 0.437 g (1 mmol) of compound $[Ni(OAc)(H_2O)_2(tmen)][OTf] \cdot H_2O$ (3) was dissolved in 5 ml of methanol. A solution of *N*-phenylacetohydroxamic acid 0.151 g (1 mmol) in 5 ml of methanol was added and the mixture stirred for 30 min. After filtering, solvent was removed under vacuum to give an oil, which was dissolved in acetonitrile. Vapour diffusion of diethylether into the solution gave bluish/green crystals of (7c). Yield: 0.463 g (41.5%). *Anal.* Calc. for C₃₁H₅₅-F₃N₆O₁₁SNi₂: C, 41.64; H, 5.97; N, 9.40. Found: C, 41.88; H, 6.10; N, 9.44%. FT-IR data (KBr, cm⁻¹) major peaks 1608, 1596.

5.4. Preparation of [*Co*₂(*OAc*)₂(*H*₂*O*)₂(*tmen*)₂][*OTf*]₂ (*4*)

The reaction was carried out under oxygen-free dry nitrogen.

Complex $[Co_2(OAc)_4(H_2O)(tmen)_2]$ (2) (3.02 g, 5.0 mmol) was reacted with 5 mmol of TMS-OTF (0.9 ml) in 20 ml of dichloromethane and stirred for 1 h. Removal of solvent gave an oil which was dissolved in acetonitrile. Vapour diffusion of diethylether into the solution resulted in pink crystals of $[Co_2(OAc)_2(H_2O)_2(tmen)_2][OTf]_2$ (4). Yield 1.9 g (47%). *Anal.* Calc. for $C_{18}H_{42}F_6N_4O_{12}S2Co_2$: C, 26.94; H, 5.28; N, 6.98. Found: C, 27.21; H, 5.29; N, 6.91%. FT-IR data (KBr, cm⁻¹) major peaks 1578, 1998–2070.

5.5. Preparation of $[Co_2(OAc)_3(urea)(tmen)_2][OTf]$ (6)

[Co₂(OAc)₂(H₂O)₂(tmen)₂][OTf]₂ (4) 2.314 g (2.22 mmol) was reacted with urea 0.199 g (3.33 mmol) in 10 ml dried methanol under nitrogen in 1:1.5 molar ratio. Removal of solvent gave a pink oil which upon extraction using *n*-pentane resulted in a pink powder which was dissolved in acetone. Vapour diffusion of petroleum spirit into the solution resulted in pink crystals of [Co₂(OAc)₃(urea)(tmen)₂][OTf] (6). Yield: 1.83 g (30%). *Anal.* Calc. for C₂₀H₄₅F₃N₆O₁₀SCo₂: C, 32.62; H, 6.16; N, 11.42. Found: C, 32.34; H, 6.06; N, 11.16%. FT-IR data (KBr, cm⁻¹) major peaks 1617, 1561, 1669.

6. Preparation of hydroxamate dinuclear tmen complexes from [Co₂(OAc)₂(H₂O)₂(tmen)₂][OTf]₂ (4)

6.1. Preparation of the dibridged acetohydroxamate dicobalt complex [Co₂(OAc)(AA)₂(tmen)₂][OTf] (8a)

Under nitrogen, 0.241 g (0.3 mmol) of compound $[Co_2(OAc)_2(H_2O)_2(tmen)_2][OTf]_2$ (4) was dissolved in 6 ml of methanol. A solution of acetohydroxamic acid 0.045 g (0.6 mmol) in 4 ml of methanol was added and the mixture stirred for 1 h. After filtering, solvent was removed under vacuum to give an oil, which was dissolved in acetonitrile. Vapour diffusion of diethylether into the solution gave pink crystals of (8a). Yield: 0.091 g (43%). *Anal.* Calc. for C₁₉H₄₃F₃N₆O₉SCo₂: C, 30.73; H, 6.38; N, 11.31. Found: C, 31.02; H, 5.81; N, 10.89%. FT-IR data (KBr, cm⁻¹) major peaks 1632, 1590.

6.2. Preparation of the dibridged benzohydroxamate dicobalt complex [Co₂(OAc)(BA)₂(tmen)₂][OTf]· 4H₂O (**8b**)

Under nitrogen, 0.351 g (0.437 mmol) of compound [Co₂(OAc)₂(H₂O)₂(tmen)₂][OTf]₂ (4) was dissolved in 10 ml of methanol. A solution of BHA 0.120 g (875 mmol) in 5 ml of methanol was added and the mixture stirred for 1 h. After filtering, solvent was removed under vacuum to give an oil, which was disacetonitrile. Vapour diffusion solved in of diethylether into the solution gave a pink solid of (8b). Yield: 0.181 g (46%). Anal. Calc. for $C_{29}H_{55}$ -F₃N₆O₁₃SCo₂: C, 38.59; H, 6.14; N, 9.31. Found: C, 38.82; H, 5.29; N, 8.75%. FT-IR data (KBr, cm⁻¹) major peaks 1614, 1581.

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Appendix A. Supplementary data

Crystallographic data for (3) and (4) have been deposited with the Cambridge Crystallographic Data Centre (12 Union Road, Cambridge CB2 1EZ, e-mail: deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk) as Supplementary Material, CCDC number 260975 for (3) and 260976 for (4). Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ica.2005.01.029.

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