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Synthesis and in vitro anti-microbial activity of manganese (II) complexes of 2,2-dimethylpentanedioic and 3,3-dimethylpentanedioic acid: X-ray crystal structure of $[Mn(3dmepda)(phen)_2] \cdot 7.5H_2O$ ($3dmepdaH_2$ = 3,3-dimethylpentanedioic acid and phen = 1,10-phenanthroline)

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Abstract

Reactions of 2,2-dimethylpentanedioic acid($2dmepdaH_2$) and 3,3-dimethylpentanedioic acid ($3dmepdaH_2$) with $Mn(CH_3COO)_2 \cdot 4H_2O$ yield the soluble complexes $[Mn(2dmepda)] \cdot 1.5H_2O$ (**1**) and $[Mn(3dmepda)] \cdot H_2O$ (**2**). Complex **1** reacts with ethanolic solutions of 2,2′-bipyridine or 1,10-phenanthroline to give $[Mn_2(2dmepda)_2(bipy)] \cdot H_2O$ (**3**) and [Mn(2dmepda)(phen)] (**4**), respectively. Similar reactions of **2** with these ligands generated $[Mn_2(3dmepda)_2(bipy)_3] \cdot 5H_2O$ (**5**) $[Mn(3dmepda)(phen)_2] \cdot 7.25H_2O$ (**6**). The molecular structure of **6** was determined by X-ray crystallography. The asymmetric unit contains two $[Mn(3dmepda)(phen)_2]$ units with 14.5 waters of crystallisation. The two manganese complexes are of very similar structure. In each case the manganese atom is ligated by four nitrogen atoms from two chelating phen molecules and two oxygen atoms, one from each of the carboxylates moieties of the $3dmepda^{2-}$ ligand. Thus, the two carboxylate functions of the two $3dmepda^{2-}$ dianionic ligands are essentially monodentate. The 2,2- and the 3,3-dimethylpentanedioate complexes, the metal free ligands and a number of simple manganese salts were each tested for their ability to inhibit the growth of *Candida albicans*. Only the "metal free" 1,10-phenanthroline and its 2,2- and the 3,3-dimethylpentanedioate complexes exhibit fungitoxic activity.

Keywords: Manganese(II) complexes; 2,2-Dimethylpentanedioic acid; 3,3-Dimethylpentanedioic acid; 2,2′-Bipyridine; 1,10-Phenanthroline; Crystal structure; Anti-*Candida* activity

1. Introduction

The state-of-the-art Azole and Polyene drugs currently used to treat candidosis and other fungal infections are often ineffective because of problems with resistance or toxicity and thus the search for alternative anti-fungal agents has gathered momentum [1]. Furthermore, pharmaceutical manufacturers are intensively seeking cheaper and more effective anti-fungal therapeutic agents. A number of publications has appeared in the literature highlighting the fungicidal activity of novel transition metal carboxylate complexes [2].

Recently, this group has shown that a range of cobalt, copper, manganese and silver complexes containing carboxylic acid and 1,10-phenanthroline ligands inhibit the growth of *Candida albicans* [3–9]. The in vitro anti-fungal activity of the metal complexes that we

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studied was comparable to that of of a number of the commercial Azole drugs. Furthermore, we have shown that by changing the structural nature of the phenanthroline molecules it is possible to generate complexes that are active at much lower concentrations [10]. Early studies on the 1,10-phenanthroline complexes have revealed that these compounds appear to have a different mode of action to the prescription Azole and Polyene drugs [11]. Compounds that kill fungal cells in a different biochemical way to these drugs may not have the same resistance and toxicity problems.

As part of our ongoing studies into the synthesis and biological activity of metal complexes of α,ω-dicarboxcylic acids we have generated a number of new manganese(II) derivatives of 2,2-dimethylpentanedioic acid and 3,3-dimethylpentanedioic acid. In addition the in vitro anti-*Candida* activities of the metal free ligands and the metal complexes are discussed.

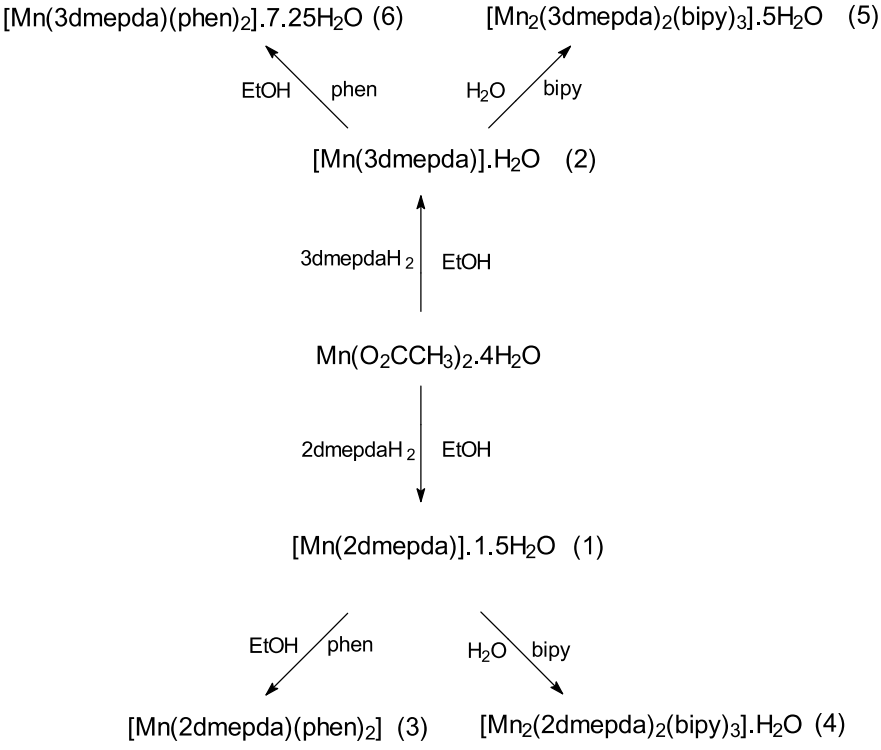
2. Results and discussion

Synthetic routes to the complexes **1–6** are shown in Scheme 1. Reaction of either 2,2-dimethylpentanedioic acid (2dmepdaH$_2$) or 3,3-dimethylpentanedioic acid (3dmepdaH$_2$) with manganese(II) acetate gave the complexes [Mn(2dmepda)]·1.5H$_2$O (**1**) and [Mn(3dmepda)]·H$_2$O (**2**), respectively. Reaction of **1** with either 2,2′-bipyridine or 1,10-phenanthroline resulted in the synthesis of [Mn$_2$(2dmepda)$_2$(bipy)]·H$_2$O (**3**) and [Mn(2dmepda)(phen)] (**4**). [Mn$_2$(3dmepda)$_2$ (bipy)$_3$]·5H$_2$O (**5**) and [Mn(3dmepda)(phen)$_2$]·7.25 H$_2$O (**6**) were obtained when **2** was treated similarly.

The X-ray crystal structure of [Mn(3dmepda)(phen)$_2$]·7.25H$_2$O **(6)** is shown in Figs. 1–3, and selected bond lengths and angles are listed in Table 1. The manganese atom is ligated by four nitrogen atoms [N(1A), N(2A), N(1B) and N(2B)] from two chelating phen molecules and two oxygen atoms [O(1) and O(3)], one from each of the carboxylates moieties of the 3dmepda^{2-} ligand (Fig. 1). Thus, the two carboxylate functions of the two 3dmepda^{2-} dianionic ligands are essentially monodentate with the two remaining carboxyl oxygens [O(2) and O(4)] uncoordinated. As a result of the bite of the phen ligands [N(2A)–Mn–N(1A) = 72.21(9)°, N(2B)–Mn–N(1B) = 72.90(9)°] the geometry of the complex is best described as irregular six-coordinate. The two manganese centres within the asymmetric unit (Fig. 2) differ in the conformation of the 3dmepda^{2-} dianion.

There is significant intermolecular association between the water solvate molecules, which are hydrogen-bonded to the uncoordinated carboxyl oxygens [O(2) and O(4)] of the 3dmepda^{2-} ligands (Table 2 and Fig. 3). Additionally, extensive π–π interactions involving all the phenanthroline groups are also present in the crystal structure.

The IR spectra of complexes (**1**)–(**6**) all contain prominent ν_{asym}(COO) stretching bands in the region 1560–1596 cm^{-1} and ν_{sym}(COO) stretching bands in the



Scheme 1.

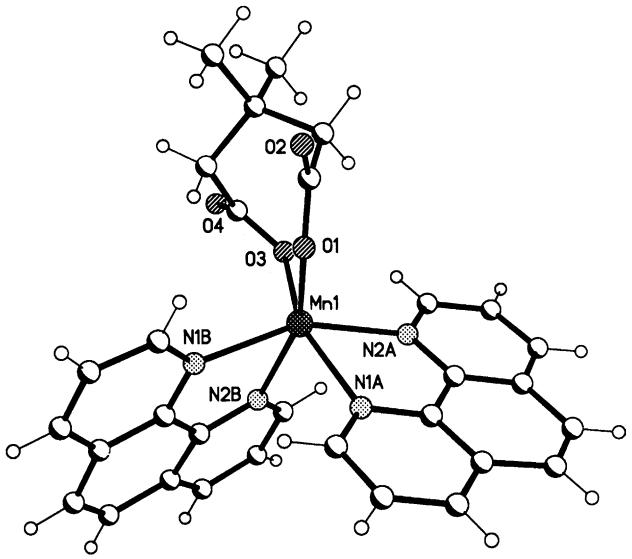


Fig. 1. The structure of one of the [Mn(3dmepda)(phen)$_2$] units in **6**.

region 1425–1385 cm^{-1} [$\Delta\nu$(COO) = 141–190 cm^{-1}]. The $\Delta\nu$(COO) values suggest that the coordination modes of the dicarboxylate ligands in these complexes may be similar [12].

The room temperature magnetic moments of powdered samples of complexes **1–6** (μ_{eff} = 5.6–6 BM) are consistent for manganese(II) complexes where there is no significant exchange interactions between adjacent metal centres [13]. Complexes **1–5** were found to be soluble in water suggesting that they are not polymeric. The molar conductivity values for aqueous solutions of complexes **1**, **2**, **4** and **6** {Λ_M = 87–143 S cm^2 mol^{-1}) suggest that these complexes probably form 1:1 electrolytes in water and may dissociate in accordance to the following equilibria:

$$[Mn(O_2C\text{–}R\text{–}CO_2)]\cdot nH_2O \overset{H_2O}{\rightleftharpoons} [Mn(H_2O)_n]^{2+} + (O_2C\text{–}R\text{–}CO_2)^{2-}$$

$$[Mn(O_2C\text{–}R\text{–}CO_2)](phen_m) \overset{H_2O}{\rightleftharpoons} [Mn(phen)_m]^{2+} + (O_2C\text{–}R\text{–}CO_2)^{2-}$$

The high molar conductivity values for complexes **3** and **5** {Λ_M = 198.16 and 355.29 S cm^2 mol^{-1}, respectively) suggest that they dissociate extensively in aqueous solution.

The complexes **1–6**, the metal free ligands and a number of simple manganese salts were each tested for their ability to inhibit the growth of *C. albicans* at a concentration of 10 μg cm^{-3} (Table 3). Both the 2,2- and the 3,3-dimethylpentanedioic acids, the simple manganese(II) salts, and the simple carboxylate complexes **1** and **2** are essentially devoid of anti-*Candida* activity. Both the uncoordinated 2,2′-bipyridine and its carboxylate derivatives (complexes **3** and **5**) are also ineffective against the pathogen. However the phenanthroline complexes **4** and **6** both exhibit discrete anti-Candida activity causing 68% and 70% inhibition of cell growth, respectively. Significantly the "metal free" 1,10-phenanthroline itself shows the greatest activity causing 89% inhibition of cell growth. However we believe that the so called metal free 1,10-phenanthroline is probably

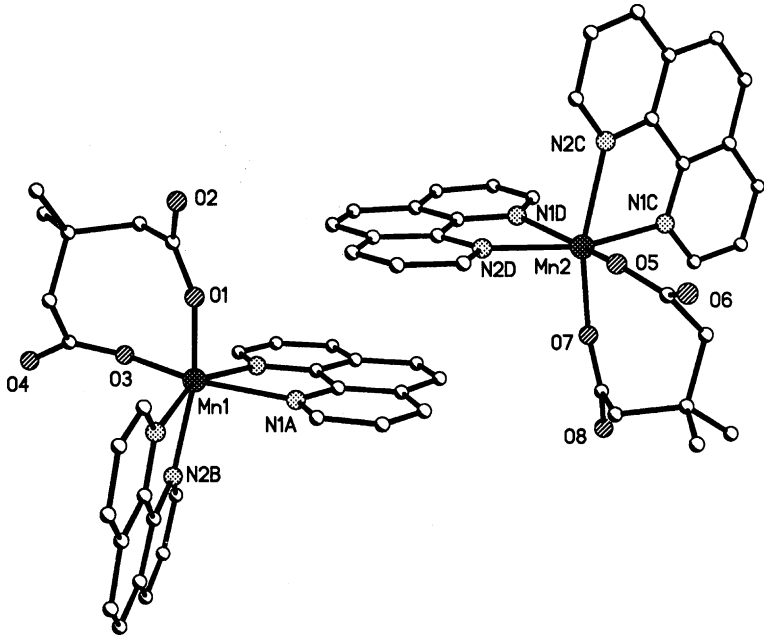


Fig. 2. Two independent [Mn(3dmepda)(phen)$_2$] units in **6** showing a π–π interaction between the phen groups.

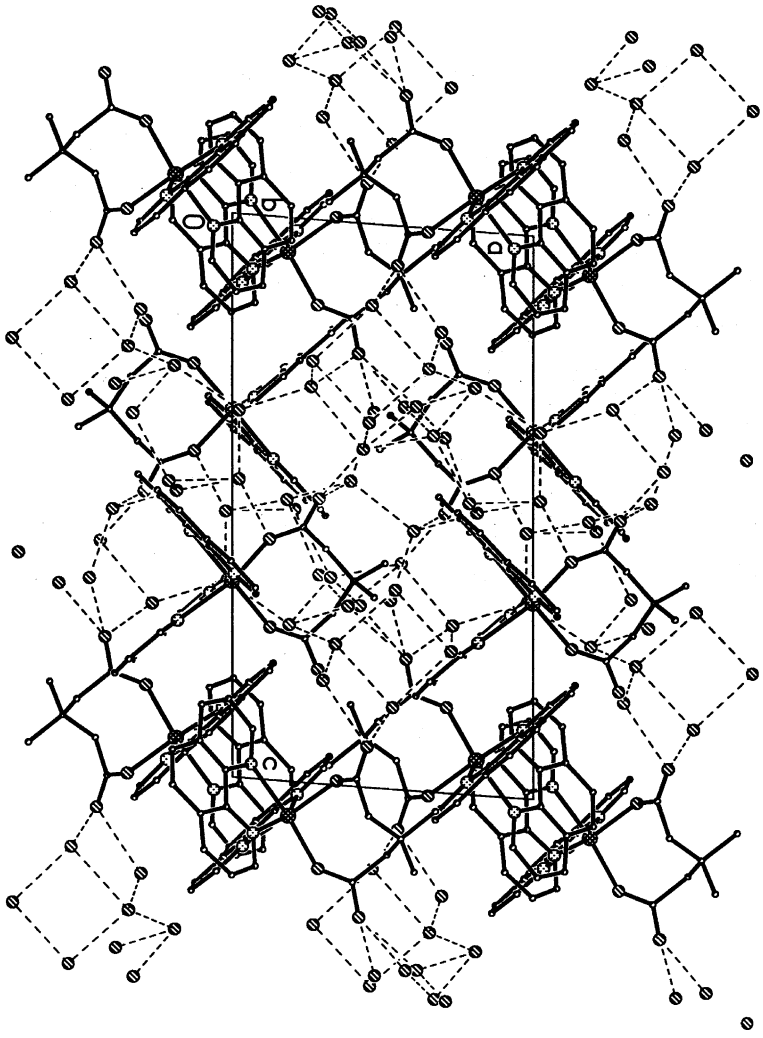


Fig. 3. The packing diagram for **6** viewed down the *b* axis, showing π–π stacking and hydrogen bonding.

coordinating to metal ions (other than the manganese) that are present in trace amounts in the growth medium and that it is these resulting metal–phenanthroline complexes that are responsible for the high anti-*Candida* activity. Studies are currently underway in our laboratories to examine this theory. The efficacy of complexes **4** and **6** are comparable to the azole drug ketoconazole at 10 μg cm^{-3} (Table 3) and as the concentration is lowered the anti-fungal activity decreases significantly.

In conclusion, it would appear that 2,2- and the 3,3-dimethylpentanedioic acids, whether coordinated or uncoordinated to manganese, do not possess any anti-*Candida* properties. Furthermore, the presence of the NN-donor 2,2′-bipyridine does not improve the activity of the complex. The 1,10-phenanthroline molecule is a potent anti-*Candida* agent and upon reaction with the manganese the 2,2- and the 3,3-dimethylpentanedioate complexes yields compounds with fungitoxic activity comparable to that of the state-of-the-art drug Ketoconazole.

3. Experimental

Chemicals were purchased from commercial sources and used without further purification. IR spectra were recorded as KBr discs in the region 4000–400 cm^{-1} on a Nicolet-400 Impact spectrometer. Magnetic susceptibility measurements were made using a Johnson Matthey Magnetic Susceptibility balance. $[HgCo(SCN)_4]$ was used as a reference. Conductivity readings were obtained using a Ciba Corning model check-mate 90 conductivity meter. Satisfactory microanalytical data for the complexes were reported by the Microanalytical Laboratory, University College Cork, Ireland.

*3.1. [Mn(2dmepda)]·1.5H_2O (**1**)*

To a solution of 2,2-dimethylpentanedioic acid {2dmepdaH_2} (1.05 g, 6.57 mmol) in ethanol (100 cm^3) was added manganese(II) acetate tetrahydrate (1.15 g, 4.28 mmol), and the mixture was refluxed for 2 h. The

Table 1
Selected bond lengths [Å] and angles [°] for **6**

Bond lengths			
Mn(1)–O(1)	2.091(2)	Mn(2)–O(5)	2.125(2)
Mn(1)–O(3)	2.108(2)	Mn(2)–N(2D)	2.281(3)
Mn(1)–N(2A)	2.262(3)	Mn(2)–N(2C)	2.293(3)
Mn(1)–N(2B)	2.265(3)	Mn(2)–N(1D)	2.302(2)
Mn(1)–N(1B)	2.265(3)	Mn(2)–N(1C)	2.312(3)
Mn(1)–N(1A)	2.329(3)	Mn(2)–O(7)	2.080(2)
Bond angles			
O(1)–Mn(1)–O(3)	95.98(9)	N(2B)–Mn(1)–N(1A)	96.18(9)
O(1)–Mn(1)–N(2A)	107.17(10)	N(1B)–Mn(1)–N(1A)	89.17(9)
O(3)–Mn(1)–N(2A)	86.85(9)	O(7)–Mn(2)–O(5)	99.97(9)
O(1)–Mn(1)–N(2B)	159.95(9)	O(7)–Mn(2)–N(2D)	101.23(9)
O(3)–Mn(1)–N(2B)	85.84(9)	O(5)–Mn(2)–N(2D)	86.73(9)
N(2A)–Mn(1)–N(2B)	92.86(9)	O(7)–Mn(2)–N(2C)	158.10(9)
O(1)–Mn(1)–N(1B)	87.94(9)	O(5)–Mn(2)–N(2C)	88.80(9)
O(3)–Mn(1)–N(1B)	111.25(9)	N(2D)–Mn(2)–N(2C)	99.26(9)
N(2A)–Mn(1)–N(1B)	155.44(9)	O(7)–Mn(2)–N(1D)	93.01(9)
N(2B)–Mn(1)–N(1B)	72.90(9)	O(5)–Mn(2)–N(1D)	157.30(9)
O(1)–Mn(1)–N(1A)	89.23(9)	N(2D)–Mn(2)–N(1D)	72.43(9)
O(3)–Mn(1)–N(1A)	159.02(9)	N(2C)–Mn(2)–N(1D)	85.85(9)
N(2A)–Mn(1)–N(1A)	72.21(9)	O(7)–Mn(2)–N(1C)	86.10(9)
O(5)–Mn(2)–N(1C)	108.49(9)		
N(2D)–Mn(2)–N(1C)	161.89(9)		
N(2C)–Mn(2)–N(1C)	72.07(9)		
N(1D)–Mn(2)–N(1C)	90.80(9)		

product formed as a colourless solid. The reaction mixture was allowed to cool to room temperature and then the product was filtered. The product was washed with two portions of ethanol and then dried in air. Yield: 0.63 g (39.93%). Complex **1** was soluble in H_2O, partially soluble in warm EtOH, and insoluble in MeOH, acetone, ether and chloroform. Found: C, 34.73; H, 5.45. Calc.: C, 35.01; H, 5.46. IR: 3382.09, 2979.10, 2925.37, 2871.64, 1561.94, 1474.63, 1414.18, 1300.00, 1138.81, 1051.49, 1031.34, 789.55, 668.66, 614.93 cm^{-1}. $\mu_{eff} = 5.99$ BM $\Lambda_M(H_2O) = 142.95$ S cm^2 mol^{-1}.

3.2. [Mn(3dmepda)]·H_2O (**2**)

To a solution of 3,3-dimethylpentanedioic acid 3dmepdaH_2 (2.00 g, 12.5 mmol) in ethanol (100 cm^3) was added manganese(II) acetate (3.03 g, 12.5 mmol), and the mixture was refluxed for 2 h. The product formed as a colourless solid. The mixture was allowed to cool to room temperature and then the product was filtered. The product was washed with two portions of ethanol and allowed to dry in air. Yield: 2.35 g (93.36%). Complex **2** was soluble in H_2O, partially soluble in warm EtOH and insoluble in MeOH, acetone, ether and chloroform. Found: C, 36.55; H, 5.15. Calc.: C, 36.38; H, 5.23. IR: 3402.24, 2972.39, 1561.94, 1454.48, 1407.46, 1313.43, 1252.99, 1145.52, 1118.66, 1038.06, 1011.19, 769.40, 735.82, 668.66 cm^{-1}. $\mu_{eff} = 5.88$ BM $\Lambda_M(H_2O) = 127.64$ S cm^2 mol^{-1}.

3.3. [Mn_2(2dmepda)$_2$(bipy)]·H_2O (**3**)

To a solution of [Mn(2dmepda)]·1.5H_2O **(1)** (1.00 g, 4.16 mmol) in ethanol (100 cm^3) was added 2,2′-bipyridine (2.04 g, 13.06 mmol), and the mixture was refluxed for 3.5 h. The product formed as a yellow solid that was then filtered and dried in air. Yield: 0.96 g (37.01%). Complex **3** was soluble in H_2O and partially soluble in warm EtOH and ether, and insoluble in MeOH, acetone and chloroform. Found: C, 48.14; H, 4.79; N, 5.3. Calc.: C, 48.01; H, 5.03; N, 4.66. IR: 3422.39, 3106.72, 3066.42, 2992.54, 2952.24, 2905.22, 1582.09, 1474.63, 1441.04, 1407.46, 1373.88, 1340.30, 1259.70, 1158.96, 1064.93, 1017.91, 823.13, 769.40, 735.82, 655.22, 628.36 cm^{-1}. $\mu_{eff} = 5.65$ BM $\Lambda_M(H_2O) = 198.16$ S cm^2 mol^{-1}.

3.4. [Mn(2dmepda)(phen)] (**4**)

To a solution of [Mn(2dmepda)]·1.5H_2O **(1)** (0.40 g, 1.66 mmol) in ethanol (50 cm^3) was added 1,10-phenanthroline (0.62 g, 3.46 mmol), and the mixture refluxed for 2 h. The product formed as a yellow solid that was then filtered off and dried in air. Yield: 0.47 g (69.07%). Complex **4** was soluble in H_2O, partially soluble in warm EtOH, ether and chloroform and insoluble in MeOH and acetone. Found: C, 58.63; H, 4.60; N, 7.02. Calc.: C, 58.02; H, 4.61; N, 7.12. IR: 3406.96, 3066.42, 2972.39, 2952.24, 2918.66, 2864.93, 1601.70,

Table 2
Hydrogen bond lengths [Å] and angles [°] for **6**

D–H···A	*d*(D–H)	*d*(H···A)	*d*(D···A)	∠(DHA)
O(1W)–H(1WA)···O(8)#1	0.94	1.94	2.867(3)	169.9
O(1W)–H(1WB)···O(4)	0.89	1.92	2.803(3)	169.5
O(2W)–H(2WA)···O(4)	0.91	1.86	2.724(3)	158.5
O(2W)–H(2WB)···O(6W)	1.00	1.96	2.958(4)	175.7
O(3W)–H(3WA)···O(6)	0.93	1.79	2.707(3)	170.1
O(3W)–H(3WB)···O(15W)#2	0.85	1.91	2.700(6)	153.4
O(3W)–H(3WB)···O(12W)#2	0.85	2.00	2.845(6)	171.7
O(4W)–H(4WA)···O(3W)#3	0.90	1.94	2.841(4)	173.9
O(4W)–H(4WB)···O(5W)	0.92	2.02	2.885(4)	156.1
O(5W)–H(5WA)···O(7W)#3	0.93	1.98	2.877(4)	161.2
O(5W)–H(5WB)···O(2W)	0.95	1.85	2.791(4)	168.0
O(6W)–H(6WA)···O(4W)	0.94	1.84	2.768(4)	167.4
O(6W)–H(6WB)···O(1W)	0.99	1.82	2.785(4)	162.7
O(7W)–H(7WA)···O(3W)	1.08	1.78	2.810(4)	157.3
O(7W)–H(7WB)···O(2)#4	0.88	1.91	2.773(4)	168.2
O(8W)–H(8WA)···O(6W)#1	0.86	2.12	2.978(4)	178.4
O(8W)–H(8WB)···O(15W)#1	1.00	1.79	2.716(6)	152.4
O(8W)–H(8WB)···O(12W)#1	1.00	1.82	2.806(6)	165.8
O(9W)–H(9WA)···O(5)	0.87	2.01	2.879(3)	175.4
O(9W)–H(9WA)···O(6)	0.87	2.59	3.195(4)	128.0
O(9W)–H(9WB)···O(10W)#1	0.84	2.24	2.777(4)	121.6
O(11W)–H(1WE)···O(14W)	0.74	1.81	2.556(7)	177.5
O(11W)–H(1WE)···O(16W)	0.74	2.46	3.137(7)	151.2
O(10W)–H(1WC)···O(7W)#1	0.98	1.85	2.805(4)	162.5
O(10W)–H(1WD)···O(9W)#1	0.87	1.91	2.777(4)	178.0
O(11W)–H(1WF)···O(6)	0.99	1.87	2.826(4)	159.6
O(12W)·····O(13W)			2.698(7)	
O(12W)·····O(16W)#5			2.739(8)	
O(13W)·····O(2)#6			2.752(6)	
O(14W)·····O(9W)			2.925(7)	
O(14W)O·····(9W)#5			2.901(6)	
O(14W)·····O(18W)#5			2.834(8)	
O(15W)·····O(2)#6			2.914(6)	
O(15W)·····O(18W)			2.693(8)	
O(16W)·····O(18W)#5			2.802(9)	
O(17W)·····O(2)#6			2.776(7)	
O(17W)·····O(18W)			2.668(11)	

Symmetry transformations used to generate equivalent atoms: #1 $-x,-y,-z+1$; #2 $x-1,y,z$; #3 $x+1,y,z$; #4 $-x,-y,-z+2$; #5 $-x,1-y,1-z$; #6 $1-x,-y,2-z$.

Table 3
Anti-*Candida* (expressed as % growth of fungal cells)

Test compound	% Cell growth		
	10 μg cm^{-3}	5 μg cm^{-3}	2.5 μg cm^{-3}
Control	100	100	100
Ketoconazole	25 ± 3	26 ± 4	47 ± 10
[Mn(2dmepda) · 1.5H_2O] (**1**)	110 ± 13		
[[Mn(3dmpeda)] · H_2O (**2**)	112 ± 15		
[Mn_2(2dmpeda)$_2$(bipy)] · H_2O (**3**)	97 ± 7		
[Mn(2dmpeda)phen] (**4**)	32 ± 2	43 ± 12	60 ± 2
[Mn(3dmpeda)$_2$(bipy)$_3$] · 5H_2O (**5**)	95 ± 3		
[Mn(3dmpeda)(phen)$_2$] · 7.5H_2O (**6**)	30 ± 2	16 ± 2	72 ± 7
2dmpedaH_2	102 ± 3		
3dmpedaH_2	105 ± 10		
1,10 phen	11 ± 1	14 ± 2	22 ± 2
2,2 bipy	114 ± 6		
$MnCl_2$	110 ± 5		
$Mn(NO_3)_2$	118 ± 12		
$MnSO_4$	108 ± 9		

1534.52, 1474.63, 1420.32, 1360.45, 1300.00, 1232.84, 1138.16, 1104.57, 910.45, 856.01, 782.84, 728.37, 635.07 cm^{-1}. $\mu_{eff} = 5.97$ BM $\Lambda_M(H_2O) = 125.86$ S cm^2 mol^{-1}.

3.5. $[Mn_2(3dmepda)_2(bipy)_3] \cdot 5H_2O$ (5)

To a solution of Mn(3dmepda) · H_2O **(2)** (0.41 g, 1.77 mmol) in deionised water (50 cm^3) was added 2,2′-bipyridine (0.50 g, 3.20 mmol). The resulting green solution was left to stand for several days at room temperature to give yellow crystals. These were filtered, washed with deionised H_2O and dried in air. Yield: 0.13 g (7.63%). Complex **5** was soluble in H_2O, EtOH and MeOH and insoluble in acetone, ether and chloroform. Found: C, 53.34; H, 5.62; N, 9.18. Calc.: C, 53.66; H, 5.53; N, 8.53. IR: 3450.5, 3066.42, 2957.9, 2864.93, 1576.2, 1474.63, 1438.1, 1385.7, 1313.43, 1252.99, 1157.1, 1118.66, 1064.93, 957.46, 910.45, 774.7, 736.8, 648.51 cm^{-1}. $\mu_{eff} = 5.73$ BM $\Lambda_M(H_2O) = 355.29$ S cm^2 mol^{-1}.

3.6. $[Mn(3dmepda)(phen)_2] \cdot 7.25H_2O$ (6)

To a solution of [Mn(3dmepda)] · H_2O **(2)** (0.8 g, 3.46 mmol) in ethanol (100 cm^3) 1,10-phenanthroline (1.10 g, 6.92 mmol) was added, and the mixture was refluxed for 2 h. Upon standing for 1 week the solvent had evaporated leaving an impure looking product. The product was recrystallised from hot water to give yellow crystals plus a brown solution. The crystals were filtered off and dried at room temperature. Yield: 0.58 g (24.04%). Complex **6** was soluble in H_2O, EtOH, MeOH and acetone, and insoluble in ether and chloroform. Found: C, 53.37; H, 5.81; N, 8.09. Calc.: C, 53.22; H, 5.76; N, 8.01. IR: 3415.67, 3052.99, 2952.24, 2858.21, 1575.37, 1514.93, 1447.76, 1420.90, 1387.31, 1340.30, 1300.00, 1246.27, 1145.52, 1105.22, 850.00, 776.12, 729.10, 641.79 cm^{-1}. $\mu_{eff} = 6.03$ BM $\Lambda_M(H_2O) = 116.53$ S cm^2 mol^{-1}.

3.7. X-ray crystallography

Crystal data for [Mn(3dmepda)$(phen)_2$] · $7.25H_2O$ (**6**) are summarised in Table 4. The data set for the complex was collected on a Siemens P4 diffractometer, solved by direct methods and refined on F^2 using SHELXTL 97 [14] and SHELXTL [15]. All the non-hydrogen atoms were refined with anisotropic atomic displacement parameters. Eleven lattice water molecules were refined with full occupancy and a further seven refined with 50% occupancy.

Hydrogen atoms bound to carbon were inserted at calculated positions; hydrogen atoms of full-occupancy

Table 4
Summary of crystal data, data collection, structure solution and refinement details for **6**

Empirical formula	$C_{31}H_{40}MnN_4O_{11.25}$
Formula weight	703.61
Temperature (K)	153(2)
Wavelength (Å)	0.71073
Crystal system	triclinic
Space group	$P\bar{1}$
Unit cell dimensions	$a = 10.4292(16)$ (Å)
	$b = 16.794(2)$ (Å)
	$c = 19.893(4)$ (Å)
	$\alpha = 77.065(12)°$
	$\beta = 83.843(16)°$
	$\gamma = 81.133(9)°$
Volume	3345.5(9)
Z	4
Density (calculated) (Mg/m^3)	1.397
Absorption coefficient (mm^{-1})	0.460
$F(000)$	1476
Crystal size (mm)	$0.82 \times 0.78 \times 0.50$
θ range for data collection	2.11° to 25.00°
Index ranges	$0 < h < 12$, $-19 < k < 19$, $-23 < l < 23$
Reflections collected	12,448
Independent reflections	11,743 [$R_{int} = 0.0292$]
Completeness to $\theta = 25.00°$ (%)	99.5
Absorption correction	empirical
Max. and min. transmission	0.8007 and 0.7558
Refinement method	full-matrix least-squares on F^2
Data/restraints/parameters	11,743/0/883
Goodness-of-fit on F^2	1.012
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0482$, $wR_2 = 0.0974$
R indices (all data)	$R_1 = 0.0853$, $wR_2 = 0.1112$
Largest differential peak and hole (e $Å^{-3}$)	0.475 and −0.433

water molecules were located from difference maps and not further refined, those on 50% occupancy water molecules {O(12w)–O(18w)} were not included.

3.8. Anti-Candida testing

Candida albicans isolate was obtained commercially from Oxid Culti-loops (ATCC 10231). The isolate was stored on Sabouraud dextrose agar (SDA) plates at 4 °C. Culture conditions and measurement of drug minimum inhibitory concentrations (MICs) were as previously described [7].

4. Supplementary data

Crystallographic data have been deposited with the CCDC. 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.uk or www: http://www.ccdc.cam.ac.uk), quoting the deposition number CCDC206030.

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