DALTON
FULL PAPER

Synthesis of water soluble DTPA complexes with pendant uracil moieties capable of forming complementary hydrogen bonds

Alexandra S. Georgopoulou,[a] Stefan Ulvenlund,[b] D. Michael P. Mingos,*[a] Ian Baxter[a] and David J. Williams[a]

[a] *Dept. of Chemistry, Imperial College of Science, Technology and Medicine, London, UK SW7 2AY. E-mail: d.mingos@ic.ac.uk*
[b] *Dept. of Explorative Pharmaceutics, Astra Draco AB, PO Box 34, S-22100 Lund, Sweden*

Received 5th October 1998, Accepted 11th January 1999

Two new DTPA (diethylenetriaminepentaacetic acid) functionalised bis(amides) with pendant uracil moieties have been synthesised from the condensation reaction between DTPA bis(anhydride) and 5-aminouracil or 5,6-diaminouracil. These ligands are representative of an increasing number of ligands capable of forming triple hydrogen bonds with complementary organic bases. However, these ligands are unusual since they form water soluble complexes with a variety of metal ions. In this paper, the syntheses of the two DTPA-uracil ligands, seven metal complexes and the crystal structure of the bismuth complex of DTPA bis(4,5-diamino-6-hydroxy-2-mercaptopyrimidine) L^1 are reported. The most important feature of this solid state structure is that the two arms on which the uracil moieties are situated have a high degree of rotational freedom and this allows these groups to form multiple hydrogen bonds involving both uracil moieties on one side of the molecule.

Introduction

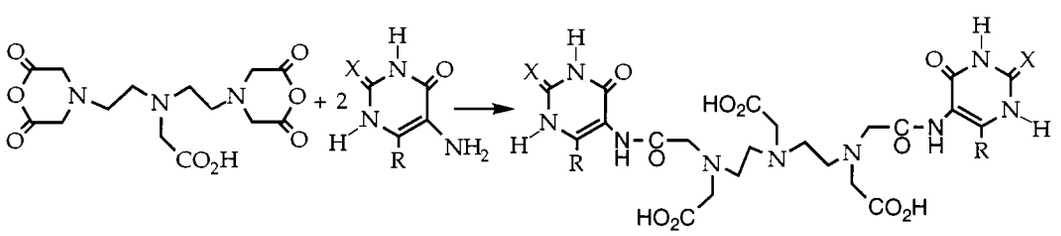
Metal complexes capable of forming complementary hydrogen bonds occupy an important position in the development of biochemically active molecules.[1] The complexes we have previously reported[2] are all either very sparingly soluble or insoluble in water, limiting their utility in biological systems. It was hoped that by functionalising DTPA with uracil based moieties the water solubilities of the complexes derived from the ligands could be improved. Polycarboxylate ligands based on DTPA have been widely used in co-ordination and analytical chemistry, as they are able to function in a polydentate fashion through both amino and carboxylate groups. Although considerable attention has been focused on the synthesis and structural studies of DTPA metal complexes, the synthesis of such complexes with ligands containing side groups capable of forming complementary hydrogen bonds has not been widely investigated. Konings and co-workers[3] have shown that the bis(anhydride) of DTPA reacts in dry DMF or DMSO to give the corresponding functionalised bis(amides) and we have extended this methodology to include EDTA analogues.[4] Previously similar ligands and metal complexes have been prepared by the condensation reaction of DTPA bis(anhydride) with isopropyl-, isobutyl-, benzyl- and phenylethyl-amine.[5,6] Derivatives with two lipophilic side-chains have been shown to have both diagnostic and therapeutic applications.[7] We herein report the synthesis of DTPA based uracil derivatives and their complexes with some s-, p-, d- and f-block metals.

Results and discussion

The bis(anhydride) of DTPA **1** reacts with 5-aminouracil derivatives in dry DMF or DMSO to give the corresponding functionalised bis(amides), as shown in Scheme 1. The 5-aminouracil derivatives were chosen since they have hydrogen bonding sites which are complementary to those found in DNA bases.

4,5-Diamino-6-hydroxy-2-mercaptopyrimidine (5,6-diamino-2-thiouracil) and 5-aminouracil were reacted with the DTPA bis(anhydride) in dry DMF at 40–45 °C for two hours.

The protonated bis(amides) H_3L^1 and H_3L^2 proved to be very soluble in water, DMF and DMSO but insoluble in all other common solvents and they are very hygroscopic when anhydrous. When exposed to moist air, the freshly precipitated anhydrous products transformed from off-white powders to brown gums. The fully hydrated, recrystallised products were however colourless or pale yellow powders.



1

R	X	
NH_2	S	H_3L^1
H	O	H_3L^2

Scheme 1

Due to their tendency to supersaturate in aqueous solutions the purification and isolation of the final products proved to be difficult. Recrystallisation from water was unsuccessful but was eventually achieved in water–acetone mixtures. Both hydrated ligands are stable towards hydrolysis and proved to have ill-defined melting points. At temperatures >170 °C the compounds started to transform to gums, which in appearance were similar to the partially hydrated products.

As expected, the complexing properties of the ligands were very similar to those of the parent DTPA carboxylate. Complexation reactions involving H_3L^1 and H_3L^2 were facile and resulted in a direct reaction between the protonated ligand and a stoichiometric amount of water-stable, basic metal compound. The neutral complexes of these ligands were water soluble and seemed to form hydrated powders rather than crystalline solids. A summary of the metal complexes synthesised is given in Table 1.

All the compounds were synthesised and recrystallised from water and consequently were isolated as hydrates. They were characterised using IR and NMR spectroscopy, mass spectrometry and elemental analyses.

As reported previously for the analogous H_4EDTA (ethylenediaminetetraacetic acid) ligands and complexes,[4] the ^{1}H NMR spectra of both the ligands and their metal complexes showed peaks between δ 2.6 and 3.6 which are characteristic for the $–CH_2–$ groups on the DTPA backbone and those observed between δ 6.6 and 12.1 are characteristic of the uracil protons. Accordingly, in the ^{13}C NMR spectra the peaks between δ 50 and 60 can be assigned to the C–C chain atoms whereas those between δ 100 and 180 to the uracil and carboxylate carbon atoms.

The infrared spectra of DTPA bis(amides) and their metal complexes have been studied extensively.[4] All these compounds exhibit three amide NH–CO bands at the following frequencies: 1686–1636 cm^{-1} (amide I), 1560–1450 cm^{-1} (amide II) and 1310–1240 cm^{-1} (amide III). Both the bis(amides) of DTPA and their metal complexes exhibit the characteristic N–H and C–H stretching bands at 3500–3100 cm^{-1} and 3100–2900 cm^{-1}, respectively. The strongest peaks in the IR spectra of these complexes are the (C=O) bands around 1700–1600 cm^{-1}. Those peaks can be assigned to the carboxylic acid, the uracil and the amide C=O's. Summaries of the infrared spectra of the ligands and their complexes are given in Tables 2 and 3, respectively.

Table 1 Summary of the metal complexes of L^1 and L^2

Complex	Starting materials	Colour
$Bi(L^1)(H_2O)\cdot 8.5H_2O$	$H_3L^1 + (BiO)_2CO_3$	Colourless
$Gd–L^1\cdot 12H_2O$	$H_3L^1 + Gd_2O_3$	Off-white
$Al–L^1\cdot 3H_2O$	$H_3L^1 + Al(CH_3CO_2)_2OH$	Pale yellow
$Cr–L^1\cdot 11H_2O$	$H_3L^1 + Cr_3(CH_3CO_2)_7(OH)_2$	Pale violet
$Fe–L^1\cdot 6H_2O$	$H_3L^1 + Fe(NO_3)_3\cdot 9H_2O$	Pale yellow
$Fe–L^2\cdot 8H_2O$	$H_3L^2 + Fe(NO_3)_3\cdot 9H_2O$	Off-white
$Al–L^2\cdot 5H_2O$	$H_3L^2 + Al(CH_3CO_2)_2OH$	Off-white

Table 2 Infrared spectra of H_3L^1 and H_3L^2

	H_3L^1	H_2L^2
ν(N–H)/cm^{-1}	3412, 3230	3436, 3224, 3095
ν(C–H)/cm^{-1}	2964, 2906	2996, 2921
ν(C=O)/cm^{-1} (uracil, acid, amide I)	1637, 1616	1681, 1662, 1622
amide II/cm^{-1}	1561	1554
ν(C–N)/cm^{-1}	1385	1357
amide III/cm^{-1}	1260	1240
ν(C–S)/cm^{-1}	1166	—

Crystal structure of $Bi(L^1)(H_2O)\cdot 8.5H_2O$

The X-ray structural analysis of the complex formed between bismuth and DTPA bis(thioaminouracil), L^1, (Fig. 1) shows L^1 to act as an octadentate chelating ligand. The relevant bond lengths derived from the crystallographic analysis are summarised in Table 4. The bismuth ion exhibits a comparatively rare nine co-ordinate geometry† and the ninth co-ordination site is occupied by an aqua ligand. The geometry at bismuth may be best described as monocapped-square antiprismatic with N(10) acting as the capping atom (Fig. 2). The Bi–O co-ordination distances are in the range 2.337 [O(25)] to 2.784 Å [O_{aqua}], whilst the Bi–N distances range between 2.440 [N(7)] and 2.617

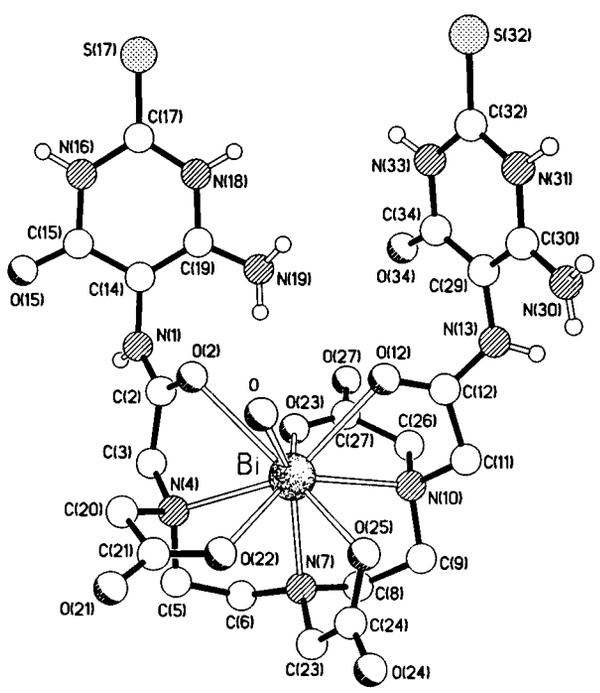


Fig. 1 The molecular structure of $Bi(L^1)(H_2O)\cdot 8.5H_2O$ showing the octadentate chelating mode of the ligand.

† In the Cambridge Crystallographic Database only 18 of the total 577 bismuth complexes exhibit nine co-ordination.

Table 3 Infrared spectra of the metal complexes of L^1 and L^2

	$Bi–L^1$	$Gd–L^1$	$Al–L^1$	$Cr–L^1$	$Fe–L^1$	$Fe–L^2$	$Al–L^2$
ν(N–H)/cm^{-1}	3546, 3471	3413, 3200	3428, 3259	3423, 3179	3434, 3249	3423, 3226	3438, 3257
ν(C–H)/cm^{-1}	2964, 2921	2900	2925	2923	2960, 2923	2966, 2923	2960, 2923
ν(C=O)/cm^{-1} (uracil, acid)	1633	1624, 1592	1641, 1565	1638	1637	1687, 1637, 1623	1658
amide II/cm^{-1}	1432	1437	1494	1463	1465	1465	1471
ν(C–N)/cm^{-1}	1384	1399	1384	1383	1382	1367	1382
amide III/cm^{-1}	1261	1260	1259	1256	1261	1263	1261
ν(C–S)/cm^{-1}	1170	1174	1170	1169	1095	—	—

Table 4 Selected bond lengths (Å) and angles (°) for $Bi(L^1)(H_2O)\cdot 8.5H_2O$

Bi–O	2.784(10)	Bi–O(2)	2.781(6)
Bi–N(4)	2.577(7)	Bi–N(7)	2.440(7)
Bi–N(10)	2.617(7)	Bi–O(12)	2.636(7)
Bi–O(22)	2.475(7)	Bi–O(23)	2.387(6)
Bi–O(25)	2.337(6)		
O–Bi–O(2)	71.7(3)	O–Bi–N(4)	101.8(3)
O–Bi–N(7)	140.5(3)	O–Bi–N(10)	126.3(3)
O–Bi–O(12)	67.0(3)	O–Bi–O(22)	63.8(3)
O–Bi–O(23)	131.2(3)	O–Bi–O(25)	82.5(3)
O(2)–Bi–N(4)	59.8(2)	O(2)–Bi–N(7)	128.3(2)
O(2)–Bi–N(10)	129.3(2)	O(2)–Bi–O(12)	91.0(2)
O(2)–Bi–O(22)	95.2(2)	O(2)–Bi–O(23)	67.8(2)
O(2)–Bi–O(25)	153.5(2)	N(4)–Bi–N(7)	72.2(2)
N(4)–Bi–N(10)	131.8(2)	N(4)–Bi–O(12)	150.8(2)
N(4)–Bi–O(22)	64.3(2)	N(4)–Bi–O(23)	80.2(3)
N(4)–Bi–O(25)	122.7(2)	N(7)–Bi–N(10)	71.4(2)
N(7)–Bi–O(12)	133.9(2)	N(7)–Bi–O(22)	79.4(3)
N(7)–Bi–O(23)	87.2(3)	N(7)–Bi–O(25)	70.1(2)
N(10)–Bi–O(12)	64.4(2)	N(10)–Bi–O(22)	135.5(2)
N(10)–Bi–O(23)	67.5(2)	N(10)–Bi–O(25)	71.2(2)
O(12)–Bi–O(22)	125.2(3)	O(12)–Bi–O(23)	87.5(3)
O(12)–Bi–O(25)	83.8(2)	O(22)–Bi–O(23)	144.4(2)
O(22)–Bi–O(25)	67.6(2)	O(23)–Bi–O(25)	137.5(2)

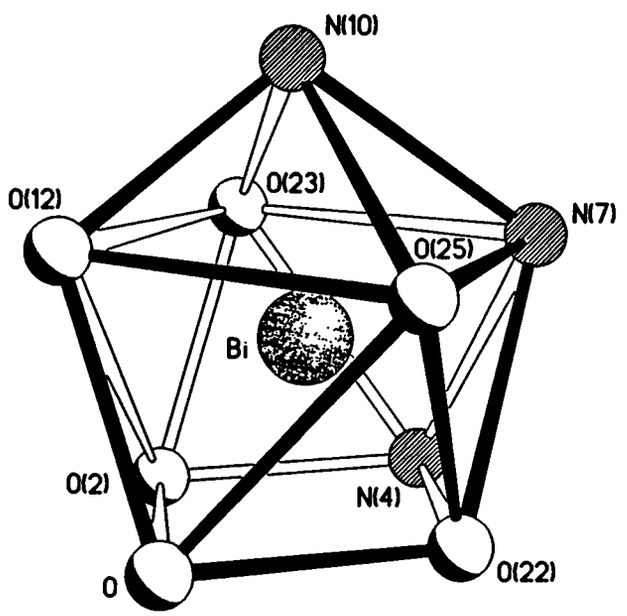


Fig. 2 The monocapped square antiprismatic geometry present in the structure of $Bi(L^1)(H_2O)\cdot 8.5H_2O$.

Å [N(10)]. The thioaminouracil ring systems are rotated by 60 [N(1)] and 65° [N(13)] out of the planes of their attached amide groups, and by 128° with respect to each other, the two C–S bonds being orientated approximately co-directionally. Despite what appears to be a favourable orientation of these two ring systems, there are no intramolecular hydrogen bonding interactions between them.

An inspection of the packing of the molecules reveals the formation of corrugated hydrogen bonded sheets of molecules (Fig. 3). A notable feature of this network is that there are only four unique N–H···O interactions—involving N(18), N(30), N(31) and N(33)—thus there is a marked redundancy in the utilisation of potential hydrogen bonding donors. The H atoms of the water molecules of crystallisation could not be reliably located so that potential hydrogen bonding interactions have not been analysed. However several of them do lie in the regions between the hydrogen bonded sheets and probably are involved in a cross-linking role.

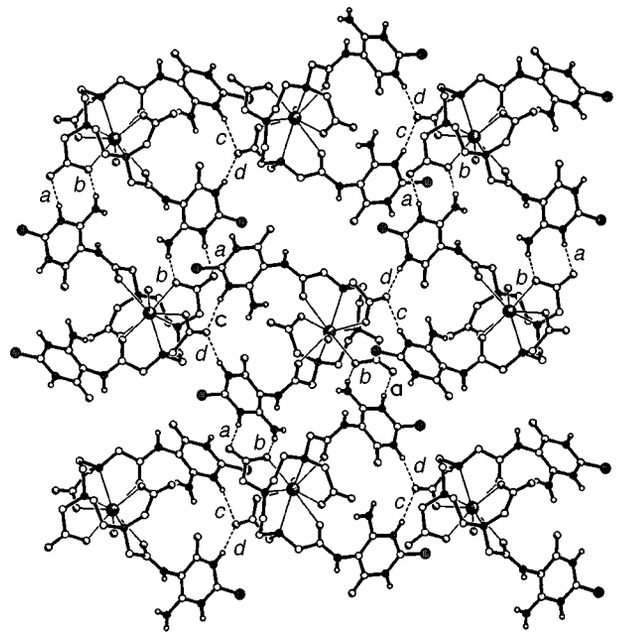


Fig. 3 Part of the corrugated hydrogen bonded sheets present in the structure of $Bi(L^1)(H_2O)\cdot 8.5H_2O$. Hydrogen bonding distances N···O, H···O (Å) and angles N–H···O (°); (*a*): 2.81, 1.92, 170; (*b*): 2.86, 1.98, 166; (*c*): 2.97, 2.10, 163; (*d*): 2.79, 1.90, 168 (all N–H distances have been normalised to 0.90 Å).

Experimental

Instrumentation

Infrared spectra were recorded on a Perkin Elmer FTIR 1720 spectrometer as KBr discs. NMR spectra were recorded on either a JEOL GS 270 MHz or a JEOL GS 500 MHz spectrometer. ^1H and ^{13}C NMR spectra were referenced internally to the residual ^1H impurity and ^{13}C present in the deuteriated solvent. Chemical shifts are reported in parts per million (δ) relative to $SiMe_4$ (δ 0). FAB(+) and FAB(−) mass spectra were recorded on a VG Autospec spectrometer using 3-nitrobenzyl alcohol for the sample matrix. The ionising radiation was a 35 keV Cs^+ primary ion beam.

Starting materials

DTPA bis(anhydride), 5-aminouracil, 5,6-diamino-2-thiouracil, $(BiO)_2CO_3$, Gd_2O_3, $(CH_3CO_2)_2AlOH$, $In(OH)_3$, $(CH_3CO_2)_7Cr_3(OH)_2$, $Fe(NO_3)_3\cdot 9H_2O$, KOH and NaOH were purchased from Aldrich Chemical Co. and were used as received.

DMSO and DMF were distilled from BaO *in vacuo* just prior to use.

Syntheses

DTPA bis(4,5-diamino-6-hydroxy-2-mercaptopyrimidine) hydrate, H_3L^1. 4,5-Diamino-6-hydroxy-2-mercaptopyrimidine (0.53 g, 3.35 mmol) was added to DTPA bis(anhydride) (0.60 g, 1.68 mmol) in DMF (20 ml, 99%). The reaction mixture was stirred at 40 °C for 2 hours, left to cool to room temperature and filtered through filter paper. The dark yellow filtrate was treated with $CHCl_3$ (150 ml, 99%) and a yellow precipitate obtained, which was filtered through a glass filter. The product was then dissolved in H_2O (15 ml) and the yellow solution produced was filtered through filter paper. The solution was heated to boiling and the volume reduced to 5 ml and then treated with acetone (200 ml). An off-white precipitate was produced which was isolated on a glass filter and dried *in vacuo* for 12 hours at 60 °C. (Yield 1.1 g, 50%.) (Found: C, 38.1; H, 4.4; N, 21.7; S, 9.2. Calc. for $C_{22}H_{31}N_{11}O_{10}S_2\cdot H_2O$: C, 38.2; H, 4.8; N, 22.3; S, 9.3%). IR (cm^{-1}): 3412(s), 3230(m), 2964(m), 2906(m), 1637(s),

1616(s), 1561(s), 1385(m), 1260(m), 1166(m). ^{1}H [d_6-DMSO, 270 MHz], δ 11.83 (2H, s, CSN*H*CO), 11.68 (2H, s, C(NH_2)-N*H*CS), 8.57 (2H, s, CH_2CONH), 6.55 (4H, s, NH_2), 3.69 (2H, s, central NCH_2CO_2H), 3.61 (4H, s, terminal NCH_2CO_2H), 3.45 (4H, s, CH_2CONH), 3.20 (4H, s, $NCH_2CH_2NCH_2CH_2N$), 3.02 (4H, s, $NCH_2CH_2NCH_2CH_2N$), 2.50 (s, DMSO). ^{13}C [d_6-DMSO, 500 MHz], δ 173.1 (terminal NCH_2CO_2H), 172.4 (central NCH_2CO_2H), 170.3 (CH_2CONH), 158.9 (uracil C4), 150.8 (uracil C2), 102.1 (uracil C6), 90.8 (uracil C5), 55.2 (CH_2CONH), 51.7 (terminal NCH_2CO_2H and central NCH_2CO_2H), 50.2 (NCH_2CH_2N), 39.8 (DMSO). Mass spectrum FAB(−): 672 {100%, $[L^1 - H]^-$}.

DTPA bis(5-aminouracil), H_3L^2. DTPA bis(anhydride) (0.70 g, 1.96 mmol) was added to 5-aminouracil (0.60 g, 4.72 mmol) in DMF (40 ml, 99%). The reaction mixture was stirred at 45 °C for 2 hours and the resulting light brown suspension was filtered through filter paper after cooling to room temperature. The filtrate was treated with $CHCl_3$ (150 ml, 99%) and the off-white precipitate obtained was isolated by filtration on a glass filter and redissolved in H_2O (15 ml). After stirring for 1 hour the cloudy yellow solution was filtered through filter paper and the product precipitated by addition of acetone (70 ml). The white solid obtained was collected on a glass filter and then recrystallised from boiling water–acetone (1 : 4 v/v) (*ca*. 25 ml). The white precipitate formed on cooling was filtered through a glass filter and dried *in vacuo* at 45 °C for 5 hours. (Yield: 0.46 g, 36.0%.) (Found: C, 40.3; H, 4.8; N, 18.8. Calc. for $L_2{\cdot}2.5H_2O$: C, 40.3; H, 5.2: N, 19.2%). IR (cm^{-1}): 3436(m), 3224(m), 3095(m), 3046(m), 2996(m), 2921(m), 1724(s), 1681(s), 1662(s), 1622(s), 1554(m), 1448(m), 1357(m), 1240(m). ^{1}H [d_6-DMSO, 270 MHz], δ 11.49 (2H, s, CON*H*CO), 10.64 (2H, d, $^2J_{H-H}$ 4.9 Hz, CHN*H*CO), 9.26 (2H, s, CH_2CONH), 8.08 (2H, d, $^2J_{H-H}$ 4.9 Hz, uracil C*H*), 3.41 (4H, s, CH_2CONH), 3.31 (6H, s, NCH_2CO_2H), 2.74 (4H, s, $NCH_2CH_2NCH_2CH_2N$), 2.72 (4H, s, $NCH_2CH_2NCH_2CH_2N$). ^{1}H [D_2O, 270 MHz, 20 °C], δ 7.95 (2H, s, uracil C*H*), 4.82 (s, H_2O), 3.83 (2H, s, central NCH_2CO_2H), 3.60 (4H, s, terminal NCH_2CO_2H), 3.46 (4H, t, $^2J_{H-H}$ 50 Hz, $NCH_2CH_2NCH_2CH_2N$), 3.37 (4H, s, CH_2CONH), 3.17 (4H, t, $^2J_{H-H}$ 50 Hz, $NCH_2CH_2NCH_2CH_2N$). ^{13}C [d_6-DMSO, 500 MHz], δ 172.2 (terminal NCH_2CO_2H), 171.7 (central NCH_2CO_2H), 169.3 (CH_2CONH), 160.3 (uracil C4), 149.4 (uracil C2), 127.6 (uracil C6), 112.9 (uracil C5), 58.2 (CH_2CONH), 55.1 (terminal NCH_2CO_2H), 54.7 (central NCH_2CO_2H), 52.1 ($NCH_2CH_2NCH_2CH_2N$), 52.0 ($NCH_2CH_2NCH_2CH_2N$), 39.8 (q, DMSO). Mass spectrum (Electrospray +): 612 {100%, $[L^2 + H]^+$}.

Bi(L^1)(H_2O)·8.5H_2O. $(BiO)_2CO_3$ (0.08 g, 0.15 mmol) was added to a solution of H_3L^1 (0.20 g, 0.30 mmol) in H_2O (20 ml). The reaction mixture was stirred at reflux for 2.5 hours after which time a yellow solution was obtained and filtered. The solution was cooled to 0 °C and the yellow precipitate obtained filtered off through a glass filter and dried. The yellow solid was redissolved in boiling water and placed in a covered Dewar flask containing boiling water and left to cool slowly. Colourless crystals were obtained after a period of four days. (Yield: 0.07 g, 53.1%.) (Found: C, 25.3; H, 4.7; N, 14.8. Calc. for $C_{22}H_{28}N_{11}O_{10}S_2Bi{\cdot}9.5H_2O$: C, 25.2; H, 4.5; N, 14.7%). IR (cm^{-1}): 3546(w), 3471(s), 3415(s), 2964(m), 2921(w), 1633(s), 1432(w), 1384(w), 1261(m), 1170(m). ^{1}H [d_6-DMSO, 270 MHz], δ 12.0 [m, CSN*H*CO and C(NH_2)N*H*CS], 9.4 (s, CH_2CONH), 8.9 (s, CH_2CONH), 6.6 (m, NH_2), 3.5 (m, central NCH_2CO_2H, terminal NCH_2CO_2H, CH_2CONH, $NCH_2CH_2NCH_2CH_2N$, $NCH_2CH_2NCH_2CH_2N$), 2.5 (s, DMSO). Mass spectrum FAB(−): 672 {12%, $[L^1 - H]^-$}, 878 {55%, $[(Bi–L^1) - H]^-$}.

Gd–L^1·12H_2O. Gd_2O_3 (0.04 g, 0.1 mmol) was added to a solution of ligand H_3L^1 (0.13 g, 0.2 mmol) in H_2O (20 ml). The reaction mixture was stirred at reflux for 2.5 hours affording a yellow solution which was filtered. The clear solution was heated to boiling and the volume reduced to 5 ml. It was then left to cool to 0 °C producing an off-white precipitate which was isolated by filtration on a glass filter, washed with acetone and dried *in vacuo*. (Yield: 0.074 g, 89.4%.) (Found: C, 25.4; H, 4.9; N, 14.5; S, 5.8. Calc. for $C_{22}H_{28}N_{11}O_{10}S_2Gd{\cdot}12H_2O$: C, 25.3; H, 5.0; N, 14.7; S, 6.1%). IR (cm^{-1}): 3413(s), 3200(s), 2900(m), 1637(s), 1624(s), 1592(s), 1561(s), 1437(m), 1399(m), 1326(m), 1260(m), 1174(m). Mass spectrum FAB(−): 827 {60%, $[(Gd–L^1) - H]^-$}.

Al–L^1·3H_2O. $Al(CH_3CO_2)_2(OH)$ (0.2 g, 0.13 mmol) was added to a solution of ligand H_3L^1 (0.09 g, 0.13 mmol) in H_2O (15 ml). The reaction mixture was stirred at reflux for 2.5 hours and the yellow solution obtained filtered. The clear solution was then heated to boiling and the volume reduced to 5 ml. The solution was left in ice overnight and the pale yellow precipitate obtained was isolated by filtration using a glass filter and dried *in vacuo*. (Yield: 0.042 g, 46.3%.) (Found: C, 35.3; H, 3.8; N, 20.6. Calc. for $C_{22}H_{28}N_{11}O_{10}S_2Al{\cdot}3H_2O$: C, 35.2; H, 4.5; N, 20.5%). IR (cm^{-1}): 3428(s), 3259(m), 3027(m), 2925(m), 1641(s), 1565(s), 1494(w), 1384(m), 1259(m), 1170(m). ^{1}H, [d_6-DMSO, 270 MHz], δ 11.5 (s, CSN*H*CO), 11.0 [s, C(NH_2)-N*H*CS], 9.1 (s, CH_2CONH), 8.1 (s, CH_2CONH), 7.2 (s, NH_2), 6.6 (s, NH_2), 3.4 (m, central NCH_2CO_2H, terminal NCH_2CO_2H), 3.2 (s, CH_2CONH), 2.9 (s, $NCH_2CH_2NCH_2CH_2N$ and $NCH_2CH_2NCH_2CH_2N$), 2.5 (s, DMSO). ^{13}C [d_6-DMSO, 500 MHz], δ 172.5 (terminal NCH_2CO_2H, central NCH_2CO_2H), 171.0 (CH_2CONH), 158.8 (uracil C4), 150.5 (uracil C2), 126.8 (uracil C6), 112.0 (uracil C5), 63.3 (CH_2CONH), 55.1 (terminal NCH_2CO_2H), 55.0 (central NCH_2CO_2H), 51.8 (NCH_2CH_2N), 48.7 (NCH_2CH_2N), 39.8 (q, DMSO). Mass spectrum FAB(−): 696 {65%, $[(Al–L^1) - H]^-$}.

Cr–L^1·11H_2O. $Cr_3(CH_3CO_2)_7(OH)_2$ (0.036 g, 0.06 mmol) was added to a solution of ligand H_3L^1 (0.121 g, 0.18 mmol) in H_2O (20 ml). After 20 min of refluxing a violet solution was obtained which was filtered through filter paper, the volume reduced to 5 ml and the solution was left to cool to 0 °C. A pale violet precipitate was obtained which was isolated by filtration and dried *in vacuo*. (Yield: 0.046 g, 97.9%.) (Found: C, 28.7; H, 4.9; N, 15.9; S, 6.7. Calc. for $C_{22}H_{28}N_{11}O_{10}S_2Cr{\cdot}11H_2O$: C, 28.7; H, 5.4; N, 16.7; S, 6.9%). IR (cm^{-1}): 3423(s), 3179(m), 2923(m), 2853(m), 1638(s), 1463(s), 1383(m), 1256(m), 1169(m). Mass spectrum FAB(−): 672{45%, $[L^1 - H]^-$}, 722 {50%, $[Cr–L^1]^-$}.

Fe–L^1·6H_2O. The ligand H_3L^1 (0.067 g, 0.1 mmol) was dissolved in 10 ml of aqueous KOH (0.017 g, 0.3 mmol) at room temperature. The solution of the deprotonated ligand was then added to an aqueous solution (20 ml) of $Fe(NO_3)_3{\cdot}9H_2O$ (0.04 g, 0.1 mmol) and the resulting yellow solution heated to reflux for 2 hours. After reducing the volume to 5 ml, the solution was left to cool in ice which resulted in the formation of a pale yellow precipitate which was isolated by filtration and dried *in vacuo*. (Yield: 0.044 g, 60.6%.) (Found: C, 32.3; H, 4.2; N, 17.8; S, 6.7. Calc. for $C_{22}H_{28}N_{11}O_{10}S_2Fe{\cdot}6H_2O$: C, 31.7; H, 4.8; N, 18.4; S, 6.9%). IR (cm^{-1}): 3434(s), 3249(m), 3191(m), 2960(m), 2923(s), 2852(m), 1637(s), 1558(m), 1465(m), 1429(m), 1382(m), 1261(s), 1095(m). Mass spectrum FAB(−): 672 {40%, $[L^1 - H]^-$}, 726 {50%, $[Fe–L^1]^-$}.

Al–L^2·5H_2O. $Al(CH_3CO_2)_2OH$ (0.041 g, 0.25 mmol) was added to a solution of H_3L^2 (0.153 g, 0.25 mmol) in H_2O and the reaction mixture was stirred at reflux for 2 hours. The yellow solution obtained was filtered through filter paper and the volume reduced to 5 ml. The solution was left to cool in ice and the resulting off-white precipitate filtered and dried *in vacuo* at 60 °C. (Yield: 0.10 g, 62.5%.) (Found: C, 36.1; H, 5.1; N, 17.9. Calc. for $C_{22}H_{26}N_9O_{12}Al{\cdot}5H_2O$: C, 36.4; H, 5.0; N, 17.4%). IR

(cm^{-1}): 3438(s), 3257(m), 2960(m), 2923(m), 2852(w), 1658(s), 1471(m), 1382(m), 1261(m). ^1H [d_6-DMSO, 270 MHz], δ 11.49 (s, CONHCO), 11.06 (s, CHNHCO), 10.67 (s, CONHCO), 10.02 (s, CHNHCO), 9.15 (s, CH_2CONH), 8.08 (s, CH_2-CONH), 7.19 (s, uracil CH), 6.58 (s, uracil CH), 3.43 (s, CH_2CONH), 3.14 (s, NCH_2CO_2H), 2.89 (s, $NCH_2CH_2NCH_2$-CH_2N), 2.61 (s, $NCH_2CH_2NCH_2CH_2N$), 2.50 (s). ^{13}C [d_6-DMSO, 500 MHz], δ 172.7 (terminal NCH_2CO_2H), 172.2 (central NCH_2CO_2H), 171.2 (CH_2CONH), 169.6 (CH_2-$CONH$), 161.5 (uracil C4), 149.6 (uracil C2), 121.7 (uracil C6), 112.7 (uracil C5), 63.2 (CH_2CONH), 60.6 (terminal NCH_2-CO_2H), 58.2 (central NCH_2CO_2H), 54.7 ($NCH_2CH_2NCH_2$-CH_2N), 54.4 ($NCH_2CH_2NCH_2CH_2N$), 39.8 (q, DMSO). Mass spectrum FAB(−): 726 {50%, $[Al–L^2]^-$}.

Fe–L^2·8H_2O. H_3L^2 (0.120 g, 0.2 mmol) was dissolved in 10 ml of aqueous NaOH (0.024 g, 0.6 mmol) at room temperature. The solution of the deprotonated ligand was then added to 20 ml of aqueous solution of $Fe(NO_3)_3$·$9H_2O$ (0.08 g, 0.2 mmol) and the yellow solution obtained heated to reflux for 2 hours. After filtering and reducing the volume to 5 ml, the solution was left to cool in ice which resulted in the formation of an off-white precipitate which was filtered and dried *in vacuo*. (Yield: 0.097 g, 72.9%.) (Found: C, 32.2; H, 4.8; N, 15.0. Calc. for $C_{22}H_{26}N_9O_{12}Fe$·$8H_2O$: C, 32.7; H, 5.2; N, 15.6%). IR (cm^{-1}): 3423(s), 3226(m), 3114(m), 2966(m), 2923(s), 1687(s), 1660(s), 1637(s), 1623(s), 1465(m), 1444(m), 1367(m), 1346(w), 1263(m). Mass spectrum FAB(−): 664 {50%, $[Fe–L^2]^-$}.

Crystal structure determination

For $Bi(L^1)(H_2O)$·$8.5H_2O$, $M = 1050.81$, monoclinic, space group $P2_1/n$, $a = 10.625(1)$, $b = 21.341(2)$, $c = 16.676(2)$ Å, $\beta = 94.80(1)°$, $U = 3767.9(7)$ $Å^3$, $Z = 4$, $D_c = 1.852$ g cm^{-3}, μ(Cu-Kα) = 11.0 mm^{-1}, $F(000) = 2108$, yellow blocks, crystal dimensions 0.27 × 0.20 × 0.10 mm.

Data collection and processing

Data were measured on a Siemens P4/PC diffractometer with Cu-Kα radiation ($\lambda = 1.54178$ Å, graphite monochromator) using ω scans. 6081 independent reflections were measured ($2\theta \leqslant 126°$) of which 4768 had $|F_o| > 4\sigma|F_o|$ and were considered to be observed. The data were corrected for Lorentz and polarisation factors and an ellipsoidal absorption correction from ψ-scan data was applied; the maximum and minimum transmission factors were 0.665 and 0.197 respectively.

Structure analysis and refinement

The structure was solved by direct methods and the non-hydrogen atoms refined anisotropically. The C–H hydrogen atoms were placed in idealised positions and allowed to ride on their parent atoms with U_{iso} tied to $1.5U_{eq}$ of the parent atom. NH_2 protons were found from the difference map and allowed to refine isotropically subject to a N–H distance constraint. The hydrogen atoms on the water molecules could not be located. Refinement was by full-matrix least squares based on F^2 to give (for the observed data) $R1 = 0.051$, $wR2 = 0.117$ ‡ for 522 parameters. The maximum and minimum residual electron densities in the final ΔF map were 1.746 and −1.423 e $Å^{-3}$ respectively. Computations were carried out using the SHELXTL PC program system.[8]

CCDC reference number 186/1307.

See http://www.rsc.org/suppdata/dt/1999/547/ for crystallographic files in .cif format.

‡ $R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$; $wR_2 = \sqrt{\{\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]\}}$.

References

1 J. M. Lehn, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 89; W. I. Sundquist and S. Lippard, *Coord. Chem. Rev.*, 1990, **100**, 293; H. Sigel, *Chem. Soc. Rev.*, 1993, **22**, 255.
2 A. D. Burrows, C. W. Chan, M. M. Chowdhry, J. E. McGrady and D. M. P. Mingos, *Chem. Soc. Rev.*, 1995, **24**, 329.
3 M. S. Konings, W. C. Dow, D. B. Love, K. N. Raymond, S. C. Quay and S. M. Rocklage, *Inorg. Chem.*, 1990, **29**, 1488.
4 S. Ulvenlund, A. S. Georgopoulou, D. M. P. Mingos, I. Baxter, S. E. Lawrence, A. J. P. White and D. J. Williams, *J. Chem. Soc., Dalton Trans.*, 1998, 1869.
5 S. W. A. Bligh, H. M. S. Chowdhury, M. McPartlin and I. J. Scowen, *Polyhedron*, 1995, **14**, 567.
6 Y. M. Wang, T. H. Cheng, C. C. Liu and P. S. Sheu, *J. Chem. Soc., Dalton Trans.*, 1997, 833.
7 F. Jasanada and F. Nepveu, *Tetrahedron Lett.*, 1992, **33**, 5745.
8 SHELXTL PC, version 5.03, Siemens Analytical X-Ray Instruments, WI, 1994.

Paper 8/07723A