Synthesis and X-ray crystal structure of a tetracyclic gem-*cis*-bis(aminal) formed from *N*,*N'*-bis(2-aminophenyl)ethylenediamine and 1,10-phenanthroline-5,6-dione

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Dedicated to Professor M. Anthony McKervey

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Abstract

The condensation reaction of 1,10-phenanthroline-5,6-dione with *N*,*N'*-bis(2-aminophenyl)ethylenediamine in a 1:1 molar ratio produces the tetracyclic gem-*cis*-bis(aminal) 7a,12c-(2,2'-bipyridin-3,3'-diyl)-1,2,7a,12c-tetrahydro-7H,8H-2a,7,8,12b-tetraazacyclopenta(fg)tetracene methanol (1:1) **(1)** (Figure 1). The X-ray crystal structure of **(1)·MeOH** (Figure 3) shows the molecule to be non-planar and chiral, and comprising three six-membered rings and one five-membered ring fused onto the back of a bipyridine moiety. Reaction of the dione with selected non-aromatic polyamines affords only 1,10-phenanthroline-5,6-diol.

Keywords: Bipyridine, 1,10-phenanthroline-5,6-dione, *N*,*N'*-bis(2-aminophenyl)ethylenediamine, gem-*cis*-bis(aminal), 7a,12c-(2,2'-bipyridin-3,3'-diyl)-1,2,7a,12c-tetrahydro-7H,8H-2a,7,8,12b-tetraazacyclopenta(fg)tetracene methanol (1:1), X-ray structure.

Introduction

Our current interest in 1,10-phenanthroline and its metal complexes centers on the *in vitro* anti-fungal activities of this class of compound.[1,2]. More recently, we have found that 1,10-phenanthroline-5,6-dione and its N,N'-chelated Cu(II) and Ag(I) complexes exhibit a marked improvement in ability to inhibit the growth of the pathogenic fungus *Candida albicans* in comparison to their 1,10-phenanthroline analogues.[3] In an effort to further enhance the anti-fungal activity it was decided to attempt to build an N4 macrocycle onto the back of 1,10-phenanthroline-5,6-dione, the resulting macrocyclic cavity having the ability to incorporate a

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second metal ion.

Results and Discussion

Chemistry

1,10-Phenanthroline-5,6-dione undergoes Schiff base condensation reactions with certain aromatic diprimary amines such as 1,2-diaminobenzene,[4] and 2,3-diaminonaphthalene.[5] However, in the present study the reaction of the dione with the tetraamine N,N'-bis(2-aminophenyl)ethylenediamine in a 1:1 molar ratio in ethanol yielded, not the expected diimine macrocycle, but the tetracyclic gem-*cis*-bis(aminal) 7a,12c-(2,2'-bipyridin-3,3'-diyl)-1,2,7a,12c-tetrahydro-7H,8H-2a,7,8,12b-tetraazacyclopenta(fg)tetracene methanol (1:1) **(1)** (Figure 1). Compound **(1)** forms with an ethanol molecule of crystallization, **(1)·EtOH**.

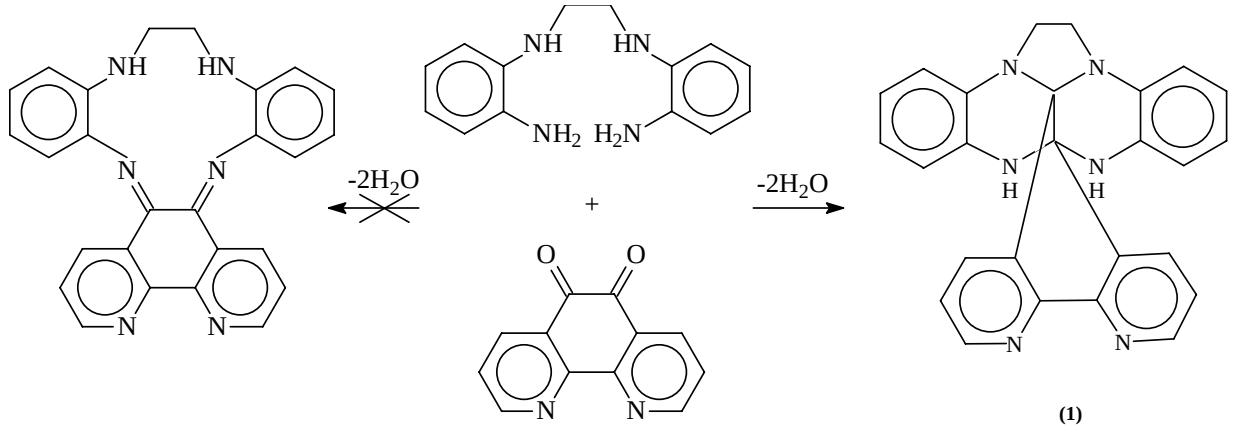

Figure 1. Reaction of 1,10-phenanthroline-5,6-dione with *N,N'*-bis(2-aminophenyl) ethylenediamine.

The preparation of **(1)·EtOH** is analogous to the bis(aminals) that form upon reacting linear tetraamines and α-dicarbonyls.[6,7] In a similar, although not identical, reaction the acid catalyzed condensation of 1,10-phenanthroline-5,6-dione with urea produces bipyridine-glycoluril (Figure 2) in high yield.[8]

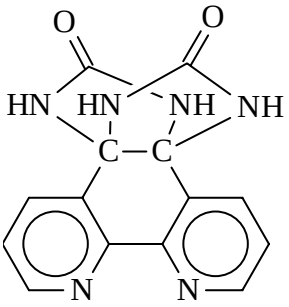

Figure 2. Bipyridine-glycoluril formed upon reaction of 1,10-phenanthroline-5,6-dione with urea.

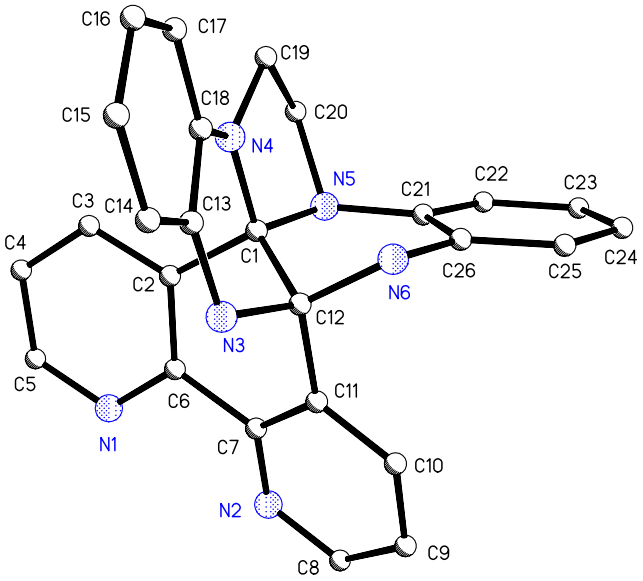

Figure 3. Structure of **(1)·MeOH** (MeOH omitted).

The methanol solvate molecule is hydrogen bonded to N1 and N6 of an adjacent molecule, so that hydrogen–bonded chains run through the structure parallel to the b axis (**Figures 4** and **5**).

X-ray crystallography

The compound crystallised as **(1)·MeOH** in the chiral space group P2(1) and the absolute configuration was not determined unambiguously. The chirality derives from the twisted conformation as is found in spiro compounds - there are no chiral carbons. Figure 3 shows the molecule to be non-planar, comprising three six-membered rings and one five-membered ring fused onto the back of the now bipyridine moiety. The bonds and angles are all quite conventional (Table 1).

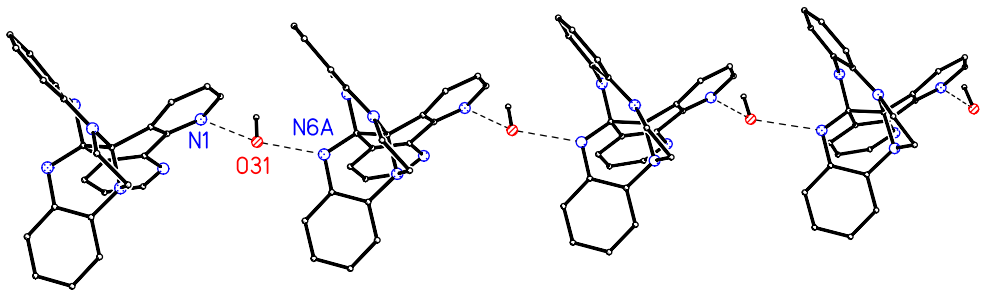

Figure 4. Placement of methanol solvate molecule in **(1)·MeOH**.

The two primary amine N atoms of N,N'-bis(2-aminophenyl)ethylenediamine have bonded with one of the carbonyl carbons of the dione to give secondary amines, whilst the two secondary amine N atoms of N,N'-bis(2-aminophenyl)ethylenediamine have attached to the carbon atom of the second carbonyl group of the dione producing two tertiary amine functions. Two molecules of water are eliminated in the overall reaction.

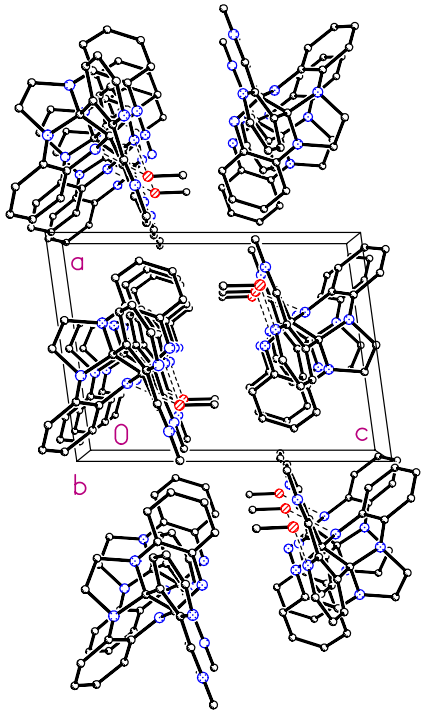

Figure 5. Stacking of **(1)**·**MeOH** molecules as viewed down the b axis.

Attempts to prepare Schiff base condensation products upon reaction of an ethanolic refluxing solution 1,10-phenanthroline-5,6-dione with tetraamines (N,N'-bis(3-aminopropyl)ethylenediamine, triethylaminetetramine, tris(2-aminoethyl)amine) resulted only in the formation of the hydroquinone 1,10-phenanthroline-5,6-diol.

Future work on **(1)**·**EtOH** will include a study its coordination chemistry and an assessment of its antimicrobial activity.

Conclusions

The condensation reaction of 1,10-phenanthroline-5,6-dione with N,N'-bis(2-aminophenyl)ethylenediamine in a 1:1 molar ratio produces the non-planar, chiral, tetracyclic gem-*cis*-bis(aminal) **1** (Figure 1) in moderate yield. Reaction of the dione with selected non-aromatic polyamines affords only 1,10-phenanthroline-5,6-diol.

Table 1. Bond lengths [Å] and angles [°] for **(1)·MeOH**.

C(1)-N(4)	1.461(2)	N(4)-C(1)-N(5)	105.47(14)
C(1)-N(5)	1.464(2)	N(4)-C(1)-C(2)	111.00(15)
C(1)-C(2)	1.533(3)	N(5)-C(1)-C(2)	108.96(14)
C(1)-C(12)	1.547(2)	N(4)-C(1)-C(12)	109.95(15)
C(2)-C(3)	1.388(3)	N(5)-C(1)-C(12)	112.51(14)
C(2)-C(6)	1.403(3)	C(2)-C(1)-C(12)	108.94(14)
C(3)-C(4)	1.389(3)	C(3)-C(2)-C(6)	117.95(17)
C(4)-C(5)	1.379(3)	C(3)-C(2)-C(1)	122.68(17)
C(5)-N(1)	1.339(3)	C(6)-C(2)-C(1)	119.35(16)
N(1)-C(6)	1.341(2)	C(2)-C(3)-C(4)	118.98(18)
C(6)-C(7)	1.479(2)	C(5)-C(4)-C(3)	118.89(18)
C(7)-N(2)	1.337(2)	N(1)-C(5)-C(4)	123.36(19)
C(7)-C(11)	1.404(3)	C(5)-N(1)-C(6)	117.61(17)
N(2)-C(8)	1.337(2)	N(1)-C(6)-C(2)	123.15(17)
C(8)-C(9)	1.382(3)	N(1)-C(6)-C(7)	117.51(16)
C(9)-C(10)	1.383(3)	C(2)-C(6)-C(7)	119.24(16)
C(10)-C(11)	1.388(3)	N(2)-C(7)-C(11)	123.61(17)
C(11)-C(12)	1.529(2)	N(2)-C(7)-C(6)	117.58(16)
C(12)-N(3)	1.452(2)	C(11)-C(7)-C(6)	118.79(16)
C(12)-N(6)	1.452(2)	C(7)-N(2)-C(8)	117.14(17)
N(3)-C(13)	1.414(2)	N(2)-C(8)-C(9)	123.64(19)
C(13)-C(14)	1.381(3)	C(8)-C(9)-C(10)	118.83(18)
C(13)-C(18)	1.417(3)	C(9)-C(10)-C(11)	119.09(19)
C(14)-C(15)	1.389(3)	C(10)-C(11)-C(7)	117.69(17)
C(15)-C(16)	1.383(3)	C(10)-C(11)-C(12)	121.34(17)
C(16)-C(17)	1.392(3)	C(7)-C(11)-C(12)	120.97(16)
C(17)-C(18)	1.397(3)	N(3)-C(12)-N(6)	111.50(15)
C(18)-N(4)	1.379(2)	N(3)-C(12)-C(11)	109.48(14)
N(4)-C(19)	1.458(2)	N(6)-C(12)-C(11)	113.38(15)
C(19)-C(20)	1.533(3)	N(3)-C(12)-C(1)	105.42(14)
C(20)-N(5)	1.492(2)	N(6)-C(12)-C(1)	106.97(14)
N(5)-C(21)	1.436(2)	C(11)-C(12)-C(1)	109.75(15)
C(21)-C(22)	1.390(3)	C(13)-N(3)-C(12)	115.34(15)
C(21)-C(26)	1.404(3)	C(14)-C(13)-N(3)	122.03(17)
C(22)-C(23)	1.388(3)	C(14)-C(13)-C(18)	119.76(17)
C(23)-C(24)	1.388(3)	N(3)-C(13)-C(18)	118.19(17)
C(24)-C(25)	1.388(3)	C(13)-C(14)-C(15)	120.84(19)
C(25)-C(26)	1.403(3)	C(16)-C(15)-C(14)	119.83(19)
C(26)-N(6)	1.395(2)	C(15)-C(16)-C(17)	120.27(18)
O(31)-C(32)	1.403(3)	C(16)-C(17)-C(18)	120.43(18)

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Table 1. Bond lengths [Å] and angles [°] for **(1)·MeOH**.(continued)

N(4)-C(18)-C(17)	121.79(17)	C(22)-C(21)-C(26)	119.11(17)
N(4)-C(18)-C(13)	119.43(16)	C(22)-C(21)-N(5)	118.93(16)
C(17)-C(18)-C(13)	118.76(18)	C(26)-C(21)-N(5)	121.93(16)
C(18)-N(4)-C(19)	124.67(16)	C(23)-C(22)-C(21)	121.47(18)
C(18)-N(4)-C(1)	121.07(14)	C(24)-C(23)-C(22)	119.48(18)
C(19)-N(4)-C(1)	111.33(14)	C(25)-C(24)-C(23)	119.95(18)
N(4)-C(19)-C(20)	101.51(15)	C(24)-C(25)-C(26)	120.79(18)
N(5)-C(20)-C(19)	104.99(15)	N(6)-C(26)-C(25)	122.32(17)
C(21)-N(5)-C(1)	116.47(15)	N(6)-C(26)-C(21)	118.58(16)
C(21)-N(5)-C(20)	113.95(14)	C(25)-C(26)-C(21)	119.11(17)
C(1)-N(5)-C(20)	103.09(14)	C(26)-N(6)-C(12)	114.19(15)

Experimental Section

General Procedures. Chemicals were purchased from commercial sources and, unless specified, were used without further purification. Literature methods were used to prepare 1,10-phenanthroline-5,6-dione[4] and N,N'-bis(2-nitrophenyl)ethylenediamine.[9] The infrared spectrum of **(1)·EtOH** (in a KBr matrix) was recorded in the region 4000-400 cm^{-1} on a Nicolet FT-IR Impact 400D infrared spectrometer and the ^1H NMR spectrum was run on a Bruker Avance 300 MHz instrument. The mass spectrum of **(1)·EtOH** was carried out on a Kratos Profile mass spectrometer and microanalytical data were provided by the Microanalytical Laboratory, National University of Ireland, Cork, Ireland. X-ray crystallographic data for **(1)·MeOH** were collected at 150(2) K on a Bruker SMART 1000 diffractometer. The structure was solved by direct methods and refined by full-matrix least-squares on F^2 using the SHELXTL suite of programs.[10] All the non-hydrogen atoms were refined with anisotropic atomic displacement parameters and hydrogen atoms bonded to carbon were inserted at calculated positions using a riding model. Hydrogen atoms bonded to oxygen or nitrogen (N3 and N6) were located from difference maps and their coordinates allowed to refine. Details of the data collection and structure refinement are given in Table 2.

Table 2. Crystal data and structure refinement for **(1)·MeOH**.

Empirical formula	C27 H24 N6 O
Formula weight	448.52
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)

Table 2. Crystal data and structure refinement for **(1)·MeOH**.(continued)

Unit cell dimensions	a = 9.2110(9) Å	α= 90°.
	b = 9.5779(9) Å	β= 97.829(2)°
	c = 12.5664(12) Å	γ = 90°.
Volume	1098.30(18) Å^3	
Z	2	
Density (calculated)	1.356 Mg/m^3	
Absorption coefficient	0.087 mm^{-1}	
F(000)	472	
Crystal size	0.34 x 0.17 x 0.05 mm^3	
Crystal description	Colourless plate	
Theta range for data collection	1.64 to 28.65°.	
Index ranges	-12<=h<=11, -12<=k<=12, -16<=l<=16	
Reflections collected	9465	
Independent reflections	4943 [R(int) = 0.0206]	
Completeness to theta = 25.00°	100.0 %	
Absorption correction	Multiscan	
Max. and min. transmission	1.00000 and 0.944615	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4943 / 1 / 317	
Goodness-of-fit on F^2	1.048	
Final R indices [I>2sigma(I)]	R1 = 0.0396, wR2 = 0.0888	
R indices (all data)	R1 = 0.0509, wR2 = 0.0946	
Absolute structure parameter	0.1(14)	
Largest diff. peak and hole	0.268 and -0.202 e.Å^{-3}	

***N,N'*-Bis(2-aminophenyl)ethylenediamine.** This is an alternative route to the compound where reduction was carried out using hydrazine hydrate rather than hydrogen gas.[9] To a suspension of N,N'-bis(2-nitrophenyl)ethylenediamine (1.0 g, 3.3 mmol) in ethanol (10 cm^3), was added Pd/C (10% wt., 0.4 g). Hydrazine monohydrate (2 cm^3) was dissolved in ethanol (20 cm^3) and added dropwise. The resulting solution was refluxed for 6 h, cooled and filtered. The filtrate was reduced to 5 cm^3 and water added (30 cm^3) to precipitate the white product. The solid was filtered off, washed with water and air-dried. Yield: 0.63 g (79%). Anal. Calcd. for $C_{14}H_{18}N_4$ (242.28): C, 69.40; H, 7.49; N, 23.11. Found: C, 69.59; H, 7.59; N, 22.83. *m/z* = 242. IR: 3361, 3308, 3254, 3052, 2945, 2911, 2844, 1608, 1508, 1454, 1320, 1273, 1125, 1024, 890, 755, 440 cm^{-1}. NMR data δ_H (ppm $CHCl_3$): 6.80 (m, 2H), 6.72, (m, 6H), 3.42 (s, 10H); δ_C (ppm $CHCl_3$): 137.44, 134.56, 120.67, 119.11, 116.58, 112.04, 43.67.

(1)·EtOH and **(1)·MeOH.** To a suspension of 1,10-phenanthroline-5,6-dione (0.17 g, 0.8 mmol) in ethanol (20 cm^3) was added N,N'-bis(2-aminophenyl)ethylenediamine (0.19 g, 0.8 mmol). The resulting yellow solution was stirred at room temperature and it gradually changed to an orange/brown colour. After 1 h the yellow product **(1)·EtOH** precipitated and the mixture was

stirred for a further 3 h. The yellow solid was filtered off, washed thoroughly with ethanol and ether and then air-dried (0.18 g, 47%), mp 288 ^{o}C (dec). Anal. Calcd. for $C_{28}H_{26}N_6O$ (462.55): C, 72.70; H, 5.67; N, 18.17. Found: C, 72.52; H, 5.30; N, 18.00. *m/z* = 417 (M + 1 without EtOH). IR: 3395, 3247, 2865, 1609, 1510, 1418, 1363, 1307, 1215, 1135, 984, 812, 753 cm^{-1}. NMR data: δ_H (ppm DMSO): 8.61 (m, 2H), 8.07 (d, *J* = 7.8, 1H), 7.55 (m, 1H), 7.30 (m 2H), 6.60 (m 8H), 4.36 (s, 1H), 3.95 (s, 1H), 3.40 (m, 7H), 1.06 (t, *J* = 7.0, 3H); δ_C (ppm DMSO): 151.68, 149.90, 149.67, 148.93, 137.69, 137.46, 136.22, 135.00, 134.75, 131.13, 130.46, 124.34, 123.82, 122.38, 120.12, 119.93, 118.94, 116.66, 115.46, 114.36, 111.62, 79.78, 64.57, 56.42, 52.51, 46.17, 18.91. Crystals of **(1)·MeOH** suitable for X-ray analysis were obtained by recrystallising **(1)·EtOH** from methanol.

Acknowledgements

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Supporting Information Available

Supplementary X-ray structural data for (**1)·MeOH** are available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, England (fax: +44-1223-336033), on request quoting the deposition number CCDC 204875.

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