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Crystal Structure, Electrospray Ionization Mass Spectrometry, Electron Paramagnetic Resonance, and Magnetic Susceptibility Study of $[Cu_2(ascidH_2)(1,2\text{-}\mu\text{-}CO_3)(H_2O)_2]\cdot 2H_2O$, the Bis(copper(II)) Complex of Ascidiacyclamide (ascidH$_4$), a Cyclic Peptide Isolated from the Ascidian *Lissoclinum patella*

**Anna L. van den Brenk,[1a] Karl A. Byriel,[1a] David P. Fairlie,[1b] Lawrence R. Gahan,*[1a]
Graeme R. Hanson,[1c] Clifford J. Hawkins,[1a] Alun Jones,[1b] Colin H. L. Kennard,[1a]
Boujemaa Moubaraki,[1d] and Keith S. Murray[1d]**

Department of Chemistry, Centre for Magnetic Resonance, and 3D Centre,
The University of Queensland, Brisbane, QLD, 4072 Australia, and Chemistry Department,
Monash University, Clayton, Victoria 3168, Australia

Received November 2, 1993®

A bis(copper(II)) complex of the naturally occurring cyclic peptide ascidiacyclamide (ascidH$_4$), isolated from the ascidian *Lissoclinum patella*, has been characterized by X-ray crystallography, magnetic susceptibility measurements, ion spray mass spectrometry, and EPR spectroscopy. The crystals are triclinic, space group $P1$, with $a = 9.9420(10)$, Å, $b = 11.808(2)$, Å, $c = 20.635(3)$ Å, $\alpha = 74.340(10)°$, $\beta = 87.520(10)°$, $\gamma = 89.460(10)°$, $V = 2330.3(6)$ Å^3, $Z = 2$, and $R = 0.058$. The geometry around one copper(II) atom is distorted square pyramidal, the metal ion coordinated by three nitrogen donors, one each from an oxazoline, a thiazole, and a deprotonated amide. A water molecule and the oxygen atom of a bridging carbonate anion complete the coordination sphere. The other copper(II) atom exhibits a similar coordination environment with an added distant Cu–O interaction making up a distorted octahedral environment. The Cu(1)···Cu(2) distance was determined as 4.43 Å. The geometry of the carbonate anion was considerably distorted from that in the free anion. The presence of the CO_3^{2-} species was confirmed with ion spray mass spectral studies by comparing the mass spectra of isolated $[Cu_2(ascidH_2)(1,2\text{-}\mu\text{-}CO_3)(H_2O)_2]\cdot 2H_2O$ with that generated *in situ* using $^{13}CO_3^{2-}$ ($[ascidH_2 + 2Cu^{2+} + CO_3^{2-} + Na^+]^+$: $^{12}CO_3^{2-}$, m/z 965.2; $^{13}CO_3^{2-}$, m/z 966.3). Magnetic susceptibility measurements (4–300 K) on the powdered sample show that weak ferromagnetic coupling ($2J = +1.6 \pm 0.4$ cm^{-1}) occurs, probably via an intramolecular superexchange pathway across the $1,2\text{-}\mu\text{-}CO_3^{2-}$ bridge. EPR spectroscopy suggests a structural reorganization of the binuclear copper site when the binuclear copper ascidiacyclamide complex is dissolved in methanol and that the formation of $[Cu_2(ascidH_2)(1,2\text{-}\mu\text{-}CO_3)(solvent)_2]$ is complicated by a series of equilibria in which other binuclear and monomeric species are involved.

Introduction

Families of cyclic peptides, possessing antineoplastic activity, have been isolated from *Lissoclinum patella*, a species of tunicate, class Ascidiacea, of the phylum Chordata.[2-13] Members of the family of cyclic peptides, patellamides, have the 24-azacrown-8 structure.[8,9] The structure of ascidiacyclamide, a patellamide, has been deduced by chemical synthesis and X-ray structural determination.[12,14] The molecule, in which the cyclic peptide chain takes on a saddle-shaped conformation, consists of alternating D-valine and L-isoleucine side chains with thiazole and oxazoline rings located alternately at each corner of the 24-azacrown-8 macrocyclic ring structure. The disposition of the N–H bonds of the amide groups and N lone pairs of the thiazole and oxazoline rings were observed to be directed toward the center of the macrocycle.[12]

It is presently unknown whether these and other marine metabolites sequester and transport metal ions *in vivo*, provide a convenient template for biological assembly of the metabolites, or have functions associated with the biological activity of the compounds.[15] Although species of the Ascidiacea have been found to concentrate a range of metal ions *in vivo*,[9,16-20] there is a paucity of information concerning both the interaction of metal ions with these marine metabolites and the roles of the metal ions.[15]

This paper reports the characterization by X-ray crystallography, ion spray mass spectrometry, magnetic moment

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* Author to whom correspondence should be addressed.

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(1) (a) Department of Chemistry, The University of Queensland. (b) 3D Centre, The University of Queensland. (c) Centre for Magnetic Resonance, The University of Queensland. (d) Department of Chemistry, Monash University.

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determination, and electron paramagnetic resonance (EPR)[21] spectroscopy of a binuclear copper(II) complex $[Cu_2(ascidH_2)(1,2\text{-}\mu\text{-}CO_3)(H_2O)_2]\cdot 2H_2O$, prepared *in vitro*, from reaction between a copper(II) salt and the cyclic peptide ascidiacyclamide ($ascidH_4$) isolated from the ascidian *L. patella*.

Experimental Section

Ascidiacyclamide was isolated and purified from *L. patella* collected from Heron Island on the Great Barrier Reef, Australia.[5]

Copper(II) nitrate–2.5-water, methanol (Mallinckrodt), and anhydrous triethylamine (Aldrich) were of analytical grade and used without further purification. $Na_2{}^{13}CO_3$ (^{13}C, 99%) and $K^{15}NO_3$ (^{15}N, 99%) were purchased from Cambridge Isotope Laboratories, Cambridge, MA.

The copper ascidiacyclamide complex was prepared from stock methanol solutions of ascidiacyclamide (4 mM, 3400 μL), copper(II) nitrate (0.02 M, 1360 μL), and triethylamine, NEt_3 (0.05 M, 100 μL × 10), with 1200 μL of methanol. Evaporation of the solvent at 22 °C over an extended period of time produced deep blue crystals suitable for X-ray crystallographic studies. The product was washed with 10 mL of water and dried between filter paper and finally in a vacuum desiccator (8.78 mg, 63%).

Magnetic Studies. Magnetic susceptibility studies were made using a Quantum Design MPMS SQUID magnetometer with an applied field of 1 T. The powdered sample was contained in a calibrated gelatine capsule which was held in the center of a soda straw fixed to the end of the sample rod. The magnetization values of the instrument were calibrated against a standard palladium sample, supplied by Quantum Design, and also against chemical calibrants such as $CuSO_4\cdot 5H_2O$ and $[Ni(en)_3](S_2O_3)$.

Electrospray Ionization Mass Spectrometry. Methanol solutions containing various ratios of ascidiacyclamide (10^{-3} M), copper triflate or copper chloride, and base (NEt_3, Na_2CO_3) were directly infused via syringe pump (2.5 $\mu L\ min^{-1}$) into an atmospheric ionization source of an API-111 triple quadrupole mass spectrometer (PE/Sciex, Thornhill, Ontario, Canada). The pneumatically assisted electrospray[22] (ion spray)[23] interface was operated at +5.0 kV to generate cations. After solvent evaporation,[24] the cations were drawn into the analyzer region of the spectrometer through a 100-μm sampling orifice of varying voltage potential difference (OR = 0–100 V). Low potential differences (0–50 V) typically produced intact molecular ions but higher potential differences fragmented them. Multiply protonated molecular ions $[M + nH]^{n+}/n$ were separated (m/z ratios) by rf and dc voltages and detected by scanning quadrupole-1 from m/z = 200 to 1200 in 6 s with a scan step of 0.2 Da.

Electron Paramagnetic Spectroscopy. EPR spectra were recorded with a Bruker ESP-300E EPR spectrometer with an X-band (*ca.* 9.40 GHz) microwave bridge. A flowthrough cryostat *in conjunction* with a Eurotherm (B-VT-2000) variable-temperature controller provided temperatures of 110–130 K at the sample position in the cavity. Calibration of the magnetic field and the microwave frequency were performed with a Bruker 035M gaussmeter and a EIP 548 B microwave frequency counter, respectively. Computer simulation of the EPR spectra arising from the binuclear copper(II) complex was performed with the similar and dissimilar ion dimer computer programs gndimer.f[25] and dissim.f[25] on a SUN SPARCstation 10/30 workstation. The quality of the final simulated spectrum can be estimated from the least-squares error parameter (LSE).[26] Spectral comparisons and the determination of LSE were carried out with the EPR software package EPR__PLOT running on The University of Queensland Prentice Computer Centre's VAX 8550 computer.

Table 1. Crystal Data for $\{[Cu_2(ascidH_2)(1,2\text{-}\mu\text{-}CO_3)(H_2O)_2]\cdot 2H_2O\}_2$

formula	$C_{37}H_{58}Cu_2N_8O_{13}S_2$
fw	1014.11
a, Å	9.9420(10)
b, Å	11.808(2)
c, Å	20.635(3)
α, deg	74.340(10)
β, deg	87.520(10)
γ, deg	89.460(10)
V, Å^3	2330.3(6)
Z	2
cryst system	triclinic
space group	$P1$
T, K	298
cryst dimens, mm	0.32 × 0.25 × 0.18
radiation, Å	0.710 73
ρ_{calcd}, g cm^{-3}	1.445
μ, cm^{-1}	10.7
$F(000)$, e$^-$	1060
θ range, deg	1.03–25.00
index ranges	$-2 \leq h \leq 11, -14 \leq k \leq 14, -24 \leq l \leq 24$
no. of reflcns collcd	8772
no. of indpdt reflcns	8665 (R_{int} = 0.0207)
goodness-of-fit on F^2	1.035
$R_1{}^a$	0.0585
$wR_2{}^b$	0.1465
max and min peaks, e Å^{-3}	0.952 and –0.594

[a] $R_1 = (\sum||F_o| - |F_c||)/\sum|F_o|$. [b] $wR_2 = [\sum[w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2]]^{1/2}$.

X-ray Crystallography. X-ray data were collected on two crystals from different preparations (data sets one and two) with an Enraf-Nonius CAD-4 diffractometer using graphite-monochromatized Mo Kα radiation (λ 0.710 73 Å). Initial cell dimensions were obtained from the angle data for 25 independent reflections (2θ). The intensities of 3 standard reflections, measured every 200 reflections throughout the data collection, showed only small random variations. The data were processed and corrected for Lorentz and polarization effects and absorption (empirical, based on azimuthal scans for 2 reflections) using the XTAL 3.2 package.[27] The structure was solved by direct methods using SHELXS-86[28] and refined by least-squares methods (F^2) using SHELXL-93.[29] All non-hydrogen atoms were refined with anisotropic atomic displacement parameters. Hydrogen atoms were generated. Secondary extinction corrections were not applied. Neutral scattering factors and anomalous dispersion corrections for non-hydrogen atoms were taken from ref 30. Absorption correction using the ψ-scan method was employed. Final refinement using 8652 observed reflections [$I > 2\sigma(I)$] yielded an R-factor of 0.0585 (data set two). Although there were two independent molecules per unit cell in the space group $P1$, checks using PLATON[31] failed to reveal additional symmetry.[32] SHELXL-93[29] was employed to check the chirality, the Flack[33] parameter of 0.03(2) indicating that the correct assignment of the chirality had been made. The four most intense peaks in the difference map (0.95–0.73 e Å^{-3}) are all 2.0 Å away from existing Cu atoms. Calculations using oxygen atoms (H_2O molecules) at these positions failed to refine. The crystallographic data are given in Table 1, the final non-hydrogen atomic coordinates are listed in Table 2, selected bond distances are listed in Table 3, and bond angles are in Table 4. Figures were drawn with PLATON.[31]

Results and Discussion

Synthesis and Magnetism. Blue crystals of a copper complex were isolated from a methanol solution containing the cyclic peptide ascidiacyclamide, copper(II) nitrate, and triethylamine. As the four amide groups of the ascidiacyclamide ligand may be deprotonated, the ligand abbreviation employed is $ascidH_4$; the doubly deprotonated ligand is therefore given the abbreviation $ascidH_2$.

The complex displays a magnetic moment close to that expected for two isolated d^9 copper(II) sites (1.86 μ_B per copper, 298 K). Variable-temperature susceptibility measurements in the range

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(21) The International EPR Society is recommending that the acronym EPR rather than ESR be used to describe this technique.

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Table 2. Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Thermal Parameters ($Å^2 \times 10^3$) of the Non-Hydrogen Atoms for $\{[Cu_2(ascidH_2)(1,2\text{-}\mu\text{-}CO_3)(H_2O)_2]\cdot 2H_2O\}_2$

	x	*y*	*z*	*U*(eq)[a]		*x*	*y*	*z*	*U*(eq)[a]
Cu(1)	2477[b]	4431[b]	5671[b]	35(1)	Cu(3)	−483(2)	7892(2)	12786(1)	36(1)
Cu(2)	2919(2)	2563(2)	7832(1)	35(1)	Cu(4)	−764(1)	9246(2)	10641(1)	34(1)
N(1)	808(12)	5051(9)	5245(6)	42(3)	N(9)	1186(11)	7914(9)	13249(6)	39(3)
C(1)	90(14)	4422(12)	4970(7)	39(3)	C(37)	1899(13)	7002(12)	13438(7)	35(3)
O(1)	−956(11)	4675(9)	4670(6)	53(3)	O(7)	2979(11)	6871(9)	13734(6)	58(3)
C(2)	724(17)	3234(12)	5062(7)	45(4)	C(38)	1359(15)	5986(11)	13184(7)	39(3)
N(2)	1872(11)	2947(9)	5381(6)	35(3)	N(10)	161(12)	6189(9)	12855(6)	38(3)
C(3)	207(16)	2310(12)	4835(8)	53(4)	C(39)	1857(15)	4911(11)	13285(8)	49(4)
S(1)	1292(5)	1150(3)	5023(2)	58(1)	S(3)	811(5)	4072(3)	12950(2)	58(1)
C(4)	2346(15)	1918(11)	5409(8)	40(4)	C(40)	−276(14)	5234(11)	12702(7)	35(3)
C(5)	3650(14)	1410(11)	5636(7)	37(3)	C(41)	−1522(15)	5146(11)	12342(8)	43(4)
C(6)	4808(17)	2179(14)	5260(9)	59(4)	C(42)	−2767(17)	5349(15)	12752(8)	58(4)
C(7)	6177(18)	1703(16)	5521(10)	73(6)	C(43)	−2880(22)	4388(17)	13431(8)	79(6)
C(8)	4799(20)	2260(16)	4501(9)	70(5)	C(44)	−4075(19)	5421(21)	12371(11)	92(7)
N(3)	3691(11)	1203(8)	6378(5)	35(2)	N(11)	−1448(12)	5965(9)	11676(5)	36(3)
C(9)	4237(13)	256(11)	6761(7)	35(3)	C(45)	−1904(13)	5708(10)	11121(7)	34(3)
O(2)	4719(12)	−569(8)	6577(5)	56(3)	O(8)	−2310(12)	4769(8)	11106(5)	62(3)
C(10)	4241(15)	211(10)	7524(7)	39(3)	C(46)	−1823(16)	6729(12)	10479(7)	40(3)
C(11)	3966(20)	−1023(12)	7973(8)	60(5)	C(47)	−1333(15)	6308(12)	9856(7)	43(3)
C(12)	4690(19)	−1348(16)	8626(9)	68(5)	C(48)	−2042(19)	6883(17)	9229(8)	67(5)
N(4)	3196(11)	936(9)	7716(5)	34(3)	N(12)	−823(12)	7637(9)	10484(6)	37(3)
O(3)	2523(11)	−930(7)	8148(6)	55(3)	O(9)	72(10)	6639(8)	9780(5)	47(2)
C(13)	2281(13)	243(11)	8019(7)	36(3)	C(49)	181(14)	7454(11)	10141(7)	38(3)
C(14)	882(16)	663(11)	8201(7)	42(3)	C(50)	1498(13)	8132(11)	10087(7)	36(3)
C(15)	−157(16)	547(14)	7701(8)	54(4)	C(51)	2543(14)	7400(12)	10548(7)	40(3)
C(16)	198(23)	1261(21)	6977(11)	107(8)	C(52)	2119(20)	7115(17)	11291(9)	80(6)
C(17)	−403(25)	−769(18)	7755(13)	100(8)	C(53)	2946(22)	6290(16)	10367(9)	75(6)
C(18)	−1634(25)	−998(23)	7412(13)	121(9)	C(54)	4150(24)	5699(21)	10672(13)	116(9)
N(5)	1208(11)	1881(10)	8197(6)	44(3)	N(13)	1058(11)	9184(8)	10287(7)	47(3)
C(19)	286(14)	2468(12)	8438(7)	40(3)	C(55)	1882(18)	10115(12)	10121(7)	49(4)
O(4)	−857(12)	2182(9)	8709(6)	61(3)	O(10)	2967(10)	10227(9)	9845(6)	54(3)
C(20)	782(15)	3719(12)	8355(8)	44(4)	C(56)	1184(12)	11088(11)	10356(7)	34(3)
N(6)	2068(12)	4005(9)	8080(6)	40(3)	N(14)	−121(13)	10904(9)	10641(6)	44(3)
C(21)	154(17)	4573(13)	8556(9)	59(4)	C(57)	1672(16)	12176(13)	10286(9)	64(5)
S(2)	1083(5)	5789(4)	8414(2)	66(1)	S(4)	570(5)	13019(3)	10591(3)	65(1)
C(22)	2358(14)	5128(12)	8089(7)	38(3)	C(58)	−540(15)	11883(11)	10804(7)	39(3)
C(23)	3708(14)	5714(11)	7871(7)	38(3)	C(59)	−1953(16)	12027(10)	11102(7)	41(4)
C(24)	4804(15)	5044(12)	8282(7)	45(4)	C(60)	−3077(14)	11976(12)	10613(8)	45(4)
C(25)	6186(17)	5604(17)	8012(9)	72(5)	C(61)	−2851(18)	12845(14)	9936(8)	61(5)
C(26)	4580(24)	4977(14)	9026(9)	77(6)	C(62)	−4418(18)	12120(20)	10931(9)	81(6)
N(7)	3952(11)	5950(9)	7137(6)	38(3)	N(15)	−2175(12)	11224(9)	11763(6)	42(3)
C(27)	3239(16)	6767(11)	6724(7)	42(3)	C(63)	−1564(15)	11360(11)	12313(7)	39(3)
O(5)	2381(11)	7356(9)	6898(5)	57(3)	O(11)	−860(13)	12210(8)	12290(5)	66(3)
C(28)	3559(15)	6860(11)	5973(7)	39(3)	C(64)	−1828(14)	10352(12)	12954(7)	36(3)
C(29)	3169(16)	8101(13)	5522(8)	53(4)	C(65)	−1501(15)	10760(13)	13587(7)	45(4)
C(30)	4066(18)	8559(13)	4929(8)	58(4)	C(66)	−2372(17)	10143(16)	14204(8)	62(5)
C(31)	1679(15)	6741(12)	5441(7)	42(3)	N(16)	−733(12)	9494(9)	12958(6)	35(3)
N(8)	2605(12)	6091(9)	5755(6)	34(3)	O(12)	−117(11)	10438(8)	13703(5)	47(2)
O(6)	1859(11)	7912(8)	5920(5)	47(2)	C(67)	168(16)	9644(13)	13341(7)	45(4)
C(32)	433(14)	6242(11)	5227(8)	41(4)	C(68)	1469(14)	9005(12)	13417(8)	39(3)
C(33)	−769(15)	6341(15)	5714(8)	53(4)	C(69)	2624(16)	9760(13)	12953(8)	49(4)
C(34)	−507(21)	5633(19)	6451(10)	89(6)	C(70)	2319(20)	10009(18)	12210(9)	86(7)
C(35)	−1158(18)	7579(16)	5652(11)	77(6)	C(71)	2851(18)	10899(15)	13171(8)	62(5)
C(36)	−2577(18)	7683(23)	5937(13)	110(9)	C(72)	4137(24)	11492(19)	12864(11)	104(8)
C(73)	4451(14)	3766(9)	6712(8)	32(3)	C(74)	−2482(14)	8688(10)	11761(7)	33(3)
O(13)	4566(9)	3241(8)	7352(4)	36(2)	O(16)	−2487(9)	9168(7)	11100(5)	40(2)
O(14)	3368(11)	3537(7)	6454(5)	45(2)	O(17)	−1398(10)	8107(8)	11969(5)	46(3)
O(15)	5325(10)	4458(8)	6410(5)	47(2)	O(18)	−3396(10)	8874(9)	12146(5)	51(3)
O(19)	3817(10)	4927(9)	4682(5)	47(3)	O(23)	−1799(12)	7103(8)	13816(5)	55(3)
O(20)	4068(12)	2087(8)	8858(5)	53(3)	O(24)	−1727(12)	9932(9)	9559(5)	53(3)
O(21)	−4373(12)	9260(11)	10104(6)	68(3)	O(25)	−3435(13)	1953(12)	8203(8)	91(4)
O(22)	−4312(11)	7841(12)	13443(6)	69(3)	O(26)	6331(12)	5099(12)	5093(6)	77(4)

[a] U_{eq} is defined as one-third of the trace of the orthogonalized U_{ij} tensor. [b] Fixed.

4.2–300 K showed the existence of weak ferromagnetic coupling ($2J = +1.6 \pm 0.4$ cm^{-1}). This can be seen in the μ_{Cu} vs T plot (Figure 1) in which the μ_{Cu} values increase from 1.86 μ_B at 300 K to 1.96 μ_B at 4.2 K on account of increased population of an $S = 1$ ground state. The coupling most likely occurs in an intramolecular fashion between Cu(1) and Cu(2) rather than by intermolecular interactions to neighboring molecules. Recent studies were done on a number of μ-carbonato-bridged Cu(II) complexes, which contain Cu···Cu separations and a μ–1,2-CO_3^{2-} bridging mode similar to that shown in Figure 2, and all show the presence of weak intramolecular ferromagnetic coupling.[34–36]

Description of Structure. The compound crystallized in the space group *P*1 with two molecules (1 and 2) per cell. There were only small differences (8 bond distances where the differences

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(34) Kruger, P. E.; Fallon, G. D.; Moubaraki, B.; Murray, K. S. Unpublished data.

(35) Kolks, G.; Lippard, S. J.; Waszczak, J. V. *J. Am. Chem. Soc.* **1980**, *102*, 4833.

Table 3. Bond Distances (Å) for $\{[Cu_2(ascidH_2)(1,2\text{-}\mu\text{-}CO_3)(H_2O)_2]\cdot 2H_2O\}_2$

Cu(1)–O(14)	1.922(10)	Cu(1)–N(1)	1.955(11)	Cu(3)–N(9)	1.954(11)	Cu(3)–N(16)	2.028(11)
Cu(1)–N(8)	2.020(10)	Cu(1)–N(2)	2.100(10)	Cu(3)–N(10)	2.073(11)	Cu(3)–O(23)	2.410(11)
Cu(1)–O(19)	2.328(11)	Cu(2)–N(5)	1.923(11)	Cu(4)–O(16)	1.913(10)	Cu(4)–N(13)	1.931(12)
Cu(2)–O(13)	1.939(9)	Cu(2)–N(4)	2.014(11)	Cu(4)–N(12)	2.013(11)	Cu(4)–N(14)	2.065(11)
Cu(2)–N(6)	2.070(11)	Cu(2)–O(20)	2.378(11)	Cu(4)–O(24)	2.399(11)	N(9)–C(37)	1.26(2)
N(1)–C(1)	1.29(2)	N(1)–C(32)	1.44(2)	N(9)–C(68)	1.45(2)	C(37)–O(7)	1.25(2)
C(1)–O(1)	1.23(2)	C(1)–C(2)	1.50(2)	C(37)–C(38)	1.54(2)	C(38)–C(39)	1.32(2)
C(2)–N(2)	1.34(2)	C(2)–C(3)	1.41(2)	C(38)–N(10)	1.38(2)	N(10)–C(40)	1.33(2)
N(2)–C(4)	1.29(2)	C(3)–S(1)	1.71(2)	C(39)–S(3)	1.73(2)	S(3)–C(40)	1.719(14)
S(1)–C(4)	1.742(14)	C(4)–C(5)	1.47(2)	C(40)–C(41)	1.49(2)	C(41)–N(11)	1.45(2)
C(5)–N(3)	1.49(2)	C(5)–C(6)	1.52(2)	C(41)–C(42)	1.52(2)	C(42)–C(44)	1.54(2)
C(6)–C(7)	1.53(2)	C(6)–C(8)	1.54(2)	C(42)–C(43)	1.55(2)	N(11)–C(45)	1.36(2)
N(3)–C(9)	1.31(2)	C(9)–O(2)	1.22(2)	C(45)–O(8)	1.19(2)	C(45)–C(46)	1.53(2)
C(9)–C(10)	1.56(2)	C(10)–N(4)	1.45(2)	C(46)–N(12)	1.47(2)	C(46)–C(47)	1.56(2)
C(10)–C(11)	1.52(2)	C(11)–O(3)	1.47(2)	C(47)–O(9)	1.44(2)	C(47)–C(48)	1.49(2)
C(11)–C(12)	1.51(2)	N(4)–C(13)	1.26(2)	N(12)–C(49)	1.25(2)	O(9)–C(49)	1.37(2)
O(3)–C(13)	1.36(2)	C(13)–C(14)	1.54(2)	C(49)–C(50)	1.53(2)	C(50)–N(13)	1.47(2)
C(14)–N(5)	1.47(2)	C(14)–C(15)	1.52(2)	C(50)–C(51)	1.53(2)	C(51)–C(53)	1.50(2)
C(15)–C(16)	1.53(2)	C(15)–C(17)	1.55(2)	C(51)–C(52)	1.52(2)	C(53)–C(54)	1.46(3)
C(17)–C(18)	1.50(3)	N(5)–C(19)	1.31(2)	N(13)–C(55)	1.34(2)	C(55)–O(10)	1.19(2)
C(19)–O(4)	1.25(2)	C(19)–C(20)	1.52(2)	C(55)–C(56)	1.52(2)	C(56)–C(57)	1.35(2)
C(20)–C(21)	1.33(2)	C(20)–N(6)	1.38(2)	C(56)–N(14)	1.40(2)	N(14)–C(58)	1.35(2)
N(6)–C(22)	1.36(2)	C(21)–S(2)	1.67(2)	C(57)–S(4)	1.69(2)	S(4)–C(58)	1.697(14)
S(2)–C(22)	1.69(2)	C(22)–C(23)	1.51(2)	C(58)–C(59)	1.54(2)	C(59)–N(15)	1.45(2)
C(23)–N(7)	1.47(2)	C(23)–C(24)	1.50(2)	C(59)–C(60)	1.55(2)	C(60)–C(62)	1.49(2)
C(24)–C(26)	1.52(2)	C(24)–C(25)	1.54(2)	C(60)–C(61)	1.50(2)	N(15)–C(63)	1.36(2)
N(7)–C(27)	1.33(2)	C(27)–O(5)	1.20(2)	C(63)–O(11)	1.22(2)	C(63)–C(64)	1.54(2)
C(27)–C(28)	1.54(2)	C(28)–N(8)	1.48(2)	C(64)–N(16)	1.48(2)	C(64)–C(65)	1.56(2)
C(28)–C(29)	1.56(2)	C(29)–O(6)	1.45(2)	C(65)–O(12)	1.44(2)	C(65)–C(66)	1.52(2)
C(29)–C(30)	1.46(2)	C(31)–N(8)	1.27(2)	N(16)–C(67)	1.26(2)	O(12)–C(67)	1.37(2)
C(31)–O(6)	1.35(2)	C(31)–C(32)	1.51(2)	C(67)–C(68)	1.48(2)	C(68)–C(69)	1.58(2)
C(32)–C(33)	1.55(2)	C(33)–C(35)	1.48(2)	C(69)–C(70)	1.52(2)	C(69)–C(71)	1.55(2)
C(33)–C(34)	1.56(2)	C(35)–C(36)	1.52(2)	C(71)–C(72)	1.49(2)	C(74)–O(18)	1.24(2)
C(73)–O(15)	1.23(2)	C(73)–O(14)	1.28(2)	C(74)–O(17)	1.30(2)	C(74)–O(16)	1.33(2)
C(73)–O(13)	1.31(2)	Cu(3)–O(17)	1.906(10)				

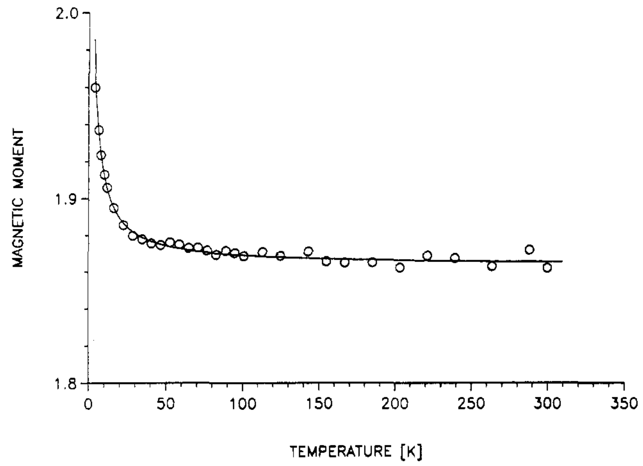

Figure 1. Temperature dependence of the magnetic moment for $\{[Cu_2(ascidH_2)(1,2\text{-}\mu\text{-}CO_3)(H_2O)_2]\cdot 2H_2O\}_2$. The best fit parameters obtained were $2J = +1.6 \pm 0.4$ cm^{-1} and $g = 2.15$ (% monomer 0.58). The best fit calculated is illustrated as a solid line.

are ≥|0.05 Å|) between the structural parameters of molecule 1 and molecule 2; the major discussion will therefore be directed toward molecule 1.

Both molecules (1 and 2) are composed of an ascidiacyclamide ligand, two copper(II) atoms, a bridging anion, and two water molecules. In addition, there are a further two water molecules associated with, and hydrogen bonded to, each molecule. Figure 2 presents a diagrammatic representation of one molecule of the complex. The identity of the bridging functionality is open to some conjecture. The synthetic methodology ($Cu(NO_3)_2$) suggested that the identity of the bridging group could be NO_3^-. The isoelectronic CO_3^{2-} represents an alternative, but no CO_3^{2-} was added to the reaction. Both bridging entities possess trigonal geometry and potentially could be isostructural. At the simplest level of differentiation between the possible bridging entities the overall charge balance of the molecule would necessitate the presence of a dianionic bridging moiety; other explanations might involve a mixed-valence molecule with separate Cu(II) and Cu(I) sites or a hydroxide coordinated to a copper(II) atom. That the bridging species was not nitrate was suggested from an experiment in which an identical product was isolated after commencing the synthesis with copper(II) chloride, with no source of nitrate present. However, when the synthesis of the complex was undertaken with rigourous exclusion of air, the typical blue

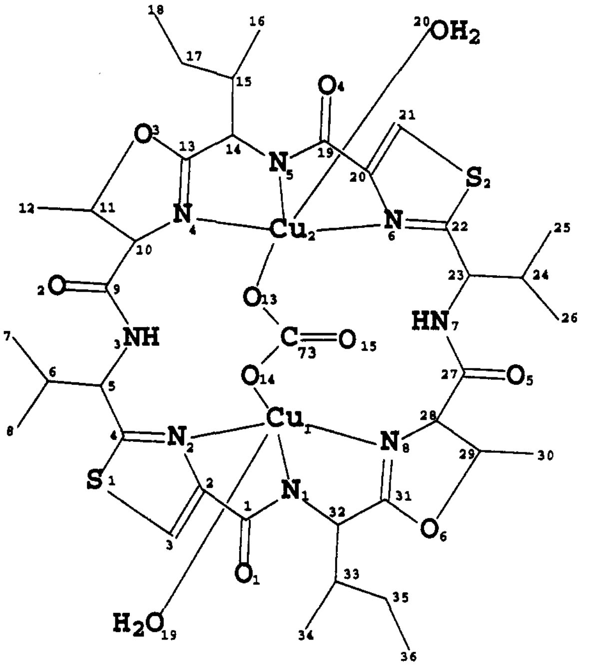

Figure 2. Diagrammatic representation and numbering scheme for $[Cu_2(ascidH_2)(1,2\text{-}\mu\text{-}CO_3)(H_2O)_2]$ (molecule 1).

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(36) Gregson, A. K.; Moxon, N. T. *Inorg. Chem.* **1982**, *21*, 3464.

Table 4. Bond Angles (deg) for $\{[\mathrm{Cu_2(ascidH_2)(1,2\text{-}\mu\text{-}CO_3)(H_2O)_2}]\cdot 2\mathrm{H_2O}\}_2$

O(14)–Cu(1)–N(1)	149.1(5)	O(14)–Cu(1)–N(8)	102.5(4)	O(17)–Cu(3)–N(16)	101.0(4)	N(9)–Cu(3)–N(16)	82.6(5)
N(1)–Cu(1)–N(8)	81.4(4)	O(14)–Cu(1)–N(2)	94.5(4)	O(17)–Cu(3)–N(10)	96.4(4)	N(9)–Cu(3)–N(10)	81.0(4)
N(1)–Cu(1)–N(2)	81.2(4)	N(8)–Cu(1)–N(2)	162.1(5)	N(16)–Cu(3)–N(10)	162.3(5)	O(17)–Cu(3)–O(23)	116.4(4)
O(14)–Cu(1)–O(19)	115.0(4)	N(1)–Cu(1)–O(19)	95.4(4)	N(9)–Cu(3)–O(23)	93.7(5)	N(16)–Cu(3)–O(23)	87.1(4)
N(8)–Cu(1)–O(19)	90.8(4)	N(2)–Cu(1)–O(19)	86.9(4)	N(10)–Cu(3)–O(23)	87.5(4)	O(16)–Cu(4)–N(13)	172.3(5)
N(5)–Cu(2)–O(13)	172.5(5)	N(5)–Cu(2)–N(4)	80.9(5)	O(16)–Cu(4)–N(12)	96.8(4)	N(13)–Cu(4)–N(12)	81.2(5)
O(13)–Cu(2)–N(4)	96.5(4)	N(5)–Cu(2)–N(6)	81.3(5)	O(16)–Cu(4)–N(14)	101.4(4)	N(13)–Cu(4)–N(14)	80.8(5)
O(13)–Cu(2)–N(6)	101.2(4)	N(4)–Cu(2)–N(6)	162.2(5)	N(12)–Cu(4)–N(14)	161.8(5)	O(16)–Cu(4)–O(24)	92.2(4)
N(5)–Cu(2)–O(20)	97.5(5)	O(13)–Cu(2)–O(20)	89.6(4)	N(13)–Cu(4)–O(24)	95.1(5)	N(12)–Cu(4)–O(24)	85.8(4)
N(4)–Cu(2)–O(20)	92.2(4)	N(6)–Cu(2)–O(20)	89.7(4)	N(14)–Cu(4)–O(24)	93.2(4)	C(37)–N(9)–C(68)	122.9(12)
C(1)–N(1)–C(32)	121.2(12)	C(1)–N(1)–Cu(1)	120.6(9)	C(37)–N(9)–Cu(3)	121.4(9)	C(68)–N(9)–Cu(3)	115.5(8)
C(32)–N(1)–Cu(1)	118.2(8)	O(1)–C(1)–N(1)	129.4(14)	O(7)–C(37)–N(9)	129.3(13)	O(7)–C(37)–C(38)	119.1(12)
O(1)–C(1)–C(2)	121.1(13)	N(1)–C(1)–C(2)	109.5(13)	N(9)–C(37)–C(38)	111.2(12)	C(39)–C(38)–N(10)	115.9(13)
N(2)–C(2)–C(3)	112.6(13)	N(2)–C(2)–C(1)	122.0(13)	C(39)–C(38)–C(37)	127.5(13)	N(10)–C(38)–C(37)	116.3(10)
C(3)–C(2)–C(1)	125(2)	C(4)–N(2)–C(2)	116.5(12)	C(40)–N(10)–C(38)	111.9(11)	C(40)–N(10)–Cu(3)	138.3(10)
C(4)–N(2)–Cu(1)	136.7(10)	C(2)–N(2)–Cu(1)	106.7(9)	C(38)–N(10)–Cu(3)	109.7(8)	C(38)–C(39)–S(3)	109.5(12)
C(2)–C(3)–S(1)	109.0(12)	C(3)–S(1)–C(4)	90.9(6)	C(40)–S(3)–C(39)	91.0(7)	N(10)–C(40)–C(41)	126.1(12)
N(2)–C(4)–C(5)	129.5(13)	N(2)–C(4)–S(1)	110.9(11)	N(10)–C(40)–S(3)	111.7(11)	C(41)–C(40)–S(3)	122.1(9)
C(5)–C(4)–S(1)	119.2(9)	C(4)–C(5)–N(3)	109.3(11)	N(11)–C(41)–C(40)	109.9(11)	N(11)–C(41)–C(42)	112.0(12)
C(4)–C(5)–C(6)	111.3(12)	N(3)–C(5)–C(6)	112.5(12)	C(40)–C(41)–C(42)	110.6(12)	C(41)–C(42)–C(44)	113.1(14)
C(5)–C(6)–C(7)	112.0(14)	C(5)–C(6)–C(8)	110.2(14)	C(41)–C(42)–C(43)	110(2)	C(44)–C(42)–C(43)	111(2)
C(7)–C(6)–C(8)	109(2)	C(9)–N(3)–C(5)	121.8(10)	C(45)–N(11)–C(41)	123.2(10)	O(8)–C(45)–N(11)	124.8(13)
O(2)–C(9)–N(3)	126.4(13)	O(2)–C(9)–C(10)	118.9(12)	O(8)–C(45)–C(46)	120.5(12)	N(11)–C(45)–C(46)	114.6(10)
N(3)–C(9)–C(10)	114.8(10)	N(4)–C(10)–C(11)	105.0(12)	N(12)–C(46)–C(45)	114.6(12)	N(12)–C(46)–C(47)	102.3(11)
N(4)–C(10)–C(9)	112.4(11)	C(11)–C(10)–C(9)	111.9(11)	C(45)–C(46)–C(47)	111.5(11)	O(9)–C(47)–C(48)	110.4(12)
O(3)–C(11)–C(12)	107.1(13)	O(3)–C(11)–C(10)	100.6(11)	O(9)–C(47)–C(46)	102.5(10)	C(48)–C(47)–C(46)	113.8(13)
C(12)–C(11)–C(10)	116(2)	C(13)–N(4)–C(10)	106.2(11)	C(49)–N(12)–C(46)	106.6(11)	C(49)–N(12)–Cu(4)	111.8(9)
C(13)–N(4)–Cu(2)	111.6(9)	C(10)–N(4)–Cu(2)	140.4(9)	C(46)–N(12)–Cu(4)	138.8(9)	C(49)–O(9)–C(47)	104.8(10)
C(13)–O(3)–C(11)	105.1(10)	N(4)–C(13)–O(3)	117.7(12)	N(12)–C(49)–O(9)	118.4(12)	N(12)–C(49)–C(50)	122.6(12)
N(4)–C(13)–C(14)	122.9(12)	O(3)–C(13)–C(14)	119.2(11)	O(9)–C(49)–C(50)	119.0(12)	N(13)–C(50)–C(49)	102.0(10)
N(5)–C(14)–C(15)	115.1(12)	N(5)–C(14)–C(13)	100.0(11)	N(13)–C(50)–C(51)	113.4(11)	C(49)–C(50)–C(51)	111.0(11)
C(15)–C(14)–C(13)	111.9(12)	C(14)–C(15)–C(16)	113.3(13)	C(53)–C(51)–C(52)	109.8(13)	C(53)–C(51)–C(50)	113.7(12)
C(14)–C(15)–C(17)	110(2)	C(16)–C(15)–C(17)	112(2)	C(52)–C(51)–C(50)	113.2(12)	C(54)–C(53)–C(51)	116(2)
C(18)–C(17)–C(15)	114(2)	C(19)–N(5)–C(14)	117.4(12)	C(55)–N(13)–C(50)	117.2(12)	C(55)–N(13)–Cu(4)	123.1(10)
C(19)–N(5)–Cu(2)	122.2(10)	C(14)–N(5)–Cu(2)	120.4(9)	C(50)–N(13)–Cu(4)	118.9(8)	O(10)–C(55)–N(13)	129.9(13)
O(4)–C(19)–N(5)	132.0(14)	O(4)–C(19)–C(20)	118.6(13)	O(10)–C(55)–C(56)	123.0(14)	N(13)–C(55)–C(56)	107.1(14)
N(5)–C(19)–C(20)	109.4(12)	C(21)–C(20)–N(6)	114.4(14)	C(57)–C(56)–N(14)	114.5(13)	C(57)–C(56)–C(55)	126.2(14)
C(21)–C(20)–C(19)	128(2)	N(6)–C(20)–C(19)	117.8(11)	N(14)–C(56)–C(55)	119.3(12)	C(58)–N(14)–C(56)	108.9(11)
C(22)–N(6)–C(20)	109.1(11)	C(22)–N(6)–Cu(2)	141.6(10)	C(58)–N(14)–Cu(4)	141.8(11)	C(56)–N(14)–Cu(4)	109.3(9)
C(20)–N(6)–Cu(2)	109.2(8)	C(20)–C(21)–S(2)	112.7(13)	C(56)–C(57)–S(4)	111.9(12)	C(57)–S(4)–C(58)	89.9(7)
C(21)–S(2)–C(22)	90.3(7)	N(6)–C(22)–C(23)	124.0(13)	N(14)–C(58)–C(59)	123.8(12)	N(14)–C(58)–S(4)	114.8(11)
N(6)–C(22)–S(2)	113.5(10)	C(23)–C(22)–S(2)	122.4(10)	C(59)–C(58)–S(4)	121.2(9)	N(15)–C(59)–C(58)	111.6(12)
N(7)–C(23)–C(24)	114.5(12)	N(7)–C(23)–C(22)	111.0(11)	N(15)–C(59)–C(60)	113.2(11)	C(58)–C(59)–C(60)	112.6(11)
C(24)–C(23)–C(22)	111.1(12)	C(23)–C(24)–C(26)	111.7(14)	C(62)–C(60)–C(61)	112.3(14)	C(62)–C(60)–C(59)	109.9(13)
C(23)–C(24)–C(25)	110.1(12)	C(26)–C(24)–C(25)	110.8(14)	C(61)–C(60)–C(59)	112.4(12)	C(63)–N(15)–C(59)	122.3(12)
C(27)–N(7)–C(23)	119.7(12)	O(5)–C(27)–N(7)	125.0(14)	O(11)–C(63)–N(15)	122.1(13)	O(11)–C(63)–C(64)	123.6(13)
O(5)–C(27)–C(28)	121.6(13)	N(7)–C(27)–C(28)	113.3(13)	N(15)–C(63)–C(64)	114.3(11)	N(16)–C(64)–C(63)	105.8(11)
N(8)–C(28)–C(27)	108.2(11)	N(8)–C(28)–C(29)	101.3(12)	N(16)–C(64)–C(65)	100.4(10)	C(63)–C(64)–C(65)	110.1(11)
C(27)–C(28)–C(29)	110.7(11)	O(6)–C(29)–C(30)	107.8(13)	O(12)–C(65)–C(66)	109.4(12)	O(12)–C(65)–C(64)	104.5(10)
O(6)–C(29)–C(28)	103.7(11)	C(30)–C(29)–C(28)	114.8(13)	C(66)–C(65)–C(64)	112.3(13)	C(67)–N(16)–C(64)	109.3(11)
N(8)–C(31)–O(6)	117.4(13)	N(8)–C(31)–C(32)	122.5(12)	C(67)–N(16)–Cu(3)	109.0(10)	C(64)–N(16)–Cu(3)	138.3(9)
O(6)–C(31)–C(32)	120.1(13)	C(31)–N(8)–C(28)	107.9(11)	C(67)–O(12)–C(65)	105.6(11)	N(16)–C(67)–O(12)	116.2(14)
C(31)–N(8)–Cu(1)	111.4(9)	C(28)–N(8)–Cu(1)	139.7(9)	N(16)–C(67)–C(68)	123.8(13)	O(12)–C(67)–C(68)	120.0(13)
C(31)–O(6)–C(29)	106.5(11)	N(1)–C(32)–C(31)	103.8(11)	N(9)–C(68)–C(67)	104.3(11)	N(9)–C(68)–C(69)	113.4(12)
N(1)–C(32)–C(33)	114.3(12)	C(31)–C(32)–C(33)	109.1(12)	C(67)–C(68)–C(69)	111.3(12)	C(70)–C(69)–C(71)	112.6(14)
C(35)–C(33)–C(32)	112.2(13)	C(35)–C(33)–C(34)	113(2)	C(70)–C(69)–C(68)	111.3(12)	C(71)–C(69)–C(68)	109.5(12)
C(32)–C(33)–C(34)	111.5(13)	C(33)–C(35)–C(36)	112(2)	C(72)–C(71)–C(69)	111.2(14)	O(18)–C(74)–O(17)	123.3(13)
O(15)–C(73)–O(14)	124.8(14)	O(15)–C(73)–O(13)	119.6(13)	O(18)–C(74)–O(16)	121.8(12)	O(17)–C(74)–O(16)	114.7(12)
O(14)–C(73)–O(13)	115.5(12)	C(73)–O(13)–Cu(2)	115.4(8)	C(74)–O(16)–Cu(4)	114.8(8)	C(74)–O(17)–Cu(3)	131.1(9)
C(73)–O(14)–Cu(1)	129.9(9)	O(17)–Cu(3)–N(9)	149.7(5)				

coloration of the methanol solution did not develop, and the blue crystalline product did not form. Other than using neutron diffraction, the X-ray technique has severe limitations for an unambiguous identification of whether an element is carbon or nitrogen. For a sample of the complex isolated from a reaction where the starting copper salt was copper(II) chloride, the structure was fully refined (data set one) with the XO_3 group being refined isotropically. With X = N, the U_{iso} for N is 0.05, 0.06 and that for O is 0.03–0.05, with $R = 0.0460$; for X = C, U_{iso} for C is 0.03, 0.03 and that for O is 0.03–0.05, with $R = 0.0455$. Assuming that in a triangular ion the central atom would have a lower U_{iso} value than the perimeter atoms, the identity of the bridging species was assumed to be carbonate at the crystallographic level. The full refinement was undertaken on the data set (data set two) obtained from crystals isolated from reaction between copper(II) nitrate and $\mathrm{ascidH_4}$, as described, which were subsequently investigated by magnetic moment determination, mass spectrometry, and EPR. The blue complex formed in the different reactions was found to be crystallographically independent of the nature of the copper(II) salt employed in the synthesis and, in each case, was found to contain carbonate.

In the $[\mathrm{Cu_2(ascidH_2)(1,2\text{-}\mu\text{-}CO_3)(H_2O)_2}]\cdot 2\mathrm{H_2O}$ molecule the coordination geometry about each copper(II) site is formed by the nitrogen atom of the deprotonated amide (N(1) or N(5)), the nitrogen atom from the oxazoline ring (N(8) or N(4)), the nitrogen atom from the thiazole ring (N(2) or N(6)), and the oxygen atom from a bridging carbonate anion; the oxygen atom of a bound water molecule occupies the apical position on each copper(II) atom. The geometry around Cu(2) may be considered as a distorted octahedron if the long Cu(2)···O(14) interaction (2.76 Å) is considered. Figures 3 and 4a,b show the structure of one

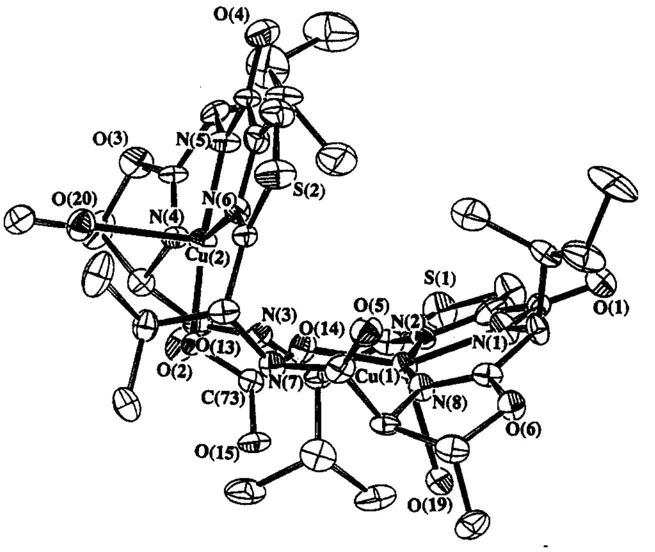

Figure 3. PLATON plot of [Cu$_2$(ascidH$_2$)(1,2-μ-CO$_3$)(H$_2$O)$_2$]·2H$_2$O (molecule 1) showing the saddle conformation. (For clarity only the Cu, O, N, and S atoms have been labeled.)

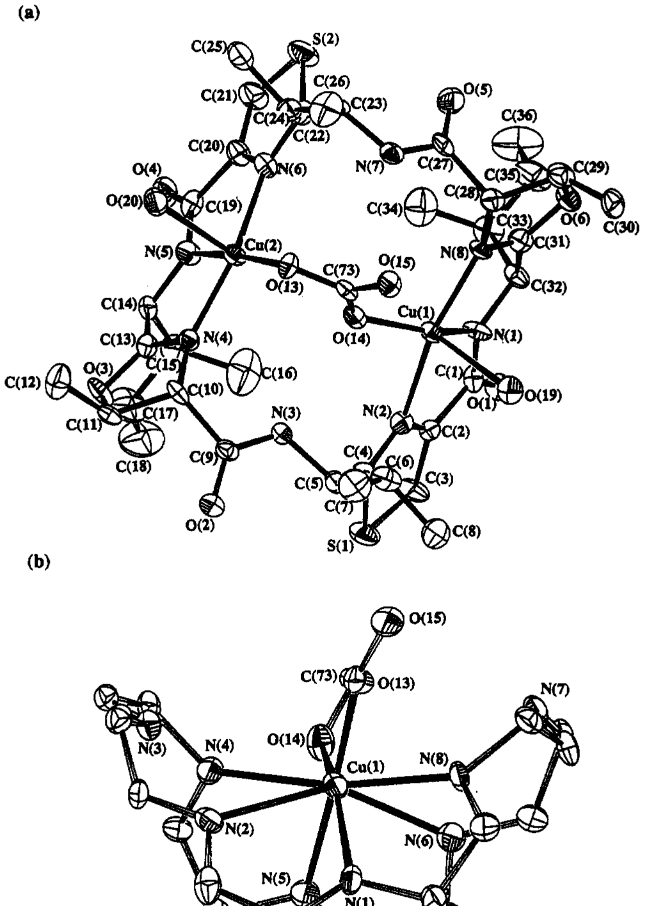

Figure 4. (a) PLATON plot of [Cu$_2$(ascidH$_2$)(1,2-μ-CO$_3$)(H$_2$O)$_2$]·2H$_2$O (molecule 1) showing the coordination of the CO_3^{2-} molecule. (b) PLATON plot of [Cu$_2$(ascidH$_2$)(1,2-μ-CO$_3$)(H$_2$O)$_2$]·2H$_2$O (molecule 1) viewed along the Cu(1)–Cu(2) axis and including only the atoms in the macrocyclic ring.

molecule. The five-coordinate geometry around Cu(1) is considerably distorted from that of a square-based pyramid, with the metal atom, N(2), and N(8) below the mean plane of the donor atoms (-0.26, -0.25, and -0.24 Å, respectively) and N(1) and O(14) above the plane (0.29 and 0.21 Å). For Cu(2) the distortion from the mean plane is significantly less than for Cu(1) (Cu(2), 0.07 Å; N(6), 0.05 Å; N(4), 0.06 Å; N(5), -0.06 Å; O(13), -0.04 Å). The most obvious manifestation of the structural difference between the two copper sites is the difference in the angles N(1)–Cu(1)–O(14) and N(5)–Cu(2)–O(13), 149.1(5) and 172.5(5)°, respectively. The Cu–N(amide) distances Å (Cu(1)–N(1) = 1.955(11); Cu(2)–N(5) = 1.923(11)) are similar to those reported for the (tetraglycinato)cuprate(II) complex with an average Cu–N$_{\text{amide}}$ distance of 1.926 Å, range 1.912–1.944 Å.[37] The amide nitrogens N(3) and N(7) remain uncoordinated. The Cu–N$_{\text{thiazole}}$ (Cu(1)–N(2) = 2.100(10); Cu(2)–N(6) = 2.070(11) Å) and Cu–N$_{\text{oxazoline}}$ distances (Cu(1)–N(8) = 2.020(10); Cu(2)–N(4) = 2.014(11) Å) are longer than those reported for the complexes *trans*-dichlorobis(2,4-dimethylthiazole)copper(II) (1.985 Å)[38] and bis(μ-bromo)tetrakis(μ-2-(4,4-dimethyl-2-oxazolin-2-yl)-4-methylphenyl-*N*,*C*,*C*)hexacopper(II) (1.980, 1.948, 1.972, 1.974 Å).[39] The planarity imposed by the conjugation of thiazole rings and associated amides has been commented on previously[11,40–42] and is retained in this structure. The Cu–O$_{\text{water}}$ distances (Cu(1)–O(19) = 2.328(11) Å; Cu(2)–O(20) = 2.378(11) Å) are similar to that reported previously for a complex in which the metal ion is square pyramidal and the solvent donor (water) axial.[43] There is at least one example, however, where an axial Cu–O$_{\text{water}}$ distance in a metal complex is extremely short (2.263(6) Å).[44]

The two metal atoms (Cu···Cu distance 4.43 Å) are bridged by the carbonate anion, the bridge being formed through the basal plane of each metal ion. Two Cu–O$_{\text{carbonate}}$ distances are similar (Cu(1)–O(14) = 1.922(10); Cu(2)–O(13) = 1.939(9) Å), the other Cu–O$_{\text{carbonate}}$ distances (Cu(2)···O(14) = 2.78 Å, and Cu(1)···O(15) = 3.28 Å) suggest a distant contact in the former case. Two C–O bonds are associated with the bridge C(73)–O(14) and C(73)–O(13) (1.28(2) and 1.31(2) Å, respectively); the third bond associated with the carbonate (C(73)–O(15) 1.23(2) Å) is shorter. The bond lengths observed are similar to those reported for copper(II) complexes containing μ-CO_3^{2-}.[45–54] The O(*n*)–C(73)–O(15) angles (*n* = 13, 14) are as anticipated,[47–51] 119.6(13) and 124.8(14)°, respectively; however, the angle O(13)–C(73)–O(14) (115.5(12)°) suggests some distortion around the bridge. The O(13)–C(73)(–O(15))–O(14) moiety does not lie symmetrically within the macrocyclic ring with C(73)–O(15) tilted toward the C(22)–C(23)–N(7)–C(27)–C(28) fragment (Figure 3b).

Two solvent water molecules in the lattice are involved in intramolecular hydrogen bonds with each [Cu$_2$(ascidH$_2$)(1,2-

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μ-$CO_3)(H_2O)_2]$ moiety. One lattice water molecule is hydrogen bonded to a bound water molecule (O(26)···O(19) = 2.68 Å) and to an oxygen atom of the bridging carbonate (O(26)···O(15), = 2.71 Å); the second water molecule is only associated with O(20) (O(25)···O(20) = 2.79 Å). There is also the possibility that the 1,2-μ-CO_3^{2-} bridge is stabilized by hydrogen bonding to the uncoordinated amides of the peptide fragments (N(7)···O(15) = 2.95 Å; N(3)···O(14) = 2.80 Å). There are no intermolecular hydrogen bonds.

The versatile nature of the coordination behavior of carbonate has been addressed previously.[50] The considerably distorted geometry (from that of the free anion (D_{3h})) of the carbonate observed in the present case is similar to that reported for $Na_2[Cu(CO_3)_2]$,[51] $Na_2[Cu(CO_3)_2(H_2O)_3]$[52,53] (described as 2L, 2M, *syn, anti*[50]), and [LZn(μ-CO_3)ZnL] (L = hydrotris(3,5-diisopropyl-1-pyrazolyl)borate).[54] For [LZn(μ-CO_3)ZnL] the carbonate is bound to one Zn site in a bidentate mode (Zn–O = 1.979(9) and 2.335(8) Å) and unidentate to the other Zn site (Zn–O = 1.907(8) Å), with a long Zn···O interaction observed (2.618(9) Å) at the formally unidentate site.[53] The Zn···Zn distance was reported as 4.580(3) Å. For the copper complex of the same ligand, [LCu(μ–CO_3)CuL], the carbonate ion is bound virtually symmetrically between the two metal atoms with Cu–O distances 2.019(4), 1.999(4) and 2.028(4), 2.000(5) Å, the Cu···Cu distance being 4.044(2) Å.[54] In the complex $[Cu_4(dpt)_4(CO_3)Cl_2]^{4+}$ (dpt = bis(3-aminopropyl)amine) CO_3^{2-} is at the center of a rectangle of copper(II) ions and bridges the four copper sites, with one O atom bonded to two Cu atoms (Cu···Cu – 3.6 Å) or two O atoms bonded to two Cu sites (Cu···Cu – 4.7 Å).[50]

The X-ray crystal structure of the ascidiacyclamide ligand itself has been reported.[12] The 24-membered macrocyclic backbone assumes a nearly square shape with the four heterocyclic rings at the corners, an arrangement classified as a type II conformation;[40] all eight nitrogen atoms are endocyclic, and the cyclic peptide chain takes on a saddle-shaped conformation.[12] There are no intramolecular hydrogen bonds. The alternate type I conformation is rectangular, stabilized by two intramolecular N–H···O hydrogen bonds.[40] For ascidiacyclamide, the type II conformation is predominant in solution.[11]

Comparison of structural parameters for free ascidiacyclamide and the bis(copper(II)) complex indicate that complexation of the metal ions causes only small changes in the bond angles and bond lengths. There are, however, significant conformational differences ($\Delta > 50°$) (Table S4, supplementary material) associated with the peptide fragments C(22)–C(23)–N(7)–C(27) and N(7)–C(27)–C(28)–N(8) in the free ligand and the metal complex. Smaller differences ($10° < \Delta < 50°$) are associated with the N(6)–C(22)–C(23)–N(7) and N(2)–C(4)–C(5)–N(3), C(27)–C(28)–N(8)–C(31) and C(9)–C(10)–N(4)–C(13), and C(31)–C(32)–N(1)–C(1) and C(13)–C(14)–N(5)–C(19) peptide residues, the distortions being associated with the accommodation of the metal ions within the macrocyclic ring. The ascidiacyclamide ligand complexes the two copper(II) atoms in an environment such that the hydrophobic saddle arrangement of the free ligand is essentially preserved (Figure 3). The screening of the metal ion by this ligand appears typical of such ionophore–metal complexes.[55]

Mass Spectrometry. Pneumatically assisted electrospray[22] ionization (ion spray)[23] mass spectrometry is a low-resolution technique involving a mild ionization method of producing unfragmented molecular ions. These readily form adducts with extraneous/exogenous ions in solution. Thus ascidiacyclamide was detected at low orifice potentials (OR = 45 V) by ion spray mass spectrometry (Table 5) as intact molecular ion adducts of either H^+, Na^+, K^+, or NEt_3H^+. At higher potentials both adducts and copper complexes tended to fragment.

Table 5. Summary of Observed Mass Spectral Data for Ascidiacyclamide and Copper(II) Complex Species

m/z	assgnt[a]
757.8	$[ascidH_4 + H^+]^+$
779.8	$[ascidH_4 + Na^+]^+$
795.8	$[ascidH_4 + K^+]^+$
858.8	$[ascidH_4 + NEt_3H^+]^+$
818.6	$[ascidH_3 + Cu^{2+}]^+$
837.6	$[ascidH_3 + Cu^{2+} + H_2O]^+$
881.0	$[ascidH_2 + 2Cu^{2+} - H^+]^+$
899.6	$[ascidH_2 + 2Cu^{2+} + H_2O - H^+]^+$
917.0	$[ascidH_2 + 2Cu^{2+} + 2H_2O - H^+]^+$
932.4	$[ascidH_2 + 2Cu^{2+} + 3H_2O - H^+]^+$
943.4	$[ascidH_2 + 2Cu^{2+} + CO_3^{2-} + H^+]^+$
965.4	$[ascidH_2 + 2Cu^{2+} + CO_3^{2-} + Na^+]^+$
979.6	$[ascidH_2 + 2Cu^{2+} + CO_3^{2-} + 2H_2O + H^+]^+$
981.4	$[ascidH_2 + 2Cu^{2+} + CO_3^{2-} + K^+]^+$
983.2	$[ascidH_2 + 2Cu^{2+} + CO_3^{2-} + H_2O + Na^+]^+$
1043.8	$[ascidH_2 + 2Cu^{2+} + CO_3^{2-} + NEt_3H^+]^+$
1079.4	$[ascidH_2 + 2Cu^{2+} + CO_3^{2-} + 2H_2O + NEt_3H^+]^+$

[a] Based on masses calculated from atomic isotopes of natural abundance.

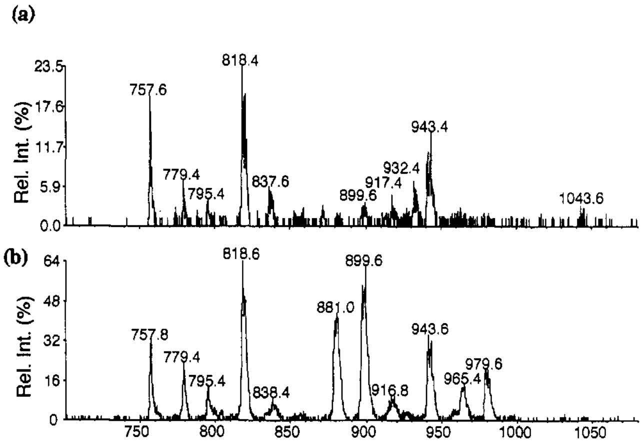

Figure 5. Ion spray mass spectrum for crystals of $[Cu_2(ascidH_2)(1,2\text{-}\mu\text{-}CO_3)(H_2O)_2]\cdot 2H_2O$ dissolved in methanol: (a) OR = 45 V; (b) OR = 100 V. Refer to the text and Table 5 for peak assignments.

The ion spray mass spectrum (OR = 45 V; Figure 5a) of crystals of $[Cu_2(ascidH_2)(1,2\text{-}\mu\text{-}CO_3)(H_2O)_2]\cdot 2H_2O$, dissolved in methanol, primarily contained peaks attributed to $[ascidH_2 + 2Cu^{2+} + CO_3^{2-} + H^+]^+$, $[ascidH_3 + Cu^{2+}]^+$, and $[ascidH_4 + H^+]^+$. As the orifice potential was raised (OR ~ 100 V; Figure 5b), signals became apparent for $[ascidH_2 + 2Cu^{2+} + CO_3^{2-} + (H^+/Na^+/K^+)]^+$, $[ascidH_2 + 2Cu^{2+} + 2H_2O - H^+]^+$, $[ascidH_2 + 2Cu^{2+} + H_2O - H^+]^+$, $[ascidH_2 + 2Cu^{2+} - H^+]^+$, $[ascidH_3 + Cu^{2+} + H_2O]^+$, $[ascidH_3 + Cu^{2+}]^+$, and $[ascidH_4 + (H^+/Na^+/K^+)]^+$ (Table 5). Peaks attributed to copper species were broad due to isotopic distributions, and this is responsible for slight differences between some calculated versus experimental m/z values. The Na^+ and K^+ ions indicated are trace impurities in methanol at the concentrations employed.

To confirm the identity of the bridging moiety, hitherto assumed to be 1,2-μ-CO_3^{2-} rather than the isostructural 1,2-μ-NO_3^-, experiments were undertaken in which methanol solutions of $ascidH_4$, copper(II) triflate, and triethylamine (ratio 1:2:2–4) were reacted with 1–2 molar equiv of $K^{14}NO_3$ versus $K^{15}NO_3$. Peaks attributed (Table 5) to $[ascidH_2 + 2Cu^{2+} + CO_3^{2-} + (H^+/K^+/NEt_3H^+)]^+$, $[ascidH_2 + 2Cu^{2+} + H_2O - H^+]^+$, $[ascidH_3 + Cu^{2+}]$, and $[ascidH_4 + (K^+/NEt_3H^+)]^+$ were detected with no $^{14}N/^{15}N$ isotope differences anywhere in the spectrum from m/z = 200 to 1200. Alternatively, when the experiments were performed using $Na_2{}^{12}CO_3$ and $Na_2{}^{13}CO_3$, in place of nitrate, the principal peaks observed in the mass spectrum at low orifice potential were attributed to $[ascidH_2 + Cu^{2+} + CO_3^{2-} + (H^+/$

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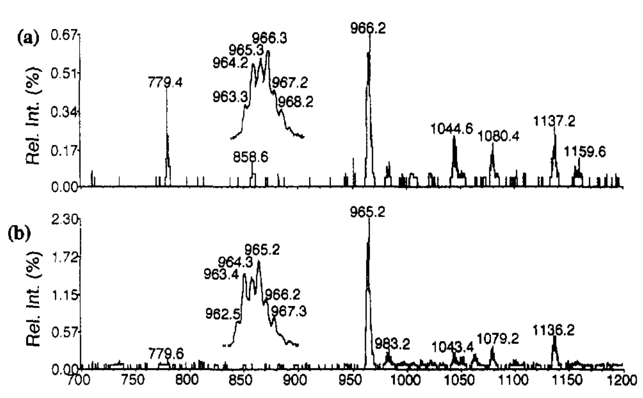

Figure 6. Ion spray mass spectrum for the reaction mixture containing ascidH_4:Cu$(CF_3SO_3)_2$:NEt_3:Na_2CO_3 (1:2:2:2) in methanol (OR = 45 V): (a) with $^{13}CO_3^{2-}$, inset [ascidH_2 + $2Cu^{2+}$ + $^{13}CO_3^{2-}$ + Na^+]$^+$; (b) $^{12}CO_3^{2-}$, inset [ascidH_2 + $2Cu^{2+}$ + $^{12}CO_3^{2-}$ + Na^+]$^+$. See Table 5 and the text for peak assignments.

Na^+/NEt_3H^+)]$^+$ and [ascidH_4 + (Na^+/NEt_3H^+)]$^+$. There was a clear ^{12}C/^{13}C isotope shift for all peaks assigned to the CO_3^{2-} species but for no other peaks in the mass spectrum (Figure 6a, $^{13}CO_3^{2-}$; Figure 6b, $^{12}CO_3^{2-}$). The result firmly establishes the identity of the bridging moiety in the complex as CO_3^{2-}. Furthermore, there was an indication that addition of progressively more NEt_3 (2, 3, and 4 equiv), or longer reaction times, led to higher concentrations of the species containing carbonate.

EPR Spectroscopy. X-band EPR spectra of the crushed crystalline solid, and of it dissolved in methanol, are shown in Figure 7a,b,d, respectively. The EPR spectra can be interpreted in terms of a spin Hamiltonian involving inter- and intramolecular dipole–dipole coupling between two copper(II) ions.[25] Assuming an axially symmetric binuclear copper(II) complex, computer simulation of the powder spectrum (Figure 7a) yields an internuclear copper–copper distance of 7.8 Å (ξ, 144°), which is consistent with the average intermolecular copper···copper distances (6.95–9.96 Å) obtained from X-ray diffraction data.

EPR spectra of dilute frozen methanol solutions were measured in order to eliminate intermolecular dipole–dipole coupling. The spectra (Figure 7b,d) reveal resonances around 3200 × 10^{-4} and 1500 × 10^{-4} T which arise from $\Delta M_s = \pm 1$ and $\Delta M_s = \pm 2$ transitions in an $S = 1$ spin system arising from intramolecular dipole–dipole coupling between two copper(II) ions. EPR studies at 120 K cannot, however, distinguish between dipole–dipole coupling and a weak ferromagnetic interaction ($2J = +1.6 \pm 0.4$ cm^{-1}) as found from the magnetic susceptibility measurements. Computer simulation (see Experimental Section) of these resonances (Figure 7c,e) assuming an axially symmetric copper dimer produces the g and A matrices ($g_\parallel = 2.31$, $g_\perp = 2.10$ and $A_\parallel = 111 \times 10^{-4}$ cm^{-1}, $A_\perp = 70 \times 10^{-4}$ cm^{-1}), an intramolecular Cu(1)···Cu(2) distance of 3.60 Å, and the angles ξ, η, and τ (144 ± 5, 0 ± 5, and 0 ± 5°, respectively) which define the relative orientation of Cu(1) with respect to Cu(2).[25]

A comparison of the intramolecular Cu(1)···Cu(2) distance and relative orientation of the two copper(II) ions obtained from X-ray crystallography and EPR studies of the crystal in frozen solution reveal significant differences. In particular the binuclear copper(II) ascidiacyclamide complex in solution, based on the simulation of the EPR spectrum, appears to have a significantly shorter intramolecular distance (3.60 compared to 4.43 Å) and an axial symmetry (ξ, 144°; η, 0°; τ, 0°) compared with triclinic symmetry (ξ, O(20)–Cu(2)–Cu(1), 154.5°; η, N(4)–Cu(2)–Cu(1), 97.6°; τ, O(20)–Cu(2)–Cu(1)–O(19), 40.5°) observed in the crystal structure. Computer simulation studies of the frozen solution EPR spectrum assuming triclinic symmetry and the parameters obtained from the X-ray structure were unable to reproduce the experimental line shape. Consequently, these differences suggest a structural reorganization of the binuclear copper site when the binuclear copper ascidiacyclamide complex is dissolved in methanol. Solution studies also indicate that the formation of [Cu_2(ascidH_2)(1,2-μ-CO_3)(solvent)$_2$] is complicated by a series of equilibria, which appear to involve reorganization of the binuclear center, and in which at least two other forms of the binuclear complex are involved. These other binuclear complexes may be those observed in the mass spectrum, [ascidH_2 + $2Cu^{2+}$ + $2H_2O$ – H^+]$^+$, [ascidH_2 + $2Cu^{2+}$ + H_2O – H^+]$^+$, and [ascidH_2 + $2Cu^{2+}$ – H^+]$^+$. Detailed equilibrium copper binding studies on the related molecule patellamide D reveal the presence of three binuclear complexes, and we believe that the formation of the 1,2-μ-CO_3^{2-} ascidiacyclamide complex occurs in a similar way.[9]

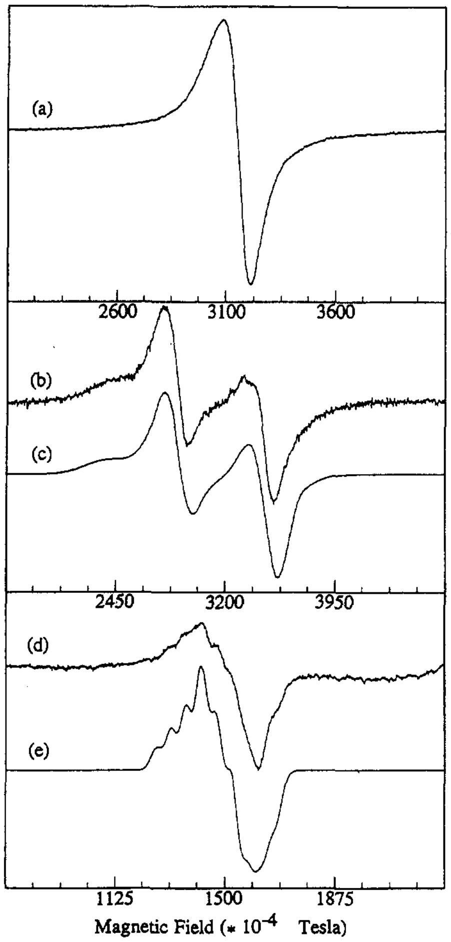

Figure 7. X-band EPR spectra of [Cu_2(ascidH_2)(1,2-μ-CO_3)$(H_2O)_2$]: (a) Room-temperature powder spectrum, ν = 9.2991 GHz; (b) frozen methanol solution spectrum showing the $\Delta M_s = \pm 1$ transitions, ν = 9.4721 GHz; (c) computer simulation of (b), LSE = 2.046 × 10^{-1}, 140- and 30-MHz line widths at half-height for the parallel and perpendicular resonances, respectively; (d) frozen methanol solution spectrum showing the $\Delta M_s = \pm 2$ transitions, ν = 9.4721 GHz; (e) computer simulation of (d), LSE = 5.482 × 10^{-2}, 20- and 22-MHz line widths at half-height for the parallel and perpendicular resonances, respectively.

The formation of (μ-carbonato)copper(II) complexes, with macrocyclic and multidentate ligands, by fixation of CO_2 has been observed previously[54,56–61] but not by a naturally occurring macrocycle. Proposed mechanisms for the spontaneous fixation of CO_2 implicate either the nucleophilic attack of a coordinated

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peroxo group[59,60] or a coordinated hydroxo group on the electrophilic carbon of CO_2, in the latter case followed by water dissociation,[61] or attack by carbonate formed in the basic solutions after absorption of atmospheric CO_2. While the mechanistic details of the incorporation of carbonate in the present case have not been investigated, potentiometric titrations involving copper(II) and ascidiacyclamide suggest the presence of a Cu–OH moiety.[62]

It is clear from the above work that the dimeric copper complex of the cyclic peptide ascidiacyclamide has an unusual affinity for carbonate. The detection of the $1,2\text{-}\mu\text{-}CO_3^{2-}$ ligand implicates *in vitro* fixation of atmospheric CO_2, absorbed by the strongly basic solutions, as carbonate in the dimeric copper complex of the cyclic peptide ascidiacyclamide. There may also be *in vivo* implications of the observation reported here. The presence of calcium carbonate spicules in the ascidians[63] offers the intriguing prospect that these cyclic ligands, in association with metal ions, are involved in the activation and mobilization of CO_2 for subsequent incorporation in the spicules.

Note Added in Proof. A novel Ag_4 cluster, with the cyclic peptide westiellamide isolated from the ascidian *Lissoclinum bistratum*, has recently been reported: Wipf, P.; Venkatraman, S.; Miller, C. P.; Geib, S. J. *Angew. Chem., Int. Ed. Engl.*, in press.

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Supplementary Material Available: Listings of full crystal data (Table S1), complete bond distances (Å), bond angles (deg), and torsion angles (deg) for molecules 1 and 2 (Tables S3 and S4), anisotropic thermal parameter (Table S5), and hydrogen coordinates and thermal parameters (Table S6) and a diagram showing the full numbering scheme for molecules 1 and 2 (Figure S1), a crystal packing diagram (Figure S2), and a PLATON plot of $[Cu_2(ascidH_2)(\mu\text{-}CO_3)(H_2O)_2]\cdot 2H_2O$ (Figure S4b) with all atoms (except H's) included (15 pages). Ordering information is given on any current masthead page.

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