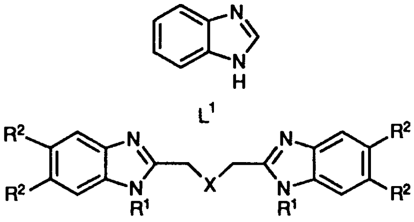
Model Studies of Benzimidazole Complexes of Cu, Zn, and Cd. Crystal Structures of 1,5-Bis(benzimidazol-2-yl)-3-thiapentane Complexes of $CuBr_2$ and $Cu(NO_3)_2$ and Nuclear Magnetic Resonance Studies of Exchange of 1,6-Bis(benzimidazol-2-yl)-2,5-dithiahexane on Cd†

Joyce C. Lockhart,* William Clegg,* M. N. Stuart Hill, and David J. Rushton
Department of Chemistry, University of Newcastle upon Tyne, Newcastle upon Tyne NE1 7RU

Some complexes of bridged bis(benzimidazole) ligands of various bridge types with Cu, Zn, and Cd have been examined as potential models of structure and mobility of biological metal binding sites. Two distinct (distorted trigonal bipyramidal and square-based pyramidal verging on distorted octahedral) environments have been found in crystal structures for copper bromide and nitrate complexes of one ligand, 1,5-bis(benzimidazol-2-yl)-3-thiapentane. N.m.r. studies of the exchange of 1,6-bis(benzimidazol-2-yl)-2,5-dithiahexane [or its ring-methylated analogue 1,6-bis(5',6'-dimethylbenzimidazolyl)-2,5-dithiahexane] in cadmium chloride mixtures show that it occurs *via* a rate-determining dissociative step, where there is cadmium salt in excess of a 1 : 1 ratio of M : L, but that bimolecular ligand exchange is rate-determining when the ratio M : L is less than unity. A hypothesis as to the minimum rearrangements necessary to explain the n.m.r. spectra is proposed. The crystal structure of 1,6-bis(1'-octylbenzimidazolyl)-2,5-dithiahexane was obtained. This ligand, lacking prototropy, served to test the role of protons in the hypothesis.



	X	R^1	R^2
L^2	$S(CH_2)_2S$	H	H
L^3	O	H	Me
L^4	CH_2SCH_2	H	H
L^5	$O(CH_2)_2O$	H	H
L^6	$S(CH_2)_2S$	H	Me
L^7	$S(CH_2)_2S$	C_8H_{17}	H
L^8	NR	H	H
	(R = alkyl)		

Classical co-ordination chemistry dealt with classical symmetrical polyhedra. The understanding of biological schemes for metal co-ordination has opened chemists' eyes to the kinetic and thermodynamic benefits of distorted metal environments. Polydentate and macrocyclic ligands have been described containing benzimidazole (L^1), together with OH, O, S, and CO_2^- donor groups which simulate the environments found in metalloproteins, and which provide a rich source of new co-ordination chemistry, with interesting stereochemistry and kinetic properties.[1] In model studies the copper sites of metalloproteins such as haemocyanin, superoxide dismutase, plastocyanin, and azurin are targeted.[2] Information from model copper(II) complexes of imidazole and benzimidazole ligands has been influential in deepening understanding of the factors causing variations on copper(II) geometry so far found, although mechanistic studies of the model binding site are few. There are many convenient features of ligands containing benzimidazole (L^1). The imidazole nitrogens of benzimidazole and histidine (His) are similar[3] with pK_a (H_2O) of 5.5 (L^1) and 6.0 (His) so that prototropy at biological pH is possible, permitting pH control of metal co-ordination to imidazole nitrogen. The extra rigidity and bulk of benzimidazole relative to imidazole may be advantageous in attempts to mimic constrained biological co-ordination spheres.[4] In a number of crystal-structure determinations it has been noted that ligands containing two benzimidazole units tend to stack with the aromatic rings parallel, and that such ligands favour a linear N–Cu–N co-ordination.[5–7] Ligand L^4 was originally synthesised to provide a model copper environment approximating to the methionine donor of certain blue copper proteins, such as plastocyanin and azurin,[7] and there are three crystal structures of copper(II) complexes of this ligand, all with different co-ordination from the same donor set,[8–10] N_2O_2S. Since then a considerable range of ligands of this type has been investigated.[4] The geometry of Cu^{II} is frequently found to be distorted five-co-ordinate, lying between the trigonal bipyramid and the tetragonal pyramid. Indeed the index τ defined by Addison *et al.*[11] has been used to give a semiquantitative assessment of the deviation of a structure along the pathway from tetragonal (value 0.0) to trigonal (value 1.0). Recently, however, Reinen and co-workers[12] have noted a symmetrical five-co-ordinate structure based on a terpyridyl ligand, which is unprecedented in this series. Where there are two thioethers in the ligand chain (as in ligand L^2), there are restrictions for example on the N–Cu–N and S–Cu–S angles, which are smaller than expected. This has been demonstrated in a range of similar ligands with substituted imidazolyl polydentates.[13–16] In two instances[17,18] ligands providing just one thioether and one imidazolyl group (bidentates) have been used to supply the required co-ordination, with two or three ligands in the copper co-ordination sphere. The restrictions of the small bite of the dithio bridge are thereby lifted and the two thio ligands in particular

---

† *Supplementary data available:* see Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1990, Issue 1, pp. xix—xxii.

Table 1. Crystallographic data

	(2)	(3)	L^7
Formula	$C_{18}H_{18}CuN_6O_6S \cdot CH_3OH$	$C_{18}H_{18}Br_2CuN_4S \cdot CHCl_3$	$C_{34}H_{50}N_4S$
M	542.0	665.2	578.9
Crystal system	Monoclinic	Orthorhombic	Triclinic
a/Å	16.299(1)	11.554 4(5)	9.328(2)
b/Å	9.573(1)	14.397 0(7)	12.536(3)
c/Å	16.162(2)	14.861 2(7)	15.780(4)
α/°			84.73(2)
β/°	119.068(5)		74.06(2)
γ/°			75.33(2)
U/Å^3	2 204.1	2 472.2	1 716.0
Z	4	4	2
D_c/g cm^{-3}	1.633	1.787	1.120
μ/mm^{-1}	1.14	4.51	0.17
F(000)/electrons	1 116	1 308	628
Space group	Cc	$Pnma$	$P\bar{1}$
Crystal size (mm)	0.4 × 0.4 × 0.5	0.1 × 0.2 × 0.55	0.35 × 0.5 × 0.55
$2\theta_{max.}$/°	50	50	50
Transmission	0.66—0.71	0.15—0.19	
Reflections measured	5 022	4 976	9 592
Unique reflections	3 867	2 264	6 022
Observed reflections	3 768	1 629	3 822
R_{int}	0.015	0.024	0.025
Extinction x	$2.8(6) \times 10^{-7}$	$2.0(6) \times 10^{-7}$	0
Weighting g	0.000 16	0.000 04	0.001 19
Parameters	306	146	381
R	0.025	0.065	0.084
R'	0.031	0.055	0.115
Slope of normal probability plot	1.44	1.92	1.79
Maximum, mean Δ/σ	0.018, 0.004	0.010, 0.001	0.22, 0.03
Maximum, minimum $\Delta\rho$/e Å^{-3}	0.57, −0.43	1.14, −1.41	0.46, −0.39

can be found *trans*. Terdentate ligands with two fewer methylenes in the bridge than found with ligand L^4 have a tighter bite, as seen in various copper(II) derivatives of L^8, where some complexes have five-co-ordination, and reduced N–Cu–N angles.[19] Distorted-octahedral environments have been found for other ligands of this series, which have (*a*) rather distant axial ligand(s), often provided in the models by a co-ordinating oxy-anion.[19] The replacement of the N-alkyl group by a pyridyl nitrogen gives an even more restricted ligand.[20] More complicated ligands of the imidazolyl or benzimidazolyl type have been used to provide a binucleating site with donors appropriate for models of haemocyanin[21,22] or for laccase and tyrosinase.[23] Crystal structures for examples of all of these have been described in the appropriate references.

Another aspect of the co-ordination of benzimidazole compounds in models concerns the role of the NH group in the release of metal ion; studies of this could be relevant in providing better functional models for biological metal binding sites. Evidence for pH control of the co-ordination of His 87 has been found in the remarkable crystal structures determined for plastocyanins crystallised at different pH.[24] Since the mechanism by which donor groups exchange when co-ordinated to metals of biological interest is of considerable importance, we have also studied the kinetics of ligand and metal exchanges, using n.m.r. spectroscopy and seeking information on prototropy of the benzimidazole ligands. Unfortunately copper(II) complexes are unsuitable for n.m.r. work because of their paramagnetism, and we had to use zinc or cadmium complexes for this; however, we were unable to obtain crystals of any complexes studied in the n.m.r. work which were suitable for crystal-structure determination. In this paper we report two new crystal structures of copper complexes of ligand L^4, and some kinetic studies by one-dimensional methods using ^{1}H n.m.r. spectroscopy with ligands L^2—L^6 and their mixtures in solution with zinc or cadmium chloride.

Experimental

The ligands L^2—L^6 were prepared as previously.[5] Ligand L^7 was obtained by alkylation of L^2 in tetrahydrofuran with sodium hydride and octyl bromide by a previous route.[25]

N.M.R. Studies.—Solutions for n.m.r. spectroscopy had varying ratios of ligand and of $ZnCl_2$ or $CdCl_2$ in an equivolume mixture of $CDCl_3$ and $(CD_3)_2SO$ which had a liquid range down to *ca.* 230 K and permitted observation of ^{1}H n.m.r. spectra at low temperatues, for these solutes. Proton and ^{13}C n.m.r. spectra were run on a Bruker WB300 spectrometer.

Complexes.—One set of crystals was obtained from an n.m.r. solution (ligand L^3 and $ZnCl_2$) after it had been stored in a refrigerator for some weeks. These analysed for $[ZnCl_2L^3] \cdot 2.5(CD_3)_2SO$. Fast atom bombardment mass spectrum: *m*/*z* 433 ($ZnClL^3$) and 335 ($L^3 + H^+$) (Found: C, 44.0; H, 5.2; N, 8.3. $C_{25}H_{22}Cl_2D_{15}N_4O_{3.5}S_{2.5}Zn$ requires C, 44.2; H + D, 5.5; N, 8.2%). Proton n.m.r. [200 MHz, $CDCl_3$–$(CD_3)_2SO$ (1:1)]: δ 2.42 (12 H, 4 CH_3), *ca.* 4.0 (wide signal, exchanging residual solvent water), 4.90 (4 H, OCH_2), and 7.5—8.0 (4 H, very wide, exchanging arene H).

The crystals of the complexes used for *X*-ray analyses were obtained by recrystallisation from methanol solutions by addition of chloroform; preparation and characterisation of these complexes $[Cu(L^4)(NO_3)_2]$ (**2**) and $[Cu(L^4)Br_2]$ (**3**), has been described previously.[5] Ligand L^7 was recrystallised from chloroform and diethyl ether.

X-*Ray Crystallography.*—Crystal data are given in Table 1,

Table 2. Atomic co-ordinates (× 10^4) for complex (**2**)

Atom	*x*	*y*	*z*
Cu	5 000	7 795(1)	7 500
N(1)	4 507(1)	9 656(2)	7 521(1)
C(2)	3 575(2)	10 104(2)	6 970(2)
C(3)	2 786(2)	9 437(3)	6 274(2)
C(4)	1 961(2)	10 197(3)	5 845(2)
C(5)	1 919(2)	11 579(3)	6 102(2)
C(6)	2 681(2)	12 253(3)	6 783(2)
C(7)	3 526(2)	11 494(3)	7 218(2)
N(8)	4 416(2)	11 838(2)	7 901(2)
C(9)	4 976(2)	10 730(2)	8 057(2)
C(10)	5 998(2)	10 743(3)	8 763(2)
C(11)	6 248(2)	9 651(3)	9 531(2)
S(12)	6 128(1)	7 860(1)	9 126(1)
C(13)	7 125(2)	7 688(3)	8 913(2)
C(14)	7 254(2)	6 186(3)	8 734(2)
C(15)	6 427(2)	5 486(3)	7 939(2)
N(16)	6 516(1)	4 195(2)	7 656(1)
C(17)	5 649(2)	3 773(3)	6 936(2)
C(18)	5 365(2)	2 556(3)	6 398(2)
C(19)	4 437(2)	2 461(3)	5 744(2)
C(20)	3 806(2)	3 536(3)	5 629(2)
C(21)	4 091(2)	4 740(3)	6 158(2)
C(22)	5 040(2)	4 871(2)	6 816(2)
N(23)	5 547(1)	5 944(2)	7 455(1)
O(24)	4 368(1)	7 917(2)	6 060(1)
N(25)	4 910(1)	8 642(2)	5 868(1)
O(26)	5 682(1)	9 007(2)	6 526(1)
O(27)	4 648(2)	8 938(3)	5 034(1)
O(28)	3 852(1)	6 596(3)	7 620(2)
N(29)	3 255(2)	6 968(3)	7 867(2)
O(30)	2 543(2)	6 312(4)	7 610(3)
O(31)	3 399(2)	8 010(3)	8 359(2)
O(32)	9 871(2)	9 374(2)	8 772(2)
C(33)	9 470(3)	9 492(4)	9 346(2)

Table 3. Atomic co-ordinates (× 10^4) for complex (**3**)

Atom	*x*	*y*	*z*
Cu	159(1)	2 500	1 028(1)
Br(1)	239(1)	2 500	2 688(1)
Br(2)	−1 100(1)	2 500	−484(1)
N(1)	71(5)	3 863(4)	1 052(4)
C(2)	−955(7)	4 342(5)	1 280(5)
C(3)	−2 067(7)	4 015(6)	1 441(6)
C(4)	−2 911(7)	4 657(6)	1 661(6)
C(5)	−2 629(8)	5 596(6)	1 721(7)
C(6)	−1 537(9)	5 938(6)	1 550(6)
C(7)	−709(8)	5 276(5)	1 327(5)
N(8)	446(5)	5 360(4)	1 159(4)
C(9)	887(7)	4 504(5)	992(5)
C(10)	2 139(6)	4 377(5)	808(6)
C(11)	2 655(6)	3 461(6)	1 121(6)
S(12)	2 144(2)	2 500	432(2)
C(13)	963(21)	2 500	6 106(23)
Cl(1)	24(5)	2 500	6 901(4)
Cl(2)	452(5)	3 463(7)	5 331(5)

with other pertinent information on the data collection and structure determination. All measurements were made at room temperature on a Stoe-Siemens diffractometer, with graphite-monochromated Mo-K_α radiation (λ = 0.710 73 Å). Unit-cell parameters were refined from 2θ values (20—25°) of 32 reflections measured at ±ω in each case. Data were collected in a ω—θ scan mode with variable scan width and time. No significant variation in intensity was observed for three periodically measured standard reflections in the case of complex (**3**) and ligand L^7; a decay of *ca.* 4% for complex (**2**) was corrected. Semiempirical absorption corrections were also applied for (**2**) and (**3**). Each data set consisted of a complete unique set of reflections [including Friedel pairs for (**2**)], together with a partial equivalent set.

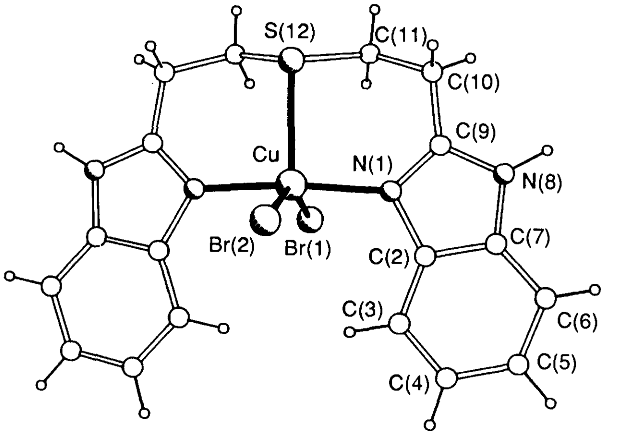


Figure 1. Molecular structure of complex (**3**), with the numbering scheme. A crystallographic mirror plane passes through Cu, S(12), and the two Br atoms

The structures were solved[26] by direct methods and refined by blocked-cascade least squares on *F*, with weighting $w^{-1} = \sigma^2(F) + gF^2$. Atomic scattering factors were taken from ref. 27. Refinement included an isotropic extinction parameter x [$F_c' = F_c/(1 + xF_c^2/\sin 2\theta)^{\frac{1}{4}}$], anisotropic thermal parameters for all non-H atoms, and constrained H atoms [C–H 0.96 Å, H–C–H 109.5°, aromatic H on ring angle external bisectors, U(H) = 1.2 U_{eq}(C)]. Two-fold disorder was resolved for two of the atoms in one octyl chain of L^7, and refined with relative occupancy factors of 0.73:0.27(2); H atoms were not included for this disordered region or for the solvent molecules in (**2**) and (**3**). The largest residual difference electron-density peaks for (**3**) were found around the $CHCl_3$ molecule.

Additional material available from the Cambridge Crystallographic Data Centre comprises H-atom co-ordinates, thermal parameters, and remaining bond lengths and angles.

Results and Discussion

Crystallography.—Crystal structures of complexes of ligand L^4 with $Cu(NO_3)_2$, (**2**), and $CuBr_2$, (**3**), and of the octylated ligand L^7, have been determined. Atomic co-ordinates are in Tables 2—4, selected bond lengths and angles for (**2**) and (**3**) in Tables 5 and 6. Crystals of both copper complexes contained solvent, but not directly co-ordinated to the metal. The co-ordination of copper in (**2**) could be described as distorted trigonal bipyramidal, or alternatively as elongated distorted octahedral, if one of the nitrates is considered as an asymmetric bidentate ligand. The copper environment in (**3**) is intermediate between trigonal bipyramidal and square-based pyramidal. In both of these structures, and in the closely related[6] lozenge-shaped structure (**1**) (which is the copper bromide complex of ligand L^5), the ligand maintains approximate coplanarity of the benzimidazoles, and an almost collinear set of N–Cu–N atoms for the tertiary nitrogens of the benzimidazole, which is usual for such systems.

The copper bromide complex, $[Cu(L^4)Br_2]\cdot CHCl_3$ (**3**). The copper bromide complex of ligand L^4 is five-co-ordinate. The geometry, as shown in Figure 1, lies between square pyramidal and trigonal bipyramidal with a Br–Cu–Br angle (α) of 149.2(1)° and an N–Cu–N angle of 173.7(3)° (β), giving a τ value of 0.408

Table 4. Atomic co-ordinates (× 10^4) for ligand L^7

Atom	*x*	*y*	*z*
S(1)	4 739(1)	5 482(1)	3 911(1)
C(11)	4 702(5)	5 776(4)	2 769(2)
C(12)	3 169(5)	4 788(4)	4 324(2)
C(13)	1 657(4)	5 527(3)	4 296(2)
N(11)	1 041(4)	5 557(3)	3 633(2)
C(14)	−331(5)	6 330(3)	3 844(3)
C(15)	−1 446(5)	6 673(4)	3 386(3)
C(16)	−2 721(6)	7 454(4)	3 760(4)
C(17)	−2 905(6)	7 924(4)	4 564(4)
C(18)	−1 776(6)	7 580(4)	5 027(3)
C(19)	−516(5)	6 776(3)	4 662(3)
N(12)	778(4)	6 245(3)	4 936(2)
C(101)	1 051(5)	6 413(4)	5 780(2)
C(102)	1 805(5)	7 342(4)	5 758(3)
C(103)	1 929(6)	7 559(4)	6 660(3)
C(104)	2 756(6)	8 392(4)	6 692(3)
C(105)	2 835(8)	8 627(5)	7 593(4)
C(106)	3 438(8)	9 594(6)	7 666(5)
C(107)	3 455(10)	9 895(8)	8 557(5)
C(108)	3 921(12)	10 862(9)	8 624(7)
S(2)	5 068(1)	5 032(1)	1 103(1)
C(21)	5 079(5)	4 750(4)	2 244(2)
C(22)	6 756(5)	5 604(5)	672(3)
C(23)	8 169(4)	4 845(4)	848(2)
N(21)	8 828(4)	5 050(3)	1 423(2)
C(24)	10 070(5)	4 158(4)	1 402(2)
C(25)	11 203(5)	3 957(4)	1 858(3)
C(26)	12 301(6)	2 997(4)	1 710(3)
C(27)	12 323(7)	2 248(5)	1 096(4)
C(28)	11 257(6)	2 435(5)	615(4)
C(29)	10 127(5)	3 416(4)	789(3)
N(22)	8 886(4)	3 876(3)	437(2)
C(201)	8 562(6)	3 449(5)	−308(3)
C(202)	7 921(9)	2 473(6)	−44(4)
C(203)	7 603(11)	2 010(7)	−847(6)
C(204)	8 895(13)	1 543(11)	−1 613(7)
C(205)	8 365(18)	823(12)	−2 173(6)
C(206)	8 741(18)	1 221(11)	−3 124(7)
C(207)	8 579(12)	373(8)	−3 719(4)
C(208)	7 018(11)	659(8)	−3 879(6)
X(205)	8 340(36)	1 564(13)	−2 457(9)
X(206)	8 499(24)	401(13)	−2 733(8)

Table 5. Selected bond lengths (Å) and angles (°) for complex (**2**)

Cu-N(1)	1.961(2)	Cu-S(12)	2.366(1)
Cu-N(23)	2.001(2)	Cu-O(24)	2.040(2)
Cu-O(26)	2.599(3)	Cu-O(28)	2.282(3)
N(1)-Cu-S(12)	93.5(1)	N(1)-Cu-N(23)	177.0(1)
S(12)-Cu-N(23)	86.8(1)	N(1)-Cu-O(24)	89.1(1)
S(12)-Cu-O(24)	162.8(1)	N(23)-Cu-O(24)	89.8(1)
N(1)-Cu-O(28)	95.5(1)	S(12)-Cu-O(28)	98.4(1)
N(23)-Cu-O(28)	87.5(1)	O(24)-Cu-O(28)	98.3(1)
N(1)-Cu-O(26)	84.5(1)	S(12)-Cu-O(26)	109.3(1)
N(23)-Cu-O(26)	92.6(1)	O(24)-Cu-O(26)	53.9(1)
O(28)-Cu-O(26)	152.3(1)		

Table 6. Selected bond lengths (Å) and angles (°) for complex (**3**)

Cu-Br(1)	2.470(2)	Cu-Br(2)	2.676(2)
Cu-N(1)	1.965(6)	Cu-S(12)	2.458(3)
Br(1)-Cu-Br(2)	149.2(1)	Br(1)-Cu-N(1)	89.1(2)
Br(2)-Cu-N(2)	89.3(2)	Br(1)-Cu-S(12)	109.0(1)
Br(2)-Cu-S(12)	101.8(1)	N(1)-Cu-S(12)	93.1(2)
N(1)-Cu-N(1')	173.7(3)		

Symmetry operator for primed atom: $x, \frac{1}{2} - y, z$.

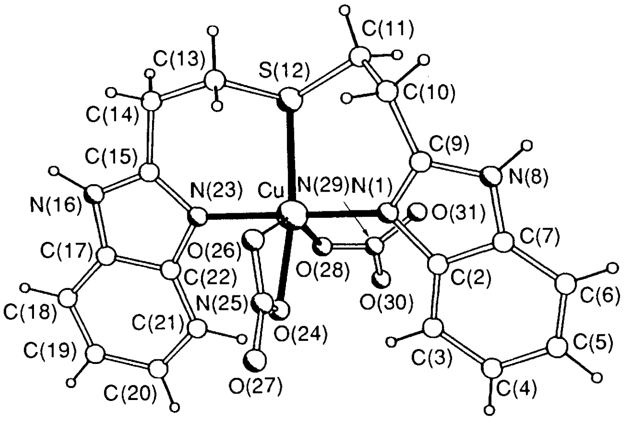
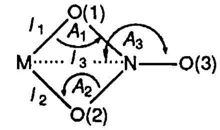


Figure 2. Molecular structure of complex (**2**), with the numbering scheme. The molecule has no crystallographically imposed symmetry

according to the criteria set in ref. 11; in this context the thioether donor would be regarded as apical. The Cu–S length of 2.458 Å is not really in the range[10] considered long, although it is longer than the corresponding distance of 2.366 Å in the nitrate (**2**) reported here; this is no doubt a reflection of the distortion from tetragonal. The shortest distance in similar models with ligand L^4 is 2.297 Å, the longest 2.696 Å, both in ref. 10. The two bromide ligands of complex (**3**) have distinctly different bond lengths to copper of 2.470 and 2.676 Å, well inside the usual range of 2.34—2.79 Å. Compare the two identical lengths of 2.465 Å in the six-co-ordinate lozenge structure of (**1**),[6] which has Br–Cu–Br of 168.2(1)° and N–Cu–N of 168.9(5)°, and two equal Cu–Br distances of 2.493 Å in the Reinen structure,[12] and one equatorial Cu–Br[15] of 2.417 Å. Shorter equatorial Cu–Br distances of 2.37 and 2.385 Å have been found for the two copper co-ordination spheres within a binucleating structure.[21] There are no significant interactions between chloroform and the complex. The major packing determinant seems to be the planar benzimidazole stacking.

The copper nitrate complex, $[Cu(L^4)(NO_3)_2]\cdot CH_3OH$ (**2**). For this complex, the molecular structure is shown in Figure 2. The bis(benzimidazole) ligand is not symmetrically placed, and the copper is in a distorted environment, with one nitrate ligand bonded in a unidentate mode through a terminal oxygen and the second in the unsymmetrically bidentate mode as identified by Addison *et al*[28]; criteria of Reedijk and co-workers[29] (see Table 7) were used to test this geometrical feature. The closest analogies in the recent literature would seem to be the complexes of ligands L^8, where R may be one of several alkyl groups.[7,19] The three compounds with R = t-butyl, isopropyl, or benzyl are distorted octahedral. The terdentate benzimidazole ligand circles the plane of the copper, and there is an unsymmetrically bidentate nitrate, the shorter Cu^{II}–O distance for this being 1.965, 1.982, and 1.998 Å, respectively, regarded as equatorial, while the longer Cu^{II}–O distance, described as apical, is 2.493, 2.602, and 2.637 Å. In each structure there is also a methanol ligand, regarded as apical, completing the octahedral co-ordination. The similarity of the distances to those of our complex (**2**) is striking. However, in our structure the elongated Cu–O distances are the asymmetric nitrate longer

Table 7. Assignment of nitrate groups on criteria of ref. 29



	1	2		Criterion for anisobidentate	Criterion for unidentate
O(24)O(26) nitrate					
$l_2 - l_1$	(2.599 −	2.040)	0.559	0.3—0.6	>0.6
$A_1 - A_2$	(106.4 −	80.81)	25.59	14—28	>28
$l_3 - l_2$	(2.695 −	2.599)	0.096	0.1—0.2	<0.1
A_3	164.68			162—168	

O(28)O(31) nitrate				Criterion for unidentate
$l_2 - l_1$	3.501	2.282	1.219	>0.6
$A_1 - A_2$	132.2	69.14	63.06	>28
$l_3 - l_2$	3.272	3.501	−0.23	<0.1
A_3	147.4			<162

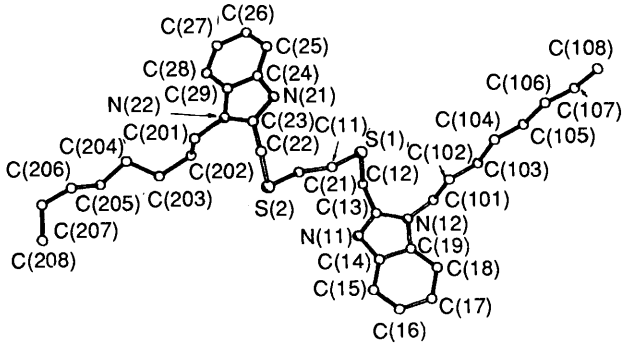
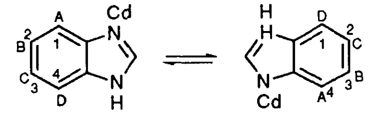


Figure 3. Molecular structure of ligand L^7, with the numbering scheme. Hydrogen atoms and the minor component of the disorder [X(205), X(206)] are not shown

distance and the unidentate nitrate distance. The angles N–Cu–N are tighter for the N_3 ligands of Nishida and Takahashi.[19] Glass *et al.*[18] have shown that a less-constricted ligand can give much more open angles in a five-co-ordinate N_3S_2 ligand set.

Hydrogen bonding appears to play a small part in the packing of the molecules of complex and solvent, with just three intermolecular contacts of less than 3 Å involving O and N atoms. The methanol oxygen atom, O(32), lies 2.783 Å from a nitrate oxygen atom [O(28), which is co-ordinated to copper] and 2.722 Å from one of the imidazole NH nitrogen atoms N(8), approximately along the N–H bond direction. The O ··· O ··· N angle subtended at methanol O(32) by its two hydrogen bonds is 114.3°, and these bonds are inclined at 93.6 and 108.8° to the methanol C–O bond. The third unique hydrogen bond of the structure is between the other imidazole NH [N(16)] and O(31) of the unidentate nitrate, with a N ··· O distance of 2.935 Å and this is also approximately along the N–H bond direction. Thus both N–H groups are involved in essentially linear hydrogen bonding, one to methanol solvent and the other to nitrate ligand. There are no N–H ··· N hydrogen bonds, and the bidentate nitrate does not take part in hydrogen bonding.

Ligand L^7. The N-octyl derivative of L^2 was obtained as white crystals for which diffraction data gave the structure shown in Figure 3, with one disordered alkyl chain. No structure for a free N-alkylated benzimidazole ligand appears to have been published previously, although there are some crystal structures of complexes of N-propyl ligands.[9] The conformation of the dithio bridge is of interest; the two sulphurs are *anti*, the torsion angle S(2)–C(21)–C(11)–S(1) being −179.3°. This feature is reproduced in modelling with molecular mechanics, and suggests that reorganisation would be required for the two sulphurs to co-ordinate in a chelate ring with a metal ion, as observed for example[29] in complexes of several metals with thioether bridged ligands related to L^2. It is common for two sulphurs linked thus in a thiacrown ether to appear *anti* in the free ligand, but *gauche* when complexed.[30]



Scheme 1. Representation of ABCD ⟷ DCBA

The structures will be valuable in the development of force-field parameters for benzimidazoles with Cu, and because solvent molecules are entrained in each unit cell there is opportunity to study non-bonded interactions.

N.M.R. Studies of Ligand-exchange Processes.—Exchange processes observable in the one-dimensional ^1H n.m.r. spectra of benzimidazole ligands correspond to rapid movement of protons between the secondary and tertiary nitrogens of the benzimidazole, such that the ABCD aromatic protons of the benzimidazole unit appear as an AA′BB′ system resulting from the process ABCD ⟷ DCBA (Scheme 1). For the free ligands the process is slowed by cooling, but it was not possible to analyse the kinetics in detail since the shift separations were insufficient for the slow-exchange region to be reached in the solvent chosen. This exchange is slowed by the presence of a metal salt, for example $ZnCl_2$, which presumably co-ordinates to the tertiary nitrogen (as in the structure in Figure 1) thus introducing greater shift separation for the aromatic signals, the signal for the proton closest to the tertiary nitrogen shifting most. The greater chemical shift difference between such signals for free and complexed ligand enabled the exchange processes evident in the temperature-variable spectra to be examined. The phenomenon was studied using the ligands L^2, L^3, L^5, and L^6, the ligands L^3 and L^6 being chosen to simplify the spectra which are reduced to AB ⟷ BA, averaging to AA′ in the fast-exchange region. A sample with deuterium on the secondary nitrogen was also used, to verify the location of the NH signal in the proton spectrum, since water was always present in the solvent, and sometimes the salts, which were added, and an exchange from NH to water was always evident in the proton spectra. A complication in the slow-exchange spectra is the appearance of the A proton in ABCD systems. This signal remains broad, without fine structure, when the D proton has sharpened to show its coupling pattern. A possible explanation is that, in the slow-exchange region, coupling to the tertiary nitrogen is evident, but that the asymmetric electric field gradient at this nitrogen causes rapid quadrupolar relaxation. Aromatic protons (A) adjacent to the secondary nitrogen do not show this effect, presumably because the secondary nitrogen has an attached proton which provides a more efficient relaxation route for it. The variation of lineshape with temperature was simulated using the DNMR3 program.[31] The rates obtained ($k_{obs.}$) for solutions with varied M:L ratio are contained in Tables 8 and 9. Activation energies are in Table 10.

Excess of cadmium region. In mixtures with a M:L ratio greater than unity the exchange was treated as ABCD ⟷ DCBA (or the corresponding AB process for ligand L^6). The rates were found to decrease as the ratio of M:L increased,

Table 8. Observed rate constants for $CdCl_2$ mixtures with ligand L^2

T/K	$[L^2]$/mol dm^{-3}	[LiCl]/mol dm^{-3}	k/s^{-1}
298	0.100		3 160
	0.050		1 240
	0.050	0.100	1 290
	0.033		890
280	0.100		1 660
	0.050		620
	0.050	0.100	710
	0.033		410
270	0.100		1 120
	0.050		400
	0.050	0.100	500
	0.033		260
260	0.100		720
	0.050		240
	0.050	0.100	330
	0.033		160
250	0.100		470
	0.050		150
	0.050	0.100	220
	0.033		90
240	0.100		290
	0.050		80
	0.050	0.100	150
	0.033		50

All samples contained 0.100 mol dm^{-3} $CdCl_2$.

Table 9. Observed rate constants for reaction of ligand L^6 and its cadmium complex

[Complex]/mol dm^{-3}	$[L^6]$/mol dm^{-3}	k*/s^{-1}
0.0167	0.0333	450
0.0250	0.0250	550
0.0333	0.0167	700

* $R = k_{obs.}/[CdL] = 26\,900, 22\,000,$ and $21\,000$ dm^3 mol^{-1} s^{-1}.

Table 10. Activation energies for data in Table 8; $[CdCl_2] = 0.100$ mol dm^{-3}

$[L^2]$/mol dm^{-3}	[LiCl]/mol dm^{-3}	E_a/kJ mol^{-1} (s.d.)
0.100		24.5(0.08)
0.050	0.100	22.3(0.17)
0.050		28.0(0.17)
0.033		29.7(0.16)

consistent with the reaction proceeding through a dissociative step in which free ligand and free metal ion are produced (Table 8). For the reaction of ligand L^2, in mixtures with $CdCl_2$, where M:L is greater than 1:1, a plot of observed rate constant ($k_{obs.}$) *versus* $[M]^{-1}$ is shown in Figure 4. The inverse dependence on [M] is explained in terms of a pre-equilibrium dissociative step for the exchange, as for example shown in equation (1).

$$[CdL]^{2+} \overset{k_d}{\rightleftharpoons} L + Cd^{2+} \quad (1)$$

$$L^* + [CdL]^{2+} \overset{k_2}{\rightleftharpoons} [CdL^*]^{2+} + L \quad (2)$$

The simple dissociation of L cannot of course exchange ABCD $\longleftrightarrow$ DCBA on a benzimidazole. The actual switch must come in a subsequent critical step, which is competing with the second-order reverse step of equation (1) for the supply of L. The critical step might be a prototropic exchange on the free ligand, or the process shown in equation (2), but there is insufficient evidence to determine this. The exchange rate constant for the 1:1 M:L mixture should correspond to the dissociative rate constant for equation (1).

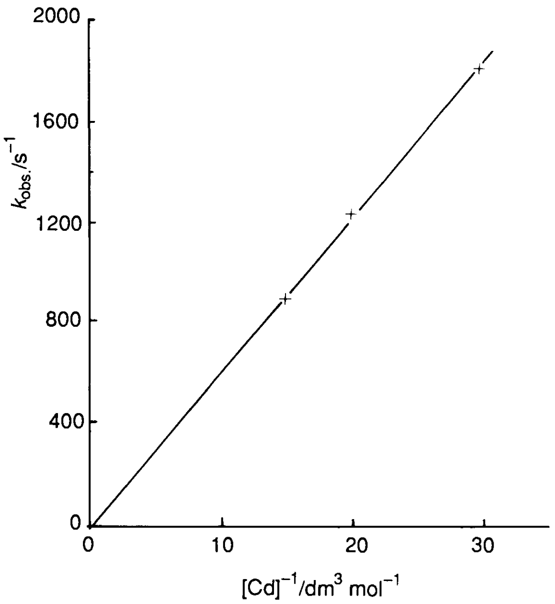


Figure 4. Plot of $k_{obs.}$ *versus* the inverse of the free cadmium concentration, based on results in Table 8

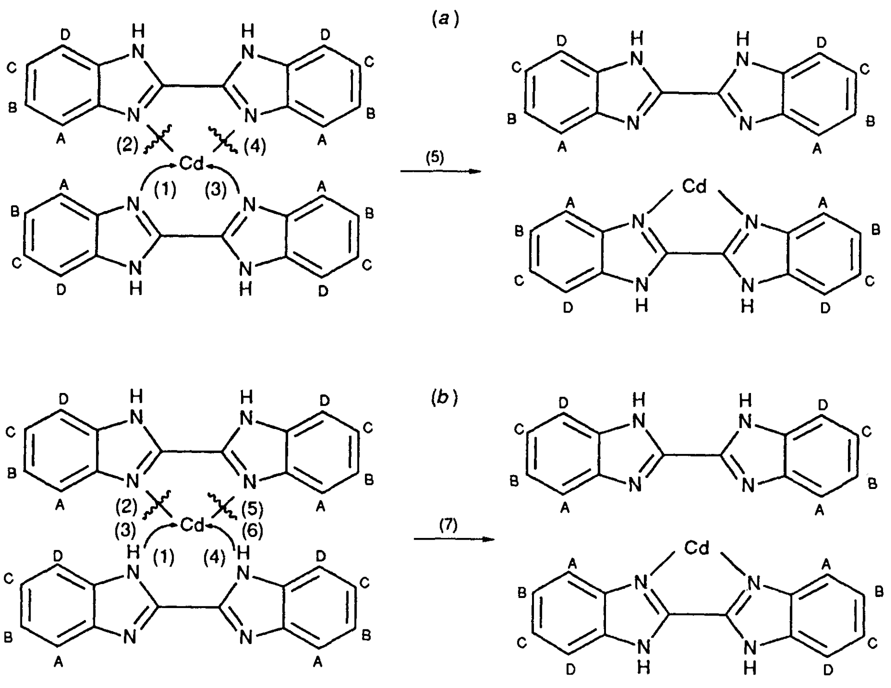
The excess of ligand region. When the M:L ratio dropped below 1.0:1 the rate of the observed aromatic proton switch increased. The system visible at the lowest temperatures studied was a simple ABCD (or AB) spectrum, sometimes with rather low resolution. In some experiments lithium chloride, equimolar with the cadmium chloride, was added to the mixture. The observed rate constant in general increased, as may be seen in Table 8. The corresponding activation energies (Table 10) were lowered by *ca.* 6 kJ mol^{-1}. The lithium chloride may be considered as an additional source of chloride, acting as a nucleophile competing with the ligand for cadmium. At no point, for any of the systems studied, was there a separation of signals pertaining to free ligand, and free complex. The significance of this observation is that the L + ML exchange is fast under these conditions. Since several mechanisms were explored it was simpler to use ligand L^6, the methylated version of ligand L^2, for the DNMR3 simulations. The observed rate constants for the mixture of ligand L^6 and $CdCl_2$ (Table 9) were treated by the Shchori method.[32] In this instance equations (1) and (2) are taken to represent the dissociative and associative pathways envisaged for the exchange. Supposing both mechanisms to be operative, equation (3) may be derived and hence (4)

$$k_{obs.} = k_2[CdL] + k_d[CdL][L]^{-1} \quad (3)$$

$$\frac{k_{obs.}}{[CdL]} = k_2 + k_d \cdot \frac{1}{[L]} \quad (4)$$

where [L] is the concentration of free ligand. The values of $k_{obs.}/[CdL]$ should be considered as a function of $[L]^{-1}$ (Table 9). They show little variation over the limited concentration range possible, indicating no dissociative contribution to the mechanism. This result is interpreted in terms of an exclusive associative contribution to the turnover of ligand, that is as shown in equation (2). This is quite different from the situation discussed previously for Cd:L greater than 1:1. A more detailed mechanism is now considered.

The detailed mechanism. In what follows it is assumed that the ligand is complexed to the metal ion *via* its tertiary nitrogen, as



Scheme 2. Mechanisms representing aromatic exchange process. (*a*) Steps: (1) attack by tertiary N; (2) bond breaks; (3) and (4) exchange of ligand complete; (5) this process does not lead to ABCD $\longleftrightarrow$ DCBA. (*b*) Steps: (1) attack by secondary N; (2) bond breaks; (3) switching of protons; (4)–(6) exchange of ligand complete; (7) this process leads to ABCD $\longleftrightarrow$ DCBA

seems to be true in complexes studied by *X*-ray crystallography. The ABCD system is used for the discussion, but the analogous situation is also presumed to apply to the AB system (ligand L^6).

It is proposed that the fast L–ML process observed (but not analysable) in mixtures with excess of L at low temperatures goes *via* the exchange of a ligand attacking a complex in the symmetrical sense, where the pyridyl nitrogen is the attacking group and also the leaving group (Scheme 2). This exchange is from ligand to complex, averaging ABCD(L) with ABCD(complex) to give an apparent single ABCD spectrum, but it cannot exchange ABCD $\longleftrightarrow$ DCBA; the latter exchange could however occur if the ligand uses the secondary nitrogen to attack the metal ion, with accompanying proton-exchange steps on either free ligand or complex. No information as to how this proceeds can be obtained from the n.m.r. spectra but a number of steps, including proton transfers, would seem to be required. It is suggested that this is the process which is observed from around 230 K to around room temperature, and the kinetics of which can be followed by the n.m.r. method. Apparently then this is an associative process, in which attack is initiated by the secondary amine of the attacking benzimidazole. These results are quite realistic for the system studied, at 240 and 230 K, where an associative contribution is more likely, and at the concentrations as quoted. The condition of excess of ligand is analogous to the conditions prevailing in a liquid membrane, and may indicate the likely mechanism by which metal is transferred through the organic membrane in membrane passive transport (three-phase transport).[25,33] It is possible that a dissociative contribution would be competitive at higher temperatures and lower concentrations, as has been proposed for an analogous ligand exchange of propeller crowns with their alkali-cation complexes.[34] Although there may be concomitant or additional exchange with attack initiated by tertiary nitrogen, evidence will not be obtained by this particular n.m.r. method. In mixtures of ligand L^7 and metal salts an exchange process became evident in the ^1H n.m.r. spectra on cooling; this ligand is unable to undergo prototropy, but still has a tertiary pyridine-type nitrogen. This low-temperature process may relate to the lower-temperature process observed for the unalkylated ligands, perhaps oligomeric association *via* intermolecular coordination of cadmium.

Acknowledgements

The authors thank the S.E.R.C. for support, and Miss Rachel Riley and Mr. Martin Sykes for help in growing crystals of complexes (**2**) and (**3**).

References

1 C. M. Groeneveld, J. van Rijn, J. Reedijk, and G. W. Canters, *J. Am. Chem. Soc.*, 1988, **110**, 4893.
2 'Copper Coordination Chemistry: Biochemical and Inorganic Perspectives,' eds. K. D. Karlin and J. Zubieta, Adenine Press, New York, 1983.
3 C. A. Bunton, Y. S. Hong, L. S. Romsted, and C. Quan, *J. Am. Chem. Soc.*, 1981, **103**, 5784.
4 J. Reedijk, W. L. Driessen, and J. van Rijn, in 'Biological and Inorganic Copper Chemistry. Volume 2,' eds. K. D. Karlin and J. Zubieta, Adenine Press, New York, 1986, pp. 143–160.
5 W. Clegg, J. C. Lockhart, and F. H. Musa, *J. Chem. Soc., Dalton Trans.*, 1986, 47.
6 W. Clegg and J. C. Lockhart, *Polyhedron*, 1987, **6**, 1149.
7 K. Takahashi, Y. Nishida, and S. Kida, *Polyhedron*, 1984, **3**, 113.
8 J. V. Dagdigian and C. A. Reed, *Inorg. Chem.*, 1979, **18**, 2623.
9 J. V. Dagdigian, V. McKee, and C. A. Reed, *Inorg. Chem.*, 1982, **21**, 1332.
10 A. W. Addison, P. J. Burke, K. Henrick, T. N. Rao, and E. Sinn, *Inorg. Chem.*, 1983, **22**, 3645.
11 A. W. Addison, T. N. Rao, J. Reedijk, J. van Rijn, and G. C. Verschoor, *J. Chem. Soc., Dalton Trans.*, 1984, 1349.
12 M. I. Arriortua, J. L. Mesa, T. Rojo, T. Debaerdemaeker, D. Beltran-Porter, H. Stratemeier, and D. Reinen, *Inorg. Chem.*, 1988, **27**, 2976.
13 E. Bouwman, R. Day, W. L. Driessen, W. Tremel, B. Krebs, J. S. Wood, and J. Reedijk, *Inorg. Chem.*, 1988, **27**, 4614.
14 E. Bouwman, A. Burik, J. C. Ten Hove, W. L. Driessen, and J. Reedijk, *Inorg. Chim. Acta*, 1988, **150**, 125.
15 P. J. M. W. L. Birker, E. F. Godefroi, J. Helder, and J. Reedijk, *J. Am. Chem. Soc.*, 1982, **104**, 7556.

16 E. Bouwman, J. C. Ten Hove, W. L. Driessen, and J. Reedijk, *Polyhedron*, 1988, **7**, 2591.

17 E. Bouwman, C. E. Westheide, W. L. Driessen, and J. Reedijk, *Inorg. Chim. Acta*, 1989, 166, 291.

18 R. S. Glass, M. Sabahi, M. Hojjatie, and G. S. Wilson, *Inorg. Chem.*, 1987, **26**, 2194.

19 Y. Nishida and K. Takahashi, *J. Chem. Soc., Dalton Trans.*, 1988, 691.

20 S. B. Sanni, H. J. Behm, P. T. Beurskens, G. A. van Albada, J. Reedijk, A. T. H. Lenstra, A. W. Addison, and M. Palaniandavar, *J. Chem. Soc., Dalton Trans.*, 1988, 1429.

21 J. van Rijn, J. Reedijk, M. Dartmann, and B. Krebs, *J. Chem. Soc., Dalton Trans.*, 1987, 2579.

22 H. P. Berends and D. W. Stephan, *Inorg. Chim. Acta*, 1985, **99**, L53.

23 A. Benzekri, P. Dubourdeaux, J-M. Latour, J. Laugier, and P. Rey, *J. Chem. Soc., Chem. Commun.*, 1987, 1564.

24 J. M. Guss, P. R. Harrowell, M. Murata, V. A. Norris, and H. C. Freeman, *J. Mol. Biol.*, 1986, **192**, 361.

25 K. I. Kinnear, J. C. Lockhart, and D. J. Rushton, *J. Chem. Soc., Dalton Trans.*, 1990, 1365.

26 G. M. Sheldrick, SHELXTL, an integrated system for solving, refining, and displaying crystal structures from diffraction data, Revision 5, University of Göttingen, 1985.

27 'International Tables for *X*-Ray Crystallography,' Kynoch Press, Birmingham, 1974, vol. 4, pp. 99, 149.

28 C. C. Addison, N. Logan, S. C. Wallwork, and C. D. Garner, *Q. Rev. Chem. Soc.*, 1971, **25**, 289.

29 G. J. Kleyweg, W. G. R. Wiesmeijer, G. J. Van Driel, W. L. Driessen, J. Reedijk, and J. H. Noordik, *J. Chem. Soc., Dalton Trans.*, 1985, 2177.

30 J. R. Hartman, R. E. Wolf, B. M. Foxman, and S. R. Cooper, *J. Am. Chem. Soc.*, 1983, **105**, 131.

31 DNMR3, D. A. Kleier and G. Binsch, *J. Magn. Reson.*, 1970, **3**, 146.

32 E. Shchori, J. Jagur-Grodzinski, and M. Shporer, *J. Am. Chem. Soc.*, 1971, **93**, 7133.

33 'Separation Processes in Hydrometallurgy,' ed. G. A. Davies, Society of Chemical Industry/Ellis Horwood, Chichester, 1987.

34 J. C. Lockhart, M. B. McDonnell, M. N. S. Hill, and M. Todd, *J. Chem. Soc., Perkin Trans. 2*, 1989, 1915.

Received 16*th May* 1990; *Paper* 0/02161J