3458 *Inorg. Chem.* **1987**, *26*, 3458–3463

Summary of Patterns in Pt(II)–Phosphite and Pt(II)–Phosphonate Complexes. 1. The lengths of the $Pt-P(O)(OMe)_2$ bonds in $Pt[P(OMe)_3]_{4-n}[P(O)(OMe)_2]_n^{(2-n)+}$, $n = 1$, 2, and 4, fall in the range 2.31–2.33 Å and are largely independent of the residual charge on the complex.

2. The $Pt-P(OMe)_3$ bond distance in $Pt[P(OMe)_3]_{4-n}[P(O)(OMe)_2]_n^{(2-n)+}$ complexes, $n = 0$, 1, and 2, fall in the range 2.29–2.31 Å, which is, on average, shorter than the Pt–phosphonate bonds.

3. On the basis of the bond distance trend, the trans influence is $P(O)(OMe)_2^- > P(OMe)_3 \gg Cl^-$. The trend for $P(OMe)_3$ and $P(O)(OMe)_2^-$ is difficult to distinguish by ^{31}P NMR spectroscopy, but the trans influence of the phosphorus ligands as a group can be easily distinguished from Cl.

4. These complexes distort away from idealized square-planar geometry by an amount that qualitatively depends on the cone angle of the ligands. The *trans*-LPtL angle order is $PtCl_4^{2-}$ (180°)[26] > *cis*-$Cl_2Pt[P(OMe)_3]_2$ (174°) $\simeq$ $[ClPt[P(OMe)_3]]_3^+$ (174°) > $[Pt[P(OMe)_3]_4]^{2+}$ (170°) $\simeq$ $[Pt[P(O)(OMe)_2][P(OMe)_3]_3]^+$ (169°) $\simeq$ $Pt[P(OMe)_3]_2[P(O)(OMe)_2]_2$ (170°) > $[Pt(PMe_3)_3Cl]^+$ (166°) > $[[Pt(PEt_3)_4]]^{2+}$ (150°). If the ligands are chelated, as in $\{Pt[P(OH)_2(OMe)_2]_2[P(O)(OMe)_2]_2\}$, the distortion is less, i.e. >175°.

5. Distortion toward both square-pyramidal and tetrahedral geometry can be found at the Pt(II) center in these complexes.

6. The correlation between $^1J_{Pt-P}$ and d(Pt–P) is crude at best. It cannot be used to predict bond distances reliably from ^{31}P NMR data and vice versa.

Supplementary Material Available: Listings of bond lengths (Tables 1S, 6S, 11S, 16S, and 21S), bond angles (Tables 2S, 7S, 12S, 17S, and 22S), anisotropic thermal parameters (Tables 3S, 8S, 13S, 18S, and 23S), and hydrogen atom parameters (Tables 4S, 9S, 14S, 19S, and 24S) for **1**–**5** (15 pages); listings of observed and calculated structure factors (Tables 5S, 10S, 15S, 20S, and 25S) for **1**–**5** (102 pages). Ordering information is given on any current masthead page.

(26) Dickenson, R. G. *J. Am. Chem. Soc.* **1922**, *44*, 2404.

(27) Sperline, R. P.; Beaulieu, W. B.; Roundhill, D. M. *Inorg. Chem.* **1978**, *17*, 2030.

Contribution from the Departments of Chemistry and Nuclear Medicine,
University of California, Davis, California 95616

X-ray Crystal Structure of a Macrocyclic Copper Chelate Stable Enough for Use in Living Systems: Copper(II) Dihydrogen 6-(*p*-Nitrobenzyl)-1,4,8,11-tetraazacyclotetradecane-1,4,8,11-tetraacetate

Min K. Moi,[†] Michael Yanuck,[†] Shrikant V. Deshpande,[†] Håkon Hope,[†] Sally J. DeNardo,[‡] and Claude F. Meares*[†‡]

Received December 22, 1986

With the goal of radioimmunotherapy using copper-67 attached to monoclonal antibodies, the title complex (I) has been synthesized and shown to retain the copper ion for days under physiological conditions.[10] Here we report the crystal structures of I and also of the binuclear complex dicopper(II) (6-*p*-nitrobenzyl)-1,4,8,11-tetraazacyclotetradecane-1,4,8,11-tetraacetate (II). Crystals of I are triclinic, with cell dimensions $a = 8.537$ (4) Å, $b = 8.684$ (6) Å, $c = 21.614$ (15) Å, $\alpha = 99.48°$, $\beta = 98.69°$, and $\gamma = 90.51°$; $Z = 2$, and space group is $P\bar{1}$. The R value with anisotropic thermal parameters for all non-hydrogen atoms is 0.066 for 2934 reflections. In I, the Cu(II) is six-coordinate, with two axial nitrogen ligands (bond lengths 2.4 Å). The other two nitrogen atoms and two carboxylate oxygens form an approximately square plane (bond lengths 2.0 Å). Crystals of II are monoclinic, with cell dimensions $a = 10.501$ (3) Å, $b = 9.216$ (3) Å, $c = 17.640$ (4) Å, and $\beta = 92.06°$; $Z = 2$, and space group is Pc. The R value is 0.055 Å for 2650 reflections. In the binuclear complex the two coppers are pentacoordinate, and the structure is polymeric.

Introduction

The attachment of metal ions to proteins, such as monoclonal antibodies, can create new tools for use in biology and medicine.[1] The reagents used for such attachment are usually called "bifunctional chelating agents" because they incorporate a strong metal-chelating group and a chemically reactive group. Bifunctional chelating agents are most often used to endow biological molecules with the nuclear,[2] physical,[3] or chemical[4] properties of chelated metal ions. In the last few years, substantial progress has been made in the application of such reagents to problems such as cancer therapy and diagnosis,[5,6] clinical immunoassays,[7] and DNA footprinting.[8]

The properties of the chelated metal ions play a major role in the application of the bifunctional chelates. Radioisotopes of Cu, such as ^{67}Cu, have been shown to be potentially useful in radioimmunotherapy.[9] ^{67}Cu releases high-energy electrons (β particles), which can cause toxic chemical reactions to target tumor cells located within approximately 100 μm of the radionuclide. In addition, the radioactive decay of ^{67}Cu releases penetrating γ rays, which are useful for tumor imaging.

We have undertaken the development of new bifunctional chelates of ^{67}Cu that, when conjugated to antitumor monoclonal antibodies, will serve as tumor-imaging and tumor-therapeutic agents. For this application it is essential that the radioactive copper ion remain attached to the antibody for periods of several days in a living system. Copper(II) is a very labile metal ion that can exchange ligands with ease. To counteract this lability, we have prepared 6-[*p*-(bromoacetamido)benzyl]-1,4,8,11-tetraaza-

---

[†] Department of Chemistry.

[‡] Department of Nuclear Medicine.

(1) Meares, C. F.; Wensel, T. G. *Acc. Chem. Res.* **1984**, *17*, 202.

(2) Sundberg, M. W.; Meares, C. F.; Goodwin, D. A.; Diamanti, C. I. *Nature (London)* **1974**, *250*, 587.

(3) Leung, C. S.-H.; Meares, C. F. *Biochem. Biophys. Res. Commun.* **1977**, *75*, 149.

(4) Dreyer, G. B.; Dervan, P. B. *Proc. Natl. Acad. Sci. U.S.A.* **1985**, *82*, 968.

(5) Scheinberg, D. A.; Strand, M.; Gansow, O. A. *Science (Washington, D.C.)* **1982**, *215*, 1511.

(6) Hnatowich, D. J.; Layne, W. W.; Childs, R. L., Lanteigne, D.; Davis, M. A.; Griffin, T. W.; Doherty, P. W. *Science (Washington, D.C.)* **1983**, *220*, 613.

(7) Siitari, H.; Hemmila, I.; Sioni, E.; Lorgen, T.; Koistinen, V. *Nature (London)* **1983**, *301*, 258.

(8) Van Dyke, M. W.; Dervan, P. B. *Biochemistry* **1983**, *22*, 2373.

(9) DeNardo, S. J.; Jungerman, J. A.; DeNardo, G. L.; Lagunas-Solar, M. C.; Cole, W. C.; Meares, C. F. In *The Developing Role of Short-Lived Radionuclides in Nuclear Medical Practice*; Paras, P., Theissen, J. W., Eds.; U.S. Department of Energy: Washington, DC, 1984.

0020-1669/87/1326-3458$01.50/0 © 1987 American Chemical Society

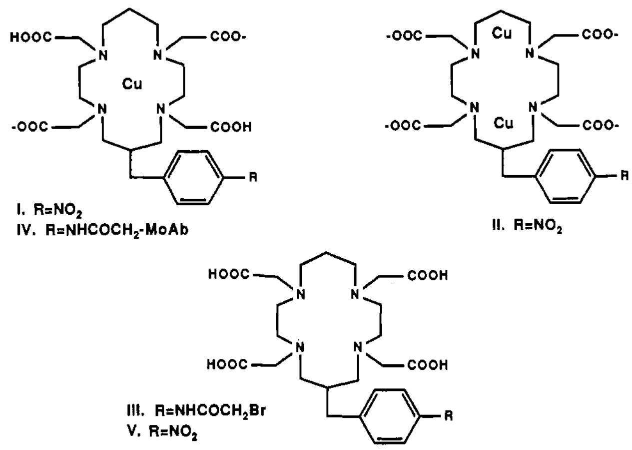


Figure 1. Compounds I–V. MoAb = monoclonal antibody.

cyclotetradecane-1,4,8,11-tetraacetic acid (III) (Figure 1), a specially designed ligand that forms a kinetically inert complex with Cu^{2+} and contains a side chain for attachment to a protein. When III is attached covalently to a monoclonal antibody, copper ions quickly and specifically bind to it in aqueous solution at neutral pH to form complex IV (Figure 1). Chelating agents based on EDTA or DTPA, which have been used previously in medical applications with other metal ions, utterly fail to retain copper under physiological conditions. In contrast, both I and IV retain approximately 95% of the copper after 6 days in human serum.[10,11]

To assist in understanding these results, we have determined the arrangement of ligands around the copper by X-ray crystallography. The metal-chelating moiety of this molecule, TETA, belongs to a class of novel cyclic polyaza ligands. Like its parent molecule, 1,4,8,11-tetraazacyclotetradecane (cyclam), TETA has a metal-selective cavity.[12] In addition to the four metal-chelating nitrogens, TETA contains four ionizable carboxylate groups that are potential ligands. Spectroscopic studies on metal complexes with this type of ligand have been reported,[13] but very few X-ray crystal structure studies on metal complexes of TETA are available. To our knowledge, the only two reported crystal structures have been those of the mononuclear Tb^{III}(TETA)[14] and binuclear Cu_2^{II}(TETA).[15]

Experimental Section

The macrocyclic ligand 6-(*p*-nitrobenzyl)-1,4,8,11-tetraazacyclotetradecane-1,4,8,11-tetraacetic acid (V) (Figure 1) was prepared as reported in ref 10, with the following modifications.

We have improved the synthesis of the intermediate cyclic diamide, a precursor to V. The improved preparation was carried out by dripping 0.4 M ethanolic solutions of 1,3-bis[(2-aminoethyl)amino]propane and *p*-nitrobenzyl malonate (each 0.0339 mol/84.7 mL) into 169.4 mL of refluxing ethanol over a period of 24 h. After 5 days of refluxing, the volume of the reaction mixture was reduced to approximately 100 mL under reduced pressure. The product precipitated to give a faintly yellowish solid. Additional product was isolated by using a silica gel column (J. T. Baker, 60–200 mesh, 2.5 × 40 cm). Application of the concentrated reaction mixture was followed by step elution with 300 mL of $CHCl_3$ and 600 mL of $CHCl_3$–MeOH (1:1). The product eluted in the $CHCl_3$–MeOH mixture. Total yield = 21.4%.

Crystallization of I. Compound V (17.6 μmol) was dissolved in 2 mL of water at pH 7, by heating to 60–70 °C. Then 4 mL of ethanol was added. A solution of $CuSO_4 \cdot 5H_2O$ (8.0 μmol) in 1 mL of water at pH 7 mixed with an equal volume of ethanol was added quickly. The resulting solution was medium blue. Crystals were observed to form after slow cooling to room temperature overnight.

Table I. Summary of Crystallographic Data

	I	II
formula	$Cu(C_{25}H_{35}N_5O_{10})(C_2H_5OH)H_2O$	$Cu_2(C_{25}H_{33}N_5O_{10}) \cdot 8H_2O$
fw	692.5	834
cryst system	triclinic	monoclinic
space group	$P\bar{1}$	Pc
conditions	none	$h0l$ absent for l odd
cryst dimens, mm	0.43 × 0.05 × 0.02	0.12 × 0.07 × 0.05
cryst color	light blue	intense deep blue
a, Å (140 K)	8.537 (4)	10.501 (3)
b, Å	8.684 (6)	9.216 (3)
c, Å	21.614 (15)	17.640 (4)
α, deg	99.48 (5)	
β, deg	98.69 (5)	92.06 (2)
γ, deg	90.51 (5)	
Z	2	2
V, Å^3	1563 (2)	1706.1 (8)
calcd d(140 K), g/cm^3	1.47	1.66
radiation	Mo Kα (λ = 0.71069 Å), graphite monochromator	Mo Kα (λ = 0.71069 Å), graphite monochromator
linear abs coeff, cm^{-1}	8.0	13.9
temp, K	140	140
scan type	ω	ω
scan speed, deg/min	5	4
scan width, deg	1.0	1.0
offset for background, deg	1.0	1.0
$2\theta_{max}$, deg	50	55
range of transmn factors	0.96–0.99	0.90–0.94
octants	$h,\pm k,\pm l$	$h,k,\pm l$
no. of params	424	209
data/parameter ratio	6.9	12.7
check refls	2 measd every 200 refls	2 measd every 200 refls
no. of uniq data	5503	4358
no. of data used	2934 ($I > 2\sigma(I)$)	2650 ($I > 3\sigma(I)$)
$R(F)$	0.066	0.055
$R_w(F)$	0.068	0.054
largest shift/esd	0.036	0.064

Crystallization of II. Compound V (17.6 μmol) was dissolved in 2 mL of water, and the solution was adjusted to pH 7 at room temperature. Then a solution of $Cu(OAc)_2$ (50.0 μmol) in 2 mL of water was added. Precipitation was observed immediately upon mixing. The precipitate was filtered out and dissolved in dilute NaOH (pH 12) at 80–90 °C. The pH was adjusted to 7 with formic acid (7 M). Crystals were observed after standing at room temperature for 5 days.

Crystal Structure Determination. Compound I. Crystal data and the parameters for X-ray data collection are summarized in Table I. A crystal was investigated by using a Syntex $P2_1$ diffractometer equipped with a low-temperature apparatus. The reported cell dimensions are based upon a least-squares fit of 14 centered reflections in the range $6.9 < 2\theta < 21.3°$. The structure was solved by using the computer programs of SHELXTL, version 4. Neutral-atom scattering factors and corrections for anomalous dispersion[16] were from common sources. A correction for absorption effects was made.[17] Solution of the structure followed from location of the copper on a Patterson map. All non-hydrogen atoms were located on Fourier maps and refined anisotropically. Positional parameters of the five hydrogen atoms involved in hydrogen bonding were refined. All other hydrogen atoms were included in the structure factor calculation at positions calculated by using a riding model, an assumed C–H distance of 0.96 Å, and idealized geometry. Isotropic thermal parameters were fixed at 1.2 times the equivalent isotropic thermal parameter of the bonded carbon. The final discrepancy index and other indicators of convergence are given in Table I. Positional parameters for non-hydrogen atoms are given in Table II.

Compound II. Crystal data and the parameters for X-ray data collection are summarized on Table I. The reported cell dimensions are based upon a least-squares fit of 12 reflections with $7.8 < 2\theta < 24.1°$. Cu was anisotropic and all other atoms were isotropic in refinement.

---

(10) Moi, M. K.; Meares, C. F.; McCall, M. J.; Cole, W. C.; DeNardo, S. J. *Anal. Biochem.* **1985**, *148*, 249.

(11) Cole, W. C.; DeNardo, S. J.; Meares, C. F.; McCall, M. J.; DeNardo, G. L.; Epstein, A. L.; O'Brien, H. A.; Moi, M. K. *J. Nucl. Med.* **1987**, *28*, 83.

(12) Izatt, R. M.; Christensen, J. J. *Synthetic Multidentate Macrocyclic Compounds*; Academic: New York, 1978.

(13) Haflinger, H.; Kaden, T. A. *Helv. Chim. Acta* **1979**, *62*, 683.

(14) Spirlet, M. R.; Rebizant, J.; Loncin, M. F.; Desreux, J. F. *Inorg. Chem.* **1984**, *23*, 4278.

(15) Riesen, A.; Zehnder, M.; Kaden, T. A. *J. Chem. Soc., Chem. Commun.* **1985**, 1336.

(16) *International Tables for X-ray Crystallography*; Kynoch: Birmingham, England, 1974; Vol. IV.

(17) The method obtains an empirical absorption tensor from an expression relating F_o and F_c: Hope, H.; Moezzi, B. Program XABS; Department of Chemistry, University of California: Davis, CA.

Table II. Positional Parameters for Non-Hydrogen Atoms of I

atom	*x*	*y*	*z*	*U*,[a] Å^2
Cu	2027 (1)	1138 (1)	1804 (1)	12 (1)
N(1)	218 (7)	−422 (7)	1576 (3)	15 (2)
N(4)	554 (7)	2522 (7)	2547 (3)	16 (2)
N(8)	3870 (7)	2698 (7)	2035 (3)	17 (2)
N(11)	3560 (7)	−290 (7)	1053 (3)	17 (2)
C(2)	−1132 (8)	320 (9)	1859 (4)	20 (3)
C(3)	−596 (9)	1229 (9)	2530 (4)	20 (3)
C(5)	1671 (9)	2861 (10)	3152 (4)	19 (3)
C(6)	3083 (10)	3923 (9)	3115 (3)	15 (2)
C(7)	4358 (9)	3169 (9)	2735 (3)	16 (3)
C(9)	5201 (9)	1846 (9)	1765 (4)	18 (3)
C(10)	4706 (9)	1017 (9)	1075 (4)	19 (3)
C(12)	2435 (9)	−625 (9)	449 (4)	19 (3)
C(13)	953 (9)	−1597 (10)	476 (4)	18 (3)
C(14)	−279 (9)	−840 (10)	873 (4)	20 (3)
C(1)	675 (9)	−1838 (9)	1872 (4)	19 (3)
C(1′)	2223 (9)	−1549 (10)	2340 (4)	18 (3)
C(4)	−247 (9)	3917 (9)	2364 (4)	16 (3)
C(4′)	−1373 (10)	4701 (10)	2783 (4)	24 (3)
C(8)	3431 (9)	4053 (9)	1704 (4)	19 (3)
C(8′)	1969 (9)	3752 (9)	1215 (4)	17 (3)
C(11)	4319 (9)	−1698 (10)	1234 (4)	21 (3)
C(11′)	5468 (9)	−2475 (10)	808 (4)	22 (3)
O(1′)	2931 (6)	−214 (6)	2428 (2)	18 (2)
O(1″)	2729 (6)	−2677 (6)	2601 (2)	21 (2)
O(4′)	−2008 (7)	5938 (8)	2542 (3)	36 (2)
O(4″)	−1690 (6)	4327 (7)	3263 (3)	26 (2)
O(8′)	1180 (6)	2468 (6)	1162 (3)	19 (2)
O(8″)	1569 (6)	4789 (6)	880 (3)	23 (2)
O(11′)	6133 (8)	−3673 (7)	1056 (3)	34 (2)
O(11″)	5761 (7)	−2090 (7)	327 (3)	25 (2)
C(15)	3930 (9)	4514 (10)	3807 (4)	22 (3)
C(16)	2911 (9)	5479 (9)	4223 (4)	21 (3)
C(17)	2773 (10)	5234 (10)	4831 (4)	25 (3)
C(18)	1843 (10)	6148 (10)	5213 (4)	27 (3)
C(19)	984 (10)	7268 (10)	4960 (4)	27 (3)
C(20)	1043 (11)	7555 (10)	4356 (4)	32 (3)
C(21)	2042 (10)	6680 (10)	3996 (4)	27 (3)
N(22)	−59 (10)	8246 (9)	5347 (4)	38 (3)
O(23)	−1267 (8)	8721 (9)	5065 (4)	52 (3)
O(24)	372 (9)	8524 (8)	5924 (3)	44 (3)
O(25)	−1726 (8)	5012 (8)	419 (3)	34 (2)
O(26)	−4134 (7)	7513 (8)	3131 (3)	36 (2)
C(27)	−3606 (14)	8970 (15)	3511 (6)	69 (5)
C(28)	−4511 (15)	9638 (16)	3988 (6)	78 (6)

[a] Equivalent isotropic *U* defined as one-third of the trace of the orthogonalized U tensor.

Table III. Positional Parameters for Non-Hydrogen Atoms of II

atom	*x*	*y*	*z*	*U*, Å^2
Cu(1)	5252 (1)	2344 (1)	7570 (1)	10 (1)[a]
Cu(2)	5000	4153 (1)	5000	9 (1)[a]
N(1)	6332 (8)	1241 (9)	6838 (5)	13 (2)
N(4)	4220 (9)	2176 (9)	5101 (5)	11 (2)
N(8)	3792 (8)	5200 (9)	5708 (4)	8 (2)
N(11)	6009 (8)	4337 (9)	7417 (5)	9 (2)
C(2)	6029 (10)	1487 (11)	6016 (5)	11 (2)
C(3)	4587 (9)	1387 (11)	5821 (5)	8 (2)
C(5)	2796 (10)	2225 (10)	5031 (5)	9 (2)
C(6)	2162 (10)	3156 (11)	5634 (6)	14 (2)
C(7)	2435 (10)	4775 (12)	5546 (6)	13 (2)
C(9)	4149 (9)	4956 (11)	6531 (5)	11 (2)
C(10)	5594 (9)	5100 (11)	6709 (5)	10 (2)
C(12)	7460 (11)	4257 (12)	7469 (7)	18 (3)
C(13)	8028 (10)	3246 (11)	6912 (6)	12 (2)
C(14)	7712 (11)	1640 (13)	7005 (6)	17 (2)
C(1)	6106 (10)	−297 (11)	7022 (6)	14 (2)
C(1′)	4778 (10)	−542 (11)	7314 (5)	12 (2)
C(4)	4747 (10)	1404 (11)	4438 (5)	10 (2)
C(4′)	6063 (10)	1906 (11)	4270 (6)	12 (2)
C(8)	3989 (9)	6759 (11)	5515 (6)	11 (2)
C(8′)	5273 (10)	7069 (11)	5212 (5)	12 (2)
C(11)	5582 (10)	5192 (12)	8097 (6)	17 (2)
C(11′)	4338 (10)	4595 (11)	8408 (6)	13 (2)
O(1′)	4218 (7)	590 (7)	7578 (4)	15 (1)
O(1″)	4331 (7)	−1790 (8)	7316 (4)	20 (2)
O(4′)	6378 (7)	3141 (8)	4531 (4)	15 (2)
O(4″)	6751 (7)	1104 (8)	3889 (4)	19 (2)
O(8′)	5861 (7)	5985 (8)	4924 (4)	14 (1)
O(8″)	5676 (7)	8324 (8)	5199 (4)	16 (2)
O(11′)	3938 (7)	3381 (7)	8151 (4)	12 (2)
O(11″)	3802 (7)	5314 (8)	8910 (4)	15 (2)
C(15)	695 (10)	2916 (11)	5549 (6)	16 (2)
C(16)	315 (10)	1356 (11)	5720 (5)	14 (2)
C(17)	−614 (10)	636 (11)	5269 (6)	18 (2)
C(18)	−1028 (10)	−760 (12)	5434 (6)	18 (2)
C(19)	−432 (11)	−1464 (12)	6050 (6)	21 (2)
C(20)	493 (11)	−792 (12)	6513 (6)	22 (2)
C(21)	849 (11)	591 (12)	6361 (6)	21 (2)
N(22)	−836 (10)	−2916 (10)	6255 (5)	23 (2)
O(23)	−100 (8)	−3705 (9)	6608 (5)	29 (2)
O(24)	−1907 (9)	−3307 (10)	6036 (5)	38 (2)
$O_w(1)$	6473 (7)	1787 (9)	8620 (4)	21 (2)
$O_w(2)$	1269 (9)	3635 (9)	7632 (5)	33 (2)
$O_w(3)$	2103 (8)	−1583 (9)	8153 (5)	29 (2)
$O_w(4)$	8942 (9)	1448 (10)	3110 (5)	41 (2)
$O_w(5)$	2417 (8)	1073 (10)	8981 (5)	35 (2)
$O_w(6)$	384 (9)	6059 (10)	8505 (5)	38 (2)
$O_w(7)$	−1152 (10)	4027 (12)	9382 (6)	53 (3)
$O_w(8)$	−110 (9)	1625 (11)	8536 (5)	45 (2)

[a] Equivalent isotropic *U* defined as one-third of the trace of the orthogonalized U tensor.

Positional parameters for non-hydrogen atoms are given in Table III.

EPR Spectra. The electron paramagnetic resonance spectrum of compound I at 77 K was recorded by a Varian E-4 X-band spectrometer. DPPH, α,α-diphenyl-β-picrylhydrazyl, was used as the internal *g* marker. To prepare the samples, 3 mM solutions of copper chloride and V were mixed in 1:1.1 molar ratio and the pH of the resulting solution was adjusted with 0.1 M NaOH (final *c* 1.5 mM). Samples with pH values between 7.0 and 10.6 were prepared. The solution was passed through a Chelex column to remove unchelated copper ions, the effluent was lyophilized, and the residue was dissolved in methanol to give a final concentration of approximately 2 mM.

Visible spectra were recorded with a Hewlett Packard 8450A UV/vis spectrophotometer.

Results and Discussion

The Cu[6-(*p*-$NO_2C_6H_4Me$)TETA] Complex (I). The crystal structure of I is shown in Figure 2. From the bond lengths and bond angles listed in Tables IV and V, it may be seen that the ligand geometry around copper is slightly distorted octahedral. The ligands consist of the four tertiary nitrogens and two carboxylate oxygen atoms. Tetragonal distortion is observed: two Cu–N bonds are elongated, to 2.428 and 2.367 Å, respectively, relative to the others (2.0 Å). These axial ligands [N(4) and N(11)] lie close to the axis perpendicular to the square plane. The arrangement of the other four ligands, N(1), N(8), O(1′), and O(8′), is somewhat distorted from square planar. The bond angles for N(1)–Cu–O(1′) and N(8)–Cu–O(8′) are 85.7 and 85.4°,

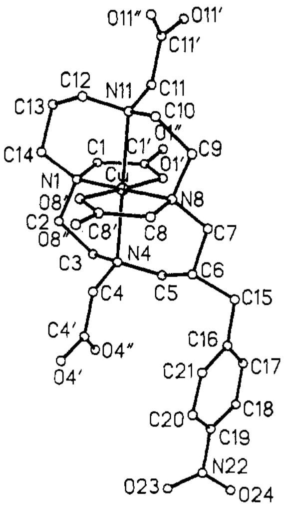


Figure 2. Crystal structure of Cu[6-(*p*-$NO_2C_6H_4Me$)TETA] (I).

Table IV. Bond Lengths (Å) of I

Cu–N(1)	1.994 (6)	Cu–N(4)	2.367 (6)
Cu–N(8)	2.016 (6)	Cu–N(11)	2.428 (6)
Cui–O(1′)	2.004 (6)	Cu–O(8′)	2.006 (6)
N(1)–C(2)	1.488 (10)	N(1)–C(14)	1.495 (9)
N(1)–C(1)	1.506 (11)	N(4)–C(3)	1.478 (10)
N(4)–C(5)	1.483 (9)	N(4)–C(4)	1.477 (10)
N(8)–C(7)	1.494 (9)	N(8)–C(9)	1.502 (10)
N(8)–C(8)	1.498 (11)	N(11)–C(10)	1.482 (10)
N(11)–C(12)	1.485 (9)	N(11)–C(11)	1.471 (11)
C(2)–C(3)	1.534 (10)	C(5)–C(6)	1.531 (12)
C(6)–C(7)	1.547 (11)	C(6)–C(15)	1.561 (10)
C(9)–C(10)	1.540 (10)	C(12)–C(13)	1.529 (11)
C(13)–C(14)	1.541 (11)	C(1)–C(1′)	1.529 (10)
C(1′)–O(1′)	1.274 (10)	C(1′)–O(1″)	1.257 (10)
C(4)–C(4′)	1.510 (12)	C(4′)–O(4′)	1.352 (11)
C(4′)–O(4″)	1.204 (11)	C(8)–C(8′)	1.499 (10)
C(8′)–O(8′)	1.277 (9)	C(8′)–O(8″)	1.264 (10)
C(11)–C(11′)	1.530 (12)	C(11′)–O(11′)	1.340 (11)
C(11′)–O(11″)	1.203 (11)	C(15)–C(16)	1.508 (11)
C(16)–C(17)	1.386 (12)	C(16)–C(21)	1.397 (12)
C(17)–C(18)	1.392 (12)	C(18)–C(19)	1.360 (13)
C(19)–C(20)	1.378 (13)	C(19)–N(22)	1.489 (12)
C(20)–C(21)	1.389 (13)	N(22)–O(23)	1.228 (11)
N(22)–O(24)	1.228 (10)	O(26)–C(27)	1.419 (13)
C(27)–C(28)	1.431 (19)		

Table V. Bond Angles (deg) of I

N(1)–Cu–N(4)	86.9 (2)	N(1)–Cu–N(8)	179.4 (3)
N(4)–Cu–N(8)	93.5 (2)	N(1)–Cu–N(11)	93.4 (2)
N(4)–Cu–N(11)	179.3 (2)	N(8)–Cu–N(11)	86.2 (2)
N(1)–Cu–O(1′)	85.7 (2)	N(4)–Cu–O(1′)	91.5 (2)
N(8)–Cu–O(1′)	93.9 (2)	N(11)–Cu–O(1′)	87.8 (2)
N(1)–Cu–O(8′)	95.0 (2)	N(4)–Cu–O(8′)	90.4 (2)
N(8)–Cu–O(8′)	85.4 (2)	N(11)–Cu–O(8′)	90.3 (2)
O(1′)–Cu–O(8′)	178.0 (2)	Cu–N(1)–C(2)	106.5 (4)
Cu–N(1)–C(14)	112.3 (5)	C(2)–N(1)–C(14)	108.4 (6)
Cu–N(1)–C(1)	108.6 (4)	C(2)–N(1)–C(1)	109.1 (6)
C(14)–N(1)–C(1)	111.7 (6)	Cu–N(4)–C(3)	95.9 (4)
Cu–N(4)–C(5)	105.3 (4)	C(3)–N(4)–C(5)	113.0 (6)
Cu–N(4)–C(4)	116.3 (5)	C(3)–N(4)–C(4)	111.5 (6)
C(5)–N(4)–C(4)	113.5 (6)	Cu–N(8)–C(7)	113.3 (5)
Cu–N(8)–C(9)	104.1 (4)	C(7)–N(8)–C(9)	108.6 (5)
Cu–N(8)–C(8)	107.3 (4)	C(7)–N(8)–C(8)	113.0 (6)
C(9)–N(8)–C(8)	110.2 (6)	Cu–N(11)–C(10)	95.4 (4)
Cu–N(11)–C(12)	104.4 (4)	C(10)–N(11)–C(12)	113.4 (6)
Cu–N(11)–C(11)	116.4 (5)	C(10)–N(11)–C(11)	113.2 (6)
C(12)–N(11)–C(11)	112.8 (6)	N(1)–C(2)–C(3)	112.0 (6)
N(4)–C(3)–C(2)	112.9 (7)	N(4)–C(5)–C(6)	112.9 (7)
C(5)–C(6)–C(7)	116.4 (6)	C(5)–C(6)–C(15)	107.8 (6)
C(7)–C(6)–C(15)	106.9 (6)	N(8)–C(7)–C(6)	116.6 (6)
N(8)–C(9)–C(10)	112.8 (6)	N(11)–C(10)–C(9)	110.0 (7)
N(11)–C(12)–C(13)	114.8 (7)	C(12)–C(13)–C(14)	118.3 (6)
N(1)–C(14)–C(13)	117.6 (6)	N(1)–C(1)–C(1′)	111.9 (6)
C(1)–C(1′)–O(1′)	118.7 (7)	C(1)–C(1′)–O(1″)	116.8 (7)
O(1′)–C(1′)–O(1″)	124.5 (6)	N(4)–C(4)–C(4′)	117.7 (7)
C(4)–C(4′)–O(4′)	109.7 (7)	C(4)–C(4′)–O(4″)	127.2 (8)
O(4′)–C(4′)–O(4″)	123.1 (8)	N(8)–C(8)–C(8′)	113.9 (6)
C(8)–C(8′)–O(8′)	118.4 (7)	C(8)–C(8′)–O(8″)	118.3 (7)
O(8′)–C(8′)–O(8″)	123.2 (6)	N(11)–C(11)–C(11′)	116.5 (7)
C(11)–C(11′)–O(11′)	109.3 (7)	C(11)–C(11′)–O(11″)	126.7 (8)
O(11′)–C(11′)–O(11″)	124.0 (8)	Cu–O(1′)–C(1′)	113.1 (4)
Cu–O(8′)–C(8′)	113.7 (4)	C(6)–C(15)–C(16)	114.1 (6)
C(15)–C(16)–C(17)	123.2 (7)	C(15)–C(16)–C(21)	119.6 (7)
C(17)–C(16)–C(21)	117.2 (8)	C(16)–C(17)–C(18)	122.6 (8)
C(17)–C(18)–C(19)	117.7 (8)	C(18)–C(19)–C(20)	122.7 (8)
C(18)–C(19)–N(22)	119.5 (8)	C(20)–C(19)–N(22)	117.9 (8)
C(19)–C(20)–C(21)	118.5 (8)	C(16)–C(21)–C(20)	121.3 (8)
C(19)–N(22)–O(23)	117.6 (7)	C(19)–N(22)–O(24)	117.1 (8)
O(23)–N(22)–O(24)	125.3 (9)	O(26)–C(27)–C(28)	118.6 (11)

Table VI. Hydrogen Bonding in I

atoms involved	dist, Å	atoms involved	dist, Å
O(1″)···O(26)	2.741	O(8′)···O(25)	2.864
O(4′)···O(26)	2.637	O(8″)···O(25)	2.858
O(11′)···O(25)	2.613		

respectively. These values are in close agreement with data for the five-membered glycine chelate ring.[18] The deviations of N(1), N(8), Cu, O(1′), and O(8) from their mean plane are 0.009, 0.009, 0.016, −0.017, and −0.017 Å, respectively. Thus, the Cu ion is located very close to the mean plane.

As might be expected, the crystal structure of Tb(TETA) reported by Spirlet et al.[14] reveals major differences from that of I. In Tb(TETA) it was found that the large Tb ion is located 1.299 Å above the mean plane of the four N atoms. Moreover, the ligands coordinated to the Tb ion consist of all four nitrogen atoms and all four carboxylate groups. For Tb(TETA), the carboxylate groups are situated on the same side of the macrocycle, indicating remarkable flexibility of the ligand.

The axial ligands in complex I are made up of nitrogens N(4) and N(11). These two "weaker" ligands are held by the carbon skeleton of the macrocyclic ring. The carboxylate oxygens O(8′) and O(1′) lie closer to the copper (bond lengths 2.0 Å). This stronger interaction of the carboxylate oxygens compared to that of the two tertiary nitrogens is surprising. Studies by Hancock et al. have shown that ligands such as hydroxide exhibit only weak interaction with copper in copper 1,4,8,11-tetraazacyclotetradecane.[19] From the crystal structure of copper 1,4,8,11-tetraazacyclotetradecane,[20] it is interesting to note that all Cu–N bond lengths are equal (2.02 Å). Their inequivalence in I suggests that the ability of the macrocycle to ligate to the metal ion is dependent on the nature of the ligands in, above, and below the plane of the macrocycle. The unique arrangement of TETA around the copper atom described above results in an unusually inert complex.

Hydrogen-bonding to solvent molecules is observed. The two solvent molecules, O(25)$_{\text{water}}$ and O(26)$_{\text{ethanol}}$, are hydrogen-bonded to the carboxyl oxygen atoms. As shown in Table VI, the water molecule, O(25), is hydrogen-bonded to both O(11′) and O(8″) while the ethanol molecule is hydrogen-bonded to O(1″) and O(4′).

The EPR spectrum of frozen I at pH 7 and 77 K shows anisotropy in g and A values, with three well-resolved peaks and one shoulder peak having a nuclear hyperfine coupling $A_{\parallel}$ value of 160 G. The $g_{\parallel}$ value (=2.237) is less than that obtained for copper chloride ($g_{\parallel}$ = 2.422), suggesting an overall increase in the metal–ligand bond covalency in the complex. The high-field spectrum of I shows that the complex has an axial symmetry with rhombic distortion, maintaining approximate D_{2h} symmetry. $g_z > g_x \gtrsim g_y$; therefore, the Cu^{2+} in I has a $d_{x^2-y^2}$ ground state.[21] The absence of any half-field spectrum ($\Delta m_s = 2$ transition) suggests that the complex is not dimeric in solution at pH 7. We were unable to observe any superhyperfine peaks due to nitrogen coupling. EPR spectra taken at different pH values do not show any significant change in the g and A values, indicating that the structure of the complex at pH 7 is not different from that at pH 10.6.

Our optical data also support the insensitivity of I to pH change. At both pH 7 and pH 12 the $\lambda_{\max}$ of this complex in the visible region is at 650 nm (ϵ = 270 M^{-1} cm^{-1}). Optical studies of the mononuclear copper complex of *meso*-5,12-dimethyl-1,4,8,11-tetraazacyclotetradecane-1,4,8,11-tetraacetic acid have suggested that the coordination sphere undergoes only slight changes, $\lambda_{\max}$ (solution) = 653 nm and $\lambda_{\max}$ (solid state) = 660 nm.[13] Thus, we believe that in solution, I maintains an octahedral geometry very similar to that determined from our X-ray crystallographic study.

The Cu_2[6-(*p*-$NO_2C_6H_4Me$)TETA] Complex (II). The crystal structure of the binuclear copper complex is given in Figure 3, and the bond lengths and bond angles are listed in Tables VII and VIII. The two coppers are situated above and below the plane of the four nitrogen atoms. The ligands coordinated to Cu(1) consist of N(1), N(11), O(1′), O(11′), and O$_w$(1). These ligands are the two nitrogen atoms located farthest away from the nitrobenzyl group, along with their carboxylate oxygen atoms. The deviations from the mean plane for N(1), N(11), O(1′), O(11′),

---

(18) Tomita, V. K.; Nitta, I. *Bull. Chem. Soc. Jpn.* **1961**, *34*, 286.

(19) Hancock, R. D.; Darling, E. A.; Hodgson, R. H.; Ganesh, K. *Inorg. Chim. Acta* **1984**, *90*, L83.

(20) Tasker, P. A.; Sklar, L. *J. Cryst. Mol. Struct.* **1975**, *5*, 329.

(21) Hathaway, B. J.; Biling, D. E. *Coord. Chem. Rev.* **1970**, *5*, 143.

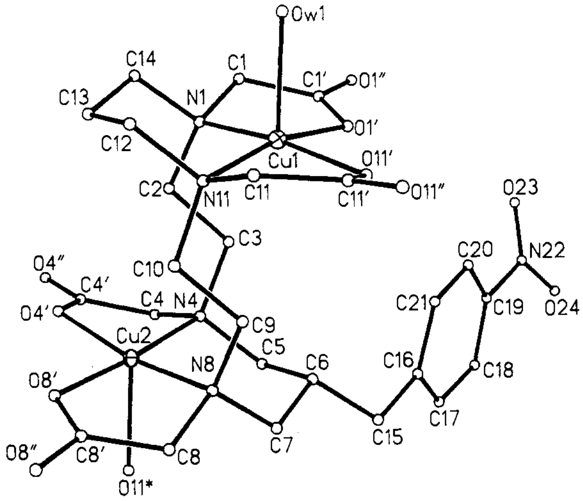


Figure 3. Crystal structure of $Cu_2[6-(p-NO_2C_6H_4Me)TETA]$ (II).

Table VII. Bond Lengths (Å) in II

Cu(1)–N(1)	2.022 (9)	Cu(1)–N(11)	2.023 (9)
Cu(1)–O(1′)	1.947 (7)	Cu(1)–O(11′)	1.992 (7)
Cu(1)–O_w(1)	2.274 (8)	Cu(2)–N(4)	2.008 (9)
Cu(2)–N(8)	2.052 (8)	Cu(2)–O(4′)	1.933 (7)
Cu(2)–O(8′)	1.922 (7)	Cu(2)–O(11*)	2.312 (7)
N(1)–C(2)	1.491 (13)	N(1)–C(14)	1.514 (14)
N(1)–C(1)	1.475 (14)	N(4)–C(3)	1.502 (13)
N(4)–C(5)	1.496 (14)	N(4)–C(4)	1.492 (13)
N(8)–C(7)	1.495 (13)	N(8)–C(9)	1.504 (12)
N(8)–C(8)	1.493 (13)	N(11)–C(10)	1.486 (13)
N(11)–C(12)	1.525 (14)	N(11)–C(11)	1.517 (14)
C(2)–C(3)	1.543 (14)	C(5)–C(6)	1.537 (15)
C(6)–C(7)	1.528 (15)	C(6)–C(15)	1.559 (15)
C(9)–C(10)	1.544 (14)	C(12)–C(13)	1.493 (15)
C(13)–C(14)	1.527 (16)	C(1)–C(1′)	1.521 (14)
C(1′)–O(1′)	1.292 (12)	C(1′)–O(1″)	1.243 (13)
C(4)–C(4′)	1.497 (14)	C(4′)–O(4′)	1.267 (13)
C(4′)–O(4″)	1.246 (13)	C(8)–C(8′)	1.496 (14)
C(8′)–O(8′)	1.288 (12)	C(8′)–O(8″)	1.232 (12)
C(11)–C(11′)	1.537 (15)	C(11′)–O(11′)	1.273 (12)
C(11′)–O(11″)	1.256 (13)	O(11″)–Cu(2a)	2.311 (7)
C(15)–C(16)	1.525 (14)	C(16)–C(17)	1.403 (14)
C(16)–C(21)	1.430 (15)	C(17)–C(18)	1.392 (15)
C(18)–C(19)	1.393 (15)	C(19)–C(20)	1.392 (16)
C(19)–N(22)	1.453 (15)	C(20)–C(21)	1.358 (16)
N(22)–O(23)	1.216 (13)	N(22)–O(24)	1.230 (13)

Table VIII. Bond Angles (deg) in II

N(1)–Cu(1)–N(11)	98.0 (4)	N(1)–Cu(1)–O(1′)	85.0 (3)
N(11)–Cu(1)–O(1′)	167.5 (3)	N(1)–Cu(1)–O(11′)	169.7 (3)
N(11)–Cu(1)–O(11′)	85.2 (3)	O(1′)–Cu(1)–O(11′)	89.9 (3)
N(1)–Cu(1)–O_w(1)	95.4 (3)	N(11)–Cu(1)–O_w(1)	95.8 (3)
O(1′)–Cu(1)–O_w(1)	96.0 (3)	O(11′)–Cu(1)–O_w(1)	94.0 (3)
N(4)–Cu(2)–N(8)	96.3 (3)	N(4)–Cu(2)–O(4′)	85.1 (3)
N(8)–Cu(2)–O(4′)	167.4 (3)	N(4)–Cu(2)–O(8′)	175.9 (3)
N(8)–Cu(2)–O(8′)	86.1 (3)	O(4′)–Cu(2)–O(8′)	91.9 (3)
N(4)–Cu(2)–O(11a)	93.2 (3)	N(8)–Cu(2)–O(11*)	94.4 (3)
O(4′)–Cu(2)–O(11a)	98.0 (3)	O(8′)–Cu(2)–O(11*)	89.9 (3)
Cu(1)–N(1)–C(2)	116.1 (6)	Cu(1)–N(1)–C(14)	108.0 (6)
C(2)–N(1)–C(14)	108.8 (8)	Cu(1)–N(1)–C(1)	104.2 (6)
C(2)–N(1)–C(1)	109.2 (8)	C(14)–N(1)–C(1)	110.5 (8)
Cu(2)–N(4)–C(3)	114.9 (6)	Cu(2)–N(4)–C(5)	112.0 (6)
C(3)–N(4)–C(5)	108.1 (8)	Cu(2)–N(4)–C(4)	101.5 (6)
C(3)–N(4)–C(4)	109.9 (8)	C(5)–N(4)–C(4)	110.3 (8)
Cu(2)–N(8)–C(7)	111.5 (6)	Cu(2)–N(8)–C(9)	112.3 (6)
C(7)–N(8)–C(9)	110.3 (7)	Cu(2)–N(8)–C(8)	102.7 (6)
C(7)–N(8)–C(8)	110.3 (8)	C(9)–N(8)–C(8)	109.4 (7)
Cu(1)–N(11)–C(10)	115.9 (6)	Cu(1)–N(11)–C(12)	110.2 (6)
C(10)–N(11)–C(12)	109.6 (8)	Cu(1)–N(11)–C(11)	103.8 (6)
C(10)–N(11)–C(11)	109.5 (8)	C(12)–N(11)–C(11)	107.6 (8)
N(1)–C(2)–C(3)	112.4 (8)	N(4)–C(3)–C(2)	112.3 (8)
N(4)–C(5)–C(6)	114.5 (8)	C(5)–C(6)–C(7)	112.8 (9)
C(5)–C(6)–C(15)	107.8 (8)	C(7)–C(6)–C(15)	108.5 (8)
N(8)–C(7)–C(6)	114.7 (8)	N(8)–C(9)–C(10)	113.1 (8)
N(11)–C(10)–C(9)	112.7 (8)	N(11)–C(12)–C(13)	114.4 (9)
C(12)–C(13)–C(14)	116.1 (9)	N(1)–C(14)–C(13)	115.1 (9)
N(1)–C(1)–C(1′)	111.9 (8)	C(1)–C(1′)–O(1)	115.9 (8)
C(1)–C(1′)–O(1″)	119.3 (9)	O(1′)–C(1′)–O(1″)	124.8 (9)
N(4)–C(4)–C(4′)	112.3 (8)	C(4)–C(4′)–O(4′)	115.8 (9)
C(4)–C(4′)–O(4″)	118.7 (9)	O(4′)–C(4′)–O(4″)	125.4 (10)
N(8)–C(8)–C(8′)	113.5 (8)	C(8)–C(8′)–O(8′)	116.4 (8)
C(8)–C(8′)–O(8″)	120.0 (9)	O(8′)–C(8′)–O(8″)	123.5 (9)
N(11)–C(11)–C(11′)	112.1 (8)	C(11)–C(11′)–O(11′)	117.5 (9)
C(11)–C(11′)–O(11″)	118.1 (9)	O(11′)–C(11′)–O(11″)	124.4 (10)
Cu(1)–O(1′)–C(1′)	114.0 (6)	Cu(2)–O(4′)–C(4′)	113.5 (7)
Cu(2)–O(8′)–C(8′)	114.9 (6)	Cu(1)–O(11′)–C(11′)	112.3 (6)
C(11′)–O(11″)–Cu(2a)	117.1 (6)	C(6)–C(15)–C(16)	112.3 (8)
C(15)–C(16)–C(17)	121.0 (9)	C(15)–C(16)–C(21)	121.5 (9)
C(17)–C(16)–C(21)	117.5 (9)	C(16)–C(17)–C(18)	122.2 (9)
C(17)–C(18)–C(19)	117.3 (10)	C(18)–C(19)–C(20)	122.3 (10)
C(18)–C(19)–N(22)	119.8 (10)	C(20)–C(19)–N(22)	117.8 (10)
C(19)–C(20)–C(21)	119.6 (10)	C(16)–C(21)–C(20)	121.0 (10)
C(19)–N(22)–O(23)	119.5 (10)	C(19)–N(22)–O(24)	117.6 (9)
O(23)–N(22)–O(24)	122.8 (10)		

and Cu(1) are –0.0185, –0.0569, –0.0576, –0.0146, and 0.1476 Å, respectively. It is seen that Cu(1) lies above the mean plane, resulting in a slightly distorted square pyramid. The square base is also distorted with angles N(1)–Cu(1)–O(1′), O(1′)–Cu(1)–O(11′), O(11′)–Cu(1)–N(11), and N(11)–Cu(1)–N(1) of 85.0, 89.9, 85.2, and 98.0°, respectively. The angles O(11′)–Cu(1)–N(11) and O(1′)–Cu(1)–N(1) are as expected for a five-membered chelate ring.[18] However, the 98° angle N(11)–Cu(1)–N(1) deviates appreciably from the expected 92° (six-membered diamino chelate ring),[22] indicating strain in the system.

The ligands around the second copper atom, Cu(2), also form a square-based pyramid. The base consists of the two nitrogen atoms and two carboxylate oxygens closest to the nitrobenzyl group. The axial ligand is a carboxylate oxygen, O(11*), from an adjacent macrocyclic unit. Because of the close proximity of the nitrobenzyl group to this second copper center, the base of the pyramid is significantly distorted. The deviations from the mean plane for N(4), N(8), O(4′), O(8′), and Cu(2) are –0.0526, 0.1044, 0.1135, –0.0581, and –0.1071, respectively.

Comparing the axial bond length of the two square-pyramidal centers, we find that the Cu(2)–O(11*) bond length is shorter than bond length Cu(1)–O_w(1). In contrast, the unsubstituted TETA molecule forms a binuclear copper complex in which the Cu–$O_{carboxylate}$ is longer than Cu–O_w.[15]

The II crystal is polymeric, with each unit attached to the next through the Cu(2)–O(11*) linkage. The other oxygen of the carboxyl group containing O(11*) is coordinated to copper in the adjacent complex. This is consistent with the studies by Haflinger et al., who suggested that the binuclear copper complex of *meso*-5,12-Me_2-1,4,8,11-TETA is polymeric.[13]

The Cu(1)–Cu(2) distance in II is 4.828 Å. This metal–metal distance is similar to that of the binuclear copper complex of the unsubstituted TETA molecule (4.78 and 4.88 Å), and it allows for antiferromagnetic interaction.[15] Although similarities exist between the Cu_2(TETA) and the alkyl-substituted chelate II, there are remarkable differences. Cu_2(TETA) in crystalline form is made up of two coordinatively different Cu_2(TETA) units. In one unit, the two coppers are ligated axially to carboxylate oxygen atoms, while in the other the two coppers are ligated axially to water oxygen atoms. In contrast, in II, each unit in the polymer is identical with the others. However, within each unit there are two coordinatively different copper centers, as described above. Interestingly, substitution of all four carboxylate pendant arms by aminoethyl groups, as in 1,4,8,11-tetrakis(2-aminoethyl)-1,4,8,11-tetraazacyclotetradecane (taec), results in a binuclear copper complex with a ligand arrangement similar to that of II.[23] However, in $[Cu_2(taec)ClO_4]_2$ the Cu(1)–Cu(2) distance is longer (~5.479 Å). Also, the amino ligands in taec, unlike carboxylates, are monodentate and therefore unable to form polymeric links.

---

[22] Curtis, N. F. *Coordination of Macrocyclic Compounds*; Plenum: New York, 1979; p 219.

[23] Murase, I.; Mikuriya, M.; Sonoda, H.; Kida, S. *J. Chem. Soc., Chem. Commun.* **1984**, 692.

Acknowledgment. We thank Dr. Marilyn Olmstead for her advice and assistance. We acknowledge support by Research Grant CA 16861 to C.F.M. from the National Cancer Institute and Research Grant DE FGO384ER60233 to S.J.D. from the Department of Energy.

Registry No. I, 110242-22-3; II, 110242-23-4; 1,3-bis[(2-aminoethyl)amino]propane, 4741-99-5; *p*-nitrobenzyl malonate, 110270-80-9; cyclic diamide, 97856-33-2.

Supplementary Material Available: Listings of anisotropic thermal parameters and hydrogen coordinates (Tables S1–S4) (3 pages); listings of structure factor amplitudes (Tables S5 and S6) (33 pages). Ordering information is given on any current masthead page.

Contribution from the Department of Chemistry and Laboratory for Molecular Structure and Bonding,
Texas A&M University, College Station, Texas 77843

Preparation, Spectroscopic Properties, and Characterization of *anti*- and *syn*-α-$Mo_2Cl_4[(C_6H_5)_2PCH_2CH_2P(p\text{-}CH_3C_6H_4)_2]$ in Solution and in the Solid State

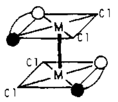
F. Albert Cotton* and Susumu Kitagawa*

Received April 1, 1987

Dimolybdenum(II) compounds containing the unsymmetrical diphosphine dpdt (1-(diphenylphosphino)-2-(di-*p*-tolylphosphino)ethane) have been synthesized. Each of the two structural isomers (α and β) exists as two geometrical isomers (syn and anti), as shown schematically by structures **1**–**4**. All isomers can be formed, and all are very soluble in CH_2Cl_2. The crystal structure of *anti*-α-$Mo_2Cl_4(dpdt)_2\cdot 2CH_3OH$, in which a dpdt ligand chelates to each of the Mo atoms of the dimer, has been determined. The space group is $P2_1/c$ with $a = 12.374$ (4) Å, $b = 9.280$ (2) Å, $c = 24.829$ (5) Å, $\beta = 102.12$ (3)°, $V = 2787$ (2) Å^3, and $Z = 2$. The Mo–Mo bond distance is 2.147 (1) Å, similar to that in the dppe compound, while the Mo–P(phenyl) and Mo–P(tolyl) distances are 2.547 (3) and 2.534 (3) Å, respectively. α-$Mo_2Cl_4(dpdt)_2$ was obtained by slow isomerization of a sample of pure β-$Mo_2Cl_4(dpdt)_2$. The ^1H NMR spectra of the α and β isomers were measured, and the spectra of the anti and syn isomers of the α form were completely assigned with the aid of aryl ring diamagnetic anisotropy. It has thus been demonstrated that essentially equal amounts of the geometrical isomers are formed in the synthesis of α-$Mo_2Cl_4(dpdt)_2$ from K_4MoCl_8. The magnetic anisotropy of the quadruple bond in the α isomers has been estimated to be -8800×10^{-36} m^3/molecule.

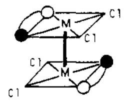
Introduction

Many quadruply bonded M_2 compounds,[1,2] $Mo_2X_4(LL)_2$, where X = Cl and Br and LL is the bridging bidentate phosphine $R_2P(CH_2)_nPR_2$, have been extensively studied in the solid state, with particular attention to how their structural properties relate to the nature of the multiple Mo–Mo bonding. The recent findings[3–5] concerning the isomerization of α-$Mo_2X_4(dppe)_2$ to β–$Mo_2X_4(dppe)_2$ have added an additional, intriguing dimension to this dimolybdenum chemistry. However, because of the general insolubility of these complexes investigations of their reactions and properties in solution have been quite limited. A complete understanding of this chemistry, especially the isomerization phenomenon, requires detailed characterization of the solution behavior of these compounds, or similar ones. In this paper, we report the successful synthesis of some $Mo_2Cl_4(LL')_2$ compounds, which have much greater solubility. As a result, we have been able to make many new observations, including discovery of the reverse isomerization reaction (from the β isomer to the α isomer) and obtain the full characterization of these compounds by ^1H NMR magnetic resonance, including the distinction between geometrical isomers (syn and anti), which arise because of the unsymmetrical ligand LL′. In the following discussion the terms α-$Mo_2Cl_4(dpdt)_2$ and β-$Mo_2Cl_4(dpdt)_2$ will signify the essentially equimolar mixture of the syn and anti geometrical isomers.



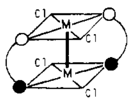
syn-α

1



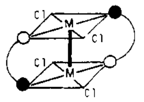
anti-α

2



syn-β

3



anti-β

4

Experimental Section

All operations were carried out under an atmosphere of purified argon. Solvents were dried by conventional methods and distilled under dinitrogen. $K_4Mo_2Cl_8$ and $Mo_2(O_2CCF_3)_4$ were prepared as described elsewhere.[6,7] Tri-*p*-tolylphosphine and 1-(diethylphosphino)-2-(diphenylphosphino)ethane (dedp) were purchased from Strem Chemicals. Diphenylvinylphosphine was purchased from Aldrich Chemicals.

Preparation of dpdt. Tri-*p*-tolylphosphine (12 g, 0.039 mol) was treated with Li wire (1.2 g, 0.17 mol) in THF.[8,9] The resultant dark red solution was hydrolyzed and extracted with ether and the ether extract washed with dilute acid and water. The organic layer was dried over Na_2SO_4 and distilled to give 4.5 g of di-*p*-tolylphosphine (54% yield, bp 124–126 °C (1.2 mmHg)), which was identified by its ^1H NMR spectrum.

A mixture of 4.1 g (0.019 mol) of diphenylvinylphosphine, 4.0 g (0.019 mol) of di-*p*-tolylphosphine, and 0.4 g of potassium *tert*-butoxide in THF was refluxed for 6 h.[10] Evaporation of the solvent gave an orange-yellow residue, which was washed with methanol, and the crude white solid was separated by filtration. This solid was recrystallized from benzene/methanol to give a white crystalline solid: yield 5.7 g (70%); mp 112.0–112.5 °C. Anal. Found: C, 79.31; P, 14.78; H, 6.66. Calcd for $C_{28}H_{28}P_2$: C, 78.86; P, 14.52; H, 6.62.

Preparation of α-$Mo_2Cl_4(dpdt)_2$. A mixture of $K_4Mo_2Cl_8$ (0.27 g, 0.43 mmol) and dpdt (0.37 g, 0.87 mmol) in 30 mL of methanol was refluxed for 3 h.[11] A precipitated green powder was separated by filtration, washed once with methanol and diethyl ether, and dried in vacuo; yield 0.27 g (55%). This powder contained small amounts of the β form and $K_4Mo_2Cl_8$; the pure α form was obtained from the second CH_2Cl_2 fraction by silica gel column chromatography.

Preparation of β-$Mo_2Cl_4(dpdt)_2$. $Mo_2(O_2CCF_3)_4$ (0.16 mg, 0.25 mmol) was dissolved in 20 mL of THF, and Me_3SiCl (0.2 mL) was added. This solution was stirred for 12 h,[12] and then 216 mg of dpdt (0.51 mmol) was added. After 10 h, a brown solution was obtained. No precipitates were observed. The solvent was evaporated, and the brown residue was washed with methanol and cold ether. The light brown powder was dried in vacuo; yield 0.17 g (60%). This powder was not yet the pure β form and was redissolved in CH_2Cl_2 and then separated by silica gel chromatography. The first brown fraction was collected, and the CH_2Cl_2 was evaporated to give the light brown, pure β form. The α- and β-$Mo_2Cl_4(dedp)_2$ compounds were prepared in a similar way.

---

(1) Cotton, F. A.; Walton, R. A. *Multiple Bonds between Metal Atoms*; Wiley: New York, 1982.
(2) Cotton, F. A.; Walton, R. A. *Struct. Bonding* (*Berlin*) **1985**, *62*, 99.
(3) Agaskar, P. A.; Cotton, F. A.; Fraser, I. F.; Peacock, R. D. *J. Am. Chem. Soc.* **1984**, *106*, 1851.
(4) Agaskar, P. A.; Cotton, F. A.; Derringer, D. R.; Powell, G. L.; Root, D. R.; Smith, T. J. *Inorg. Chem.* **1985**, *24*, 2786.
(5) Agaskar, P. A.; Cotton, F. A. *Inorg. Chem.* **1986**, *25*, 15.
(6) Cotton, F. A.; Norman, J. G., Jr. *Coord. Chem.* **1972**, *1*, 161.
(7) Cotton, F. A.; Brencic, J. V. *Inorg. Chem.* **1970**, *9*, 351.
(8) Wittenberg, D.; Gilman, H. *J. Org. Chem.* **1958**, *23*, 1063.
(9) Grim, S. O.; Molenda, R. P. *Phosphorus Relat. Group V Elem.* **1974**, *4*, 189.
(10) Kapoor, P. N.; Pathak, D. D.; Gaur, G.; Kutty, M. *J. Organomet. Chem.* **1984**, *276*, 167.
(11) Best, S. A.; Smith, T. J.; Walton, R. A. *Inorg. Chem.* **1978**, *17*, 99.
(12) Agaskar, P. A.; Cotton, F. A. *Inorg. Chem.* **1984**, *23*, 3383.