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Syntheses and Characterization of Two Dioxygen-Reactive Dinuclear Macrocyclic Schiff-Base Copper(I) Complexes

Diana Utz,[†] Frank W. Heinemann,[†] Frank Hampel,[‡] David T. Richens,[§] and Siegfried Schindler*[,†,||]

Institut für Anorganische Chemie, Universität Erlangen-Nürnberg, Egerlandstrasse 1, 91058 Erlangen, Germany, Institut für Organische Chemie, Universität Erlangen-Nürnberg, Henkestrasse 42, 91054 Erlangen, Germany, and School of Chemistry, University of St. Andrews, Purdie Building, North Haugh, St. Andrews, Fife KY169ST, Scotland

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The dinuclear copper(I) complex $[Cu_2L^1(CH_3CN)_2](ClO_4)_2$ (**1**, L^1 = 3,6,9,17,20,23-hexaazatricyclo[23.3.1.1]triaconta-1(29),2,9,11(30),12(13),14,16,23,25,27-decaene) has been structurally characterized. As previously described, intramolecular ligand hydroxylation (at the aromatic ring) was observed when **1** was reacted with dioxygen. A stopped-flow analysis of the reaction of **1** with dioxygen under different conditions did not allow a "dioxygen intermediate" to be spectroscopically detected. Detailed NMR and electrochemical data on **1** are also presented and evaluated for the first time. No copper(II) complexes of L^1 could be characterized due to hydrolysis of the compounds. In contrast, complex **2**—differing from **1** only in an increase in the size of the chelate rings—did not undergo intramolecular hydroxylation when it was oxidized. The crystal structure of **2** is also described.

Introduction

A dinuclear copper center forms the active site of the enzyme tyrosinase, a monooxygenase which activates dioxygen for the *ortho*-hydroxylation of monophenols (tyrosine) and further oxidizes the *o*-diphenol to an *o*-quinone.[1−5] Efforts to functionally model this protein and the related dioxygen transport protein hemocyanin led to the development of a series of mononuclear and dinuclear copper model complexes. However the detailed mechanism for the aromatic ring hydroxylation reaction still remains unclear.[4−16] The interest in modeling these proteins derives from their possible use as catalysts for selective oxidations of organic substrates with dioxygen.[17] Tyrosinase activity was first modeled successfully by Karlin and co-workers, who found that an intramolecular ligand hydroxylation occurred during the reaction of dioxygen with the dinuclear copper(I) complex $[Cu_2(XYL\text{-}H)]^{2+}$ wherein a *m*-xylyl group links two bis[2-(2-pyridyl)ethyl]amine units.[18,19] The occurrence of a peroxo complex as an intermediate during this reaction was proven spectroscopically in a detailed stopped-flow kinetics study

* To whom correspondence should be addressed. E-mail: Siegfried.Schindler@anorg.chemie.uni-giessen.de. Fax: +49-(0)641-99-34149.

[†] Institut für Anorganische Chemie, Universität Erlangen-Nürnberg.

[‡] Institut für Organische Chemie, Universität Erlangen-Nürnberg.

[§] School of Chemistry, University of St. Andrews.

[||] Current address: Institut für Anorganische und Analytische Chemie, Justus-Liebig-Universität Giessen, Heinrich-Buff-Ring 58, 35392 Giessen, Germany.

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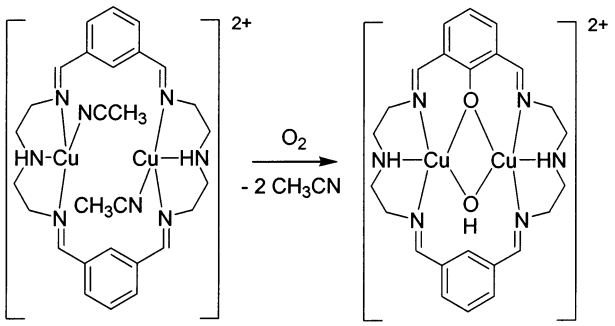

Figure 1. Reaction of $[Cu_2L^1(CH_3CN)_2](ClO_4)_2$ (**1**) with dioxygen.

at low temperatures.[20−22] Resonance Raman spectroscopic studies indicate that this intermediate is a μ-η^2: η^2-peroxo-bridged dicopper(II) species.[23]

To gain further understanding of this reaction dinuclear copper(I) complexes with the *m*-xylyl group linking different donor units have been investigated. For many of these compounds intramolecular aromatic ring hydroxylation was observed during their reaction with dioxygen.[11,24−35] This kind of reactivity is also described for the macrocyclic dicopper(I) complex $[Cu_2L^1(CH_3CN)_2](ClO_4)_2$ (**1**) (Figure 1).[34,36,37] Until now no detailed structural characterization of this complex has been available. Herein we report the crystal structures of $[Cu_2L^1(CH_3CN)_2](ClO_4)_2$ and of the related compound $[Cu_2L^2](ClO_4)_2$ as well as further details on the solution chemistry and the reactivity of both complexes toward dioxygen.

Experimental Section

Materials and Methods. Reagents and solvents used were of commercially available reagent quality. Organic solvents used in the syntheses of the copper(I) complexes were dried in the usual way. Diethylenetriamine (dien) and bis(3-aminopropyl)amine were distilled prior to use. $[Cu(CH_3CN)_4]ClO_4$ was synthesized according to a literature procedure.[38] Preparation and handling of air-sensitive compounds was carried out in a glovebox filled with argon (Braun, Garching, Germany; water and dioxygen less than 1 ppm). Samples for NMR spectra were prepared in the glovebox. ^{1}H and ^{13}C NMR spectra were recorded on a DXP 300 AVANCE spectrometer or Bruker AVANCE DRX-400 spectrometer with a wide-bore magnet, respectively. Infrared spectra were recorded as KBr pellets on a ATJ Mattson Infinity 60 AR-FT-IR instrument. Elemental analyses were carried out on a Carlo Erba model 1106 element analyzer, and FD mass spectra were measured on a JEOL JMS 700 instrument at 70 eV and a source temperature of 200 °C.

Electrochemical measurements were carried out at 20.0 °C on oxygen-free 0.005 M solutions of L^1 in dichloromethane or acetonitrile in the presence of varying amounts of $[Cu(CH_3CN)_4]ClO_4$ (added via syringe addition from a 0.2 M stock solution) using a glassy carbon disk working electrode (i.d. 0.5 mm), a Pt wire auxiliary electrode, and a Ag/0.1 M $AgNO_3$/MeCN reference electrode with a BAS 100B instrument. The supporting electrolyte was 0.1 M tetrabutylammonium perchlorate. Potentials are reported referenced to ferrocene (+0.38 V vs the $Ag/AgNO_3$ reference) used as the internal standard. Solvents (Merck, HPLC grade) for the electrochemical studies were distilled onto freshly dried 4 Å molecular sieves prior to use.

Aromatic Ring Hydroxylation Studies. To a 0.005 M solution of L^1 in oxygen-free dichloromethane (50 mL) was added varying amounts of $[Cu(CH_3CN)_4]ClO_4$ (from a 0.2 M stock solution in acetonitrile). The mixture was stirred, and then air was bubbled through the solution briefly before being left to stir open to air for 12 h. The initial pale-yellow colored solution of the mixture turned a bright olive-green color. The mixture was then evaporated to dryness and treated with dilute HCl (0.5 M) causing complete hydrolysis of both the copper complex and any free Schiff-base ligand to give Cu^{2+}(aq), $dienH_3^{3+}$, and a mixture of isophthalaldehyde and 2-hydroxy-1,3-benzenedicarbaldehyde. The carbaldehyde mixture was then extracted with dichloromethane, dried over anhydrous Na_2SO_4, evaporated again to dryness, and finally taken up in $CDCl_3$/TMS for the ^{1}H NMR studies. The relative ratio of the two aldehydes, found from integrating the two aldehydic C−H resonances and the OH resonance in the low-field region of the spectrum above 10 ppm, gives a measure of the % hydroxylation at one ring. This was plotted against the number of equivalents of Cu(I) added to L^1 in the original mixture.

Variable-Temperature Stopped-Flow Measurements. Solutions of complexes for the collection of time-resolved UV−vis spectra were prepared in the glovebox and transferred using syringes to the low-temperature stopped-flow instrument. A dioxygen saturated solution was prepared by bubbling dioxygen through methanol or acetone in a syringe (solubility of dioxygen at 25 °C: methanol, 0.0104 M;[39] acetone, 0.0102 M[40]). The reaction was studied under pseudo-first-order conditions ([complex] $\ll$ [O_2]), and time-resolved UV−vis spectra of the reactions of dioxygen with copper(I) complexes were recorded with a modified Hi-Tech SF-3L low-temperature stopped-flow unit (Salisbury, U.K.) equipped with a J&M TIDAS 16-500 photodiode array spectrophotometer (J&M, Aalen, Germany). Data fitting was performed using the integrated J&M software Kinspec.

X-ray Structure Determination of $[Cu_2L^1(CH_3CN)_2](ClO_4)_2$ (1) and $[Cu_2L^2](ClO_4)_2$ (2). Single crystals were coated with

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Table 1. Crystal Data and Structure Refinement for $[Cu_2L^1(CH_3CN)_2](ClO_4)_2$ (**1**) and $[Cu_2L^2](ClO_4)_2$ (**2**)

param	**1**	**2**
chem formula	$C_{28}H_{36}N_8Cu_2Cl_2O_8$	$C_{28}H_{36}N_6Cu_2Cl_2O_8$
fw	810.63	782.61
temp (K)	294(2)	173(2)
wavelength (Å)	0.710 73	0.710 73
space group	*C*2/*c*	$P2_1/c$
a (Å)	36.242(4)	13.9342(5)
b (Å)	11.391(3)	7.9472(3)
c (Å)	19.065(2)	15.0109(6)
α (deg)	90	90
β (deg)	116.89(1)	102.008(2)
γ (deg)	90	90
V (Å^3)	7020(2)	1625.90(11)
Z	8	2
D_{calcd} (Mg/m^3)	1.534	1.599
abs coeff. (mm^{-1})	1.422	1.530
R indices [$I > 2\sigma(I)$]	$R1(F_o) = 0.0551$	$R1(F_o) = 0.0532$
	$wR2(F_o^2) = 0.1332$	$wR2(F_o^2) = 0.1313$
R indices (all data)	$R1(F_o) = 0.0914$	$R1(F_o) = 0.0894$
	$wR2(F_o^2) = 0.1538$	$wR2(F_o^2) = 0.1510$

Table 2. Bond Lengths (Å) and Angles (deg) for **1** and **2**

Bond Lengths for **1**			
Cu(1)−N(1)	2.081(4)	Cu(1)−N(3)	1.996(3)
Cu(1)−N(2)	2.193(4)	Cu(1)−N(7)	1.894(4)
Cu(2)−N(4)	2.048(4)	Cu(2)−N(5)	2.219(5)
Cu(2)−N(6)	2.039(4)	Cu(2)−N(8)	1.912(4)
Bond Angles for **1**			
N(7)−Cu(1)−N(3)	137.9(2)	N(8)−Cu(2)−N(6)	129.1(2)
N(3)−Cu(1)−N(1)	103.1(2)	N(6)−Cu(2)−N(4)	103.3(2)
N(3)−Cu(1)−N(2)	85.1(2)	N(6)−Cu(2)−N(5)	80.7(2)
N(7)−Cu(1)−N(1)	116.2(2)	N(8)−Cu(2)−N(4)	125.8(2)
N(7)−Cu(1)−N(2)	114.4(2)	N(8)−Cu(2)−N(5)	113.3(2)
N(1)−Cu(1)−N(2)	80.8(2)	N(4)−Cu(2)−N(5)	84.6(2)
C(25)−N(7)−Cu(1)	177.4(4)	C(27)−N(8)−Cu(2)	173.8(5)
Bond Lengths for **2**			
Cu(1)−N(1)	1.942(3)	Cu(1)−N(3)	1.943(4)
Cu(1)−N(2)	2.110(3)		
Bond Angles for **2**			
N(1)−Cu(1)−N(3)	158.80(14)	N(1)−Cu(1)−N(2)	104.72(15)
N(3)−Cu(1)−N(2)	96.27(14)		

polyfluoroether oil and mounted on a glass fiber. Data for **1** were collected on a Siemens P4 diffractometer at 294(2) K and for **2** on a Nonius Kappa diffractometer with a CCD array detector at 173(2) K (graphite-monochromator) (see Tables 1 and 2). Lorentz, polarization, and empirical absorption corrections were applied. Space groups were determined from systematic absences and subsequent least-squares refinement. The structures were solved by direct methods and refined on F^2 using full-matrix least-squares techniques.[41] Non-hydrogen atoms were refined with anisotropic thermal parameters. For **1** all hydrogen atom positions were taken from a difference Fourier map but were not refined. The crystallographic data were deposited as supplementary publication nos. CCDC 180448 (**1**), CCDC 181311 (**2**), and CCDC 183547 (**3**) at the Cambridge Crystallographic Data Centre and are available on request from the following: CCDC, 12 Union Road, Cambridge CB2 1EZ. Fax: (+44)1223-336-033. E-mail: deposit@ccdc.cam.ac.uk.

Syntheses of Ligands and Complexes. **Caution!** *Perchlorate salts are potentially explosive and should be handled with great care*.

3,6,9,17,20,23-Hexaazatricyclo[23.3.1.1]triaconta-1(29),2,9,11(30),12(13),14,16,23,25,27-decaene (L^1). L^1 was synthesized in a manner similar to previously published procedures.[34,36] A solution of 5.32 g (39.7 mmol) of isophthalaldehyde in 650 mL of CH_3CN was added dropwise (over 8 h) to a solution of 4.10 g (39.7 mmol) of freshly distilled diethylenetriamine in 1000 mL of CH_3CN. The reaction mixture was stirred for 17 h at room temperature. The resulting yellow precipitate was filtered off and recrystallized from a mixture of CH_3CN/CH_2Cl_2 (1:3) to yield 5.88 g (14.60 mmol) of a white solid (yield: 74%). The 300-MHz ^{1}H NMR spectra in $CDCl_3$ are complex because of a ring-forming tautomeric equilibrium of the Schiff-base in solution.[34] Anal. Calcd: C, 71.61; H, 7.52; N, 20.88. Found: C, 71.72; H, 7.50; N, 20.93. FD-MS ($CHCl_3$, 70 eV): m/z = 201/202 $[L^1]^{2+}$, 403/404 $[L^1]^+$. IR (KBr, cm^{-1}): 3274 ν(N−H), 3057/3034 ν(C−H), 2926/2891/2839/2789 ν(C−H), 1649 ν(C═N), 1444 δ(C−H), 793/700 δ(C−H).

$[Cu_2L^1(CH_3CN)_2](ClO_4)_2$ (1). To a suspension of 0.402 g (1 mmol) of L^1 in 20 mL of MeOH was added a suspension of 0.654 g (2 mmol) of $[Cu(CH_3CN)_4]ClO_4$ in 40 mL of MeOH and heated for 5 min at 60 °C. After the mixture was stirred for 2 h at room temperature, a yellow precipitate was obtained in 98% yield (0.800 g, 0.98 mmol). Yellow crystals suitable for X-ray diffraction studies were obtained by diffusion of THF into a solution of **1** in a mixture of MeOH, CH_3CN, and CH_2Cl_2 (2:2:1). Anal. Calcd for $C_{28}H_{36}N_8Cu_2Cl_2O_8$: C, 41.49; H, 4.48; N, 13.82. Found: C, 41.39; H, 4.99; N, 13.50. IR (KBr, cm^{-1}): 3355 ν(N−H), 3034 ν(C−H), 2928/2857 ν(C−H), 1636 ν(C═N), 1443 δ(C−H), 1090 ν(Cl−O), 783/691 δ(C−H).

$[Cu_2L^2](ClO_4)_2$ (2). A solution of 0.394 g (3 mmol) of bis(3-aminopropyl)amine in 10 mL of MeOH and 0.982 g (3 mmol) of $[Cu(CH_3CN)_4]ClO_4$ was added to a solution of 0.402 g (3 mmol) of isophthalaldehyde in 15 mL of methanol. The reaction mixture was heated at 60 °C for 15 min and then stirred for 3 h at room temperature. The resulting orange solid was filtered off and dried in vacuo to yield 0.563 g (0.718 mmol) of **2** (48%). Red single crystals suitable for X-ray diffraction studies were obtained by diffusion of Et_2O into a solution of **2** in a mixture of $MeOH/CH_3CN$ (1:1). Anal. Calcd for $C_{28}H_{38}N_6Cu_2Cl_2O_8$: C, 42.86; H, 4.88; N, 10.71. Found: C, 42.75; H, 5.08; N, 10.63. FD-MS (CH_3CN, 70 eV): m/z = 459 $[L^2]^+$, 522 $[CuL^2]^+$. IR (KBr, cm^{-1}): 3271 ν(N−H), 3045 ν(C−H), 2919/2862 ν(C−H), 1624 ν(C═N), 1458 δ(C−H), 1092 ν(Cl−O), 788/689 δ(C−H).

Results and Discussion

Synthesis and Characterization of $[Cu_2L^1(CH_3CN)_2](ClO_4)_2$ (1) and $[Cu_2L^2](ClO_4)_2$ (2). Metal complexes of Schiff-base macrocycles have been used successfully in the past for modeling metallobiosites.[42] General procedures to synthesize such complexes were established by Nelson and co-workers.[43] The macrocyclic ligand L^1 was readily prepared in good yields similar to published procedures.[34,36,44] NMR spectra of L^1 in $CDCl_3$ are complex and suggest the existence of several isomeric/tautomeric species in solution.[34,44] The crystal structure of one of the isomers was determined and revealed a ring contraction from the 24-membered macrocycle to an 18-membered macrocycle due to a ring-forming tautomerism resulting from reaction of the secondary amine group with one of the imines.[34,44] However these Schiff-base tautomers are in equilibrium with the 24-membered tetraimine form which is the form that complexes with copper(I).

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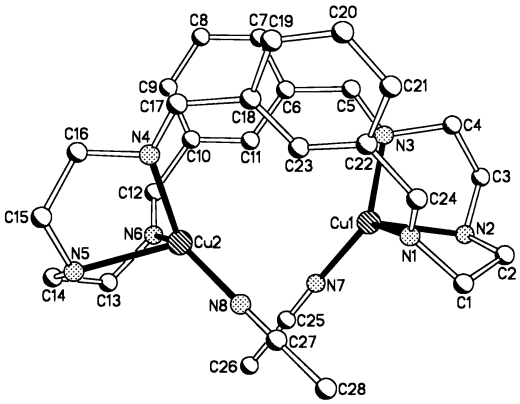

Figure 2. Molecular structure of the cation of $[Cu_2L^1(CH_3CN)_2](ClO_4)_2$ (**1**). (Hydrogen atoms are omitted for clarity.)

Although reaction of the copper(I) complex of L^1 with dioxygen has been previously reported, a detailed characterization of this complex has so far been lacking.[34,36,37,45] This is mainly a consequence of the high reactivity of **1** in solution toward dioxygen. However, under the inert conditions of a glovebox we obtained crystals of this complex suitable for X-ray analysis. The complex can also be synthesized by a template reaction following the procedure described for $[Cu_2L^2](ClO_4)_2$ (**2**) above. The molecular structure of the cation of $[Cu_2L^1(CH_3CN)_2](ClO_4)_2$ (**1**) with the atomic numbering scheme is shown in Figure 2.

Each copper ion is coordinated in a distorted tetrahedral manner by two imine donors, an amine donor, and one acetonitrile molecule. The ClO_4^- counterions do not interact with the copper(I) ions. One ClO_4^- counterion was found to be disordered over two positions. These two positions were refined with occupancies of 73(3)% and 27(3)%. The Cu−N_{imine} and Cu−N_{amine} bond distances compare well with other crystallographically characterized copper(I) imine complexes (only some examples are given in the references).[33,45,46] The Cu−Cu separation of 4.250(3) Å is smaller than the experimental value for deoxyhemocyanin (4.6 Å) but quite close to the 4.4 Å reported for the reduced form of catechol oxidase, an enzyme related to tyrosinase (the crystal structure of tyrosinase has not been reported yet).[47−49] It is much shorter than in a related nonmacrocyclic complex (4.952(2) Å)[33] and the macrocyclic *p*-phenylene isomer of **1** (7.04 Å).[45] This must be a consequence of the "bowl shape" of the complex that results from the distortion of the phenyl rings against each other.

It is interesting to note that, due to the difficulties obtaining crystals of **1** in the past, the structure of this complex was predicted by molecular mechanics calculations which were based on simulations of the *p*-phenylene isomer.[45] It is seen that the calculated structure correctly describes the important features of the experimentally determined crystal structure of **1** such as the "bowl shape" of the complex which brings the copper(I) ions into relatively close proximity. Small deviations in bond lengths and angles are apparent by replacing acetonitrile by ammonia to simplify the calculations.[45] However, the calculated Cu−Cu separation of 3.4 Å is 0.8 Å shorter than the experimental value, a feature conceivably due to accommodation of the larger acetonitrile ligands.

Use of other spectroscopic and analytical methods have failed to characterize complex **1** in detail. While elemental analysis data indicate that the complex is formed, no information on solvent coordination can be gained. IR spectroscopy also supported the formation of **1**, but again it was not possible to ascertain if acetonitrile molecules are coordinated or not. The role played by any coordinated acetonitrile molecules in these copper(I) complexes is perhaps more important to consider. In earlier work on **1** it was assumed that acetonitrile molecules are not coordinated to the copper(I) ions.[34,36] For the MM calculations on **1** the coordination of a solvent ligand on each copper(I) ion was included because of the known coordination of acetonitrile in the isomeric *p*-phenylene copper(I) complex.[45] However, such a variation in the ligand system can lead to a quite different reactivity of the copper(I) complex and furthermore can cause a completely different behavior toward coordination of additional acetonitrile molecules (see below and for example refs 50 and 51).

A ring-enlarged 28-membered Schiff-base macrocyclic ligand, L^2, similar to L^1 has been reported earlier using bis(3-aminopropyl)amine instead of diethylenetriamine in the synthesis.[52] The general reactivity of its copper(I) complex has been investigated, but a detailed structural characterization of this compound was not apparent.[53] In this work the copper(I) complex $[Cu_2L^2](ClO_4)_2$ (**2**) was prepared directly by a template reaction of $[Cu(CH_3CN)_4]ClO_4$, bis(3-aminopropyl)amine, and isophthalaldehyde under inert conditions. The molecular structure of **2** with the atomic numbering scheme is presented in Figure 3. The complex exhibits a center of inversion. In the dinuclear complex each copper(I) ion is coordinated in a distorted trigonal planar manner by two imine donors and one amine donor. Clearly in contrast to **1** no acetonitrile molecules are coordinated in **2** as additional coligands. The phenyl rings in this complex are coplanar to each other and therefore provide a large cavity in which the two copper(I) ions are included. The copper(I) ions are separated from one another by 7.700(2) Å and shifted 0.043 Å out of the N_3 plane. This distance is much larger than in **1** and even larger than that found for the *p*-phenylene isomer of **1** (7.04 Å).[45] Each copper(I) ion shows

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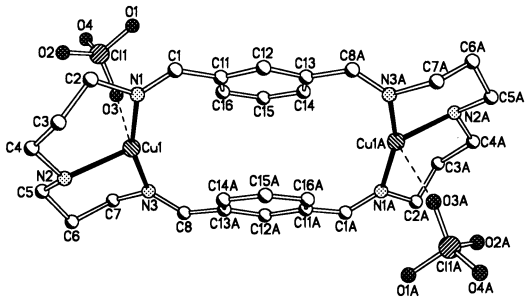

Figure 3. Molecular structure of $[Cu_2L^2](ClO_4)_2$ (**2**). (Hydrogen atoms are omitted for clarity.)

weak interaction to one oxygen atom of the ClO_4^- counterion at a distance of 2.935(3) Å.

Reactivity toward dioxygen. In an earlier communication we reported a kinetic analysis of the intramolecular ligand hydroxylation during the reaction of dioxygen with **1** (formed in situ by mixing stoichiometric amounts of $[Cu(CH_3CN)_4]ClO_4$ with L^1 under inert conditions) in methanol.[37] From the kinetic findings we postulated a dinuclear copper peroxo intermediate similar to the one that was observed spectroscopically during the reaction of $[Cu_2(XYL\text{-}H)]^{2+}$ with dioxygen at low temperatures.[20−22] With the isolation of the well-defined starting material **1** we have reinvestigated this reaction at low temperatures using stopped-flow techniques hoping to detect the occurrence of a "dioxygen adduct" as an intermediate. Unfortunately, during the kinetic experiments in methanol, acetone, or dichloromethane no oxygen-derived intermediate could be observed spectroscopically even when the temperature was lowered to −90 °C. A similar result was observed earlier for two nonmacrocyclic imine complexes.[10,13,54] We conclude that the rate-determining step in the reaction of these dicopper(I) imine complexes with dioxygen is the formation of the "dioxygen adduct" (at all temperatures studied). This behavior contrasts with the reaction of $[Cu_2(XYL\text{-}H)]^{2+}$ with dioxygen wherein formation of a "dioxygen adduct" is readily observed.[20−22] It is apparent however that the isolated complex **1** reacts faster than the same complex prepared in situ from L^1 and solutions of $[Cu(CH_3CN)_4]ClO_4$ in acetonitrile. Indeed the reaction in pure acetonitrile needs hours for completion compared with the immediate oxidation in methanol. Furthermore the intramolecular aromatic ring hydroxylation was suppressed as was reported earlier for $[Cu_2(XYL\text{-}H)]^{2+}$.[20−22] This provides clear evidence that acetonitrile competes significantly with dioxygen as a ligand on the copper(I) center. The oxidation of **1** with dioxygen in dichloromethane or in acetone is very similar to the same reaction in methanol and was not studied in more detail.[37]

Comparison of the reactivity of **1** toward dioxygen with the same reaction on the ring-expanded complex **2** and the *p*-phenylene isomer of **1** is also of interest. **2** reacts in methanol with dioxygen, but in contrast to **1**, no intramolecular aromatic ring hydroxylation was observed.[53] The reaction product was not characterized in detail, but it is believed that a bis(μ-methoxy)-bridged dicopper(II) complex is the final product in methanol.[53] A kinetic analysis of the reaction of **2** with dioxygen in methanol or acetone proved to be complex with several reaction steps detected. Simple fitting of the data to successive exponential functions under pseudo-first-order conditions was not successful. Nonetheless, the kinetics clearly showed that under the conditions employed no reactive "dioxygen intermediate" could be detected.

Despite the presence of a coordination sphere at copper(I) identical to that in **1** the *p*-phenylene isomer of **1** does not react with dioxygen.[45] The analogous copper(I) cryptates of **1** and **2** (via reaction with tren and trpn, respectively) have also been structurally characterized.[55,56] In these complexes no additional acetonitrile molecules are coordinated although a noncoordinating acetonitrile molecule is found in the crystal structure of the copper(I) cryptate analogue of **1**. The copper(I) ions are separated by 4.23 and 4.44 Å, distances similar to that found in **1**. Neither complex reacts with dioxygen.[56,57]

NMR Studies. The poor solubility of **1** in noncoordinating solvents has precluded a detailed study of its solution chemistry. ^{1}H NMR spectra from **1** in the coordinating solvents CD_3CN, DMSO-d_6, and DMF-d_7 showed broad signals at room temperature, suggesting equilibria involving a number of different species in solution. These equilibria could also result from exchange reactions of the coordinated acetonitrile molecules or copper(I) ions. Therefore we tried to push the equilibria to one side by addition of $[Cu(CH_3CN)_4]ClO_4$, but these attempts failed in contrast to earlier studies on a related nonmacrocyclic complex.[10]

Low-temperature NMR spectra of **1** in CD_3CN down to −20 °C remained complex. However corresponding NMR spectra obtained in DMF-d_7 down to −55 °C were more informative although there still remain open questions. Figure 4 shows the ^{1}H NMR spectra of **1** in DMF-d_7 at −55, −25, and +25 °C.

The existence of two different species in solution in a 1:1 ratio is suggested by the appearance of 3 signals from N−H groups at 4.43 (1H), 4.54 (2H), and 4.84 ppm (1H) which are shifted with increasing temperature and which show coalescence at −15 °C. The signals in the aliphatic region however remained complex except for the broad signal at 2.33 ppm (6H) and a sharp singlet at 2.51 ppm (6H) for the coordinated acetonitrile molecules. These signals show coalescence at −25 °C.

With the help of a ^{1}H,^{1}H-COSY NMR spectrum recorded at −45 °C in DMF-d_7, we were able to assign the different signals in the aromatic region unambigiously to the corresponding aromatic protons. We find for the H_c protons two broad signals at 6.86 (2H) and 7.74 ppm (2H) and for the H_b protons two dublets at 7.61 (2H) and 8.09 ppm (2H) and

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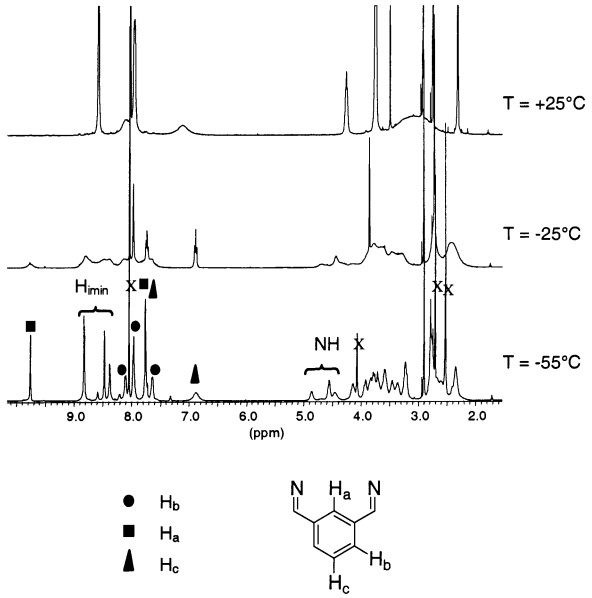

Figure 4. Low-temperature ^{1}H NMR spectra of **1** in DMF-d_7 at −55, −25, and +25 °C, respectively. (X marks solvent or water peaks.)

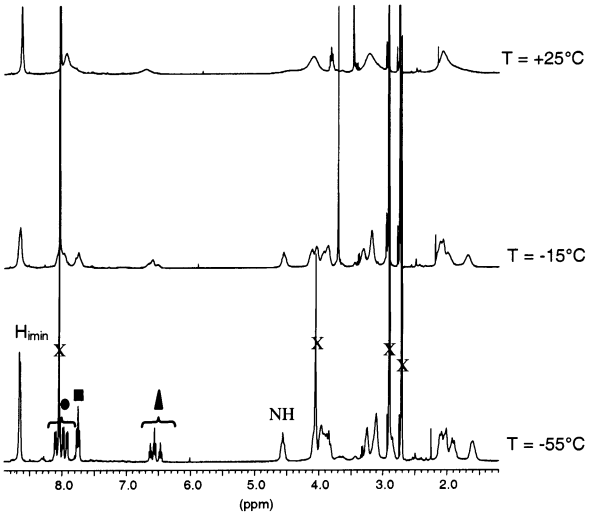

Figure 5. Low-temperature ^{1}H NMR spectra of **2** in DMF-d_7 at −55, −15, and +25 °C, respectively. (X marks solvent or water peaks.)

a broad signal at 7.94 ppm (4H). One peak for H_a at 7.74 ppm (2H) is overlaid by the signal for two H_c protons, while the other signal at 9.74 ppm (2H) shows a striking low-field shift due to a strong deshielding of H_a. The imine protons give peaks at 8.36, 8.46, 8.80, and 8.81 ppm.

The strong deshielding of H_a could result either from electronic or anisotropic effects. Because of the little importance of the aromatic ring current for ^{13}C chemical shifts, we measured the ^{1}H,^{13}C-HMQC spectrum of **1** in DMF-d_7 at −45 °C. The signal corresponding to C_a was found at 121.14 ppm, while the other aromatic nonquaternary C atoms caused peaks between 128.41 and 136.47 ppm. This high-field shift suggests a quite high electron density for the C_a atoms and therefore indicates that upon oxidation of **1** an electrophilic attack of the postulated peroxo moiety can take place at least in one species of **1**. Because of equilibria in solution at room temperature, complete oxidation of **1** can occur. The other chemical shifts are given for completion: 1.58; 2.17 (CH_3CN); 48.08; 49.98; 50.87; 51.02; 59,69; 60.41; 61.96; 64.92 (CH_2); 121.14 (C_a); 128.41 (C_b); 129.28 (C_c); 130.39 (C_a or C_c); 132.50 (C_b); 136.47 (C_a or C_c); 162.89; 164.03; 164.42; 167.12 (C═N).

To explore the effects of macrocyclic ring enlargement within the ligand donors around the copper(I) centers, the ^{1}H NMR behavior of complex **2** was also investigated in DMF-d_7 down to −55 °C. Unlike **1**, complex **2** shows well-resolved signals at low temperatures in the aromatic region, while the aliphatic region remained complex. Figure 5 shows the NMR spectra of **2** in DMF-d_7 at −55, −15, and +25 °C.

At −55 °C three doublets of doublets at 6.45 (1H), 6.54 (2H), and 6.61 ppm (1H) are found for H_c, which show coalescence at 15 °C, and three singlets for H_a at 7.71 (1H), 7.73 (2H), and 7.76 ppm (1H), which show coalescence at 5 °C. Therefore, we suggest here in analogy to **1** the existence of two different species in solution in a 1:1 ratio, but the nature of the assumed conformers is unknown. Furthermore, there are two singlets at 8.63 and 8.65 ppm (4H each) for H_{imin} and four doublets for H_b at 7.91, 7.96, 8.00, and 8.02 ppm (8H). The NH protons give one broad signal at 4.54 ppm (4H).

Interestingly, **2** does not show such a strong low-field shift for H_a. Together with the longer Cu−Cu distance in the complex this might be responsible for the fact that hydroxylation of the phenyl ring does not occur upon oxidation.

Electrochemistry. A cyclic voltammogram of the free ligand L^1 in either dichloromethane or acetonitrile is characterized by a broad irreversible oxidation wave at +0.56 V which disappears upon the addition of varying equivalents of Cu(I) salt (syringe addition) to be replaced by a new irreversible oxidation wave (to Cu(II)) for the Cu(I) complex at +0.12 V accompanied by a number of irreversible reduction waves on the return scan at −0.11, −0.34, and −1.31 V. In dichloromethane the height of the +0.12 V wave increases linearly with the equivalents of Cu(I) added up to a sharp break leveling off at exactly 2.0 equiv. The linear nature of the increase of the wave height up to 2.0 equiv of Cu(I) indicates that a single complex, the Cu(I) species **1**, is relevant over all ratios of Cu(I) to L^1 in this solvent. However, in acetonitrile different behavior is observed, with more than 2.0 equiv of Cu(I) required to maximize the height of the +0.12 V wave of the dicopper(I) species. The growth of the peak with Cu(I) concentration is now curved without the appearance of a sharp break. Here it is believed that acetonitrile competes with **1** for coordination to Cu(I) thus setting up an equilibrium between **1** and acetonitrile-solvated Cu(I)—quite feasable since acetonitrile is known to be an effective ligand for Cu(I). Furthermore, this finding correlates with the observation that intramolecular aromatic ring hydroxylation is suppressed in acetonitrile (see above).

The profile of the cyclic voltammetric experiments in dichloromethane parallels exactly that of the % hydroxylation study described in the Experimental Section, showing that exclusive formation of a dicopper(I) complex is essential for aromatic ring hydroxylation to be observed. If two or more copper(I) ions are present with one molecule of L^1, an

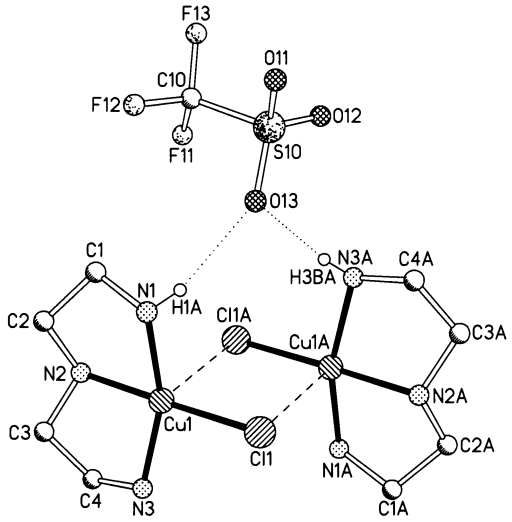

Figure 6. Molecular structure of $[Cu_2(dien)_2Cl_2](SO_3CF_3)_2$ (**3**). (One triflate anion is omitted for clarity.)

intramolecular aromatic ring C−H hydroxylation of 100% is observed (the lower hydroxylation yields reported earlier[34] most likely are either a consequence of not adding enough copper(I) salt or using acetonitrile as a cosolvent). Thus, it is clear that the reactive C−H hydroxylating species is directly derived from the dinuclear complex **1**.

Copper(II) Complexes. As discussed earlier, the "dioxygen adduct complex", most likely a copper(II) peroxo complex which forms during the reaction of **1** with dioxygen according to our kinetic data, could not be isolated or characterized spectroscopically.[37] Therefore, the isolation of different copper(II) complexes of L^1 was attempted in the hope that they could provide an excellent structural description of the postulated analogous peroxo complexes.[50,51] Unfortunately all attempts to isolate a stable dicopper(II) complex with L^1 under different conditions and using various anions failed. This is not surprising because imine hydrolysis in such ligands is enhanced dramatically by the presence of copper(II) ions. The reaction of $Cu(ClO_4)_2$ in dry methanol with L^1 precipitates a bluish-green moisture-sensitive solid analyzing for $[Cu_2L^1](ClO_4)_4$ and with infrared evidence of weak ClO_4^- coordination. This and other related complexes rapidly turn bright blue in the air due to formation of copper dien complexes as a result of hydrolysis of the macrocyclic ligand. The isolation of solid $[Cu_2L^1(X)_2](X)_2$ ($X = Cl^-$ or NO_3^-) has also been claimed, but as there is no crystal structure, these results should be regarded critically.[58] From one of these reactions for example we only could isolate the chloride-bridged copper(II) complex $[Cu_2(dien)_2Cl_2](SO_3CF_3)_2$. The structure of this complex in Figure 6 (omitting one triflate anion for clarity) shows the hydrogen-bonded network. The cationic unit has however been described in the literature as the nitrate[61] and chloride[45] salt, so structural data for this compound are only deposited with the CCDC as described at the end of the Experimental Section.

A dinuclear copper(II) complex of L^2 was postulated to form by reacting $CuCl_2$ with L^2 in methanol, but characterization of this compound was not reported; however, the product $[Cu_2(dpt)_2Cl_2]Cl_2$ (dpt = dipropylenetriamine) of the quantitative hydrolysis of this complex was described.[54,61]

Summary/Conclusions

Previous work had shown that the macrocyclic dinuclear copper(I) complex **1** underwent intramolecular ligand hydroxylation upon reaction with dioxygen, but a detailed characterization of **1** was still missing. We were now able to structurally characterize **1** which adopts a "bowl shape" in the solid state. This allows a relatively close proximity of the copper(I) ions with a copper−copper distance of 4.250(3) Å. In solution low-temperature NMR measurements reveal an equilibrium of two not further identified species. One species clearly shows a high electron density for the C_a atom which indicates that upon oxidation of **1** an electrophilic attack of the postulated peroxo moiety can take place at least in that species. Electrochemical studies allowed us to optimize the conditions for hydroxylation up to nearly a 100% yield. Compound **2** with the enlarged macrocyclic ligand does not undergo the intramolecular hydroxylation reaction of an aromatic ring upon oxidation. The molecular structure of **2** shows that the phenyl rings are coplanar to each other and therefore provide a larger cavity in which the two copper(I) ions are embedded. The copper(I) ions are separated from one another by 7.700(2) Å. Low-temperature NMR studies also reveal the presence of two different species in solution, but in contrast to **1**, H_a does not show such a strong low-field shift. It is obvious that the distance of the two copper ions as well as the distance of the copper "dioxygen" moiety to an aromatic ring must play an important role for successful ligand hydroxylation reactions.

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