Monatshefte für Chemie (2002)
DOI 10.1007/s00706-002-0471-1

Monatshefte für Chemie
Chemical Monthly
Printed in Austria

Synthesis of Hexadentate Hexahydro-1,3,5-triazine-Based Ligands and their Copper(I) Complexes

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Received January 22, 2002; accepted (revised) March 22, 2002
Published online July 15, 2002 © Springer-Verlag 2002

Summary. Hexadentate ligands were formed by the reaction of primary dimethylaminoethyl- or methoxyethylamines with formaldehyde. The resulting N,N',N''-functionalized hexahydro-1,3,5-triazines contain pending amino or ether functionalities which are able to coordinate to metals in addition to the ring nitrogen atoms. Both ligands were reacted with CuBr, and novel tricopper clusters were isolated and characterized by X-ray structure analysis. In these compounds a ring nitrogen atom, the pending amino or ether functionality, and two bridging bromine atoms coordinate each of the copper atoms.

Keywords. Complexes; Heterocycles; Ligands; X-Ray structure determination.

Introduction

The chemistry of coordination compounds between copper and amines has recently gained much interest due to its importance in biological systems [1]. Especially copper complexes with multidentate ligands have been used as model compounds for metalloenzyms [2–4]. On the other hand, the combination of copper halides and multidentate amine ligands is also used in controlled radical polymerization methods, *i.e.* atom transfer radical polymerization (ATRP), in which the copper complex serves as an activating and controlling species and where there is a search for new ligands which extend the activity of the commonly used copper compounds [5, 6].

A frequently used multidentate amine ligand with four coordination sites is the commercially available compound tris(2-aminoethyl)amine and its derivatives. However, a higher number of coordination sites is sometimes desirable. Examples of such ligands are cryptands that cover the metal in a cage-like surrounding. While cryptands are quite expensive, difficult to synthesize, and toxic, new ligand systems which have a similar ability to bind metal centers show a high potential for different applications. As good starting points for ligands with a larger number of

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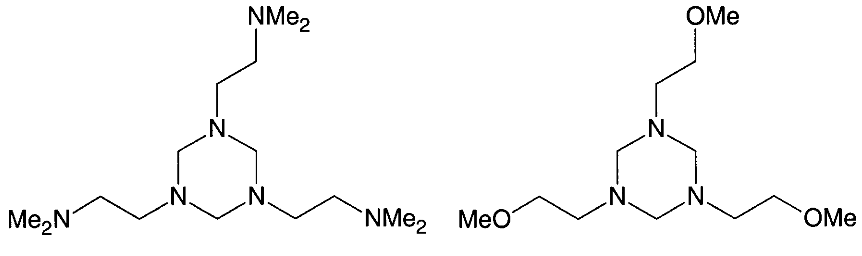
coordination sites, derivatives of 1,3,5-triazacyclohexanes (triazines) seem to be a good choice due to their straightforward preparation starting from cheap chemicals [7, 8]. Copper complexes of simple triazines with alkyl substituents at the nitrogen atom are already known and have been structurally characterized [8, 9]. In these compounds the copper atom is coordinated to the three nitrogen atoms in the triazine ring and to one (in the case of Cu(I)) or two (in the case of Cu(II)) additional ligands. The triazacyclohexane behaves in these complexes as a rigid six-membered ring ligand in the chair conformation with an η^2 or η^3 bonding mode. However, most of these coordinating heterocycles contain only alkyls or aryls as substituents at the nitrogen atoms. *N,N′,N″*-Functionalized triazines with additional coordination sites such as methoxycarbonylmethylpropyl [9] or hydroxy-functionalized ligands [10] and their metal complexes have already been described in the literature. However, only in more complex macrocyclic systems the additional coordination sites are bonded to the metal center [11, 12]. In this report we describe the synthesis of triazine ligands with additional ether or amine functionalities and their use in the preparation of Cu(I) complexes.

Results and Discussions

Synthesis of N,N′,N″-functionalized hexahydro-1,3,5-triazines

N,N′,N″-Functionalized triazines were prepared according to a procedure of *Kaufmann* [7] by reaction of primary amines with formaldehyde in water. 3-Dimethylamino-1-ethylamine and 2-aminoethyl-methylether were used as the primary amines. The applied one-pot synthesis resulted in colorless liquids in good yields. An accurate purification of the crude products by fractional distillation under high vacuum was necessary because the target molecules had to be separated from contaminations of cyclic ether side-products probably resulting from uncompleted condensation reactions. The existence of such products was verified by ^{1}H and ^{13}C analysis and is a known phenomenon in the synthesis of triazines from formaldehyde [7]. Depending on the amines used, two different types of ligands were obtained: (*i*) those with solely amine coordination sites (**1**) and those which offer two different coordination sites (nitrogen atoms in the ring and oxygen atoms in the terminal positions; **2**) (Scheme 1).



1 **2**

Scheme 1

Synthesis of the tricopper complexes

For first investigations of the capability of the ligands to coordinate metals, copper was used because of its variety of different possible coordination spheres. Whereas Cu(I) with its d^{10} electron configuration prefers a tetrahedral surrounding, typical coordination spheres of Cu(II), depending on the number of ligands, are distorted tetrahedral [13], square planar [14], trigonal bipyramidal [15], quadratic pyramidal [16], or distorted octahedral [17]. As a source of Cu(I) the halide CuBr was used which can easily be purified from traces of Cu(II) and supports our interest in its catalytic activities in ATRP [5, 6]. CuBr was dissolved in acetonitrile and reacted with the ligands at room temperature. From the solution with ligand **1** immediate precipitation occurred. The resulting copper complex was air-stable but moisture sensitive, insoluble in all solvents, and decomposed in coordinating solvents such as *DMSO* which is a known property of other metal complexes of triazines [10]. Therefore, a characterization with solution NMR techniques was not possible. However, due to the good crystallization behaviour the molecular structure could be obtained by a single crystal X-ray analysis (Fig. 1); selected structural data can be found in Table 1. A tricopper cluster complex was formed, although a 1:1 ratio of CuBr and ligand was used. The geometry of each of the Cu atoms in this complex is best described as a distorted tetrahedron formed by one triazine ring nitrogen atom, one of the terminal amine N atoms, and two Br atoms bridging two adjacent Cu atoms. Quite large differences in the angles reveal distortions of the tetrahedral surrounding of the copper atoms, *e.g.* the $N_{triazine}$–Cu–$N_{terminal}$ angles are 82–83°, whereas the $N_{triazine}$–Cu–Br angles are around 116°. Generally, the Cu–N distances are in the same range as in comparable Cu(I) complexes [18, 19]. The whole structure shows C_3 symmetry in the limits of the standard deviations of the crystal structure analysis (Fig. 2). The overall morphology of the structure is crown-like with the triazine ring forming the base and the Cu–Br ring building the top of the crown with the Br atoms as spikes. A similar motif of coordination in a triazine-based ligand system has been obtained applying a dodecaaza macrotetracycle incorporating a Cu_3O core [11]. However, in the latter compound Cu(II) was used, and each metal atom had a trigonal bipyramidal environment.

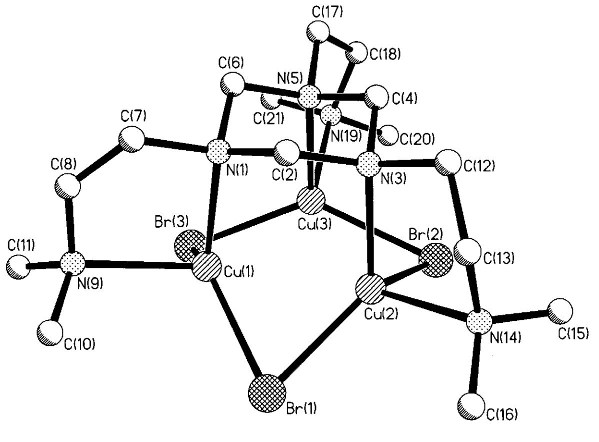


Fig. 1. Molecular structure of **3**

Table 1. Selected distances (pm) and angles (°) of **3**

Cu(1)–N(1)	221.9(11)	Br(1)–Cu(1)–N(9)	105.9(3)
Cu(1)–N(9)	227.3(13)	N(1)–Cu(1)–Br(3)	116.8(2)
Cu(1)–Br(1)	242.03(19)	Br(3)–Cu(1)–N(9)	102.8(3)
Cu(1)–Br(3)	243.73(19)	Br(1)–Cu(1)–Br(3)	121.71(9)
Cu(1)–Cu(2)	277.1(2)	Cu(1)–Br(1)–Cu(2)	69.98(6)
Cu(1)–Cu(3)	277.2(2)	N(3)–Cu(2)–N(14)	83.0(4)
Br(1)–Cu(2)	241.2(2)	Br(1)–Cu(2)–N(3)	119.4(3)
Br(2)–Cu(2)	244.4(2)	Br(1)–Cu(2)–N(14)	102.9(3)
Br(2)–Cu(3)	244.7(2)	Br(2)–Cu(2)–N(3)	105.1(3)
Cu(2)–N(3)	224.4(1)	Br(2)–Cu(2)–N(14)	105.1(3)
Cu(2)–N(14)	225.7(1)	Br(1)–Cu(2)–Br(2)	129.55(9)
Cu(2)–Cu(3)	284.0(2)	Cu(1)–Br(3)–Cu(3)	70.01(6)
Br(3)–Cu(3)	239.39(19)	N(5)–Cu(3)–N(19)	82.8(4)
Cu(3)–N(5)	222.4(1)	Br(3)–Cu(3)–N(5)	113.3(3)
Cu(3)–N(19)	227.0(1)	Br(3)–Cu(3)–N(19)	104.0(3)
		Br(2)–Cu(3)–N(5)	108.1(3)
N(1)–Cu(1)–N(9)	82.4(4)	Br(2)–Cu(3)–N(19)	101.7(3)
N(1)–Cu(1)–Br(1)	116.4(2)	Br(2)–Cu(3)–Br(3)	133.33(8)

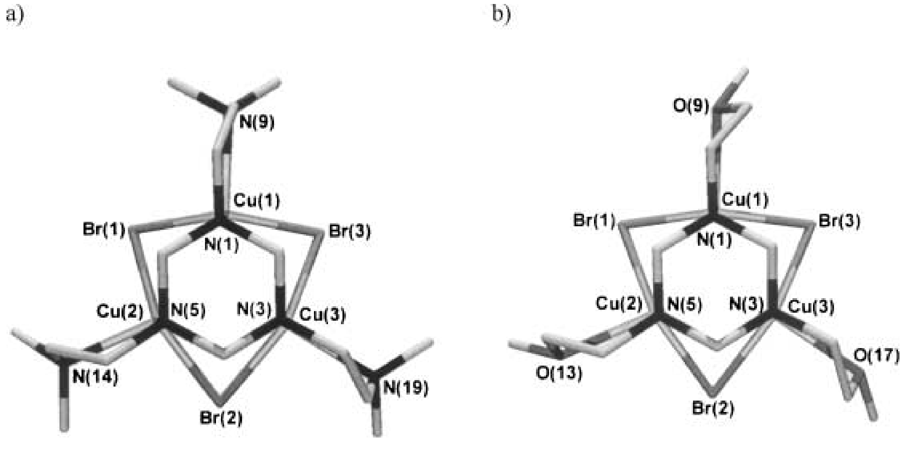


Fig. 2. Schematic representation of **3** (a) and **4** (b) along the C_3 axis

For a comparison of different Cu(I) sources and to investigate the importance of the bromine bridge, $[(CH_3CN)_4Cu]ClO_4$ was used as a different metal source. In contrast to the former reaction, the acetonitrile solution became a slightly green suspension after addition of the ligand, and no obvious precipitation occurred under the same conditions as in the reaction with CuBr. No crystals were formed, even if the reaction mixture was allowed to rest for several weeks.

Contrary to compound **3**, the reaction of CuBr with ligand **2** results in a much slower precipitation of **4**. The precipitate was again crystalline, and a single crystal X-ray structure determination was possible. The molecular structure is similar to that of **3** (Fig. 3); selected bond lengths and angles are shown in Table 2. Similar to the structure of **3** the copper atoms have a distorted tetrahedral environment

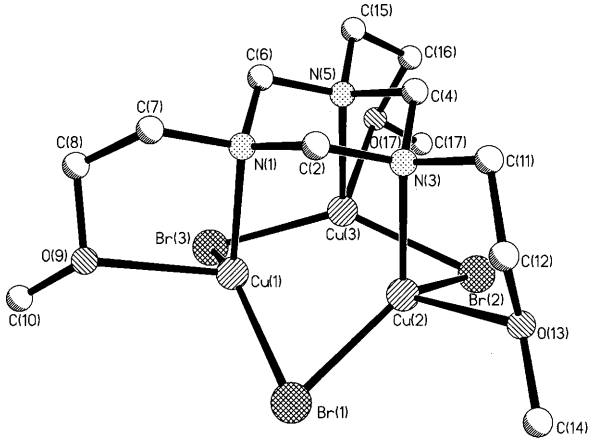


Fig. 3. Molecular structure of **4**

Table 2. Selected distances (pm) and angles (°) of **4**

Cu(1)–Br(1)	237.39(8)	Br(1)–Cu(1)–Br(3)	131.42(3)
Cu(2)–Br(1)	240.95(8)	Cu(2)–Br(2)–Cu(3)	67.51(2)
Cu(1)–N(1)	220.5(3)	N(3)–Cu(2)–O(13)	79.52(13)
Cu(1)–O(9)	235.7(3)	N(3)–Cu(2)–Br(2)	106.95(10)
Cu(1)–Br(3)	241.51(8)	O(13)–Cu(2)–Br(2)	105.56(9)
Cu(1)–Cu(2)	265.91(9)	N(3)–Cu(2)–Br(1)	115.39(10)
Cu(1)–Cu(3)	266.27(8)	O(13)–Cu(2)–Br(1)	98.15(8)
Cu(2)–Br(2)	239.06(8)	Br(2)–Cu(2)–Br(1)	134.41(3)
Cu(3)–Br(2)	242.18(8)	Cu(3)–Br(3)–Cu(1)	67.47(2)
Cu(2)–N(3)	219.0(3)	N(5)–Cu(3)–O(17)	79.18(14)
Cu(2)–O(13)	234.5(3)	N(5)–Cu(3)–Br(3)	109.62(10)
Cu(2)–Cu(3)	267.42(8)	O(17)–Cu(3)–Br(3)	104.64(9)
Cu(3)–Br(3)	237.92(8)	N(5)–Cu(3)–Br(2)	108.72(10)
Cu(3)–N(5)	220.5(3)	O(17)–Cu(3)–Br(2)	96.78(9)
Cu(3)–O(17)	236.7(3)	Br(3)–Cu(3)–Br(2)	138.80(3)
		Br(1)–Cu(1)–Br(3)	131.42(3)
Cu(1)–Br(1)–Cu(2)	67.54(2)	Cu(2)–Br(2)–Cu(3)	67.51(2)
N(1)–Cu(1)–O(9)	78.96(13)	N(3)–Cu(2)–O(13)	79.52(13)
N(1)–Cu(1)–Br(1)	114.13(10)	N(3)–Cu(2)–Br(2)	106.95(10)
O(9)–Cu(1)–Br(1)	103.87(9)	O(13)–Cu(2)–Br(2)	105.56(9)
N(1)–Cu(1)–Br(3)	111.45(10)	N(3)–Cu(2)–Br(1)	115.39(10)
O(9)–Cu(1)–Br(3)	100.36(9)		

coordinated by one nitrogen ring atom, the terminal ether functionality, and two bridging bromine ligands from adjacent copper atoms. The $N_{triazine}$–Cu–O angles are 79–80° and the $N_{triazine}$–Cu–Br angles vary from 107 to 115°. Whereas in compound **3** the Cu–N distances from the ring and the terminal nitrogen atoms had approximately the same values, the Cu–O bonding distances in **4** are about 15 pm longer than those of the ring nitrogen atoms.

An interesting observation was made when the two complexes were stored in air for a couple of weeks. The crystals decomposed, and a dark green viscous product was formed. NMR spectroscopic investigations were only partially successful due to the content of paramagnetic Cu(II). However, the ^{13}C spectrum revealed the existence of carbonyl C atoms. A possible explanation for this observation is the fixation of CO_2 as CO_3^{2-} under simultaneous oxidation of Cu(I) which has already been observed in other amine complexes [20].

Conclusions

In summary, two types of 1,3,5-triazacyclohexanes with additional pending amine or ether groups were synthesized and used as hexadentate ligands. In reactions with CuBr trinuclear copper complexes were formed in which the metal is coordinated by a distorted tetrahedral surrounding. The formation of crystalline complexes of this type were not observed with $[(CH_3CN)_4Cu]ClO_4$ as the Cu(I) source. The reaction with $CuBr_2$ resulted in no molecular products; the obtained suspension indicates the formation of a polymer-like structure.

Experimental

General

All chemicals were obtained from Aldrich. CuBr was stirred in glacial acetic acid overnight, filtered, and washed with absolute EtOH. Amines were distilled prior to use. CH_3CN was distilled over CaH_2, stored over molecular sieve, and degassed prior to use. All other chemicals were used without further purification. All reactions with Cu(I) salts were carried out under an Ar atmosphere using *Schlenk* techniques. Microanalyses were carried out by Microanalytical Laboratory, University of Vienna; the results agreed with the calculated values within experimental error.

N,N′,N″-Tris(dimethylaminoethyl)hexahydro-s-triazine (**1**; $C_{15}H_{36}N_6$)

1 was prepared following the procedure of *Kaufman* [7]. To a stirred solution of HCHO in H_2O (37%; 25.0 g, 0.308 mol), dimethylaminoethylamine (27.1 g, 0.308 mol) was added at a rate to keep the temperature below 45°C. After the addition was complete, the reaction mixture was stirred for an additional hour, cooled in an ice bath, and KOH was added slowly so that the temperature did not exceed 15°C. After stirring for an additional hour the organic layer was separated, and the aqueous layer was extracted three times with diethyl ether. The combined organic layers were dried over $MgSO_4$, and the ether was removed under vacuum. The solution was distilled under high vacuum using a *Vigreux* column.

Yield: 18.61 g (60.3%); ^1H NMR (250 MHz, $CDCl_3$): $\delta = 2.21$ (s, 18H, CH_3), 2.36 (t, 6H, CH_2), 2.54 (t, 6H, CH_2), 3.38 (s, 6H, CH_2) ppm; ^{13}C NMR (62 MHz, $CDCl_3$): $\delta = 46.06$ ($N(CH_3)_2$), 51.03 (CH_2), 58.10 (CH_2–NMe_2), 75.18 (N–CH_2–N) ppm.

N,N′,N″-Tris(methoxyethyl)hexahydro-s-triazine (**2**; $C_{12}H_{27}N_3O_3$)

2 was prepared similar to **1**. Yield: 19.4 g (72.4%); ^1H NMR (250 MHz, $CDCl_3$): $\delta = 2.67$ (t, 6H, CH_2), 3.32 (s, 9H, CH_3), 3.46 (m, 12H, O–CH_2/N–CH_2–N) ppm; ^{13}C NMR (62 MHz, $CDCl_3$): $\delta = 52.45$ (OCH_2), 59.02 (OCH_3), 71.60 (N–CH_2), 75.16 (N–CH_2–N) ppm.

Reaction of CuBr with N,N′,N″-tris(dimethylaminoethyl)hexahydro-s-triazine (→ **3**) *or N,N′,N″-tris(methoxyethyl)hexahydro-s-triazine* (→ **4**)

0.143 g (1 mmol) CuBr, 7.5 cm^3 of CH_3CN, and 1 mmol of the triazine were stirred until the copper bromine had completely dissolved. In the case of **3**, colorless crystals of the composition

$C_{15}H_{36}Br_3Cu_3N_6$ precipitated immediately. Compound **4** precipitated after the colorless solution was left under Ar for one week ($C_{12}H_{27}Br_3Cu_3N_3O_3$). Both products did not dissolve in any of the usual solvents for NMR analysis.

X-Ray crystallography

Selected crystals were mounted on a Siemens SMART diffractometer with a CCD area detector. Graphite-monochromated MoK_α radiation (71.073 pm) was used for all measurements. The nominal crystal-to-detector distance was 4.40 cm. A hemisphere of data was collected by a combination of three sets of exposures at 293 K. Each set had a different ϕ angle for the crystal, and each exposure took 20 s and covered 0.3° in ω. The data were corrected for polarization and *Lorentz* effects, and an empirical absorption correction (SADABS) was applied. The cell dimensions were refined with all unique

Table 3. Crystal data and structure refinement

	3	**4**
Empirical formula	$C_{15}H_{36}Br_3Cu_3N_6$	$C_{12}H_{27}Br_3Cu_3N_3O_3$
Formula weight	730.85	691.72
Crystal system	orthorhombic	orthorhombic
Space group	$Pna2_1$	$P2_12_12_1$
Unit cell dimensions	$a = 1965.35(7)$ pm	$a = 982.89(13)$ pm
	$b = 1789.09(6)$ pm	$b = 1414.3(2)$ pm
	$c = 736.58(2)$ pm	$c = 1516.4(3)$ pm
	$\alpha = 90°$	$\alpha = 90°$
	$\beta = 90°$	$\beta = 90°$
	$\gamma = 90°$	$\gamma = 90°$
V/pm^3	$2589.95(14) \cdot 10^6$	$2108.0(6) \cdot 10^6$
Z	4	4
Calculated density/$\mathrm{g \cdot cm^{-1}}$	1.874	2.180
Absorption coefficient/$\mathrm{mm^{-1}}$	7.082	8.700
$F(000)$	1440	1344
Crystal size/mm	0.50×0.10×0.10	0.22×0.20×0.06
Theta range for data collection	1.54°–20.82°	1.97°–24.74°
Limiting indices	$0 \leq h \leq 19$	$-11 \leq h \leq 11$
	$0 \leq k \leq 17$	$-16 \leq k \leq 13$
	$0 \leq l \leq 7$	$-17 \leq l \leq 17$
Reflections collected/unique	8435/1502	11337/360
	(R(int) = 0.0530)	(R(int) = 0.0360)
Completeness to max. Θ	100.0%	99.9%
Max. and min. transmission	0.5378 and 0.1258	0.6233 and 0.2505
Data/restraints/parameters	1502/1/245	3604/0/221
Goodness-of-fit on F^2	1.252	1.024
Final R indices ($I > 2\sigma(I)$)	$R_1 = 0.0292$	$R_1 = 0.0237$
	$wR_2 = 0.0916$	$wR_2 = 0.0523$
R indices (all data)	$R_1 = 0.0330$	$R_1 = 0.0275$
	$wR_2 = 0.0953$	$wR_2 = 0.0538$
Absolute structure parameter	0.04(3)	0.028(11)
Extinction coefficient	0.00092(19)	0.00117(11)
Largest diff. peak and hole/$\mathrm{e \cdot A^{-3}}$	0.458 and −0.335	0.496 and −0.307
Weighting scheme $P = (\mathrm{Max}(F_0^2, 0) + 2\,F_c^2)/3$	$W = 1/(\sigma^2(F_0^2) + (0.0559P)^2 + 2.77P)$	$W = 1/(\sigma^2(F_0^2) + (0.0251P)^2 + 0.93P)$

reflections. The structure was solved by direct methods (SHELXS86). Refinement was carried out with the full-matrix least-squares method based on F^2 (SHELXL93) with anisotropic thermal parameters for all non-hydrogen atoms. Hydrogen atoms were inserted in calculated positions and refined riding with the corresponding atom. Due to a low scattering intensity in the high Θ range of the measured data set of compound **3**, a high-resolution limit of 1.0 Å was employed; this modified data set was used for the refinement. For details, see Table 3.

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication Nos. CCDC-174672 and CCDC-174674. Copies of the data can be obtained free of charge upon application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44(1223)336-033; E-mail: deposit@ccdc.cam.ac.uk).

Acknowledgments

We thank Dr. *Michael Puchberger* and *Dieter Holzinger* for technical assistance and the *Fonds zur Förderung der wissenschaftlichen Forschung*, Austria, for financial support.

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