Copper(II)-Promoted Chemical Transformations of 3-Substituted 5-(2′-Pyridyl)-1,4-benzodiazepin-2-one Derivatives. Crystal Structures and Spectroscopic Characterisation of Metal Complexes

Aleksandar Višnjevac,[a] Ljerka Tušek-Božić,[a] Maja Majerić-Elenkov,[a] Vitomir Šunjić,[a] and Biserka Kojić-Prodić*[a]

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Enantiomerically pure 7-bromo-1,3-dihydro-3-hydroxymethyl-1-methyl-5-(2′-pyridyl)-2*H*-1,4-benzodiazepin-2-one, (+)-**1**, affords the dichloro adduct **3**, [$CuCl_2$(**1**)], when treated with a solution of $CuCl_2 \cdot 2H_2O$ in ethanol. Complex **3** is isolated as a racemic compound. The replacement of one chlorine atom with DMSO gives complex **4**, [CuCl(**1**-H)(DMSO)]. The C(3)-oxygenated product appears as a racemic *N,N,O*-tridentate ligand in the square-pyramidal complex **5**. Oxidative ring contraction of (+)-**1** yields 6-bromo-4-ethoxy-1,4-dihydro-1-methyl-4-(2′-pyridyl)-1,3-quinazoline, which acts as an *N,N*-bidentate ligand in the tetrahedral complex **6**. Reaction of 3-acetoxymethyl-7-bromo-1,3-dihydro-1-methyl-5-(2′-pyridyl)-2*H*-1,4-benzodiazepin-2-one, (±)-**2**, with $CuCl_2 \cdot 2H_2O$, affords the square-pyramidal complex **7**, [$CuCl_2$(**2**)]. In this complex the lactam oxygen atom of a neighbouring molecule binds to the fifth coordination site, hence forming an infinite chain of connected polyhedra in the crystal. Oxidative ring contraction of **2** leads to 6-bromo-1,4-dihydro-4-hydroxy-1-methyl-4-(2′pyridyl)-1,3-quinazoline, which acts as an *N,N*-bidentate ligand in the centrosymmetric binuclear five-coordinate Cu^{II} complex **8**. In this complex the di-μ-chloro bridges are asymmetrical: one Cl atom is in an apical position [Cu–Cl, 2.820 (7) Å], whereas the other is in an equatorial position [Cu–Cl, 2.252 (5) Å]. The complexes are characterised by IR spectroscopy and X-ray structure analysis. Mechanisms of racemisation, oxygenation and ring contraction are discussed.

Introduction

The tranquilising and sedative-hypnotic activity of 1,4-benzodiazepines prompted chemists to investigate their complexation properties with transition metals,[1−3] in an attempt to prepare even more potent drugs. Among the first isolated was $Cu^{II}Cl_2$(diazepam)$_2$ (diazepam known as Valium®), with a square-planar geometry around Cu^{II}.[4] To the best of our knowledge, few crystal structures of 1,4-benzodiazepine complexes are known so far.[5,6] Generally, it has been of practical interest to design ligands which can enforce specific metal coordinations of suitable geometry and electronic properties which lead to desired catalytically active coordination compounds. Such complexes can also serve as good models for studying the activity of metalloenzymes.[7,8] Thus, it was interesting to examine the chelation properties of 5-substituted 1,4-benzodiazepin-2-one ligands, and to study the substitution effect at the stereogenic centre (C3) on metal complexation.[9,10] In our previous studies we investigated the use of metal complexes of C(3)-substituted 5-phenyl- and 5-pyridyl-1,4-benzodiazepin-2-ones in non-catalytic, catalytic, and biocatalytic reactions.[9−16] We have already reported on the oxidative C(3)-acetoxylation of the 5-pyridyl-1,4-benzodiazepine derivative to the 3-acetoxy derivative promoted by a mixed reagent [$Pb^{IV}(AcO)_4$]/I_2.[17] In vitro metal-catalysed C(3)-oxygenation of 1,4-benzodiazepin-2-ones has been unprecedented. However, the stereochemistry of an analogous in vivo process, which is catalysed by cytochrome P450, has already been described in detail.[18−20]

In this work we report on the preparation and characterisation of Cu^{II} complexes with ligands (+)-**1** and (±)-**2** (Scheme 1), which have undergone oxygenation at C(3) and a ring contraction. The mechanism for ligand transformations in the presence of the copper ion is explained (Scheme 2). The understanding of the mechanism is based upon the structure of the initial components and the isolated complexes. This mechanism is strongly supported in similar transformations of (5-phenyl)-1,4-benzodiazepin-2-ones already reported.[21−25]

Results and Discussion

Preparation of the Complexes

The reactions of benzodiazepine ligands (+)-**1** and (±)-**2** with $CuCl_2$ dihydrate in ethanol have yielded various types of complexes as presented in Scheme 1. It was observed that both ligands (+)-**1** and (±)-**2** initially formed the dichloro adduct (±)-**3** and (±)-**7**, respectively. Recrystallisation of (±)-**3** in ethanol at room temperature gave a mixture of the complexes (±)-**5** and (±)-**6**. Heating (±)-**7** in a mixture of ethanol and acetonitrile afforded the complex (±)-**8**. The green dichloro adduct (**3**), containing ligands bonded through two α-diimine nitrogens, a hydroxymethyl oxygen and two chlorine atoms, was isolated immediately after its formation, i.e. after about 5 minutes of stirring the reactants

[a] Rudjer Bošković Institute,
P. O. B. 180, 10002 Zagreb, Croatia
E-mail: kojic@rudjer.irb.hr

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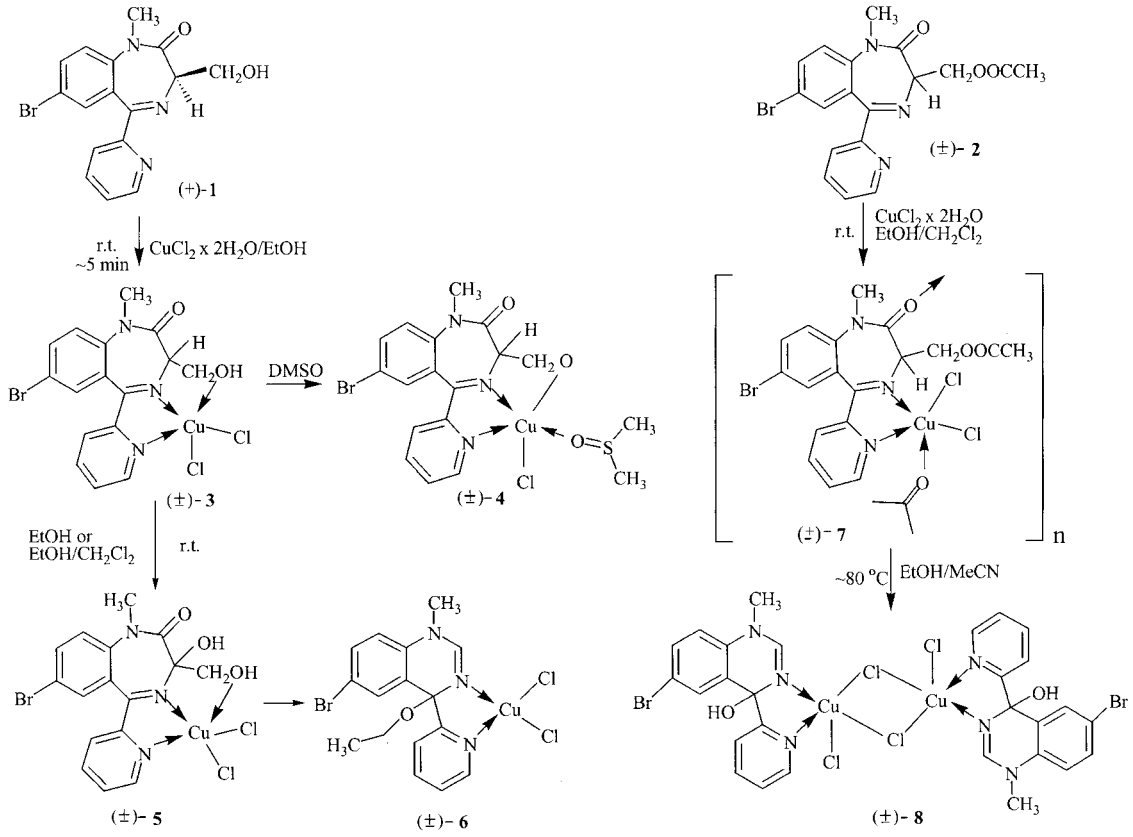
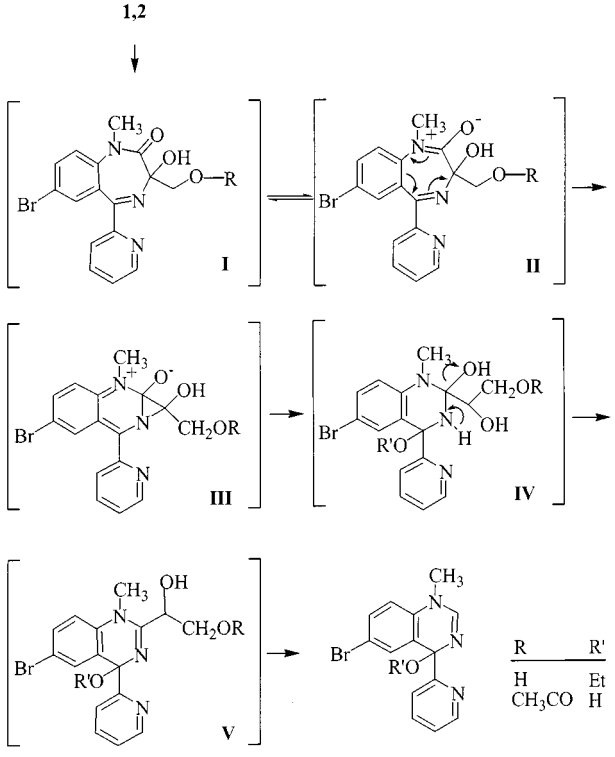


Scheme 1. Chemical diagrams of ligands and copper(II) complexes



Scheme 2. Possible transition states on the route of chemical modifications of **1** and **2** to 1,3-quinazolines in the presence of Cu^{II}

in absolute ethanol at room temperature. Prolonged stirring caused the slow dissolution of this complex and the formation of a mixture of complexes; a green square-pyramidal complex **5**, dichloro-[7-bromo-1,3-dihydro-3-hydroxy-3-hydroxymethyl-1-methyl-5-(2′-pyridyl)-2*H*-1,4-benzodiazepin-2-one-*N*,*N*,*O*]copper(II) and a black tetrahedral complex **6**, dichloro-[6-bromo-4-ethoxy-1,4-dihydro-1-methyl-4-(2′-pyridyl)-1,3-quinazoline-*N*,*N*]copper(II). Recrystallisation of the complex **3** from DMSO yielded a reddish-brown complex **4**, in which one chlorine atom is replaced by a DMSO molecule (coordinated via an oxygen atom). The reaction of ligand **2** with $CuCl_2$ in a mixture of ethanol and dichloromethane, without an inert atmosphere, gave a green dichloro adduct **7**, which is insoluble in pure ethanol. Complex **7** dissolved on heating a mixture of ethanol and acetonitrile. The benzodiazepine ligand **2** was converted into the 1,3-quinazoline derivative in an ethanol and acetonitrile mixture, which then formed a dark-brown chloro-bridged dinuclear complex **8**, di-μ-chloro-bis[6-bromo-1,4-dihydro-4-hydroxy-1-methyl-4-(2′-pyridyl)-1,3-quinazoline-*N*,*N*]dichlorodicopper(II). Ligand (+)-**1** undergoes a Cu^{II} catalysed oxygenation at C(3), which is detected in the complex **5**. The amide-imide enolate equilibrium (Scheme 2, **I** ⇄ **II**) of 3-hydroxy benzodiazepine derivatives, presumably proceeds pericyclic ring-contraction leading to a tricyclic intermediate **III**, which after nucleophilic attack by an alcohol or water molecule undergoes opening of the cyclopropane ring and rearomatisation to

IV. This intermediate easily eliminates a molecule of water to form **V**, in which oxidative carbon-carbon bond splitting affords the 4-substituted 1,3-quinazoline derivatives found in the complexes **6** and **8**. Since racemisation has not been observed with C(3)-alkyl-5-pyridyl-1,4-benzodiazepines in the presence of Cu^{I} or Cu^{II} ions,[16] the racemisation and formation of complexes **5** and **6** reveal a key role of the C(3)−CH_2OH 'arm' in these processes. They probably comprise the coordination of Cu^{II}, and thus the activation of the C(3)−H bond for racemisation and oxygen insertion. However, under an inert N_2 atmosphere, similar chiral 1,4-benzodiazepines and Cu^{II} ions act catalytically in a cyclopropanation reaction, without oxygenation of the ligand.[16] The role of the Cu^{II} ion as an oxidising agent in biological and chemical catalytic systems has been repeatedly described; at the active site of galactose oxidase, the Cu^{II} ion oxidises primary alcohols to aldehydes.[21,22] Cu^{II} complexes containing *N,N*- and *N,O*-bidentate ligands proved effective in the chiral variant of Bayer−Villiger-type metal-catalysed oxidation of ketones to lactones with molecular oxygen.[23] Racemisation of (+)-**1** is a result of enolisation, since it was observed during C(3) enantiomerisation of 3-carbethoxy-1,4-benzodiazepines.[24] Ring contraction of a 1,4-benzodiazepin-2-one system has been repeatedly observed, either under acidic,[24] basic,[25] or thermal[25] conditions. A pericyclic process has already been postulated in the key ring contraction step.[24] Ring contraction is followed by substitution at the benzylic cation and elimination of the 2C fragment from the C(2) position in 1,4-dihydro-1,3-quinazoline ring, as already observed in similar substrates.[24,25]

The Crystal Structures

Both ligands **1** and **2** are chiral molecules and were used in the preparation of complexes (+)-**1** and (±)-**2**. In separate experiments we proved that enantiomerically pure compounds undergo fast racemisation in an ethanol solution and in the presence of Cu^{II} ions. Thus, during the preparation of the Cu^{II} complexes, racemic compounds were obtained from both homochiral (**1**) and racemic (**2**) ligands. Crystals of all the complexes and the ligand **2** (Scheme 1) crystallise in the centrosymmetric space groups (details given in the Experimental section, X-ray structure analysis, Tables 2 and 3). This indicates that on complexation the configurational stability of the C(3) stereogenic centre is lowered, presumably by the Cu^{II}-promoted enolisation. The Cu^{II} ion enhances the C(3)-acidity during complexation and promotes the above enolisation, which results in the racemisation of the optically active structures. In the crystal structure of **2** (Figure 1), the molecule appears in a *boat*

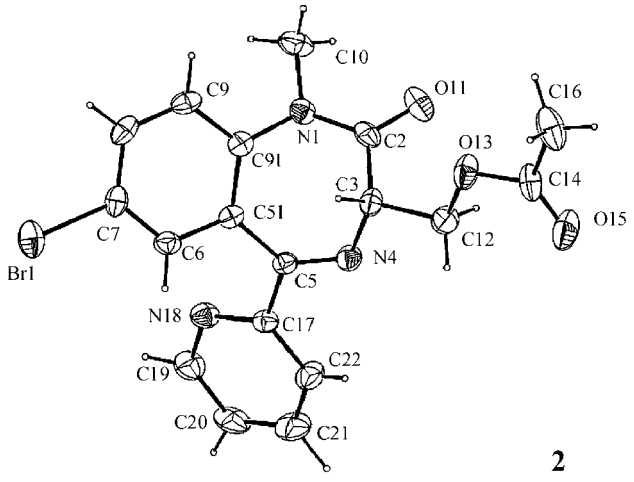


Figure 1. The ORTEP drawing of the ligand (±)-**2**; thermal ellipsoids are scaled at the 30% probability level

Table 1. Bond lengths [Å] and angles [°] in Cu^{II} coordination spheres of the benzodiazepine (**4**, **5**, **7**) and quinazoline (**6**, **8**) complexes

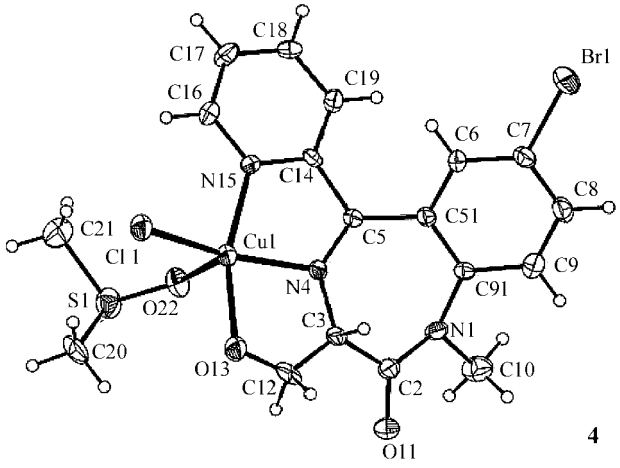
Bond/Angle	**4**	**5**	**7**	Bond/Angle	**6**	**8**
Cu−Cl1	2.235(3)	2.206(5)	2.237(3)	Cu−Cl1	2.257(2)	2.282(7)
Cu−Cl2	−	2.518(5)	2.222(5)	Cu−Cl2	2.236(2)	2.252(5)
Cu−N4	1.972(6)	1.93(1)	2.05(1)	Cu−Cl1[a]	−	2.820(7)
Cu−N_{Py}	1.994(6)	1.99(1)	2.02(1)	Cu−N3	1.984(4)	1.98(2)
Cu−O	1.981(6)	2.01(1)	2.27(1)	Cu−N_{Py}	2.032(5)	2.04(2)
Cu−O_{DMSO}	2.259(5)	−	−			
N_{py}−Cu−N4	79.3(2)	81.4(5)	78.9(5)	N_{py}−Cu−N3	78.7(2)	79.2(7)
N_{py}−Cu−Cl1	97.7(2)	97.3(4)	93.1(4)	N_{py}−Cu−Cl1	169.5(1)	169.7(5)
N_{py}−Cu−O_{DMSO}	93.5(2)	−	−	N_{py}−Cu−Cl2	94.0(2)	95.1(5)
N_{py}−Cu−Cl2	−	98.6(4)	162.4(4)	N3−Cu−Cl1	92.6(1)	91.8(6)
N4−Cu−Cl1	161.4(2)	165.3(4)	171.7(4)	N3−Cu−Cl2	162.4(1)	158.4(6)
N4−Cu− O_{DMSO}	95.8(2)	−	−	Cl1−Cu−Cl2	96.05(1)	95.0(2)
N4−Cu−Cl2	−	92.4(4)	94.7(4)	N_{py}−Cu− Cl1[a]	−	86.5(6)
Cl1−Cu−O_{DMSO}	102.8(2)	−	−	N3−Cu− Cl1[a]	−	99.8(5)
Cl1−Cu−Cl2	−	102.3(2)	92.2(2)	Cl1−Cu− Cl1[a]	−	90.4(2)
N_{py}−Cu−O	161.2(2)	155.2(5)	92.9(5)	Cl2−Cu− Cl1[a]	−	100.7(2)
N4−Cu−O	83.0(2)	78.4(5)	84.2(5)			
Cl1−Cu−O	97.2(2)	97.3(4)	98.7(3)			
O_{DMSO}−Cu−O	94.4(2)	−	−			
Cl2−Cu−O	−	97.7(4)	102.9(3)			

[a] $-x, -y, -z$.

conformation which is preserved in the crystal structure of its complex **7** and also in the complexes **4** and **5**. In spite of numerous efforts, crystallisation of ligand **1** and its complex **3** failed to produce good quality crystals needed for X-ray structure analysis.

Complexation with Cu^{II} ions resulted in structural changes of the ligands as was unambiguously proven by the X-ray structure analysis of the isolated complexes. The coordination geometries of the complexes are given in Table 1. The crystal structures of the complexes **5** (Figure 2) and **7** (Figure 3) reveal a distorted square-pyramidal Cu^{II} coordination. The five coordination sites are occupied by two chlorine atoms, azomethine and pyridine nitrogen atoms in both complexes, and by the hydroxymethyl oxygen in **5** and the lactam oxygen of the neighbouring molecule in **7**. Thus, in the crystal structure of **7** the coordination polyhedra are connected through a common corner into an infinite chain (Figure 3) running along the *b* axis.

In order to prove the mode of coordination of the ligand (+)-**1** in the complex **3**, it was recrystallised from DMSO, yielding the complex **4**. The crystal structure of **4** reveals



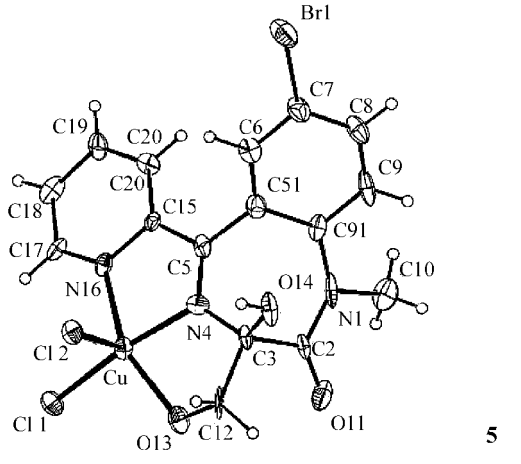


Figure 2. The ORTEP drawings of the five-coordinated chloro-{[7-bromo-1,3-dihydro-1-methyl-3-oxomethyl-5-(2′-pyridyl)-2*H*-1,4-benzodiazepin-2-one-*N*,*N*](dimethylsulfoxide)}copper(II) (**4**) and dichloro-[7-bromo-1,3-dihydro-3-hydroxy-3-hydroxymethyl-1-methyl-5-(2′-pyridyl)-2*H*-1,4-benzodiazepin-2-one-*N*,*N*,*O*]copper-(II) (**5**). Thermal ellipsoids are scaled at the 30% probability level

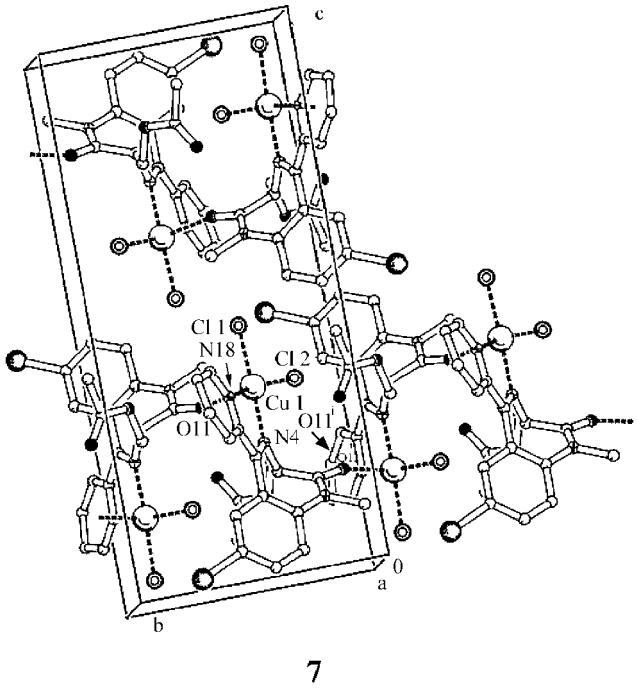


Figure 3. An infinite chain with the five-coordinated Cu^{II} coordination polyhedra of dichloro-[3-acetoxymethyl-7-bromo-1,3-dihydro-1-methyl-5-(2′-pyridyl)-2*H*-1,4-benzodiazepin-2-one-*N*,*N*,*O*]-copper(II) (**7**), connected through a common corner occupied by a lactam oxygen $O11^{i}$ of 1,4-benzodiazepine ligand running along the crystallographic axis *b*. The symmetry operation *i* is defined as $0.5 + x$, $0.5 + y$, $0.5 - z$

that the five coordination sites are occupied by the deprotonated hydroxymethyl oxygen, both nitrogen atoms of the azomethine and pyridine moieties, the chlorine atom, and the oxygen atom of a DMSO molecule (Figure 2).

The crystal structure analysis of complexes **6** and **8** reveal the ring contraction of 5-(2′-pyridyl)-1,4-benzodiazepin-2-one of **1** and **2**, respectively, into the 1,4-dihydro-1,3-quinazoline derivatives (Scheme 1, Scheme 2 and Figure 4). The tetrahedral coordination in **6** involves two nitrogens of the 1,4-dihydro-4-pyridyl-1,3-quinazoline derivative and two chlorine atoms. However, the ring contraction of ligand **2**, detected in **8**, was accompanied by the formation of the centrosymmetric dinuclear Cu^{II} complex with di-μ-chloro bridges. The Cu−Cl bond lengths are 2.252 (5) and 2.820 (7) Å (Table 1), and the Cu···Cu distance is 3.62 Å. The apical chlorine atom with the Cu^{II}−Cl distance of 2.820 (7) Å is part of a bridging system. The asymmetrical bond lengths are common in Cu^{II} binuclear species.[26−28] Such a species, with a distant ligand, might be considered as a stable transition state formed on conversion from a four to five, or vice versa, coordination complex. The third terminal chlorine atom, which completes the five-coordination, has a Cu−Cl bond length of 2.282 (7) Å.

In the crystal structures of **4** and **5**, the benzodiazepine ligands act as ***N,N,O***-tridentate ligands whereas the 1,4-dihydro-1,3-quinazoline ligand acts as an *N,N*-bidentate ligand. Both types of ligands introduce considerable distortions of the Cu^{II}-coordination polyhedra. Bite angles of these chelating ligands are in the range of 78.7(2) to 81.4(5)°

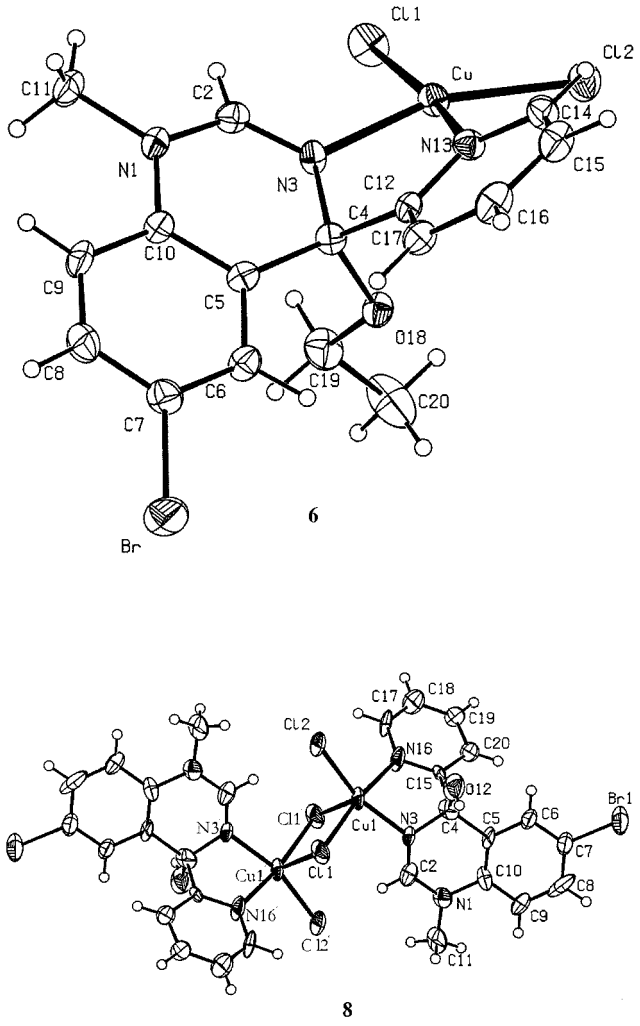


Figure 4. The ORTEP drawings of dichloro-[6-bromo-4-ethoxy-1,4-dihydro-1-methyl-4-(2′-pyridyl)-1,3-quinazoline-*N,N*]copper(II) (**6**) and di-μ-chloro-bis[6-bromo-1,4-dihydro-4-hydroxy-1-methyl-4-(2′-pyridyl)-1,3-quinazoline-*N,N*]dichlorodicopper(II) (**8**). Thermal ellipsoids are scaled at the 30% probability level

(Table 1). The atoms in the equatorial positions, as well as the Cu^{II} atom, of the square-pyramidal geometry are not coplanar (in the structures studied deviations are larger than 0.1 Å). The only exception is the structure of **5**, where deviations from the equatorial plane range from 0.012 (4) to 0.018 (9) Å.

Infrared Spectra

The IR spectra of the complexes provide some structural information of these compounds, whereas the ^1H NMR spectra show broad and badly resolved signals of little diagnostic value. When comparing the spectroscopic data of complexes with those of the free ligands,[16] the greatest changes may be noticed in the range 1750−1500 cm^{-1}. In this region bands arising from the stretching modes of the azomethine and pyridine C=N groups, as well as those from the lactam and acetate C=O, and the aromatic C=C vibrations, occur.[13,29,30] A very strong band at 1675 cm^{-1} and three weak bands at 1611, 1588, and 1562 cm^{-1} are characteristic of the free ligand (+)-**1**. On coordination of both nitrogen atoms, most of these bands in complexes **3** and **5** shift slightly to higher frequencies, and the intensity of the lower frequency bands increases. This behaviour is associated with a general π-electronic redistribution by metallation. The OH stretching mode over the 3000 cm^{-1} region is not informative due to the presence of the crystalline solvent. The spectra of the acetoxy derivative of **2** and its complex **7**, show a more complicated spectral pattern due to the strong absorptions of the acetate group. The transformation of ligand **1** to the 1,3-quinazoline derivative in complex **6** is supported by the absence of the lactam carbonyl band at 1675 cm^{-1}, as well as by the appearance of the very strong absorption at 1267 cm^{-1} due to the ν_{as}(C−O−C) vibration of the 4-substituted ethoxy group.

The far-IR spectra of the complexes show a number of bands in the 400−200 cm^{-1} region, where stretching modes of the metal-ligand vibrations occur. The low symmetry of the present complexes, particularly that of the [*N,N,O*] chelates **3**, **5**, and **7**, does not allow the characterisation of the copper-specific vibrations. In complexes **3** and **5**, a broad band around 325 cm^{-1} with a few shoulders on the lower frequency side, as well as absorption at 276 cm^{-1}, could be assigned to the ν(Cu−Cl) and ν(Cu−N) vibrations. The metal-halogen/nitrogen stretching frequency is observed over a wide range. This may be due to the variation in the two Cu−Cl and Cu−N bonds in the structure of the complex(Table 1). On the other hand coupled Cu−Cl and Cu−N bands could also be expected. The band at 364 cm^{-1} may be assigned to the ν(Cu−O) vibration, since it was found that ν(Cu−O) > ν(Cu−N) for this kind of metal complex.[31,32] The situation is more complicated in complex **7**, where the internal deformation modes of the acetate ligand also falls into the same spectral region as the metal-ligand vibrations.

Conclusion

Generally, the understanding of the structural and catalytic properties of copper complexes contributes to a better understanding of the catalytic reactions and functions of copper containing enzymes. We focused on the use of substituted 1,4-benzodiazepin-2-ones as the complexing agents for Cu^{II}. An unexpected reactivity of the 5-pyridyl-1,4-benzodiazepin-2-one derivatives (+)-**1** and (±)-**2** in the presence of Cu^{II} ions in ethanol was observed. Both starting compounds can coordinate through two oxygen atoms (hydroxy/acetoxy and lactam) and two nitrogen atoms (azomethine and pyridine) to Cu^{II}. Coordination through specific functional groups of the ligands used, and the electronic properties of the copper ions favour racemisation, (in complex **3**), oxygenation (in complex **5**) and ring contraction leading to the 1,4-dihydro-1,3-quinazoline derivatives (complexes **6** and **8**). The study presented suggests that 5-pyridyl-1,4-benzodiazepin-2-one chiral ligands in metal complexes, which are used as catalysts in enantioselective reactions, have to be employed with great caution.

Experimental Section

Materials and Instrumentation: (+)-7-Bromo-1,3-dihydro-3-hydroxymethyl-1-methyl-5-(2′-pyridyl)-2*H*-1,4-benzodiazepin-2-one, (+)-**1**, was prepared by lipase-catalysed kinetic resolution[16], whereas *rac*-3-acetoxymethyl-7-bromo-2,3-dihydro-1-methyl-5-(2′-pyridyl)-2*H*-1,4-benzodiazepin-2-one, (±)-**2**, was prepared according to the reported method.[15] All other reagents and solvents were of analytical grade and were used without purification. − FTIR spectra were recorded on a Perkin−Elmer 2000 spectrophotometer using KBr (4000−400 cm^{-1}) and polyethylene (400−200 cm^{-1}) pellets. − Elemental analyses were performed with a Perkin−Elmer Elemental Analyser E-2400 Series 2 (CHN) and thermogravimetric analyses with a Cahn RG electromicrobalance in an air atmosphere.

Preparation of Complexes 3 and 4: A solution of (+)-**1** (0.080 g, 0.22 mmol) in absolute EtOH (2 mL) was added dropwise to a stirred solution of $CuCl_2·2H_2O$ (0.038 g, 0.22 mmol) in absolute EtOH (3.0 mL) at ambient temperature, whereupon the colour of the reaction mixture changed to brown. After ca. 5 minutes the stirred solution became green again, and a green precipitate was observed. The precipitate was immediately separated by filtration, washed with cold absolute EtOH and the hygroscopic solid stored overnight under vacuum at ambient temperature. Elemental and thermogravimetric analyses indicated the formation of complex **3** as a trihydrate (yield 0.055 g, 46%). − $C_{16}H_{14}BrCl_2CuN_3O_2·3H_2O$ (548.95): calcd. C 35.00, H 3.67, N 7.69, H_2O 9.84; found C 34.80, H 3.08, N 7.30, H_2O 9.29. − IR (KBr): $\tilde{\nu}$ = 3420 m br [ν(OH], 1684 vs br [ν(C=O)], 1635 m, 1629 m, 1596 m and 1559 w-m [δ(HOH), ν(C=N), ν(C=C)], 1486 m, 1469 m, 1446 m, 1402 m, 1340 s, 1301 w, 1253 m, 1123 m, 1106 m, 1035 w, 1024 m, 972 w, 925 w, 890 w, 831 m, 800 m, 756 w-m, 741 w, 725 w, 673 m, 649 w cm^{-1}. − IR (polyethylene): $\tilde{\nu}$ = 364 w, 322 w-m br, 300 sh, 288 sh and 275 w cm^{-1}. Recrystallisation of complex **3** from DMSO gave reddish-brown single crystals of complex **4**.

Preparation of Complexes 5 and 6: Recrystallisation of complex **3**, either from absolute EtOH or a mixture of absolute EtOH and CH_2Cl_2, afforded a mixture of green (complex **5**) and black (complex **6**) crystals, both suitable for X-ray structural analysis. The solutions were subjected to slow solvent evaporation in a desiccator over silica gel. A small amount of the mixture of complexes **5** and **6** was also gradually formed from the mother solution (ethanol), after the preparation and isolation of complex **3**. Complexes were separated by hand under a microscope. Complex **5**: − IR (KBr): $\tilde{\nu}$ = 3300 w [ν(OH], 1688 vs [ν(C=O)], 1626 m, 1596 m, and 1560 w [δ(HOH), ν(C=N), ν(C=C)], 1487 m, 1468 m, 1445 m, 1399 m, 1332 s, 1303 w, 1252 m-s, 1146 m, 1100 s, 1070 m, 1026s, 1008 w-m, 989 w, 891 w, 848 w-m, 822 m, 793 m, 754 w, 684 m, 659 w, 650 w cm^{-1}. − IR (polyethylene): $\tilde{\nu}$ = 364 w, 324 w-m br, 300 sh, 286 sh, 276 w cm^{-1}. Complex **6**: − IR (KBr): $\tilde{\nu}$ = 1629s, 1595m-s, 1553m-s, 1503vs [ν(C=N), ν(C=C)], 1458 m-s, 1439 w-m, 1425 w, 1391 m, 1328 m, 1297 s, 1267 vs, 1245 m, 1202 w-m, 1175 w, 1117 w-m, 1092 w, 1039 w, 1024 m, 1001 m, 965 w, 916 w, 861 m, 825 m, 788 m, 754 w-m, 731w, 655 w-m, 643 w, 619 w cm^{-1}. − IR (polyethylene): $\tilde{\nu}$ = 340 w, 314 w, 301 w, 290 sh, 280 w cm^{-1}.

Table 2. Crystallographic data, crystallisation details, structure solution, and refinement of compounds **2**, **4**, and **5**

Compound	**2**	**4**	**5**
Formula	$C_{18}H_{16}BrN_3O_3$	$C_{18}H_{19}BrCl_2CuN_3O_3S \times 0.125\ H_2O$	$C_{16}H_{14}BrCl_2CuN_3O_3 \times 0.25\ C_2H_5OH$
M_r	402.25	536.33	510.66
Crystal system	monoclinic	monoclinic	monoclinic
Space group	*C*2/*c*	*C*2/*c*	$P2_1/n$
a [Å]	19.07(1)	10.250(3)	8.348(2)
b [Å]	7.461(3)	20.333(4)	15.030(6)
c [Å]	25.366(8)	20.036(2)	17.243(7)
α [°]	90.00	90.00	90.00
β [°]	105.32(4)	93.23(2)	91.52(4)
γ [°]	90.00	90.00	90.00
V [Å^3]	3481(3)	4169(1)	2163(1)
Z	8	8	4
D_x [Mg·m^{-3}]	1.542	1.715	1.568
Colour	colourless	reddish-brown	green
Crystallization solvent(s)	diisopropyl ether, dichloromethane, 1:1	DMSO	absolute ethanol
Temp. of crystallization	293(1) K	293 (1) K	293(1)K, dessicator
θ range [°]for cell det.	13.57−37.38	3.98−10.09	13.37−45.90
μ [mm^{-1}]	2.38	3.22	3.12
Temp. during data collection [K]	293(2)	293(2)	100(7)
Absorption correction	ψ-scan	ψ-scan	no correction
Total data collected	7852	4484	4719
Unique data	3526	4236	4387
Observed data [$I > 2\sigma(I)$]	1357	1474	1641
θ_{max} [°]	26.32	26.30	26.32
Range of *h*, *k*, *l*	−23.0; 0.9; −31.31;	−12.12; −25.0; 0.24;	−10.10; 0.18; 0, 21;
Intensity decay [%]	0.2	0.9	1.1
R_1 [$F_o > 4\sigma(F_o)$]	0.0453	0.0551	0.1146
wR_2 (F^2), all data	0.1297	0.1472	0.3267
S	0.911	0.917	1.417
No. of parameters	290	260	240
Δρ [e·Å^{-3}]	0.40, −0.46	0.53, −0.99	1.84, −2.36

Table 3. Crystallographic data, crystallisation details, structure solution, and refinement of compounds **6**, **7**, and **8**

Compound	**6**	**7**	**8**
Formula	$C_{16}H_{16}BrCl_2CuN_3O$	$C_{18}H_{16}BrCl_2CuN_3O_3$	$C_{14}H_{12}BrCl_2CuN_3O \times 0.5\ H_2O$
M_r	480.68	536.70	452.62
Crystal system	monoclinic	monoclinic	triclinic
Space group	$P2_1/n$	$P2_1/n$	$P\bar{1}$
a [Å]	10.073(2)	10.815	9.69(1)
b [Å]	13.027(3)	9.072	9.797(4)
c [Å]	14.020(3)	19.985	10.63(2)
α [°]	90.00	90.00	70.82(5)
β [°]	105.71(1)	98.64	61.93(9)
γ [°]	90.00	90.00	86.32(6)
V [Å^3]	1770.8(7)	1939(2)	836(2)
Z	4	4	2
D_x [Mg·m^{-3}]	1.803	1.841	1.796(1)
Colour	black	green	brown
Crystallization solvent(s)	absolute ethanol	acetonitrile	acetonitrile
Temp. of crystallization	293(1)K, dessicator	277.15 K	277.15 K
θ range [°]for cell det.	13.20−52.63	9.62−47.17	5.10−20.78
μ [mm^{-1}]	3.80	3.49	3.95
Temp. during data collection [K]	293(2)	100(7)	293(2)
Absorption correction	ψ-scan	ψ-scan	ψ-scan
Total data collected	5780	4332	3588
Unique data	5358	3949	3380
Observed data [$I > 2\sigma(I)$]	2104	1245	848
θ_{max} [°]	30.44	26.32	26.32
Range of h, k, l	−14, 14; 0, 18; 0, 20;	−13.13; 0.11; 0, 25;	0.12; −12.12; −13.13;
Intensity decay [%]	−0.7	−1.4	−0.2
R_1 [$F_o > 4\sigma(F_o)$]	0.0572	0.0768	0.0769
wR_2 (F^2), all data	0.1650	0.2347	0.2697
S	0.907	0.944	0.892
No. of parameters	235	207	205
Δρ [e·Å^{-3}]	0.69, −0.86	1.46, −1.62	0.72, −0.97

Preparation of Complexes 7 and 8: A solution of **2** (0.080 g, 0.20 mmol) in a 1:1 mixture of absolute EtOH and CH_2Cl_2 (5 mL) was added dropwise to a stirred solution of $CuCl_2{\cdot}2H_2O$ (0.034 g, 0.20 mmol) in the same solvent mixture (5 mL). After complete addition, the reaction mixture was continuously stirred for 1 h at ambient temperature, and the green precipitate formed was filtered off, washed with cold CH_2Cl_2 and dried under vacuum (yield 0.103 g, 96%). Green single crystals of complex **7** were obtained from MeCN on cooling at 4 °C. − $C_{18}H_{16}BrCl_2CuN_3O_3$ (536.70): calcd. C 40.28, H 3.01, N 7.83; found C 39.83, H 3.14, N 7.60. − IR (KBr): $\tilde{\nu}$ = 1750 vs and 1727 vs [ν(C=O) acetate], 1686 vs br [ν(C=O) lactam, ν_{as}(COO)], 1589 s, 1568 m, and 1557 m [ν(C=N), ν(C=C)], 1480 m, 1470 m-s, 1429 m, 1404 m, 1389 w, 1369 m, 1340 m, 1261 s, 1250 s, 1187 w, 1119 m-s, 1107 m-s, 1050 m, 1038 m, 1023 m, 980 w, 955 w, 888 w, 876 w, 835 m, 802 m, 782 w, 760 m, 743 w, 714 w, 677 m, 647 w-m, 605 w cm^{-1}. − IR (polyethylene): $\tilde{\nu}$ = 338 m, 315 m br, 294 m-s, 276 m cm^{-1}. Recrystallisation of complex **7** from a hot mixture of MeCN and absolute EtOH yielded a mixture of complex **7** (predominantly) and dark-brown single crystals of complex **8**, which were separated manually under a microscope.

X-ray Structure Analysis: Suitable single crystals were obtained by slow evaporation from different solvents; solvents used and crystallisation temperatures are listed in Table 2 and Table 3, which also summarises crystal data, experimental details of data collections and refinements. Intensities were measured on an Enraf−Nonius CAD4 diffractometer, with graphite monochromated Mo-K_α radiation, wavelength 0.71083 Å, using ω/2θ scan technique. For the compounds **5** and **7** data collections were at 100 K, whereas the others were performed at 293(±2) K. During data collections there were no significant variations in intensities of the three control reflections, which were measured every 120 minutes. The data were corrected for Lorentz and polarisation effects.[33] The absorption correction was based on a ψ-scan of seven reflections. Structures were solved using the package SIR97[34] and refined by the package SHELXL97.[35] The crystal quality of **5** was rather poor and in spite of low-temperature data the final R [for $F_o > 4\sigma$ (F_o)] was 0.1146. However, electron density maps unambiguously revealed the molecular structure of the complex. Molecular geometry calculations and illustrations of the crystal packing were prepared by PLATON98.[36] Plots of the molecules with thermal ellipsoids scaled at the probability level 30% were prepared by ORTEP.[37] Atomic scattering factors were those included in SHELXL97. The H-atom coordinates were calculated geometrically and refined using the SHELX97 riding model.

Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-158707 (**2**), CCDC-158708 (**4**), CCDC-158709 (**5**), CCDC-158710 (**6**), CCDC-158711 (**7**) and CCDC-158712 (**8**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) +44−1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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