# Synthesis, crystal structures, and electrochemistry of $Cu^{II}$ complexes with tetradentate $N_2O_2$ ligands derived from 3,7-diazabicyclo[3.3.1]nonan-9-one

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New copper(II) complexes with tetradentate ligands derived from 1,5-diphenyl-3,7-diazabicyclo[3.3.1]nonan-9-one and containing the N,N'-2-hydroxyethyl, 2-methoxyethyl, and carboxymethyl substituents were synthesized. The crystal structures of the complexes were established and the complexes were studied by cyclic voltammetry. The ligands are preorganized for complexation and are highly complementary for a divalent copper cation.

**Key words:** diazabicyclononane, bispidine, copper complexes, amino acids, structure, electrochemistry.

3,7-Diazabicyclo[3.3.1]nonane (DABCN, bispidine) is a functional building block, which has been extensively studied in organic chemistry and is widespread in living nature.<sup>1</sup> It combines the complexation properties of the nitrogen atoms included in the chelating configuration and rigid geometry of the bicyclic moiety, which fixes the directionality of the lone pairs of heteroatoms and the volume of the coordination sphere.<sup>2,3</sup> This provides selectivity and strength of complexation with appropriate metal cations and even neutral atoms fitting into the coordination sphere.<sup>4</sup> A wide range of possible modifications, varying the nature of substituents in the skeleton, and controlling the conformational equilibrium between the constituent six-membered rings allow one to make bispidine derivatives suitable for solving certain problems. In particular, diazabicyclononane-based pharmaceuticals, which control signal transduction in synapses and are used for the treatment of certain diseases, were designed.<sup>5</sup> It is conceivable that complexation of bispidines with metal cations in heart tissues plays a decisive role in the management of cardiac arrhythmia with the use of appropriate pharmaceuticals.<sup>6</sup> Complexes with (-)sparteine, which is a naturally occurring chiral alkaloid containing

DABCN as the key fragment, have been studied most thoroughly. Sparteine complexes with transition and main-group metals have found use as enantioselective catalysts.<sup>7</sup> An essential drawback, which limits the synthetic potential of the natural alkaloid, is that the (+)enantiomer is inaccessible, resulting in the formation of only one type of stereoisomers. This has stimulated a search for synthetic analogs of sparteine.<sup>8</sup> Although bispidines have been studied in-depth, data on their complexes are surprisingly scarce. Studies in this field have been intensified in the past decade because of diversity of bispidines and prospects of their use as ligands.

As part of our continuing studies of the complexation properties of 1,5-diphenyl-3,7-diazabicyclo[3.3.1]nonanes containing various substituents at the nitrogen atoms,<sup>9</sup> we turned our attention to  $N_2O_2$ -type tetradentate ligands, which, like  $N_4$ -type bispidine ligands,<sup>2,3,10</sup> are expected to possess a pronounced chelating effect and high affinity for divalent copper cations. At the same time, the presence of oxygen atoms lowers the symmetry of the coordination environment of the copper cations and opens up possibilities for the synthesis of inner-complex salts. The steric volume of the environment of the oxygen atoms is smaller than that of the nitrogen atom because it has only two substituents. As a result, additional ligands can

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more easily approach the copper atom, which is of importance in catalytic processes.



R = H (1, 3), Me (2, 4)

We used the simplest  $\alpha$ -amino acids, such as glycine and alanine, and their reduced derivatives, such as ethanolamine and 2-methoxyethylamine, as bicyclononanebridged chelating moieties. These DABCN ligands were synthesized by double Mannich condensation with the use of the corresponding primary amine, dibenzyl ketone, and paraformaldehyde. The reactions with ethanolamine and its methyl ether afforded ligands 1 and 2, respectively.<sup>11,12</sup> The glycine derivative of bispidone **3** has been described for the first time by Stetter,<sup>13</sup> who prepared its complex salts with Co<sup>II</sup>, Ni<sup>II</sup>, and Cu<sup>II</sup> and measured their stability constants. However, the structural data were lacking. Attempts to incorporate other amino acids into the bicyclononane structure failed, except for  $\alpha, \alpha$ -dimethylglycine.<sup>14</sup> The Mannich reaction of amino acids are difficult to perform because of the influence of the carboxy group, which is manifested, in particular, in low nucleophilicity of the amino group. This is confirmed by the fact that reactions with amino acid esters, as well as with aromatic amines,<sup>15</sup> proceed even more difficultly.<sup>16</sup> The yields of the reaction products are very low. The influence of the carboxy group of amino acids on the Mannich reaction cannot be attributed exclusively to the (-I) effect, because the reactions with  $\beta$ - and  $\gamma$ -amino



acids (in which this effect is smaller) do not afford the expected condensation products as well.<sup>17</sup> Earlier,<sup>18</sup> we have succeeded in performing the Mannich reaction with alanine to prepare bispidone **4** containing chiral substituents at the nitrogen atoms.

## **Results and discussion**

We synthesized ligands 1-4 using procedures described in the studies<sup>11-13</sup> and in our earlier publications.<sup>18</sup> Complex compounds 5 and 6 were synthesized from copper(II) chloride and perchlorate, respectively, by heating mixtures of solutions of the corresponding salt and the ligand followed by crystallization of the product upon cooling of the reaction mixture. Chelated salt 7 was prepared by deprotonation of chloride complex 5 with alkali. Compounds 8 and 9 were synthesized by heterogeneous reactions of solutions of the ligands with copper hydroperoxide.

## Structures of complexes

The crystal structures of complexes 5-7 and 9 were established by X-ray diffraction analysis. The crystallographic data are given in Table 1. Selected bond lengths, bond angles, and torsion angles are listed in Tables 2–4. The structures of complexes 5-7 and 9 are shown in Figs 1–4. Since we failed to grow single crystals of compound 8 suitable for X-ray diffraction study, the geometry of 8 was calculated by two quantum-chemical methods, the semiempirical PM3(tm) method and the density functional theory (DFT).

Generally, complexation of bispidine leads to the transformation of the bicyclic moiety into the exclusively rigid tricyclic skeleton, in which only slight variations in



Fig. 1. Structure of complex 5.

Га	ble	e 1		Crystal	lographic	data	for	compound	s 5—7	7 and	9
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Parameter	5	6	7	9
Molecular formula	C <sub>25</sub> H <sub>36</sub> Cl <sub>2</sub> CuN <sub>2</sub> O <sub>5</sub>	C <sub>25</sub> H <sub>32</sub> Cl <sub>2</sub> CuN <sub>2</sub> O <sub>11</sub>	C <sub>23</sub> H <sub>36</sub> CuN <sub>2</sub> O <sub>8</sub>	C <sub>50</sub> H <sub>52</sub> Cu <sub>2</sub> N <sub>4</sub> O <sub>14</sub>
Molecular weight	579.00	670.97	532.08	1060.04
Temperature	293(2)	213(2)	293(2)	298(2)
Radiation	Μο-Κα	Cu-Ka	Μο-Κα	Μο-Κα
Wavelength/Å	0.71073	1.54178	0.71073	0.71073
Crystal dimensions/mm	$0.4 \times 0.2 \times 0.2$	$0.6 \times 0.1 \times 0.1$	$0.4 \times 0.1 \times 0.1$	$0.2 \times 0.2 \times 0.2$
Crystal system	Triclinic	Triclinic	Monoclinic	Orthorhombic
Space group	$P\overline{1}$	$P\overline{1}$	Cc	$P2_{1}2_{1}2_{1}$
a/Å	8.991(1)	10.636(1)	14.472(1)	9.164(2)
b/Å	12.725(1)	10.646(1)	21.792(1)	17.558(4)
c/Å	13.232(1)	13.258(1)	8.768(1)	29.392(6)
α/deg	114.37(1)	104.15(1)	90.00	90.00
β/deg	95.89(1)	91.77(1)	119.38(1)	90.00
γ/deg	103.54(1)	108.09(1)	90.00	90.00
$V/Å^3$	1306.4(2)	1374.4(2)	2409.5(4)	4729.2(18)
Z	2	2	4	4
$d_{\rm calc}/{\rm g~cm^{-3}}$	1.472	1.621	1.467	1.489
$\mu/mm^{-1}$	1.079	3.479	0.957	0.973
<i>F</i> (000)	606	694	1124	2200
θ Scan range	2.39-25.12	3.46-64.99	2.52 - 25.00	2.32 - 27.50
Ranges of indices of measured	$-10 \le h \le 10$	$-12 \le h \le 13$	$-12 \le h \le 17$	$0 \le h \le 12$
reflections	$-15 \le k \le 13$	$-13 \le k \le 12$	$-5 \le k \le 25$	$0 \le k \le 24$
	$0 \le l \le 15$	0 <i>≤ l ≤</i> 16	$-10 \le l \le 10$	$0 \le l \le 41$
Number of measured reflections	4837	3472	3622	6026
Number of independent reflections $(R_{int})$	4619 (0.0366)	3334 (0.0489)	2841 (0.0448)	6023 (0.0025)
Number of parameters in refinement	317	333	452	634
$R_1 \left[ I \ge 2\sigma(I) \right]$	0.0789	0.1065	0.0282	0.0359
$wR_2$ (based on all reflections)	0.2185	0.3746	0.0710	0.1100
Goodness-of-fit on $F^2$	1.044	1.033	1.036	1.013
Flack absolute structure parameter	_	_	-0.01(1)	-0.01(2)
Residual electron density				
$(max/min)/e Å^{-3}$	1.263/-2.364	1.441/-0.762	0.450/-0.545	0.469/-0.300

 Table 2. Selected geometric parameters of molecules 1 and 4

 determined by X-ray diffraction analysis

Parameter	1	<b>4</b> <sup><i>a</i></sup>	<b>4</b> <sup>b</sup>	4 <sup>c</sup>
Bond		d	/Å	
N(1) - N(2)	3.476(4) <sup>19</sup>	2.713(4)	2.665(4) <sup>20</sup>	2.689
O(1) - O(2)	7.650(4) <sup>19</sup>	6.050(4)	6.108(4) <sup>20</sup>	6.079
Angle <sup>d</sup>	. ,	ω/	deg	
	11.5(3) <sup>18</sup>	13.2(3)	7.9(3) <sup>19</sup>	10.5

<sup>*a,b*</sup> Two crystallographically independent molecules.

<sup>c</sup> The average value for two molecules.

<sup>d</sup> The N(1)-N(2)-O(1)-O(2) dihedral angle.

structural parameters at the Cu atom are possible, primarily, due to asymmetry of the bonds between the nitrogen atoms and the metal. The presence of additional carbon bridges between the oxygen atoms and the diazabicyclononane skeleton provides alternative conformational possibilities for the ligand and, correspondingly, gives rise to additional types of coordination geometry, for example, as a result of deviation of the metal atom from the mean  $N_2O_2$  plane. In addition, the ethanolamine and  $\alpha$ -amino acid fragments differ in both the electronic and steric properties.

The available structural data<sup>19,20</sup> for ligands 1 and 4 provide a possibility of comparing these ligands with the corresponding complexes 5, 7, and 9. In the crystal, molecules 1 adopt a chair-boat conformation, which is, apparently, the major conformation in solution as well.<sup>17</sup> Upon complexation, the ligand molecule is forced to adopt a chair-chair conformation. Molecules 4, like other amino acids, exist in the zwitterionic form. The proton bound to the nitrogen atom forms an intramolecular hydrogen bond with another nitrogen atom, thus fixing a chair-chair conformation. Therefore, the bicyclic skeleton of **4** is spatially preorganized for complexation, *i.e.*, minimal changes in the geometry of the ligand are required for the complex formation. Correspondingly, the change in the entropy of the reaction is small. An analogous effect would be expected for molecule 3. The free

Parameter	5	6	7	8,	8,	<b>9</b> <sup>a</sup>	<b>9</b> <sup>b</sup>	<b>9</b> <sup>c</sup>	10,	11,
	XDA			DFT	PM3	XDA			XDA <sup>21</sup>	XDA <sup>22</sup>
Cu-N(1)	2.008(3)	2.017(12)	2.015(2)	2.03	1.90	2.027(4)	2.025(4)	2.026	1.979(8)	1.984(10)
Cu-N(2)	2.012(4)	1.965(13)	2.030(3)	2.06	1.96	1.989(4)	1.983(4)	1.986	1.979(8)	2.021(11)
$Cu-N^d$	2.010	1.991	2.023	2.05	1.93	2.008	2.004	2.006	1.979	2.003
Cu-O(1)	1.993(3)	1.975(12)	1.926(3)	1.93	1.86	1.922(3)	1.911(4)	1.917	1.944(7)	1.946(9)
Cu-O(2)	2.012(3)	1.979(11)	1.928(2)	1.96	1.86	1.952(4)	1.958(3)	1.955	1.950(7)	1.957(9)
$Cu-O^d$	2.003	1.977	1.927	1.95	1.86	1.937	1.936	1.936	1.947	1.952
N(1) - N(2)	2.771(4)	2.776(16)	2.760(4)	2.90	2.71	2.841(5)	2.808(5)	2.825	3.000(9)	2.989(14)
O(1) - O(2)	2.958(5)	3.012(15)	2.871(4)	3.09	2.39	2.821(5)	2.818(5)	2.820	2.804(9)	2.831(12)
Cu-X(1)	2.416(1)	2.51(1)	2.408(3)	2.49	2.02	2.218(4)	2.213(4)	2.216	2.390(7)	2.404(11)
$X(1)^e$	Cl	$O(ClO_4)$	$O(H_2O)$	$O(H_2O)$	$O(H_2O)$	O(OCO)	$O(H_2O)$	_	O(OCO)	$O(H_2O)$
Cu-X(2)	3.826(7)	2.54(1)				_		_	_	
$X(2)^e$	$O(H_2O)$	$O(ClO_4)$	_	_	_	_	_	_	_	_
$\Delta^f$	0.369(2)	0.019(6)	0.201(2)	0.08	0.26	0.345(2)	0.343(2)	0.344	0.13(1)	0.05(1)

Table 3. Selected bond lengths (Å) in the ligand molecules and complexes 5-11 (XDA is X-ray diffraction analysis)

<sup>*a,b*</sup> Two crystallographucally independent molecules.

<sup>c</sup> The average value for two molecules.

<sup>d</sup> The average value.

<sup>e</sup> The extra ligand.

<sup>*f*</sup> The deviation of the copper atom from the N(1)-N(2)-O(1)-O(2) plane.

Table 4. Selected bond angles (deg) in the ligand molecules and complexes 5–11 (XDA is X-ray diffraction analysis)

Parameter	5	6	7	8,	8,	<b>9</b> <sup>a</sup>	<b>9</b> <sup>b</sup>	<b>9</b> <sup>c</sup>	10,	11,
		XDA		DFT	PM3		XDA		XDA <sup>21</sup>	XDA <sup>22</sup>
N(1) - Cu - N(2)	87.21(13)	88.8(5)	86.05(11)	90.083	89.155	90.1(2)	89.0(2)	89.6	98.6(3)	96.6(4)
O(1) - Cu - O(2)	95.24(14)	99.2(5)	102.23(13)	105.15	80.113	93.5(2)	93.5(2)	93.5	92.1(3)	92.9(4)
X(1) - Cu - X(2)	162.5(1)	158.3(4)	_	_	—	_	_	_	_	_
Cu-N-Cexo	104.4(3)	105.9(10)	103.9(2)	103.9	104.4	105.4(3)	105.6(3)	105.5	108.1(4)	109.4(5)
NCuN/OCuO	30.6(1)	7.3(3)	16.9(3)	29.86	23.95	29.4(2)	29.5(1)	29.5	11.04(3)	4.82(4)
Dihedral angle	1.38(1)	7.2(5)	1.97(13)	27.89	9.99	4.28(15)	6.45(15)	5.37	1.0(3)	2.2(4)
N(1)-N(2)-O(1)-O(2)	)					. ,	. ,			

<sup>*a,b*</sup> Two crystallographycally independent molecules.

<sup>c</sup> The average value for two molecules in the asymmetric unit.

energies of complexation for 3 and 4 decrease due to an increase in the entropy term, thus increasing stability of the resulting complexes. To estimate the geometric complementarity for copper(II) and preorganization of the ligands for complexation with copper(II), it is necessary to compare the structural parameters of the complexes with those of the free complexation agents and with the ideal values for the bonds with the metal atom. The latter can be determined, on the one hand, by ab initio calculations of the geometry of the appropriate model molecules and, on the other hand, from experimental data for related compounds, whose structures can be considered as unstrained. It is reasonable to compare the compounds under study with complexes, in which the bicyclononane skeleton linking two chelate fragments is absent, *i.e.*, there are no restrictions imposed by the bicyclic fragment on the coordination sphere of the metal atom. The structures of copper alanine (10) and glycine (11) complexes and the structure of compound 9 have been established earlier.<sup>21–23</sup> The copper complexes with ephedrine<sup>24</sup> and tris-hydroxymethylaminomethane<sup>25</sup> are the closest analogs of compound 7. The crystallographic data for copper ethanolaminate and analogs of complexes 5 and 6 are lacking. In addition, the copper(II) complex with an alanine derivative of urotropine<sup>26</sup> and the nickel(II) complex with a glycine derivative of urotropin<sup>27</sup> were documented.

The principal bond lengths and bond angles for compounds 1, 4, and 5-11 are given in Tables 2-4. It should be noted that the diazabicyclononane backbone remains virtually unchanged upon complexation, and the main difference is observed in the orientation of the substitu-



Fig. 2. Structure of complex 6.

ents at the nitrogen atoms. The substituents can adopt different conformations in the free ligand depending on the crystal packing. Apparently, several stable conformers exist in solution, but both substituents in the complex adopt similar conformations fixed by the five-membered chelate rings.



Fig. 3. Structure of complex 7.

The coordination environment of the metal atoms in complexes 5, 7, and 9 can be considered as a distorted tetragonal pyramid. The coordination environment of the metal atom in complex 6 can be described as a tetragonal bipyramid or as an elongated octahedron. The apical positions of the bipyramid are occupied by the oxygen atoms of the  $ClO_4^-$  anions. In this interpretation, the coordination environment of copper in 6 has a distorted square-planar geometry, because the perchlorate anions are at a large distance from the metal atom (2.5 Å) and form weak



Fig. 4. Structure of complex 9.



bonds determined, apparently, by electrostatic forces. The coordination plane is slightly tetrahedrally distorted, which is typical of four-coordinate copper(11). The N-N-O-O dihedral angle is 7.25°, which corresponds to the angle between the N-Cu-N and O-Cu-O planes (7.33°). The tetrahedral distortion characteristic of four-coordinate copper(II) (unlike six-coordinate copper) argues in favor of considering complex  $\mathbf{6}$  as having a square-planar structure and the bonds between Cu and  $ClO_4^-$  as secondary bonds. In complex 5, the apical position of the pyramid is occupied by the Cl<sup>-</sup> anion. In other structures, the fifth coordination site in the coordination sphere of copper is occupied by the water molecule. The structure of dimeric compound 9 is somewhat different. In one molecule of 9, the copper cation is coordinated by the water molecule, whereas the carbonyl oxygen atom of the carboxylate group of the first molecule is present as the fifth ligand in another molecule of 9. The base of the pyramid is virtually undistorted, and the metal atom is at a distance of 0.20-0.35 Å from the base of the pyramid.

The geometry of the coordination sphere in 9 is similar to that in copper *cis*-bisalaninate complex 10. The following differences can be mentioned: the Cu–N dis-

tances in 9 differ by 0.042(6) Å, whereas these distances in 10 are identical, both Cu-N bonds in 9 being longer than those in **10** but being similar to the Cu–N distance in bisglycinate 11. The Cu–O bond lengths in 9 are, on the average, slightly shorter than those in 10 and 11  $(\sim 0.01 \text{ Å})$ . However, the average difference in the bond lengths in two complexes is substantially smaller than the asymmetry of the bonds in 9. The bonds between the copper cation and the apical ligands in 9 are substantially shorter (by more than 0.17 Å), and the Cu atom is located above the plane of the base of the coordination pyramid. The N–Cu–N bond angle in **9** is close to  $90^{\circ}$  (89.6°) and is substantially larger in 10 (98.6°), whereas the O-Cu-O bond angles in both compounds have similar values (93.5(2) and 92.1(2)°, respectively). An essential difference is observed only in the geometric parameters of the alanine fragments of complexes 9 and 10. The amino acid substituents in 10 are characterized by considerable asymmetry of the bond lengths and bond angles with respect to each other. In both complexes, two alanine fragments adopt different conformations. In one fragment, the Me substituent is in an equatorial position, whereas this substituent in another fragment is in an unfavorable axial position. It should be noted that the bond with the Me group in the axial position in 10 is substantially longer than the other bonds,<sup>21</sup> whereas all analogous bonds in 9 are virtually equal in length.<sup>22</sup>

The molecules of all complexes have symmetry  $C_1$ . However, molecule **6** has the pseudosymmetry axis  $C_2$ passing through the copper atom and the keto group, whereas molecule 5 has a pseudosymmetry plane, which relates two six-membered rings of the bicyclic skeleton and two  $\beta$ -hydroxyethyl substituents to one another. Complex 7 also has pseudosymmetry  $C_s$ . In this complex, the coordinated water molecule slightly violates the almost ideal symmetry  $C_{\rm s}$ . The geometry of complex 8 in the gas phase optimized by the semiempirical PM3 method is close to  $C_s$ , whereas calculations by the DFT method gave symmetry  $C_2$  characteristic of the tetrahedrally distorted tetragonal symmetry of the ligand environment, *i.e.*, for four- and six-coordinate copper. This is attributed to an increase in the bond length between the copper atom and the water molecule, which is transferred into the second coordination sphere. Apparently, these two coordination polyhedra with different symmetry are energetically similar, because both type of complexes exist, and the existence of a particular coordination mode depends primarily on the crystal forces. In all complexes, the Cu-N bond lengths, as well the parameters of the bicyclononane skeleton, have very similar values. In all compounds, the N-Cu-N angle is close to 90°. The Cu-O bond length varies depending on the charges of the oxygen atoms and additional ligands. The shortest Cu-O bonds are observed in the anionic ligands, the bond lengths being virtually equal for the oxide and carboxy binding centers.

The longest Cu–O bond is observed for the hydroxy binding center, whereas the analogous bond for the methoxy center is somewhat shorter. This is associated with the fact that the copper atom in complex **6** is less coordinatively saturated, because it has four atoms in the first coordination sphere rather than five atoms involved in the first coordination sphere in complex **5**.

Taking into account that the structure of copper glycinate 11 is unstrained, its parameters can be used as a model for estimating the deviations of the coordination polyhedra in 8 and 9 from the model values. The parameters of the ligand in complex 11 are virtually equal to those of free glycine, except for the carboxy group, in which the C–O bonds differ in length due to complexation. The average Cu-O and Cu-N bond lengths in complex 9 are similar to those observed in 11. The deviation of the copper atom from the plane passing through the donor atoms, apparently, indicates that the size of the Cu<sup>II</sup> dication does not match the size of the the coordination cavity. This assumption is confirmed by an increase in the distance between the nitrogen atoms (by 0.16 Å) upon complexation and by the longer N-N distances in complexes 10 and 11. However, the deviation of the geometric complementarity between the ligands and the divalent copper cation from the ideal case is small and is compensated by the displacement of the metal atom from the  $N_2O_2$  plane. Since the bond angles at the metal atoms in the complexes are rather flexible,<sup>2</sup> the above fact does not cause strain in the coordination sphere of the cation. Therefore, all ligands are characterized by high geometric complementarity for copper(II). Electronic complementarity, *i.e.*, complementarity at the level of electronic interactions, reflects complementarity of electron distribution responsible for the interaction energy.<sup>28</sup> The generalized double complementarity is responsible for stability of the complexes,<sup>28</sup> which was studied by electrochemical methods.

The geometry of molecule 8 was calculated using the atomic coordinates of one of molecules 9 determined by X-ray diffraction analysis. In this model, the copper atom is coordinated by the water molecule, and the Me group is replaced with the hydrogen atom. The geometry optimization was carried out by the DFT method with the use of the hybrid functional B3LYP. To accelerate calculations, we used the two-level ONIOM approach, in which the copper atom and its closest environment are represented with the use of the LanL2DZ basis set, whereas the bicyclic skeleton and the Ph groups are described using the minimal STO-3G basis set. The bond lengths in the coordination sphere of complex 8 calculated by the nonempirical method are similar to those for copper(II) bisglycinate. The parameters of the bicyclononane moiety differ substantially from the experimental data known for other compounds, which is reasonable considering the minimal basis set used. The type of the coordination polyhedron differs substantially from that in complex 9 and is characterized by tetrahedral distortion of the  $N_2O_2$  plane with the simultaneous displacement of the water molecule to a distance corresponding to secondary interactions. Therefore, the calculated structure of single molecule 8 *in vacuo* can be described as a tetrahedrally distorted planar square. The geometry optimization by the semiempirical method (PM3tm) retains the pyramidal geometry of the coordination polyhedron but underestimates the bond lengths of the metal atom, the parameters of the organic moiety of the molecule corresponding to standard values. The calculated structure of 8 is shown in Fig. 5.

Complexes with the amino acid bispidine ligands can be related to their methylpyridine analogs. To date, copper(II) complexes with 3,7-bis(2-pyridylmethyl)-3,7diazabicyclo[3.3.1]nonane are the most stable of complexes with acyclic tetramines.<sup>29</sup> This is associated with rigidity and preorganization of the ligand and its complementarity for Cu<sup>II</sup>. Compounds **3** and **4** have a similar geometry. However, there are no van der Waals repul-



Fig. 5. Calculated structures of complex 8.

sions in complexes 8 and 9, whereas such repulsions between the  $\alpha$ -hydrogen atoms of the pyridine rings contribute to strain in the structures of the pyridine complexes. Hence, complexes 8 and 9 would also be expected to be highly thermodynamically stable.

# Electrochemistry

Earlier,<sup>30</sup> we have studied the redox properties of a series of  $Cu^{II}$  complexes with general formula  $LCuCl_2$  (12; L is 3,7-dialkyl-3,7-diazabicyclo[3.3.1]nonan-9-one).

It was hypothesized that oxidation of these complexes occurs at the lone pairs of the nitrogen atoms giving rise to  $CuCl_2$ , whereas reduction leads to electron transfer from the electrode to the copper atom, both leading to decomposition of the complex.

In the present study, we examined the electrochemical properties of complexes **5–9** by cyclic voltammetry (CV) in MeCN at Pt and glassy-carbon electrodes against  $0.05 M Bu_4 NBF_4$ .

#### Oxidation

The complexes under consideration are irreversibly oxidized at high anodic potentials (Table 5), except for complex **8**, which is not oxidized under these conditions. Apparently, the ligand is oxidized in the anodic scan analogously to complexes **12**.<sup>30</sup> The CV curves for solutions of complex **9** in MeCN at a Pt electrode are shown in Fig. 6 (curve 1). Electrochemical oxidation of this compound (peak A) affords a product, which gives rise to a reduction peak (peak B) in the reverse cathodic scan of the CV curve at -0.68 V, which is 180 mV less negative than the reduction peak of compound **9** (peak D). Reduction at the peak B is accompanied by elimination of copper metal, as evidenced by the appearance of the peak C

**Table 5.** Oxidation potentials  $(E_p^{\text{Ox}})$  and reduction potentials  $(E_p^{\text{Red}})$  of complexes **5**–**9** at a Pt electrode (MeCN, Bu<sub>4</sub>NBF<sub>4</sub>, Ag/AgCl,KCl<sub>sat</sub>, 20 °C, scan rate was 200 mV s<sup>-1</sup>)

Com-	$E_{\rm p}^{\rm Ox}$	$E_{1/2}^{\operatorname{Red} a}$	$E_{\rm p}^{\rm Red}$			
pound		V				
5	1.84 <sup>b</sup>	_	0.50; -0.60; -1.40			
6	2.23	0.48; -0.53	0.23; -0.52; -1.55			
7	2.31	1.09	-0.89			
8	Sharp oxidation waves are absent	1.14	-1.18			
9	1.81; 1.76	1.05	$-0.87; -2.46^{c}$			

<sup>a</sup> The half-wave potentials at a rotating disk Pt electrode.

<sup>b</sup> At a glassy-carbon electrode.

<sup>*c*</sup> A small peak was also observed at -1.01 V.



Fig. 6. The CV curves for oxidation (1) and reduction (2) of complex 9 at a Pt electrode in MeCN against  $0.05 M Bu_4 NBF_4$  at 20 °C.

in the reverse anodic scan. This peak has a triangular shape without a diffusion tail, which is characteristic of oxidative desorption of metal deposited on the surface of the electrode. Earlier, we have observed an analogous behavior for copper complexes with 3,7-dialkyl-3,7-diazabicyclo[3.3.1]nonan-9-one.<sup>30</sup>

### Reduction

As can be seen from Table 5, the complexes under consideration behave differently at the cathode. At a platinum electrode, complexes 7-9 are reduced in one oneelectron quasireversible step (see Fig. 6, curve 2). The difference between the potentials of the reverse and direct peaks  $(E_{pE}^{Ox} - E_{pD}^{Red}; E \text{ and } D \text{ are the cathodic and}$ anodic peaks, respectively, of the quasireversible redox pair 9/9<sup>•-</sup> in Fig. 6) is rather large (450 mV for complex 9, 350 mV for complex 8, and 330 mV for 7), which may be indicative of a structural rearrangement of the initially formed radical anion. No anodic peaks, which could be assigned to oxidation of copper metal, were observed in the CV curves of complexes 7 and 8 during the reverse potential scan, whereas the oxidation peak  $Cu^0/Cu^1$  (-0.29 V) was observed upon reduction of complex 9 in the reverse anodic branch of the CV curve after six—eight potential scans from 0.0 to -1.3 V and in the opposite direction. The anodic branch of the CV curves also has an anodic peak ( $E_p^{Ox} = 0.15$  V) corresponding, apparently, to the Cu<sup>I</sup>/Cu<sup>II</sup> transition. When the potential was scanned from -1.3 to +0.4 V and then in the opposite direction, both anodic peaks virtually disappeared. This fact can be explained as follows. The formation of copper metal by one-electron reduction of the CuII complex occurs, apparently, due to disproportionation of the complex-free Cu<sup>I</sup>, as was observed in aqueous media.<sup>31</sup> Presumably, interactions between the d orbitals of the

copper atom and the n orbitals of the nitrogen atoms in radical anion  $9^{-}$  become weaker. However, oxidation of copper metal to Cu<sup>2+</sup> is accompanied by regeneration of the starting complex. Stability of radical anion  $9^{-}$  appeared to be dependent on the material of the working electrode. In experiments with the use of a glassy-carbon electrode, oxidation peaks of copper metal were observed neither after the first reduction peak of complex 9 nor after the second reduction peak at high cathodic potentials (-2.46 V, see Table 5).

Reduction of complexes 5 and 6 occurs analogously to reduction of complexes 12.<sup>30</sup> Two one-electron reduction peaks are observed. The first peak is quasireversible  $(E_p^{Ox} - E_p^{Red} = 80 \text{ mV} \text{ for complex 5 and 190 mV} \text{ for complex 6})$ . The transfer of the second electron results in deposition of copper metal on the electrode. The third cathodic peak (see Table 5) corresponds, apparently, to reduction of the ligand.

High negative reduction potentials of chelated salts **7–9** compared to those of complexes **5** and **6** are indicative of high stability of these compounds and high complementarity of metal—ligand interactions. Data obtained under the same conditions are necessary for a direct comparison with other ligands. Complexes **5** and **6** have positive first reduction potentials, which may be indicative of their lower stability. The reduction peaks are nearly thermodynamically reversible (when  $E_p^{Ox} - E_p^{Red} = 60 \text{ mV}$ ). Apparently, copper(1) complexes formed in the first step are much better stabilized by neutral ligands than those in the case of complexes **7–9** containing the dianions as ligands. Therefore, the electronic complementarity for Cu<sup>II</sup> ions in complexes **5** and **6** is lower than that in complexes **7–9**, whereas the complementarity for Cu<sup>I</sup> ions is higher, the steric parameters being similar.

Since bispidines based on substituted  $\alpha$ -amino acids have chiral centers near the nitrogen atoms, their complexes can be used as catalysts for enantioselective reactions. The accessibility of the starting reagents, viz., natural amino acids, and the ease and simplicity of the onepot synthesis of ligands based on these compounds hold promise for the design of this type of enantioselective catalysts. Only N<sub>4</sub>-type ligands derived from dipeptide Schiff bases, which also contain  $\alpha$ -amino acids as the key fragments, are characterized by a comparable combination of useful structural parameters, the ease of the synthesis, and accessibility of the starting reagents.<sup>32</sup> In the study,<sup>32</sup> the authors called these ligands "privileged" ligands without data on the catalytic activity at their disposal. The efficiency of the use of complexes analogous to those described in the present study was demonstrated for bicyclononanes, which are derivatives of substituted ethanolamine and which catalyze the addition of diethylzinc to aldehydes with enantiomeric excess of 83-98%.<sup>33</sup>

To summarize, we synthesized copper(II) complexes with tetradentate ligands 1-4. The structural study dem-

onstrated that these ligands are characterized by high geometric complementarity for copper(II). Electrochemical investigation revealed high electronic complementarity of chelated salts 7-9 and substantially lower complementarity of complexes 5 and 6.

# **Experimental**

Single crystals were grown by crystallization from ethanol. X-ray diffraction data sets were collected on an Enraf-Nonius CAD4 diffractometer (graphite monochromator, ω scanning technique). The crystallographic data, characteristics of X-ray data collection, and details of structure refinement for compounds 5-7 and 9 are given in Table 1. The absorption corrections were applied using experimental azimuthal scan curves. The structures were solved by direct methods (SHELXS-86)34 and refined anisotropically by the full-matrix least-squares method against  $F^2$  (SHELXL-93).<sup>35</sup> The hydrogen atoms in the structures of 5, 6, and 9 were placed in geometrically calculated positions and refined using a riding model. The hydrogen atoms in the structure of 7 were refined isotropically. In compound 6, one of the Me groups is disordered over two positions with occupancies of 0.55 and 0.45. The structure of 5 contains ethanol solvate molecules. In the structures of 7 and 9, water molecules were revealed.

Quantum-chemical calculations of the geometry of compound **8** were carried out by the DFT method with the use of the B3LYP hybrid functional and the two-level ONIOM procedure implemented in the Gaussian-98 program package.<sup>36</sup> The geometry optimization was performed using the Berny algorithm and intrinsic coordinates. The PM3(tm) calculations were carried out using the Hyperchem 7.5 program.<sup>37</sup>

Electrochemical measurements were performed with the use of a PI-50-1.1 potentiostat, a platinum electrode (3.5 mm in diameter), and a glassy-carbon electrode (50 nm in diameter). A silver chloride electrode was used as the reference electrode, and  $Bu_4NBF_4$  was used as the supporting electrolyte. All measurements were carried out in MeCN, which was purified by successive treatment with a nitrating mixture, potassium hydride, and phosphorus pentoxide. The potentials are given taking into account iR compensation. The numbers of electrons were determined by comparing the oxidation peaks of ferrocene taken at an equal concentration.

The complexes and ligands were synthesized with the use of solvents purified according to standard procedures.<sup>38</sup> Ligands 1-4 were synthesized according to procedures described earlier.<sup>11-13,18</sup>

*N,N'*, *O,O'*-3,7-Bis(2-hydroxyethyl)-9-oxo-1,5-diphenyl-3,7-diazabicyclo[3.3.1]nonanocopper(II) dichloride (5). Compound 1 (1.6 g, 4.2 mmol) was dissolved in ethanol (40 mL) and heated to boiling. Then a warm solution of anhydrous copper(II) chloride (0.56 g, 4.2 mmol) was added. The solution was refluxed for 3 h and then allowed to stand for 18 h. The blue crystals that precipitated were filtered off, washed with ethanol, and recrystallized from ethanol. The product was obtained in a yield of 1.9 g. After recrystallization from aqueous ethanol, the solvate with one ethanol molecule and one water molecule was obtained. M.p. 176–179 °C. Found (%): C, 51.57; H, 6.29; N, 4.89.  $C_{25}H_{36}Cl_2N_2O_5Cu$ . Calculated (%): C, 51.86; H, 6.27; N, 4.84. *N,N'*, **0**,**0***'*-**3**,**7**-Bis(2-methoxyethyl)-9-oxo-1,5-diphenyl-**3**,**7**-diazabicyclo[3.3.1]nonanocopper(II) diperchlorate (6). *Caution! This procedure uses explosive perchlorates!* Compound **2** (0.61 g, 1.5 mmol) was dissolved in chloroform (5 mL) and mixed with a solution of copper(II) perchlorate hexahydrate (0.55 g, 1.5 mmol). The reaction mixture was heated to boiling and then allowed to stand for 18 h. The blue crystals that precipitated were filtered off. The product was obtained in a yield of 1.01 g. Complex **6** is stable up to 210 °C. Heating at high temperature may cause explosion! Found (%): C, 44.60; H, 4.70; N, 4.25.  $C_{25}H_{32}Cl_2N_2O_{11}Cu$ . Calculated (%): C, 44.75; H, 4.81; N, 4.17.

**Copper(II)** 9-oxo-1,5-diphenyl-3,7-diazabicyclo[3.3.1]non-3,7-ylenediacetate (8). Compound 3 (3.0 g, 7.3 mmol) was dissolved in a mixture of DMF (100 mL) and isopropyl alcohol (30 mL). Then freshly precipitated copper hydroxide (1.5 g, 15 mmol) was added and the mixture was stirred at 30-40 °C for 3 h. The precipitate was filtered off, washed with diethyl ether, and dried in a vacuum desiccator for 10 h. Purple crystals of complex 8 were obtained in a yield of 3.5 g. M.p. 276–278 °C. Found (%): C, 58.51; H, 4.79; N, 6.20.  $C_{23}H_{22}N_2O_5Cu$ . Calculated (%): C, 58.78; H, 4.72; N, 5.96.

Copper(II) (+)-(*S*,*S*')- $\alpha$ , $\alpha$ '-(9-oxo-1,5-diphenyl-3,7-diazabicyclo[3.3.1]non-3,7-ylene)dipropionate (9). Compound 4 (4.8 g, 11 mmol) was dissolved in a mixture of DMF (15 mL) and methanol (150 mL). Then freshly precipitated copper hydroxide (1.5 g, 15 mmol) was added and the mixture was stirred at 30-40 °C for 3 h. The precipitate was filtered off, washed with diethyl ether, and dried in a vacuum desiccator. Dark-blue crystals, which were obtained in a yield of 5.0 g, were recrystallized from aqueous DMF. M.p. 284-286 °C. Found (%): C, 58.02; H, 5.61; N, 5.46. C<sub>25</sub>H<sub>28</sub>N<sub>2</sub>O<sub>6</sub>Cu. Calculated (%): C, 58.19; H, 5.47; N, 5.43.

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#### References

- 1. N. S. Zefirov and V. A. Palyulin, *Topics in Stereochemistry*, 1991, **20**, 171.
- 2. P. Comba and W. Schiek, *Coord. Chem. Rev.*, 2003, 238-239, 21.
- 3. P. Comba, B. Nuber, and A. Ramlow, J. Chem. Soc., Dalton Trans., 1997, 347.
- 4. K.-J. Haack, R. Goddard, and K.-R. Porschke, *J. Am. Chem. Soc.*, 1997, **119**, 7992.
- W. H. Bunnelle, D. B. Cristina, J. F. Daanen, M. J. Dart, M. D. Meyer, K. B. Ryther, M. R. Schrimpf, K. B. Sippy, and R. B. Toupence, US Pat., 2003225268, 2003.
- 6. S. Weidmann, Annu. Rev. Physiol., 1993, 55, 1.

- 7. J. Spieler, O. Huttenloch, and H. Waldmann, *Europ. J. Org. Chem.*, 2000, 391.
- J.-P. R. Hermet, D. W. Porter, M. J. Dearden, J. R. Harrison, T. Koplin, P. O'Brien, J. Parmene, V. Tyurin, A. C. Whitwood, J. Gilday, and N. M. Smith, *Org. Biomol. Chem.*, 2003, 1, 3977.
- 9. S. Z. Vatsadze, V. K. Bel'skii, S. E. Sosonyuk, N. V. Zyk, and N. S. Zefirov, *Khim. Geterotsikl. Soedin.*, 1997, 356 [*Chem. Heterocycl. Compd.*, 1997, **33**, 300 (Engl. Transl.)].
- G. D. Hosken, C. C. Allan, J. C. A. Boeyens, and R. D. Hancock, J. Chem. Soc., Dalton Trans., 1995, 3705.
- 11. Z.-Y. Kyi and W. Wilson, J. Chem. Soc., Abstracts, 1951, 1706.
- S. Chiavarelli, H. F. Toeffler, R. Landi-Vittory, and P. Mazzeo, *Ist. Super. Sanita, Rome. Farmaco, Edizione Scientifica*, 1965, 20, 421.
- 13. H. Stetter and K. Dieminger, Chem. Ber., 1959, 92, 2658.
- 14. S. Chiavarelli, G. P. Valsecchi, F. Toffler, and L. Gramiccioni, *Bollettino Chimico Farmaceutico*, 1967, 106, 301.
- A. Gogoll, H. Gernnberg, and A. Axen, *Organometallics*, 1997, 16, 1167.
- D. S. C. Black, G. B. Deacon, and M. Rose, *Tetrahedron*, 1995, **51**, 2055.
- S. Z. Vatsadze, Ph. D. (Chem.) Thesis, Department of Chemistry of the M. V. Lomonosov Moscow State University, Moscow, 1995, 146 pp. (in Russian).
- N. S. Zefirov, N. V. Zyk, S. Z. Vatsadze, and V. S. Tyurin, *Izv. Akad. Nauk, Ser. Khim.*, 1992, 2687 [*Bull. Russ. Acad. Sci., Div. Chem. Sci.*, 1992, **41**, 2131 (Engl. Transl.)].
- N. S. Zefirov, V. A. Palyulin, S. V. Starovoitova, K. A. Potekhin, and Yu. T. Struchkov, *Dokl. Akad. Nauk*, 1996, **347**, 637 [*Dokl. Chem.*, 1996, **347**, 98 (Engl. Transl.)].
- 20. A. N. Chekhlov, Zh. Strukt. Khim., 2000, 41, 140 [Russ. J. Struct. Chem., 2000, 41, 116 (Engl. Transl.)].
- R. D. Gillard, R. Mason, N. C. Payne, and G. B. Robertson, J. Chem. Soc. (A), 1969, 1864.
- 22. H. C. Freeman, M. R.Snow, I. Nitta, and K. Tomita, *Acta Crystallogr.*, 1964, **17**, 1463.
- A. N. Chekhlov, *Zh. Strukt. Khim.*, 2000, **41**, 359 [*Russ. J. Struct. Chem.*, 2000, **41**, 294 (Engl. Transl.)].
- 24. J. F. Malone, M. Miskelly, and M. Parvez, Proc. R. Ir. Acad. Sect. B, 1978, 77, 499.
- 25. M. F. Colombo, L. Austrilino, O. R. Nascimento, E. E. Castellano, and M. Tabak, *Can. J. Chem.*, 1987, 65, 821.
- 26. Z. Travnicek and J. Marek, *Acta Crystallogr., Sect. C (Cr. Str. Commun.)*, 1994, **50**, 1211.
- 27. Soon-Beng Teo, Chew-Hee Ng, and E. R. T. Tiekink, *Inorg. Chim. Acta*, 1989, **163**, 129.
- J.-M. Lehn, Supramolecular Chemistry. Concepts and Perspectives, Weinheim, New York—Basel—Cambridge— Tokyo, 1995.
- 29. G. D. Hosken and R. D. Hancock, J. Chem. Soc., Chem. Commun., 1994, 1363.
- 30. S. Z. Vatsadze, N. V. Zyk, R. D. Rakhimov, K. P. Butin, and N. S. Zefirov, *Izv. Akad. Nauk, Ser. Khim.*, 1995, 456 [*Russ. Chem. Bull.*, 1995, **44**, 440 (Engl. Transl.)].
- Ch. K. Mann and K. K. Barnes, *Electrochemical Reactions in Nonaqueous Systems*, Marcel Dekker, New York, 1970.

- 32. R. Polt, B. D. Kelly, B. D. Dangel, U. B. Tadikonda, R. E. Ross, A. M. Raitsimtring, and A. V. Astashkin, *Inorg. Chem.*, 2003, 42, 566.
- 33. J. Spieler, O. Huttenloch, and H. Waldmann, *Europ. J. Org. Chem.*, 2000, 391.
- 34. G. M. Sheldrick, Acta Crystallogr., 1990, A46, 467.
- 35. G. M. Sheldrick, SHELXL-93. Program for the Refinement of Crystal Structures, University of Göttingen. Germany, 1993.
- 36. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck,

K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle, and J. A. Pople, *GAUSSIAN-98, Revision A.7,* Gaussian, Inc., Pittsburgh (PA), 1998.

- 37. Hyperchem 6.1. Hypercube, Inc., Gainesville, FL (USA), 1999.
- 38. A. J. Gordon and R. A. Ford, *The Chemist's Companion*, Wiley and Sons, New York, 1972, 293 p.

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