Complexation properties of 3,7-diazabicyclo[3.3.1]nonanes
1. Investigation of copper(II) complexes by cyclic voltammetry

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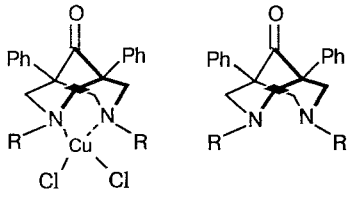
The electrochemical behavior of some 3,7-diazabicyclo[3.3.1]nonanes and their complexes with copper(II) chloride was investigated. The composition and stability of complexes are discussed.

Key words: 3,7-diazabicyclo[3.3.1]nonanes, coordination compounds of copper, cyclic voltammetry, complex stability constants.

The 3,7-diazabicyclo[3.3.1]nonane moiety is the basis of alkaloids of the sparteine series that exhibit physiological activity of various types.[1] These features of 3,7-diazabicyclo[3.3.1]nonanes have been intensely studied since 1951.[2] Many authors relate the anesthetic and antiarrhythmic activity displayed by these compounds to the ability of diazabicyclononanes to form stable complexes with various metals.[3–8] However, very little is known about the quantitative estimation of the stability constants of these complexes.[9] In the present work we start a series of studies of the complexation properties of 3,7-diazabicyclo[3.3.1]nonane derivatives.

We chose cyclic voltammetry (CVA) as the method of investigation. We studied the redox behavior of copper(II) complexes, **1** and **2**, and the cathodic and anodic behavior of anhydrous copper(II) chloride **3** and the corresponding bispidones **4** and **5**. The oxidation and reduction potentials are presented in Table 1.



1: R = Me
2: R = Et

4: R = Me
5: R = Et

Experimental

^{1}H and ^{13}C NMR spectra were recorded on a Varian VXR-400 spectrometer with working frequencies of 400 and 100 MHz, respectively. IR spectra were obtained on a UR-20 spectrophotometer.

Electrochemical measurements were performed on a ZF-2 polarograph with a platinum electrode 3.5 mm in diameter. A silver/silver chloride reference electrode and Bu_4NBF_4 supporting electrolyte were used. All measurements were carried out in acetonitrile preliminarily treated with a nitrating mixture, calcium hydride, and phosphorus pentoxide. The potentials were corrected for the *iR*-compensation. The number of electrons was measured by comparison with the oxidation current of ferrocene at the same concentration.

3,7-Dimethyl-1,5-diphenyl-3,7-diazabicyclo[3.3.1]nonane-9-one (4) was obtained according to the procedure in Ref. 4, yield 41.7%, m.p. 149—151 °C (from ethanol; Ref. 2: m.p. 151 °C). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 7.4—7.2 (m, 10 H, C_6H_5); 3.55 (d, 4 H, J = 11.2 Hz); 3.10 (d, 4 H, J = 11.2 Hz); 2.50 (s, 6 H, CH_3). ^{13}C NMR ($CDCl_3$), δ: 210.92 (C-9); 142.2; 127.8, 126.88, 126.55 (arom.); 67.59 (C-2, C-4, C-6, C-8); 54.03 (C-1, C-5); 45.47 (methyl). IR (vaseline oil), ν/cm^{-1}: 1730 (C=O); 1505 and 1450 (C=C arom.).

3,7-Diethyl-1,5-diphenyl-3,7-diazabicyclo[3.3.1]nonane-9-one (5). Paraform (6.46 g, 0.215 mol) and ethylamine hydrochloride (7.01 g, 0.086 mol) were added to a solution of dibenzylketone (9.05 g, 0.043 mol) in ethanol (60 mL), and the mixture was heated to boiling. A solution of potassium hydroxide (4 g) in ethanol (20 mL) was added, and the mixture was refluxed for 4 h. The solution was filtered, concentrated on a rotary evaporator, and worked-up with 20 % KOH (100 mL). The mixture was extracted with chloroform

Table 1. Oxidation (E^{Ox}) and reduction (E^{Red}) potentials of copper complexes and the corresponding amines (Ag/AgCl/KCl satur., Bu_4NBF_4, Pt, 20 °C)

Compound	E_o^{Ox}/V	$-E_o^{Red}$/V
1	2.12	0.03; 0.54
2	2.07	−0.01; 0.78
4	0.78; 2.09	— *
5	0.97; 2.17	— *

* No reduction occurs.

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(3×20 mL). The organic fractions were combined, washed with water, and dried with sodium sulfate. The solvent was distilled off, and the residue was dissolved with heating in ethanol (50 mL). The solution was kept for 12 h in a refrigerator, and the resulting crystals were filtered off and recrystallized from ethanol to give 4.07 g (27.2 %) of a crystalline product, m.p. 133—135 °C (from ethanol). Found (%): C, 79.56; H, 8.43; N, 7.90. $C_{23}H_{28}N_2O$. Calculated (%): C, 79.28; H, 8.09; N, 8.04. ^{1}H NMR (400 MHz, CD_2Cl_2), δ: 7.38—7.20 (m, 10 H, C_6H_5); 3.52 (d, 4 H, J = 10.8 Hz); 3.09 (d, 4 H, J = 10.8 Hz); 2.63 (q, 4 H, CH_2, J = 7.2 Hz); 1.17 (t, 6 H, CH_3, J = 7.2 Hz). ^{13}C NMR (CD_2Cl_2), δ: 212.22 (C-9); 144.23; 128.20, 127.34, 126.87 (arom.); 65.24 (C-2, C-4, C-6, C-8); 54.70 (C-1, C-5); 51.50; 12.87 (ethyl). IR (vaseline oil), ν/cm^{-1}: 1730 (C=O); 1510 and 1460 (C=C arom.).

The complex of compound 4 with copper(II) chloride (1) was obtained according to the reported procedure[10] in 98 % yield, m.p. 180—182 °C (dec). (from ethanol; Ref. 10: m.p. 180—182 °C). IR (vaseline oil), ν/cm^{-1}: 1750 (C=O), 1510 and 1455 (C=C arom.).

The complex of compound 5 with copper(II) chloride (2). Anhydrous copper(II) chloride (0.39 g, 2.87 mmol) was added to a solution of compound **5** (1.00 g, 2.87 mmol) in chloroform (30 mL). The mixture was refluxed for 3 h until the copper dichloride dissolved completely. The solution was concentrated to half its volume and kept in a refrigerator. The resulting crystals were filtered off, washed with chloroform, and recrystallized from chloroform to give 1.6 g (92 %) of green crystals, m.p. 139 °C (dec.) (from chloroform). Found (%): C, 47.37; H, 4.96; N, 4.55. $C_{23}H_{28}N_2OCuCl_2 \cdot CHCl_3$. Calculated (%): C, 47.85; H, 4.85; N, 4.65. IR (vaseline oil), ν/cm^{-1}: 1750 (C=O); 1510 and 1450 (C=C arom.).

Results and Discussion

Bispidones **4** and **5** undergo irreversible oxidation involving two one-electron steps. Oxidation of copper(II) chloride also occurs irreversibly and involves the transfer of one electron. When the potential is repeatedly scanned from +1.60 V to +0.60 V and *vice versa*, a pair of peaks appear on the CVA curve. These peaks correspond to the $2Cl^- \rightleftharpoons Cl_2$ transitions. One can assume the following scheme of the oxidation of copper(II) chloride:

$$CuCl_2 - \bar{e} \xrightarrow{1.50} CuCl^+ + 1/2Cl_2$$

$$1/2Cl_2 \underset{-e^-\ 0.98}{\overset{+e^-\ 0.81}{\rightleftharpoons}} Cl^-$$

The reduction of the chloride involves two monoelectron steps. One of these is reversible, while the other results in the irreversible loss of zero-valent copper, whose adsorption oxidation peak was detected at −0.24 V:

$$Cu^{II}Cl_2 + e^- \underset{+0.70}{\overset{+0.52}{\rightleftharpoons}} Cu^{I}Cl + Cl^-$$

$$Cu^{I}Cl + e^- \xrightarrow{-0.77} Cu^0 + Cl^-$$

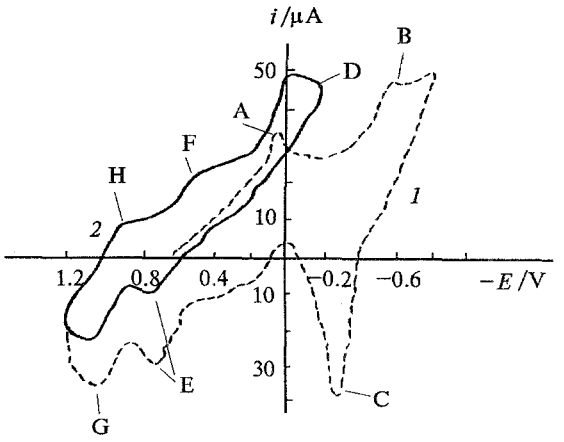

Fig. 1. CVA curves for the reduction of complex **2** ($2 \cdot 10^{-3}$ mol L^{-1}) in MeCN, Bu_4NBF_4, Ag/AgCl/KCl · HCl. *1* (dashed line), during potential scanning from 0.6 to −0.8 V and from −0.8 V to 1.2 V; *2* (solid line), during subsequent scanning from 1.2 V.

The peak at 1.10 V on the anodic scan of the CVA curve corresponds to the oxidation of Cl^-.

The potentials of the electrochemical oxidation and reduction of complexes **1** and **2** suggest that the interaction of the d-orbitals of the copper ion with the lone electron pairs of the nitrogen atom results in a considerable cathodic shift (by *ca.* 500 mV) of the Cu^{II}/Cu^{I} reduction potential and in an even higher shift of the oxidation potential of the nitrogen electron pair (by *ca.* 1 V).

An analysis of the literature data shows that complexation of the divalent copper ion with bidentate nitrogen-containing ligands results in a considerable cathodic shift of the potential of the Cu^{II}/Cu^{I} transition, which ranges from +0.20 V to −0.20 V.[11—14] The potential of the Cu^{I}/Cu^{0} transition should be between −1.60 and −1.70 V (SCE).[15]

The reduction of complexes **1** and **2** involves two one-electron steps (peaks A and B, Fig. 1, curve *1*). The transfer of the second electron leads to the liberation of metallic copper on the surface of the platinum electrode (peak C corresponds to the oxidation of copper, Fig. 1). If we then reverse the direction of the potential sweep at point D, two pairs of peaks are observed corresponding to $Cu^{I}Cl \rightleftharpoons Cu^{II}Cl^+$ (peaks E and F) and $2Cl^- \rightleftharpoons Cl_2$ transitions (peaks G and H).

The potentials of peaks B and C are close to those recorded for copper(II) chloride. Probably, the chloride of monovalent copper, unlike $CuCl_2$, does not form stable complexes with the ligand, which results in the liberation of the corresponding amines (compounds **4** and **5**) and in the generation of free copper(I) chloride in the near-electrode layer.

The oxidation of complexes **1** and **2** is also accompanied by their destruction, specifically, the oxidized ligand eliminates $CuCl_2$. Because the oxidation potentials of the complexes (peak A, Fig. 2) are more anodic than

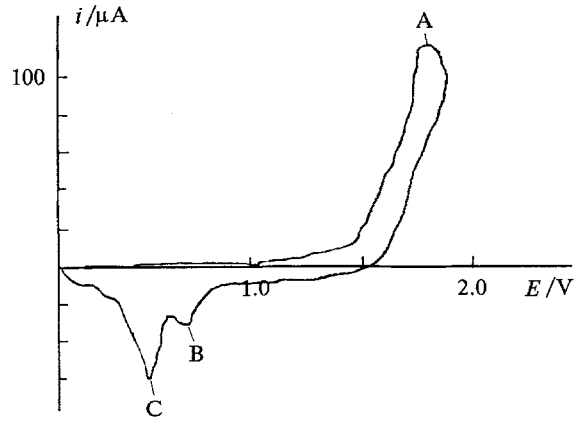

Fig. 2. Curve of the oxidation of complex **1** ($2 \cdot 10^{-3}$ mol L^{-1}).

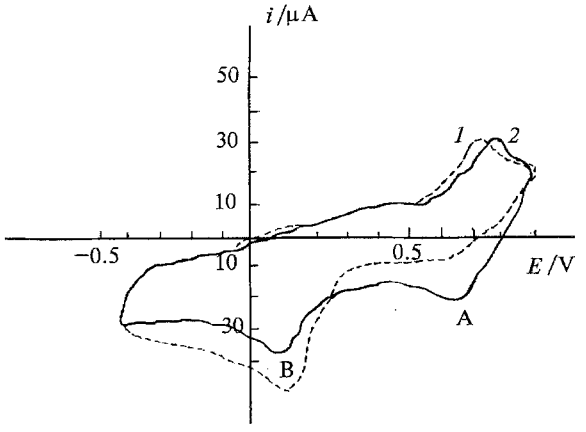

Fig. 3. Curves of the reduction of $CuCl_2$ ($2 \cdot 10^{-3}$ mol L^{-1}) in the presence of bispidone **5**: *1*, $8 \cdot 10^{-4}$; *2*, $1 \cdot 10^{-3}$ mol L^{-1}.

that of copper(II) chloride, the latter is instantly oxidized into $CuCl^+$ and Cl_2, which undergo reduction during the reverse scanning (peaks B and C, Fig. 2).

Subsequently, we studied the concentration dependence by adding increasing amounts of bispidone **5** to a cell containing $2 \cdot 10^{-3}$ mol L^{-1} of $CuCl_2$. Starting from an amine concentration of $1 \cdot 10^{-4}$ mol L^{-1}, the height of peak A corresponding to the reduction of copper(II) chloride decreases, while peak B, corresponding to the reduction of the ion bound in the complex, increases (Fig. 3). When the $CuCl_2$: bispidone ratio reaches 1 : 1, the peak at +0.52 V disappears completely. It can thus be assumed that copper(II) chloride forms a 1 : 1 complex with compound **5** in solution (see the elemental analysis data for complex **2**). Judging by the similar behavior of both complexes studied, we can also assume that they have the same type of coordination and similar structures (complex **1** has previously been studied by X-ray diffraction).[16]

The complexation constants calculated by the standard equation amount to $1.8 \cdot 10^{18}$ (**1**) and $3.5 \cdot 10^{16}$ (**2**), they are significantly higher than the corresponding value for ethylenediamine, and they are comparable to the previously reported values for analogous systems.[9]

Thus, it can be stated that ligands of the 3,7-diazabicyclo[3.3.1]nonane series are promising complexation reagents for divalent copper compounds, and this feature of these compounds should be studied more thoroughly.

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