Determination of stability constants of intermediates by coordination capillary GLC. Chiral complexes of Ni^{II} and Cu^{II} with Schiff's bases (1*R*,2*R*)-*N*,*N*′-bis(3′-*tert*-butylsalycilidene)diaminocyclohexane and (1*R*,2*R*)-*N*,*N*′-bis[(4-hydroxy[2.2]paracyclophanyl)-5-methylene]diaminocyclohexane as GLC phases

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Chiral Ni^{II} and Cu^{II} salen complexes dissolved in the polymethylphenylsiloxane phase OV-17 were used as the phases for capillary chromatography. Chiral salen ligands are Schiff's bases obtained from salicylaldehyde (SA) and (1*R*,2*R*)-diaminocyclohexane and Schiff's bases obtained by condensation of (1*R*,2*R*)- or (1*S*,2*S*)-diaminocyclohexane with (*R*)-4-hydroxy-5-formyl[2.2]paracyclophane (HFPC). The stability constants of the intermediates were calculated from the retention times. The complexes based on HFPC are stronger Lewis acids than those based on SA. The ability of the substrates to form intermediates decreases in the sequence: aromatic aldehydes > halogen-substituted aromatic compounds > halogen-substituted aliphatic compounds.

Key words: capillary chromatography, chiral salen complexes, paracyclophane; stability constants of intermediates.

Interest in studies in the field of asymmetric organic synthesis has been observed in recent years, being caused to a considerable extent by the success of asymmetric organometallic catalysis.[1–3] When a catalytically active complex contains a chiral ligand, conditions for asymmetric catalysis appear. The interactions manifested in these processes are of the same nature as those in recognition of enantiomer-ligands by chiral transition metal complexes.[4,5] A simple and efficient method for the estimation of the ability of chiral complexes to coordinate with the Lewis bases and recognize the enantiomers of these bases is required for the creation of novel asymmetric metal-containing catalysts for asymmetric synthesis.

Among chiral metal-containing catalysts, complexes with Schiff's bases based on substituted salicylaldehyde and chiral amines play an important role. For example, the Mn^{III} complex with (1*R*,2*R*)-*N*,*N*′-bis(3′-*tert*-butylsalicylidene)diaminocyclohexane efficiently catalyzes epoxidation of nonactivated C=C bonds[6] and asymmetric opening of the epoxide cycle of racemic oxiranes.[7] The Ti^{IV} complex with the same ligand catalyzes trimethylsilyl-cyanation of aldehydes,[8] and the Ti^{IV} complexes with Schiff's bases obtained from salicylaldehyde and dipeptides are efficient catalysts for asymmetric addition of HCN to aldehydes.[9]

This work studied the possibility of using chiral Cu^{II} and Ni^{II} salen complexes, which are thermally stable up to 200 °C, as stationary phases (SP) for GLC, and used GLC to study the ability of these complexes to interact additionally with the Lewis bases.

Experimental

Gas-chromatographic analysis was carried out on a 3700-00 chromatograph (Khromatograf plant, Moscow) with two flame-ionization detectors and a system of simultaneous injection of a sample into two capillary columns; helium was used as the carrier gas, with pressure of 0.1 MPa for compounds **1** and **2** (reference columns 012) and 0.11 MPa for compounds **3** and **4** (reference columns 034). The temperature of the columns was 100 °C, and the temperature of the evaporator and detectors was 230 °C. The organic compounds, which were studied along with an inert standard *n*-octane (2 : 1 vol/vol, volume of a sample 0.1 μL), were simultaneously injected into a reference column and a column containing a metal complex. Pre-deactivated Pyrex capillary columns 40 m×0.23 mm (for 012, **1**, **2**) and 40 m×0.21 mm (for 034, **3**, **4**) were used. The columns were covered by a film of the stationary phase (SP) by the method of "high-pressure statics."[10] The film thickness was 0.12 mm. The content of a metal complex in SP for **1** and **2** was 0.1269 mg; for **3**, 0.0729 mg; and for **4**, 0.0738 mg (weighed samples were prepared by the method of successive dilutions). Columns were conditioned at 130 °C for 8 h. The

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Table 1. Corrected retention times of compounds

Compound	$t'_1/t'_2/t'_{012}$	$t'_3/t'_4/t'_{034}$
	s	
1-Chloropentane	32.5/32.5/30.8	39.2/40.0/39.2
1-Bromopentane	62.5/61.7/56.7	75.9/75.9/74.2
1-Iodopentane	129.2/128.3/115.0	151.7/155.9/151.7
Methyl propionate	13.7/13.7/13.7	19.2/19.2/19.2
Methyl chloroacetate	52.5/51.7/47.5	63.4/64.2/62.5
Methyl bromoacetate	93.7/90.8/80.8	111.7/113.4/109.2
Methyl α-bromopropionate	107.5/105.8/95.8	125.9/128.4/125.9
Benzene	21.7/21.7/21.7	28.4/28.4/28.4
Chlorobenzene	86.7/84.2/76.7	103.4/105.9/101.7
Bromobenzene	171.7/170.0/151.7	203.4/208.4/201.7
Iodobenzene	400.8/396.7/351.7	460.9/477.5/459.2
Benzaldehyde	268.3/261.7/225.0	314.2/325.9/309.0
o-Fluorobenzaldehyde	210.0/205.0/182.5	250.0/257.5/246.7
m-Fluorobenzaldehyde	220.0/215.0/190.8	259.2/268.4/255.9
p-Fluorobenzaldehyde	245.8/241.7/211.7	294.2/302.5/289.2
p-Trifluoromethylbenzaldehyde	190.0/188.3/164.2	226.7/233.4/223.4
Anisole	154.2/152.5/136.7	182.5/185.9/180.0
o-Methoxybenzaldehyde	1989.2/1965.0/1765.8	2237.5/2369.5/2192.5
m-Methoxybenzaldehyde	1442.5/1413.3/1230.8	1728.4/1801.7/1705.0
p-Methoxybenzaldehyde	2317.5/2285.8/2027.5	2650.0/2775.9/2592.5
Styrene oxide	499.2/492.5/422.5	579.2/602.5/573.4

Note. t'_1, t'_2, t'_3, t'_4, t'_{012}, and t'_{034} are corrected retention times of compounds on columns containing the metal complex and on reference columns, respectively. Retention times (τ/s) of methane (t_m) and octane (t_o) for **1** and **2** and reference columns: t_m = 207.5, t_o = 235.5; for **3** and **4** and their references columns: t_m = 203.3, t_o = 237.5. The average values of 3—6 injections of samples are presented. In all cases, a deviation is not greater than 0.5% of the indicated value.

efficiency of columns with respect to *n*-octane (t.p. m^{-1}) was the following: for **1**, 6480; **2**, 7750; 012, 6170; **3**, 6120; **4**, 6390; and 034, 6730.

Chromatographic data were processed by a CP-403 computer program, which determines retention times of components of a chromatographed mixture with an accuracy of 0.01 s. The values of the corrected retention times of the organic compounds are presented in Table 1.

Synthesis of Schiff's base from 4-hydroxy-formyl[2.2]paracyclophane and 1,2-diaminocyclohexane. A solution of MeONa (0.56 mmol) in MeOH (1 mL) was added to a solution of (*R*)-4-hydroxy-5-formyl[2.2]paracyclophane (0.070 g, 0.28 mmol) and (*S,S*)-1,2-diaminocyclohexane dihydrochloride (0.026 g, 0.14 mmol) in MeOH (4 mL). The reaction mixture was refluxed for 1.5 h and left to stand overnight. The solvent was distilled off *in vacuo*, and the residue was dissolved in CH_2Cl_2, washed with water, and dried with $CaCl_2$. Yield 0.076 g (93.2%).

Schiff's base (0.077 g, 94.5%) was obtained similarly from (*S*)-4-hydroxy-5-formyl[2.2]paracyclophane (0.070 g, 0.28 mmol) and (*R,R*)-1,2-diaminocyclohexane dihydrochloride (0.026 g, 0.14 mmol).

Synthesis of Cu^{II} complexes with Schiff's bases obtained from 4-hydroxy-5-formyl[2.2]paracyclophane and 1,2-diaminocyclohexane. $Cu(ClO_4)_2 \cdot 6H_2O$ (0.032 g, 0.086 mmol) and MeONa (0.172 mmol) were added to a solution of Schiff's (*R*),(*S,S*)- or (*R*),(*R,R*)-base (0.05 g, 0.086 mmol) in a mixture of MeOH (1 mL) and toluene (1 mL). The reaction mass was stirred at room temperature for 2 h, then was diluted with CH_2Cl_2, washed with a 5% solution of MeCOOH and water, and dried with Na_2SO_4.

The complexes were purified on a column packed with the sorbent Sephadex LH-20: (*R*),(*S,S*)-complex, benzene—methanol (3 : 1) and (*R*),(*R,R*)-complex, toluene—dichloromethane (10 : 1). The complexes were recrystallized from toluene. Yield 0.32 g (50%).

(*R*),(*S,S*)-Diastereoisomer (**1**), $[\alpha]^D_{25}$ +1725. Found (%): C, 74.82; H, 6.36; N, 4.16. $C_{40}H_{40}CuN_2O_2$. Calculated (%): C, 74.56; H, 6.26; N, 4.35.

(*R*),(*R,R*)-Diastereoisomer (**2**), $[\alpha]^D_{25}$ +1500. Found (%): C, 74.42; H, 6.35; N, 4.22. $C_{40}H_{40}CuN_2O_2$. Calculated (%): C, 74.56; H, 6.26; N, 4.35.

Synthesis of Cu^{II} and Ni^{II} complexes with Schiff's base obtained from (1*R*,2*R*)-diaminocyclohexane and 3-*tert*-butylsalicylaldehyde. A 4.3 *N* solution of MeONa (1.1 mL, 4.6 mmol) in MeOH was added to a solution of Schiff's base (1 g, 2.3 mmol) and $Cu(NO_3)_2 \cdot 3H_2O$ (0.56 g, 2.3 mmol) in MeOH (20 mL). The solvent was distilled off *in vacuo*, and the residue was dissolved in benzene and washed with water. After the solvent was removed, the complex was recrystallized from a benzene—methanol mixture. $[\alpha]^D_{25}$ −400.0. Found (%): C, 67.48; H, 7.25; Cu, 12.91; N, 5.54. $C_{28}H_{30}CuN_2O_2 \cdot 0.5H_2O$. Calculated (%): C, 67.33; H, 6.21; Cu, 12.83; N, 5.61.

The Ni^{II} complex (**3**) was obtained and purified similarly, $[\alpha]^D_{25}$ −740.9. Found (%): C, 68.37; H, 7.53; N, 5.63; Ni, 9.50. $C_{28}H_{30}N_2NiO_2 \cdot 0.5H_2O$. Calculated (%): C, 68.01; H, 6.27; N, 5.66; Ni, 11.94.

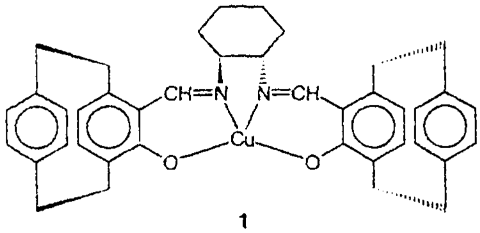
X-ray analysis of complex 2. The single crystals were obtained by crystallization from toluene. $C_{40}H_{40}CuN_2O_2$, M = 644.3, rhombic single crystals, space group $C222_1$, Z = 4, at

152 K: a = 10.203(4) Å, b = 12.452(7) Å, c = 24.864(13) Å, V = 3159(3) Å^3, d_{calc} = 1.355 g cm^{-3}. Cell parameters and intensities of 2212 independent reflections were measured on a Siemens P3/PC diffractometer (λ(Mo-Kα), graphite monochromator, $\theta/2\theta$-scan, $\theta \leq 30.0°$). The structure was solved by the direct method and refined in the anisotropic approximation for nonhydrogen atoms by the least-squares method. Hydrogen atoms were localized directly and included in the isotropic approximation. The resulting values of divergence factors: R = 0.0388 and wR = 0.0414 for 1724 observed reflections with $I > 2\sigma(I)$. All calculations were performed on an IBM PC/AT by the SHELXTL PLUS program (PC Version).[11]

Results and Discussion

Cu^{II} and Ni^{II} complexes **1—4** were chosen as the models for the study.

(*R*)-4-Formyl-5-hydroxy[2.2]paracyclophane was synthesized and separated by a known procedure.[12] Schiff's bases based on this aldehyde and (1*S*,2*S*)- and (1*R*,2*R*)-diaminocyclohexane, as well as Schiff's bases from 3-*tert*-butylsalicylaldehyde and (1*R*,2*R*)-diaminocyclohexane,[8] were obtained similarly to the previously published procedures. The complexes were synthesized from the corresponding Schiff's bases and Ni^{II} and Cu^{II} salts (see Experimental). Red crystalline products were obtained. The Cu^{II} compounds are paramagnetic, and the Ni^{II} compounds are diamagnetic, which is typical of planar-square Ni^{II} complexes with "strong" ligands. As should be expected for compounds with a similar structure,[13,14] the ligand occupies four sites in the main coordination plane of the complex, which is confirmed by the X-ray diffraction data for crystals **2** (Fig. 1, Table 2). The rest sites in the coordination plane of this crystalline complex are free. It can be expected that in solution, the Cu^{II} ion will retain its ability for weak interaction with the Lewis bases, and solutions of **1**, **2**, and **4** will serve as efficient SP for GLC. The Ni^{II} ion in diamagnetic complex **3** should possess a considerably lower withdrawing ability.[13] Nevertheless, during the chromatographic study, we hoped to observe weak donor-acceptor type interactions in the case of compound **3** as well.



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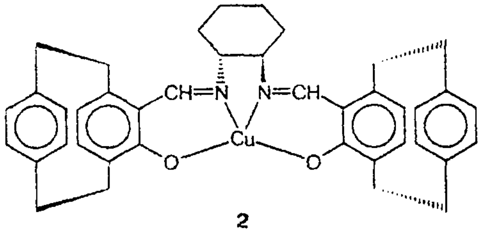

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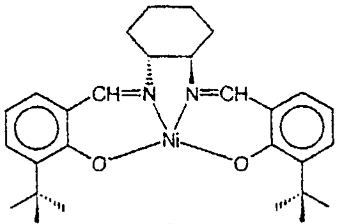

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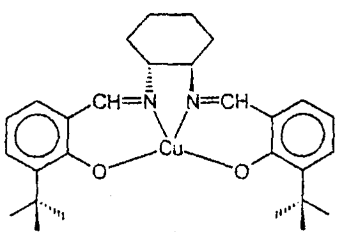

4

In practice, Ni^{II}, Co^{II}, and Mn^{II} bisterpenoketonates or lanthanide β-diketonates dissolved in nonpolar or low-polar stationary phases of the squalane, OV-101, or OV-1701 types are mainly used for studying molecular association processes by complex GLC.[15—19] As our experiments showed, the Cu^{II} and Ni^{II} complexes are almost insoluble in the nonpolar SP of the OV-101 or SE-30 type. Therefore, we used the comparatively low-polar SP OV-17 for the capillary columns.

The process of molecular association is determined by the stability constant (K_m) of an intermediate[15] formed due to the interaction of a substrate passing through a gas-chromatographic column with a metal complex dissolved in SP. The comparison of K_m values makes it possible to compare the ability of complex formation of both metal compounds and substrates and to draw conclusions on the influence of the nature of a metal and of steric and polar effects of ligands and substrates on the coordination and chiral recognition. The K_m value was calculated from the equation:[15]

$$K_m \cdot m = r/r_0 - 1 = R',$$

where m is the molal concentration of the complex in SP; $r = t'_s/t'_0$ is the ratio of corrected retention times of the substrate and inert standard (n-octane) on the column containing the metal complex; $r_0 = t'_{s0}/t'_{00}$ is the ratio of corrected retention times of the substrate and inert standard (n-octane) on a column containing no metal complex; and R' is the increase in the retention time of the substrate due to the formation of a complex.

As can be seen from the data in Table 3, complexes **1—4** retain their ability to coordinate with the Lewis bases. Even complex **3** turned out to be capable of coordination, although to a considerably lower extent than the Cu^{II} compounds. The difference in the com-

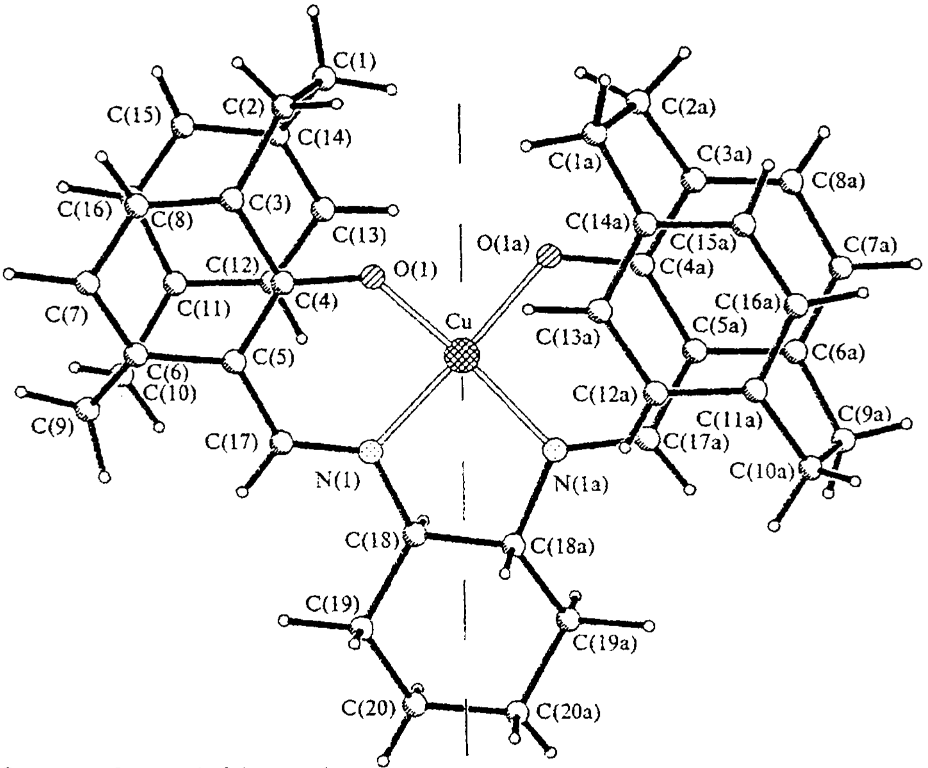

Fig. 1. Structure of molecule **2** in crystal.

Table 2. Main bond lengths (*d*) and bond angles (ω) in molecule **2**

Bond	*d*/Å	Angle	ω/deg
Cu—O(1)=Cu—O(1a)	1.866(3)	O(1)—Cu—N(1)=	
Cu—N(1)=Cu—N(1a)	1.925(3)	=O(1a)—Cu—N(1a)	93.5(1)
N(1)—C(17)=N(1a)—C(17a)	1.292(5)	N(1)—Cu—O(1a)=	
O(1)—C(4)=O(1a)—C(4a)	1.306(4)	=O(1)—Cu—N(1a)	164.8(1)
C(4)—C(5)=C(4a)—C(5a)	1.428(6)	N(1)—Cu—N(1a)	86.0(2)
		O(1)—Cu—O(1a)	90.9(2)

plex formation ability of diastereomeric compounds **1** and **2** (see Table 3) indicate that the Cu^{II} ion is more accessible in the case of **1**. It was unexpected that the shielding of the Cu^{II} ion in complex **4** was stronger than that in compounds **1** and **2**. All bases studied form more stable complexes with **1** and **2** than with **4**.

For alkyl halides and halogen-substituted benzenes, the ability to form complexes with Cu^{II} increases in the series RCl < RBr < RI. This tendency is also retained on going from methyl chloroacetate to methyl bromoacetate. Thus, the order of the relative efficiency of complex formation of covalently linked halogen atoms is the same as that for halide ions in the formation of complexes with Cu^{II} and some other transition metal ions.[20,21] An increase in the size of a substituent in a alkyl halide molecule decreases its complex formation ability. For example, methyl bromoacetate has a considerably higher complex formation constant than methyl α-bromopropionate. The carbonyl group of aromatic aldehydes is the better Lewis base with respect to Cu^{II} than the CO group of esters. The introduction of electronegative F atoms and the CF_3 group into the aromatic ring of benzaldehyde decreases its complex formation ability toward Cu^{II}. This can be explained by a decrease in the negative charge on the O atom of the aldehyde group when electronegative substituents are introduced into the ring. The introduction of the MeO group into the aromatic ring increases the complex formation constant on going from benzene to anisole, and in the case of substituted benzaldehydes, it somewhat decreases their complex formation ability. The electronegativity of the MeO group and a decrease in the charge on the carbonyl C atom of substituted benzaldehydes also is a probable reason for these facts. Styrene oxide, in whose molecule the O atom is shielded to a lower extent than in anisole and is bound to the aliphatic C atoms, has greater K_m values with the Cu^{II} complexes than the latter.

Table 3. Stability constants (K_m) of intermediates based on complexes **1—4** (T_{col} = 100 °C, $m = 5 \cdot 10^{-2}$ mol kg^{-1})

Compound	K_m/kg mol^{-1}			
	1	**2**	**3**	**4**
1-Chloropentane	1.10	1.10	0	0.51
1-Bromopentane	2.05	1.76	0.46	0.46
1-Iodopentane	2.47	2.31	0	0.55
Methyl propionate	0	0	0	0
Methyl chloroacetate	2.11	1.77	0.29	0.54
Methyl bromoacetate	3.19	2.48	0.46	0.77
Methyl α-bromopropionate	2.44	2.09	0	0.40
Benzene	0	0	0	0
Chlorobenzene	2.61	1.96	0.33	0.83
Bromobenzene	2.64	2.41	0.17	0.66
Iodobenzene	2.79	2.56	0.07	0.80
Benzaldehyde	3.85	3.26	0.34	1.09
o-Fluorobenzaldehyde	3.01	2.47	0.27	0.88
m-Fluorobenzaldehyde	3.06	2.54	0.28	0.98
p-Fluorobenzaldehyde	3.22	2.83	0.35	0.92
p-Trifluoromethylbenzaldehyde	3.14	2.94	0.30	0.90
Anisole	2.56	2.31	0.28	0.66
o-Methoxybenzaldehyde	2.53	2.26	0.41	1.61
m-Methoxybenzaldehyde	3.44	2.97	0.27	1.13
p-Methoxybenzaldehyde	2.86	2.55	0.44	1.41
Styrene oxide	3.63	3.31	0.20	1.01

The reason for the lower ability of compound **4** for complex formation than that of compounds **1** and **2** is the possibility of a partial dimerization of less hindered **4** and a decrease in the amount of the reactive complex.

The complex formation ability of Ni$^{\mathrm{II}}$ in compound **3** in many aspects repeats the tendencies observed for the systems involving **1** and **2**; however, there are substantial differences. For Cu$^{\mathrm{II}}$, the stability of complexes with alkyl halides increases on going from RBr to RI, while for the Ni$^{\mathrm{II}}$ complexes the opposite phenomenon is observed. The sensitivity of the complex formation constant of aldehydes to the introduction of fluorine-containing substituents is negligible in the case of the Ni$^{\mathrm{II}}$ complexes. Perhaps weak interaction forces in the F—Ni$^{\mathrm{II}}$ system stabilize these complexes.

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