Molecular Complexes of Hydrazides with Copper(II)

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Summary. The reaction of substituted hydrazides with copper(II) chloride was investigated in the solid state or in solution in order to account for substituent effects. Spectroscopic results and values of the formation constants indicate the occurrence of strong complexes.

Keywords. Molecular complexes; Formation constant; Copper(II) choride.

Molekulare Komplexe von Hydraziden mit Kupfer(II)

Zusammenfassung. Die Reaktionen von substituierten Hydraziden mit Kupfer(II)chlorid wurden im Festzustand und in Lösung untersucht. Die spektroskopischen Ergebnisse und die Werte der Bildungskonstanten zeigen die Koordinierung zu starken Komplexen an.

Introduction

The inhibition of the enzymatic activity of transition metals by means of aroylhydrazines and other hydrazine derivatives has been studied and mainly attributed to the formation of stable chelates [1, 2]. The reaction of sodium borohydride with metal salts of aroylhydrazines induces the transformation of the hydrazide to carbonyl groups under mild conditions [3]. For this purpose, complexes of hydrazides with copper(II) chloride appear to be particularly suitable [4, 5]. In an earlier work, structural features of some solid aroylhydrazines/Cu(II) systems have been discussed on the basis of vibrational evaluations; in particular, the shift of the amide I vCO band has been related to the behaviour of the carbonyl group as chelating site [6].

In this work the influence of the substituent and the effect of the interposition of an alkyl chain between the aromatic and the hydrazide groups on the spectral and thermodynamic properties of aroylhydrazines/copper(II) chloride complexes are investigated in solution and in the solid state.

Results and Discussion

The reaction of aroylhydrazines 1 — 7 (Table 1) with copper(II) chloride in *THF* at room temperature afforded the salts 1* — 7* as powders; the colour of the complexes,

Table 1. Charge-transfer maxima (λ_{max}, nm) and formation constants (K_f, $l\,mol^{-1}$) of complexes 1*–7* in H_2O at 20°C

	1*	2*	3*	4*	5*	6*	7*
λ_{max}	670	700	720	672	768	740	728
K_f	54	64		66		146	

in solution and in the solid state, ranged from light blue to deep green, going from weak to more basic ligands in accordance with the Sone and Fokuda scale [7]. For the determination of spectroscopic and thermodynamic properties water was chosen as a solvent for two reasons: the good solubility and the fact that this is the medium in the human cells. Table 1 reports the λ_{max} and the formation constants of the complexes 1*–7*, while Table 2 lists data for the determination of the equilibrium constant in the complex 1*. The solubility of the reactants and the low extinction coefficients of the complexes limited the determination of the equilibrium constants (K_f) to the systems 1*, 2*, 4*, and 6*. With respect to the complex 1*, the following conclusions can be drawn: (i) the presence of methylene bridges (complexes 2*, 3*) or of a p-methoxy group (4*) causes λ_{max} to shift to lower frequencies; (ii) pyridine or pyrrole rings decrease the energy of the transition, too; (iii) the absorption at higher frequencies of the system 5* may be due to the fact that the nitro group is involved in some hydrogen bonding (with an additional decrease of the donor character of the hydrazide moiety). From points (i) − (iii) it is evident that the charge-transfer transition depends from substituent effects. Although the number of data is limited, the values of the formation constants are in satisfactory agreement with points (i), (ii) and with the reactivity of these complexes [5].

Table 2. Data for the determination of K_f for the complex 1* in H_2O at 20°C; $\lambda_{max} = 670\,nm$

| $[A]_0 \cdot 10^2$	d	$[D]_0 \cdot 10^2$	$1/[D]_0$	$([A]_0/d) \cdot 10^3$
0.5257	0.129	0.7345	136.15	40.75
0.5013	0.157	0.8569	116.70	31.93
0.5760	0.169	0.9793	102.11	34.08
0.5581	0.782	1.102	90.77	30.67
0.5403	0.797	1.224	81.69	27.42
0.5257	0.210	1.469	68.07	25.03
0.6473	0.270	1.747	58.35	23.98
0.5549	0.266	1.959	51.06	20.86
0.3196	0.174	2.448	40.85	18.37
0.5354	0.288	2.938	34.04	18.59
0.5435	0.296	3.427	29.17	18.36
0.7009	0.394	3.917	25.53	17.79
0.4770	0.278	4.896	22.69	17.16
0.3115	0.193	4.896	20.42	16.14
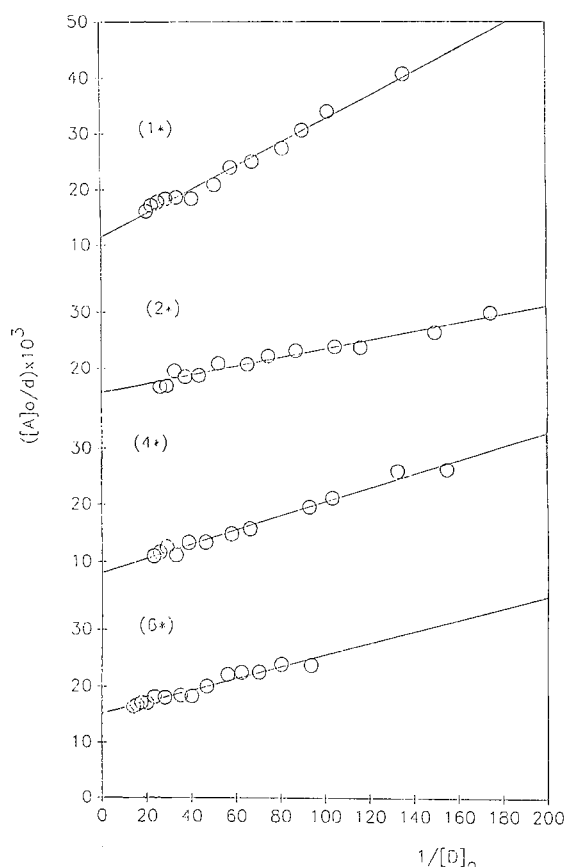
Fig. 1. Benesi-Hildebrand plots used in the calculation of the formation constants for complexes 1*, 2*, 4*, and 6* at 20°C

The stoichiometry of the complexes ligand/Cu(II), 1/1 was determined: a) in solution, from plots of the Benesi-Hildebrand equation (Fig. 1) [8] and from the Job method [9, 10]; b) in the solid state, from elemental analysis.

Results from diffuse reflectance infrared spectra of compounds 1 − 7 and 1* − 7* are reported in Table 3. In complexes 1* − 7*, both NH_2 and NH stretching vibrations are red shifted with respect to the parent bases; a similar behaviour is shown by the amide I band (vC = O) with higher shifts in presence of an electron releasing group (donor 4) or methylene bridges (donors 2, 3); the smallest shift is found for nitroaroylhydrazine, 5. A qualitative sequence of the results for the amide I bands is the following:

Ligand 6 > 1 > 7 > 3 > 4 > 2 > 5
Chelate 6* > 1* > 7* > 5* > 4* ≳ 3* > 2*

In the complexes the discrete s-donor character but the poor π-acceptor ability of the ligand causes a decrease of the effective nuclear charge of the metal atom and, consequently, an increase in energy and size in its d-orbitals. This fact, enhancing the π-character of the Cu-C bond, decreases the CO bond stretching force constant and, consequently, its stretching frequency [11].

A similar behaviour is found in the case of NH_2 and the amide II band bending modes but the results are less correlable. The non correspondence between the vCO values in the nitro systems 5 and 5* may be due to the formation of hydrogen bonds by the nitro group, so weakening the chelate.

Table 3. IR absorptions (cm^{-1}) of aroylhydrazines (Ar-CO-NH-NH$_2$), 1 − 7, and their CuCl$_2$ complexes 1* − 7*

Ar		vNH$_2$	vNH	vCO Amide I	δNH$_2$	δNH Amide II
Phenyl	1	3296 s	3220 b, 3204 s 3195 b, 3154	1660	1614	1564
	1*	3362 s	3223 sh 3151, 3117 3096	1625	1584	1550
Benzyl	2	3288 s	3196, 3175 3084 w	1641		1527
	2*		3162 b	1583		1516
2-Phenylethyl	3	3280 s	3194 sh, 3170 3082 w, 3059	1653 sh	1628	1526
	3*		3148 3082, 3026	1601	1582	1515 w
p-Methoxyphenyl	4	3311 s	3175 b 3080 w	1650	1621	1559
′	4*		3162 3047 w, 3025	1602		1558 sh
p-Nitrophenyl	5	3344 s 3301 s	3270 w, 3227 s 3129 sh 3084 w, 3055 w, 3029 w	1628	1617	1560 − 40
	5*	3342 ws 3301 s	3213 s 3117	1606		
4-Pyridyl	6	3299 s	3207 b 3170 b, 3106 s 3047	1666	1632	1557
	6*	3393 b	3174 w 3098 s, 3074 w	1638	1612	1553
3-Pyrrolyl	7	3340 s 3297 sh	3233 3139, 3103, 3027	1656	1634	1531
	7*	3337 3293	3162 3141	1619 w	1582	

From the IR data we can assert the following: (i) in the association, the ligand involves either the NH$_2$ or the CO bonds, the latter interacting in its keto form; (ii) the presence of methylene groups between phenyl and hydrazide groups makes the complex stronger and, consequently, the reduction of the hydrazide into the corresponding aldehyde proceeds with lower yields [5].

All the spectroscopic results confirm that the hydrazide group, as a whole, is the donor centre. In order to achieve further conformational details, e.s.r. spectra of complexes 1* − 7* were recorded. All the complexes − dissolved in water − showed a stable signal. Figure 2 shows the spectrum of the complex benzoylhy-drazine/Cu(II) chloride, 1*, characterized by four lines with a 47.5 G spacing and
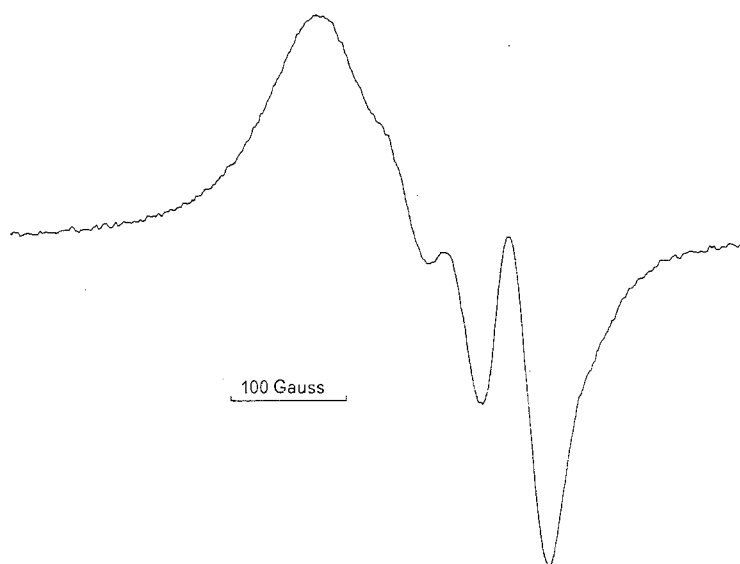
Fig. 2. E.s.r. spectrum of the complex benzoylhydrazine, 1/Cu(II)Cl$_2$ in water at 20°C

$g = 2.1709$ (*DPPH* as a standard). These e.s.r. data are consistent with the presence of Cu(II) ions in a square-pyramidal conformation [12, 13].

Experimental

Aroylhydrazines 1 − 7 were prepared according to Vogel [14]. Anhydrous copper(II) chloride was obtained by boiling the dihydrate salt with thionyl chloride in benzene. All solvents were Fluka RP-ACS grade reagents and were purified and dried before use [14].

Solid state infrared spectra were obtained using a Nicolet Fourier Transform Infrared 20-SX spectrometer equipped with a Spectra Tech. Multiple Internal Reflectance "Collector": resolution 1 cm^{-1}, 256 scans. UV-VIS spectra in solution were carried out on a Perkin Elmer 554 spectrophotometer equipped with a MgW-K2R thermostatting system for circulating water. E.s.r. spectra were recorded on a Varian E-4 ESR spectrometer using a deaerated two-leg inverted cell described previously [15].

Synthesis of Complexes 1 − 7*

Aroylhydrazides/Cu(II) chloride salts were prepared according the Ref. 4; the crude product was stirred in *THF* to eliminate the starting hydrazide.

E.s.r. Determinations of Complexes 1 − 7*

Few milligrams of the complex were dissolved in water and the solution was carefully deoxygenated before recording the spectrum.

UV-VIS Spectrophotometric Measurements of Complexes of 1, 2, 4, *and* 6 *with Copper(II) Chloride in Water. K$_f$ Determinations*

The formation constants (K$_f$ of donors 1, 2, 4, and 6 with copper(II) chloride were measured spectrophotometrically in water. According to the Benesi-Hildebrand method [8], the concentration dependence of the absorbance of the charge-transfer band (*d*) is given by the equation:

$$[A]_0/d = 1/K_f\varepsilon[D]_0 + 1/\varepsilon$$

under conditions in which the total concentration of the electron donor $[D]_0$ is in excess relative to the total concentration of the acceptor $[A]_0$ and for a 1 cm light path. K_f is the formation constant and ε is the extinction coefficient of the complex at the monitoring wavelength. Plots of $[A]_0/d$ against $1/[D]_0$ for solution in which $[D]_0 \gg [A]_0$ should be linear.

As general procedure, measurements of the complex 1* are reported in Table 2.

A stock solution of 1 (0.0735 M) was prepared. Due to the instability in water, the acceptor was weighed out directly in fourteen 3 ml flasks (approximately, $3 \cdot 10^{-3}$ g/3 ml). To each flask, a certain volume of donor solution was added, ranging from 0.3 to 2.0 ml, and for these solutions the absorbances (d), at the λ_{max} of the complex, were measured at 20°C. Linear correlations were obtained by plotting $[A]_0/d$ against $1/[D]_0$ (Fig. 1); the correlation coefficient was greater than 0.998.

For the remaining complexes the range of concentrations of donor and acceptor solutions was approximately the same.

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