169. Complex Formation of Copper(II) and Nickel(II) with Pyrrole Ligands in Aqueous Solution

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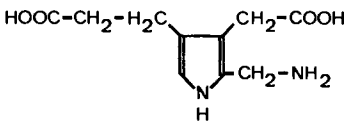
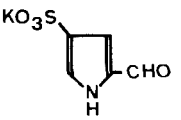
Summary. Four new ligands, namely the N-substituted 2-(4-sulfonyl)-pyrrylmethyl derivatives of methylamine, glycine, ethylenediamine and iminodiacetic acid, were synthesized to investigate the coordinating tendency of pyrrolic nitrogen in aqueous solution. The complex formation of these ligands with Cu^{++} and Ni^{++} was studied by means of alkalimetric titrations. It is shown that the coordinating tendency of the deprotonated pyrrole group is similar to that of a deprotonated amide group. The deprotonated pyrrole group stabilizes the Cu^{++} complexes of its iminodiacetate and ethylenediamine derivatives to an extent similar to that of a 2-pyridylmethyl or 2'-aminoethyl group, despite the different basicity of these substituents. On the other hand, the neutral pyrrole group shows no coordinating tendency.

1. Introduction. – Nothing appears to be known about the stability of complexes with monopyrrolic ligands in aqueous solution, though some pyrroles play an important role in biological systems, *e.g.* porphobilinogen, a precursor in porphyrin

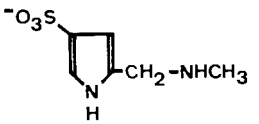


synthesis [1]. Several investigations have been done on the coordinating geometry of complexes with pyrrole derivatives (mostly aldimines), *e.g.* by studying their spectra in nonaqueous solvents [2] [4], and determination of their crystal structure [3]. As pyrrolate anion cannot be investigated in water, because it precipitates metal ions as hydroxides, some derivatives containing additional complexing groups (methylamine, glycine, ethylenediamine and iminodiacetate) at an α-methylene group were synthesized. Sulfonated pyrroles were used, because pyrroles without electron attracting groups are easily oxidized by atmospheric oxygen, especially in acidic solution [5]. Moreover, the charge of the sulfonate group causes ligands and complexes to be water-soluble. All the ligands are new and were prepared as follows: Sulfonation [6] of pyrrole-2-aldehyde gave potassium 2-formylpyrrole-4-sulfonate (KPSA). Reductive amination [7] with methylamine, glycine or ethylenediamine yielded PSMA, PSG or PSEN respectively (isolated as HPSMA, KHPSG, H_2PSEN(NO_3)). PSIDA was prepared by reaction of PSG with chloroacetic acid in alkaline medium and isolated as K_2HPSIDA. This paper describes the complex formation of these ligands with copper(II) and nickel(II). The equilibria were studied by means of alkalimetric

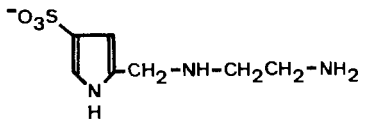
KPSA



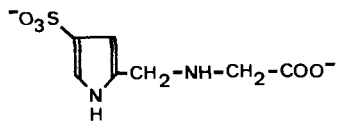
PSMA



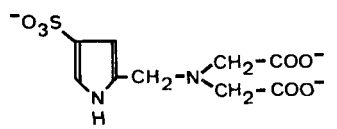
PSEN



PSG



PSIDA



titrations of the ligands in presence of the metal ion. Information about the coordinating tendency of the pyrrole was obtained by comparison of the determined equilibrium constants with those of methylamine, ethylenediamine, glycinate and iminodiacetate and their derivatives.

2. Definitions [8].

$[\,], [\,]_t$ = concentration, respectively total concentration in mol/l of the species in brackets;

$\beta_{q,p,n}$ = cumulative stability constant for $M_qH_pL_n$: $[M_qH_pL_n]/([M]^q \cdot [H]^p \cdot [L]^n)$

The charges of the species $M_qH_pL_n$ are omitted.

3. Protonation and deprotonation of the ligands. – Titrations of the protonated ligands with KOH lead exclusively to deprotonation of the carboxyl and ammonium groups[1]). Thus, H_3PSIDA is considered to be a threefold protonated acid without consideration of the pyrrole group. Table 1 shows the corresponding protonation constants K_p.

The aromatic pyrrole ring does not influence the log K_p of the carboxylate groups, which are below 3 as expected, but decreases the pK values of the ammonium groups

[1]) Pyrrole as such has pK = 17.5 [9].

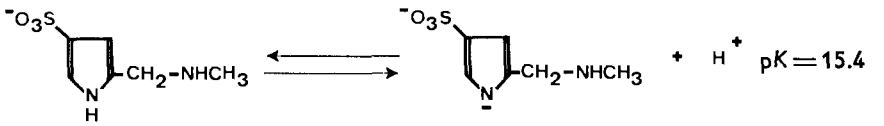
Table 1. *Protonation constants of the ligands* (25°, 1 M KNO_3)

	log K_1	log K_2	log K_3
PSMA	9.58		
PSEN	9.74	6.56	
PSG	8.71	2.25	
PSIDA	8.30	2.30	1.46 ± 0.05

Standard deviations are smaller than 0.03, unless otherwise stated.

(log K_2 for PSEN) by about one unit [10–13]. Thus, PSEN has pK values similar to N-benzylethylenediamine (9.80, 6.70 [14]) and PSIDA is comparable to N-pyridylmethyliminodiacetate (log K_1 = 8.22 [15]). PSG, PSMA and PSEN are somewhat more basic than their pyridylmethyl analogues [14] [16] [17], probably because of the charge on the sulfonate group.

The pK value of the pyrrole in PSMA was estimated by UV. spectrophotometric measurements in solutions containing different concentrations of KOH (0.1 to 11 M). Below 260 nm the deprotonated species absorbs much stronger than its conjugate acid, but neither a maximum nor an isobestic point could be observed, since solutions of KOH absorb below 300 nm and are not transparent below 230 nm. Evaluation



was carried out between 245 and 250 nm, at the end of an absorption band with maximum below 230 nm. The ratio I = [HL]/[L] is equal to 1 at 4.8 M KOH, corresponding to H_{2-} = 15.95 by using the H_{2-} scale which has been developed from measurements with indole derivatives [18]. The experimental points (E = f (H_{2-})), however, do not fit the theoretical curve for this function. The use of the H_- scale [18] lead to pK = 15.4 Because of the good fit to the theoretical curve, this value is regarded as reliable (log I *vs.* – H_- = 1.0).

4. The complex formation. – The stability constants obtained are summarised in Table 2. In the discussion these values are compared with those of similar ligands given in Table 3.

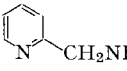
4.1. *Cu^{++}/PSEN.* Titrations of H_2PSEN^+ in presence of equimolar concentrations of Cu^{++} (Fig. 1) show at first the formation of $CuPSEN^+$ with a stability constant similar to $CuDMEN^{++}$ and $CuBEN^{++}$. Then for each mol of complex two further mol of base are consumed with two distinct buffer regions at pH 6 to 7 and 9 to 10.5 respectively. The analysis of the *first buffer region* with pK = 6.48 indicates primarily a deprotonation of $CuPSEN^+$ and small amounts of a dimer with $\beta_{2,-2,2} = 10^{7.4 \pm 0.3}$. The deprotonation can either be due to the formation of a hydroxo complex CuLOH (I) or $CuH_{-1}L$ with a deprotonated pyrrole group (II) or a mixture of both processes.

Table 2. *Equilibrium constants*[a]) *of the pyrrole ligands with* Cu^{++} *and* Ni^{++} *at 25° and I = 1 M* (KNO_3)

Reaction	L = M =	PSEN Cu	PSG Cu	PSIDA Cu	PSEN Ni
$M + L = ML$	$\log K_1$	9.49	6.90	9.6 ± 0.1	6.52
$ML + L = ML_2$	$\log K_2$	7.84	6.13	5.79	5.06
$ML = MH_{-1}L + H$	$pK(ML)$	6.48	6.75	8.01	9.19 ± 0.05
$MH_{-1}L = MH_{-1}LOH + H$	$pK(MH_{-1}L)$	9.86	9.71 ± 0.05	9.91	(10.5)
$ML_2 = M(H_{-1}L)L + H$	$pK(ML_2)$	9.46 ± 0.06	9.03 ± 0.05	–	9.14 ± 0.06
$M(H_{-1}L)L =$ $M(H_{-1}L)_2 + H$	$pK(MH_{-1}L_2)$	12.3 ± 0.4	12.2 ± 0.5	–	11.2 ± 0.2
$MH_{-1}L + MH_{-1}LOH =$ $(MH_{-1}L)_2OH$	$\log K_{d,OH}$	1.8 ± 0.3	2.2 ± 0.4	1.6 ± 0.5	–

[a]) Standard deviations are smaller than 0.04, unless otherwise stated.

Table 3. *Equilibrium constants of comparable ligands with* Cu^{++}

L	ligand	log K_1	log K_2	pK (ML)	pK ($MH_{-1}L$)	pK (ML_2)	log K_d	m[a])	Ref.
BEN	$C_6H_5CH_2NHCH_2CH_2NH_2$	9.43	7.71					2	[14]
DMEN	$H_3CNHCH_2CH_2NHCH_3$	9.69	6.65	8.09[c])			3.8[b])	1	[19]
									[20]
DIEN	$(H_2NCH_2CH_2)_2NH$	15.94		9.39[c])				3	[21]
		16.34						4	[22]
G	$H_2NCH_2COO^-$	8.33	6.87					4	[12]
MIDA	$H_3CN(CH_2COO^-)_2$	11.09	6.83	8.89[c])				2	[24]
BIDA	$C_6H_5CH_2N(CH_2COO^-)_2$	9.88	4.85					1	[25]
NPGA		9.70	5.15	7.11[d])	9.57	8.50		3	[16]
GA	$H_2NCH_2CONH_2$	5.29	4.16	6.92[d])		6.91		1	[26]
GG	$H_2NCH_2CONHCH_2COO^-$	5.68		4.21[d])	9.24		2.15[e])	1	[27]
$H_{-1}GGA$	$H_2NCH_2CON{=}CH_2CONH_2$			8.01[d])	9.82			1	[26]
AIDA	$H_2NCOCH_2N(CH_2COO^-)_2$	9.68	3.26					2	[24]
				7.88[d])	9.95			2	[28]

[a]) m = Ionic strength and temperature. m = 1: 0.1 M, 25°; m = 2: 0.1 M, 20°; m = 3: 0.5 M, 25°; m = 4: 1 M, 25°.
[b]) $K_d = [M_2L_2(OH)_2]/[MLOH]^2$.
[c]) Formation of MLOH.
[d]) Formation of $MH_{-1}L$.
[e]) $K_d = [(MH_{-1}L)_2OH]/([MH_{-1}L] \cdot [MH_{-1}LOH])$.

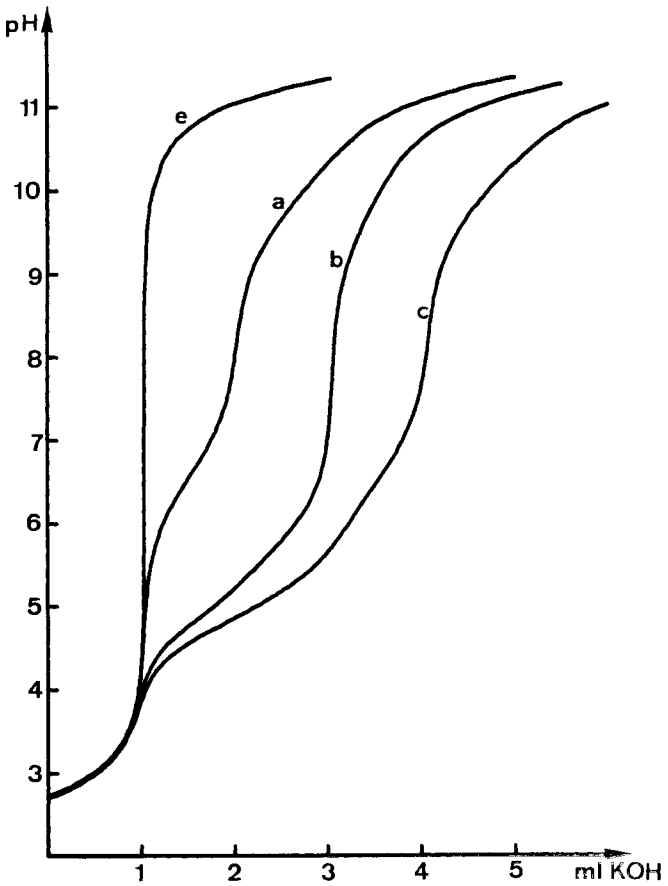


Fig. 1. *Titration curves of 0.00201* M $H_2PSEN(NO_3)$ (100 ml) *in presence of* $Cu(NO_3)_2$ *and 0.00204* M HNO_3 *with 0.2* M *KOH at 25° and I = 1* M (KNO_3)
$[Cu]_t$ = 0 (a), 0.001 (b), 0.002 M (c) e: calibration curve (titration of 0.00204 M HNO_3)

In the definitions of the cumulative formation constants $\beta_{1,-1,1}$ and $\beta_{2,-2,2}$ both possibilities have to be considered. Comparison of both constants with those of similar complexes of known

$$CuPSEN^+ = CuPSEN(OH) + H^+ \quad (I)$$

$$CuPSEN^+ = CuH_{-1}PSEN + H^+ \quad (II)$$

structure allows an interpretation of the data. For this purpose it is assumed that the hydroxo-complex CuPSEN(OH) behaves like other copper diamine hydroxocomplexes. As found by

$$\beta_{1,-1,1} = \frac{[CuLOH] + [CuH_{-1}L]}{[Cu] \cdot [H]^{-1} \cdot [L]} = \beta_{CuLOH} + \beta_{CuH_{-1}L}$$

$$\beta_{2,-2,2} = \frac{[Cu_2L_2(OH)_2] + [Cu_2H_{-2}L_2]}{[Cu]^2 \cdot [H]^{-2} \cdot [L]^2}$$

Martell [20], these complexes show a pronounced tendency to form dimeric compounds $Cu_2L_2(OH)_2$ *e.g.* with DMEN $K_d = [Cu_2L_2(OH)_2]/[CuLOH]^2 = 10^{3.8}$. For $CuPSEN^+$ $K_d = \beta_{2,-2,2}/(\beta_{1,-1,1})^2 = 10^{1.4}$, *i.e.* it is much smaller than for other Cu diamine complexes. Furthermore, the pK of

$CuDMEN^{++}$ (8.1) is much higher than for $CuPSEN^{+}$ (6.48). If it is assumed that $CuH_{-1}PSEN$ does not dimerize and that K_d of CuPSEN(OH) has the same value as found for $CuDMEN(OH)^{+}$, calculations give $\log \beta_{CuLOH} = 1/2 \cdot (\log \beta_{2,-2,2} - \log K_d) = 1.8$ and $\log \beta_{CuH_{-1}L} = 2.98$. Thus, the p$K$ values for reactions (I) and (II) are found: 6.51 for the formation of $CuH_{-1}PSEN$ and 7.7 for the formation of CuPSEN(OH) respectively.

Therefore, this first deprotonation of $CuPSEN^{+}$ corresponds mainly to the formation of $CuH_{-1}PSEN$ with a complexed deprotonated pyrrole group, whereby small amounts of $Cu_2(PSEN)_2(OH)_2$ are present[2]).

The *second buffer region* with pK = 9.86 indicates the formation of the hydroxo-complex $CuH_{-1}PSEN(OH)^{-}$. This pK value is comparable to those of other 1:1 complexes of Cu^{++} with three coordinated nitrogen atoms ($CuDIEN^{++}$: pK = 9.39; $CuH_{-1}NPGA^{+}$: pK = 9.57) if one takes into account the charge differences. Titrations with different total concentrations $[M]_t$ and $[L]_t$ reveal the formation of a dimeric complex $(CuH_{-1}PSEN)_2OH^{-}$. Its formation constant $K_{d,OH} = 10^{1.8}$ (Table 2) is comparable to that of the similar complex $(CuH_{-1}GG)_2OH^{-}$ which has $K_{d,OH} = 10^{2.15}$.

For a complete explanation of the equilibria, solutions with a metal to ligand ratio of 1:2 were titrated (Fig. 1). The buffer region below pH = 7.5 corresponds to the formation of $Cu(PSEN)_2$ with a formation constant similar to that of $Cu(BEN)_2^{++}$. As BEN has about the same protonation constants as PSEN and the steric relations in the two systems are similar, the close agreement of their complex formation constants shows that neutral pyrrole does not exhibit any coordinating tendency. Then for each mol of $Cu(PSEN)_2$ two further mol of strong base are consumed. In a first step, with pK = 9.46, five coordinated $CuH_{-1}(PSEN)_2^{-}$ (III) is formed. The formation of a hydroxo complex CuL_2OH is very unlikely because the corres-

$$Cu(PSEN)_2 \rightleftarrows CuH_{-1}(PSEN)_2^{-} + H^{+} \qquad \text{(III)}$$

ponding complex $Cu(EN)_2^{++}$ has a pK value of 13 [23]. The available pyrrole nitrogen of L seems to be preferred to the hydroxyl ion of the solvent. For the deprotonation of $CuH_{-1}(PSEN)_2^{-}$ the two competing reactions (IV) and (V) can occur. Fig. 2a and 2b show the pH-dependence of the concentrations of the different complexes for

$$Cu(H_{-1}PSEN)_2^{--} + H^{+} \underset{\text{(V)}}{\rightleftarrows} CuH_{-1}(PSEN)_2^{-} \underset{\text{(IV)}}{\rightleftarrows} CuH_{-1}PSEN(OH)^{-} + PSEN^{-} + H^{+}$$

mixtures having metal to ligand ratios of 1:1 and 1:2. The latter shows the liberation of ligand in the alkaline region according to reaction (IV). Within our experimental conditions the four coordinated $CuH_{-1}PSEN(OH)^{-}$ is preferred to a probably six coordinated $Cu(H_{-1}PSEN)_2^{--}$. Electronic spectra provide support for the postulated species. Thus $CuPSEN^{+}$ (λ_{max} = 665 nm, ε = 55) and $Cu(PSEN)_2$ (λ_{max} = 560 nm, ε = 122) absorb at wavelengths similar to $CuEN^{++}$ (660 nm) and $Cu(EN)_2^{++}$ (549 nm) [29] respectively. The spectrum of $CuH_{-1}PSEN$ (λ_{max} = 608 nm, ε = 90) is comparable to that of $Cu(H_{-1}GA)GA^{+}$ (λ_{max} = 605 nm), both having one deprotonated nitrogen group, two amine groups and an O donor. The deprotonation of complexed water does not produce significant spectral changes: $CuH_{-1}PSEN(OH)^{-}$ has λ_{max} = 590 nm and ε = 92. Spectra of alkaline solutions of $Cu(PSEN)_2$ show similar maxima at about 600 nm with $\varepsilon \approx 100$.

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[2]) The formation of $Cu_2L_2H_{-1}(OH)$ is very unlikely because its estimated cumulative formation constant is 10 times smaller than that of $Cu_2L_2(OH)_2$.

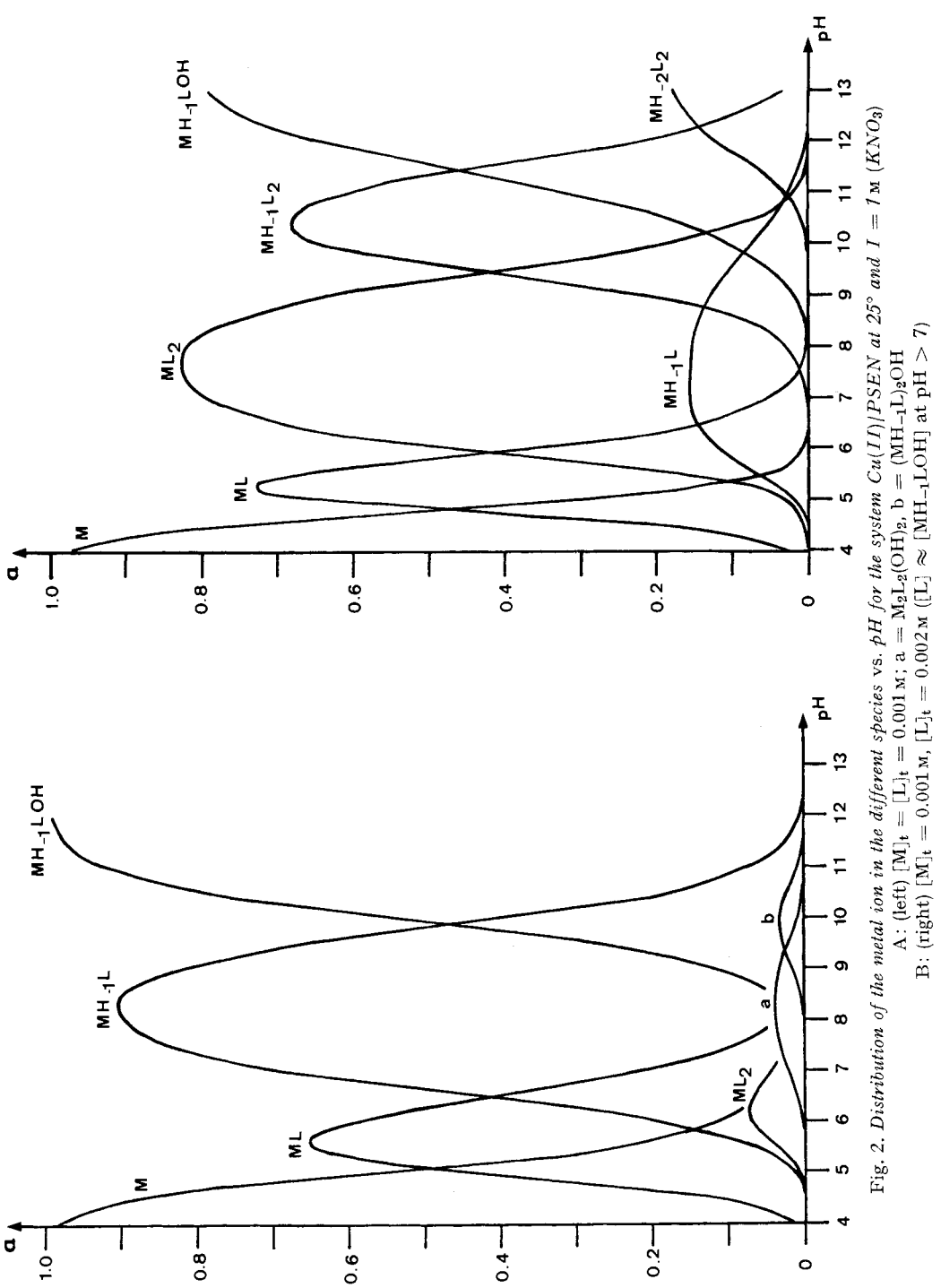
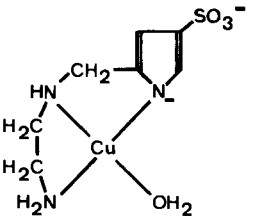
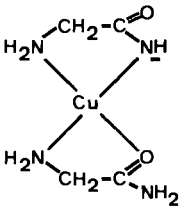


Fig. 2. *Distribution of the metal ion in the different species* vs. *pH for the system Cu(II)|PSEN at 25° and I = 1 M (KNO_3)*
A: (left) $[M]_t = [L]_t = 0.001$ M; a = $M_2L_{-2}(OH)_2$, b = $(MH_{-1}L)_2OH$
B: (right) $[M]_t = 0.001$ M, $[L]_t = 0.002$ M ($[L] \approx [MH_{-1}LOH]$ at pH > 7)



CuH$_{-1}$PSEN



Cu(H$_{-1}$GA)GA$^{\bullet}$

4.2. *Cu^{++}/PSG.* The system Cu^{++}/PSG behaves analogously to that of Cu^{++}/PSEN, but the complexes are weaker. Titrations of solutions with equimolar concentrations of Cu(II) and H_2PSG are limited by precipitation of copper hydroxide at pH 6.4. The formation of CuH$_{-1}$PSG(OH)$^{--}$ could only be observed in solutions containing an excess of ligand[3]). The complexes CuPSG and Cu(PSG)$_2^{--}$ are weaker than those of glycinate as expected from the different acidities of the ammonium groups. The formation of CuH$_{-1}$PSG$^-$ takes place with a pK value similar to that of the PSEN complex. The corresponding glycinate complex hydrolyses at about pH = 6.5 without any indication of formation of CuG(OH). (pK of CuG$^+$ > 7.5). Also dimeric complexes with similar formation constants are found: log $\beta_{2,-2,2}$ is 2.1 $\pm$ 0.5, giving log K_d = 1.7 and log $K_{d,OH}$ = 2.2 $\pm$ 0.4. The pK value of CuH$_{-1}$PSG$^-$ is higher than that of CuH$_{-1}$GG, as expected from the different charges of the complexes. Surprisingly, the pK value of Cu(PSG)$_2^{--}$ is smaller than that of the uncharged Cu(PSEN)$_2$. Thus, Cu(PSG)$_2^{--}$ accepts a fifth ligand group more easily than the more stable PSEN complex. The corresponding complex CuG_2 shows no formation of $CuG_2(OH)^-$ up to pH = 10, then the solution becomes turbid.

4.3. *Cu^{++}/PSIDA.* Titrations of H_3PSIDA in the presence of equimolar concentrations of Cu^{++} show a degree of complexation greater than 0.8 (log K_1 = 9.9 $\pm$ 0.3 [30]). The constant was therefore determined using reaction (VI) [31]. The protonation constants of TREN and its stability constant with Cu^{++} were determined for 25° and I = 1 M (KNO_3)[4]). Thus, log K_1 was found to be 9.6, similar to that with BIDA, as expected. Deprotonation of CuPSIDA$^-$ (pK = 8.01) gives CuH$_{-1}$PSIDA. Hydroxo-

$$CuPSIDA^- + H_3TREN^{3+} \rightleftharpoons CuTREN^{++} + HPSIDA^{--} + 2\,H^+ \qquad (VI)$$

complexes should be formed in more alkaline region only (CuMIDA: pK = 8.9). CuH$_{-1}$PSIDA^{--} is formed less easily than CuH$_{-1}$PSEN and CuH$_{-1}$PSG$^-$, because either an axial coordination site has to be occupied or a molecular rearrangement has to occur. The pK of CuH$_{-1}$PSIDA^{--} (9.91) is higher than that of the corresponding CuH$_{-1}$PSG$^-$ (9.71) because of the charge difference.

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[3]) Therefore $\beta_{2,-2,2}$, $K_{d,OH}$ and the pK of CuH$_{-1}$PGS$^-$ have relative big standard deviations.

[4]) Protonation constants of TREN (25°, I = 1 M KNO_3): 10.39, 9.81, 8.89. pK of CuHTREN^{3+}: 4.16, log K_1 (CuTREN^{++}): 19.27, pK of CuTREN^{++}: 9.51.

Dimeric compounds are also found: log $\beta_{2,-1,2} = 12.5$ probably corresponds to the formation of Cu_2L_2OH. If the complex $CuPSIDA(OH)^{--}$ is formed with $pK = 9$ (as with MIDA) then $K_d = [Cu_2L_2(OH)]/([CuL] \cdot [CuLOH])$ is $10^{2.3}$, *i.e.* a similar value to that of $(CuH_{-1}GG)_2OH^-$. Log $\beta_{2,-2,2} = 5.1 \pm 0.3$ gives log $K_d = 1.1$ for a complex $Cu_2H_{-2}(PSIDA)_2^{4-}$. The occurrence of this complex is reasonable if in this species one ligand can occupy three coordinating sites of one metal and one of the other metal, each metal having a square planar geometry.

K_2 is derived from titrations with a metal to ligand ratio of 1:2 (log $K_2 = 5.79$). The value log K_1 – log K_2 is similar to that of other Cu(II) iminodiacetate complexes with non-coordinating N-substituents [24].

In alkaline solution $Cu(PSIDA)_2^{4-}$ looses one ligand giving $CuH_{-1}PSIDA^{--}$ and $CuH_{-1}PSIDA(OH)^{3-}$.

The electronic spectra support these structural assignements: $CuPSIDA^-$ ($\lambda_{max} = 720$, $\varepsilon = 75$), $CuH_{-1}PSIDA^{--}$ ($\lambda_{max} = 725$, $\varepsilon = 75$) and $CuH_{-1}PSIDA(OH)^{3-}$ ($\lambda_{max} = 740$, $\varepsilon = 90$). $CuH_{-1}GG$ ($\lambda_{max} = 660$) has also one deprotonated peptide

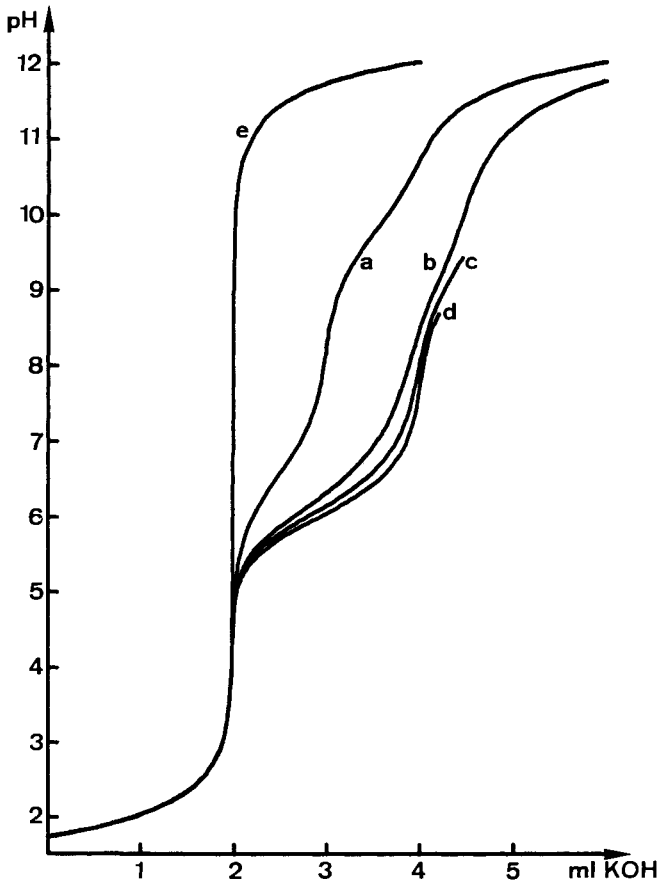


Fig. 3. *Titration curves of 0.0100 M $H_2PSEN(NO_3)$* (50 ml) *in presence of $Ni(NO_3)_2$ and 0.0198 M HNO_3 with 0.5 M KOH at 25° and I = 1 M (KNO_3)*
$[Ni]_t = 0$ (a), $= 0.0050$ M (b), $= 0.0075$ M (c), $= 0.0097$ M (d)
(e) calibration curve (titration of 0.0198 M HNO_3)

group, one amino group but only one carboxyl group. The larger λ_{max} found for $CuH_{-1}PSIDA^{--}$ is due to the axial ligand, which causes a shift to longer wavelength of 1.4 KK [32]. As with AIDA [33] the colour changes from blue to green when formation of $MH_{-1}L$ takes place.

4.4. *Ni^{++}/PSEN.* Titrations of solutions with equimolar concentrations of PSEN and Ni^{++} can be performed only up to the beginning of the buffer region for the formation of $NiH_{-1}PSEN$ (Fig. 3) with pK = 9.19. In solutions with a metal to ligand ratio of 1:2 or 1:3 $NiPSEN^+$ and $Ni(PSEN)_2$ are formed with log K_1 = 6.52 and log K_2 = 5.06. They are less stable than the Ni-EN complexes [34] because of the decreased basicity of PSEN. $Ni(PSEN)_3^-$ is not formed, in contrast to the corresponding $Ni(EN)_3^{++}$ (log K_3 = 4.4),because of the formation of $Ni(H_{-1}PSEN)PSEN^-$ and $Ni(H_{-1}PSEN)_2^{--}$ with pK values of 9.14 and 11.2. Solutions of $Ni(EN)_2^{++}$ show no indication of formation of a hydroxocomplex $Ni(EN)_2OH^+$, but precipitation of nickel hydroxide occurs (pH > 10.5). This is in agreement with our postulate of the formation of PSEN complexes with coordinated pyrrole instead of hydroxocomplexes. The inclusion of the complex $NiH_{-1}PSEN(OH)^-$ improved the fit to the experimental titration curves, when the pK value of $NiH_{-1}PSEN$ was set equal to that of $NiH_{-2}GGA$: 10.5 [27].

4.5. *The further systems.* In the systems Cu(II)/PSMA, Ni(II)/PSMA, Ni(II)/PSG and Ni(II)/PSIDA precipitation of metal hydroxide limits the measurements and disproportionation (*e.g.* 2 ML + 2 OH^- → ML_2 + $M(OH)_2$) prevents the coordination of the pyrrole nitrogen.

5. Discussion. – We have shown that in the investigated ligands the pyrrole group can coordinate a metal ion by simultaneous loss of the proton bound to the pyrrole nitrogen. This reaction (VIII) takes place in a separate process after the primary coordination of the donors of the basic ligands, reaction (VII), and can be accompanied by formation of hydroxo complexes according to (IX). The experimental

$$M^{\nu+} + L^{\mu-} \rightarrow ML^{\nu-\mu} \qquad \text{(VII)}$$

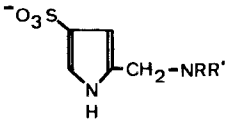
$$ML^{\nu-\mu} \rightarrow MH_{-1}L^{\nu-\mu-1} + H^+ \qquad \text{(VIII)}$$

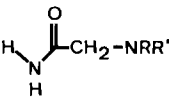
$$ML^{\nu-\mu} \rightarrow MLOH^{\nu-\mu-1} + H^+ \qquad \text{(IX)}$$

data of Table 2 indicate a smaller pK value for (VIII) than for (IX), *i.e.* that the complexation of the pyrrolate anion is preferred as shown for $CuH_{-1}PSEN$ by spectrophotometric measurements. Copper(II) complexes of N-2'-hydroxyethyl-ethylenediamine and -iminodiacetate show also the distinct reaction sequence (VII) and (VIII) (pK values: 7.3 [20] and 8.6 [24] respectively).

The complexes $CuH_{-1}L$ with the amide ligands NPGA and GA (Table 3) are formed from CuL with pK values somewhat higher than those of the corresponding complexes with terdentate PSEN and PSG, whereas the deprotonation of $CuH_{-1}GGA^+$ has a distinctly higher pK value. The Cu^{++} complexes of quadridentate PSIDA and its amide analogue (AIDA) behave very similarily, even for their second deprotonation. Also $NiPSEN^+$ and $NiH_{-1}GGA^+$ [27] have similar pK values (9.19

and 9.34), the products being $NiH_{-1}PSEN$ and $NiH_{-2}GGA$. In contrast to the pyrrole group, the amide group is coordinated even in its neutral form, by means of the >C=O group [21] *e.g.* CuAIDA is 1.5 logarithmic units more stable than it would be expected if the carbonyl group did not coordinate [24]. This stabilization, together with a different basicity of the ligand, is the reason why Cu-GA complexes are stable in contrast to the Cu-PSMA complexes. Thus, pyrrole exhibits a complexing behaviour similar to an amide with a comparable low acidity (pK of acetic acid amide is about 15.1 [35]). This similarity extends to the electronic spectra of Cu(II) complexes with deprotonated pyrrole and amide (see $CuH_{-1}PSEN$ and $Cu(H_{-1}GA)GA$).





If one takes into consideration, the pK value of the pyrrole group (15.4) or the amide group (14.3)[5]) the stability constant K^* for the complexes with deprotonated pyrrole or amide group can be evaluated ($K^* = [MH_{-1}L]/([M] \cdot [H_{-1}L])$. Comparison of these values with those of the corresponding N-2′-aminoethyl and N-(2-pyridylmethyl) substituted basic ligands (Table 4) shows the superiority of the ligands with

Table 4. *Logarithms of the stability constants* K^* *of the pyrrole substituted ligands and* K_1 *of comparable ligands* $K^* = [MH_{-1}L]/([M] \cdot [H_{-1}L])$

N-substituent	glycinate	ethylenediamine		iminodiacetate
	Cu	Cu	Ni	Cu
2-(4-sulfonyl)-pyrrylmethyl-	15.6	18.4	12.7	17.0
2-pyridyl-methyl-	11.8	14.6		14.2
2′-aminoethyl-	13.4 [a])	16.3	10.7 [b])	15.9
Carbamoylmethyl-				16.1

[a]) [36]; [b]) [37].

a pyrrole group. The complexes of the terdentate ligands with the negatively charged pyrrole (PSEN, PSG) are more stable than their pyridine or aminoethyl analogoues by 4 respectively 2 logarithmic units. With the quadridentate iminodiacetate derivatives the differences are smaller.

A comparison between pyrrolate anion, amine and pyridine as ligands can be done on the assumption that the corresponding ligands form unstrained chelate five rings. Some problems arise in considering the different basicity of the attached basic ligand. These effects are discussed taking the copper(II) complexes of the iminodiacetate derivatives as example: The logarithms of the stability constants of Cu^{++} complexes of iminodiacetate derivatives with non-coordinating N-substituents show a linear

[5]) The substituent effect of a β-amino group on the pK value of an ammonium group is 0.8 [38]. The same correction applied to acedamide gives 14.3 as estimated pK value for AIDA.

relationship with the pK values of the ammonium groups ([24], Fig. 4). Log K_1 of $CuPSIDA^-$ lies on the straight line a, as expected for a non-coordinated neutral pyrrole substituent. If a coordinating N-substituent is present and the first protonation constant of L or $H_{-1}L$ does not correspond to the protonation of the iminodiacetate group, a calculated value for this last process must be used:

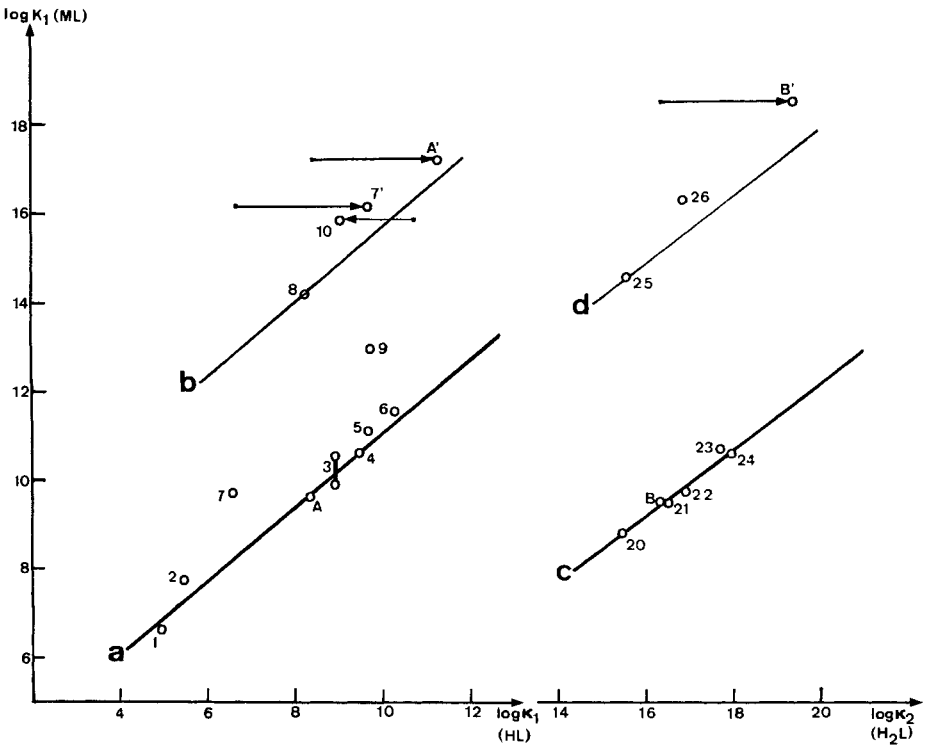


Fig. 4. *Stability constants of Cu(II) complexes of N-substituted iminodiacetate* (at left) *and ethylenediamine* (at right) *derivatives as function of their protonation constants* (log $\varkappa_1$ or log $\varkappa_2$). Iminodiacetate: 1: phenyl-, 2: β-trimethylammonio-methyl-, 3: benzyl-, 4: H, 5: methyl-, 6: cyclohexyl-, 7: carbamoylmethyl-(AIDA), 8: 2-pyridylmethyl-, 9: carboxymethyl-(NTA), 10: β-amino-ethyl-, A = PSIDA, A', 7' values for log K^* [13] [15] [24].
Ethylenediamine: 20: 4-pyridylmethyl-, 21: benzyl-, 23: H-, 24: methyl-, 25: 2-pyridylmethyl-, 26: β-aminoethyl- (DIEN, calculated value), 22: DMEN, B = PSEN, B' value for log K^* [11] [14] [19] [21] [22].

For the pyridylmethyl derivative this is just the logarithm of the first protonation constant, because the pyridyl group is protonated only in acidic solution. For the 2'-aminoethyl derivative the situation is more complicated because of the presence of two amino groups. In [24] they have been considered equivalent, which implied a statistic correction (– 0.3) leading to a $pK_1 = 10.75$ for the tertiary ammonium group. This value is certainly to high, in the case of iminodiacetate ligands, the acetate groups acting as basicity decreasing substituents. For instance, the logarithm of the protonation constant of methyliminodiacetate (9.65) is lower than that of methylamine (10.95) by 1.3 log units. Taking into account the 'base weakening effects' of a methyl group (– 0.2) and of the 2'-aminoethyl group (– 0.8) [38] the sought pK value is likely be 9.65 (MIDA) – (– 0.2) + (– 0.8) = 9.0. The experimental value pK = 11.05 corresponds mainly

to the protonation of the primary amino group, in which the protonated species is stabilized by hydrogen bonding [38]. This interpretation is corroborated by the fact, that the further protonation constant ($10^{5.6}$) is similar to that of the equally charged β-trimethylammonio-ethyl-iminodiacetate ($10^{5.5}$) [24]. For AIDA it is supposed that the pK of the ammonium group with deprotonated amide group is the same as for nitrilotriacetate (9.7 [24]). For PSIDA the effect of deprotonating the pyrrole group on the basicity of the amine group is estimated as follows: The difference between the base weakening effect of a β-aminoethyl group and a β-ammonio-ethyl group is – 2.8 while with a neutral acetic acid substituent and an acetate group this difference is – 3.1. Therefore a mean correction of 3.0 is applied giving pK = 11.3 for the sought pK value.

In Fig. 4, arrows link the experimental pK values to those calculated for the ligands with deprotonated N-substituents. The points corresponding to log K_1 are situated above the expected point (log K_1') on the straight line a. Log K_1 – log K_1' is considered a measure of the complexing power of the N-substituents. These stabilizations can then be read from this diagram and are listed in Table 5. Because

Table 5. *Stabilizations of the Cu(II) complexes of iminodiacetates and ethylenediamines by coordinating N-substituents* (log K_1 – log K_1' or log K^* – log K_1')

	iminodiacetate	ethylenediamine
N-2-(4-sulfonyl-)-pyrrylmethyl-	5.0	6.7
N-2-pyridylmethyl-	4.6	5.7
N-β-aminoethyl-	5.6	6.4
N-carbamoylmethyl-	5.2	

of the rough approximations used, these values are considered accurate to $\pm$ 0.5. Although these stabilizations are of the same order of magnitude, the value for the aminoethyl group is larger than that of the pyridylmethyl group, as is the case for the complexes of ammonia and pyridine [10] [39]. Surprisingly, the high basicity of the pyrrolate group does not enhance the stabilization.

Fig. 4 shows also a similar correlation for the N-substituted ethylenediamine derivatives in which log $\varkappa_2$ = log ($[H_2L]/([L] \cdot [H]^2)$) is used. (For DIEN the protonation constant $\varkappa_2$ is calculated for protonation of two adjacent amine groups [38]). The corresponding stabilizations (Table 5) show the same feature as for the iminodiacetate derivatives, but are larger by 1.5 units, which we attribute to the formation of complexes with square planar structure. For the Ni(II) complexes there are not enough values to establish a correlation, but similar tendencies are expected, as the difference between log K^* for NiH$_{-1}$PSEN and log K_1 for NiDIEN^{++} is the same as that for the corresponding Cu(II) complexes.

6. Experimental part. – 6.1. *Determination of stability constants.* All the ligands were investigated in concentrations from 0.001 to 0.02 M, which increased the significance of the results and allowed the detection of the dimeric complexes. Calculations were done on the computer of the Rechenzentrum of the ETH, Zürich. The protonation constants and parts of the other stability constants were calculated by minimization of the weighted protonation and complex formation functions [40]. With complicated equilibria the stability constants are evaluated by varying the wanted constants to a minimum of Σ $(([H]_{t,calc} - [H]_{t,exp})/[L]_t)^2$ [41]. If species were present only in small concentrations (high pK values or dimeric compounds) the minimum is flat and the corresponding constant has a large standard deviation. pH measurements are done in the concentration scale (pH = – log $[H^+]$) as described in [42].

6.2. *Synthesis.* – *Generalities.* IR. spectra were run on a *Perkin Elmer* 257 (intensities: s = strong, m = medium), ^{1}H-NMR. spectra at 60 MHz in D_2O; chemical shifts are given in ppm (δ, TMS = 0), coupling constants in Hz (s = singlet, d = doublet, m = multiplet). Electronic

spectra were recorded on a *Techtron* spectrophotometer. Abbreviation: i.V. = in vacuo; i.HV. = in high vacuo; RT. = room temperature.

Potassium 2-formyl-pyrrole-(4)-sulfonate (KPSA). 38 g (0.4 mol) of pyrrole-2-aldehyde were added slowly to a stirred mixture of 180 g conc. sulfuric acid and 290 g 20% oleum in an ice bath, at such a rate that the temp. did not exceed 50°. Stirring was continued until the solution reached 10°. The solution was slowly poured to 3 l of a mixture of ice, water and 934 g of $KHCO_3$. The mixture was brought to pH = 6 with KOH and precipitated K_2SO_4 was filtered off. The solution was taken to dryness i.V. Soxhlet extraction of the residue with methanol for 2 months yielded 83 g of crude product collected in several fractions and recrystallized in hot water (33 g in 100 ml). The crystalline precipitate was filtered off, washed with methanol and dried i.V. Yield: 74 g (87%) of pure KPSA. – ^{1}H-NMR.: 9.81 (*d*, J = 1.5, 1H, (CHO)); 7.99 (*m*, 1H, (C(5)); 7.61 *d*, J = 2, 1H, (C(3)) [43]. – IR. (KBr): 3175s, 3160s, 3045m, 2995m, 2960m, 1675s (CHO). – UV.: (H_2O) λ_{max} = 285 nm (ε = 16000), (1M KOH) λ_{max} = 308 nm (ε = 20000).

$C_5H_4NO_4SK$	Calc.	C 28.16	H 1.89	N 6.57	S 15.04%
(213.3)	Found	,, 28.02	,, 1.99	,, 6.57	,, 14.42%

2-Methylaminomethyl-pyrrole-(4)-sulfonic acid (HPSMA). 10.65 g (0.05 mol) of KPSA were dissolved in 100 ml of 30% aqueous solution of methylamine and hydrogenated with alkaline *Raney*-Nickel [7] at RT. and atmospheric pressure for 2 days. The resulting solution was filtered and concentrated to 40 ml to remove excess of methylamine. The solution was brought to pH = 9 with 1M hydrochloric acid and heated. After cooling the precipitated aluminium hydroxide was removed by filtration and the solution was brought to pH 5, while crystals were formed. The mixture (100 ml) was heated to dissolve the precipitate, filtered and allowed to cool slowly. The crystals were separated by filtration, washed with ice-cold water and dried i.HV. over $CaCl_2$. Yield 5.2 g. The mother liquor was concentrated to 30 ml and gave additional 2 g of product. The products were recrystallized from 45 ml of water and yielded 5.4 g (57%) of pure PSMA (colorless crystals). – ^{1}H-NMR.: 7.30 (*d*, J = 2, 1H (C(5)); 6.62 (*d*, J = 2, 1H, (C(3)), 4.25 (*s*, 2H, (CH_2)); 2.72 (*s*, 3H, (CH_3)). Mol.-Wt. (by titration): 190 ± 1.

$C_6H_{10}N_2O_3S$	Calc.	C 37.90	H 5.30	N 14.73	S 16.86%
(190.2)	Found	,, 37.64	,, 5.29	,, 14.57	,, 16.68%

N-2-(4-sulfonyl)-pyrrylmethyl-ethylenediamine hydrochloride monohydrate ($H_2PSEN(Cl) \cdot H_2O$). A warm solution of 21.3 g (0.1 mol) of KPSA in 170 ml of water was poured into a cold, stirred solution of 100 g ethylenediamine in 125 ml of water. The resulting solution was hydrogenated with alkaline *Raney*-nickel at RT. and atmospheric pressure for two days. The catalyst was removed by filtration and the solution was taken to dryness. The residue was dissolved in water and concentrated again (3 ×) to remove excess of ethylenediamine as azeotrope with water. The residue was dissolved in 400 ml of water and brought to pH 8–9 with 6M hydrochloric acid. The solution was allowed to stand overnight, and the precipitated aluminium hydroxide filtered off. The solution was concentrated to 50 ml, brought to pH 3–4, and a slimy product separated. After several days in a refrigerator the product coagulated and was separated by filtration, washed with methanol and dried over $CaCl_2$ i.HV. Yield 22 g. The crude product was dissolved in 60 ml of hot water (70°) and a rather insoluble byproduct was filtered off. On chilling the product separated. Yield: 11.2 g (41%). From the mother liquors another 2 g product were obtained. The product crystallises with one mole of water.

$C_7H_{16}ClN_3O_4S$	Calc.	C 30.71	H 5.89	N 15.35	S 11.71%
(273.7)	Found	,, 30.64	,, 5.83	,, 15.52	,, 11.66%

Mol.-Wt. (by titration): 274 ± 1.

N-2-(4-sulfonyl)-pyrrylmethyl-ethylenediamine hydronitrate monohydrate ($H_2PSEN(NO_3) \cdot H_2O$). 4.8 g $NaNO_3$ in 5 ml of water were added to a warm solution of 13 g of H2PSEN(Cl) in 60 ml of water. Immediately a precipitate appeared. The mixture was chilled for several days, the solid was filtered off and dried over $CaCl_2$ i.HV. Yield 10.9 g. Recrystallization from 50 ml of water gave 9.0 g of $H_2PSEN(NO_3) \cdot H_2O$.

$C_7H_{16}N_4O_7S$	Calc.	C 28.08	H 5.37	N 18.66	S 10.68%
(300.3)	Found	,, 28.22	,, 5.20	,, 18.74	,, 10.78%

Mol.-Wt. (by titration): 300 ± 1. The hydronitrate, as well as the hydrochloride, should be kept in a refrigerator because they become red on leaving at RT. This red decomposition product could not be removed on further recrystallization.

Potassium N-2-(4-sulfonyl)-pyrrylmethyl-glycinate (*KHPSG*). 17.3 g of glycine (0.23 mol) were dissolved in 30 ml of water and 25 ml of 8.4 M KOH. This solution was added to a stirred solution of 43 g (0.2 mol) KPSA in 250 ml of water. Alkaline *Raney*-nickel was added and the mixture was hydrogenated for two days. The catalyst was removed by filtration and the filtrate was brought to pH 9 with 2 M hydrochloric acid. Aluminium hydroxide separated and was filtered off. The solution was brought to pH 6 with a cation exchange resin in H^+ form, as the product has a solubility similar to KCl. The solution was concentrated to dryness. The residue was dissolved in 105 ml of water and filtered. 105 g of ethanol were added and the mixture (2 phases) was vigorously stirred at RT. for one day. The product separated slowly. It was filtered off, washed with methanol and dried over $CaCl_2$ i.HV. Yield: 30.3 g. The product was recrystallized by the above procedure by using 85 ml of water and 85 g of ethanol. Yield: 23.6 g (43%).

$C_7H_9KN_2O_5S$	Calc.	C 30.87	H 3.33	N 10.29	S 11.78%
(272.3)	Found	,, 30.69	,, 3.33	,, 10.36	,, 11.52%

Mol.-Wt. (by titration): 275 ± 2.

Dipotassium N-2-(4-sulfonyl)-pyrrylmethyl-iminodiacetate (K_2HPSIDA). 27.2 g KHPSG (0.1 mol) were dissolved in 25 ml of 4 M KOH. 11 g chloroacetic acid (0.115 mol) were added and a precipitate appeared. The mixture was cooled in an ice-bath and 25 ml of 4 M KOH were slowly added; the precipitate dissolved. 17.2 ml of 8.4 M KOH were added slowly and under vigorous stirring to the solution. The temperature rose to 40°. The mixture was left for 3 h, heated for 30 min to 70° to complete the reaction and was brought to pH 5 with a cation exchange resin in H^+ form. The solution was evaporated to dryness, dissolved in 44 ml of water and filtered. 22 g of ethanol were added and the mixture was vigorously stirred overnight. The precipitated product was filtered off and dried. Yield: 22.6 g. The crude product was dissolved in 29 ml of hot water and filtered. 29 g of methanol were added and the mixture was stirred for 3 days. The product was isolated by filtration, washed with methanol and dried over $CaCl_2$ i.HV. Yield: 16.5 g. Further recrystallisation gave 13.6 g (36%) of pure product.

$C_9H_{10}K_2N_2O_7S$	Calc.	C 29.34	H 2.74	N 7.67	S 8.70%
(368.5)	Found	,, 29.22	,, 2.80	,, 7.62	,, 8.81%

Mol.-Wt. (by titration): 370 ± 2.

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170. Thermolysis of 1,3,4-Oxadiazole-5-ones, a New Precursor of Nitrilimines. A Novel Synthesis of Indazoles

Preliminary communication

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(1. VI. 76)

Summary. Thermolyses of the title compounds at various temperatures have been investigated. At the lower end of the temperature range studied indazoles **5a, b** are formed in nearly quantitative yields, while at the upper end formal carbene-type reaction-products **6, 7, 8** have been isolated in just as high yields.

The most commonly used method of preparation of the highly reactive transient 1,3-disubstituted nitrilimines **3** is based on the facile thermal elimination of nitrogen from the corresponding 1,3-disubstituted tetrazoles **1** [1]. Some of these precursors (**1**) are fairly easily available; however, they all involve preparation and handling of somewhat hazardous azides [2]. An alternative method involves base-induced 1,3-elimination of hydrogen halide from hydrazonoyl halides **2** [2] [3].

The search for new precursors of **3** led us to examine the thermal behaviour of 1,3,4-oxadiazole-5-ones **4**. In spite of being easily accessible and for providing a number of rearrangement possibilities their chemistry has so far been neglected.