73. Synthesis and Copper(I) Complexes of a Series of 9- to 13-Membered N_3 Macrocycles

by **Markus Briellmann, Susan Kaderli, Charles J. Meyer,** and **Andreas D. Zuberbühler***

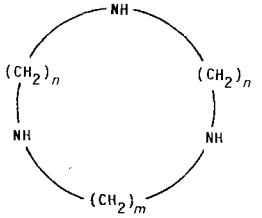
Institut für Anorganische Chemie der Universität, Spitalstr. 51, CH-4056 Basel

(27. I. 87)

Eight cyclic triamines with ring sizes between 9 and 13 were synthesized by the *p*-toluenesulfonate method. The open-chain triamines bis(2-aminoethyl)amine (dien) and bis(3-aminopropyl)amine (diprop) were used as starting materials. In some cases, the corresponding dimeric cyclic hexaamines have been isolated and characterized as major by-products. The complexation of Cu(I) by the triamines has been studied potentiometrically in CH_3CN/H_2O. All ligands L form ternary complexes $[Cu(CH_3CN)L]^+$. The corresponding association constants vary between 10^{11} and 10^7, decreasing with increasing ring size. In addition, complexes $[Cu(CH_3CN)_yLH]^{2+}$, $y = 1$ or 2, are found as less important species with maximum concentrations of 7 to 50%.

Introduction. – The coordination chemistry of tetraazamacrocycles has been studied in great detail. In relation, the analogous triazamacrocycles, suitable for facial coordination, are less well known, although some protonation constants and some stability constants with Cu^{2+}, Ni^{2+}, Zn^{2+}, Cd^{2+}, Pb^{2+}, and Co^{3+} [1–14] have been determined. No equilibrium studies involving Cu^+ as the central atom have been described so far. In the solid state, and especially with π-acceptor ligands, Cu^+ prefers tetrahedral or pseudotetrahedral coordination. This geometry also seems to be important in cuprous enzymes, as has been shown by X-ray analysis, *e.g.* for plastocyanin [15]. In solution, linear 1:2 complexes are more common [16–18], however, with typical donor ligands such as NH_3 and imidazole derivatives. This preference is exemplified, *e.g.*, by the formation of a trimeric species $[Cu_3L_2]^{3+}$ with *cis,cis*-1,3,5-cyclohexanetriamine (chta) where both the ligand (conformation with equatorial substituents) and the Cu^+ ion (linear coordination of 2 amino donors) are in their favorite states [19].

Nevertheless, with tripod-like, facially coordinating ligands, a pyramidal structure may be enforced or at least strongly favored. This leaves a fourth position for easy accommodation of small monodentate ligands. One such example has again been described with chta, where a ternary complex $[Cu(CH_3CN)\cdot chta]^+$ is formed at higher pH [19]. Here, we report on a series of 8 cyclic triaza ligands (**1–8**), which differ in ring size



1 $m = 2, n = 2$, 1,4,7-triazacyclononane
2 $m = 3, n = 2$, 1,4,7-triazacyclodecane
3 $m = 4, n = 2$, 1,4,7-triazacycloundecane
4 $m = 5, n = 2$, 1,4,7-triazacyclododecane
5 $m = 6, n = 2$, 1,4,7-triazacyclotridecane
6 $m = 2, n = 3$, 1,4,8-triazacycloundecane
7 $m = 3, n = 3$, 1,5,9-triazacyclododecane
8 $m = 4, n = 3$, 1,5,9-triazacyclotridecane

and also in the position of the donor atoms in the ring. Ligand protonation and the complexation with Cu^+ have been studied by potentiometric titration in aqueous CH_3CN. A detailed description of the syntheses is included, since only part of the ligands has previously been obtained in pure form.

Experimental. – *Materials and Instrumentation.* The following starting compounds were prepared according to the literature: *N,N*-bis[2-(tosylamino)ethyl]-*p*-toluenesulfonamide (**9**), m.p. 174° ([1]: 173°); *N,N*-bis[3-(tosylamino)propyl]-*p*-toluenesulfonamide (**10**), m.p. 114° ([1]: oil; [9]: 114°); 1,2-ethanediyl bis(*p*-toluenesulfonate) (**11**), m.p. 126° ([20]: 126°); 1,3-propanediyl bis(*p*-toluenesulfonate) (**12**), m.p. 92° ([21]: 92–93°); 1,4-butanediyl bis-(*p*-toluenesulfonate) (**13**), m.p. 81° ([21]:81–82°); 1,5-pentanediyl bis(*p*-toluenesulfonate) (**14**), m.p. 73° ([20]: 79°); 1,6-hexanediyl bis(*p*-toluenesulfonate) (**15**), m.p. 72° ([22]: 71–72°). $[Cu(CH_3CN)_4][BF_4]$ [23] was the source of Cu^+, m.p. 161°. Other chemicals (*Fluka* or *Merck*) were used as obtained. M.p.: *Büchi-510* apparatus; corrected. ^{1}H-NMR spectra: *Varian EM 360* instrument using TMS or sodium 3-(trimethylsilyl)-propanesulfonate as internal standard.

Syntheses. All cyclic triamines **1–8** were synthesized by the *p*-toluenesulfonate method of *Koyama* and *Yoshino* [1], modified by *Richman* and *Atkins* [29]. *N*-Detosylation and purification proved problematic in several cases, however, and not all procedures described in the literature were successful.

a) At 100°, 0.1 mol of the dry disodium salt prepared from the open-chain *N,N*-bis(tosylaminoalkyl)-*p*-toluenesulfonamide and $NaOCH_3$ in dry CH_3OH were dissolved in 0.5 l of DMF under N_2. Then, 0.1 mol of the alkanediyl bis(*p*-toluenesulfonate) were added dropwise within 4 h, and the mixture was let to stand for another 3 h at 100°. The cyclic *N,N',N''*-tritosyl derivative was obtained by adding H_2O up to beginning turbidity in the hot soln., cooling, and filtration. The precipitate was suspended in 0.5 l of boiling CH_3OH and the solvent decanted from a usually viscous paste. This raw product is a complicated mixture of roughly 6 different compounds according to TLC.

b) For the ligands **1, 4, 7,** and **8**, the *N,N',N''*-tritosyl derivative (see *a*) was taken up in EtOH/$CHCl_3$ 4:1 (for **1, 4, 7**) or 3:4 (for **8**), filtered hot from insoluble by-products and recrystallized twice. Of this partially purified material, 25 mmol were detosylated at 120° in 0.5 mol 96% H_2SO_4 under N_2. The soln. was treated with 1.5 mol of NaOH in 200 ml of ice/H_2O, keeping the temp. always below 10°, and extracted with Et_2O (**1**, *Kutscher-Steudel*, 12 h) or several portions of $CHCl_3$ (**4, 7, 8**). The free amines **4, 7,** and **8** were dissolved in dil. HCl soln., treated with activated C, filtered through *Celite (Fluka)*, evaporated, and then recrystallized from H_2O/EtOH/conc. HCl. The diperchlorate of **1** was obtained directly by dissolving the free amine in EtOH, slow addition of a 5-fold excess of 60% $HClO_4$ soln., and washing the crystals with abs. EtOH.

c) With ligands **2, 3, 5,** and **6**, procedure *b*) was not successful. Their *N,N',N''*-tritosyl derivative was dissolved in CH_2Cl_2 and chromatographed on a silica gel *60 (Fluka)* column with CH_2Cl_2/AcOEt 95.5:4.5 (monitoring by UV (λ = 254 nm) in a flow cell). For **3** and **5**, the first separation was incomplete, and the procedure had to be

Table 1. *Cyclisations*

N,N-Bis-(tosylamino)-*p*-toluene-sulfonamide	Alkanediyl bis(*p*-toluene-sulfonate)	Product	Yield [%]	M.p. [°C]	Elemental analyses	C	H	N	O	S
9	**11**	**1**·3Tos	50	220	found[a]):	54.66	5.67	7.09	–	–
			([29]: 71)	([29]: 223)	calc.:	54.80	5.62	7.10	–	–
9	**12**	**2**·3Tos	57	237		–	–	–	–	–
			([29]: 84)	([29]: 234–236)		–	–	–	–	–
9	**13**	**3**·3Tos	38	172	found:	56.37	6.01	7.00	15.55	15.35
			([30]: 81)		calc.:	56.20	6.02	6.78	15.49	15.52
9	**14**	**4**·3Tos	31	173–174	found[a]):	56.5	6.3	6.4	–	–
			([29]: 55)	([29]: 172–173)	calc.:	56.85	6.20	6.63	–	–
9	**15**	**5**·3Tos	23	207	found:	57.55	6.21	6.59	14.70	14.67
			([29]: 50)	([29]: 205–206)	calc.:	57.47	6.38	6.49	14.82	14.85
10	**11**	**6**·3Tos	53	217	found:	56.12	5.96	6.95	15.64	15.36
			([1]: 25)	([1]: 213)	calc.:	56.20	6.02	6.78	15.49	15.52

Table 1 (cont.)

N,N-Bis-(tosylamino)-*p*-toluene-sulfonamide	Alkanediyl bis(*p*-toluene-sulfonate)	Product	Yield [%]	M.p. [°C]	Elemental analyses	C	H	N	O	S
10	**12**	**7**·3Tos	35 ([1]: 8)	171 ([1]: 172)	[a])	– –	– –	– –	– –	– –
10	**13**	**8**·3Tos ·H_2O	45 ([31]: 76; [32]: 33)	220–221 ([31]: 213–214; [32]: 232–235)	found[a]): calc.:	55.80 55.91	6.34 6.50	6.14 6.31	– –	– –
9	**13**	**16**·6Tos	11 ([33]: 25)	261 ([33]: 245–250)	found: calc.:	56.21 56.20	5.79 6.02	6.80 6.78	15.20 15.49	15.24 15.52
9	**15**	**17**·6Tos	3	210	found: calc.:	57.40 57.47	6.26 6.38	6.38 6.49	14.67 14.82	14.64 14.85

[a]) Not purified by column chromatography.

Table 2. *Detosylations*

Product	Reaction time [h]	Yield [%]	M.p. [°C]	^{1}H-NMR (D_2O)	Elemental analyses	C	H	N	Cl
1·2$HClO_4$	30	87	276	3.60 (*s*, 12H, C–CH_2–N)	found: calc.:	21.95 21.83	5.20 5.19	12.50 12.73	21.19 21.48
2·3HCl	26	56	242 ([7]: 239)	2.20 (*quint.*, 2H, C–CH_2–C) 3.35 (*m*, 12H, C–CH_2–N)	found: calc.:	33.29 33.28	8.02 7.98	16.50 16.63	41.52 42.10
3·3HCl[a])	53	78	246	1.95 (*m*, 4H, C–CH_2–C) 3.20 (*t*, 4H, N–CH_2–C–C) 3.50 (*s*[b]), 8H, N–CH_2–C–N)	found: calc.:	36.24 36.04	8.43 8.32	15.90 15.76	39.73 39.89
4·3HCl ·1.5H_2O	91	34	255 ([34]: 230)	1.75 (*m*, 6H, C–CH_2–C) 3.12 (*m*, 12H, N–CH_2–C)	found: calc.:	35.06 35.13	8.51 8.84	13.53 13.65	34.61 34.57
5·3HCl[a])	10	50	261	1.60 (*m*, 4H, C–C–CH_2–C–C) 1.80 (*m*, 4H, C–C–CH_2–C–N) 3.25 (*t*, 4H, N–CH_2–C–C) 3.60 (*s*[b]), 8H, N–CH_2–C–N)	found: calc.:	40.99 40.76	8.92 8.89	14.12 14.26	35.94 36.09
6·3HCl	22	83	247 ([7]: 243)	2.10 (*m*, 4H, C–CH_2–C) 3.25 (*m*, 12H, N–CH_2–C)	found: calc.:	36.08 36.04	8.28 8.32	15.84 15.76	39.61 39.89
7·3HCl	117	58	286 ([7]: 260)	2.10 (*quint.*, 6H, C–CH_2–C) 3.25 (*t*, 12H, N–CH_2–C)	found: calc.:	38.62 38.51	8.32 8.62	14.97 14.97	37.63 37.89
8·3HCl	70	46	282	2.10 (*m*, 8H, C–CH_2–C) 3.25 (*m*, 12H, N–CH_2–C)	found: calc.:	40.78 40.76	8.94 8.89	14.09 14.26	35.89 36.09
16·6HCl·2H_2O		70	266	1.90 (*m*, 8H, C–CH_2–C) 3.25 (*t*, 8H, N–CH_2–C–C) 3.60 (*s*[b]), 16H, N–CH_2–C–N)	found: calc.:	34.07 33.75	8.43 8.49	14.83 14.76	37.66 37.36
17·6HCl·H_2O		83	298	1.55 (*m*, 8H, C–C–CH_2–C–C) 1.80 (*m*, 8H, C–C–CH_2–C–N) 3.20 (*t*, 8H, N–CH_2–C–C) 3.60 (*s*, 16H, N–CH_2–C–N)	found: calc.:	39.62 39.54	9.10 8.96	13.93 13.83	34.89 35.02

[a]) ^{1}H-NMR in 1M DCl/D_2O.
[b]) Theoretically, 2 nearly identical *t*.

repeated for the middle fractions. The purified *N,N',N''*-tritosyl derivative was crystallized from CH_2Cl_2/EtOH, subsequently detosylated as under *b*), and the free amine extracted with Et_2O as for **1**, omitting the treatment with activated C and filtration through *Celite*.

From the cyclisation mixtures of **9** with **13** and **15**, a second substance was isolated which could not be distinguished from the *N,N',N''*-tritosyl derivatives of **3** and **5**, resp., by NMR or elemental analysis, but differed in the m.p. and on TLC (R_f). It was shown by fast atom bombardment (FAB) mass spectroscopy that these more slowly eluting materials were the hexatosylated dimers **16** and **17** of **3** and **5**. They were detosylated and recrystallized as the hexachlorides from H_2O/EtOH/conc. HCl.

Yields, m.p., elemental analyses, detosylation times, and ^{1}H-NMR characteristics are collected in *Tables 1* (cyclisation) and *2* (detosylation).

Measurements. – The protonation constants of the ligands and the stability constants of the complexes were determined by potentiometric titration with 0.4M NaOH under N_2. The experiments were done at 20.0 ± 0.1° and at an ionic strength of 0.2M (Na_2SO_4). Instrumentation and programs used for data acquisition and data reduction have been described elsewhere [24] [25]. Titration curves were obtained at overall ligand concentrations (c_L) of 0.002 and 0.004M (**1**, **2**) or 0.001 and 0.002M (**3–8**). The metal concentrations (c_M) were 40% and 25% of c_L. In order to prevent precipitation of Cu_2O or disproportionation of Cu^+, 1, 2, or 4% (*v/v*) CH_3CN were added. All experiments were done in duplicates. For the calculation of the complex formation constants, the titration curves were collected into 2 batches for every concentration of CH_3CN, and the model function was fitted to all curves of one batch simultaneously. The formation constants presented here are the weighted means of 2 corresponding batch calculations.

For several ligands, deprotonation of LH_3^{3+} to LH_2^{2+} or of LH^+ to L could not be followed potentiometrically since the corresponding reactions take place in strongly acidic (pH < 3) or basic (pH > 11) solutions. In these cases, an ^{1}H-NMR method [26] [27], based on the chemical shifts of the methylene H-atoms adjacent to the N-atom(s) in question, was applied. To obtain the fully protonated and deprotonated species, 6M DCl and 4M NaOD were used, resp., dioxane served as internal standard. Protonation constants K^H were calculated through least-squares fit based on *Eqn. 1* where δ_A and δ_B are

$$\delta = (\delta_A [H^+] + \delta_B K^H) / ([H^+] + K^H) \quad (1)$$

the chemical shifts of corresponding acidic and basic species (LH_3 and LH_2 or LH and L, resp.). Protonation constants obtained by ^{1}H-NMR, thus, are based on a pD rather than pH scale. Despite the availability of suggestions for relating pD to pH [28], no such corrections were applied since the relative deuterium effect on the solvent and the ligand would be difficult to judge, and since the corresponding protonation constants agreed quite well, when a determination was done by both methods (see below).

Results and Discussion. – The cyclic triamines **1–8** could all be synthesized by the general *p*-toluenesulfonate method of *Richman* and *Atkins* [29] [30], but the workup proved to be rather problematic. Reported yields of 70–85% [29–31] could be verified for the cyclisation step, but related only to raw products, which typically consisted of at least 6 compounds according to TLC. The average yield of purified or partially purified material was only 42%, however, ranging between 23 and 57%, *cf. Table 1*. Purification at the stage of the *N,N',N''*-tritosyl derivatives was essential since the free cyclic amines could not be easily separated from large amounts of by-products. For ligands **1**, **4**, **7**, and **8**, recrystallisation of the tosyl derivatives preceded by filtration from insoluble materials was sufficient, at the cost of a more complicated workup of the detosylated amines. The

other 4 compounds had to be purified by column chromatography prior to detosylation. In this process, the hexatosyl derivatives **16** and **17**, *i.e.* the dimeric analogs of **3** and **5**, were also isolated and transformed into the corresponding hexaamines. The problem of by-products in the *Richman-Atkins* synthesis and the formation of dimeric compounds has been addressed before [11] [35] [36], but the dimeric hexaamines or other by-products have not been actually worked up so far. While only the two compounds **16** and **17** have been isolated in the present study, it seems very likely that the same would have been possible for the other ligands, perhaps with the exception of **1** and **2** where there was no indication of larger amounts of dimers. Some analogous macrocyclic hexaamines have been synthesized before [33] [37], but based on specific multistep syntheses. It seems possible that, after appropriate optimisation, the present way would yield a just as efficient, but much more simple access to this general class of hexaamines. As is shown in *Table 2*, most of the cyclic amine hydrochlorides have not been isolated in pure form so far. Either they have not been described at all (**3**, **5**, **8**, **16**, **17**) or considerably lower m.p. are indicating a mixture of species (**4**, **7**). In addition, heterogeneity of earlier preparations of **2** has been revealed by spectroscopic titration of the Cu^{2+} complexes [38]. Thus, only compounds **1** and **6** seem to have been reasonably free from by-products before.

Protonation Constants of the Cyclic Triamines. They are summarized in *Table 3*. For discussion, the ligands are conveniently grouped into two sets, **1–5** being derived from

Table 3. *Ligand Protonation Constants and Standard Deviations of the Cyclic Triamines* **1–8** *at 20° and* I = *0.2* M (Na_2SO_4). Weighted mean of determinations in aqueous solutions with 1, 2, or 4% *(v/v)* CH_3CN.

Ligand	$\log K^H_{LH}$	($\sigma_{\log K}$)	$\log K^H_{LH_2}$	($\sigma_{\log K}$)	$\log K^H_{LH_3}$	($\sigma_{\log K}$)
1	*11.03*	(0.02)	*7.37*	(0.02)	*0.7*[a])	
	10.42[b])		6.82[b])		–[b])	
	10.59[c])		6.88[c])		–[c])	
2	*13.2*[d])		*6.96*	(0.01)	*0.1*[a])	
	12.02[b])[e])		6.59[b])		–[b])	
	10.85[c])		6.76[c])		–[c])	
3	*13.2*[a])		*6.94*	(0.01)	*–0.4*[a])	
	11.96[b])[e])		7.61[b])		–[b])	
4	*11.53*	(0.01)	*8.95*	(0.01)	*0.2*[a])	
5	*10.98*	(0.01)	*9.50*	(0.01)	*0.9*[a])	
6	*12.8*[a])		*8.03*	(0.01)	*0.2*[a])	
7	*12.7*[d])		*7.99*	(0.01)	*3.30/3.2*[a])	(0.01)
	12.60[b])[e])		7.57[b])		2.41[b])	
8	*12.2*[a])		*8.79*	(0.01)	*4.76*	(0.01)
	9.79[f])		8.13[f])		4.18[f])	
dien	10.18[g])		9.41[g])		4.83[g])	
diprop	10.65[h])		9.57[h])		7.72[h])	

[a]) From ^{1}H-NMR measurements, estimated uncertainty 0.2 log units.
[b]) From [7].
[c]) From [8].
[d]) The $\log K^H_{LH}$ for **2** and **7** taken from [26] [27] were interchanged because of wrong assignment in the original work.
[e]) Special potentiometric method.
[f]) From [3].
[g]) From [43].
[h]) From [44].

diethylenetriamine (dien) and **6–8** from bis(3-aminopropyl)amine (diprop). For both sets, only the second protonation is typical for chelating aliphatic amines with $\log K^{H}_{LH_2}$ values between 7 and 10. In relation, the first protonation is unusually strong ($\log K^{H}_{LH} = 11 - 13.2$), the third one extremely weak, $\log K^{H}_{LH_3} < 3$, with the exception of **7** and **8**. High and low $\log K^{H}$ values were determined by ^{1}H-NMR. With **7**, $\log K^{H}_{LH_3}$ was obtained both by ^{1}H-NMR and potentiometrically, and the results (3.2 and 3.30, resp.) compare quite well, taking into account the uncertainties of the ^{1}H-NMR approach and the change of pH to pD. High $\log K^{H}_{LH}$ values have been observed before with other cyclic polyamine ligands such as 1,4,8,11-tetraazacyclotetradecane ($\log K^{H}_{LH} = 11.5$ [39] or 11.83 [40]) or with 2,2,4,10,10,12-hexamethyl-1,5,9,13-tetraazacyclohexadecane ($\log K^{H}_{LH} = 12.2$ [41]). The extra stabilisation of LH^+ has been explained by the formation of intramolecular H-bonds [26] [42].

There is some general trend of decreasing $\log K^{H}_{LH}$ with increasing ring size in the two sets **1–5** and **6–8**, but the effect is not very strong in the latter. A noticeable exception is given by **1** whose first protonation is practically equal to that of **5**, although the C-chain used for cyclisation differs by 4 units in the two ligands. The basicity of L with **1** approaches that of aliphatic amines, a fact which has been ascribed to the inability of **1** to form optimum H-bonds [42].

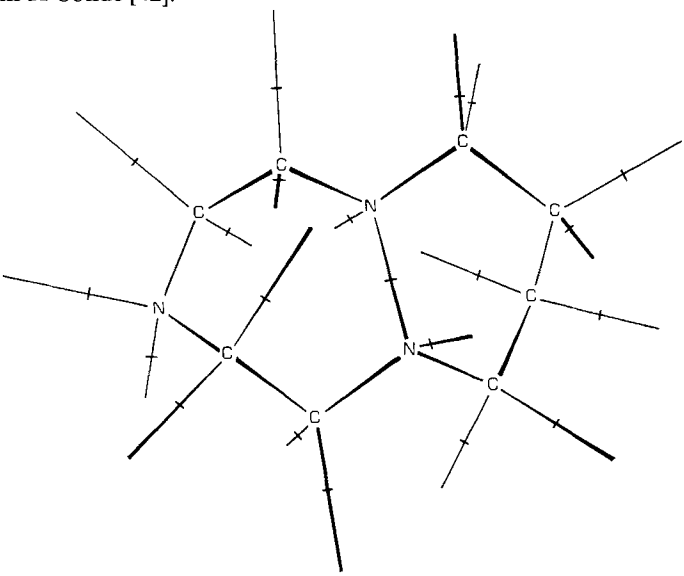


Fig. 1. *Molecular model of H-bonded species LH_2 of* **3**. Hydrogen *van der Waals* radii are indicated. LH is obtained by deprotonation of the non-bridgehead N-atom. The dash | indicates estimated position of H-atoms.

Hydrogen bonding in LH_2 must be an important factor in the relative instability of LH_3. The values of $\log K^{H}_{LH_3}$ pass a significant minimum for the 11-membered ligand **3**. As is shown in *Fig. 1*, an ideal H-bond is possible with this ligand for both LH_2 and LH.

Inspection of molecular models showns that the situation is not nearly as good with any other ligand of set **1–5** and that a linear H-bond is quite impossible in LH_2 of **1**. It is, therefore, concluded that the extremely low $\log K^{H}_{LH_3}$ and high $\log K^{H}_{LH}$ are due to specific

stabilisation of LH_2 and LH by H-bonding and not primarily to the instability of LH_3 and L, resp. Of course, this effect is supplemented by changes in electrostatic repulsion in LH_3 and LH_2 with varying ring size. One would expect that with sufficiently long C-chains, the $\log K^H$ values would approach those of the corresponding open-chain amines. The results compiled in *Table 3* are supporting this assumption, but the limiting values of dien and diprop are not actually reached for $\log K^H_{LH_3}$ and $\log K^H_{LH}$.

Values for some of the protonation constants have already been described in the literature. As may be concluded from *Table 3*, reported values compare well with the present results in a very few cases only. Some of the deviations (0.1–0.5 log units) may be correlated with differences in experimental parameters such as temperature and ionic strength. Other discrepancies, especially low values for $\log K^H_{LH}$ (**2**: 10.85 [8]; **3**: 11.96 [7]; **8**: 9.79 [32] and $\log K^H_{LH_3}$ (**7**: 2.41 [7]) are ascribed to the inadequacy of the potentiometric method used by these authors, at the extremes of the pH scale. If part of the problems should be traced to dimeric impurities in older preparations (see above), this cannot be ruled out at the moment.

Complex Formation Constants. With all ligands, we could observe species of the general formula $[Cu(CH_3CN)_xL]^+$ and $[Cu(CH_3CN)_yLH]^{2+}$ *(Table 4)*. The number of CH_3CN bound to the complexes, x and y, can be derived from the apparent equilibrium constants $K^*_{[CuL]}$ *(Eqn. 2)* and $K^*_{[CuLH]}$ *(Eqn. 3)*, respectively, determined at different CH_3CN concentrations.

$$Cu^+_{tot} + LH^+ \rightleftharpoons [CuL]^+_{tot} + H^+ \colon K^*_{[CuL]} \tag{2}$$

$$Cu^+_{tot} + LH^+ \rightleftharpoons [CuLH]^{2+}_{tot} \colon K^*_{[CuLH]} \tag{3}$$

$$[Cu^+_{tot}] = \sum_{i=0}^{3} [[Cu(CH_3CN)_i]^+]; \quad [[CuL]^+_{tot}] = \sum_{i=0}^{2} [[Cu(CH_3CN)_iL]^+];$$

$$[[CuLH]^{2+}_{tot}] = \sum_{i=0}^{2} [[Cu(CH_3CN)_iLH]^{2+}]$$

With the formation constants of the Cu^+/CH_3CN complexes ($\log K_1 = 3.28$ [45], $\log\beta_2 = 4.35$ [46], $\log\beta_3 = 4.39$ [47]), $\Delta\log K = \log K^*_{1\%} - \log K^*_{2\%}$ (0.60, 0.30, and 0 for 0, 1, and 2 CH_3CN, resp., bound per Cu^+) and $\Delta\log K = \log K^*_{2\%} - \log K^*_{4\%}$ (0.68, 0.38, and 0.07 for 0, 1, and 2 CH_3CN, resp.) can be calculated [19] [48] from the CH_3CN-dependent constants of *Eqn. 2* and *3* obtained at different $[CH_3CN]$ (1, 2, or 4%). Once the number of bound CH_3CN is known, the CH_3CN-independent constants $K_{[Cu(CH_3CN)_xL]}$ *(Eqn. 4)* and $K_{[Cu(CH_3CN)_yLH]}$ *(Eqn. 5)* may be derived.

$$[Cu(CH_3CN)_x]^+ + L \rightleftharpoons [Cu(CH_3CN)_xL]^+ \colon K_{[Cu(CH_3CN)_xL]} \tag{4}$$

$$[Cu(CH_3CN)_y]^+ + LH^+ \rightleftharpoons [Cu(CH_3CN)_yLH]^{2+} \colon K_{[Cu(CH_3CN)_yLH]} \tag{5}$$

Some of the $\Delta\log K$ are relatively far from the theoretical values (*cf. Table 4*). This either reflects experimental uncertainties in the underlying $\log K^*$ or points to a mixture of ternary complexes with different numbers of bound CH_3CN. The correct explanation is not generally obvious, but for the well defined species $[Cu(CH_3CN)_xL]^+$, experimental errors are less likely than for the complexes $[Cu(CH_3CN)_yLH]^{2+}$ which are formed with maximum concentrations between 7 (**4**) and 50% (**1**) under our conditions. With each ligand, $[Cu(CH_3CN)_xL]^+$ is the main species. It is formed above pH 6–8, while $[Cu(CH_3CN)_yLH]^{2+}$ is formed between pH 5 and 9.

Table 4. *Formation Constants and Standard Deviations of the Cu^+ Complexes with* **1–8** *in Aqueous CH_3CN*

Ligand	$\log K^*_{[CuL]}$		$\Delta\log K$[a])	No. of CH_3CN (x)	$\log K_{[Cu(CH_3CN)_xL]}$ ($\sigma_{\log K}$)
	2% CH_3CN	4% CH_3CN			
1	−1.02 (0.03)	−0.57 (0.01)[b])	0.45[c])	1 (0)	10.93 (0.08)
2	−3.20 (0.01)[d])	−3.63 (0.01)[d])	0.43	1	10.85 (0.03)[e])
3	−5.05 (0.01)	−5.42 (0.04)	0.37	1	9.05 (0.01)[e])
4	−3.08 (0.02)	−3.50 (0.02)	0.42	1	9.29 (0.03)
5	−4.20 (0.02)	−4.67 (0.01)	0.47[c])	1 (0)	7.56 (0.02)
6	−3.29 (0.01)	−3.71 (0.01)	0.42	1	10.33 (0.02)[e])
7	−5.13 (0.01)	−5.46 (0.01)	0.33	1	8.46 (0.01)[e])
8	−4.92 (0.01)	−5.28 (0.01)	0.36	1	8.14 (0.01)[e])

Ligand	$\log K^*_{[CuLH]}$		$\Delta\log K$[a])	No. of CH_3CN (y)	$\log K_{[Cu(CH_3CN)_yLH]}$ ($\sigma_{\log K}$)
	2% CH_3CN	4% CH_3CN			
1	4.80 (0.04)	4.98 (0.05)[b])	0.18[c])	1 (2)	5.63 (0.06)
2	2.55 (0.06)[d])	2.53 (0.05)[d])	0.02	2	2.80 (0.03)
3	2.37 (0.09)	2.25 (0.04)	0.12	2	2.55 (0.04)
4	3.60 (0.03)	3.18 (0.04)	0.42	1	4.45 (0.02)
5	3.59 (0.08)	3.16 (0.06)	0.43	1	4.43 (0.05)
6	3.56 (0.02)	3.34 (0.01)	0.22[c])	1 (2)	4.50 (0.08)
7	2.56 (0.02)	2.48 (0.03)	0.08	2	2.78 (0.01)
8	2.81 (0.06)	2.54 (0.03)	0.27[c])	1 (2)	3.76 (0.04)

[a]) $\Delta\log K = \log K^*_{2\%} - \log K^*_{4\%}$ or $\log K^*_{1\%} - \log K^*_{2\%}$.
[b]) With 1% CH_3CN instead of 4% CH_3CN.
[c]) $\Delta\log K$ may point to a mixture of two species.
[d]) From single batch only.
[e]) Neglecting uncertainty of $\log K^H_{LH}$ (^{1}H-NMR results).

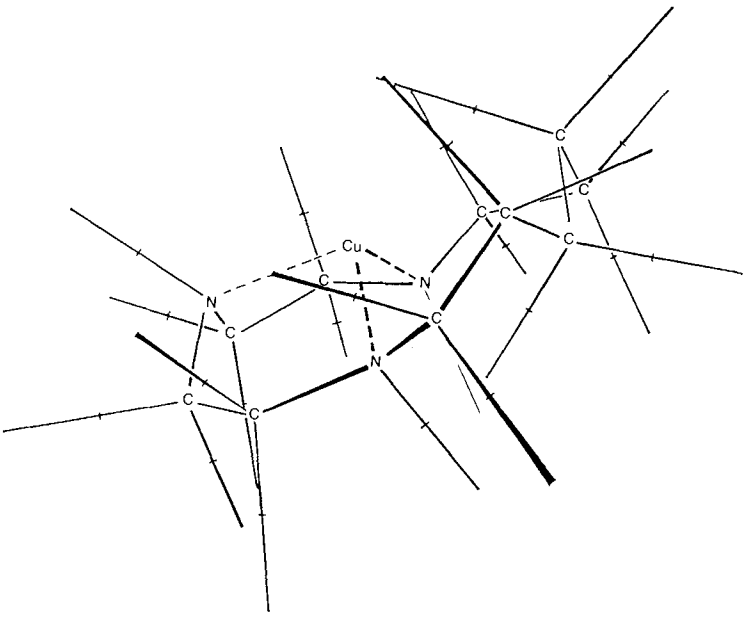


Fig. 2. *Molecular model of $[CuL]^+$ from* **5**, *indicating crowding at fourth coordination site*

With the fully deprotonated ligands L, the ternary 1:1:1 complexes $[Cu(CH_3CN)_xL]^+$ ($x = 1$) are predominant in each case. For ligands **1** and **5**, *i.e.* the compounds derived from dien containing the shortest and the longest C-chain, resp., there is indication of a binary complex $[CuL]^+$ without CH_3CN. $\Delta \log K$ values of 0.37, 0.42, and 0.47 for **3**, **4**, and **5**, respectively, might point to a decreasing CH_3CN-binding capacity with increasing ring size. This would fit well with a corresponding increase in planarity and steric crowdance as is implied by molecular models. As is shown in *Fig.2*, the H-atoms of the C_6-chain in the complex with **5** would seem to interfere strongly with any bound CH_3CN at the fourth coordination site, but the data are not sufficient for definite conclusions. As for the ligand protonation constants, the result with **1** does not fit well with the other members of the set, considering that $\Delta \log K = 0.30$ would be expected for **1**, but $\Delta \log K = 0.38$ for the other ligands in complexes with 1 CH_3CN. Most likely, this is again due to the special situation with this rather small macrocycle.

For $[Cu(CH_3CN)_yLH]^{2+}$, a similar trend as for $[Cu(CH_3CN)_xL]^+$ can be observed with the ligands **2–5**: The number of CH_3CN is 2 with the smaller rings (**2**, **3**) but only 1 with the larger ones (**4**, **5**). Again, the species with ligand **1** is an exception. With the ligands **6–8**, 1 or 2 CH_3CN are bound in $[Cu(CH_3CN)_yLH]^{2+}$, and no specific trend is observed. No binary complexes $[Cu(LH)]^{2+}$ without CH_3CN are indicated by the results of *Table 4*.

The stability of $[Cu(CH_3CN)L]^+$ decreases with increasing ring size of the ligands. This can be observed with the ligands of both sets (**1–5** and **6–8**). The stabilities are significantly higher than for the 1:1 complexes $[CuL]^+$ with NH_3 ($\log K_{[CuL]} = 5.93$) [49], or imidazole ($\log K_{[CuL]} = 5.78$ [50]) or with substituted imidazoles ($\log K_{[Cu(CH_3CN)L]} = 4.7 - 5.0$) [18]. This high stability implies a trigonal pyramidal structure for $[Cu(CH_3CN)L]^+$ with **1–8**. Inspection of molecular models shows that a bidentate coordination is unlikely. Either the third amino group is rather near the metal ion or the complex is in an unfavourable conformation.

Comparing ligands with identical ring size but different position of the amino groups (*i.e.* **3** with **6**, **4** with **7**, and **5** with **8**) does not reveal any consistent trend. No special preference can, therefore, be implied for Cu^+ for either 5- or 6-membered chelates in pyramidal complexes of the type proposed here.

The stabilities of all species $[Cu(CH_3CN)_yLH]^{2+}$ are much smaller, with no obvious trend. Interpretation of the results is complicated by the varying number of CH_3CN ($y = 1$ or 2) bound in the complexes. The values of $\log K_{[Cu(CH_3CN)LH]}$ are of the same order as those of the complexes $[Cu(CH_3CN)L]^+$ with monodentate N-donors [18] [19] for which a linear structure has been proposed. Chelate formation is theoretically possible of course for $[Cu(CH_3CN)LH]^{2+}$ and $[Cu(CH_3CN)_2LH]^{2+}$, but the protonated uncomplexed amino group would have to be rather close, leading to unfavourable electronic repulsion. A linear structure is, therefore, postulated throughout for $[Cu(CH_3CN)LH]^{2+}$, and a trigonal planar coordination, as established for crystalline Cu^+ amine complexes [51], is assumed for $[Cu(CH_3CN)_2LH]^{2+}$.

Financial support by the *Swiss National Science Foundation* (grant No. 2.357-085) is gratefully acknowledged. We thank the *Ciba-Geigy AG* for the FAB spectra (*F. Raschdorf* and *R. Dahinden*) and for the elemental analyses.

REFERENCES

[1] H. Koyama, T. Yoshino, *Bull. Chem. Soc. Jpn.* **1972,** *45,* 481.
[2] M.S. Okamoto, E.K. Barefield, *Inorg. Chim. Acta* **1976,** *17,* 91.
[3] R. Yang, L.J. Zompa, *Inorg. Chem.* **1976,** *15,* 1499.
[4] M. Nonoyama, *Trans. Met. Chem.* **1976,** *1,* 70.
[5] M. Nonoyama, *Inorg. Chim. Acta* **1976,** *20,* 53.
[6] M. Kodama, E. Kimura, *J. Chem. Soc., Dalton Trans.* **1977,** 1474.
[7] L. Zompa, *Inorg. Chem.* **1978,** *17,* 2531.
[8] M. Kodama, E. Kimura, *J. Chem. Soc., Dalton Trans.* **1978,** 1081.
[9] T.J. Riedo, Dissertation, Basel, 1979.
[10] K. Wieghardt, W. Schmidt, B. Nuber, J. Weiss, *Chem. Ber.* **1979,** *112,* 2220.
[11] M.E. Angley, M. Dwyer, S.F. Lincoln, G.H. Searle, R.J. Geue, F.R. Keene, *Inorg. Chim. Acta* **1980,** *45,* L91.
[12] M. Kodama, T. Yatsunami, E. Kimura, *Inorg. Chem.* **1980,** *19,* 1600.
[13] P.G. Graham, D.C. Weatherburn, *Aust. J. Chem.* **1981,** *34,* 291.
[14] P.G. Graham, D.C. Weatherburn, *Aust. J. Chem.* **1984,** *37,* 2243.
[15] P.M. Colman, H.C. Freeman, J.M. Guss, M. Murata, V.A. Norris, J.A.M. Ramshaw, P. Venkatappa, *Nature (London)* **1978,** *272,* 319.
[16] A.D. Zuberbühler, *Helv. Chim. Acta* **1967,** *50,* 466.
[17] A.D. Zuberbühler, *Chimia* **1969,** *23,* 416.
[18] M. Güntensperger, A.D. Zuberbühler, *Helv. Chim. Acta* **1977,** *60,* 2584.
[19] Z. Szeverényi, U. Knopp, A.D. Zuberbühler, *Helv. Chim. Acta* **1982,** *65,* 2529.
[20] R. Gerdill, *Helv. Chim. Acta* **1973,** *56,* 1859.
[21] T.M. Laakso, D.D. Reynolds, *J. Am. Chem. Soc.* **1951,** *73,* 3518.
[22] F. Drahowzal, D. Klamann, *Ann. Chem.* **1951,** *82,* 460.
[23] Ger. Pat. 1230025 (*Chem. Abstr.* **1967,** *66,* 46487e).
[24] H.Gampp, M. Maeder, A.D. Zuberbühler, T.A. Kaden, *Talanta* **1980,** *27,* 513.
[25] A.D. Zuberbühler, T.A. Kaden, *Talanta* **1982,** *29,* 201.
[26] T.J. Riedo, T.A. Kaden, *Chimia* **1977,** *31,* 220.
[27] T.J. Riedo, T.A. Kaden, *Helv. Chim. Acta* **1979,** *62,* 1089.
[28] R.G. Bates, 'Determination of pH', J. Wiley Interscience, New York, 1979.
[29] J.E. Richman, T.J. Atkins, *J. Am. Chem. Soc.* **1974,** *96,* 2268.
[30] T.J. Atkins, J.E. Richman, W.F. Oettle, *Org. Synth.* **1978,** *58,* 86.
[31] F.L. Weitl, K.N. Raymond, *J. Am. Chem. Soc.* **1979,** *101,* 2728.
[32] E. Kimura, T. Yatsunami, *Chem. Pharm. Bull.* **1980,** *28,* 994.
[33] A.E. Martin, T.M. Ford, J.E. Bulkowsky, *J. Org. Chem.* **1982,** *47,* 412.
[34] J.E. Richman, Offenlegungsschrift 2447279, BRD, 1975.
[35] T.N. Margulis, L.J. Zompa, *J. Chem. Soc., Chem. Commun.* **1979,** 430.
[36] G.H. Searle, R.J. Geue, *Aust. J. Chem.* **1984,** *37,* 959.
[37] J. Comarmond, P. Plumeré, J.-M. Lehn, Y. Agnus, R. Louis, R. Weiss, O. Kahn, I. Morgenstern-Badarau, *J. Am. Chem. Soc.* **1982,** *104,* 6330.
[38] T.A. Kaden, S. Kaderli, A.D. Zuberbühler, in preparation.
[39] F.P. Hinz, D.W. Margerum, *Inorg. Chem.* **1974,** *13,* 2941.
[40] A.P. Leugger, L. Hertli, T.A. Kaden, *Helv. Chim. Acta* **1978,** *61,* 2296.
[41] A.P. Leugger, Dissertation, Basel, 1977.
[42] R.W. Renfrew, R.S. Jamison, D.C. Weatherburn, *Inorg. Chem.* **1979,** *18,* 1584.
[43] H. Gampp, H. Sigel, A.D. Zuberbühler, *Inorg. Chem.* **1982,** *21,* 1190.
[44] A. Vacca, D. Arenare, P. Paoletti, *Inorg. Chem.* **1966,** *5,* 1384.
[45] A. Günter, A.D. Zuberbühler, *Chimia* **1970,** *24,* 340.
[46] P. Hemmerich, C. Sigwart, *Experientia* **1963,** *19,* 488.
[47] A.D. Zuberbühler, *Helv. Chim. Acta* **1970,** *53,* 473.
[48] K.P. Balakrishnan, T.A. Kaden, L. Siegfried, A.D. Zuberbühler, *Helv. Chim. Acta* **1984,** *67,* 1060.
[49] J. Bjerrum, *Kgl. Danske Videnskab Selskab, Mat-Fys. Medd.* **1934,** *12* No. 15.
[50] C.J. Hawkins, D.D. Perrin, *J. Chem. Soc.* **1962,** 1351.
[51] K.D. Karlin, Y. Gultneh, J.P. Hutchinson, J. Zubieta, *J. Am. Chem. Soc.* **1982,** *104,* 5240.