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Ternary Complexes in Solution. 50.[1] Dependence of Intramolecular Hydrophobic Ligand–Ligand Interactions on Ligand Structure, Geometry of the Coordination Sphere of the Metal Ion, and Solvent Composition. Opposing Solvent Effects

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Received February 24, 1988

Stability constants of mixed-ligand M(phen)(*i*-AlCA)$^+$ complexes [M = Cu^{2+}, Zn^{2+}; phen = 1,10-phenanthroline; *i*-AlCA$^-$ = 2-methylpropionate (2-MPr$^-$), 3-methylbutyrate, 4-methylvalerate, 5-methylhexanoate, 6-methylheptanoate (6-MHp$^-$)] have been determined by potentiometric pH titration in aqueous solution and in 50% (v/v) ethanol–water or dioxane–water and compared with the stabilities of the corresponding formate or acetate complexes. The ternary complexes containing isoalkanecarboxylates (*i*-AlCA$^-$) are significantly more stable due to intramolecular hydrophobic interactions between the alkyl residue of the *i*-AlCA$^-$ ligands and the phen molecule. These intramolecular hydrophobic interactions have been confirmed by ^{1}H NMR shift measurements in water and 50% (v/v) ethanol–water for the whole series of the Zn(phen)(*i*-AlCA)$^+$ complexes. The formation degree of the intramolecular hydrophobic adducts in the Cu^{2+} and Zn^{2+} complexes (closed species) was calculated, and the position of the intramolecular equilibrium between the opened and closed forms was determined: the closed forms occur between a trace percent and about 50%, depending on the geometry of the coordination sphere of the bridging metal ion (Cu^{2+}, tetragonal; Zn^{2+}, tetrahedral or octahedral), on the number of methylene units between the isopropyl residue and the coordinating carboxylate group (i.e., on the size of the alkyl moiety), and on the solvent composition. The influence of the solvent composition has been further studied by measuring the complex stabilities for M(phen)(2-MPr)$^+$ and M(phen)(6-Mhp)$^+$ (M = Cu^{2+}, Zn^{2+}) in water and in 30–90% (v/v) ethanol–water. There are indications, and these are discussed, that the structure of the closed species is solvent-dependent: in water, a "simple" (though not rigid) intramolecular hydrophobic ligand–ligand adduct is formed, while in the mixed solvents, in addition, probably a series of structurally somewhat different closed species (orientation of the ligand moieties, degrees of solvation, intercalated organic solvent molecules, etc.) may occur. As there is at present no way to identify with certainty such different structures, the whole observed stability increase between M(phen)(*i*-AlCA)$^+$ and M(phen)(Ac)$^+$ or M(phen)(HCOO)$^+$ was simply attributed to a (single) so-called "closed" species. The formation degree of the closed species is influenced by the solvent: *addition of some ethanol (or dioxane) to an aqueous solution favors their formation*, contrary to the experience with simple unbridged hydrophobic adducts, which are destabilized. Such a destabilization of the closed ternary species occurs only at high concentrations of the organic solvent (usually more than 70%). It should be noted that the overall stability of the interaction between M^{2+} and *i*-AlCA$^-$ is governed by the polarity of the solvent, while the position of the intramolecular equilibrium is influenced by the hydrophobic solution properties of the solvent molecules. The relevance of the present results with regard to biological systems is indicated.

Introduction

Hydrophobic interactions determine in part the selectivity as observed in biological systems, and great efforts are made to understand and to quantify hydrophobic effects. These efforts encompass a wide variety of approaches, like model studies,[3,4] evaluation of distances between relevant groups in proteins,[5,6] protein engineering,[7] and many kinds of theoretical considerations.[8-11] Intramolecular hydrophobic interactions in metal ion complexes have so far received much less attention, though, e.g., in the active center of many proteins a metal ion like $Cu^{+/2+}$, Zn^{2+}, or Ca^{2+} (cf. ref 12–14) is located, and it has been shown that metal ion bridging is promoting the interaction between suitable hydrophobic residues, e.g., of amino acids.[15-17]

The ligand 1,10-phenanthroline (phen) has proved especially suitable for model studies in the presence of metal ions because the hydrophobic interaction between its aromatic ring system and alkyl chains is quite pronounced; e.g., M(phen)$_3^{2+}$ forms 1:1 aggregates with cationic surfactants containing long alkyl chains[18] and also (of a larger stability) with anionic 1-alkanesulfonates[19] or dodecyl sulfate.[20] The effects operating here are certainly also of importance in M(phen)$^{n+}$/nucleic acid interactions.[21] Again, by the formation of a direct link between phen and an alkyl residue as in M(phen)(valerate)$^+$ complexes,[22] the hydrophobic interaction may be promoted. This type of structural interaction allows also an intramolecular shielding of charge-transfer excited states of rhenium(I) photosensitizers.[23]

To learn more about the factors that govern and determine the extent of intramolecular hydrophobic ligand–ligand interactions, we initiated a comprehensive study that involves the components shown in Figure 1. The indicated series of isoalkanecarboxylates (*i*-AlCA$^-$)[24] allows a systematic variation of the overall size of

(1) Part 49: Tribolet, R.; Martin, R. B.; Sigel, H. *Inorg. Chem.* **1987**, *26*, 638–643.
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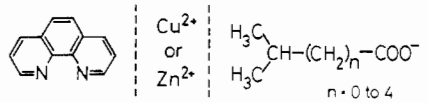

Figure 1. Metal ions and ligands used in this study.

the alkyl residue, as well as of the distance between the isopropyl moiety and the coordinating carboxylate group. Both properties, overall size and distance, are expected to influence the extent of the interaction. Similarly, the geometry of the coordination sphere of the bridging metal ion is also expected to have an influence: Cu^{2+} has a tetragonal coordination sphere allowing four equatorial and nearby donor atoms and possibly one or two more distant axial donors, while Zn^{2+} has a tetrahedral or octahedral geometry. Indeed, these differences are reflected in the stability of those ternary complexes that involve short-chain alkanecarboxylates; in these cases differences in the overlap of the hydrophobic groups are enforced.

Another aspect in the focus of this study is the influence of organic solvents on the extent of the intramolecular hydrophobic ligand–ligand interactions. It is now well established that the "equivalent solution" or "effective" dielectric constant is lower in an active-site cavity of an enzyme than in water.[25,26] It is also known that addition of organic solvents like ethanol or dioxane to an aqueous solution not only reduces the polarity of the solvent but also inhibits hydrophobic and stacking interactions in unbridged binary adducts.[27,28] That this may be quite different in metal ion bridged stacks was shown recently[28] for the ternary complexes formed by phen, Cu^{2+} or Zn^{2+}, and 2-phenylacetate or 3-phenylpropionate; certain amounts of dioxane or ethanol favor the intramolecular ligand–ligand interaction. Similar observations have been made now also for the hydrophobic interactions of isoalkanecarboxylates.

Experimental Section

Materials. 2-Methylpropionic acid and 3-methylbutyric acid were from Fluka AG, Buchs, Switzerland. 4-Methylvaleric acid was purchased from BDH Chemicals Ltd, Poole, England, and 5-methylhexanoic acid and 6-methylheptanoic acid were obtained from ICN Pharmaceuticals Inc., Plainview, NY. All these ligands were purchased in the highest purity available. Ethanol (absolute; pro analysi) and 1,4-dioxane (extra pure) were obtained from Merck AG, Darmstadt, FRG. All other reagents were the same as used in ref 29; the stock solutions were also prepared as described.[29]

Potentiometric pH Titrations. The pH titrations were carried out at 25 °C and an ionic strength (I) of 0.1 M ($NaNO_3$) under a nitrogen atmosphere with Metrohm potentiograph E536, dosimat E535, and macro EA 121 glass electrodes. The buffers (pH 4.64 and 7.00) used for calibration were also from Metrohm AG, Herisau, Switzerland. The direct pH-meter readings were used in the calculations for the acidity constants; no "corrections" were applied for the change in solvent from water to aqueous dioxane or ethanol, though correction factors have been published[30] for both solvent mixtures.[31]

The determination of the equilibrium constants, including their calculation, was carried out as described recently:[29] 50 mL of 0.2 mM HNO_3 was titrated in the presence and absence of 0.6 mM (or in some cases 0.45 mM) carboxylic acid with 1 mL of 0.05 M NaOH. This means, always a pair of titration curves obtained by titrating corresponding solutions in the presence and absence of ligand was evaluated; in other words, the titration curve of the strong acid (HNO_3) was not calculated but each time again experimentally determined. In the case of formic acid (as well as with several of the other carboxylic acids), several of the titrations were carried out by titrating 50 mL of 0.9 (or 1.8) mM HNO_3 in the presence and absence of 0.6 mM carboxylate with 1 (or 2) mL of 0.05 M NaOH. In addition, depending on the extent of the depression of the buffer region for a carboxylic acid (i.e., depending on the stability of the complexes), the concentrations of $M(NO_3)_2$ (or $M(NO_3)_2$/phen) were varied between 2.5 and 25 mM by keeping I always at 0.1.

^{1}H NMR Measurements. The ^{1}H NMR spectra were recorded on a Varian Anaspect EM-360 spectrometer (60 MHz) at 34 °C in water and in 50% (v/v) aqueous ethanol as solvents, with the center peak of the tetramethylammonium ion triplet as an internal reference (0.02 M). However, all chemical shifts were converted to a sodium 3-(trimethylsilyl)propanesulfonate reference by adding 3.174 ppm (H_2O) or 3.188 ppm (50% aqueous ethanol). The last mentioned reference is not directly usable due to its hydrophobic interaction with Zn^{2+}/phen.[32]

In the ^{1}H NMR measurements the change in the chemical shift of the terminal methyl group(s) of the carboxylic acids was followed; in all cases a set of four different experiments were carried out in order to see the influence of protonation and of the coordination of Zn^{2+} or $Zn(phen)^{2+}$. Always the center position of the multiplets corresponding to these methyl groups was evaluated. On the basis of the shifts measured in the experiments and the concentrations of the various carboxylic acid species, the extrapolated shifts for $Zn(CA)^+$ and $Zn(phen)(CA)^+$ were calculated (analogous to eq 4 of ref 15)[17,33] by using the equilibrium constants determined from the potentiometric pH titrations for this study.

Results and Discussion

1. Definition of Constants and Stabilities of Binary $M(CA)^+$ and Ternary $M(phen)(CA)^+$ Complexes. The equilibrium constants were determined by potentiometric pH titrations (I = 0.1 M, $NaNO_3$; 25 °C). The acidity constants of the carboxylic acids, H(CA), and the stability constants of their binary (eq 2) and ternary (eq 3) complexes with Cu^{2+} and Zn^{2+}, the ternary complexes containing also 1,10-phenanthroline (phen),[34] are defined by equilibria 1–3. A significant excess concentration of M^{2+} or

$$H(CA) \rightleftharpoons CA^- + H^+ \quad (1a)$$

$$K^{H}_{H(CA)} = [H^+][CA^-]/[H(CA)] \quad (1b)$$

$$M^{2+} + CA^- \rightleftharpoons M(CA)^+ \quad (2a)$$

$$K^{M}_{M(CA)} = [M(CA)^+]/[M^{2+}][CA^-] \quad (2b)$$

$$M(phen)^{2+} + CA^- \rightleftharpoons M(phen)(CA)^+ \quad (3a)$$

$$K^{M(phen)}_{M(phen)(CA)} = [M(phen)(CA)^+]/[M(phen)^{2+}][CA^-] \quad (3b)$$

M^{2+}/phen[34] over that of the carboxylate ligands, CA^-, was used in the experiments; hence, all observations may be fully characterized by eq 2 and 3.

The relative stability of mixed-ligand or ternary complexes toward their binary parent complexes is best quantified by considering equilibrium 4a.[37,38] Both sides of this equilibrium contain

$$M(phen)^{2+} + M(CA)^+ \rightleftharpoons M(phen)(CA)^+ + M^{2+} \quad (4a)$$

(24) Abbreviations: Ac^-, acetate; $AlCA^-$, alkanecarboxylate; CA^-, carboxylate ligand; $CHAc^-$, 2-cyclohexylacetate; i-$AlCA^-$, isoalkanecarboxylate (e.g., $3\text{-}MBu^-$ or 6-MHp); L, general ligand; M^{2+}, general divalent metal ion; $3\text{-}MBu^-$, 3-methylbutyrate; 6-MHp, 6-methylheptanoate; 5-MHx, 5-methylhexanoate; $2\text{-}MPr^-$, 2-methylpropionate; $4\text{-}MVa^-$, 4-methylvalerate = 4-methylpentanoate; PAc^-, 2-phenylacetate; $PheCA^-$, phenylalkanecarboxylate (e.g., PAc^- or PPr^-); phen, 1,10-phenanthroline; PPr^-, 3-phenylpropionate; Pr^-, propionate; Va^-, valerate = pentanoate.

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Table I. Negative Logarithms of the Acidity Constants (Eq 1) of Several Carboxylic Acids (Figure 1),[24] Logarithms of the Stability Constants of the Corresponding Binary $Cu(CA)^+$ (Eq 2) and Ternary $Cu(phen)(CA)^+$ Complexes (Eq 3), and the Resulting Values for $\Delta \log K_{Cu}$ (Eq 4, 5)[a] in Water, 50% (v/v) Ethanol–Water (Corresponding to a Mole Fraction of 0.237), and 50% (v/v) Dioxane–Water (Mole Fraction 0.175) at I = 0.1 M ($NaNO_3$) and 25 °C

CA^-	*n* of Figure 1	$pK^H_{H(CA)}$	$\log K^{Cu}_{Cu(CA)}$	$\log K^{Cu(phen)}_{Cu(phen)(CA)}$	$\Delta \log K_{Cu}$	$\log K^{Zn}_{Zn(CA)}$	$\log K^{Zn(phen)}_{Zn(phen)(CA)}$	$\Delta \log K_{Zn}$
				In Water				
$HCOO^-$		3.58 ± 0.01	1.58 ± 0.04	1.55 ± 0.03	−0.03 ± 0.05	0.95 ± 0.03	0.83 ± 0.07	−0.12 ± 0.08
Ac^-		4.57 ± 0.01	1.73 ± 0.04	1.73 ± 0.03	0.00 ± 0.05	0.93 ± 0.03	0.81 ± 0.04	−0.12 ± 0.05
2-MPr$^-$	0	4.67 ± 0.01	1.79 ± 0.03	1.84 ± 0.03	0.05 ± 0.04	1.01 ± 0.02	0.90 ± 0.03	−0.11 ± 0.04
3-MBu$^-$	1	4.61 ± 0.01	1.70 ± 0.03	1.78 ± 0.02	0.08 ± 0.04	0.96 ± 0.03	0.93 ± 0.03	−0.03 ± 0.04
4-MVa$^-$	2	4.68 ± 0.01	1.73 ± 0.04	1.85 ± 0.03	0.12 ± 0.05	0.99 ± 0.04	0.96 ± 0.04	−0.03 ± 0.06
5-MHx$^-$	3	4.69 ± 0.01	1.79 ± 0.07	1.94 ± 0.03	0.15 ± 0.08	0.99 ± 0.04	0.98 ± 0.04	−0.01 ± 0.06
6-MHp$^-$	4	4.72 ± 0.01	1.80 ± 0.04	1.97 ± 0.03	0.17 ± 0.05	1.02 ± 0.05	1.07 ± 0.02	0.05 ± 0.05
				In 50% Ethanol–Water[b]				
$HCOO^-$		4.31 ± 0.01	2.24 ± 0.03	2.31 ± 0.03	0.07 ± 0.04	1.49 ± 0.03	1.38 ± 0.04	−0.11 ± 0.05
Ac^-		5.55 ± 0.01	2.70 ± 0.01	2.78 ± 0.02	0.08 ± 0.02	1.86 ± 0.01	1.81 ± 0.02	−0.05 ± 0.02
2-MPr$^-$	0	5.99 ± 0.01	2.80 ± 0.01	3.05 ± 0.01	0.25 ± 0.01	2.00 ± 0.02	2.01 ± 0.02	0.01 ± 0.03
3-MBu$^-$	1	5.94 ± 0.01	2.74 ± 0.01	2.96 ± 0.01	0.22 ± 0.01	1.94 ± 0.02	1.96 ± 0.01	0.02 ± 0.02
4-MVa$^-$	2	6.02 ± 0.01	2.78 ± 0.02	3.02 ± 0.01	0.24 ± 0.02	1.91 ± 0.02	2.03 ± 0.01	0.12 ± 0.02
5-MHx$^-$	3	6.02 ± 0.01	2.79 ± 0.01	3.06 ± 0.02	0.27 ± 0.02	1.91 ± 0.02	2.06 ± 0.02	0.15 ± 0.03
6-MHp$^-$	4	6.06 ± 0.01	2.79 ± 0.03	3.07 ± 0.01	0.28 ± 0.03	1.95 ± 0.01	2.10 ± 0.01	0.15 ± 0.01
				In 50% Dioxane–Water				
$HCOO^-$		4.77 ± 0.01	2.65 ± 0.01	2.65 ± 0.01	0.00 ± 0.01	1.87 ± 0.01	1.76 ± 0.01	−0.11 ± 0.01
Ac^-		5.99 ± 0.01	3.15 ± 0.01	3.20 ± 0.01	0.05 ± 0.01	2.21 ± 0.01	2.11 ± 0.01	−0.10 ± 0.01
2-MPr$^-$	0	6.40 ± 0.01	3.27 ± 0.01	3.47 ± 0.01	0.20 ± 0.01	2.37 ± 0.01	2.37 ± 0.02	0.00 ± 0.02
3-MBu$^-$	1	6.37 ± 0.01	3.23 ± 0.01	3.39 ± 0.01	0.16 ± 0.01	2.32 ± 0.01	2.36 ± 0.01	0.04 ± 0.01
4-MVa$^-$	2	6.45 ± 0.01	3.29 ± 0.01	3.47 ± 0.01	0.18 ± 0.01	2.34 ± 0.01	2.38 ± 0.01	0.04 ± 0.01
5-MHx$^-$	3	6.51 ± 0.01	3.29 ± 0.01	3.51 ± 0.01	0.22 ± 0.01	2.35 ± 0.01	2.45 ± 0.01	0.10 ± 0.01
6-MHp$^-$	4	6.53 ± 0.01	3.33 ± 0.01	3.52 ± 0.01	0.19 ± 0.01	2.36 ± 0.01	2.45 ± 0.01	0.09 ± 0.01

[a] The error given is *3 times* the standard error of the mean value or the sum of the probable systematic errors, whichever is larger. The values of the error limits for $\Delta \log K_M$ were calculated according to the error propagation after Gauss. [b] The equilibrium constants for the formate and acetate systems are from ref 39.

species of the same charge type, minimizing any electrostatic contribution to the corresponding equilibrium constant, which is defined by eq 4b and calculated with eq 5. In general, the position

$$10^{\Delta \log K_M} = \frac{[M(phen)(CA)^+][M^{2+}]}{[M(phen)^{2+}][M(CA)^+]} \quad (4b)$$

$$\Delta \log K_M = \log K^{M(phen)}{}_{M(phen)(CA)} - \log K^{M}{}_{M(CA)} = \log K^{M(CA)}{}_{M(CA)(phen)} - \log K^{M}{}_{M(phen)} \quad (5)$$

of equilibrium 4a is expected[16,37,38] to lie on the left side with negative values for $\Delta \log K_M$ due to the general rule that $K^{M}{}_{M(L)} > K^{M(L)}{}_{M(L)_2}$. Indeed, statistical considerations[39] for $\Delta \log K_M$, assuming an octahedral (oh) coordination sphere for Zn^{2+}, lead to $\Delta \log K_{oh} = \log (4{:}1/6{:}1) = -0.18$; should the coordination sphere of Zn^{2+} be tetrahedral (th), then $\Delta \log K_{th} = \log (2{:}1/4{:}1) = -0.3$. For the tetragonal or Jahn–Teller distorted octahedral coordination sphere of Cu^{2+}, one estimates[39] $\Delta \log K_{Cu/statist} \simeq -0.5$.

To learn something about the influence of the solvent on the stability of complexes, the equilibrium constants of (1)–(4) were determined in water, as well as in 50% (v/v) aqueous ethanol or dioxane. Table I contains these results for the isoalkanecarboxylate ligands of Figure 1 and also for formate ($HCOO^-$) and acetate (Ac^-); the data for these two latter ligands are needed for comparisons. The negative logarithms of the acidity constants for the carboxylic acids increase in all three solvents, as expected, from formic acid to acetic acid and then further to 2-methylpropionic acid; separation of the isopropyl residue from the carboxylic group by a single methylene unit leads to a slight decrease in pK_a and then again to further small increases with the increasing size of the alkyl residues. It is evident that these alterations are also reflected in the stability constants of the binary $M(CA)^+$ complexes.

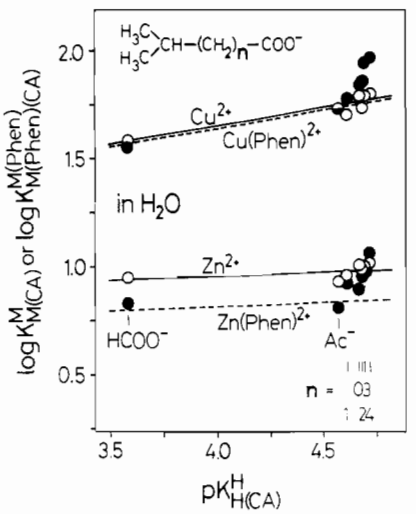

Figure 2. Relationship between $\log K^{M}{}_{M(CA)}$ or $\log K^{M(phen)}{}_{M(phen)(CA)}$ and $pK^{H}{}_{H(CA)}$ in aqueous solution for the binary complexes, $M(CA)^+$ (○), or the ternary complexes, $M(phen)(CA)^+$ (●), with *simple* carboxylates, i.e. $HCOO^-$ and Ac^-, and the isoalkanecarboxylates (see formula above) with n = 0–4. The plotted data are from Table I, and those of the binary complexes fit on straight lines (*solid* lines) (regression: m_{Cu} = 0.170 ± 0.035 (±1σ), $y_{0/Cu}$ = 0.965 ± 0.159; m_{Zn} = 0.039 ± 0.031, $y_{0/Zn}$ = 0.802 ± 0.141); the reference lines for the ternary complexes (*broken* lines) are drawn with the corresponding slopes but only through the points of $HCOO^-$ and Ac^- (see text).

2. Some Conclusions from the Stability of the Complexes and Indirect Evidence for Hydrophobic Ligand–Ligand Interactions. For a series of structurally related ligands it is expected[40,41] that plots of $\log K^{M}{}_{M(L)}$ versus $pK^{H}{}_{H(L)}$ result in straight lines. Indeed,

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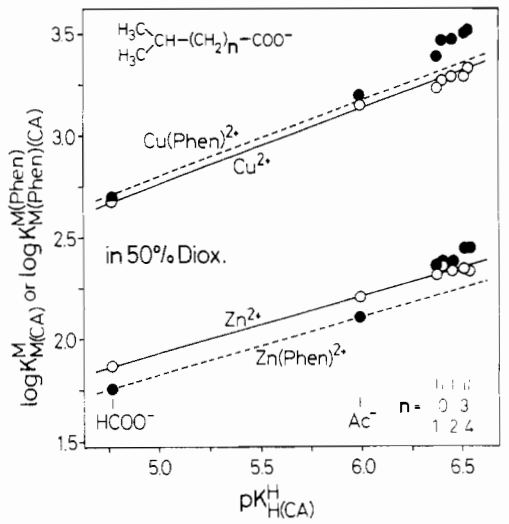

Figure 3. Relationship between log $K^{M}_{M(CA)}$ or log $K^{M(phen)}_{M(phen)(CA)}$ and $pK^{H}_{H(CA)}$ in 50% (v/v) dioxane–water for the binary complexes, $M(CA)^+$ (○), or the ternary complexes, $M(phen)(CA)^+$ (●), with *simple* carboxylates, i.e. $HCOO^-$ and Ac^-, and the isoalkanecarboxylates (see formula above) with $n = 0$–4. The plotted data are from Table I, and those of the binary complexes fit on straight lines (*solid* lines) (regression: $m_{Cu} = 0.374 \pm 0.015$ (1σ), $y_{0/Cu} = 0.875 \pm 0.091$; $m_{Zn} = 0.283 \pm 0.012$, $y_{0/Zn} = 0.519 \pm 0.075$); the reference lines for the ternary complexes (*broken* lines) are drawn with the corresponding slopes but only through the points of $HCOO^-$ and Ac^- (see text).

all the binary carboxylate complexes with Cu^{2+} and Zn^{2+} fit within experimental error on individual straight lines in the three solvents employed; Figures 2 and 3 demonstrate this for water and 50% (v/v) dioxane–water, respectively. In the mixed solvents the fit is somewhat better as the stability of the binary complexes is somewhat larger and therefore the experimental error smaller (Table I). But even for the aqueous solution the values of the Cu^{2+} and Zn^{2+} complexes of all carboxylates fit within ±0.04 log unit on the two corresponding straight lines.

Figures 2 and 3 show also that the ternary complexes behave differently: only the values of $Cu(phen)(CA)^+$ and $Zn(phen)(CA)^+$ with formate and acetate fit within experimental error on straight lines (broken lines) parallel to the reference lines of the binary complexes (solid lines). Already the points due to $M(phen)(2\text{-}MPr)^+$ are above the corresponding broken lines in all three solvents. Hence, these two ternary Cu^{2+} and Zn^{2+} complexes are more stable than expected on the basis of the basicity of the carboxylate group of 2-methylpropionate; this parallels the earlier observation[22] made with unsubstituted propionate (Pr^-). It is evident that an extra stabilization within these ternary complexes must occur. In fact, this extra stabilization may be attributed to intramolecular hydrophobic ligand–ligand interactions between the alkyl chains of the carboxylates and the aromatic ring system of phen. This interpretation is in accord with ^1H NMR shift studies,[16a,33] which prove such hydrophobic interactions for $Zn(phen)(Pr)^+$ and similar complexes.[16a,22]

In summary, two important conclusions are evident from Figures 2 and 3 (and also from the measurements in 50% ethanol–water): (i) The properties of $M(phen)(HCOO)^+$ and $M(phen)(Ac)^+$ are representative for ternary complexes resulting from the coordination of a carboxylate group to $M(phen)^+$. (ii) All the ternary complexes of the isoalkanecarboxylates of Figure 1 are more stable than expected on the basis of their carboxylate basicity in the three solvents. In fact, this confirms the expected intramolecular ligand–ligand interactions between the alkyl moieties and the aromatic ring system of phen. In addition, the increase in stability for $M(phen)(i\text{-}AlCA)^+$ obviously depends to some extent on the number of methylene groups between the terminal isopropyl residue and the coordinating carboxylate group, and this is further evidence that hydrophobic interactions are the source of the increased stabilities. A simplified structure for such a "closed" species is shown in Figure 4.

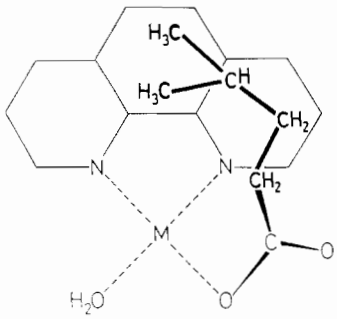

Figure 4. Possible (schematic) structure of $M(phen)(4\text{-}MVa)^+$ for the isomer with the intramolecular hydrophobic ligand–ligand interaction between the alkyl residue of 4-methylvalerate and the aromatic ring system of 1,10-phenanthroline.

As emphasized above, the stabilities of $M(phen)(HCOO)^+$ and $M(phen)(Ac)^+$ are governed by the basicity of the carboxylate group and *not* by intramolecular ligand–ligand interactions. With this in mind, the $\Delta \log K_M$ values for these complexes in Table I should shortly be considered: for Zn^{2+} the values vary between −0.12 and −0.05 log unit and for Cu^{2+} between −0.03 and +0.08 log unit. Hence, in comparison with the statistical expectation of $\Delta \log K_{Zn/statist} = -0.3$ to −0.18 and $\Delta \log K_{Cu/statist} \simeq -0.5$ (see section 1), an increased stability is observed for the formate and acetate complexes. This result corresponds to the well-known fact that the combination of heteroaromatic N bases and O ligands in ternary complexes with Cu^{2+} or Zn^{2+} and related metal ions leads to an increased stability.[37,38,42] Consequently, the evaluation of the intensity of the hydrophobic interaction in the ternary $M(phen)(i\text{-}AlCA)^+$ complexes has to be done in relation to the $\Delta \log K_M$ values of the corresponding formate and acetate complexes (see section 4).

3. ^1H NMR Studies of Ternary Zn^{2+} Complexes Composed of phen and Isoalkanecarboxylates: Direct Evidence for Intramolecular Hydrophobic Interactions. An ideal method to more directly establish hydrophobic interactions of the kind indicated in section 2 for mixed-ligand complexes involves the use of ^1H NMR shift measurements.[15,17] Protonation or coordination of a metal ion shifts the signals of the ligand hydrogens close to the binding site *downfield*. However, in a complex in which the aliphatic side chain of a carboxylate is located above or below the plane of an aromatic ring system (Figure 4), the signals of the aliphatic hydrogens should be shifted *upfield*, relative to those of the free alkanecarboxylate or $Zn(AlCA)^+$, due to the ring current of the aromatic system.[43]

In order to confirm the hydrophobic intramolecular ligand–ligand interaction in the ternary $Zn(phen)(i\text{-}AlCA)^+$ complexes the following experiments were made in H_2O and in 50% (v/v) ethanol–H_2O: The effects on the side of the carboxylate ligands through protonation and Zn^{2+} or $Zn(phen)^{2+}$ coordination were measured by monitoring the relative position of the signal of the terminal methyl group(s) of the alkanecarboxylates as a function of H^+, Zn^{2+}, and $Zn(phen)^{2+}$. The experimentally determined shifts of $AlCA^-$ and H(AlCA), as well as the extrapolated shifts (see Experimental Section) of $Zn(AlCA)^+$ and $Zn(phen)(AlCA)^+$ are compiled in Table II, together with the *downfield* shifts due to protonation or Zn^{2+} coordination and the *upfield* shifts resulting from $Zn(phen)^{2+}$ coordination. The data for Ac^-, $2\text{-}MPr^-$, $3\text{-}MBu^-$, and $4\text{-}MVa^-$ in water agree well with previous results.[33]

It is obvious that the extent of the intramolecular hydrophobic interaction in the ternary $Zn(phen)(i\text{-}AlCA)^+$ complexes should be dependent on the length and possibly also on the volume of the aliphatic residue of the carboxylate ligand. To facilitate

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Table II. Measured Chemical Shifts of the Terminal Methyl Groups[a] of Various Protonated ($\delta_{H(AlCA)}$) and Free Alkanecarboxylate Anions (δ_{AlCA}), Together with the Extrapolated[b] Shifts of Their Binary Zn^{2+} ($\delta_{Zn(AlCA)}$) and Ternary $Zn(phen)^{2+}$ ($\delta_{Zn(phen)(AlCA)}$) Complexes in Water and in 50% (v/v) Ethanol–Water at I = 0.1–0.2 M ($NaNO_3$) and 34 °C, and the Resulting Relevant Shift Differences (in ppm)

AlCA	δ_{AlCA}[c]	$\delta_{H(AlCA)}$[d]	$\delta_{AlCA} - \delta_{H(AlCA)}$	$\delta_{Zn(AlCA)}$[e,f]	$\delta_{AlCA} - \delta_{Zn(AlCA)}$	$\delta_{Zn(phen)(AlCA)}$[f,g]	$\delta_{Zn(AlCA)} - \delta_{Zn(phen)(AlCA)}$
			In Water				
Ac	1.915 ± 0.004	2.094 ± 0.004	−0.179 ± 0.006	1.99 ± 0.02	−0.07 ± 0.02	1.85 ± 0.02	0.14 ± 0.03
2-MPr	1.061 ± 0.004	1.152 ± 0.004	−0.091 ± 0.006	1.11 ± 0.01	−0.05 ± 0.01	0.91 ± 0.02	0.20 ± 0.02
3-MBu	0.910 ± 0.004	0.955 ± 0.004	−0.045 ± 0.006	0.93 ± 0.01	−0.02 ± 0.01	0.63 ± 0.02	0.30 ± 0.02
4-MVa	0.878 ± 0.004	0.893 ± 0.004	−0.015 ± 0.006	0.91 ± 0.02	−0.03 ± 0.02	0.45 ± 0.02	0.46 ± 0.03
5-MHx	0.867 ± 0.004	0.871 ± 0.004	−0.004 ± 0.006	0.87 ± 0.03	0.00 ± 0.03	0.33 ± 0.03	0.54 ± 0.04
6-MHp	0.859 ± 0.004	0.855 ± 0.004	0.004 ± 0.006	0.86 ± 0.04	0.00 ± 0.04	0.32 ± 0.05	0.54 ± 0.06
			In 50% Ethanol–Water				
Ac	1.891 ± 0.004	2.057 ± 0.004	−0.166 ± 0.006	1.97 ± 0.01	−0.08 ± 0.01	1.92 ± 0.01	0.05 ± 0.01
2-MPr	1.047 ± 0.005	1.13 ± 0.01	−0.083 ± 0.011	1.08 ± 0.04	−0.03 ± 0.04	0.93 ± 0.03	0.15 ± 0.05
3-MBu	0.904 ± 0.004	0.944 ± 0.004	−0.040 ± 0.006	0.93 ± 0.01	−0.03 ± 0.01	0.72 ± 0.01	0.21 ± 0.01
4-MVa	0.872 ± 0.004	0.883 ± 0.004	−0.011 ± 0.006	0.88 ± 0.02	−0.01 ± 0.02	0.65 ± 0.02	0.23 ± 0.03
5-MHx	0.858 ± 0.004	0.864 ± 0.004	−0.006 ± 0.006	0.86 ± 0.02	0.00 ± 0.02	0.63 ± 0.01	0.23 ± 0.02
6-MHp	0.845 ± 0.004	0.852 ± 0.004	−0.007 ± 0.006	0.85 ± 0.02	0.00 ± 0.02	0.65 ± 0.02	0.20 ± 0.03

[a] Always the midpoint of the multiplets is given, relative to 3-(trimethylsilyl)propanesulfonate, but the actual measurements were made with $(CH_3)_4N^+NO_3^-$ (0.02 *M*) as internal standard (see Experimental Section). The results are the average of at least two independent measurements. The error limits are estimates; those of the differences were calculated according to the error propagation after Gauss. [b] See the Experimental Section. [c] Measured with [AlCA$^-$] = 0.05 M in H_2O at pH 7.0 and in 50% (v/v) ethanol–water at pH 8.5. [d] Measured in H_2O at pH 2.0 and in 50% (v/v) ethanol–water at pH 3.0 (=pH-meter reading; see Experimental Section) with [H(AlCA)] = 0.05 M. In the cases of H(5-MHx) and H(6-MHp) in water, saturated solutions were used; i.e., the concentration was on the order of 0.01 M. [e] The Zn^{2+}:AlCA ratio was always 1:1, and usually [AlCA] = 0.05 and 0.08 M, but in water [4-MVa] = 0.03 M, [5-MHx] = 0.02 M, and in the case of [6-MHp] = 0.01 M, the solution was still slightly turbid; hence, the corresponding value must be considered as an estimate; in 50% (v/v) ethanol–water, [6-MHp] = 0.05 M. [f] The measurements in water were made at pH 6.0, and those in the ethanol–water mixture, at pH 5.0. The values given in the table are the extrapolations toward complete complex formation from at least two measurements.[b] [g] The reactant ratio was always 1:1:1, and usually [AlCA] = 0.05 and 0.08 M, but in water [5-MHx] = 0.03 and 0.05 M and [6-MHp] = 0.01 M.

comparisons in this respect, the results of Table II, together with some related earlier results,[33] are plotted in Figure 5 *relative* to the shift position of the terminal methyl group(s) of the free alkanecarboxylates. The upper part of the figure summarizes some previous results[33] for nonbranched alkanecarboxylates in water, and the middle and lower parts summarize those for the iso-alkanecarboxylates in water and 50% (v/v) ethanol–water, respectively.

As expected, protonation (Table II) and Zn^{2+} coordination (Figure 5) lead to a *downfield* shift and the shift difference decreases with increasing distance between the methyl group(s) and the site of coordination. Actually, the effect is large only with acetate and falls off rapidly with increasing chain length, being already small for four-carbon chains (butyrate, 3-methylbutyrate; n = 1) and negligible for longer chains. However, the *upfield* shift caused by $Zn(phen)^{2+}$ increases rapidly with increasing chain length; i.e., the aliphatic chain undergoes a hydrophobic interaction with the aromatic rings of phen within the ternary complexes. This interaction is very poor or even (nearly) absent in $Zn(phen)(Ac)^+$, but with an increasing chain length the terminal methyl group or groups reach over the aromatic ligand (Figure 4) and the upfield shift differences become larger. For the hexanoates (n = 3 in Figure 5) the maximum upfield shifts are reached, and there are indications in Figure 5 that with the heptanoates (n = 4) the shifts are already slightly smaller; this indicates that the length of the chain is now such that the methyl group or groups reach beyond the aromatic ring system of phen.

A good fit between the aliphatic moiety and the aromatic system of phen in the ternary Zn^{2+} complexes is evidently already reached with the valerates (n = 2 in Figure 5; Figure 4), and it is interesting to compare for this chain length the extent of the upfield shift for the branched and nonbranched carboxylates in water: The upfield shift with 2-methylvalerate is clearly somewhat more pronounced than for valerate. The reason for this observation is probably that a somewhat higher proportion of the complex exists in the "closed" form (see section 4) due to the increased hydrophobicity of the isopropyl moiety compared with that of an ethyl group.

Two further points must be made: (i) The extent of the upfield shifts is smaller in 50% (v/v) ethanol–water (lower part of Figure 5) than in water as solvent (middle). However, it is evident that a hydrophobic interaction is also occurring in the ethanol–water mixture; these systems will be further discussed in sections 6 and 7. (ii) As shown previously,[33] it is also possible to prove by ^1H NMR measurements that the aliphatic residues of such carboxylate ligands (L) interact with phen also in the absence of metal

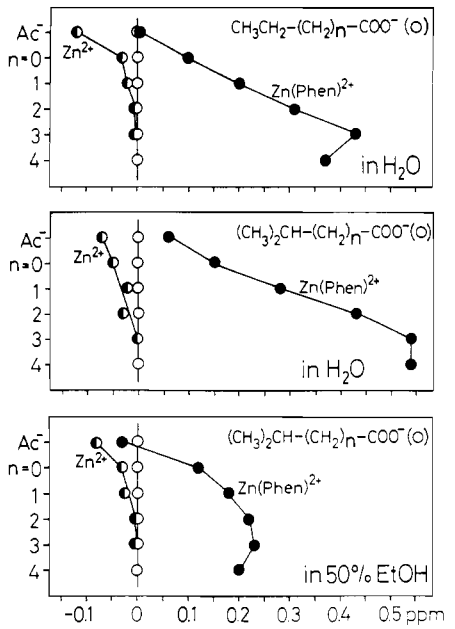


Figure 5. Up- and downfield shifts of the terminal methyl group(s) in the ^1H NMR spectra of straight-chain (upper part) and of branched-chain (middle and lower parts) alkanecarboxylate ligands for Zn^{2+} (◐) or $Zn(phen)^{2+}$ (●) coordination in water (upper and middle parts) and in 50% (v/v) ethanol–water (lower part) relative to the resonance positions of the uncoordinated carboxylates (○). The measurements were carried out at I = 0.1–0.2 M ($NaNO_3$) and 34 °C; the data for the upper part are from ref 33, and those of the middle and lower parts, from Table II.

ions. However, as expected, the adduct formation is very weak and stability constants could only be estimated: $K^{phen}_{(phen)(L)} \simeq 2\ M^{-1}$ (in water).[33] This agrees with theoretical calculations[8] for the hydrophobic interaction between leucine and phenylalanine in aqueous solution at 25 °C: $K^{Phe}_{(Phe)(Leu)} \simeq 2\ M^{-1}$.[44]

4. Intramolecular Equilibria: Formation Degree of the Isomer with the Hydrophobic Interaction in the Ternary M(phen)(*i*-

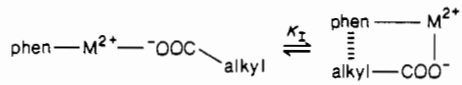
(44) It may be added that comparison of the stability of these binary adducts with the stability of the ternary Zn^{2+} complexes (Table I) indicates that in aqueous solution (but not in the mixed solvents) in the mixed-ligand systems also traces of unbridged adducts, i.e. without a carboxylate coordination, might coexist.

Table III. Extent of the Intramolecular Hydrophobic Ligand–Ligand Adducts in Ternary Cu^{2+} Complexes Containing 1,10-Phenanthroline (phen) and an Alkanecarboxylate ($AlCA^-$): Intramolecular and Dimensionless Equilibrium Constant K_I (Eq 7–9) and Percentage of the Closed Form, $Cu(phen)(AlCA)^+_{cl}$ (Eq 6), in Water, 50% (v/v) Ethanol–Water, and 50% (v/v) Dioxane–Water at I = 0.1 M ($NaNO_3$)[a] and 25 °C

no.	complex	*n* of Figure 1	$\Delta \log K_{Cu}$[a]	$\Delta\Delta \log K$[b,c]	K_I[c]	% $Cu(phen)(AlCA)^+_{cl}$[c]
			In Water			
1	$Cu(phen)(HCOO)^+$		−0.03 ± 0.05	−0.01 ± 0.04[d]		
2	$Cu(phen)(Ac)^+$		0.00 ± 0.05			
3a	$Cu(phen)(Pr)^+$				0.10 ± 0.08 (0.17)	9 ± 7 (14)
3	$Cu(phen)(2\text{-}MPr)^+$	0	0.05 ± 0.04	0.06 ± 0.04 (0.06)	0.15 ± 0.11 (0.15)	13 ± 8 (11)
4	$Cu(phen)(3\text{-}MBu)^+$	1	0.08 ± 0.04	0.09 ± 0.04 (0.05)	0.23 ± 0.10 (0.14)	19 ± 7 (9)
5	$Cu(phen)(4\text{-}MVa)^+$	2	0.12 ± 0.05	0.13 ± 0.05 (0.06)	0.38 ± 0.16 (0.19)	26 ± 9 (10)
6	$Cu(phen)(5\text{-}MHx)^+$	3	0.15 ± 0.08	0.16 ± 0.08 (0.08)	0.45 ± 0.25 (0.28)	31 ± 12 (13)
7	$Cu(phen)(6\text{-}MHp)^+$	4	0.17 ± 0.05	0.18 ± 0.05 (0.06)	0.51 ± 0.17 (0.21)	34 ± 8 (9)
			In 50% Ethanol–Water			
8	$Cu(phen)(HCOO)^+$		0.07 ± 0.04	0.08 ± 0.02[d]		
9	$Cu(phen)(Ac)^+$		0.08 ± 0.02			
10	$Cu(phen)(2\text{-}MPr)^+$	0	0.25 ± 0.01	0.17 ± 0.01 (0.03)	0.48 ± 0.05 (0.09)	32 ± 2 (4)
11	$Cu(phen)(3\text{-}MBu)^+$	1	0.22 ± 0.01	0.14 ± 0.01 (0.03)	0.38 ± 0.04 (0.09)	28 ± 2 (5)
12	$Cu(phen)(4\text{-}MVa)^+$	2	0.24 ± 0.02	0.16 ± 0.02 (0.03)	0.45 ± 0.07 (0.11)	31 ± 4 (5)
13	$Cu(phen)(5\text{-}MHx)^+$	3	0.27 ± 0.02	0.19 ± 0.02 (0.03)	0.55 ± 0.08 (0.12)	35 ± 3 (5)
14	$Cu(phen)(6\text{-}MHp)^+$	4	0.28 ± 0.03	0.20 ± 0.03 (0.04)	0.58 ± 0.12 (0.14)	37 ± 5 (6)
			In 50% Dioxane–Water			
15	$Cu(phen)(HCOO)^+$		0.00 ± 0.01	0.03 ± 0.01[d]		
16	$Cu(phen)(Ac)^+$		0.05 ± 0.01			
17a	$Cu(phen)(Pr)^+$				0.15 ± 0.07 (0.09)	13 ± 6 (7)
17	$Cu(phen)(2\text{-}MPr)^+$	0	0.20 ± 0.01	0.17 ± 0.01 (0.02)	0.48 ± 0.05 (0.06)	32 ± 2 (3)
18	$Cu(phen)(3\text{-}MBu)^+$	1	0.16 ± 0.01	0.13 ± 0.01 (0.02)	0.35 ± 0.05 (0.05)	26 ± 2 (3)
19a	$Cu(phen)(Va)^+$				0.35 ± 0.09 (0.10)	26 ± 5 (6)
19	$Cu(phen)(4\text{-}MVa)^+$	2	0.18 ± 0.01	0.15 ± 0.01 (0.02)	0.41 ± 0.05 (0.06)	29 ± 2 (3)
20	$Cu(phen)(5\text{-}MHx)^+$	3	0.22 ± 0.01	0.19 ± 0.01 (0.02)	0.55 ± 0.05 (0.06)	35 ± 2 (3)
21	$Cu(phen)(6\text{-}MHp)^+$	4	0.19 ± 0.01	0.16 ± 0.01 (0.02)	0.45 ± 0.05 (0.06)	31 ± 2 (3)
22a	$Cu(phen)(CHAc)^+$				0.62 ± 0.08 (0.11)	38 ± 3 (4)

[a] The $\Delta \log K_{Cu}$ values and their errors ranges (*3 times* the standard error) are from Table I. The results of entries 3a, 17a, 19a, and 22a (I = 0.1 M, $NaClO_4$; 25 °C) are from ref 22. [b] The values for $\Delta\Delta \log K$ were calculated according to eq 8. [c] The error limits given with these data correspond to the errors of the individual values of $\Delta \log K_{Cu}$. The error limits in parentheses include also the error in $\Delta \log K_{Cu/op}$;[d] these latter error limits should be used in external comparisons. However, for internal comparisons the error based only on the individual $\Delta \log K_{Cu}$ values is more reasonable because $\Delta \log K_{Cu/op}$ is the same for a whole series of data,[b] and therefore any error in $\Delta \log K_{Cu/op}$ will lead to a systematic correction for all these values. [d] This value for $\Delta \log K_{Cu/op}$ is the average of $\Delta \log K_{Cu}$ determined for the $HCOO^-$ and Ac^- systems.

$AlCA)^+$ Complexes. The determined stability constants, i.e. especially the values of $\Delta \log K_M$ (Table I), provide indirect evidence for intramolecular hydrophobic ligand–ligand interactions in $M(phen)(i\text{-}AlCA)^+$ complexes (section 2). Unequivocally confirmed is this interaction by the results described in the preceding ^1H NMR section. However, it is clear that the occurrence of a complex species with a structure similar to the one shown in Figure 4, which is responsible for the increase in stability (Table I) and for the observed upfield shifts in the ternary complexes (Table II), does not mean that all of the $M(phen)(i\text{-}AlCA)^+$ species must exist in this folded form. For example, the influence of the different solvents on the values of $\Delta \log K_M$ (Table I) indicates that the formation degree of this folded species can vary. Hence, there is certainly an intramolecular equilibrium in solution between an "opened" and a "closed" form as indicated in



(6a)

If these two forms are designated as $M(phen)(AlCA)^+_{op}$ and $M(phen)(AlCA)^+_{cl}$, the dimensionless constant of this equilibrium is defined by

$$K_I = [M(phen)(AlCA)^+_{cl}]/[M(phen)(AlCA)^+_{op}] \quad (6b)$$

Values of K_I may be calculated from[15]

$$K_I = \frac{K^{M(phen)}_{M(phen)(AlCA)}}{K^{M(phen)}_{M(phen)(AlCA)_{op}}} - 1 \quad (7a)$$

$$= \frac{10^{\Delta \log K_{M/phen/AlCA}}}{10^{\Delta \log K_{(M/phen/AlCA)op}}} - 1 \quad (7b)$$

The values of $K^{M(phen)}_{M(phen)(AlCA)}$ are known (eq 3), and those of $K^{M(phen)}_{M(phen)(AlCA)_{op}}$ could be estimated according to Figures 2 and 3: the acidity constant of a given $AlCA^-$ ligand allows one to read from the intercept with the reference line the stability constant expected for a simple carboxylate coordination.

However, experience shows[15] that use of the $\Delta \log K_M$ formulation (eq 7b)[45] is preferable because systematic errors cancel to a large part. The values due to $\Delta \log K_{M/phen/AlCA}$ are known; they correspond to those calculated from eq 5. There is also no problem regarding $\Delta \log K_{(M/phen/AlCA)_{op}}$; this value is certainly well represented by those determined for $M(phen)(HCOO)^+$ and $M(phen)(Ac)^+$. Clearly, in $M(phen)(HCOO)^+$ no intramolecular interaction is possible and in $M(phen)(Ac)^+$ an interaction with the methyl group, if it occurs at all, is small and insignificant (Figures 2, 3, and 5; sections 2 and 3). Hence, $\Delta \log K_{(M/phen/AlCA)_{op}}$ is obtained by averaging the $\Delta \log K_M$ values measured for the $M^{2+}/phen/HCOO^-$ and $M^{2+}/phen/Ac^-$ systems (Table I).

The crucial parameter obtained by calculating K_I from eq 7b is the difference given in eq 8. Equation 7b may then be rewritten

$$\Delta\Delta \log K = \Delta \log K_{M/phen/AlCA} - \log K_{(M/phen/AlCA)_{op}} \quad (8)$$

$$K_I = 10^{\Delta\Delta \log K} - 1 \quad (9)$$

as eq 9. Obviously, any error will be more significant as the difference in eq 8 becomes smaller. In addition, it is evident[15] that $10^{\Delta\Delta \log K}$ is the equilibrium constant that determines the position of equilibrium 10 (where CA^- represents $HCOO^-$ or

$$M(AlCA)^+ + M(phen)(CA)^+ \rightleftharpoons M(phen)(AlCA)^+ + M(CA)^+ \quad (10)$$

(45) Usually the difference of eq 5 is referred to as $\Delta \log K_M$; only in those cases where further identification is needed are additional subscripts given, like $\Delta \log K_{M/phen/AlCA}$.

Table IV. Extent of the Intramolecular Hydrophobic Ligand–Ligand Adducts in Ternary Zn^{2+} Complexes Containing 1,10-Phenanthroline (phen) and an Alkanecarboxylate ($AlCA^-$): Intramolecular and Dimensionless Equilibrium Constant K_I (Eq 7–9) and Percentage of the Closed Form, $Zn(Phen)(AlCA)^+_{cl}$ (Eq 6), in Water, 50% (v/v) Ethanol–Water, and 50% (v/v) Dioxane–Water at I = 0.1 M ($NaNO_3$)[a] and 25 °C

no.	complex	*n* of Figure 1	$\Delta \log K_{Zn}$[a]	$\Delta\Delta \log K$[b,c]	K_I[c]	% $Zn(phen)(AlCA)^+_{cl}$[c]
			In Water			
1	$Zn(phen)(HCOO)^+$		−0.12 ± 0.08	−0.12 ± 0.05[d]		
2	$Zn(phen)(Ac)^+$		−0.12 ± 0.05			
3	$Zn(phen)(2\text{-}MPr)^+$	0	−0.11 ± 0.04	0.01 ± 0.04 (0.06)	0.02 ± 0.08 (0.14)	2 ± 8 (13)
4	$Zn(phen)(3\text{-}MBu)^+$	1	−0.03 ± 0.04	0.09 ± 0.04 (0.06)	0.23 ± 0.12 (0.18)	19 ± 8 (12)
5	$Zn(phen)(4\text{-}MVa)^+$	2	−0.03 ± 0.06	0.09 ± 0.06 (0.08)	0.23 ± 0.16 (0.21)	19 ± 11 (14)
6	$Zn(phen)(5\text{-}MHx)^+$	3	−0.01 ± 0.06	0.11 ± 0.06 (0.08)	0.29 ± 0.17 (0.22)	22 ± 10 (13)
7	$Zn(phen)(6\text{-}MHp)^+$	4	0.05 ± 0.05	0.17 ± 0.05 (0.07)	0.48 ± 0.18 (0.25)	32 ± 8 (11)
			In 50% Ethanol–Water			
8	$Zn(phen)(HCOO)^+$		−0.11 ± 0.05	−0.08 ± 0.03[d]		
9	$Zn(phen)(Ac)^+$		−0.05 ± 0.02			
10	$Zn(phen)(2\text{-}MPr)^+$	0	0.01 ± 0.03	0.09 ± 0.03 (0.04)	0.23 ± 0.08 (0.11)	19 ± 5 (7)
11	$Zn(phen)(3\text{-}MBu)^+$	1	0.02 ± 0.02	0.10 ± 0.02 (0.04)	0.26 ± 0.06 (0.10)	21 ± 4 (6)
12	$Zn(phen)(4\text{-}MVa)^+$	2	0.12 ± 0.02	0.20 ± 0.02 (0.04)	0.58 ± 0.08 (0.13)	37 ± 3 (5)
13	$Zn(phen)(5\text{-}MHx)^+$	3	0.15 ± 0.03	0.23 ± 0.03 (0.04)	0.70 ± 0.11 (0.15)	41 ± 4 (5)
14	$Zn(phen)(6\text{-}MHp)^+$	4	0.15 ± 0.01	0.23 ± 0.01 (0.03)	0.70 ± 0.06 (0.12)	41 ± 2 (4)
			In 50% Dioxane–Water			
15	$Zn(phen)(HCOO)^+$		−0.11 ± 0.01	−0.10 ± 0.01[d]		
16	$Zn(phen)(Ac)^+$		−0.10 ± 0.01			
17a	$Zn(phen)(Pr)^+$				0.10 ± 0.06 (0.07)	9 ± 5 (5)
17	$Zn(phen)(2\text{-}MPr)^+$	0	0.00 ± 0.02	0.10 ± 0.02 (0.02)	0.26 ± 0.06 (0.07)	21 ± 4 (4)
18	$Zn(phen)(3\text{-}MBu)^+$	1	0.04 ± 0.01	0.14 ± 0.01 (0.02)	0.38 ± 0.04 (0.06)	28 ± 2 (3)
19a	$Zn(phen)(Va)^+$				0.35 ± 0.09 (0.10)	26 ± 5 (5)
19	$Zn(phen)(4\text{-}MVa)^+$	2	0.04 ± 0.01	0.14 ± 0.01 (0.02)	0.38 ± 0.04 (0.06)	28 ± 2 (3)
20	$Zn(phen)(5\text{-}MHx)^+$	3	0.10 ± 0.01	0.20 ± 0.01 (0.02)	0.58 ± 0.05 (0.06)	37 ± 2 (3)
21	$Zn(phen)(6\text{-}MHp)^+$	4	0.09 ± 0.01	0.19 ± 0.01 (0.02)	0.55 ± 0.05 (0.06)	35 ± 2 (3)
22a	$Zn(phen)(CHAc)^+$				0.58 ± 0.05 (0.07)	37 ± 2 (3)

[a–d] These footnotes are the same as those given in Table III. To facilitate comparisons, the above entry numbers are also the same as those used for the corresponding Cu^{2+} complexes in Table III.

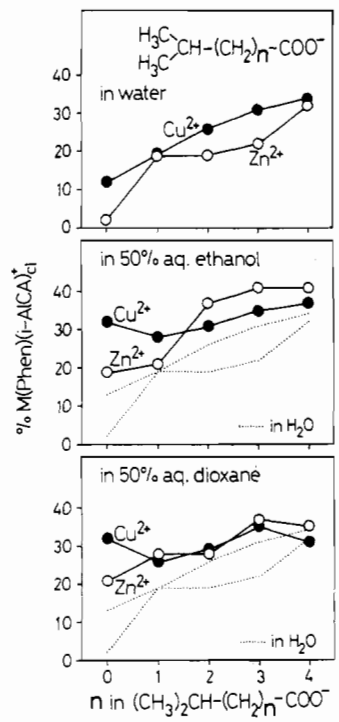


Figure 6. Dependence of the formation degree of the intramolecularly closed species in ternary M(phen)(*i*-AlCA)$^+$ complexes (eq 6) of Cu^{2+} (●) and Zn^{2+} (○) in water (top), 50% (v/v) ethanol–water (middle), and 50% (v/v) dioxane–water (bottom) on the number of methylene units present in the isoalkanecarboxylates (the formula is shown in the top part). The situation in water is repeated by dotted lines in the middle and lower parts to facilitate comparisons. The data are taken from Tables III and IV (I = 0.1, $NaNO_3$; 25 °C). The average error of the plotted percentages is about ±5. Note, in this figure and in Figure 7, % M(phen)(*i*-AlCA)$^+_{cl}$ is based on $[M(phen)(i\text{-}AlCA)^+]_{tot}$ = 100%.

CH_3COO^-). The coordination spheres of the complexes in this equilibrium, i.e. the donor atoms bound to the metal ions, are identical on both sides; consequently, the values for $\Delta\Delta \log K$ (eq 8) are a true reflection of the extent of the intramolecular ligand–ligand interaction in the ternary M(phen)(AlCA)$^+$ complexes.

The results of the calculations based on eq 9 and the constants listed in Table I for the isoalkanecarboxylates are summarized in Tables III and IV for the ternary Cu^{2+} and Zn^{2+} complexes, respectively. These tables contain in addition some previous results[22] for nonbranched alkanecarboxylates, i.e. for propionate (entries 3a and 17a) and valerate (19a), as well as for the voluminous 2-cyclohexylacetate (22a). It is evident that the knowledge of the dimensionless equilibrium constant K_I (eq 6) easily allows calculation of the percentage[46] of the closed form in equilibrium 6a; these results are also listed in Tables III and IV.

5. Influence of Ligand Structure, Metal Ion Coordination Sphere, and Solvent on the Formation Degree of the Closed Isomer. To facilitate comparisons between the different complex systems, as well as between the solvents employed, in Figure 6 the percentages of the closed forms of the M(phen)(*i*-AlCA)$^+$ complexes are plotted in dependence on the number of methylene groups between the isopropyl residue and the coordinating carboxylate group (Figure 1). The following conclusions are evident:

(1) *The ligand structure*, i.e. the distance between the coordinating carboxylate group and the isopropyl residue (being especially able to undergo hydrophobic interactions), influences complex stability and hence the percentage of M(phen)(*i*-AlCA)$^+_{cl}$ only if the overall length of the alkyl chain is short. The percentages of M(phen)(*i*-AlCA)$^+_{cl}$ with *i*-$AlCA^-$ = 4-MVa^-, 5-MHx^-, or 6-MHp^- (i.e., n = 2–4) are identical within the error limits (Tables III and IV) for given conditions (solvent and M^{2+} not varied). In fact, for all these systems the formation degree of the closed species is in the order of about 30%. It appears that about four aliphatic carbon units may be suitably arranged and located above the aromatic rings of phen for an optimal interaction; with more carbon units as available, e.g. in 6-MHp^-, no larger

(46) Martin, R. B.; Sigel, H. *Comments Inorg. Chem.* **1988**, *6*, 285–314.

Table V. Negative Logarithms of the Acidity Constants (Eq 1) of Several Carboxylic Acids, Logarithms of the Stability Constants of the Corresponding Binary $M(CA)^+$ (Eq 2) and Ternary $M(phen)(CA)^+$ Complexes (Eq 3), and the Resulting Values for $\Delta \log K_M$ (Eq 4, 5),[a-c] Depending on the Amount of Ethanol Added to Water and on the Resulting Dielectric Constant at I = 0.1 M ($NaNO_3$) and 25 °C

CA^-	% (v/v) ethanol	mol fract	ϵ[c]	$pK^H_{H(CA)}$	log $K_{Cu(CA)}$	log $K^{Cu(phen)}_{Cu(phen)(CA)}$	$\Delta \log K_{Cu}$	log $K^{Zn}_{Zn(CA)}$	log $K^{Zn(phen)}_{Zn(phen)(CA)}$	$\Delta \log K_{Zn}$
$HCOO^-$	0	0	78.5	3.58 ± 0.01	1.58 ± 0.04	1.55 ± 0.03	−0.03 ± 0.05	0.95 ± 0.03	0.83 ± 0.07	−0.12 ± 0.08
	30	0.117	63.7	3.90 ± 0.02	1.97 ± 0.02	1.97 ± 0.02	0.00 ± 0.03	1.12 ± 0.04	1.08 ± 0.04	−0.04 ± 0.06
	50	0.237	52.1	4.31 ± 0.01	2.24 ± 0.03	2.31 ± 0.03	0.07 ± 0.04	1.49 ± 0.03	1.38 ± 0.04	−0.11 ± 0.05
	70	0.420	40.8	4.82 ± 0.01	2.65 ± 0.02	2.68 ± 0.02	0.03 ± 0.03	1.92 ± 0.01	1.81 ± 0.02	−0.11 ± 0.02
	90	0.736	29.1	5.36 ± 0.01	3.34 ± 0.02	3.33 ± 0.01	−0.01 ± 0.02	2.62 ± 0.02	2.43 ± 0.02	−0.19 ± 0.03
Ac^-	0	0	78.5	4.57 ± 0.01	1.73 ± 0.04	1.73 ± 0.03	0.00 ± 0.05	0.93 ± 0.03	0.81 ± 0.04	−0.12 ± 0.05
	30	0.117	63.7	5.06 ± 0.01	2.33 ± 0.01	2.37 ± 0.01	0.04 ± 0.01	1.46 ± 0.01	1.36 ± 0.01	−0.10 ± 0.01
	50	0.237	52.1	5.55 ± 0.01	2.70 ± 0.01	2.78 ± 0.02	0.08 ± 0.02	1.86 ± 0.01	1.81 ± 0.02	−0.05 ± 0.02
	70	0.420	40.8	6.08 ± 0.01	3.22 ± 0.01	3.25 ± 0.01	0.03 ± 0.01	2.38 ± 0.01	2.25 ± 0.01	−0.13 ± 0.01
	90	0.736	29.1	6.73 ± 0.02	4.07 ± 0.03	4.08 ± 0.01	0.01 ± 0.03	3.35 ± 0.02	3.10 ± 0.02	−0.25 ± 0.03
$2\text{-}MPr^-$	0	0	78.5	4.67 ± 0.01	1.79 ± 0.03	1.84 ± 0.03	0.05 ± 0.04	1.01 ± 0.02	0.90 ± 0.03	−0.11 ± 0.04
	30	0.117	63.7	5.34 ± 0.01	2.28 ± 0.01	2.53 ± 0.01	0.25 ± 0.01	1.50 ± 0.02	1.57 ± 0.01	0.07 ± 0.02
	50	0.237	52.1	5.99 ± 0.01	2.80 ± 0.01	3.05 ± 0.01	0.25 ± 0.01	2.00 ± 0.02	2.01 ± 0.02	0.01 ± 0.03
	70	0.420	40.8	6.59 ± 0.01	3.35 ± 0.01	3.59 ± 0.01	0.24 ± 0.01	2.56 ± 0.01	2.57 ± 0.01	0.01 ± 0.01
	90	0.736	29.1	7.22 ± 0.01	4.29 ± 0.03	4.41 ± 0.03	0.12 ± 0.04	3.61 ± 0.02	3.46 ± 0.02	−0.15 ± 0.03
$6\text{-}MHp^-$	0	0	78.5	4.72 ± 0.01	1.80 ± 0.04	1.97 ± 0.03	0.17 ± 0.05	1.02 ± 0.05	1.07 ± 0.02	0.05 ± 0.05
	30	0.117	63.7	5.42 ± 0.01	2.30 ± 0.01	2.60 ± 0.01	0.30 ± 0.01	1.47 ± 0.01	1.69 ± 0.01	0.22 ± 0.01
	50	0.237	52.1	6.06 ± 0.01	2.79 ± 0.03	3.07 ± 0.01	0.28 ± 0.03	1.95 ± 0.01	2.10 ± 0.01	0.15 ± 0.01
	70	0.420	40.8	6.52 ± 0.01	3.29 ± 0.02	3.49 ± 0.01	0.20 ± 0.02	2.47 ± 0.02	2.51 ± 0.02	0.04 ± 0.03
	90	0.736	29.1	7.04 ± 0.01	4.13 ± 0.03	4.26 ± 0.03	0.13 ± 0.04	3.49 ± 0.02	3.32 ± 0.01	−0.17 ± 0.02

[a] The error given is *3 times* the standard error of the mean value or the sum of the probable systematic errors, whichever is larger. The values of the error limits for $\Delta \log K_M$ were calculated according to the error propagation after Gauss. [b] The values in water and in 50% (v/v) ethanol–water are from Table I, and those for $HCOO^-$ and Ac^- in the other ethanol–water mixtures from Table II of ref 28. [c] The dielectric constants for the ethanol–water mixtures are interpolated from the data given in Table XII of ref 47.

formation degree is achieved (see also section 3). This conclusion agrees with the results obtained for $M(phen)(CHAc)^+$ (entries 22a in Tables III and IV); it appears that in this case the four methylene groups forming the "plane" of the cyclohexyl chair interact favorably with the aromatic plane of phen. With very small alkyl groups only, the addition of a single carbon unit, e.g. to propionate, resulting in 2-methylpropionate, will lead to a significant increase in the formation degree (cf. entries 3 and 3a or 17 and 17a in Tables III and IV).

(2) *The geometry of the coordination sphere* of the metal ion has a remarkable influence on the formation degree of the closed species only if the alkyl residue of *i*-$AlCA^-$ is short. It is evident from Figure 6, as well as from entries 3, 10, and 17 of Tables III and IV, that Cu^{2+} and Zn^{2+} give only with 2-methylpropionate clearly different formation degrees for $M(phen)(2\text{-}MPr)^+_{cl}$. This is understandable; only a small alkyl residue is not flexible and adaptable enough that the geometry of the metal ion coordination sphere can influence its interaction with the phen rings. In agreement herewith, the percentages of the closed forms are always relatively similar or even identical within the error limits for the ternary Cu^{2+} and Zn^{2+} complexes with the larger ligands, i.e. $4\text{-}MVa^-$, $5\text{-}MHx^-$, and $6\text{-}MHp^-$ (n = 2–4). It may be added that stacking interactions depend much more on the geometry of the coordination sphere of the bridging metal ion[39] because aryl moieties are considerably less flexible.

(3) *The influence of the solvent*, originating in different solvation properties, is also evident from Figure 6. The intramolecular ligand–ligand interaction in $M(phen)(2\text{-}MPr)^+$ is clearly favored, if the solvent is changed from water to 50% (v/v) ethanol–water or dioxane–water. A similar effect is observed for the other ligand systems, though less pronounced. This result is very surprising and warrants further studies (see section 6) because the stability of unbridged adducts with hydrophobic and stacking interactions is inhibited by the addition of ethanol or dioxane.[27,28] On the other hand, the present result is similar to observations made with $M(phen)(PAc)^+$ and related complexes.[24,28]

6. Influence of Increasing Amounts of Ethanol on the Formation Degree of the Closed Species in Ternary $M(phen)(i\text{-}AlCA)^+$ Complexes. The results of the previous section (Tables III and IV; Figure 6) show that intramolecular ligand–ligand interactions in $M(phen)(i\text{-}AlCA)^+$ complexes are substantial also in 50% (v/v) aqueous ethanol or dioxane, and the ^1H NMR experiments (section 3) prove that the alkyl residues are still located on the aromatic rings of phen such that hydrophobic interactions occur (Figure 5). From Figure 6 it is evident that the most substantial influence of the organic solvent component occurs with $M(phen)(2\text{-}MPr)^+$, while the least effect is observed with $M(phen)(6\text{-}MHp)^+$; i.e., the complexes with the smallest and the largest alkyl residues show the greatest difference in their properties; this does not have to be so a priori; with arylalkanecarboxylates this was somewhat different.[28] However, in this latter study the influences of ethanol and dioxane were quite comparable. Therefore, we restricted these tedious and time-consuming measurements now to ethanol mixtures and determined in these solvents the stability constants for the (Cu^{2+} or Zn^{2+})/phen/(2-MPr or 6-MHp) systems; the results are summarized in Table V.[47]

From the equilibrium constants given in Table V it is evident that the overall stability of the binary and ternary complexes is governed by the polarity of the solvent; with increasing amounts of ethanol, complex stability increases. This result corresponds to our previous observation made with similar ligating systems; as everything is quite analogous, the corresponding plots, evaluations, and discussions given there[25,28] are also valid here; they are therefore not repeated. However, in combination with eq 9 the experimental data of Table V may be used to calculate the intramolecular equilibrium constants K_I (eq 6) and the percentages of the closed species formed in the different systems by attributing the stability increase (calculated via $\Delta \log K_M$) between the $M(phen)(i\text{-}AlCA)^+$ and the $M(phen)(HCOO \text{ or } Ac)^+$ complexes to the intramolecular ligand–ligand interaction (see section 4). The results of these calculations are listed for the several ethanol–water mixtures in Table VI.

The percentages for the closed species of equilibrium 6a dependent on the mole fractions of ethanol are plotted in the left parts of Figure 7 for the ternary $M(phen)(2\text{-}MPr)^+$ and $M(phen)(6\text{-}MHp)^+$ complexes. The right parts of Figure 7 show for comparison the corresponding results of an earlier study[28] with phenylalkanecarboxylates ($PheCA^-$), i.e. for the ternary $M(phen)(PheCA)^+$ complexes containing 2-phenylacetate (PAc^-) or 3-phenylpropionate (PPr^-); in these complexes intramolecular

(47) Åkerlöf, G. *J. Am. Chem. Soc.* **1932**, *54*, 4125–4139.

Table VI. Extent of the Intramolecular Hydrophobic Ligand–Ligand Interaction in the Ternary Complexes Containing Cu^{2+} or Zn^{2+}, 1,10-Phenanthroline (phen), and 2-Methylpropionate (2-MPr^-) or 6-Methylheptanoate (6-MHp^-) Depending on the Amount of Ethanol Added to Water: Intramolecular and Dimensionless Equilibrium Constant K_I (Eq 7–9) and Percentage of the Closed Species, Cu(phen)(i-AlCA)$^+_{cl}$ (Eq 6), in Different Solvents at I = 0.1 M ($NaNO_3$) and 25 °C

no.	complex	% (v/v) ethanol	$\Delta \log K_M$[a]	$\Delta \log K_{M/op}$[b]	$\Delta\Delta \log K$[c]	K_I[c]	% M(phen)-(i-AlCA)$^+_{cl}$[c]
1	Cu(phen)(2-MPr)$^+$	0	0.05 ± 0.04	−0.01 ± 0.04	0.06 ± 0.04 (0.06)	0.15 ± 0.11 (0.15)	13 ± 8 (11)
2		30	0.25 ± 0.01	0.02 ± 0.02	0.23 ± 0.01 (0.02)	0.70 ± 0.06 (0.08)	41 ± 2 (3)
3		50	0.25 ± 0.01	0.08 ± 0.02	0.17 ± 0.01 (0.03)	0.48 ± 0.05 (0.09)	32 ± 2 (4)
4		70	0.24 ± 0.01	0.03 ± 0.01	0.21 ± 0.01 (0.02)	0.62 ± 0.05 (0.08)	38 ± 2 (3)
5		90	0.12 ± 0.04	0.00 ± 0.02	0.12 ± 0.04 (0.05)	0.32 ± 0.13 (0.14)	24 ± 7 (8)
6	Zn(phen)(2-MPr)$^+$	0	−0.11 ± 0.04	−0.12 ± 0.05	0.01 ± 0.04 (0.06)	0.02 ± 0.08 (0.14)	2 ± 8 (13)
7		30	0.07 ± 0.02	−0.07 ± 0.03	0.14 ± 0.02 (0.04)	0.38 ± 0.07 (0.12)	28 ± 4 (6)
8		50	0.01 ± 0.03	−0.08 ± 0.03	0.09 ± 0.03 (0.04)	0.23 ± 0.08 (0.11)	19 ± 5 (7)
9		70	0.01 ± 0.01	−0.12 ± 0.01	0.13 ± 0.01 (0.02)	0.35 ± 0.04 (0.06)	26 ± 2 (3)
10		90	−0.15 ± 0.03	−0.22 ± 0.02	0.07 ± 0.03 (0.03)	0.17 ± 0.08 (0.09)	15 ± 6 (7)
11	Cu(phen)(6-MHp)$^+$	0	0.17 ± 0.05	−0.01 ± 0.04	0.18 ± 0.05 (0.06)	0.51 ± 0.17 (0.21)	34 ± 8 (9)
12		30	0.30 ± 0.01	0.02 ± 0.02	0.28 ± 0.01 (0.02)	0.91 ± 0.06 (0.09)	48 ± 2 (3)
13		50	0.28 ± 0.03	0.08 ± 0.02	0.20 ± 0.03 (0.04)	0.58 ± 0.12 (0.14)	37 ± 5 (6)
14		70	0.20 ± 0.02	0.03 ± 0.01	0.17 ± 0.02 (0.03)	0.48 ± 0.08 (0.09)	32 ± 3 (4)
15		90	0.13 ± 0.04	0.00 ± 0.02	0.13 ± 0.04 (0.05)	0.35 ± 0.13 (0.14)	26 ± 7 (8)
16	Zn(phen)(6-MHp)$^+$	0	0.05 ± 0.05	−0.12 ± 0.05	0.17 ± 0.05 (0.07)	0.48 ± 0.18 (0.25)	32 ± 8 (11)
17		30	0.22 ± 0.01	−0.07 ± 0.03	0.29 ± 0.01 (0.03)	0.95 ± 0.06 (0.15)	49 ± 2 (4)
18		50	0.15 ± 0.01	−0.08 ± 0.03	0.23 ± 0.01 (0.03)	0.70 ± 0.06 (0.12)	41 ± 2 (4)
19		70	0.04 ± 0.03	−0.12 ± 0.01	0.16 ± 0.03 (0.03)	0.45 ± 0.09 (0.10)	31 ± 4 (5)
20		90	−0.17 ± 0.02	−0.22 ± 0.02	0.05 ± 0.02 (0.03)	0.12 ± 0.06 (0.08)	11 ± 5 (6)

[a] These values and error ranges (*3 times* the standard error) are from Table V. [b] The values of $\Delta \log K_{M/op}$ are the averages of $\Delta \log K_M$ determined for the systems with $HCOO^-$ and Ac^- in each individual solvent (see Table V). [c] The error limits given with these data (eq 8) result from the errors of the individual values of $\Delta \log K_M$. The error limits in parentheses include also the error in $\Delta \log K_{M/op}$; these errors should be used in external comparisons. For internal comparisons, e.g., between the complexes containing 2-MPr^- or 6-MHp^- in the *same* solvent, the errors based only on the individual $\Delta \log K_M$ value are more appropriate because $\Delta \log K_{M/op}$ has then the same value and therefore any error in $\Delta \log K_{M/op}$ will influence the result in the same (systematic) way. Regarding the meaning of the formula, M(phen)(i-AlCA)$^+_{cl}$, and the possible formation of closed complexes with somewhat different structures, see the discussion in section 7.

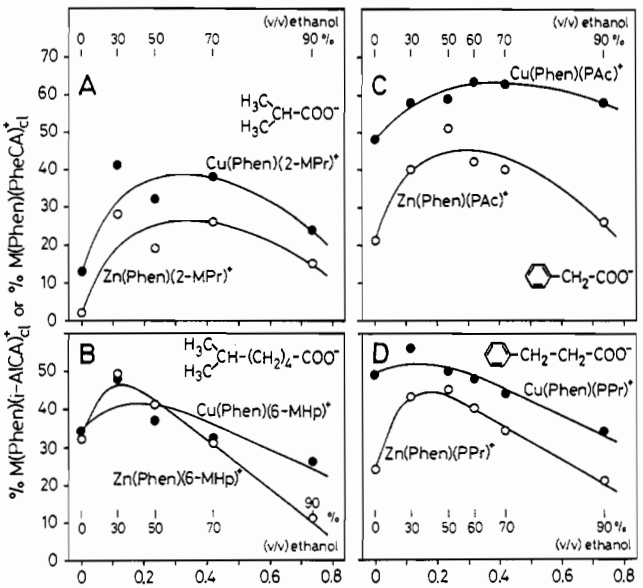


Figure 7. Formation degree of the intramolecularly closed species (eq 6) in ternary M(phen)(2-MPr)$^+$ (A), M(phen)(6-MHp)$^+$ (B), M(phen)(PAc)$^+$ (C), and M(phen)(PPr)$^+$ (D) complexes of Cu^{2+} (●) and Zn (○) depending on the mole fractions of ethanol; the second solvent component is always water. The data are taken from Table VI for parts A and B and from ref 28 for parts C and D (I = 0.1; 25 °C).

stacks are formed between the phenyl residue and the aromatic rings of 1,10-phenanthroline. It is evident that addition of (some) ethanol to an aqueous solution of these ternary complexes *favors* the formation degree of the closed species. This formation degree reaches a maximum, depending on the complex system considered, between about 30 and 70% (v/v) ethanol–water. Only in solutions that contain more than about 70% ethanol does the concentration of the closed species decrease, though it may still be of the order found in aqueous solution.

It should be emphasized that the rather general description given in the preceding paragraph holds for all eight ternary complexes considered in Figure 7, despite the fact that the absolute formation degrees of the closed species differ due to the different coordination geometries of Cu^{2+} and Zn^{2+} and due to the different structures of the alkyl and aryl residues of the carboxylate ligands. It may be added that for M(phen)(6-MHp)$^+$ with Cu^{2+} or Zn^{2+} even the absolute formation degrees of the closed species are identical within experimental error at least up to 70% ethanol (Table VI; Figure 7B). This agrees with the conclusions given in section 5: a large alkyl residue is flexible and adaptable enough to overcome the restrictions (otherwise) imposed by the coordination geometry of the metal ion.

Finally, it must be added that the results described in this section are not unique for ethanol–water mixtures. Tentatively it is evident from sections 4 and 5 (Figure 6) that for dioxane–water mixtures corresponding properties must be expected. In fact, for ternary complexes with phenylalkanecarboxylates this has been proven.[28]

7. Opposing Solvent Effects. Why Do Certain Amounts of Ethanol Favor the Formation of the Intramolecularly Closed Complexes? These problems have been discussed in ref 28 (see also ref 22) for ternary complexes containing intramolecular stacks. From Figure 7 it is evident that the main difference between stacking and hydrophobic ligand–ligand interactions is only in the formation degree of the closed species: as one might expect, intramolecular stacking adducts between aromatic ring systems are somewhat more stable, i.e. reach a larger formation degree, than "simple" hydrophobic adducts involving alkyl residues. Therefore, the reasonings given earlier[28] for stacking adducts are also valid here, though through the present results the effects are receiving a much broader and generally more valid basis. Hence, with this information taken into account, some of the earlier conclusions are reformulated and summarized below.

In case of unbridged stacking/hydrophobic adducts, increasing amounts of ethanol or dioxane clearly *weaken* the stability of the adducts.[28] This observation is easily rationalized as the addition of these organic solvents leads to a solvation of the aryl and/or alkyl moieties by the alkyl units of the solvent molecules. Hence, this "hydrophobic" solvation competes with the formation of the

unbridged adducts and thus reduces their formation degree.

The influence of organic solvents on the formation degree of the closed species in the M(phen)(*i*-AlCA)$^+$ and M(phen)(PheCA)$^+$ complexes is obviously more complicated (Figure 7). There is the unexpected result that some ethanol (or dioxane)[28] favors the intramolecular interaction (eq 6a), and only at high concentrations of the organic solvent does inhibition occur. It is evident that there must be two opposing solvent effects, and on the basis of the experience with *unbridged* adducts, it is also evident that the bridging metal ion must be the cause for the effects.

A simple explanation of the observations may be based directly on equilibrium 6a. Addition of small amounts of an organic solvent may lead to a preferred hydrophobic solvation of the intramolecular aromatic/aliphatic adduct because the lypophilicity of this adduct will act as a germ and attract the organic molecules forming a micelle-like hydrophobic unit close to the metal ion; the formation of this "micelle" will favor the formation of the closed species. It is evident that, as soon as this micelle-like unit has reached a size where it is coming into conflict with the hydration sphere of the bridging metal ion, no further organic solvent molecules can favorably be added. Now, with increasing and already relatively large amounts of organic solvent molecules, the hydrophobic residues of the open isomer in equilibrium 6a are individually solvated; this of course favors the left side of the equilibrium and inhibits also the recombination of the residues to form the intramolecular adduct.

This whole process must obviously be governed by the bridging metal ion because this can be the only cause for the apparent initial inhibition of the solvation of the aliphatic/aromatic residues of the ligands by the organic solvent molecules in the *open* isomers; note, in the *unbridged* adducts the individual organic moieties are obviously preferably solvated. It appears that the aqueous solvation shell of the metal ion in the open isomer initially inhibits the lypophilic solvation of the organic ligand residues; in the closed isomer this hydration shell is possibly already reduced or at least distorted; i.e., one side of the hydration shell is already shielded by the intramolecular adduct. In accord with this view is the observation that the promotional effect of the organic solvent becomes smaller with an increasing length of the organic ligand residue (i.e., the distance to the hydration shell is increasing), and the maximum of the promotional effect moves to lower concentrations of the organic solvent and most probably disappears if the organic ligand residue is large enough. Needless to say, in those systems where the effect operates, at higher concentrations of the organic solvent the hydration shell will be reduced, allowing then an individual solvation of the organic ligand residues and thus giving rise to the expected inhibition. With this relatively simple picture the experimental observations (i.e. the shape of the curves in Figure 7) for the ternary complexes may be rationalized.

It must be emphasized, however, that this "picture" implies for the micelle-like closed species in the organic solvents a more complicated structure than the one suggested for aqueous solution (Figure 4). It is to be expected that different hydrophobic solvation degrees mean somewhat different structures for the closed adduct, leading even to species in which organic solvent units intercalate between the aryl/alkyl residues of the ternary complex.[48] This type of separation of the aryl/alkyl residues via intercalation is in accordance with the ^{1}H NMR observations (section 3): the upfield shifts are less pronounced in 50% (v/v) ethanol–water than in water (Figure 5), and this may reflect a larger average distance between the interacting moieties in the bridged adduct. To conclude: the so-called "closed" species in the organic solvent mixtures must actually be viewed as a whole series of species,[49] all of which however still contribute to the increased stability of the complex; i.e., they have an intramolecular ligand–ligand interaction. Species in which the aromatic and/or aliphatic residues do not "feel" each other's presence anymore are expected to cancel in the evaluation of the results, which is based on the constants measured for M(phen)(HCOO)$^+$ and M(phen)(Ac)$^+$, and these latter complexes form only the open isomer.

A further finer, though possibly most important, detail may be added. The promotion of the stability of the closed species could occur in an indirect way through the hydrophobic environment created by the micelle-like structure close to the metal ion: this could reduce the *effective* dielectric constant at the metal ion and consequently the M^{2+}/O^- binding would be stabilized; in fact, this would be quite a powerful mechanism.[25,28] One might also think that with an increasing concentration of the organic solvent a facilitated reduction not only of the aqueous coordination sphere but also of the coordination number of the metal ion occurs especially in the closed species. However, this seems *not* so because one would expect that Cu^{2+} and Zn^{2+} change their coordination number at different organic solvent:water ratios, and this contrasts with the experimental observations: the properties of the Cu^{2+} and Zn^{2+} complexes parallel each other rather well in all systems (Figure 7). More of a parallelism as observed is expected, however, if the stability increase occurs via an alteration of the effective dielectric constant as indicated above.

Conclusions

It seems worthwhile to refer here also to some other studies that appear relevant in connection with the presented results. For example, the *intra*molecular hydrophobic association of two alkyl chains (of oligoethylene glycol diethers and diesters) in aqueous solution has been described.[4] This observation corresponds to the intramolecular hydrophobic interaction of the two isopropyl groups in the Cu(L-leucinate)$_2$ complex.[22] Recently, also the dimerization of the 1:2 Cu^{2+}–decanoate complex (CuA_2) according to

$$2CuA_2 \rightleftharpoons Cu_2A_4$$

was quantified: it was observed[50] that the dimerization constant increased with the dioxane content of the aqueous solution, i.e. from 0.3 to 0.4 and 0.5 mole fraction of dioxane. In view of the results described in the present study (Figure 7), it appears, aside from other effects,[50] that dioxane is promoting the intramolecular association of the alkyl chains in the dimeric complex; there are unfortunately no data for larger dioxane concentrations given; it would have been interesting to see if the dimerization tendency is decreasing again.

Another study[3] of interest here deals with cyclodextrin–adamantanecarboxylate inclusion complexes, which have been used as models for studying the hydrophobic effect. Addition of methanol to an aqueous solution weakens the adamantanecarboxylate/β-cyclodextrin interaction, and this gradual trend is reflected in the $\Delta G°$ values; however, the values for $\Delta H°$ and $T\Delta S°$ vary dramatically, passing through a maximum at approximately 30% methanol. This indicates, despite the fact that not only hydrophobic effects are involved in this complex formation,[3] that it is difficult to predict from stability measurements (which correspond to $\Delta G°$ values) as discussed in the present study, if enthalpy or entropy changes are the main source of the solvent dependence and the observed maximum regarding the formation degree of the closed species (eq 6a).

As indicated already in the Introduction, the importance of hydrophobic and stacking interactions in systems of biological origin is now well recognized,[3-11] but the interplay between these interactions and the coordination of metal ions is evidently only at the brink of recognition.[15-17,38] The latter is even more true if the influence of mixed aqueous/organic solvents on such systems is considered.[22,27,28]

The cooperative effects that may be created by the interplay between metal ion coordination, hydrophobic or stacking inter-

(48) (a) For the intercalation of water molecules, crystal[48b] and theoretical[48c] studies of hydrophobic interactions support the idea that the hydrophobic effect in aqueous solution can act over longer distances (than originally expected) via solvent-separated associations involving alkyl groups or aromatic ring systems. (b) Srikrishnan, T.; Parthasarathy, R. *Arch. Biochem. Biophys.* **1985**, *239*, 38–45. (c) Ravishanker, G.; Beveridge, D. L. *J. Am. Chem. Soc.* **1985**, *107*, 2565–2566.

(49) This description does not imply that the structure of the closed "isomer" in *aqueous* solution is a rigid situation (Figure 4). Of course, also a whole series of conformers is possible here.

(50) Fujii, Y.; Jimbo, K.; Yamada, H.; Mizuta, M. *Polyhedron* **1985**, *4*, 491–496.

actions, and reduced solvent polarity or lower effective dielectric media have recently been discussed[28] for active-site cavities of enzymes, especially for carboxypeptidase A. The possibility of reducing the effective dielectric constant close to a metal ion via a nearby hydrophobic micelle offers a very subtle tool for nature, especially as the energy differences[46] involved are very small. For example, in the present study the maximum stability increase observed equals only 0.29 log unit, corresponding to −1.7 kJ/mol, but this leads already to a formation degree for the closed species (eq 6a) of 49%. Assuming that such a closed conformation of a complex is the reactive species in an enzymic process, it is evident that some few percent of this species are enough for a continuous flow of the reaction, and the desired selectivity is in this way also achieved.

Acknowledgment. The support of this research by a grant from the Swiss National Science Foundation and a fellowship to G.L. from the University of Basel within the exchange program between the People's Republic of China and Switzerland is gratefully acknowledged.

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Novel Drums and Mixed-Drum Organooxotin Clusters from Carboxylic, Phosphinic, and Phosphoric Acids[1,2]

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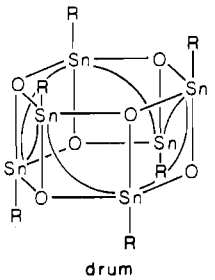
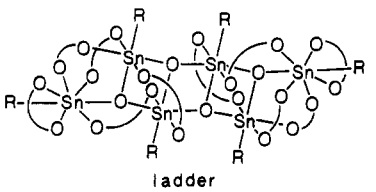
Received January 29, 1988

A variety of new "drum" geometries were synthesized by a condensation reaction of an alkylstannonic acid with either a carboxylic acid or a phosphorus-based acid. The structures of $[MeSn(O)O_2CMe]_6$ (**1**), $[(MeSn(O)O_2CMe)(MeSn(O)O_2P(t\text{-}Bu)_2)]_3$ (**2**), and $[n\text{-}BuSn(O)O_2P(OPh)_2]_6$ (**3**) were revealed by X-ray analysis. Interestingly, the mixed-drum composition **2** resulted from the reaction of the drum formulation **1** with di-*tert*-butylphosphinic acid. Also an oxygen-capped cluster $[(n\text{-}BuSn(OH)O_2P(OPh)_2)_3O][(PhO)_2PO_2]$ (**8**) is formed when the same reaction that was used to prepare **3** is conducted at 25 °C rather than at reflux. **1** crystallizes in the rhombohedral space group $R\bar{3}$ with a_H = 17.420 (5) Å, c_H = 9.963 (2) Å, and Z = 3. **2** crystallizes in the monoclinic space group $C2/c$ with a = 21.495 (4) Å, b = 28.032 (6) Å, c = 10.013 (2) Å, β = 95.34 (2)°, and Z = 4. **3** crystallizes in the monoclinic space group $P2_1/n$ with a = 14.252 (3) Å, b = 17.346 (2) Å, c = 21.987 (3) Å, β = 91.62 (1)°, and Z = 2. The conventional unweighted residuals were 0.023 (**1**), 0.036 (**2**), and 0.040 (**3**).

Introduction

In several recent articles,[1b,3-6] we have identified new structural forms of organotin compounds. X-ray analysis reveals all are oxotin derivatives and possess hexacoordinated tin atoms in a four-membered stannoxane ring, $(-Sn-O-)_2$, as a common structural feature. "Drum" compositions $[R'Sn(O)O_2CR]_6$ and "ladders" $[(R'Sn(O)O_2CR)_2R'Sn(O_2CR)_3]_2$ result from the reaction of an aryl- or alkylstannonic acid with a carboxylic acid.[1b,c] An alternate route makes use of an organotin trichloride in reaction with a salt of the carboxylic acid.





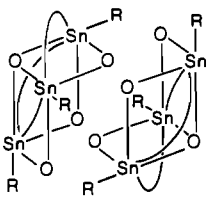
When phosphorus-based acids are used instead of a carboxylic acid, the geometrical forms isolated are more diverse, although a ladder structure has not been obtained thus far with this type of ligand. We have reported a cube[6] and an oxygen-capped cluster[5] resulting from the reactions of *n*-butylstannonic acid with dicyclohexylphosphinic acid and diphenylphosphinic acid, respectively. The cube has the composition $[n\text{-}BuSn(O)O_2P(C_6H_{11})_2]_4$ while the oxygen-capped cluster exhibits the ionic formula $[(n\text{-}BuSn(OH)O_2PPh_2)_3O][Ph_2PO_2]$. Hydrogen bonding is present between the hydroxyl groups in the cationic portion and the oxygen atoms of the phosphinate anion.

The drum and open-drum or "ladder" forms, $[n\text{-}BuSn(O)O_2C(C_6H_{11})]_6$ and $[(n\text{-}BuSn(O)O_2CC_6H_{11})_2(n\text{-}BuSn(O_2CC_6H_{11})_3)]_2$, which contains the same organotin group and cyclohexanoate ligand, interconvert as shown by ^{119}Sn NMR.[1b] Hydrolytically, the drum form is more stable. The hydrolysis reaction in eq 1 illustrates this. In excess carboxylic acid, the

$$[(R'Sn(O)O_2CR)_2R'Sn(O_2CR)_3]_2 + 2H_2O \rightarrow [R'Sn(O)O_2CR]_6 + 4RCO_2H \quad (1)$$

reaction may be reversed and the drum opens up, yielding the open drum or ladder.

Examination of the structural relationships among the forms that have been isolated suggests that additional oligomers in other cluster arrangements are possible. For example, the tin–oxygen framework of the oxygen-capped cluster[5] can be viewed as a cube with one corner removed.



In this paper we explore further routes to these interesting new oligomeric oxotin compounds using acetate, di-*tert*-butyl-

(1) (a) Organotin Clusters 3. (b) Part 2; Chandrasekhar, V.; Schmid, C. G.; Burton, S. D.; Holmes, J. M.; Day, R. O.; Holmes, R. R. *Inorg. Chem.* **1987**, *26*, 1050–1056. (c) Part 1: Holmes, R. R.; Schmid, C. G.; Chandrasekhar, V.; Day, R. O.; Holmes, J. M. *J. Am. Chem. Soc.* **1987**, *109*, 1408–1414.
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