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TERNARY COMPLEXES IN SOLUTION: INTRAMOLECULAR HYDROPHOBIC AND STACKING INTERACTIONS IN MIXED LIGAND COMPLEXES FORMED BY COPPER(II), 2,2'-BIPYRIDYL OR 1,10-PHENANTHROLINE, AND *n*-BUTYL DIPHOSPHATE ($BuDP^{3-}$) OR PHENYL DIPHOSPHATE ($PhDP^{3-}$)[1,2]

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ABSTRACT. The stability constants of the 1:1 complexes formed between Cu^{2+} or $Cu(Arm)^{2+}$, where Arm = 2,2'-bipyridyl or 1,10-phenanthroline, and phenyl diphosphate ($PhDP^{3-}$) or *n*-butyl diphosphate ($BuDP^{3-}$) [$R\text{-}DP^{3-}$ = $PhDP^{3-}$ or $BuDP^{3-}$], were determined by potentiometric pH titrations in aqueous solution (25°C; I = 0.1 M, $NaNO_3$). It is shown that the stability of the binary $Cu(R\text{-}DP)^-$ complexes is solely determined by the basicity of the diphosphate group; this is different for the ternary $Cu(Arm)(R\text{-}DP)^-$ complexes. It is demonstrated that the equilibrium, $Cu(Arm)^{2+} + Cu(R\text{-}DP)^- \rightleftharpoons Cu(Arm)(R\text{-}DP)^- + Cu^{2+}$, is considerably displaced to its right hand side. Part of this displacement is due to the well known experience that mixed ligand complexes formed by a divalent 3d ion, a heteroaromatic N base and an O donor ligand possess an increased stability. However, the other part of this displacement is due to an intramolecular ligand-ligand interaction between parts of the phenyl or *n*-butyl residues and the aromatic rings of Bpy or Phen. The formation degree of the intramolecular stacks in the $Cu(Arm)(PhDP)^-$ complexes corresponds to approximately 35%, whereas the formation degree of the intramolecular hydrophobic adducts in the $Cu(Arm)(BuDP)^-$ species reaches only about 15%. The relevance of these results regarding biological systems is shortly indicated.

INTRODUCTION

Hydrophobic and stacking interactions belong to the prominent noncovalent interactions which determine to a large part the shape of molecules in biological systems and which affect the selectivity of reactions as well [3,4]. In low molecular weight metal ion complexes such interactions can also be observed [1,2,4-8], e.g., in mixed ligand complexes consisting of Cu^{2+}, 2,2'-bipyridyl (Bpy) or 1,10-phenanthroline (Phen), i.e., of a heteroaromatic nitrogen base (= Arm) and of ligands, like phenyl phosphate or uridine 5'-monophosphate [9].

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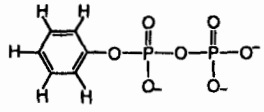
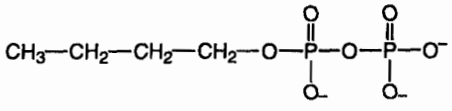
[1] Contributed on the occassion of the 10th Anniversary of the *Bulletin of the Chemical Society of Ethiopia* with the very best wishes of the authors for continuing success.

[2] This is part 61 of the series 'Ternary Complexes in Solution'; for parts 60 and 59, 58 see [1] and [2], respectively.

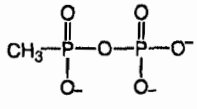
In our attempts to learn more about the complexing properties of nucleotides [10,11] and also about the effects which govern noncovalent interactions in mixed ligand complexes in aqueous solution [4,7], we have now determined via potentiometric pH titrations the stability of the complexes formed by Cu^{2+}, Bpy or Phen, and phenyl diphosphate ($PhDP^{3-}$) (see Figure 1) or *n*-butyl



$PhDP^{3-}$



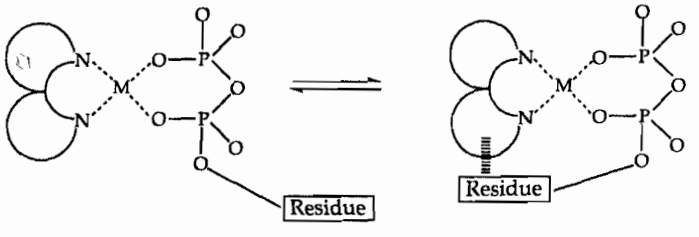
$BuDP^{3-}$



$MePP^{3-}$

Figure 1. Chemical structures of phenyl diphosphate ($PhDP^{3-}$), and *n*-butyl diphosphate ($BuDP^{3-}$). The ligand methylphosphonylphosphate ($MePP^{3-}$) will be used for comparisons (*vide infra*).

diphosphate ($BuDP^{3-}$) [$R\text{-}DP^{3-}$ = $PhDP^{3-}$ or $BuDP^{3-}$]. The results show that the stability of the indicated ternary complexes is larger than expected for the coordination of $Cu(Arm)^{2+}$ to the diphosphate residue of $R\text{-}DP^{3-}$. In this way evidence is obtained that the following intramolecular equilibrium (1) exists:



(1)

EXPERIMENTAL

The trisodium salts of phenyl diphosphate and *n*-butyl diphosphate were synthesized (by F.G.) according to published procedures [12]. All the other reagents were the same as used recently [1,13].

The preparation of the solutions and the determination of their exact concentrations were carried out as before [1,13].

The equipment used for the potentiometric pH titrations was from Metrohm AG, Herisau, Switzerland, as described in [1,13]. The equilibrium constants were determined from solutions which were 0.3 mM in R-DP ($I = 0.1$ M, $NaNO_3$; 25 °C). The experiments and their evaluations were carried out exactly as given previously [1]. It should be emphasized that in the pH range used for the calculations of the stability constants of the mixed ligand complexes, complex formation between Cu^{2+} and Bpy or Phen is already complete due to the high stability of the corresponding binary $Cu(Arm)^{2+}$ complexes [14,15]. This was also evident from the identity of the titration curves obtained from a pair of solutions, one which only contained HNO_3 and the other with Cu^{2+}/Arm in addition [13]. Of course, in the upper pH range such a pair of titrations begins to differ due to the formation of hydroxo complexes of $Cu(Arm)^{2+}$; at the corresponding pH the collection of data for the calculations was stopped. Hence, in the calculations [1,13] only complex formation between $Cu(Arm)^{2+}$ and R-DP had to be considered.

The final results for the acidity constants are the averages of at least 30 independent pairs of titrations and in the case of the stability constants for all systems at least seven independent pairs of titrations were made and the results averaged.

RESULTS AND DISCUSSION

For the diphosphate monoesters, $R\text{-}DP^{3-}$, considered in this study (Figure 1) only the release of the proton from the monoprotonated species according to equilibrium (2) is of relevance in the present context:

$$H(R\text{-}DP)^{2-} \rightleftharpoons R\text{-}DP^{3-} + H^+ \qquad (2a)$$

$$K^{H}_{H(R\text{-}DP)} = [R\text{-}DP^{3-}][H^+]/[H(R\text{-}DP)^{2-}] \qquad (2b)$$

Of course, the monoprotonated diphosphate group can be further protonated, but these protons are released with $pK_a \leq 1.3$ [16], i.e., far below the physiological pH range and therefore, these reactions are not considered further here, though we have measured the corresponding acidity constants [16].

If one defines $M^{2+} = Cu^{2+}$, $Cu(Bpy)^{2+}$ or $Cu(Phen)^{2+}$, one can treat simultaneously the formation of the binary and ternary complexes considered here. Of course, this is possible only because of the high stability of the $Cu(Arm)^{2+}$ species (see Experimental) which are practically completely formed before the onset of complex formation with R-DP occurs. Under the present experimental conditions the data of the potentiometric pH titrations may be completely described by taking into account equilibrium (2a) as well as equilibria (3a) and (4a):

$$M^{2+} + H(R\text{-}DP)^{2-} \rightleftharpoons M(H;R\text{-}DP) \qquad (3a)$$

$$K^{M}_{M(H;R\text{-}DP)} = [M(H;R\text{-}DP)]/([M^{2+}][H(R\text{-}DP)^{2-}]) \qquad (3b)$$

$$M^{2+} + R\text{-}DP^{3-} \rightleftharpoons M(R\text{-}DP)^{-} \qquad (4a)$$

$$K^{M}_{M(R\text{-}DP)} = [M(R\text{-}DP)^{-}]/([M^{2+}][R\text{-}DP^{3-}]) \quad (4b)$$

The results concerning equilibria (2a) through (4a) for the ligands $PhDP^{3-}$ and $BuDP^{3-}$ are collected in Table 1. To our knowledge [17-19] none of the equilibrium constants listed in Table 1 has been determined before.

Table 1. Negative logarithms of the acidity constants (equation 2) of monoprotonated phenyl diphosphate ($PhDP^{3-}$) and *n*-butyl diphosphate ($BuDP^{3-}$) and logarithms of the corresponding binary $Cu(R\text{-}DP)^{-}$ and ternary $Cu(Arm)(R\text{-}DP)^{-}$ complexes (equation 4), as determined by potentiometric pH titrations in aqueous solution at 25 °C and I = 0.1 M ($NaNO_3$)[a,b].

$R\text{-}DP^{3-}$	$pK^{H}_{H(R\text{-}DP)}$	$\log K^{Cu}_{Cu(R\text{-}DP)}$	$\log K^{Cu(Bpy)}_{Cu(Bpy)(R\text{-}DP)}$	$\log K^{Cu(Phen)}_{Cu(Phen)(R\text{-}DP)}$
$PhDP^{3-}$	6.32±0.02	5.17± 0.05	5.82± 0.03	5.79±0.06
$BuDP^{3-}$	6.65± 0.02	5.59± 0.04	6.12± 0.03	6.11± 0.06

[a] The errors given are three times the standard error of the mean value or the sum of the probable systematic errors whichever is larger. The error limits of the derived data (see Table 2) were calculated according to the error propagation after Gauss.

[b] The stability constants of the monoprotonated complexes (equation 3) of both ligands could only be estimated; i.e. $\log K^{Cu}_{Cu(H;R\text{-}DP)} \approx 2.4$ and $\log K^{Cu(Bpy)}_{Cu(Bpy)(H;R\text{-}DP)} \approx \log K^{Cu(Phen)}_{Cu(Phen)(H;R\text{-}DP)} \approx 2.5$. The estimated error limits are in the order of ± 0.2 to 0.3 log units.

At first we shall consider the binary $Cu(PhDP)^{-}$ and $Cu(BuDP)^{-}$ species. It is well known that for a series of structurally related ligands (L) the stability of the complexes should solely depend on the basicity of the binding sites; i.e., a plot of $\log K^{M}_{ML}$ *versus* pK^{H}_{HL} should result in a straight line [20]. Indeed, if one takes into account also the data pairs obtained recently for cytidine 5'-diphosphate (CDP^{3-}), uridine 5'-diphosphate (UDP^{3-}) and thymidine 5'-diphosphate ($dTDP^{3-}$) [1], the plot seen in Figure 2 results in a straight line. This confirms also the earlier observation made with the corresponding nucleoside 5'-monophosphates [9] that the nucleobases of the above mentioned nucleotides do not participate in complex formation. In other words, the stability of these binary $Cu(R\text{-}DP)^{-}$ complexes is solely governed by the basicity of the diphosphate residue.

With the described results in mind it is interesting to view the data points due to the ternary $Cu(Arm)(R\text{-}DP)^{-}$ complexes which are also inserted in Figure 2 (empty and filled circles). Indeed, in this instance all four data points are considerably above the straight line valid for the binary complexes, which means that the stability difference defined in equation (5) is positive for all four mixed ligand complexes considered in this study.

$$\Delta\log K_{Cu/Arm/R\text{-}DP} = \log K^{Cu(Arm)}_{Cu(Arm)(R\text{-}DP)} - \log K^{Cu}_{Cu(R\text{-}DP)} \quad (5)$$

Of course, the difference between the logarithms of two equilibrium constants must also be a constant

[6,7,21,22]; in fact, this constant quantifies the position of equilibrium (6a):

$$Cu(Arm)^{2+} + Cu(R\text{-}DP)^{-} \rightleftharpoons Cu(Arm)(R\text{-}DP)^{-} + Cu^{2+} \quad (6a)$$

$$10^{\Delta \log K_{Cu/Arm/R\text{-}DP}} = \frac{[Cu(Arm)(R\text{-}DP)^{-}][Cu^{2+}]}{[Cu(Arm)^{2+}][Cu(R\text{-}DP)^{-}]} \quad (6b)$$

According to the general rule that $K_1 > K_2$, etc., one expects that equilibrium (6a) is on its left side with negative values for $\Delta\log K_{Cu/Arm/R\text{-}DP}$; this agrees with statistical estimations based on two bidentate ligands A and B [5], i.e. $\Delta\log K_{Cu/statist} \simeq -0.9$.

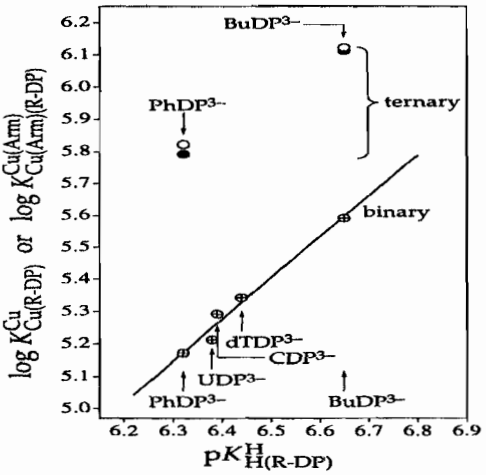


Figure 2. Evidence for an increased stability of the ternary Cu(Bpy)(R-DP)$^-$ (○) and Cu(Phen)(R-DP)$^-$ (●) complexes based on the relationship between log $K^{Cu(Arm)}_{Cu(Arm)(R\text{-}DP)}$ (○,●) or log $K^{Cu}_{Cu(R\text{-}DP)}$ (⊕) and $pK^{H}_{H(R\text{-}DP)}$ in aqueous solution at 25°C and $I = 0.1$ M ($NaNO_3$). The reference line represents the log $K^{Cu}_{Cu(R\text{-}DP)}$ versus $pK^{H}_{H(R\text{-}DP)}$ relationship for the binary Cu(R-DP)$^-$ complexes (⊕) which also includes Cu(CDP)$^-$, Cu(UDP)$^-$ and Cu(dTDP)$^-$, where CDP^{3-} = cytidine 5'-diphosphate, UDP^{3-} = uridine 5'-diphosphate and $dTDP^{3-}$ = thymidine 5'-diphosphate. The plotted equilibrium constant values are from Table 1; those for the CDP^{3-}, UDP^{3-} and $dTDP^{3-}$ systems are from [1].

From the data given in Table 1, and as also seen in Figure 2, it follows that $\Delta\log K_{Cu/Arm/R\text{-}DP}$ varies between about 0.5 and 0.65 log units; hence, equilibrium (6a) is displaced for all four ternary complexes considered here far to its right hand side. Indeed, due to previous experience an increased stability is actually expected for mixed ligand complexes formed by a divalent 3d metal ion, a heteroaromatic N base and an O donor ligand [5,6,21-25].

Therefore, it is necessary to evaluate the mentioned stability increases by comparing these with the situation in a complex formed with ligands which are unable to undergo any hydrophobic or stacking interaction. We use the Cu^{2+}/Arm/$MePP^{3-}$ systems, where $MePP^{3-}$ represents methylpho-

sphonylphosphate (see Figure 1) as a basis. For these we have recently obtained the following results [2]:

$$Cu(Bpy)^{2+} + Cu(MePP)^{-} \rightleftharpoons Cu(Bpy)(MePP)^{-} + Cu^{2+} \quad (7a)$$

$$\Delta \log K_{Cu/Bpy/MePP} = 0.42 \pm 0.05 \quad (7b)$$

$$Cu(Phen)^{2+} + Cu(MePP)^{-} \rightleftharpoons Cu(Phen)(MePP)^{-} + Cu^{2+} \quad (8a)$$

$$\Delta \log K_{Cu/Phen/MePP} = 0.45 \pm 0.05 \quad (8b)$$

It is evident that the metal ion coordination spheres in the systems of equilibria (7a) and (8a) are identical with those in equilibrium (6a). In all instances, aside from the N donor sites in Arm, only the O sites of the $-P(O)_2^-$-O-PO_3^{2-} residue are involved. The only difference between $MePP^{3-}$ and $BuDP^{3-}$ or $PhDP^{3-}$ is the presence of the aliphatic or aromatic residues, respectively, in the latter two ligands. Hence, the extra stability difference as defined in equation (9),

$$\Delta\Delta \log K = \Delta \log K_{Cu/Arm/R\text{-}DP} - \Delta \log K_{Cu/Arm/MePP} \quad (9)$$

has to be attributed to these residues because they can participate in an intramolecular ligand-ligand interaction what the methyl group of $MePP^{3-}$ can not. Indeed, for the Cu^{2+}/Arm/$PhDP^{3-}$ systems the difference according to equation (9) amounts to approximately 0.2 log units and is thus clearly outside of the error limits. This result provides convincing evidence that the intramolecular equilibrium (1) exists for these systems. Certainly, the ligand-ligand interaction indicated in equilibrium (1) could in addition be proven by other methods [26] as has been done for related systems, like Zn(Phen)(2-phenylacetate)$^+$ via ^{1}H-NMR shift experiments [27] or Cu(Phen)(2-phenylacetate)$^+$ via UV difference spectrophotometry (charge transfer) [28]. In the present case we have not carried out such additional measurements, but preferred to achieve a quantitative information about the actual position of equilibrium (1).

Taking into account that values for $\Delta \log K_{Cu/Arm/R\text{-}DP}$ define the position of equilibrium (6a) and those for $\Delta \log K_{Cu/Arm/MePP}$ that of equilibria (7a) and (8a) it is obvious [1] that the difference defined in equation (9) must also quantify the position of an equilibrium, namely that of (10):

$$Cu(R\text{-}DP)^{-} + Cu(Arm)(MePP)^{-} \rightleftharpoons Cu(Arm)(R\text{-}DP)^{-} + Cu(MePP)^{-} \quad (10)$$

Since the coordination spheres of the Cu^{2+} ions on both sides of equilibrium (10) are identical, the value for $\Delta\Delta$ log K (equation 9) is a true reflection of the extent of the intramolecular ligand-ligand interaction in the Cu(Arm)(R-DP)$^-$ complexes; in other words, positive values for $\Delta\Delta$ log K indicate that equilibrium (10) is shifted to its right hand side. Of course, if there is no ligand-ligand interaction in Cu(Arm)(RDP)$^-$, then equilibrium (10) will be exactly in the middle, i.e.$\Delta\Delta$ log K = 0, due to the identity of the coordination spheres.

If we designate now the two isomers which occur in equilibrium (1) as $Cu(Arm)(R\text{-}DP)^-_{op}$ and $Cu(Arm)(R\text{-}DP)^-_{cl}$, where op = open and cl = closed (i.e., via a hydrophobic or stacking interaction), we can define the corresponding intramolecular and dimensionless equilibrium constant K_I by equation (11):

$$K_I = [Cu(Arm)(R\text{-}DP)^-_{cl}]/[Cu(Arm)(R\text{-}DP)^-_{op}] \quad (11)$$

Values for K_I can then be obtained with equation (12),

$$K_I = \frac{10^{\Delta \log K_{Cu/Arm/R-DP}}}{10^{\Delta \log K_{(Cu/Arm/R-DP)op}}} - 1 \qquad (12a)$$

$$= \frac{10^{\Delta \log K_{Cu/Arm/R-DP}}}{10^{\Delta \log K_{Cu/Arm/MePP}}} - 1 \qquad (12b)$$

$$= 10^{\Delta\Delta \log K} - 1 \qquad (12c)$$

as shown previously [9,29-31]. Of course, if $\Delta\Delta \log K = 0$, as discussed above, K_I according to equation (12c) will then also become zero, meaning that equilibrium (1) is completely at its left side and only the open isomer, $Cu(Arm)(R\text{-}DP)^-_{op}$, forms.

Table 2. Extent of intramolecular ligand-ligand interaction (equilibrium 1) in ternary Cu(Arm)(R-P) complexes[a] as calculated from stability constants (Table 1) determined via potentiometric pH titrations: Stability enhancement $\Delta\Delta$ log K (equation 9) and data from which it is derived (equations 5, 7, and 8), intramolecular and dimensionless equilibrium constant K_I (equations 11 and 12), and percentage[b] of the species, $Cu(Arm)(R\text{-}P)_{cl}$, with the ligand-ligand interaction in aqueous solution at 25°C and I = 0.1 M ($NaNO_3$)[c]. For comparison some results[d] obtained under the same conditions for related systems are also given.

No [d]	Cu(Arm)(R-P)	$\Delta\log K_{Cu/Arm/R\text{-}P}$	$\Delta\log K_{Cu/Arm/MePP}$	$\Delta\Delta$ logK	K_I	%Cu(Arm) -$(R\text{-}P)_{cl}$
1a	Cu(Bpy)(CDP)$^-$	0.82±0.09	0.42±0.05	0.40±0.10	1.51±0.60	60± 9
b	Cu(Phen)(CDP)$^-$	0.83±0.10	0.45±0.05	0.38±0.11	1.40±0.62	58±11
2a	Cu(Bpy)(dTDP)$^-$	0.77±0.06	0.42±0.05	0.35±0.08	1.24±0.40	55± 8
b	Cu(Phen)(dTDP)$^-$	0.75±0.05	0.45±0.05	0.30±0.07	1.00±0.32	50± 8
3a	Cu(Bpy)(PhDP)$^-$	0.65±0.06	0.42±0.05	0.23±0.08	0.70±0.31	41±11
b	Cu(Phen)(PhDP)$^-$	0.62±0.08	0.45±0.05	0.17±0.09	0.48±0.32	32±15
4a	Cu(Bpy)(BuDP)$^-$	0.53±0.05	0.42±0.05	0.11±0.07	0.29±0.21	22±13
b	Cu(Phen)(BuDP)	0.52±0.07	0.45±0.05	0.07±0.09	0.17±0.23	15±17
5a	Cu(Bpy)(PhP)			0.29±0.03	0.95±0.14	49± 4
b	Cu(Phen)(PhP)			0.26±0.04	0.82±0.15	45± 5
6a	Cu(Bpy)(BuP)			0.10±0.09	0.26±0.25	21±16
b	Cu(Phen)(BuP)			0.07±0.08	0.17±0.21	15±15

[a] R-P = $R\text{-}MP^{2-}$ or $R\text{-}DP^{3-}$ = monoester of monophosphate or diphosphate, respectively. PhP^{2-} = phenyl phosphate. BuP^{2-} = *n*-butyl phosphate. For the definition of the other abbreviations see Figure 1 and legend of Figure 2. [b] % $Cu(Arm)(R\text{-}P)_{cl} = 100\ K_I/(1+K_I)$. [c] Regarding the error limits see footnote 'a' of Table 1. [d] Entries 1, 2 and 5, 6 are from references [1] and [9], respectively.

The results based on equations (5), (9), and (12) are summarized in Table 2, together with some previous results obtained for related systems [1,9]. From entries 3 (and other related ones) in Table 2 it is evident that there is no difference in the formation degree of the stacked species between the Cu(Bpy)(PhDP)$^-$ and the Cu(Phen)(PhDP)$^-$ complexes. This is not surprising, as the phenyl residue of PhDP^{3-} has a size which allows stacking in a "satisfactory fit" already with one of the pyridine-like rings of Bpy or Phen. Here it is worthwhile to view the structures of Cu(Bpy)(PhDP)$^-$ shown at the top in Figure 3:

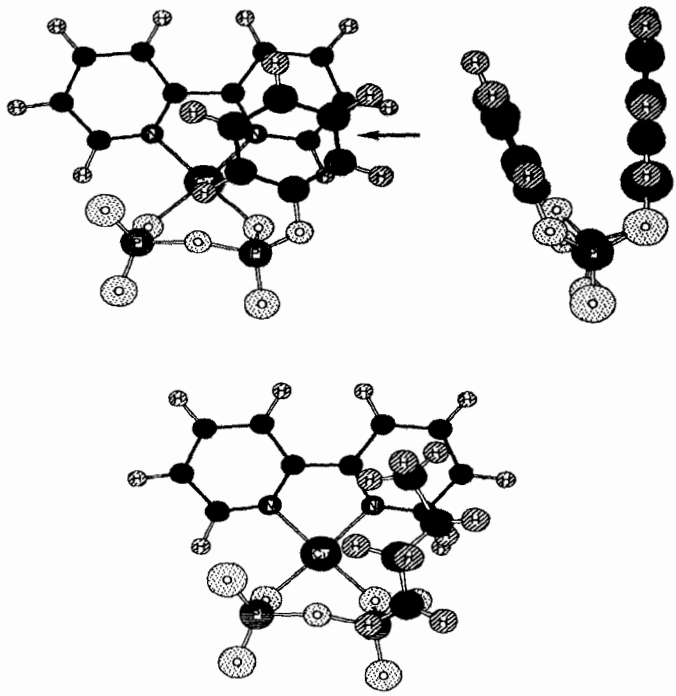


Figure 3. Schematic structures of the species with an intramolecular ligand-ligand interaction according to equilibrium (1) for Cu(Bpy)(PhDP)$^-$ (top) and Cu(Bpy)(BuDP)$^-$ (bottom) in solution. The structure at the right hand side at the top provides a view into the stack (see arrow) of Cu(Arm)(PhDP)$^-_{cl}$; the "bite" of the phosphate residue appears to be a bit too small to allow a parallel orientation of the aromatic-ring planes. It may be noted in this connection that in solution certainly a whole series of complexes with an intramolecular ligand-ligand interaction occur in which the orientation of the various interacting moieties differs somewhat; of course, the expression Cu(Arm)(R-DP)$^-_{cl}$, and the quantifications given for it (Table 2) encompass all of these species. The above structures were drawn with the program CS Chem3D, Version 3.5, from Cambridge Soft Corporation.

Due to the restrictions imposed by the Cu^{2+}-coordinated diphosphate residue, the aromatic rings overlap only partially and it appears further that the planes of the aromatic rings cannot reach a

parallel orientation. Such a bent or "butterfly"-type orientation of aromatic rings in stacks is known in the solid state [28,32,33] and occurs probably also here in solution. Indeed, in the Cu(Arm)(phenyl phosphate) complexes (entries 5 of Table 2) or in the Cu(Arm)(pyrimidine-nucleoside 5'-diphosphate)$^-$ systems (entries 1 and 2), which either have also a phenyl residue or a pyrimidine moiety (that is of a similar size) but which are sterically somewhat less restricted, it appears that the formation degree of the stacks is on average by about 15% higher despite the rather large error limits, if compared with the Cu(Arm)(PhDP)$^-$ species (entries 3).

The formation degrees of the hydrophobic adducts in Cu(Arm)(BuDP)$^-$ (entries 4 in Table 2) are small and hardly outside of the error limits, but the agreement with the results obtained previously [9] for the Cu(Arm)(*n*-butyl phosphate) systems (entries 6) is amazingly good. The formation degrees of these hydrophobic adducts have to be small because (most probably) only the terminal methyl group of the *n*-butyl residue is actually able to interact with a ring of Bpy or Phen as is evident from the structure given in the lower part of Figure 3. However, it may be added here that for several Zn(Phen)(alkanecarboxylate)$^+$ systems adduct formation has been proven by ^{1}H-NMR shift experiments [34]. Furthermore, the increasing tendency for hydrophobic adduct formation in the series, Cu(Phen)(3-methylbutyrate)$^+$ ($19 \pm 9\%$) < Cu(Phen)(4-methylvalerate)$^+$ ($26 \pm 10\%$) < Cu(Phen)(6-methylheptanoate)$^+$ ($34 \pm 9\%$), is also revealing [34].

To conclude, the present results show that the aromatic and aliphatic residues considered here are well suited for undergoing adduct formation, provided they are sterically well positioned. With regard to the potential interactions between nucleobase residues of nucleotides or nucleic acids and amino acid-side chains of proteins the described observations are meaningful [35] because they demonstrate that well defined structures can be created despite the fact that the interactions are weak.

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