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Discrimination of Metallosupramolecular Architectures in Solution by Using Diffusion Ordered Spectroscopy (DOSY) Experiments: Double-Stranded Helicates of Different Lengths

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Abstract: The translational diffusion coefficients of various helicates have been determined by using NMR diffusion spectroscopy (Diffusion Ordered SpectroscopY, DOSY), in order to investigate the individual behaviour of the helicates according to their length (different nuclearities; 1–5 metals), to the nature of the metal involved (Cu^I or Ag^I), as well to their bulkiness due to the presence of substituents on the periphery of the assembly. Furthermore, the spectrum of a mixture of helicates belonging to the same series, but with different lengths and nuclearities, showed the signals of each component, with no observable cross-linking, confirming the self-recognition properties of the helicates.

Keywords: diffusion coefficients · helical structures · NMR spectroscopy · self-recognition · supramolecular chemistry

Introduction

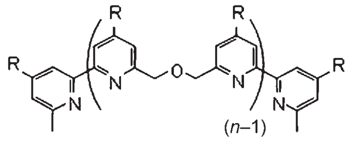
The generic term "helicate" was introduced[1] to designate metallosupramolecular architectures in which ligand strands organize around metal ions in a helical fashion.[1,2] Various types of helicates have been described involving different ligand strands and metal ions.[2] The first such entities were double helicates[1,3] formed from two identical ligand strands based on 2,2′-bipyridine-type coordination subunits linked through the 6,6′-positions by oxapropylene bridges.[4] These ligands can bear substituents such as carboxylic acid derivatives, in the 4,4′-position, thus allowing attachment of various functional residues.[4]

Upon complexation with cations (M) imposing a tetrahedral coordination geometry (Cu^I or Ag^I), blunt-ended helicates $[M_n(\mathbf{L})_2]$ are formed in which the substituents are projected out on the periphery, as, for instance, in deoxyribonucleohelicates (DNH).[5]

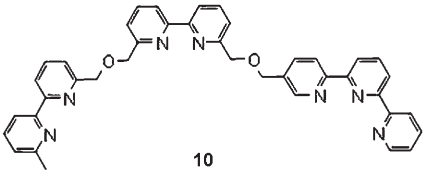
The solid-state structures of several such helicates have been described, most of them being dinuclear and a few trinuclear.[1,2,6] No crystallographic structures are available for helicates with a nuclearity higher than three, or for helicates formed from ligands bearing substituents.

It was therefore of interest to investigate unsubstituted as well as substituted helicates of different lengths by using other physical methods. Herein, we describe a DOSY (Diffusion Ordered SpectroscopY) NMR study of a homogeneous series of double-stranded helicates of increasing length ranging from mononuclear to pentanuclear $[M_n(\mathbf{L})_2]$ ($n=1$–5), formed by self-assembly from oligotopic strands **L**, either unsubstituted parent ligands (R = H) or bearing COX (X = OEt or NEt_2) substituents, and Cu^I or Ag^I cations.

Supramolecular systems, as well as combinatorial systems, were previously studied by using this technique,[7] in particu-



L	n	R
1	1	H
2	2	H
3	3	H
4	4	H
5	5	H
6	1	$CONEt_2$
7	2	$CONEt_2$
8	3	$CONEt_2$
9	3	CO_2Et



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lar, analogues of the first trinuclear double helicate $[Cu^I_3(\mathbf{3})_2]$[1] in which bipyridine groups of the ligand were replaced by phenanthroline units.[6b,c]

In the liquid state, the proton NMR spectra of all the present helicates containing diamagnetic cations exhibit the expected shifts and splitting compatible with a double-helical structure.[1,3] Furthermore, their electrospray (ES) mass spectra display the typical sets of signals and charges (m/z) corresponding to the ion pairs of helicates of charge $n+$ associated with 0 to $(n-1)$ anions.

In order to gain information on the features of these systems in solution, we used DOSY NMR experiments as a tool for determining their molecular volume, with a threefold goal: 1) to estimate the size of the helicates in solution, 2) to study a homogeneous series of species that have an incremental size difference and consequently to check the implementation and internal coherence of the methodology for charged coordination entities, 3) to discriminate the different species in a mixture, as a function of their individual diffusion coefficients.

We studied 1) individual double helicates of different nuclearities (1–5 metal ions) assembled from the same type of strand, 2) a mixture of these helicates, 3) trinuclear helicates containing the same metal ions, but with different ligands, 4) trinuclear helicates formed with the same ligands, but with different metal cations, and finally 5) a heterometallic helicate $[Cu^I_2Zn^{II}(\mathbf{10})_2]$ that differs from the parent tris-helicate $[Cu^I_3(\mathbf{3})_2]$ by having an additional pyridine group in the ligand strand and a bis-terpyridine-type Zn^{II} coordination centre.

Results and Discussion

The Pulsed-Field Gradient STimulated Echo (PFGSTE) NMR sequence[8] was used to measure the translational diffusion coefficient (D), which is a function of the molecular size and shape.[9]

The Stokes–Einstein equation [Eq. (1)], in which k_B is the Boltzmann constant, T is the absolute temperature and $f°$ is the friction coefficient, was used to determine the values of the spherical hydrodynamic radii (r_{sph}). For a spherical model, $f° = 6\pi\eta r_{sph}$ (η is the viscosity of the medium).

$$D = \frac{k_B T}{f^\circ} = \frac{k_B T}{6\pi\eta r_{sph}} \qquad (1)$$

The spherical equivalent radius (r_{eq}) may be calculated from the partial specific volume (ν) of the species and its molecular weight (M) by using Equation (2), in which N_A is the Avogadro constant.[9]

$$r_{eq} = \sqrt[3]{\frac{3M\nu}{4\pi N_A}} \qquad (2)$$

To fit with the real shape of the molecule in solution, all helicates were considered as ellipsoidal molecular objects. Relative to the spherical model, the ellipsoidal model (see footnote in Table 1) imposes a shape factor to extract the molecular dimensions from the measurement of D obtained by using NMR spectroscopy, as given in Equation (3), in which P is the ratio of the semimajor to the semiminor axis of the ellipsoids, with P being always greater than one.[10]

$$f = f^\circ \left(\frac{P^{-1/3}(P^2-1)^{1/2}}{\ln [P + (P^2-1)]^{1/2}} \right) \qquad (3)$$

This calculation needs a prior knowledge of one dimension of the molecular ellipsoidal object (a or b, see Table 1) to deduce the other from the r_{sph} value.

Table 1 summarises the measured diffusion coefficient (D), the associated spherical hydrodynamic radii (r_{sph} and r_{eq}) and the values of $2a$ and $2b$ corresponding to an ellipsoidal model (prolate), for solutions of each studied helicate in CD_3CN. Parameters a and b are deduced from the calculation of the frictional coefficient f in the case of an average ellipsoidal molecular shape.[10]

For the double-stranded Cu^I helicates formed with the unsubstituted ligands **1**–**5**, one dimension of the molecular ellipsoidal object was fixed at 5.5 Å, as derived from the crystal structure of the trinuclear helicate $[Cu^I_3(\mathbf{3})_2](PF_6)_3$ determined by using X-ray crystallography[1] and taking into account the van der Waals radii. This fixed length corresponds to the transverse distance, that is, 11 Å, which is expected to remain constant along the series.

Determination of the partial specific volume from the crystallographic parameters allowed calculation of the spherical equivalent radius (r_{eq}) [Eq. (2)] for comparison with the determined r_{sph} from DOSY experiments.

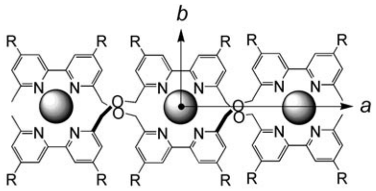
For the other helicates (**6**–**9**) formed with Cu^I and substituted ligands or with other metal ions, we made use of the results obtained from the unsubstituted series to fix one dimension, which is expected to stay constant in the molecular ellipsoid model (Table 1).

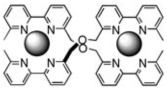
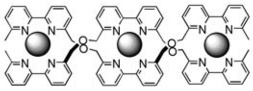
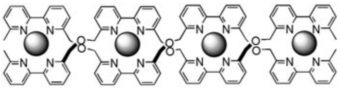
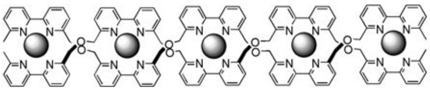
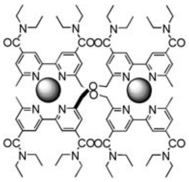
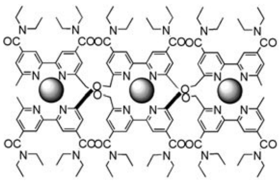
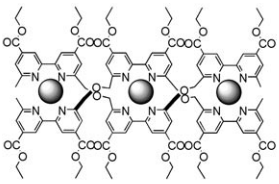
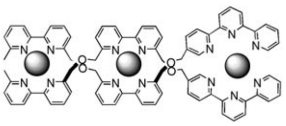
In the case of $[Cu^I_2Zn(\mathbf{10})_2]$, only a rough volume can be deduced from its hydrodynamic radius (r_{sph}), as there is no access to its transverse axis, nor to its longitudinal one.

Unsubstituted helicates: The spherical radii (r_{sph}) deduced from the NMR-measured diffusion coefficients, as well as the equivalent radii (r_{eq}) calculated from Equation (2), with-

Abstract in French: *Les coefficients de diffusion translationnelle de plusieurs groupes d'hélicates à double brin ont été mesurés par RMN DOSY (Diffusion Ordered SpectroscopY), en faisant varier leur nucléarité dans une même série, les métaux impliqués (Cu^I ou Ag^I), ainsi que leur encombrement stérique par adjonction de substituants à la périphérie. De plus, en analysant un mélange d'hélicates de même famille, mais de longueurs différentes, aucune espèce hybride n'est observée, confirmant ainsi la propriété d'auto-reconnaissance de ces assemblages.*

Table 1. Diffusion coefficients (D), spherical hydrodynamic radii (r_{sph}), calculated equivalent radii (r_{eq}) and lengths of the $2a$ and $2b$ axes of the ellipsoid obtained from DOSY measurements for double-stranded helicates. For clarity, the values $2a$ and $2b$ in Table 1 correspond to the scheme below, even for $2a$ shorter than $2b$, the shape factor being then that calculated with $P=$(semimajor axis)/(semiminor axis).[a]



	Helicate	D [$\mu m^2 s^{-1}$]	r_{sph} [Å]	r_{eq} [Å]	$2a$ [Å]	$2b$ [Å]
$[\mathrm{Cu^I}(\mathbf{1})_2]$		1550	4.1	4.8	6.5	11.0*
$[\mathrm{Cu^I_2}(\mathbf{2})_2]$		1260	5.0	6.1	9.5	11.0*
$[\mathrm{Cu^I_3}(\mathbf{3})_2]$		1010	6.3	7.0	16.0	11.0*
$[\mathrm{Ag^I_3}(\mathbf{3})_2]$		953	6.6	7.3	18.0	11.0*
$[\mathrm{Cu^I_4}(\mathbf{4})_2]$		950	6.7	7.7	18.0	11.0*
$[\mathrm{Cu^I_5}(\mathbf{5})_2]$		830	7.6	8.3	24.5	11.0*
$[\mathrm{Cu^I}(\mathbf{6})_2]$		1250	5.1	5.9	7.5	16.0*
$[\mathrm{Cu^I_2}(\mathbf{7})_2]$		880	7.2	7.3	13.5	16.0*
$[\mathrm{Cu^I_3}(\mathbf{8})_2]$		790	8.0	8.6	16.0	16.0*
$[\mathrm{Cu^I_3}(\mathbf{9})_2]$		852	7.4	8.2	16.0*	14.0
$[\mathrm{Ag^I_3}(\mathbf{9})_2]$		889	7.1	8.4	16.0*	13.5
$[\mathrm{Cu^I_2Zn}(\mathbf{10})_2]$		849	7.4	–	–	–

[a] According to the ellipsoidal model applied to the molecular shape, the lengths marked with * are fixed and allow the other dimension to be deduced from the r_{sph} value. Estimated error: ±0.5 Å on each axis a and b.

out contribution of the associated PF_6^- anions, are in good agreement with the nuclearity of the unsubstituted helicates (Figure 1). They increase linearly as one might expect for a homologous series of compounds in which molecular weight and size increase incrementally. The equivalent spherical radii (r_{eq}) are slightly greater than the determined r_{sph} values, due to the fact that in Equation (2) the partial specific volume is overestimated because the ellipsoidal model does not fit exactly to the real shape of the helicate assembly.

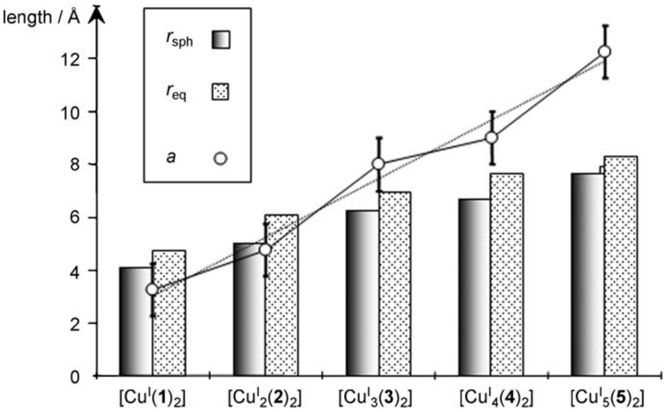


Figure 1. Evolution of the spherical hydrodynamic radii (r_{sph}) obtained from DOSY measurements, of r_{eq} calculated from Equation (2) (Table 1) and of the calculated longitudinal radii a (○), as a function of the nuclearity ($n=1$–5) of the double-stranded Cu^I helicates $[Cu^I_n(\mathbf{L})_2]$ formed from the unsubstituted ligands $\mathbf{L}=\mathbf{1}$–$\mathbf{5}$.

The calculated longitudinal (along the axis of the metal ions) radii (a) in the ellipsoidal model follow a mainly linear progression (with an average increment of 4 Å per coordination centre) as a function of the nuclearity of the helicates, keeping in mind that b is fixed at 5.5 Å for this series. The slope is higher than that for r_{sph} as the increase in nuclearity translates into an increase in the length of the double-helical species, leaving the transverse dimension more or less constant. These results provide a coherent set of data on the diffusion behaviour of the helicates and their relationship to the structural features of the metallosupramolecular entity. The value of $2a$ for $[Cu^I_3(\mathbf{3})_2]$ agrees with the length of the helicate obtained from crystal-structure data (Figure 2).[1]

Substituted helicates: A second series of helicates formed with the substituted ligands **6**–**8** and Cu^I was also investigated by using NMR diffusion measurements. As only UV, ^1H NMR and ES-MS spectral data, but no direct structural information, were available for complexes $[Cu^I(\mathbf{6})_2]$, $[Cu^I_2(\mathbf{7})_2]$ and $[Cu^I_3(\mathbf{8})_2]$, the molecular sizes were calculated from the diffusion NMR measurements, leading to estimates of the values of a and b in the ellipsoidal molecular-shape model from the determined spherical radius (r_{sph}), assuming that the transverse axis remains constant along the series, and keeping 16 Å for $2a$ in the case of $[Cu^I_3(\mathbf{8})_2]$.

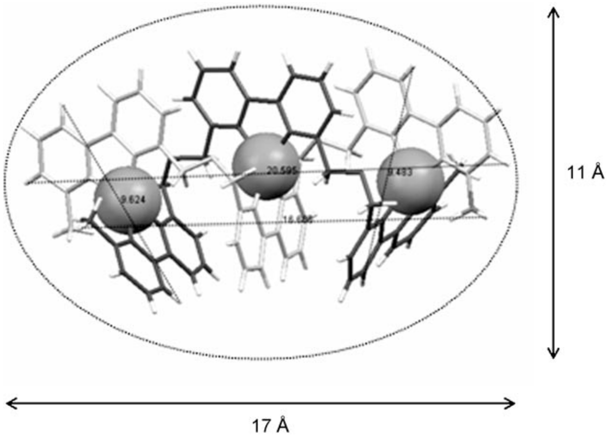


Figure 2. Solid-state molecular structure of the double-stranded trinuclear helicate cation $[Cu^I_3(\mathbf{3})_2]^{3+}$ determined by using X-ray crystallography data (from ref. [1]).

Again, the spherical radii (r_{sph}) as well as the r_{eq} values for the three helicates are in good agreement with their nuclearity (Table 1, Figure 3).

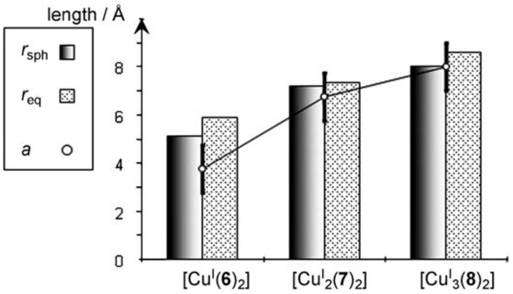


Figure 3. Evolution of the spherical hydrodynamic radii (r_{sph}) obtained from DOSY measurements, of r_{eq} calculated from Equation (2) (Table 1) and of the calculated longitudinal radii a (○), as a function of the nuclearity ($n=1$–3) of the double-stranded substituted helicates $[Cu^I_n(\mathbf{L})_2]$ formed from the ligands $\mathbf{L}=\mathbf{6}$–$\mathbf{8}$.

The introduction of bulky $CONEt_2$ substituents onto the bipyridine units of ligands **6**–**8** markedly increases the diameter of the complexes from 11 to 16 Å.

Trinuclear helicates formed with the same ligands, but with different metal cations: The tris-copper and tris-silver helicates formed with either ligands **3** or **9** gave, for the same ligand, similar spherical radii (r_{sph}) values determined from translational diffusion measurements (6.3 and 6.6 Å for **3**; 7.4 and 7.1 Å for **9**) within the experimental error (±0.5 Å), as well as similar equivalent radii (r_{eq}) values calculated from Equation (2) (Table 1). This is in agreement with the dimensions deduced from the crystallographic structures of $[Cu_3(\mathbf{3})_2]^{3+}$[1] and $[Ag_3(\mathbf{3})_2]^{3+}$.[6a]

Analysis of a mixture of unsubstituted helicates: A DOSY experiment (Figure 4) was performed on an equimolar (1.0 mm) mixture of the unsubstituted helicates $[Cu(\mathbf{1})_2]^+$, $[Cu_2(\mathbf{2})_2]^{2+}$, $[Cu_3(\mathbf{3})_2]^{3+}$, $[Cu_4(\mathbf{4})_2]^{4+}$ and $[Cu_5(\mathbf{5})_2]^{5+}$ in

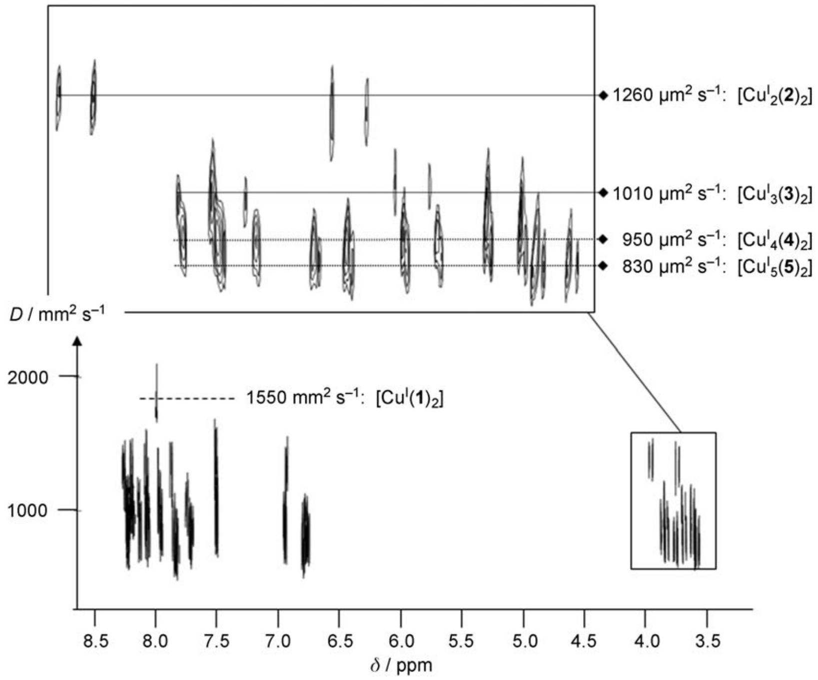


Figure 4. ^{1}H NMR DOSY spectrum of the unsubstituted helicate mixture.

CD_3CN. The resulting ^{1}H NMR spectrum shows a very complicated pattern due to the multiple spectral overlap. The 2D DOSY spectrum decomposes the 1D pattern into a vertical stacking of spectra, each level representing a different species in solution, distinguishable by its diffusion coefficient. The signals in the spectral region of the methylene-group protons ($\delta = 3.5$–4 ppm) are especially well separated, without any detectable cross-linking between ligands **1**–**5**. These results nicely illustrate the ability of the DOSY analysis to resolve a mixture of metallosupramolecular entities into its components. The 2D DOSY spectrum appears here like spectral "chromatography" allowing the NMR information to be read for a mixture of five components whereas the corresponding 1D spectrum was unreadable because of the multiresonance overlaps. The absence of signals associated with cross-links in the DOSY spectrum confirms the self-recognition property previously described for analogous mixtures of helicates.[11]

Conclusion

NMR diffusion experiments and especially DOSY spectra are of particular interest for the study of supramolecular assemblies like helicates *in solution*. They provided information about the dimensions of a series of helicates directly in solution, in the absence of solid-state crystal-structure data. Furthermore, the DOSY experiment was able to separate "spectrally" the five components of a helicate mixture by discriminating their diffusion coefficients. The example of the helicate series illustrated here can be easily expanded to other supramolecular as well as molecular systems for which solid-state characterization is unavailable or not possible, even if the system is a mixture of compounds. Furthermore, comparison of diffusion data with available solid-state structural data gives information about the eventual occurrence of specific solution effects such as aggregation, ion pairing and so forth.

Experimental Section

Materials and general methods: The following compounds were prepared as previously described: **1**–**9**,[4] **10**.[14] The following reagents were purchased from commercial sources: $[Cu^I(CH_3CN)_4]PF_6$ (Aldrich), $[Ag^I(CF_3SO_3)]$ (Aldrich) and $[Zn^{II}(BF_4)_2]\cdot 8H_2O$. ^{1}H NMR spectra (400 MHz) were recorded on a Bruker Ultrashield Avance 400 spectrometer. The residual solvent signal was used as an internal reference for ^{1}H NMR spectra.

Spectrometric analysis of the helicate mixtures

DOSY NMR experiments: The spectra were recorded on a Bruker Avance500 spectrometer, at 11.7 tesla, at the resonating frequency of 500.13 MHz for ^{1}H, using a BBI Bruker 5 mm gradient probe. The temperature was regulated at 298 K and no spinning was applied to the NMR tube. The diffusion NMR experiments were performed with a Pulsed-Field Gradient STimulated Echo (PFGSTE) sequence, using bipolar gradients.[8,12] The bipolar gradient duration and the diffusion time were optimized for each sample and were in the range of 1 to 1.5 ms and 100 to 200 ms, respectively. The evolution of the pulsed-field gradient during the NMR diffusion experiments was established in 30 steps, applied linearly between 1 and 50 $G\,cm^{-1}$. The duration of each NMR diffusion experiment was adjusted to finally obtain a minimum signal-to-noise ratio of 20. DOSY spectra were generated by using the program GIFA 5.2 (DOSY module), developed by the NMRTec company, using adapted algorithms, such as the inverse Laplace transform and maximum entropy, to build the diffusion dimension.[13]

Syntheses

*Preparation of helicate complexes formed by ligands **1**–**10** (see Table 1)*: Stock solutions of ligands **1**–**10** in CH_2Cl_2 (10^{-2} M, 20 mL) and of $[Cu^I(CH_3CN)_4]PF_6$, $[Ag^I(CF_3SO_3)]$ and $[Zn^{II}(BF_4)_2]\cdot 8H_2O$ in CH_3CN (10^{-2} M, 20 mL) were prepared. The appropriate amounts of ligand and metal salt were mixed, and the resulting solution was evaporated and redissolved in pure CD_3CN (0.500 mL) so that the concentration in the complex would be 2.5×10^{-3} M. The samples were then analysed by using ^{1}H NMR spectrometry without any further purification.

*Preparation of a mixture of unsubstituted Cu^I helicate complexes formed from ligands **1**–**5***: Appropriate volumes of solutions of complexes $[Cu(\mathbf{1})_2]^+$, $[Cu_2(\mathbf{2})_2]^{2+}$, $[Cu_3(\mathbf{3})_2]^{3+}$, $[Cu_4(\mathbf{4})_2]^{4+}$ and $[Cu_5(\mathbf{5})_2]^{5+}$ in CD_3CN were mixed, so that the concentration of each of them was 1.0×10^{-3} M. The resulting mixture was then analysed by using ^{1}H NMR spectrometry without any further purification.

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