Published in Chemistry - A European Journal 11 (1) : 185-194, 2005

Protonation Behaviour of Chiral Tetradentate Polypyridines Derived from α-Pinene. Chiralization of the Proton

Mathias Düggeli, Tobias Christen, Alexander von Zelewsky*

Department of Chemistry, University of Fribourg, Pérolles, 1700 Fribourg, Switzerland.
Fax: +41- 26-300 97 38; Tel: +41-26-300 87 32; E-mail: alexander.vonzelewsky@unifr.ch

Detailed protonation experiments of the [5,6]-pinene-bipyridine molecule and of the unsubstituted [4,5]-, and [5,6]-CHIRAGEN[0] ligands in various solvents indicate a variety of structures for the protonated species. UV/Vis- and NMR-measurements (including ^{15}N chemical shifts) show the transition from *trans* to *cis* conformation of [5,6]-pinene-bipyridine upon protonation, due to chelation of the proton. The [4,5]-CHIRAGEN[0] ligand, where the protonation sites of the nitrogen donors are at opposite side of the molecule, behave essentially like two independent bpy-moieties, when monitored by UV/Vis-, CD- and NMR-spectroscopy (including ^{15}N). In the case of the [5,6]-CHIRAGEN[0], a pocket of donor atoms provides a chiral environment for two protons per ligand.

Introduction

Only a few examples are known, where the proton is exchanged between four donor atoms of one or two ligands and the conformation of the ligand remained fixed. Sauvage *et al.* published in 1986 a mono-protonated catenane.[1] The macrocycles are interlocked and the 2,9-diphenyl-1,10-phenanthroline fragments are entwined. The molecular topography is strikingly similar to its copper(I)-analogue, the two phenanthroline units are facing each other with a dihedral angle of 61°. Although in the solid state, the acidic hydrogen atom is located on one of the four nitrogen sites, the ^{1}H-NMR spectrum corresponds to a symmetrical species, indicating a fast exchange of the binding between the four nitrogen atoms.

Another example was reported by Albrecht-Gary *et al.*.[2] They observed a mono-protonated species of a ligand containing six binding sites. The ^{1}H-NMR of this mono-protonated species is highly symmetrical, consistent with a folding of the flexible strand of the ligand around a single proton coordinated to two bpy subunits. This observation was confirmed by molecular modelling calculations with Hyperchem, which showed that the most stable conformation in a vacuum is a folded structure with stacking interactions between the aromatic parts.

The most recent example was published by Kress *et al.* in 2001.[3] These authors reported an unexpected protonation of a macrocycle containing four bindings sites pointing into the cavity, its crystal structure was published by Che *et al.* in 1994.[4] This mono-protonated structure (syn boat-boat) is markedly different from the free ligand (syn chair-chair), suggesting that the proton is exchanged between the four nitrogen atoms, maintaining the ligand in its unusual conformation. These examples show that a proton can act in the time average as a coordinating centre for up to four nitrogen donor atoms. In one case a helical structure of two phenantroline moieties was observed,[1] whereas in the other structurally characterized cases a symmetrical coordination occurs located on a mirror plane, again in the time average.

[5,6]-CHIRAGEN[0]-ligands studied in our group with respect to coordination of metal ions are able to bind protons in a similar way as the nitrogen donor ligands mentioned above. In addition they can provide a chiral environment to the proton. The present study can therefore be considered as an attempt to “chiralize” a proton.

Results and discussion

Protonation studies

The ability of **3** (chart 1) to form mononuclear complexes with several metal cations has been studied.[5] Cations such as Ag(I), Pd(II), Cu(II) and Zn(II) fit into the pocket defined by both pinene-bpy-units. Ligand **3** wraps around the metal in a helical fashion. This was the motivation to investigate the protonation behaviour of the ligand **3**. Can the proton, as smallest cation, act as a complexing agent and fix the conformation of the ligand? If the ligand can be fixed in one conformation, does it correspond to a helical conformation comparable to that in metal complexes?

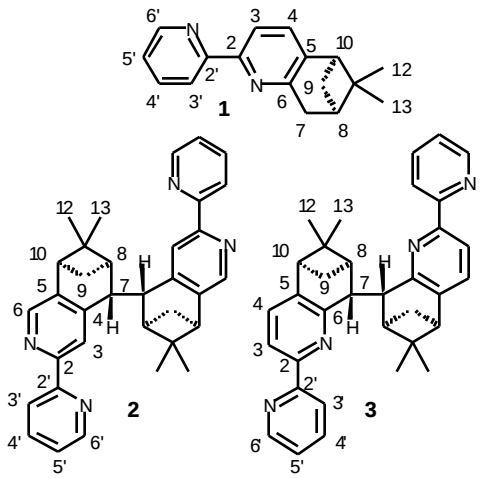


Chart 1: ligands used for extended protonation studies.

In order to understand the protonation behaviour of **3**, an extended study was carried out not only for **3**, but also for bpy, **1**[6] and **2**[7] (chart 1).

Since ligand **1** has a similar structure to bpy, similar protonation behaviour should be observed. It was used as a reference for the other cases (**2** and **3**).

2 and **3** have similar structures; both consist of two directly linked pinene-bpy-moieties. While in **3** all four nitrogen donor atoms can point into the pocket and therefore can bind cations therein, the nitrogen atoms in **2** are arranged to be in opposite sides of the molecule and both bpy units react independently.

The methods to study the protonation behaviour were spectrophotometric titration's (UV/Vis and CD-spectroscopy) and NMR-experiments. In the latter, two different nuclei were the object of the observation. ^{1}H-NMR-spectra were used to gain an initial insight into the protonation behaviour. The use of NMR-inverse-detection techniques allowed the observation of other nuclei (especially ^{15}N), obtaining results in a reasonable time and with small amounts of product.

Protonation behaviour of [5,6]-pinene-bpy (1)

First of all, [5,6]-pinene-bpy (**1**)[6] and bpy will be discussed. Both ligands contain two nitrogen donor atoms, which can be protonated. From bpy it is known, that the first protonation changes the conformation from *trans* to *cis*. The proton is shared between both nitrogens.[8-10] The second protonation leads again to a *trans*-conformation. The pK_a-value for the mono–protonated bpy in water is $pK_a = 4.5$,[11] but varies depending on the percentage of organic solvents in aqueous solution and the ionic strength.[9, 11-22]

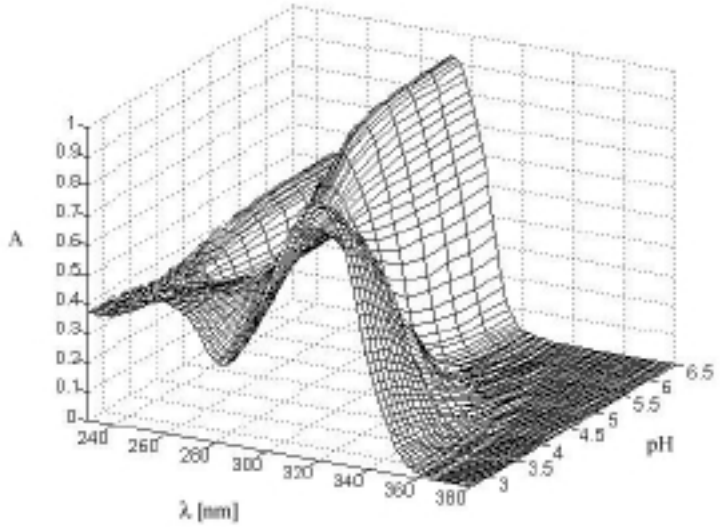


Fig. 1: UV/Vis spectra **1** upon protonation.

The UV-spectra of bpy and [5,6]-pinene-bpy (**1**) were measured in 60% (v/v) methanol/water solution with an ionic strength of 0.1M (NaCl). Hydrochloric acid was used as proton source (Fig. 1). Since both ligands show similar behaviour upon protonation, only **1** will be discussed.

The UV-spectrum of the free ligand **1** shows an absorption maximum at 293 nm (Fig. 1). Upon protonation a bathochromic shift appears (from 293 nm to 312 nm). An analogous phenomenon was described for bpy.[8, 9, 22-25] The UV-spectra were recorded in a pH-range from 10 to 2, in which only mono-protonated species are formed.[8, 9, 11] The pK_a were calculated with the programme Specfit. (pK_a = 3.9±0.1 for bpy; pK_a = 4.2±0.1 for **1**), which is in accordance with the literature.[21]

The NMR protonation studies were carried out for **1**. A ^{1}H-NMR-spectrum was recorded after each addition of 0.1 equivalent of the trifluoroacetic acid solution (TFA) to the ligand **1** (Fig. 2). Large shifts in the spectra were observed until the addition of two equivalents of acid. Only the aromatic protons show a remarkable shift, whereas the aliphatic ones are almost uninfluenced. The signals of the protons in *para*-position (4, 4’) with regard to the nitrogen and in *meta*-position (5’) show similar downfield shifts (Fig. 2).

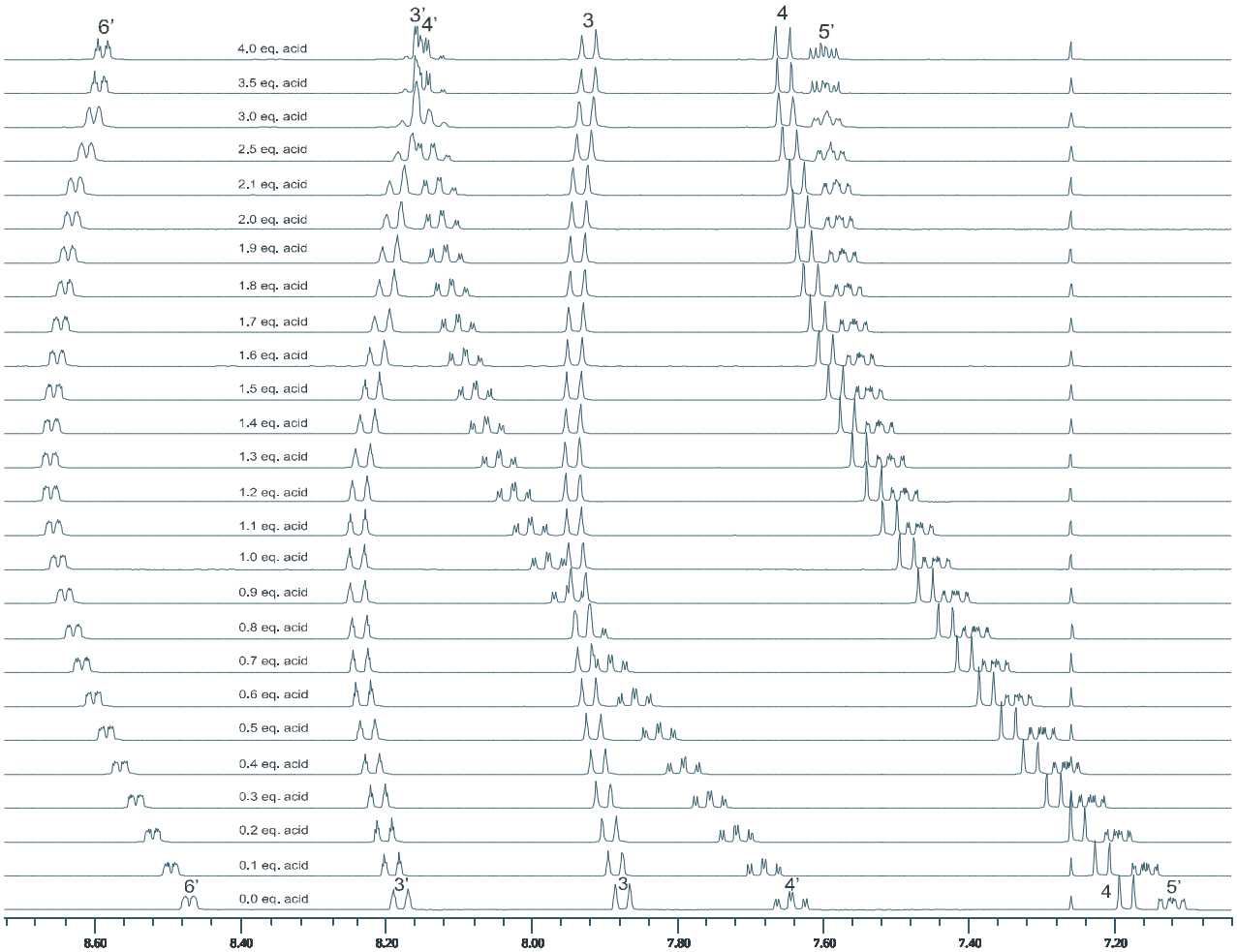


Fig. 2: ^{1}H-NMR-titration of **1**.

The signal of proton 6’ in *ortho*-position shows a less pronounced downfield shift. The signals of the protons 3 and 3’ in *meta*-positions show initially a slight downfield shift but afterwards they return to their original position.

The most important information about protonation can be obtained by the observation of the chemical shift of ^{15}N. ^{1}H-^{15}N-HMBC were recorded either on a 700 MHz Bruker Avance DRX spectrometer[‡], which allowed these 2D indirect-detection experiments to be measured in a short time, or on a 400 MHz Bruker Avance DRX with the ^{15}N-labelled product ^{15}N-**1**.

The chemical shifts of the nitrogen nuclei signals in the free ligand are at –77 and –72 ppm for N(A) and N(B) respectively (nitromethane as reference). They are shifted upfield (–134 ppm) upon protonation (Fig. 3).

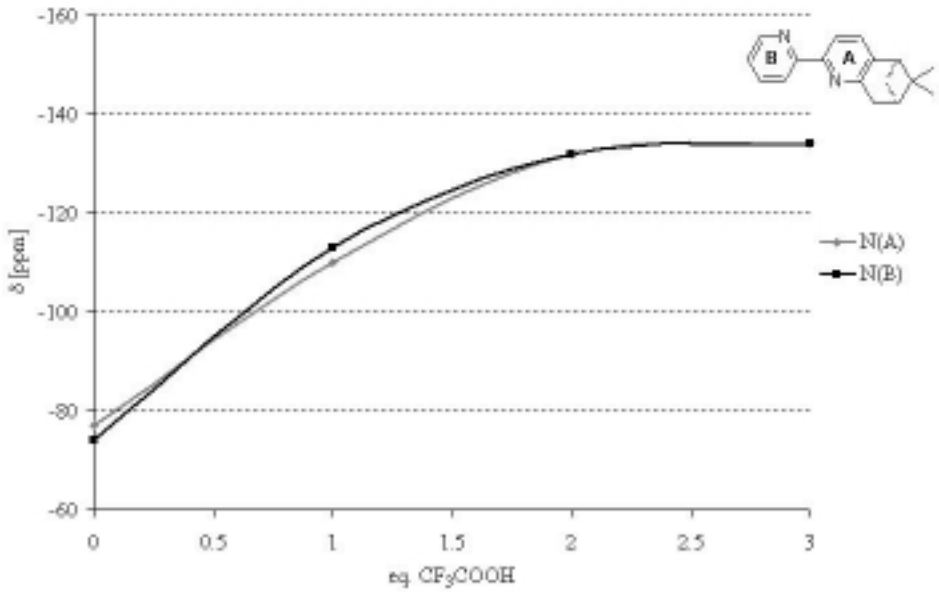
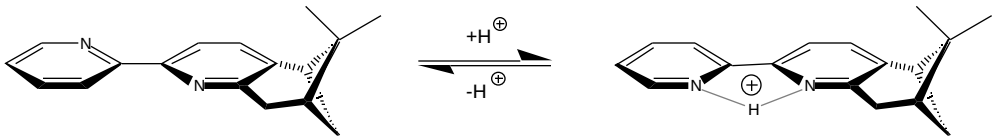


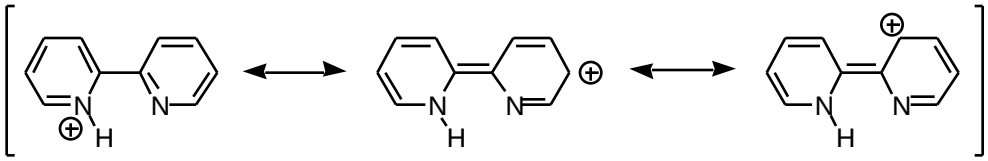
Fig. 3: ^{15}N-chemical shifts of **1** upon protonation.

All these observations lead to the following conclusion: The free ligand **1** and the mono-protonated species are in equilibrium upon protonation, as it can be seen in the UV-spectra (Fig. 1). The mono-protonated form is stabilised in the *cis*-conformation of the ligand by hydrogen bonding (scheme 1) and the proton is shared between both nitrogens, which is in accordance with the ^{15}N-experiments (Fig. 3).



Scheme 1: equilibrium between **1** and its mono-protonated form H**1**$^{+}$.

This is in accordance with the bathochromic shift observed in the UV-spectra. This bathochromic shift can be explained as follows. Although the free ligand is mostly in the *trans*-conformation, it can rotate around the bond between both pyridine rings. Therefore in the experimental time scale, the aromatic system is not conjugated over both rings. Upon protonation the coplanar *cis*-conformation is stabilised and π-conjugation through both pyridine rings occurs (scheme 2).[9] Therefore the energy difference of the π-π*-*trans*ition is reduced, and a red-shift is observed.



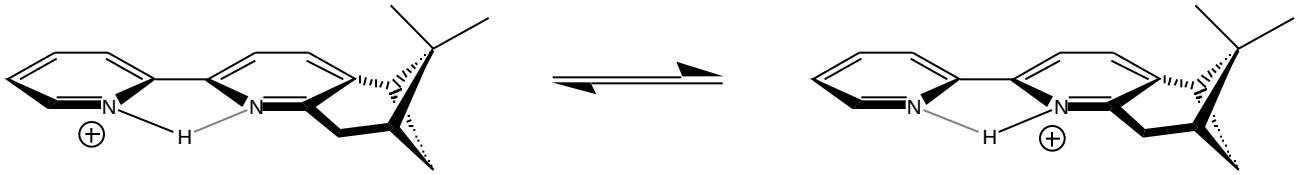
Scheme 2: π-conjugation of the mono-protonated bpy.

By analysing the NMR-spectra, it is not easy to determine if **1** is protonated once or twice upon the addition of two equivalents of trifluoroacetic acid (TFA). Nevertheless, it should be taken into account, that the solvent is not water and therefore the acid/base behaviour changes. In water TFA is a strong acid (pK_a = -2), but in acetonitrile (a protophobic solvent) this behaviour changes dramatically. TFA with a pK_a of 12.65, in acetonitrile, is no longer a strong acid and it is less acidic than the protonated pyridinium cation (pK_a = 12.33).[26] In addition, TFA forms with its conjugated base a dimeric species (HA_2^-).[†] In the solvent used in the present investigation ($CHCl_3/CH_3CN$: 3/1) the acid strength of TFA is probably even lower. Therefore, the protonation of **1** follows the equilibrium (cf. equation):

$$2\,HA + \mathbf{1} \rightleftharpoons H\mathbf{1}^{\oplus} + H(A)_2^{\ominus}$$

This is in agreement with all NMR-titrations, where always two equivalents of TFA were needed to reach the mono-protonated species.

The conclusion with a mono-protonated species in a *cis*-conformation is in line with the ^{15}N-NMR-spectra. The identical chemical shift of both nitrogen atoms is consistent with a sharing of the proton between them (scheme 3).



Scheme 3: sharing of the proton between both nitrogen donor atoms in H**1**$^+$**.**

From the ^{1}H-NMR-spectra it can be seen, that the signals of the protons in *meta* (5')- and *para* (4, 4')-positions are influenced strongly upon protonation, whereas proton 6' undergoes only a slight downfield shift (Fig. 2). This is in accordance with the chemical shifts observed for pyridine and its protonated form.[27] The exceptions are represented by proton 3 and 3'. Other effects cancel the expected downfield shift upon protonation.

Protonation behaviour of [4,5]-CHIRAGEN[0] (2)

Ligand **2** represents an analogous case to the [5,6]-pinene-bpy (**1**), which consists of two [4,5]-pinene-bpy moieties linked directly together. The four nitrogen donor atoms of both bpy-units are orientated in such a way, that the formation of mononuclear complexes is inhibited (chart 1). The protonation behaviour is expected to be similar to that of the [5,6]-pinene-bpy (**1**). No intramolecular proton *trans*fer between the two bpy units can take place and therefore each bpy-unit will be independently protonated. In addition to the techniques (UV/Vis and NMR-spectroscopy) used for [5,6]-pinene-bpy (**1**), CD-spectroscopy was performed to study the protonation behaviour.

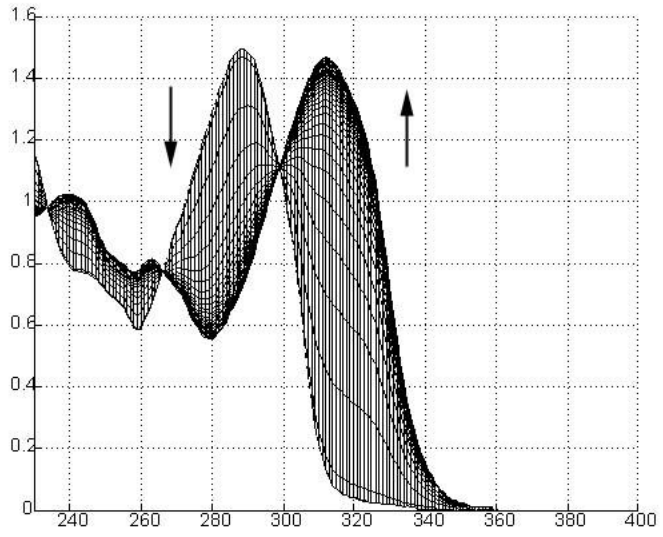


Fig. 4: UV/Vis spectra of **2** upon protonation.

The spectrophotometric titration's were carried out under the same conditions as those described for the [5,6]-pinene-bpy (**1**). Only the solvent mixture was changed to methanol/water (90% v/v) because of solubility reasons. The UV-spectra (Fig. 4) show a bathochromic shift from 288 nm for the free ligand to 312 nm in the protonated species. In the pH-range of 10 to 1.5, **2** can be protonated twice.

The CD-spectra of **2** show as well an analogous bathochromic shift (from 295 for the free ligand to 324 nm for the protonated species). The nature and the intensity of the CD-signals do not change upon protonation (Fig. 5).

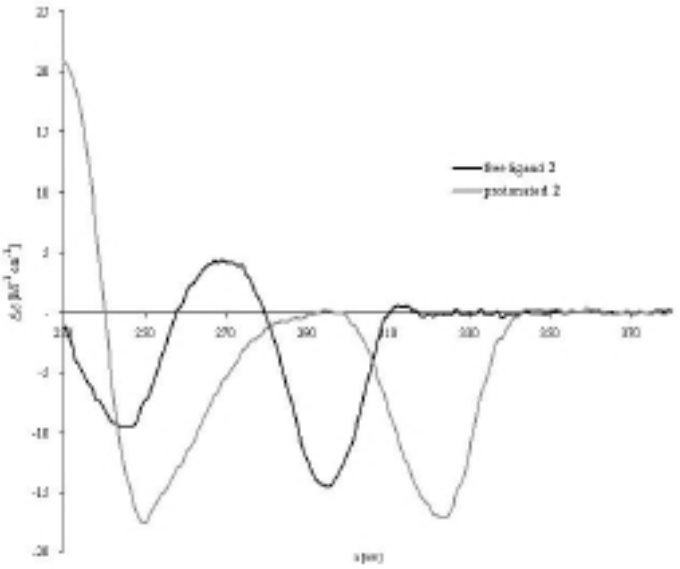


Fig. 5: CD-spectra of the free ligand **2** and its protonated species.

The ^{1}H-NMR-titrations were carried out in the same manner as for [5,6]-pinene-bpy (**1**). After each addition of the acid (TFA) solution which corresponds to 0.2 equivalents, a ^{1}H-NMR-spectrum was recorded (Fig. 6). After 3 equivalents, the addition were made in 1.0 equivalent steps.

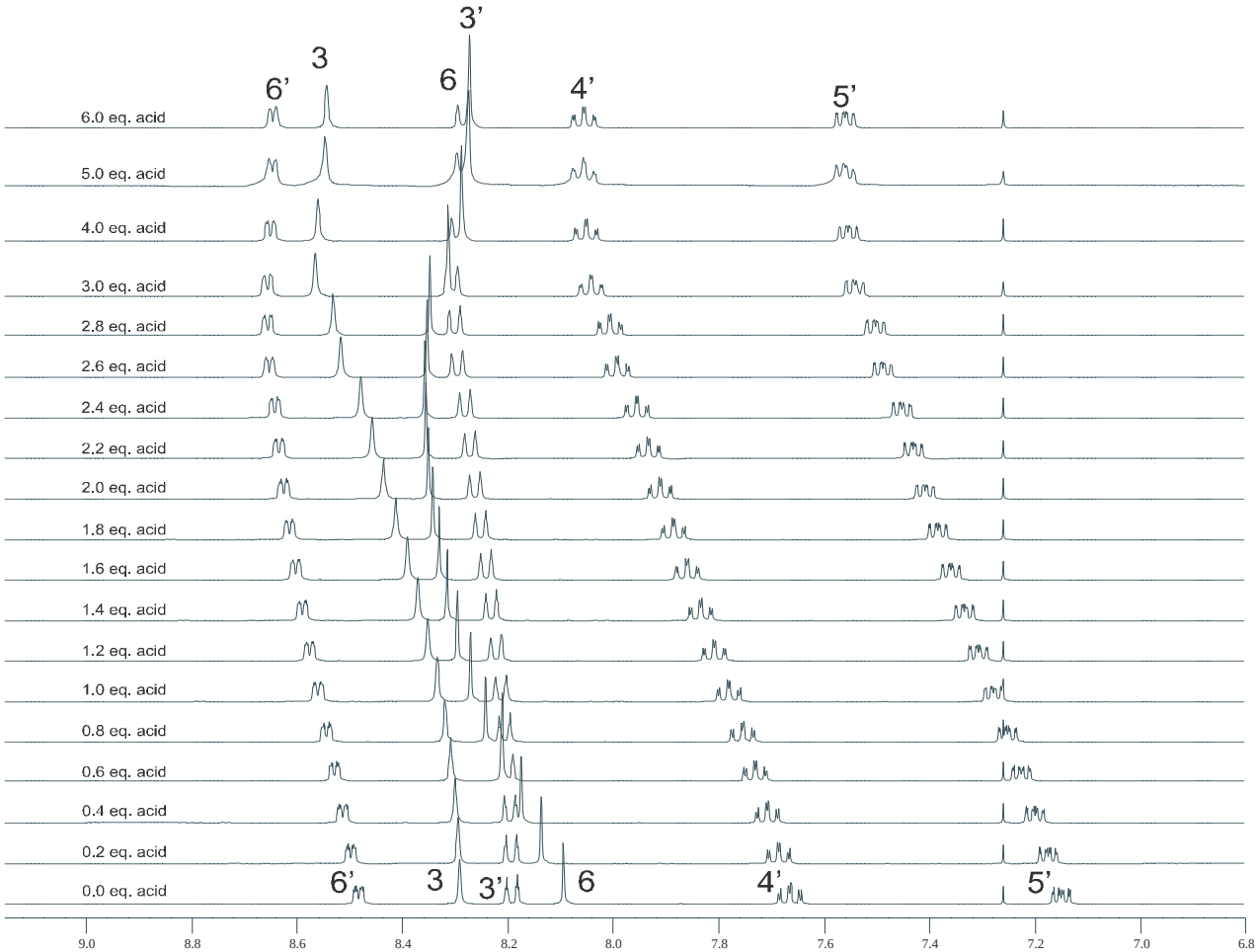


Fig. 6: ^{1}H-NMR-titration of **2**

The ^{1}H-NMR-spectra do not show any doubling of the signals, ligand **2** keeps its C_2-symmetry upon protonation due to the fast proton exchange between both bpy units on the NMR time scale. Large changes in the spectra can be observed upon the addition of 4-5 equivalents of acid (Fig. 6), mostly in the aromatic part. The signals of the proton in *para*-position (4', $\Delta\delta$ = 0.39 ppm) and in *meta*-position (5', $\Delta\delta$ = 0.40 ppm) are shifted downfield upon protonation. The signals of the protons in *ortho*-position (6, $\Delta\delta$ = 0.19 ppm; 6', $\Delta\delta$ = 0.17 ppm) show a less pronounced downfield shift, but proton 6 is more influenced upon protonation (firstly, to lowfield and then back to highfield). Proton 3' (*meta*-position) remains at the same chemical shift ($\Delta\delta$ = 0.11 ppm), whereas 3 is slightly shifted to low field ($\Delta\delta$ = 0.27 ppm). The proton at the bridge (7) shows a slight high field shift upon protonation ($\Delta\delta$ = 0.28 ppm).

From the ^{1}H-^{15}N-HMBC-experiment, the chemical shifts of the nitrogens can be determined (Fig. 7). Both nitrogens of the two bpy-moieties show a large shift to high field. The nitrogen N(A) (up to –158 ppm) is more influenced than N(B) (up to –112 ppm).

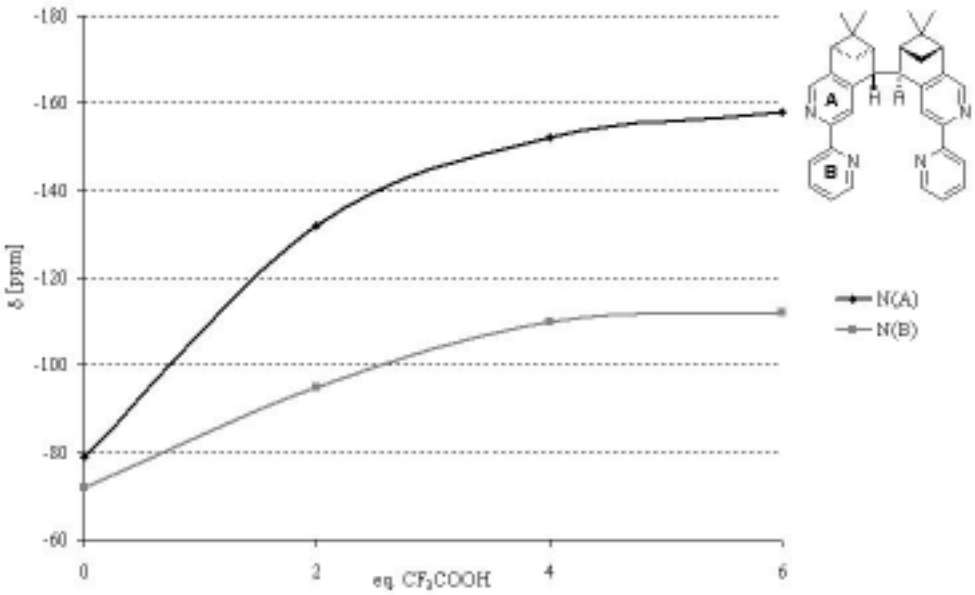
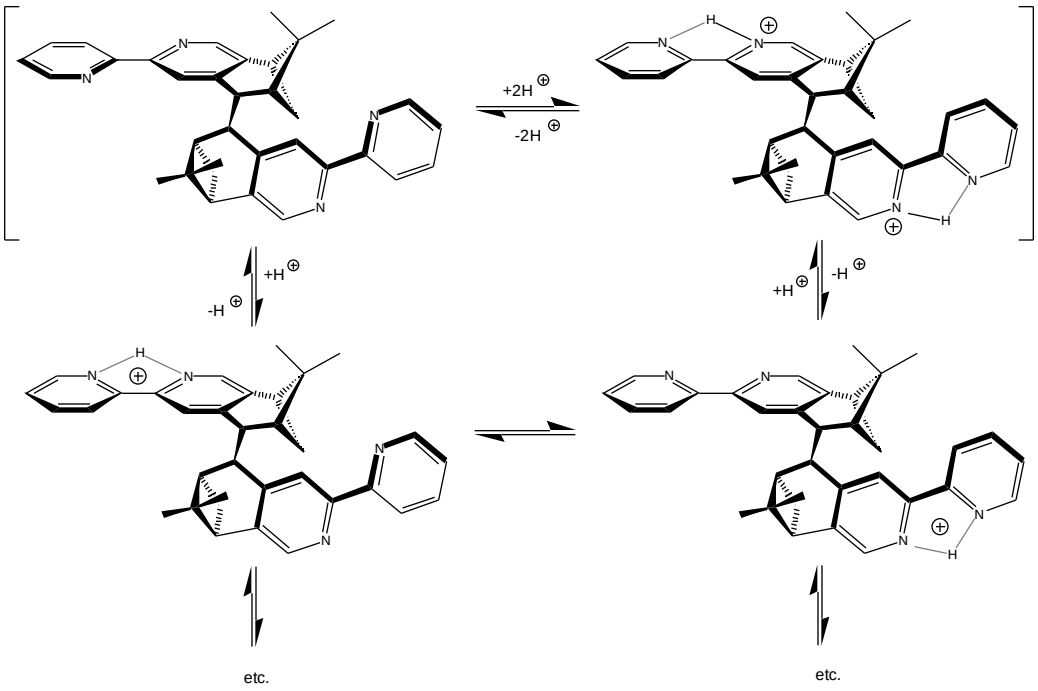


Fig. 7: ^{15}N-chemical shifts of **2** upon protonation.

These observations lead to the following conclusion: Upon protonation, the free ligand and the di-protonated species are in equilibrium. Both bpy units of the di-protonated species are in the *cis*-conformation. This protonation takes place via several other equilibria, where mono-protonated species can be present (scheme 4).



Scheme 4: equilibria between **2** and its protonated forms.

This is in accordance with the UV/Vis- (Fig. 4) and CD-measurements (Fig. 5), where no intermediate spectrum can be attributed to a mono-protonated form. The bathochromic shift in the UV-spectra (Fig. 4) and also in the CD-spectra (Fig. 5) can be explained by the *cis*-conformation of both bpy-moieties (analogous to [5,6]-pinene-bpy (**1**), Fig. 1). The protonated ligand retains in a similar conformation as the free ligand (open form), since the intensity and the nature of the CD-signal does not change. If **2** did change the conformation, which is comparable to metal complexes described with **3** [5] a similar large CD-signal should appear, due to a strong exciton coupling.

The information obtained from the NMR-experiments supports the conclusion. As in the previous case (**1**), twice the number of acid equivalents is needed, due to the formation of the relatively stable dimer:

The ^{15}N-experiments indicate that the acidic proton is favourably located on the nitrogen N(A) (larger shift to high field, Fig. 7). But a sharing of the proton between the nitrogens N(A) and N(B) can be taken into account. This is in agreement with the ^{1}H-NMR, where the protons 3 and 6 show a more pronounced shift compared to 3’ and 6’. The similarities of the proton and carbon-spectra for **2** and **1** support the model, where each bpy unit is independently mono-protonated. No intramolecular proton exchange between both bpy units of **2** is observed.

Protonation behaviour of [5,6]-CHIRAGEN[0] (3)

3 is the most interesting case of all three pinene-bpy derivatives. Its geometry allows an intramolecular proton exchange between both bpy-moieties and therefore particular protonation behaviour is expected.

3 is the least soluble of all pinene-bpy derivatives. In the solvent mixture used for **1** and bpy (methanol/water 60% v/v), it was impossible to dissolve **3**. The solvent mixture used for UV/Vis and CD-titration was methanol/water (90% v/v). But also for NMR-measurements solubility problems occurred. The free ligand is only soluble in chloroform, the protonated species in acetonitrile. A solvent mixture ($CDCl_3$, CD_3CN; 3:1) was finally used for these NMR-investigations.

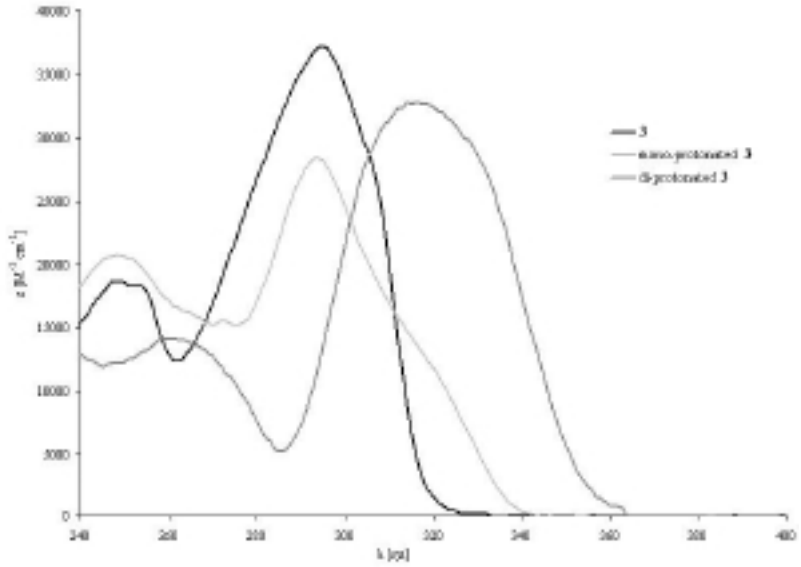


Fig. 8: UV/Vis spectra of **3** upon protonation.

In spectrophotometric titrations, two different protonation steps could be observed. In the UV-titration (Fig. 8), a hypochromic effect appears upon the first protonation, but with the addition of more acid a bathochromic effect leads to the final spectrum. All these spectra were fitted with the programme Specfit and the pK_a values were calculated (pK_{a1} = 8.2±0.1, pK_{a2} = 2.5±0.1 (methanol/water 90% v/v).

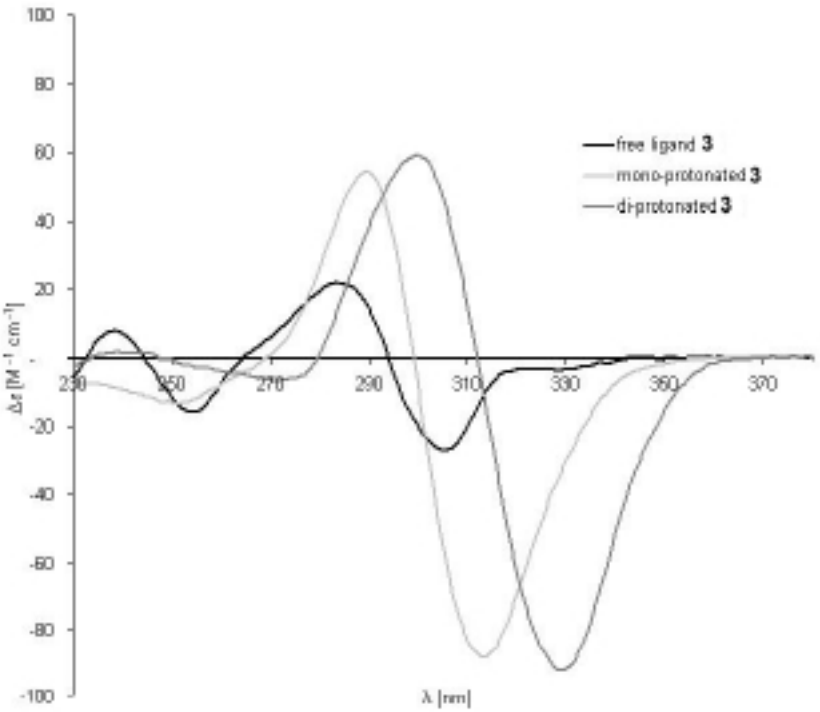


Fig. 9: CD-spectra of the free ligand **3** and its protonated species.

An interesting effect was observed in the CD-spectra (Fig. 9). While the free ligand shows only slight CD-activity, a large intensity increase is observed upon protonation.

The second protonation leads to a bathochromic shift, which was already observed in the UV-spectra. The CD-signal does not change its intensity upon the second protonation. Analogous UV- and CD-spectra were observed for the same solvent mixture and acid (TFA) used in the NMR-spectroscopy.

The ^{1}H-NMR-titrations (and ^{1}H-^{15}N-HMBC-NMR-experiments) were carried out in the same manner as described previously. The ^{1}H-NMR-spectra (Fig. 10) do not show a doubling of the signals. Ligand **3** keeps its C_2-symmetry upon protonation due to the fast proton exchange between both bpy-moieties on the NMR time scale. Two opposite trends are observable in the ^{1}H-NMR-titrations (Fig. 10). Up to the addition of two equivalents, most of the proton signals are shifted upfield. An opposite effect leads to a low field shift of these protons by adding six equivalents of acid. These protons are 6’, 5’, 4’, 3’ and 7. Proton 4 shows the opposite shift (first to low field and then back to high field). The broad signals of the protons 3’, 7 and 9_a in the free ligand sharpens upon protonation.

The most important and significant experiments were again the indirect detected ^{1}H-^{15}N-HMBC-experiments (Fig. 11). The two nitrogen atoms N(A) and N(B) show quite different behaviour. While the signal of the nitrogen N(A) is first shifted to highfield (-125 ppm) the second signal corresponding to N(B) is not influenced upon the first protonation.

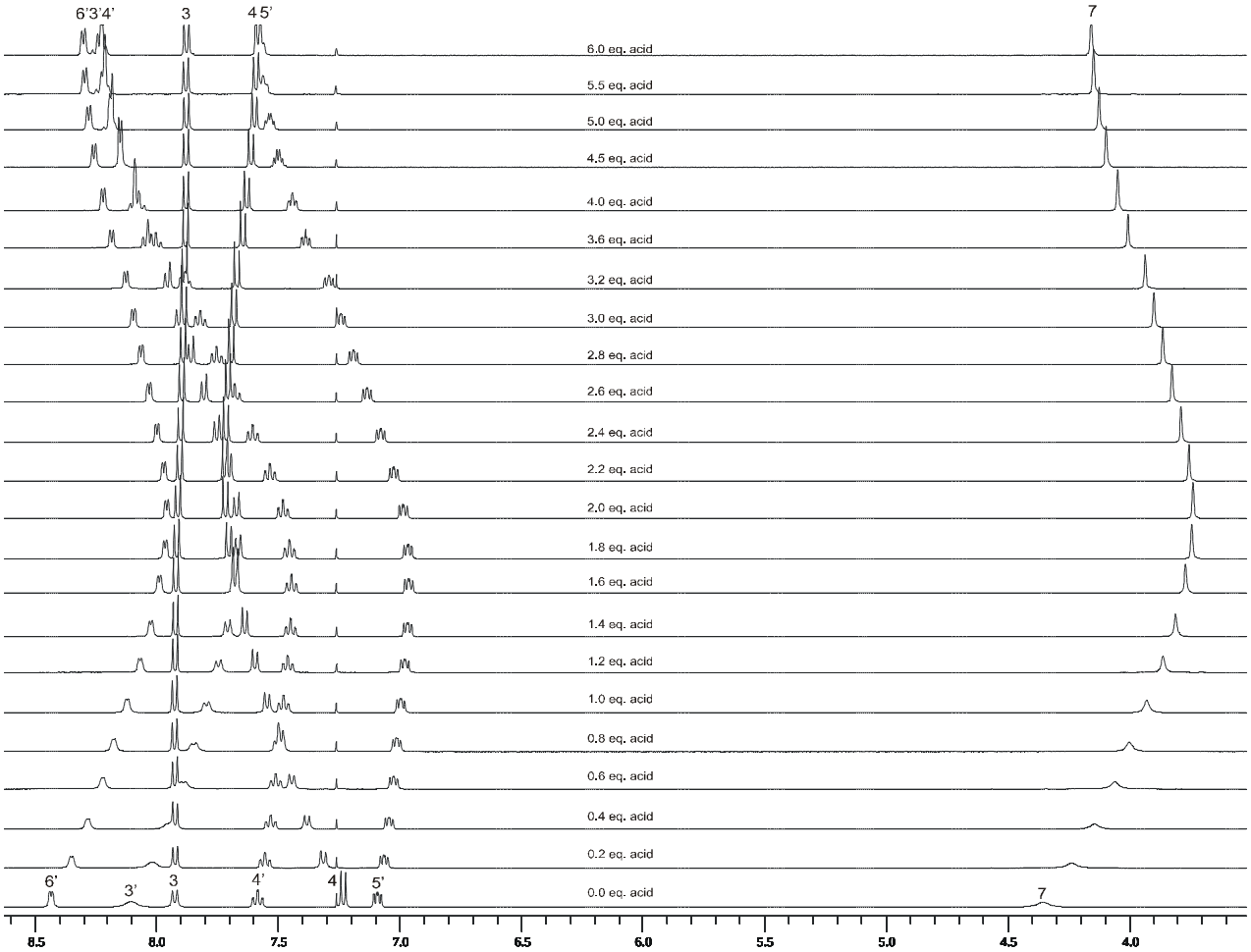


Fig. 10: ^{1}H-NMR-titration of **3**.

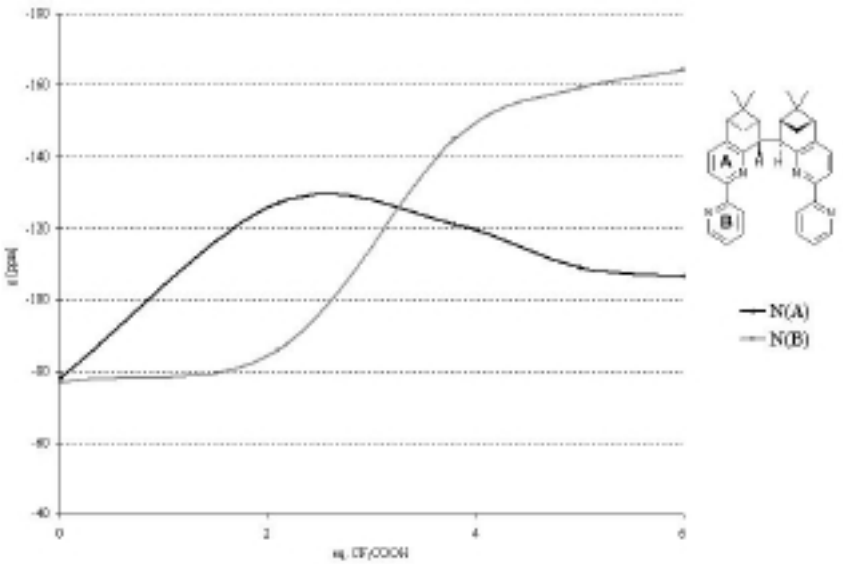
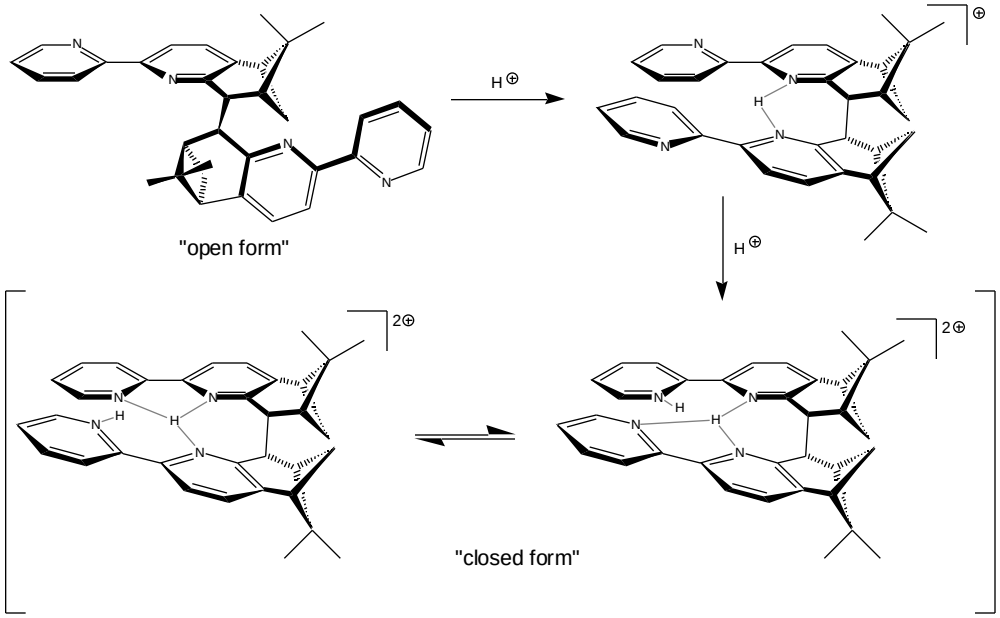


Fig. 11: ^{15}N-chemical shifts of **3** upon protonation. Some measurements are carried out using ^{15}N(A) enriched (10%) samples.

The opposite effect occurs in the second protonation step. N(B) is shifted dramatically to highfield ($\Delta\delta$ = -164 ppm), whereas N(A) is slightly shifted back to low field ($\Delta\delta$ = -107 ppm).

All these observations lead to the following conclusions: The first protonation leads to a change of the conformation of the ligand (closed form, scheme 5). The second protonation does not influence this closed conformation, but leads to the *cis*-conformer of both bpy units.



Scheme 5: conformation change of 3 upon protonation.

This is consistent with the UV-spectra (Fig. 8). The first protonation leads only to a slight hypochromic effect. The pyridine rings B can still freely rotate and therefore no π-conjugation over both pyridine rings of each bpy unit is taking place. The large change in the CD-activity upon the first protonation is due to a strong exciton coupling (Fig. 9). Similarly, this exciton coupling is observed in the metal complexes with **3**, where the cation is fixed in the cavity of the ligand. The proton is therefore able to play a similar role, as the metals.

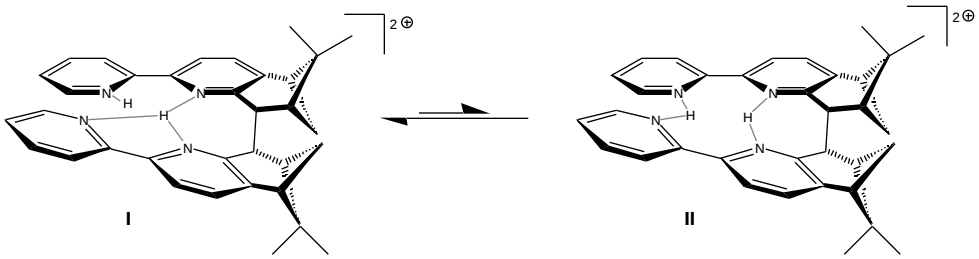
In contrast to the metal complexes, where the cations are bound to all four nitrogen donor atoms, the proton is only bound to the two N(A) nitrogen atoms near to the bridge. This can be explained by the large chemical shift of N(A) in the ^{15}N-experiment, whereas N(B) is not influenced by this proton. Both nitrogen atoms N(A) share the proton.

^{1}H-NMR-spectra are in accordance with the explanation described above (Fig. 10). Signals of the protons 4 and 3, attached to the pyridine ring (A), where the first protonation occurs, show comparable influences as those of the previously studied ligands **1** and **2**. Signal of the proton 4 is shifted lowfield (cf. proton 4 of **1** in Fig. 10, and signal of the proton 4 of **2** in Fig. 10), whereas proton 3 remains unchanged. The protons of the unprotonated pyridine rings are shifted to highfield,

which can be explained by the conformation change to the closed form. Another indication for a fixed conformation is given by the protons 3’, 7 and 9_a. All these signals are broad in the free ligand and give sharp signals upon protonation.

The second protonation leads to the *cis*-conformation of the bpy moieties (bathochromic shift in the UV- (Fig. 8) and CD-spectra (Fig. 9). The bpy-moieties are now conjugated through both pyridine rings in a similar way as already seen in **1** (Fig. 1) and **2** (Fig. 4). The conservation of the large CD-intensity can be explained by an analogous conformation as that in the mono-protonated species. Despite of an expected strong electronic repulsion of the two positive charges in the pocket, no reopening of the ligand occurs. One reason could be the distribution of the positive charges by π-conjugation (scheme 2).

The ^{15}N-chemical shifts show a strong highfield shift of N(B) upon the second protonation. The slight shift to low field of N(A) can be explained by a small participation of N(B) at the proton mainly bound to N(A). This is another reason for the *cis*-conformation of the bpy-moieties (scheme 5). A second proton distribution II can be taken into account, where the two protons are bound in the pocket (scheme 6). This distribution II would lead to a sharing of the two protons over all four nitrogen atoms (the same chemical shift of N(A) and N(B) is expected (scheme 6). From the chemical shifts observed in ^{15}N-experiments, the following distribution of the two protons can be assumed, which is in line with the proposed one (I).



I		II	
N(A)1: 0.4	N(A)2: 0.4	N(A)1: 0.5	N(A)2: 0.5
N(B)1: 1.0	N(B)2: 0.2	N(B)1: 0.5	N(B)2: 0.5

Scheme 6: two possible proton distributions in the closed form of **3**.

The protons of the pyridine ring B (3’, 4’, 5’ and 6’) are downfield shifted upon the second protonation (Fig. 10). This is in accordance with the ^{15}N-experiments, where nitrogen B is strongly downfield shifted (Fig. 11). The protons in ligand **1** (Fig. 2) and **2** (Fig. 6) behave in a similar way. Proton 4 is slightly shifted back to high field (Fig. 10), which is in line with the chemical shift of nitrogen N(A) (Fig. 11).

Conclusion

An extended protonation study was carried out with the ligands **1**, **2** and **3**.

1 show the same protonation behaviour as bpy. Upon protonation, the free ligand **1** is in equilibrium with its mono-protonated analogue. The mono-protonated species is stabilised in the cis-conformation by hydrogen bonding.

2 consists of two pinene-bpy moieties, which are arranged in such a way, that no proton exchange can take place between them. Both pinene-bpy moieties are independently mono-protonated upon protonation. The conformation of the ligands does not change considerably.

3 has the ability to form helical mononuclear complexes with several metal cations. But not only are metal cations able to fit into the pocket of the ligand, but also a proton, as the smallest cation, can fix the ligand in a helical conformation. Upon a first protonation, the ligand changes its conformation to a closed form, where the proton is shared between the two nitrogen atoms near the bridge. Upon the second protonation, the bpy-moieties are arranged in the cis-conformation, but the ligand keeps its conformation in a closed form.

Experimental part

Protonation studies

NMR-Titrations

Measurements

The NMR-spectra (^{1}H, ^{1}H-^{15}N-HMBC) were measured either on a Bruker Avance DRX 400 (with 10% ^{15}N-enriched material) or on a Bruker Avance DRX 700 NMR spectrometer. The spectrometers operate at 400.13 MHz or 700.13 MHz for ^{1}H, at 100.62 MHz for ^{13}C and at 40.54 MHz or 70.96 MHz for ^{15}N. $CDCl_3$ was used as internal reference for ^{1}H (7.26 ppm) and ^{13}C (77.0 ppm). For the ^{15}N-experiments nitromethane at (0.0 ppm) was used as internal reference.

Preparation of the solutions

From commercially available trifluoroacetic acid (Aldrich) a solution (2.7 M) in CD_3CN was freshly prepared for each acidic titration. The ligands **1** (100.0 mM), **2** (50.0 mM) and **3** (50.0 mM) were dissolved in a mixture of $CDCl_3/CD_3CN$= 3:1.

Titrations

Titrations were carried out by adding small aliquots (typically 2.23 µl) of the TFA-solution to the ligand solutions (0.6ml). 22.30µl of TFA solution corresponds to 1.0 equivalent of **1**, 11.16µl to 1.0 equivalent of **2** and **3**.

Spectrophotometric titrations

Measurements

UV/Visible spectra were measured on a Perkin Elmer Lambda 40 spectrometer. Wavelength are given in nm and molar absorption coefficients (ε) in M^{-1} cm^{-1}. Circular dichroism (CD) spectra were recorded on a Jasco J-715 spectropolarimeter and the results are given in Δε M^{-1} cm^{-1}. The pH was measured with a micro-combination pH electrode (Orion model 9863). UV-titrations were carried out with a Mettler Titrator DL21 with 1ml and 10ml burettes.

Calibration of the electrode

Assuming that hydrochloric acid is completely dissociated forming H_3O^+ in aqueous solution containing methanol. The calculated H^+-concentration was attributed to the measured potential E_{meas} according to the following equation: $pH = a*E_{meas} + b$. For further titrations the pH was calculated with the measured potential.

Preparation of the solutions

0.1 M HCl (methanol/water (60% v/v)), 1M HCl (methanol/water (60% v/v)), 0.1M (methanol/water (90% v/v)) and 1M (methanol/water (90% v/v)) were used for the titrations. The ligand solutions for **1** and bpy consisted of 0.001M NaOH, 0.1M NaCl and $5*10^{-5}$M **1** and bpy in a mixture of methanol water (60% v/v). The ligand solutions for **2** and **3** consisted of 0.001M NaOH, 0.1M NaCl and $2.5*10^{-5}$ M or $5*10^{-5}$ M of **2** and **3** in methanol water (90% v/v).

Titrations

In the pH-range from 10 to 3, HCl solution (0.1M) was added in 2_l steps to 2ml of the ligand solutions by the Mettler Titrator DL21 (1ml burette) for the UV/Vis- titration. In the pH-range from 3 to 1 HCl solution (1M) was used. pH of the stirred solution was measured directly in the cuvette by a micro electrode. The CD-titrations were carried out by adding the corresponding aliquots of acid with a micropipette without pH-measurements. Acid solutions in methanol/water (60% v/v) were used for **1** and bpy, acid solutions in methanol/water (90% v/v) for **2** and **3**.

All spectra represented of the UV/Vis- and CD-Titrations are baseline and volume corrected. Calculations of the equilibrium constants were carried out with the program Specfit®.

Spectral data of 1, 2 and 3 (incl. protonation)

*[5,6]-Pinene-bpy (**1**)*

Free Ligand 1 ^{1}H-NMR (400 MHz, $CDCl_3/CD_3CN$): δ 8.47 (d, 1H, H(6')), 8.18 (ddd, 1H, H(3')), 7.87 (d, 1H, H(3), $^3J_{3,4}$ = 8.0 Hz), 7.64 (ddd, 1H, H(4')), 7.18 (d, 1H, H(4), $^3J_{4,3}$ = 8.0 Hz), 7.12 (d,

1H, H(5'), $^3J_{5',4'}$ = 7.1 Hz, $^3J_{5',6'}$ = 7.1 Hz, $^4J_{5',3'}$ = 2.0 Hz), 3.00 (m, 2H, H(7)), 2.67 (dd, 1H, H(10), $^3J_{10,9b}$ = 5.6 Hz, $^3J_{10,8}$ = 5.6 Hz), 2.56 (ddd, 1H, H(9_b), $^2J_{9b,9a}$ = 10.4 Hz, $^3J_{9b,10}$ = 5.8 Hz, $^3J_{9b,8}$ = 5.8 Hz), 2.24 (ddt, 1H, H(8), $^3J_{8,9b}$ = 5.8 Hz, $^3J_{8,10}$ = 5.8 Hz, $^3J_{8,7}$ = 2.8 Hz), 1.26 (s, 3H, H(12)), 1.13 (d, 1H, H(9_a), 0.51 (s, 3H, H(13)). ^{15}N-NMR (40 and 71 MHz, $CDCl_3/CD_3CN$): δ -77 (N), -74 (N'). UV/Vis: λ_{max} (MeOH/H_2O (60% v/v) / nm) 293 (ε/ dm^3 mol^{-1} cm^{-1} 1.9*10^4).

Mono-protonated ligand H**1**$^+$ (3 eq. CF_3COOH) ^{1}H-NMR (400 MHz, $CDCl_3/CD_3CN$): δ 8.60 (d, 1H, H(6')), 8.17 (ddd, 1H, H(3')), 8.14 (ddd, 1H, H(4')), 7.93 (d, 1H, H(3), $^3J_{3,4}$ = 8.0 Hz), 7.65 (d, 1H, H(4), $^3J_{4,3}$ = 8.0 Hz), 7.60 (d, 1H, H(5'), $^3J_{5',4'}$ = 7.1 Hz, $^3J_{5',6'}$ = 7.1 Hz, $^4J_{5',3'}$ = 2.0 Hz), 3.16 (m, 2H, H(7)), 2.87 (dd, 1H, H(10), $^3J_{10,9b}$ = 5.6 Hz, $^3J_{10,8}$=5.6 Hz), 2.65 (ddd, 1H, H(9_b), $^2J_{9b,9a}$ = 10.4 Hz, $^3J_{9b,10}$ = 5.8 Hz, $^3J_{9b,8}$ = 5.8 Hz), 2.31 (ddt, 1H, H(8), $^3J_{8,9b}$ = 5.8 Hz, $^3J_{8,10}$ = 5.8 Hz, $^3J_{8,7}$ = 2.8 Hz), 1.29 (s, 3H, H(12)), 1.15 (d, 1H, H(9_a), $^2J_{9a,9b}$ = 10.4 Hz), 0.51 (s, 3H, H(13)). ^{15}N-NMR (40 and 71 MHz, $CDCl_3/CD_3CN$): δ –134 (N, N'). UV/Vis: λ_{max} (MeOH/H_2O (60% v/v) / nm) 312 (ε/ dm^3 mol^{-1} cm^{-1} 2.0*10^4).

*[4,5]-CHIRAGEN[0] (**2**)*

Free ligand 2: ^{1}H-NMR (400 MHz, $CDCl_3/CD_3CN$): δ 8.48 (ddd, 2H, H(6')), 8.29 (s, 2H, H(3)), 8.19 (ddd, 2H, H(3')), 8.10 (s, 2H, H(6), $^3J_{3,4}$ = 8.0 Hz), 7.66 (ddd, 2H, H(4'), $^3J_{4',3'}$ = 7.8 Hz, $^3J_{4',5'}$ = 7.8 Hz, $^4J_{4',6'}$ = 1.5 Hz), 7.15 (ddd, 2H, H(5'), $^3J_{5',4'}$ = 7.6 Hz, $^3J_{5',6'}$ = 5.3 Hz, $^4J_{5',3'}$ = 1.0 Hz), 3.88 (s, 2H, H(7)), 2.69 (dd, 2H, H(10), $^3J_{10,9b}$ = 5.3 Hz, $^3J_{10,8}$ = 5.3 Hz), 2.36 (ddd, 2H, H(9_b), $^2J_{9b,9a}$ = 10.4 Hz, $^3J_{9b,10}$ = 5.8 Hz, $^3J_{9b,8}$ = 5.8 Hz), 1.94 (dd, 2H, H(8), $^3J_{8,9b}$ = 5.6 Hz, $^4J_{8,10}$ = 5.6 Hz), 1.14 (s, 6H, H(12)), 1.09 (d, 2H, H(9_a), $^2J_{9a,9b}$ = 10.4 Hz), 0.54 (s, 6H, H(13)). ^{15}N-NMR (40 and 71 MHz, $CDCl_3/CD_3CN$): δ –79 (N), -72 (N'). UV/Vis: λ_{max} (MeOH/H_2O (90% v/v) / nm) 288 (ε/ dm^3 mol^{-1} cm^{-1} 3.0*10^4). CD: λ_{max} (MeOH/H_2O (90% v/v) / nm) 295 (Δε/ dm^3 mol^{-1} cm^{-1} -15), 247 (-10).

Di-protonated ligand $H_2$2^{2+} (5 eq. CF_3COOH) ^{1}H-NMR (400 MHz, $CDCl_3/CD_3CN$): δ 8.65 (ddd, 2H, H(6')), 8.56 (s, 2H, H(3)), 8.30 (ddd, 2H, H(3')), 8.29 (s, 2H, H(6), $^3J_{3,4}$ = 8.0 Hz), 8.05 (ddd, 2H, H(4'), $^3J_{4',3'}$ = 7.8 Hz, $^3J_{4',5'}$ = 7.8 Hz, $^4J_{4',6'}$ = 1.5 Hz), 7.55 (ddd, 2H, H(5'), $^3J_{5',4'}$ = 7.6 Hz, $^3J_{5',6'}$ = 5.3 Hz, $^4J_{5',3'}$ = 1.0 Hz), 4.16 (s, 2H, H(7)), 2.90 (dd, 2H, H(10), $^3J_{10,9b}$ = 5.3 Hz, $^3J_{10,8}$ = 5.3 Hz), 2.49 (ddd, 2H, H(9_b), $^2J_{9b,9a}$ = 10.4 Hz, $^3J_{9b,10}$ = 5.8 Hz, $^3J_{9b,8}$ = 5.8 Hz), 1.95 (dd, 2H, H(8), $^3J_{8,9b}$ = 5.6 Hz, $^4J_{8,10}$ = 5.6 Hz), 1.18 (s, 6H, H(12)), 1.09 (d, 2H, H(9_a), $^2J_{9a,9b}$ = 10.4 Hz), 0.56 (s, 6H, H(13)). ^{15}N-NMR (40 and 71 MHz, $CDCl_3/CD_3CN$): δ –158 (N), -112 (N'). UV/Vis: λ_{max} (MeOH/H_2O (90% v/v) / nm) 312 (ε/ dm^3 mol^{-1} cm^{-1} 3.0*10^4). CD: λ_{max} (MeOH/H_2O (90% v/v) / nm) 324 (Δε/ dm^3 mol^{-1} cm^{-1} -17), 251 (-18).

*[5,6]-CHIRAGEN[0] (**3**)*

Free Ligand 3: ^{1}H-NMR (400 MHz, $CDCl_3/CD_3CN$): δ 8.43 (d, 2H, H(6')), 8.10 (s, br, 2H, H(3')), 7.93 (d, 2H, H(3), $^{3}J_{3,4}$ = 7.6 Hz), 7.59 (ddd, 2H, H(4'), $^{3}J_{4',3'}$ = 7.8 Hz, $^{3}J_{4',5'}$ = 5.8 Hz, $^{4}J_{4',6'}$ = 1.8 Hz), 7.23 (d, 2H, H(4), $^{3}J_{4,3}$ = 7.6 Hz), 7.09 (ddd, 2H, H(5'), $^{3}J_{5',4'}$ = 5.8 Hz, $^{3}J_{5',6'}$ = 4.8 Hz, $^{4}J_{4',3'}$ = 1.0 Hz), 4.36 (s, br, 2H, H(7)), 2.68 (dd, 2H, H(10), $^{3}J_{10,9b}$ = 5.6 Hz, $^{3}J_{10,8}$ = 5.6 Hz), 2.39 (ddd, 2H, H(9_b), $^{2}J_{9b,9a}$ = 9.6 Hz, $^{3}J_{9b,10}$ = 5.6 Hz, $^{3}J_{9b,8}$ = 5.6 Hz), 2.00 (dd, 2H, H(8), $^{3}J_{8,9b}$ = 5.6 Hz, $^{3}J_{8,10}$ = 5.6 Hz), 1.29 (s, br, 2H, H(9_a)), 1.17 (s, 6H, H(12)), 0.61 (s, 6H, H(13)). ^{15}N-NMR (40 and 71 MHz, $CDCl_3/CD_3CN$): δ –78 (N), -77 (N'). UV/Vis: λ_{max} (MeOH/H_2O (90% v/v) / nm) 295 (ε/ dm^3 mol^{-1} cm^{-1} 3.7*10^4). CD: λ_{max} (MeOH/H_2O (90% v/v) / nm) 305 (Δε/ dm^3 mol^{-1} cm^{-1} -27), 284 (22).

Mono-protonated ligand H3^{+} (2 eq. CF_3COOH) ^{1}H-NMR (400 MHz, $CDCl_3/CD_3CN$): δ 7.96 (d, 2H, H(6')), 7.91 (d, 2H, H(3), $^{3}J_{3,4}$ = 7.8 Hz), 7.67 (ddd, 2H, H(3'), $^{3}J_{3',4'}$ = 7.6 Hz), 7.72 (d, 2H, H(4), $^{3}J_{4,3}$ = 8.1 Hz), 7.48 (ddd, 2H, H(4'), $^{3}J_{4',3'}$ = 7.6 Hz, $^{3}J_{4',5'}$ = 7.6 Hz, $^{4}J_{4',6'}$ = 1.5 Hz), 6.98 (ddd, 2H, H(5'), $^{3}J_{5',4'}$ = 7.3 Hz), 3.74 (s, 2H, H(7)), 2.94 (dd, 2H, H(10), $^{3}J_{10,9b}$ = 5.6 Hz, $^{3}J_{10,8}$ = 5.6 Hz), 2.66 (ddd, 2H, H(9_b), $^{2}J_{9b,9a}$ = 10.1 Hz, $^{3}J_{9b,10}$ = 5.6 Hz, $^{3}J_{9b,8}$ = 5.6 Hz), 2.21 (dd, 2H, H(8), $^{3}J_{8,9b}$ = 5.6 Hz, $^{3}J_{8,10}$ = 5.6 Hz), 1.19 (d, 2H, H(9_a), $^{2}J_{9a,9b}$ = 10.1 Hz), 1.33 (s, 6H, H(12)), 0.61 (s, 6H, H(13)). ^{15}N-NMR (40 and 71 MHz, $CDCl_3/CD_3CN$): δ –127 (N), -87 (N'). UV/Vis: λ_{max} (MeOH/H_2O (90% v/v) / nm) 294 (ε/ dm^3 mol^{-1} cm^{-1} 2.7*10^4). CD: λ_{max} (MeOH/H_2O (90% v/v) / nm))313 (Δε/ dm^3 mol^{-1} cm^{-1} -88), 289 (54).

Di-protonated ligand H_23^{2+} (6 eq. CF_3COOH) ^{1}H-NMR (400 MHz, $CDCl_3/CD_3CN$): δ 8.30 (d, 2H, H(6')), 8.24 (ddd, 2H, H(3')), 8.24 (ddd, 2H, H(4')), 7.88 (d, 2H, H(3), $^{3}J_{3,4}$ = 7.8 Hz), 7.57 (ddd, 2H, H(5')), 7.48 (d, 2H, H(4)), 4.16 (s, 2H, H(7)), 2.83 (dd, 2H, H(10), $^{3}J_{10,9b}$ = 5.3 Hz, $^{3}J_{10,8}$ = 5.3 Hz), 2.52 (ddd, 2H, H(9_b), $^{2}J_{9b,9a}$ = 10.1 Hz, $^{3}J_{9b,10}$ = 5.6 Hz, $^{3}J_{9b,8}$ = 5.6 Hz), 2.02 (dd, 2H, H(8), $^{3}J_{8,9b}$ = 5.8 Hz, $^{3}J_{8,10}$ = 5.8 Hz), 1.20 (s, 6H, H(12)), 1.16 (d, 2H, H(9_a), $^{2}J_{9a,9b}$ = 10.1 Hz), 0.50 (s, 6H, H(13)). ^{15}N-NMR (40 and 71 MHz, $CDCl_3/CD_3CN$): δ -164 (N'), –107 (N). UV/Vis: λ_{max} (MeOH/H_2O (90% v/v) / nm) 312 (ε/ dm^3 mol^{-1} cm^{-1} 2.9*10^4). CD λ_{max}: (MeOH/H_2O (90% v/v) / nm) 329 (Δε/ dm^3 mol^{-1} cm^{-1} -92), 299 (59).

Acknowledgements

We thank Dr. Detlef Moskau from Bruker Biospin for the possibility to measure some spectra on a 700 MHz Bruker spectrometer in Fällanden.

This work was supported by Swiss National Science Foundation

References

1 M. Cesario, O. C. Dietrich, A. Edel, J. Guilhem, J.-P. Kintzinger, C. Pacard, J.-P. Sauvage, *J. Am. Chem. Soc.* 1986, **108**, 6250.

2 N. Fatin-Rouge, S. Blanc, E. Leize, A. Van Drosselaer, P. Baret, J.-P. Pierre, A.-M. Albrecht-Gary, *Inorg. Chem.* 2000, **39**, 5771.

3 S. P. Meneghetti, P. J. Lutz, J. Fischer, J. Kress, Polyhedron 2001, **20**, 2705.

4 C.-M. Che, Z.-Y. Li, K.-Y. Wong, C.-K. Poon, T. C. W. Mak, S.-M. Peng, *Polyhedron* 1994, **13**, 771.

5 O. Mamula, A. Von Zelewsky, T. Bark, H. Stoeckli-Evans, A. Neels, G. Bernardinelli, *Chem. Eur. J.*, 2000, **6**, 3575.

6 P. Hayoz, A. Von Zelewsky, *Tetrahedron Lett.* 1992, **33**, 5165.

7 N. C. Fletcher, F. R. Keene, M. Ziegler, H. Stoeckli Evans, H. Viebrock, A. Von Zelewsky, *Helv. Chim. Acta* 1996, **79**, 1192.

8 H. Uchimura, A. Tajiri, M. Hatano, *Bull. Chem. Soc. Jpn.*, 1984, **57**, 341.

9 K. Nakamoto, *J. Phys. Chem.*, 1960, **64**, 1420.

10 O. Borgen, B. Mestvedt, I. Skauvik, *Acta. Chem. Scand. A*, 1976, **30**, 43.

11 P. Krumholz, *J. Am. Chem. Soc.*, 1951, **73**, 3487.

12 D. K. Hazra, S. C. Lahiri, *Anal. Chim. Acta*, 1975, **79**, 335.

13 L. H. Abdel-Rahman, G. G. Herman, A. M. Goeminne, M. Mahmoud, *Bull. Soc. Chim. Belg.*, 1990, **99**, 73.

14 D. K. Hazra, S. C. Lahiri, *J. Indian Chem. Soc.*, 1976, **53**, 787.

15 D. K. Hazra, S. C. Lahiri, *J. Indian Chem. Soc.*, 1976, **53**, 567.

16 R. Mandal, S. C. Lahiri, *Z. Phys. Chem.*, 1999, **210**, 157.

17 S. Bandyopadhyay, A. K. Mandal, S. Aditya, *J. Indian Chem. Soc.*, 1981, **58**, 467.

18 G. V. Budu, L. V. Nazarova, *Russ. J. Inorg. Chem. (Engl. Ed,)* 1973, **18**, 1574.

19 S. K. Chakravorty, D.Sengupta, S. C. Lahiri, *Z. Phys. Chem.*, 1986, **267**, 969.

20 S. C. Lahiri, C. C. Deb, D. K. Hazra, *Z. Phys. Chem.* 1985, **1**, 158.

21 J. Fan, J. Wang, C. Ye, *Talanta* 1998, **46**, 1285.

22 D. H. Buisson, R. J. Irving, *J. Chem. Soc., Faraday Trans. I*, 1977, **73**, 157.

23 M. Maestri, D. Sandrini, V. Balzani, A. Von Zelewsky, C. Deuschel-Cornioley, P. Jolliet, *Helv. Chim. Acta* 1988, **71**, 1053.

24 N. N. Vlasova, N. K. Davidenko, V. I. Bogomaz, *Russ. J. Phys. Chem.*, 1995, **69**, 2001.

25 C. C. Deb, D. K. Hazra, S. C. Lahiri, *Indian J. Chem.*, 1992, **21**, 26.

26 K. Izutsu, Acid-base dissociation constants in dipolar aprotic solvents; Blackwell Scientific Publications (IUPAC Chemical data Series No. 35): Oxford, 1990.

27 M. Hesse, H. Meier, B. Zeeh, Spektroskopische Methoden in der organischen Chemie; 4. Auflage ed.; Gerorge Thieme Verlag: Stuttgart, 1991.

‡ These measurements were carried out at Bruker Biospin in Fällanden.

† Equilibrium constant of the dimerisation in acetonitrile is $\log Kf(HA_2^-) = 3.88$.[26]