Protonation Behaviour of Chiral Tetradentate Polypyridines Derived from α-Pinene

Mathias Düggeli, Tobias Christen, and Alexander von Zelewsky*[a]

Abstract: Detailed protonation experiments of the [5,6]-pinenebipyridine molecule and the unsubstituted [4,5]- and [5,6]-CHIRAGEN[0] ligands in various solvents indicate a variety of structures of the protonated species. UV-visible and NMR measurements (including ^{15}N chemical shifts) show the transition from *trans* to *cis* conformation of [5,6]-pinenebipyridine upon protonation. The [4,5]-CHIRAGEN[0] ligand, in which the protonation sites of the nitrogen atom donors are at opposite sides of the molecule, behave essentially like two independent bipyridine moieties; this behaviour was monitored by UV-visible, CD and NMR spectroscopy (including ^{15}N data). In the case of the [5,6]-CHIRAGEN[0], a pocket of donor atoms provides a chiral environment for two protons per ligand.

Keywords: bipyridine · chirality · N ligands · pinene · protonation

Introduction

The smallest cation known is the proton. An interesting question is: Is it possible for a proton to act as a coordinating centre and, therefore, can a ligand induce helicity to this proton core?

Only a few examples are known in which the proton is exchanged between four donor atoms of one or two ligands and the conformation of the ligand remained fixed. In 1986 Sauvage et al. published a monoprotonated catenane.[1a] 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,[1b] in which 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 ^1H 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 monoprotonated species of a ligand that contained six binding sites. The ^1H NMR spectrum of this monoprotonated species is highly symmetrical, consistent with a folding of the flexible strand of the ligand around a single proton coordinated to two bipyrdine subunits. This observation was confirmed by molecular modelling calculations with Hyperchem, which showed that the most stable conformation in a vacuum was 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 macrocycle containing four bindings sites pointing into the cavity; its crystal structure was published by Che et al. in 1994.[4] This monoprotonated structure (*syn* boat–boat) is markedly different from the free ligand (*syn* chair–chair), suggesting 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.

The ability of these [5,6]-CHIRAGEN[0] ligands to form mononuclear complexes[5] with different cations has attracted our interest to study their protonation behaviour.

Results and Discussion

Protonation studies: The ability of **3** 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

[a] Dr. M. Düggeli, T. Christen, Prof. A. von Zelewsky
Department of Chemistry, University of Fribourg
Pérolles, 1700 Fribourg (Switzerland)
Fax: (+41) 26-300-9738
E-mail: alexander.vonzelewsky@unifr.ch

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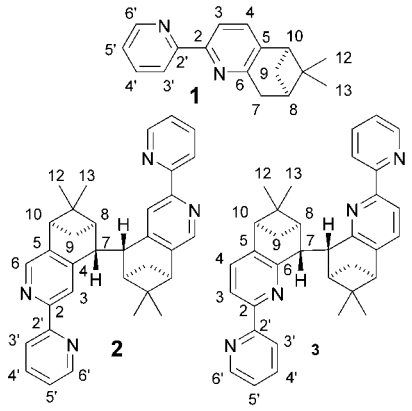
the metal in a helical fashion. This was the motivation to investigate the protonation behaviour of the ligand **3**. Can the proton, as the smallest cation, act as a complexing agent and fix the conformation of the ligand? If the ligand can be fixed in one conformation, does it correspond to a helical conformation comparable to that in metal complexes?



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

Ligands **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 on opposite sides of the molecule and both bpy units react independently.

The methods to study the protonation behaviour were spectrophotometric titrations (UV-visible and CD spectroscopy) and NMR experiments. In the latter, two different nuclei were observed (^{1}H direct and ^{15}N indirect techniques). ^{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), so that we could obtain 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 that 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 nitrogen atoms.[8–10] The second protonation leads again to a *trans*-conformation. The pK_a value for the monoprotonated bpy in water is 4.5,[11] but varies depending on the percentage of organic solvents in aqueous solution and the ionic strength.[9,11–22] The UV-visible spectra of bpy and **1** were measured in 60% (v/v) methanol/water solution with an ionic strength of 0.1 M (NaCl). Hydrochloric acid was used as proton source. Since both ligands show similar behaviour upon protonation, only **1** will be discussed.

The UV-visible spectrum of the free ligand **1** shows an absorption maximum at 293 nm. Upon protonation a bathochromic shift appears (from 293 to 312 nm). An analogous phenomenon was described for bpy.[8,9,22–25] The UV-visible spectra were recorded in a pH-range from 10 to 2, in which only monoprotonated species are formed.[8,9,11] The pK_a values were calculated with the programme Specfit: pK_a = 3.9 ± 0.1 for bpy and pK_a = 4.2 ± 0.1 for **1**; these values are 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 equivalents of trifluoroacetic acid (TFA) to the ligand **1** (Figure 1). 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*-positions (H(4), H(4′)) with regard to the nitrogen atom and in the *meta*-position (H(5′)) show similar downfield shifts (Figure 1). The signal of proton H(6′) in the *ortho*-position shows a less pronounced downfield shift. The signals of the protons H(3) and H(3′) in *meta*-positions initially show a slight downfield shift, but afterwards they return to their original positions.

The most important information about protonation can be obtained by the observation of the chemical shift of ^{15}N. ^{1}H-^{15}N-HMBC spectra 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 (Figure 2).

All these observations lead to the following conclusion: The free ligand **1** and the monoprotonated species are in equilibrium upon protonation, as can be seen in the UV-visible spectra. The monoprotonated form is stabilised in the *cis*-conformation of the ligand by hydrogen bonding (Scheme 1) and the proton is shared between both nitrogen atoms; these observations are in accordance with the ^{15}N experiments (Figure 2).

This is also indicated the bathochromic shift observed in the UV-visible 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 on the experimental timescale, 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* transition is reduced, and a red-shift is observed.

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

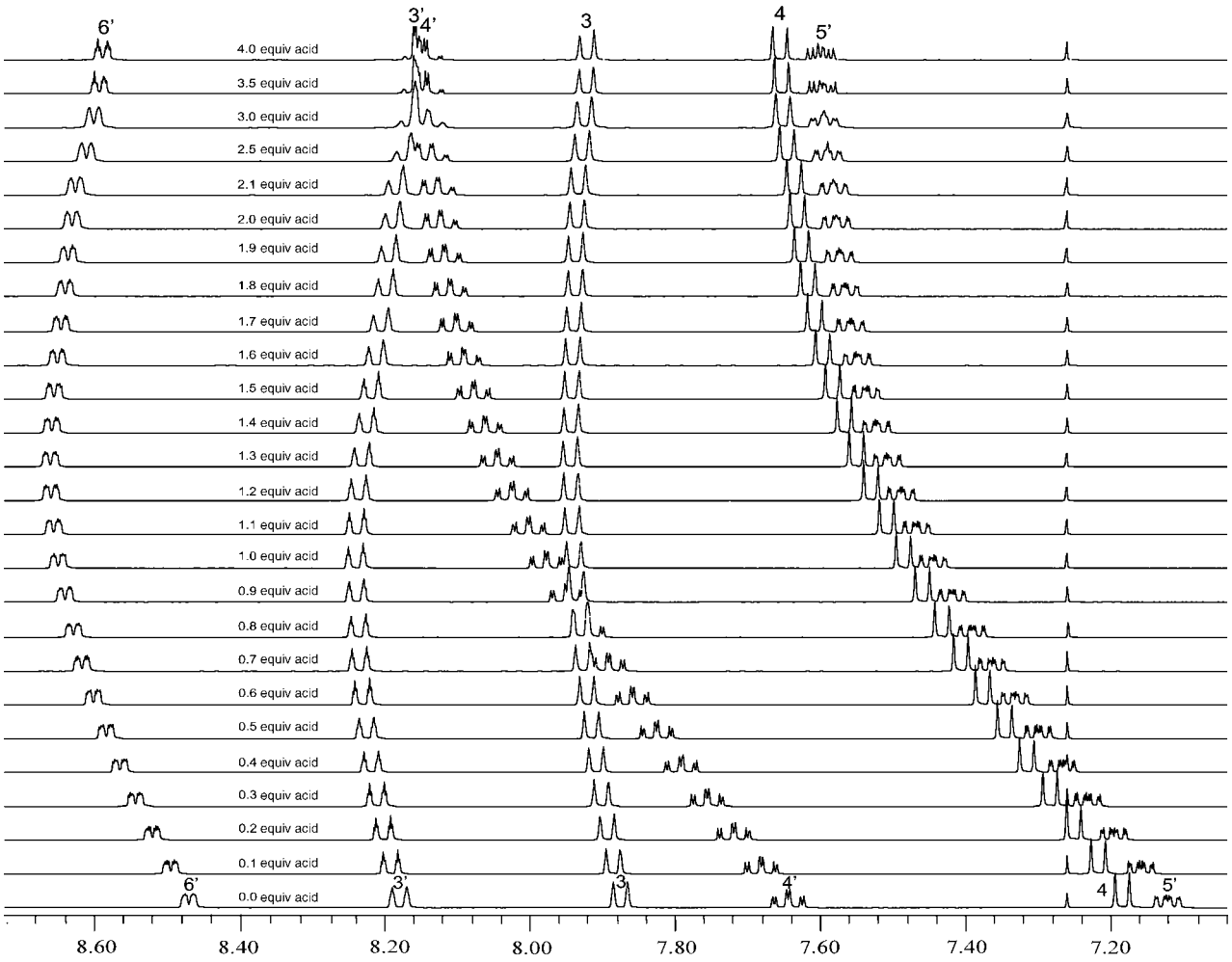


Figure 1. ^{1}H NMR titration of **1**.

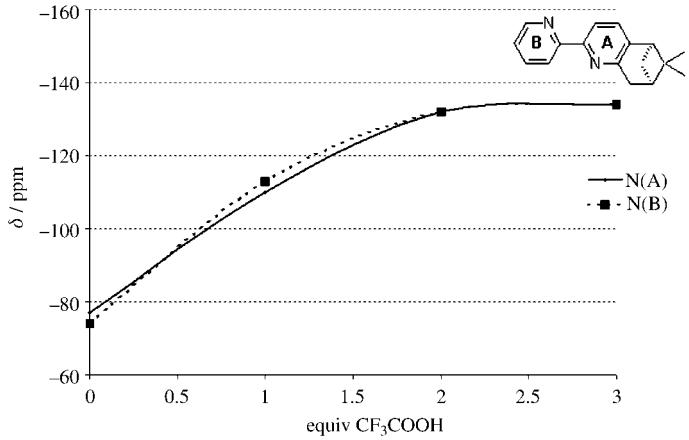
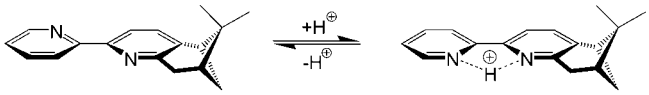
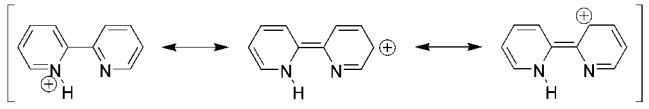


Figure 2. ^{15}N chemical shifts of **1** upon protonation.



Scheme 1. Equilibrium between **1** and its monoprotonated form H**1**$^{+}$.



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

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 a dimeric species (HA_2^-) with its conjugated base (equilibrium constant of the dimerisation in acetonitrile is $\log Kf(HA_2^-) = 3.88$[26]). 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 given in Equation (1).

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

This is in agreement with all NMR titrations, for which two equivalents of TFA were always needed to reach the monoprotonated species.

The conclusion that a monoprotonated species takes a *cis*-conformation is in line with the data obtained from 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 $H\mathbf{1}^{+}$.

From the ^1H NMR spectra it can be seen, that the signals of the protons in *meta*- and *para*-positions (H(5′) and H(4), H(4′), respectively) are influenced strongly upon protonation, whereas proton H(6′) undergoes only a slight downfield shift (Figure 1). This is in accordance with the chemical shifts observed for pyridine and its protonated form.[27] The exceptions are represented by the protons H(3) and H(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. The protonation behaviour is expected to be similar to that of the **1**. No intramolecular proton transfer between the two bpy units can take place and, therefore, each bpy unit will be independently protonated. In addition to the techniques (UV-visible and NMR spectroscopy) used for the investigation of **1**, CD spectroscopy was also performed to study the protonation behaviour.

The spectrophotometric titrations were carried out under the same conditions as those described for **1**. Only the solvent mixture was changed to methanol/water (90 % v/v) for solubility reasons. The UV-visible spectra 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, ligand **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 (Figure 3).

The ^1H NMR titrations were carried out in the same manner as for **1**. After each addition of the acid (TFA), which corresponds to 0.2 equivalents, a ^1H NMR spectrum was recorded (Figure 4). After three equivalents were added, the addition were made in steps of one equivalent.

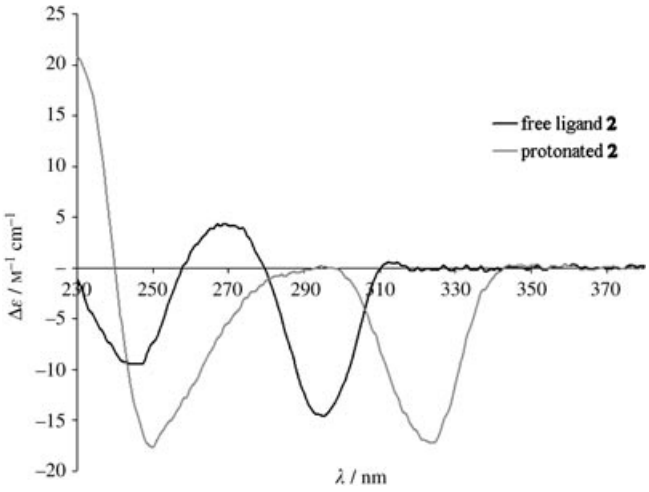


Figure 3. CD spectra of the free ligand **2** and its protonated species.

The ^1H 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 timescale. Large changes in the spectra can be observed upon the addition of 4–5 equivalents of acid (Figure 4), mostly in the aromatic part. The signals of the proton in *para*- (H(4′)) and *meta*-position (H(5′)) shift downfield upon protonation ($\Delta\delta = 0.39$ and 0.40 ppm, respectively). The signals of the protons in *ortho*-position (H(6), H(6′)) show a less pronounced downfield shift ($\Delta\delta = 0.19$ and 0.17 ppm), but proton H(6) is more influenced upon protonation (firstly, to low field and then back to high field). The signal for proton H(3′) (*meta*-position) remains at the same chemical shift ($\Delta\delta = 0.11$ ppm), whereas that for H(3) is slightly shifted to low field ($\Delta\delta = 0.27$ ppm). The signal for the proton at the bridge (H(7)) is shifted slightly to high field upon protonation ($\Delta\delta = 0.28$ ppm).

From the ^1H-^{15}N-HMBC experiment, the chemical shifts of the nitrogen atoms can be determined (Figure 5); they both show a large shift to high field. The nitrogen atom N(A) (up to −158 ppm) is more influenced than N(B) (up to −112 ppm).

All these observations lead to the following conclusion: Upon protonation, the free ligand and the diprotonated species are in equilibrium. Both bpy units of the diprotonated species are in the *cis*-conformation. This protonation takes place through several other equilibria, in which monoprotonated species can be present (Scheme 4).

This is in accordance with the UV-visible and CD measurements (Figure 3), for which no intermediate spectrum can be attributed to a monoprotonated form. The bathochromic shift in the UV-visible spectra and also in the CD spectra (Figure 3) can be explained by the *cis*-conformation of both bpy moieties (analogous to **1**). The protonated ligand retains a conformation similar to that of the free ligand (open form), since the intensity and the nature of the CD signal does not change. If **2** did change conformation,

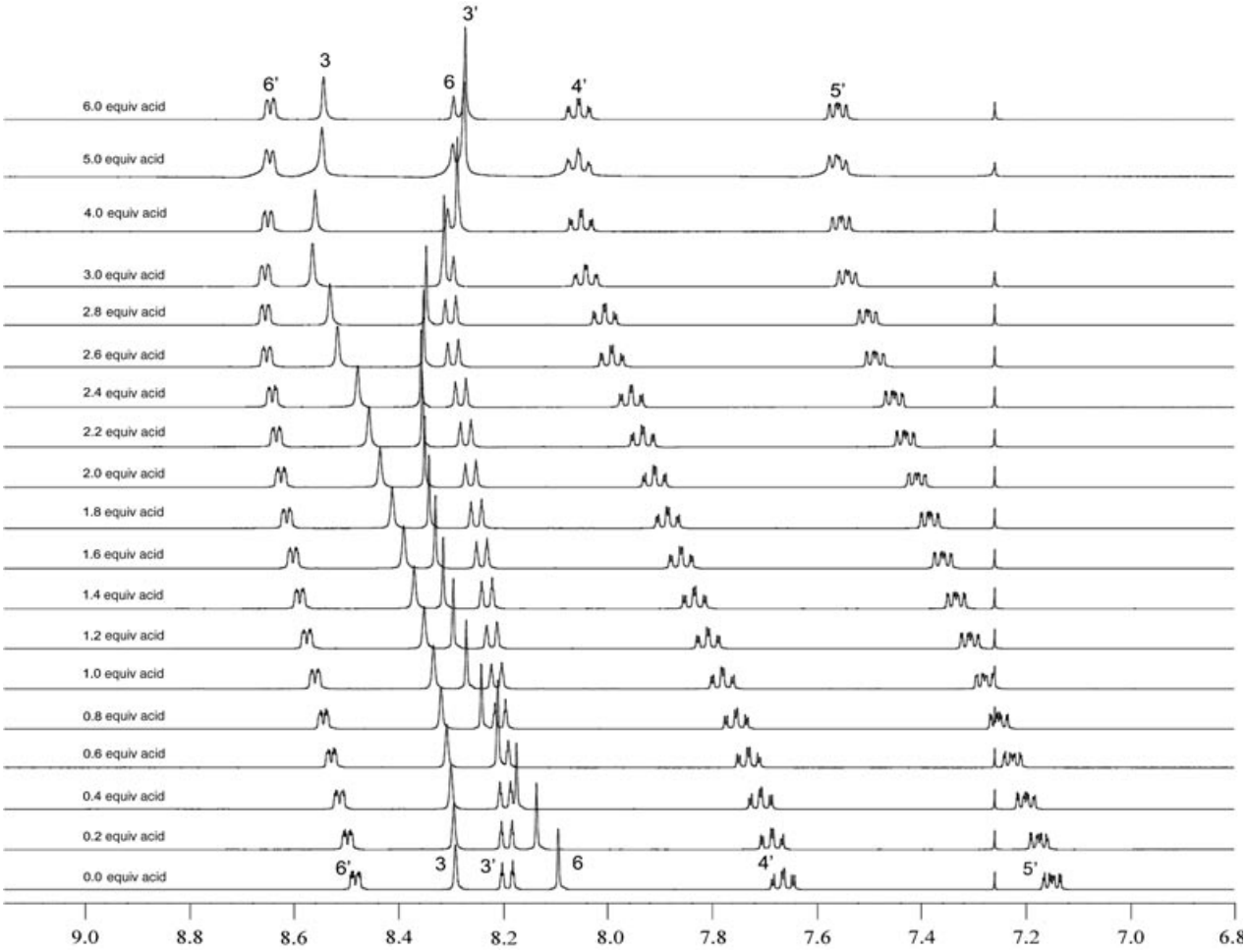


Figure 4. ^{1}H NMR titration of **2**.

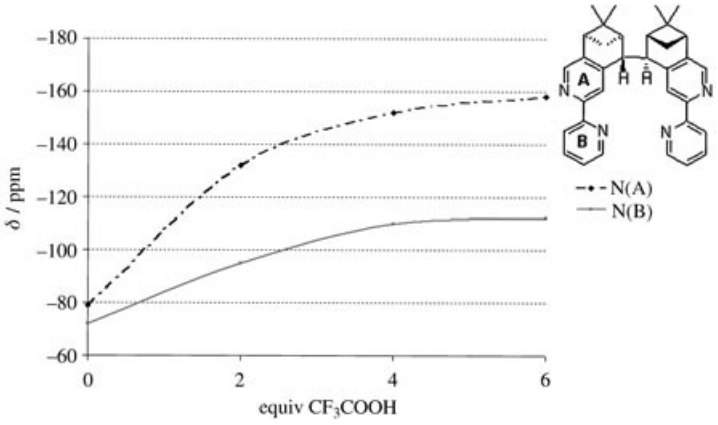
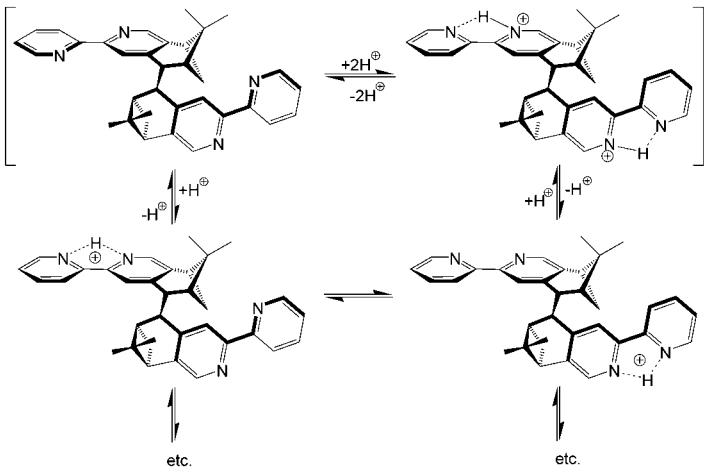


Figure 5. ^{15}N chemical shifts of **2** upon protonation.



Scheme 4. Equilibria between **2** and its protonated forms.

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 are needed, due to the formation of the relatively stable dimmer. The ^{15}N-experiments indicate that the acidic proton is favourably located on the N(A) nitrogen atom (larger shift to high field, Figure 5). However, a sharing of the proton between the N(A) and

N(B) nitrogen atoms can be taken into account. This is in agreement with the ^{1}H NMR, where the protons H(3) and H(6) show a more pronounced shift relative to H(3′) and H(6′).

The similarities of the proton spectra for **2** and **1** support the model, in which each bpy unit is independently monoprotonated. No intramolecular proton exchange between the bpy units of **2** is observed.

Protonation behaviour of [5,6]-CHIRAGEN[0] (3): Compound **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.

Compound **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-visible and CD titration measurements was methanol/water (90% v/v). Solubility problems occurred also for NMR measurements. 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.

In spectrophotometric titrations, two different protonation steps could be observed. In the UV-titration (Figure 6), a hypochromic effect appears upon the first protonation, but

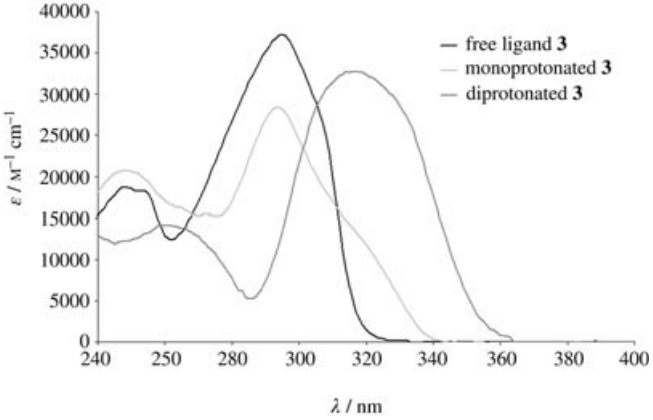


Figure 6. UV-visible spectra of **3** upon protonation.

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)).

An interesting effect was observed in the CD spectra (Figure 7). 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, already observed in the UV spectra. The CD signal does not change its intensity upon the second protonation. Analogous UV-visible and CD spectra were observed for the same solvent mixture and acid (TFA) used in the NMR spectroscopy.

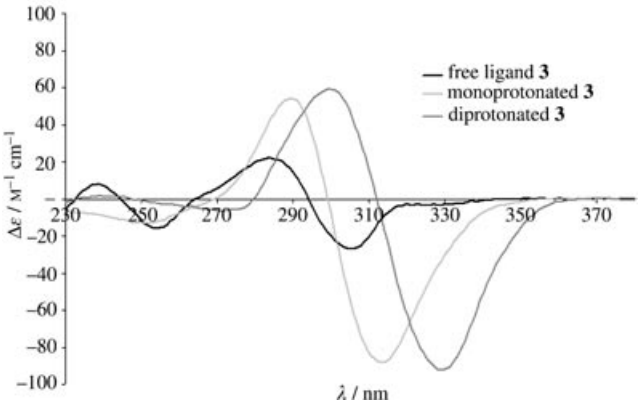


Figure 7. CD spectra of the free ligand **3** and its protonated species.

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 (Figure 8) 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 timescale. Two opposite trends are observable in the ^{1}H NMR titrations (Figure 8). 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 H(6′), H(5′), H(4′), H(3′) and H(7). Proton H(4) shows the opposite shift (first to low field and then back to high field). The broad signals of the protons H(3′), H(7) and H(9_a) in the free ligand sharpen upon protonation.

The most important and significant experiments were again the indirect detected ^{1}H-^{15}N-HMBC experiments (Figure 9). The two nitrogen atoms N(A) and N(B) show quite different behaviour. While the signal of the N(A) nitrogen atom is first shifted to high field (−125 ppm) the second signal corresponding to N(B) is not influenced upon the first protonation. The opposite effect occurs in the second protonation step. N(B) is shifted dramatically to high field ($\Delta\delta = -164$ 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.

These conclusions are consistent with the UV-visible spectra (Figure 6). 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 takes place. The large change in the CD activity upon the first protonation is due to a strong exciton coupling (Figure 8). Similarly, this exciton coupling is observed in the metal complexes with **3**, in which the cation is fixed in the cavity of the ligand. The proton is therefore able to play a similar role, as the metals.

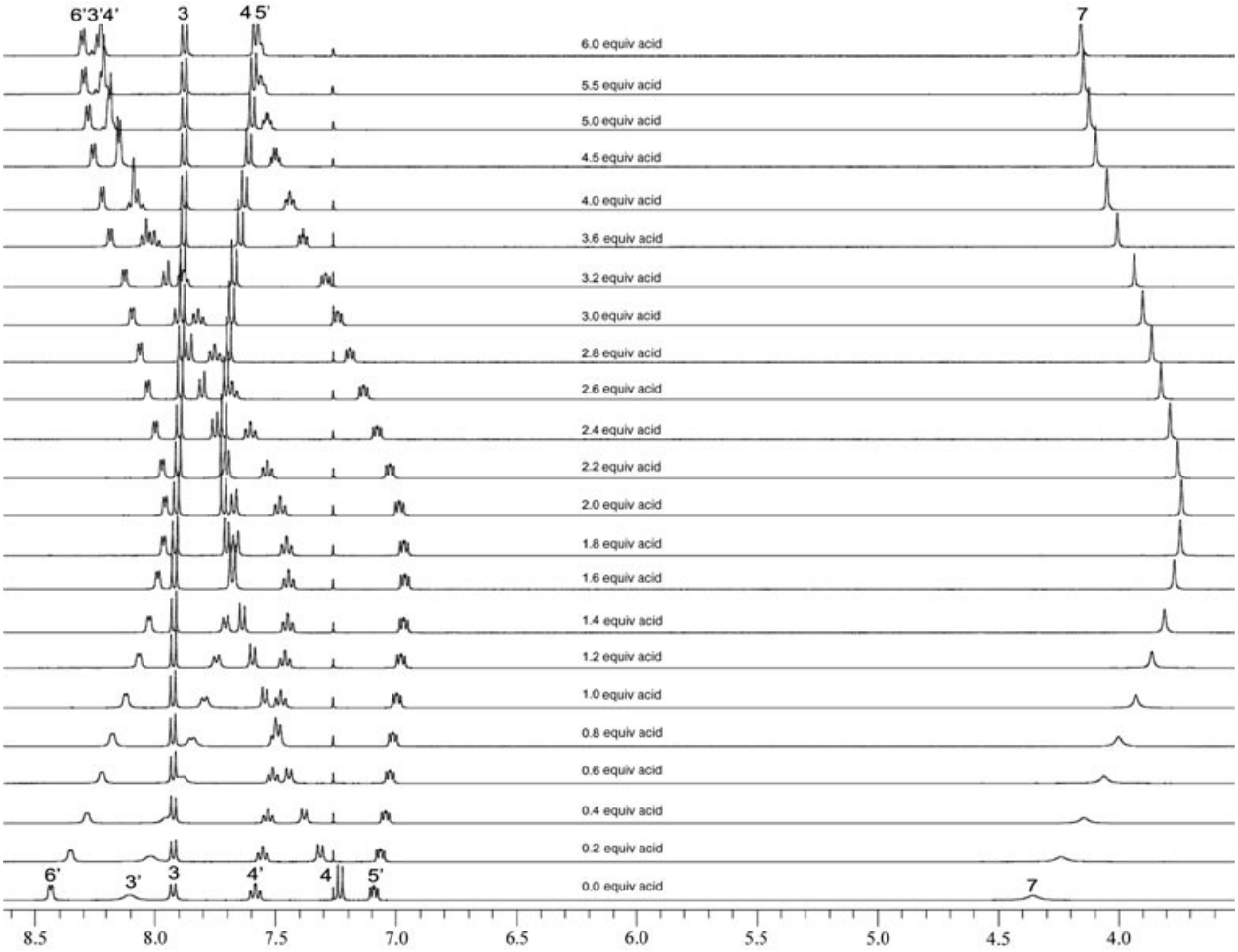


Figure 8. ^{1}H NMR titration of **3**.

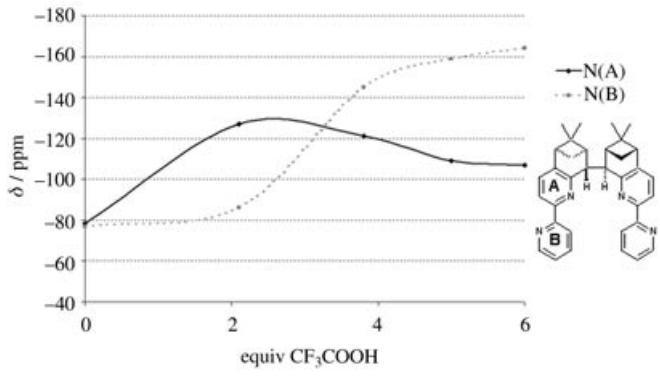
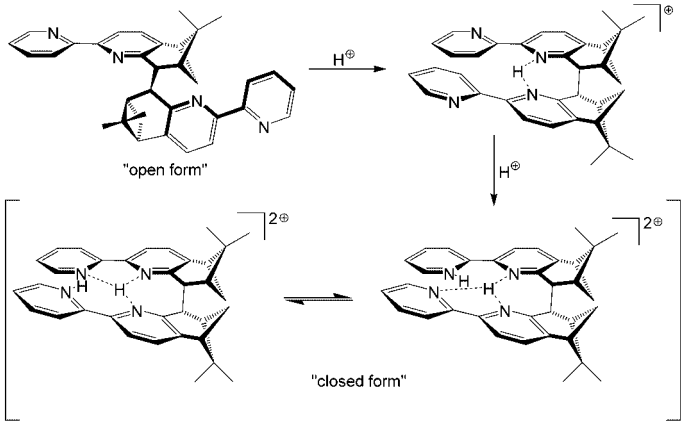


Figure 9. ^{15}N chemical shifts of 3 upon protonation. Some measurements were carried out using ^{15}N(A) enriched (10%) samples.



Scheme 5. Conformation change of **3** upon protonation.

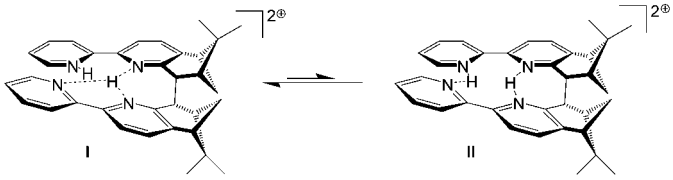
In contrast to the metal complexes, in which the cations are bound to all four nitrogen donor atoms, the proton is only bound to the two N(A) nitrogen atoms near to the bridge. This can be explained by the large chemical shift of N(A) in the ^{15}N experiment, whereas N(B) is not influenced by this proton.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

^{1}H NMR spectra are in accordance with the explanation described above (Figure 8). Signals of the protons H(4) and H(3), attached to the pyridine ring (A), in which the first protonation occurs, show comparable influences as those of the previously studied ligands **1** and **2**. The signal of the proton H(4) is shifted to low field (cf. proton H(4) of **1** in

Figure 1, and signal of the proton H(4) of **2** in Figure 4), whereas proton H(3) remains unchanged. The protons of the unprotonated pyridine rings are shifted to high field, which can be explained by the conformation change to the closed form. Another indication for a fixed conformation is given by the protons H(3′), H(7) and H(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-visible, Figure 6, and CD spectra, Figure 7). The bpy moieties are now conjugated through both pyridine rings in a similar way as already seen in **1** and **2**. The conservation of the large CD intensity can be explained by an analogous conformation as in the monoprotonated 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 high field 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, in which 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 that proposed (distribution I).



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

The protons of the pyridine ring B (H(3′), H(4′), H(5′) and H(6′)) are shifted downfield upon the second protonation (Figure 8). This is in accordance with the ^{15}N experiments, in which the N(B) nitrogen atom is strongly shifted downfield (Figure 9). The protons in ligansd **1** (Figure 1) and **2** (Figure 4) behave in a similar way. Proton H(4) is slightly shifted back to high field (Figure 8), which is in line with the chemical shift of nitrogen N(A) (Figure 9).

Conclusion

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

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

Ligand **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 monoprotonated independently. The conformation of the ligands does not change considerably.

Ligand **3** has the ability to form helical mononuclear complexes with several metal cations. However, not only are metal cations able to fit into the pocket of the ligand, but also a proton, which 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, in which 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 Section

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 (these measurements were carried out at Bruker Biospin in Fällanden). 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 (0.6 mL). 22.30 mL of the TFA solution corresponds to 1.0 equivalent of **1**, 11.16 μL to 1.0 equivalent of **2** and **3**.

Spectrophotometric titrations

Measurements: UV-visible spectra were measured on a Perkin–Elmer Lambda 40 spectrometer. Wavelengths 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 $\Delta\varepsilon$ $M^{-1}cm^{-1}$. The pH was measured with a micro-combination pH electrode (Orion model 9863). UV titrations were carried out with a Mettler Titrator DL21 with 1 mL and 10 mL burettes.

Calibration of the electrode: We assumed that hydrochloric acid 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)), 1 M HCl (methanol/water (60% v/v)), 0.1 M HCl (methanol/water (90% v/v)) and 1 M HCl (methanol/water (90% v/v)) were used for the titrations. The ligand solutions for **1** and bpy consisted of 0.001 M NaOH, 0.1 M NaCl and 5×10^{-5} M **1** and bpy in a mixture of methanol and water (60% v/v). The ligand solutions for **2** and **3** consisted of 0.001 M NaOH, 0.1 M 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 (0.1 M) was added in 2 μL steps to 2 mL of the ligand solutions by the Mettler Titrator DL21 (1 mL burette) for the UV-visible titration. In the pH range from 3 to 1 the 1 M HCl solution was used. The 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-visible 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 (including protonation)

Free ligand 1: ^{1}H NMR (400 MHz, $CDCl_3/CD_3CN$): $\delta = 8.47$ (dm, $^3J_{6',5'} = 7.1$ Hz, 1H; CH(6′)), 8.18 (dm, $^3J_{3',4'} = 8.0$ Hz, 1H; CH(3′)), 7.87 (d, $^3J_{3,4} = 8.0$ Hz, 1H; CH(3)), 7.64 (ddd, $^3J_{4',3'} = 8.0$ Hz, $^3J_{4',5'} = 7.1$ Hz, $^3J_{4',6'} = 1.8$ Hz, 1H; CH(4′)), 7.18 (d, $^3J_{4,3} = 8.0$ Hz, 1H; CH(4)), 7.12 (d, $^3J_{5',4'} = 7.1$ Hz, $^3J_{5',6'} = 7.1$ Hz, $^4J_{5',3'} = 2.0$ Hz, 1H; CH(5′)), 3.00 (m, 2H; CH(7)), 2.67 (dd, $^3J_{10,9b} = 5.6$ Hz, $^3J_{10,8} = 5.6$ Hz, 1H; CH(10)), 2.56 (ddd, $^2J_{9b,9a} = 10.4$ Hz, $^3J_{9b,10} = 5.8$ Hz, $^3J_{9b,8} = 5.8$ Hz, 1H; CH(9_b)), 2.24 (ddt, $^3J_{8,9b} = 5.8$ Hz, $^3J_{8,10} = 5.8$ Hz, $^3J_{8,7} = 2.8$ Hz, 1H; CH(8)), 1.26 (s, 3H; CH_3(12)), 1.13 (d, 1H; CH(9_a)), 0.51 ppm (s, 3H; CH_3(13)); ^{15}N NMR (40 and 71 MHz, $CDCl_3/CD_3CN$): $\delta = -77$ (N(A)), −74 ppm (N(B)); UV/Vis ($MeOH/H_2O$ (60% v/v)): λ_{max} (ε) = 293 nm (1.9×10^4 dm^{3}mol^{-1}cm^{-1}).

Monoprotonated ligand H1$^+$ (3 equiv CF_3COOH): ^{1}H NMR (400 MHz, $CDCl_3/CD_3CN$): $\delta = 8.60$ (dm, $^3J_{6',5'} = 7.1$ Hz, 1H; CH(6′)), 8.17 (m, 1H; CH(3′)), 8.14 (m, 1H; CH(4′)), 7.93 (d, $^3J_{3,4} = 8.0$ Hz, 1H; CH(3)), 7.65 (d, $^3J_{4,3} = 8.0$ Hz, 1H; CH(4)), 7.60 (d, $^3J_{5',4'} = 7.1$ Hz, $^3J_{5',6'} = 7.1$ Hz, $^4J_{5',3'} = 2.0$ Hz, 1H; CH(5′)), 3.16 (m, 2H; CH(7)), 2.87 (dd, $^3J_{10,9b} = 5.6$ Hz, $^3J_{10,8} = 5.6$ Hz, 1H; CH(10)), 2.65 (ddd, $^2J_{9b,9a} = 10.4$ Hz, $^3J_{9b,10} = 5.8$ Hz, $^3J_{9b,8} = 5.8$ Hz, 1H; CH(9_b)), 2.31 (ddt, $^3J_{8,9b} = 5.8$ Hz, $^3J_{8,10} = 5.8$ Hz, $^3J_{8,7} = 2.8$ Hz, 1H; CH(8)), 1.29 (s, 3H; CH_3(12)), 1.15 (d, $^2J_{9a,9b} = 10.4$ Hz, 1H; CH(9_a)), 0.51 ppm (s, 3H; CH_3(13)); ^{15}N NMR (40 and 71 MHz, $CDCl_3/CD_3CN$): $\delta = -134$ ppm (N(A), N(B)); UV/Vis ($MeOH/H_2O$ (60% v/v)): λ_{max} (ε) = 312 (2.0×10^4 dm^{3}mol^{-1}cm^{-1}).

Free ligand 2: ^{1}H NMR (400 MHz, $CDCl_3/CD_3CN$): $\delta = 8.48$ (dm, $^3J_{6',5'} = 5.3$ Hz, 2H; CH(6′)), 8.29 (s, 2H; CH(3)), 8.19 (dm, $^3J_{3',4'} = 7.8$ Hz, 2H; CH(3′)), 8.10 (s, 2H; CH(6)), 7.66 (ddd, $^3J_{4',3'} = 7.8$ Hz, $^3J_{4',5'} = 7.8$ Hz, $^4J_{4',6'} = 1.5$ Hz, 2H; CH(4′)), 7.15 (ddd, $^3J_{5',4'} = 7.6$ Hz, $^3J_{5',6'} = 5.3$ Hz, $^4J_{5',3'} = 1.0$ Hz, 2H; CH(5′)), 3.88 (s, 2H; CH(7)), 2.69 (dd, $^3J_{10,9b} = 5.3$ Hz, $^3J_{10,8} = 5.3$ Hz, 2H; CH(10)), 2.36 (ddd, $^2J_{9b,9a} = 10.4$ Hz, $^3J_{9b,10} = 5.8$ Hz, $^3J_{9b,8} = 5.8$ Hz, 2H; CH(9_b)), 1.94 (dd, $^3J_{8,9b} = 5.6$ Hz, $^4J_{8,10} = 5.6$ Hz, 2H; CH(8)), 1.14 (s, 6H; CH_3(12)), 1.09 (d, $^2J_{9a,9b} = 10.4$ Hz, 2H; CH(9_a)), 0.54 ppm (s, 6H; CH_3(13)); ^{15}N NMR (40 and 71 MHz, $CDCl_3/CD_3CN$): $\delta = -79$ (N(A)), −72 ppm (N(B)); UV/Vis ($MeOH/H_2O$ (90% v/v)): λ_{max} (ε) = 288 nm (3.0×10^4 dm^{3}mol^{-1}cm^{-1}); CD ($MeOH/H_2O$ (90% v/v)): λ_{max} (ε) = 295 (−15), 247 nm (−10 dm^{3}mol^{-1}cm^{-1}).

Diprotonated ligand H_22^{2+} (5 equiv CF_3COOH): ^{1}H NMR (400 MHz, $CDCl_3/CD_3CN$): $\delta = 8.65$ (dm, $^3J_{6',5'} = 5.3$ Hz, 2H; CH(6′)), 8.56 (s, 2H; CH(3)), 8.30 (m, 2H; CH(3′)), 8.29 (s, 2H; CH(6)), 8.05 (ddd, $^3J_{4',3'} = 7.8$ Hz, $^3J_{4',5'} = 7.8$ Hz, $^4J_{4',6'} = 1.5$ Hz, 2H; CH(4′)), 7.55 (ddd, $^3J_{5',4'} = 7.6$ Hz, $^3J_{5',6'} = 5.3$ Hz, $^4J_{5',3'} = 1.0$ Hz, 2H; CH(5′)), 4.16 (s, 2H; CH(7)), 2.90 (dd, $^3J_{10,9b} = 5.3$ Hz, $^3J_{10,8} = 5.3$ Hz, 2H; CH(10)), 2.49 (ddd, $^2J_{9b,9a} = 10.4$ Hz, $^3J_{9b,10} = 5.8$ Hz, $^3J_{9b,8} = 5.8$ Hz, 2H; CH(9_b)), 1.95 (dd, $^3J_{8,9b} = 5.6$ Hz, $^4J_{8,10} = 5.6$ Hz, 2H; CH(8)), 1.18 (s, 6H; CH_3(12)), 1.09 (d, $^2J_{9a,9b} = 10.4$ Hz, 2H; CH(9_a)), 0.56 ppm (s, 6H; CH_3(13)); ^{15}N NMR (40 and 71 MHz, $CDCl_3/CD_3CN$): $\delta = -158$ (N(A)), −112 ppm (N(B)); UV/Vis ($MeOH/H_2O$ (90% v/v)): λ_{max} (ε) = 312 nm (3.0×10^4 dm^{3}mol^{-1}cm^{-1}); CD ($MeOH/H_2O$ (90% v/v)): λ_{max} (ε) = 324 (−17), 251 nm (−18 dm^{3}mol^{-1}cm^{-1}).

Free ligand 3: ^{1}H NMR (400 MHz, $CDCl_3/CD_3CN$): $\delta = 8.43$ (dm, $^3J_{6',5'} = 4.8$ Hz, 2H; CH(6′)), 8.10 (brs, 2H; CH(3′)), 7.93 (d, $^3J_{3,4} = 7.6$ Hz, 2H; CH(3)), 7.59 (ddd, $^3J_{4',3'} = 7.8$ Hz, $^3J_{4',5'} = 5.8$ Hz, $^4J_{4',6'} = 1.8$ Hz, 2H; CH(4′)), 7.23 (d, $^3J_{4,3} = 7.6$ Hz, 2H; CH(4)), 7.09 (ddd, $^3J_{5',4'} = 5.8$ Hz, $^3J_{5',6'} = 4.8$ Hz, $^4J_{4',3'} = 1.0$ Hz, 2H; CH(5′)), 4.36 (brs, 2H; CH(7)), 2.68 (dd, $^3J_{10,9b} = 5.6$ Hz, $^3J_{10,8} = 5.6$ Hz, 2H; CH(10)), 2.39 (ddd, $^2J_{9b,9a} = 9.6$ Hz, $^3J_{9b,10} = 5.6$ Hz, $^3J_{9b,8} = 5.6$ Hz, 2H; CH(9_b)), 2.00 (dd, $^3J_{8,9b} = 5.6$ Hz, $^3J_{8,10} = 5.6$ Hz, 2H; CH(8)), 1.29 (brs, 2H; CH(9_a)), 1.17 (s, 6H; CH_3(12)), 0.61 ppm (s, 6H; CH_3(13)); ^{15}N NMR (40 and 71 MHz, $CDCl_3/CD_3CN$): $\delta = -78$ (N(A)), −77 ppm (N(B)); UV/Vis ($MeOH/H_2O$ (90% v/v)): λ_{max} (ε) = 295 nm (3.7×10^4 dm^{3}mol^{-1}cm^{-1}): CD ($MeOH/H_2O$ (90% v/v)): λ_{max} (ε) = 305 (−27), 28 nm (22 dm^{3}mol^{-1}cm^{-1}).

Monoprotonated ligand H3$^+$ (2 equiv CF_3COOH): ^{1}H NMR (400 MHz, $CDCl_3/CD_3CN$): $\delta = 7.96$ (dm, $^3J_{6',5'} = 4.8$ Hz, 2H; CH(6′)), 7.91 (d, $^3J_{3,4} = 7.8$ Hz, 2H; CH(3)), 7.67 (ddd, $^3J_{3',4'} = 7.6$ Hz, 2H; CH(3′)), 7.72 (d, $^3J_{4,3} = 8.1$ Hz, 2H; CH(4)), 7.48 (ddd, $^3J_{4',3'} = 7.6$ Hz, $^3J_{4',5'} = 7.6$ Hz, $^4J_{4',6'} = 1.5$ Hz, 2H; CH(4′)), 6.98 (ddd, $^3J_{5',4'} = 7.3$ Hz, 2H; CH(5′)), 3.74 (s, 2H; CH(7)), 2.94 (dd, $^3J_{10,9b} = 5.6$ Hz, $^3J_{10,8} = 5.6$ Hz, 2H; CH(10)), 2.66 (ddd, $^2J_{9b,9a} = 10.1$ Hz, $^3J_{9b,10} = 5.6$ Hz, $^3J_{9b,8} = 5.6$ Hz, 2H; CH(9_b)), 2.21 (dd, $^3J_{8,9b} = 5.6$ Hz, $^3J_{8,10} = 5.6$ Hz, 2H; CH(8)), 1.19 (d, $^2J_{9a,9b} = 10.1$ Hz, 2H; CH(9_a)), 1.33 (s, 6H; CH_3(12)), 0.61 ppm (s, 6H; CH_3(13)); ^{15}N NMR (40 and 71 MHz, $CDCl_3/CD_3CN$): $\delta = -127$ (N(A)), −87 ppm (N(B)); UV/Vis ($MeOH/H_2O$ (90% v/v)): λ_{max} (ε) = 294 nm (2.7×10^4 dm^{3}mol^{-1}cm^{-1}); CD ($MeOH/H_2O$ (90% v/v)): λ_{max} (ε) = 313 (−88), 289 nm (54 dm^{3}mol^{-1}cm^{-1}).

Diprotonated ligand H_23^{2+} (6 equiv CF_3COOH): ^{1}H NMR (400 MHz, $CDCl_3/CD_3CN$): $\delta = 8.30$ (dm, $^3J_{6',5'} = 4.8$ Hz, 2H; CH(6′)), 8.24 (m, 2H; CH(3′)), 8.24 (m, 2H; CH(4′)), 7.88 (d $^3J_{3,4} = 7.8$ Hz, 2H; CH(3),), 7.57 (m, 2H; CH(5′)), 7.48 (m, 2H; CH(4)), 4.16 (s, 2H; CH(7)), 2.83 (dd, $^3J_{10,9b} = 5.3$ Hz, $^3J_{10,8} = 5.3$ Hz, 2H; CH(10)), 2.52 (ddd, $^2J_{9b,9a} = 10.1$ Hz, $^3J_{9b,10} = 5.6$ Hz, $^3J_{9b,8} = 5.6$ Hz, 2H; CH(9_b)), 2.02 (dd, $^3J_{8,9b} = 5.8$ Hz, $^3J_{8,10} = 5.8$ Hz, 2H; CH(8)), 1.20 (s, 6H; CH_3(12)), 1.16 (d, $^2J_{9a,9b} = 10.1$ Hz, 2H; CH(9_a)), 0.50 ppm (s, 6H; CH_3(13)); ^{15}N NMR (40 and 71 MHz, $CDCl_3/CD_3CN$): $\delta = -164$ (N(B)), −107 ppm (N(A)); UV/Vis: ($MeOH/H_2O$ (90% v/v)): λ_{max} (ε) = 312 nm (2.9×10^4 dm^{3}mol^{-1}cm^{-1}); CD ($MeOH/H_2O$ (90% v/v)): λ_{max} (ε) = 329 (−92), 299 nm (59 dm^{3}mol^{-1}cm^{-1}).

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