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Carbonate binding to copper(II) in solution: mixed-ligand complex formation and its application to the isolation and separation of the three isomers of $[Cu(bpp)(H_2O)][ClO_4]_2$ [bpp = 2,6-bis(pyrrolidin-2-yl)pyridine]

Klaus Bernauer,* Amel Cabort, Nathalie Guicher, Helen Stoeckli-Evans and Georg Süss-Fink

Institut de Chimie, Université de Neuchâtel, Case postale 2, CH-2007 Neuchâtel, Switzerland

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The binding of the carbonate anion to [Cu(*meso*-bpp)$(H_2O)]^{2+}$ and *rac*-[Cu(bpp)$(H_2O)]^{2+}$ [bpp = 2,6-bis(pyrrolidin-2-yl)pyridine] in aqueous solution has been investigated. Formation constants of the carbonato complexes [Cu(*meso*-bpp)(CO_3)] and *rac*-[Cu(bpp)(CO_3)] (1.02×10^3 M^{-1} and 1.77×10^3 M^{-1}, respectively, $\mu = 0.70$ M) have been calculated from spectrophotometric measurements. The formation of these Cu^{2+} complexes can also be used for an improved synthesis and an easy isolation of the three diastereoisomers of bpp. The mixture of [Cu(*meso*-bpp)$(H_2O)]^{2+}$ and *rac*-[Cu(bpp)$(H_2O)]^{2+}$ is separated by elution from SP Sephadex C-25, either as hydroxo or carbonato derivatives. *rac*-[Cu(bpp)$(H_2O)]^{2+}$ is then resolved into the enantiomers [Cu(*S*,*S*-bpp)$(H_2O)]^{2+}$ and [Cu(*R*,*R*-bpp)$(H_2O)]^{2+}$, again on SP Sephadex C-25, by means of L-(+)-tartrate as chiral eluent. The three stereoisomers, *meso*-bpp, (*S*,*S*)-bpp and (*R*,*R*)-bpp are liberated from the corresponding copper(II) complexes by ligand displacement using *trans*-1,2-diaminocyclohexane-*N*,*N*,*N*′,*N*′-tetraacetic acid (H_4cdta). The structure of the *meso* isomer was solved by a single crystal X-ray analysis using the perchlorate salt [*meso*-bppH_2][$ClO_4]_2 \cdot 2H_2O$.

Introduction

Binding of HCO_3^-/CO_3^{2-} to metal centres has been a subject of intense research, given the interest in the enzymatic hydration/dehydration reaction of carbon dioxide catalysed by carbonic anhydrase.[1] In order to get a better understanding of the enzymatic activity, Cu^{2+} complexes have been used as model compounds.[2] It has been demonstrated that the ability of these complexes to react with HCO_3^- depends on the position of the coordinated water molecule in the coordination sphere of the Cu^{2+} centre. Bi-, tri- and tetra-dentate ligands have been used for these model compounds, and various binding modes in mono- or oligo-meric compounds have been identified.[2a] Linear triamines and their derivatives have also found a steadily increasing interest as auxiliary ligands in asymmetric synthesis,[3] as ligands for complexes with predetermined chirality,[4,5] or as building blocks in the formation of heteronuclear,[6] helical[7] and dendrimeric complexes.[8] Often these ligands contain a central pyridine unit to ensure meridional coordination and to reduce the number of possible structural isomers. Furthermore this aromatic unit allows the formation of manifold derivatives by substitution of the aromatic moiety.

Several years ago, we reported the synthesis and the separation of the three stereoisomers of the triamine 2,6-bis(pyrrolidine-2-yl)pyridine (bpp) (Fig. 1).[9] The measurements of complex formation equilibria with a chiral isomer of this ligand and different metal ions such as Ni(II), Co(II), Zn(II) revealed high stereoselectivity in the formation of homoleptic 1 : 2 complexes.[10] Nevertheless, the method used for the synthesis showed several disadvantages. The separation of the two diastereoisomers has been achieved by chromatography of the *p*-nitrobenzoyl derivatives, but deprotection of the ligand causes significant loss of the product. Finally, the racemate was separated into the two enantiomers by crystallisation as the *O*,*O*-dibenzoyltartate.

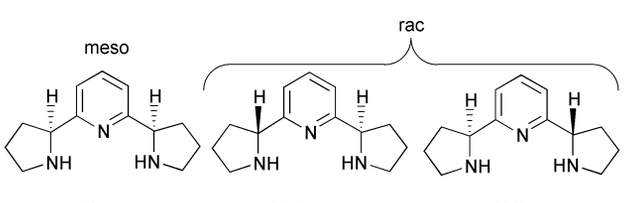

Fig. 1 Steroisomers of 2,6-bis(pyrrolidin-2-yl)pyridine (bpp).

In the present paper we report on the formation constants of the binding equilibria of the carbonate anion to [Cu(*meso*-bpp)$(H_2O)]^{2+}$ and *rac*-[Cu(bpp)$(H_2O)]^{2+}$ and the use of these equilibria for the chromatographic separation of the three complexes [Cu(*meso*-bpp)$(H_2O)]^{2+}$, [Cu(*S*,*S*-bpp)$(H_2O)]^{2+}$ and [Cu(*R*,*R*-bpp)$(H_2O)]^{2+}$ which, after decomplexation, allows the preparation of the three stereoisomers *meso*-bpp [*i.e.* (*R*,*S*)-bpp], (*S*,*S*)-bpp and (*R*,*R*)-bpp.

Experimental

Spectroscopic measurements

UV/Vis absorption spectra were recorded on a Varian Cary-1E. Circular dichroism (CD) spectra were recorded on spectropolarimeters JASCO J-700 and J-500-C. ^1H and ^{13}C NMR measurements were performed on a Varian Gemini spectrometer (200 MHz).

Materials

SP and QAE Sephadex were obtained from Amersham-Pharmacia-Biotech. The precursor of bpp, 2,6-bis(3,4-dihydro-2*H*-pyrrol-5-yl)pyridine (bdpp), was prepared as previously described.[9]

Syntheses

2,6-Bis(pyrrolidin-2-yl)pyridine (bpp). The mixture of *rac*- and *meso*-bpp was obtained as reported earlier.[9] However,

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instead of a 1 : 2 *rac* : *meso* mixture, a 1 : 1 mixture of the two diastereoisomers can be obtained by the following modification of the reduction step of the precursor 2,6-bis(3,4-dihydro-2*H*-pyrrol-5-yl)pyridine (bdpp): 2.54 g (1.19×10^{-2} mol) of bdpp were dissolved in 500 ml dried ethanol, and $NaCNBH_3$ (2.21 g; 3.58×10^{-2} mol) was added under N_2. The pH of the solution was kept at 4 by addition of 2 M HCl. After 4 hours the pH was raised to 12 by the addition of aqueous 2 M NaOH, and the organic fraction was extracted with CH_2Cl_2, washed with a saturated solution of NaCl and dried over $MgSO_4$. The solvent was removed by evaporation, and the residue was dried *in vacuo*. The resulting mixture of the bpp diastereoisomers (1.3 g, 53%) was directly used for the synthesis of the copper complexes.

Warning: Perchlorates can be dangerous and should be handled in small amounts with screen protection!

[Cu(bpp)(H_2O)][ClO_4]$_2$. The crude mixture of bpp (1.3 g, 6.3×10^{-3} mol) was dissolved in water (100 ml), and an excess of aqueous copper sulfate was added. The solution was stirred for 1 h at pH = 8.0 in order to precipitate unreacted copper as $Cu(OH)_2$. The mixture was filtered over Celite, and the pH of the solution fixed at a value between 5.0 and 6.0 by addition of diluted $HClO_4$ (*ca.* 10%). The deep blue solution of [Cu(bpp)(H_2O)][ClO_4]$_2$ was further diluted with water to five to ten times its volume in order to enhance the retention of the bivalent copper complexes. The solution was introduced into a SP Sephadex C-25 column which was then extensively washed with water. After complete elution of the copper complexes with a 0.2 M buffer ($NaHCO_3/Na_2CO_3$, pH = 10), 3 g of the pure diastereoisomeric mixture were obtained almost quantitatively as solid perchlorate salts which crystallised after acidification to pH = 5.0 with $HClO_4$ (10%).

Separation of [Cu(*meso*-bpp)(H_2O)]$^{2+}$ and *rac*-[Cu(bpp)(H_2O)]$^{2+}$

First method. A solution of the perchlorate salts of the mixture of diastereoisomers (2 g) in water (2000 ml) was introduced into a SP Sephadex C-25 column (l = 120 cm, $\varnothing$ = 8 cm). Elution with a buffer (H_3BO_3 0.1 M, Na_2SO_4 0.5% at pH = 8.35) allowed quantitative separation; the first fraction was identified as *meso*, and the second as *rac*. The fractions were separately acidified by diluted $HClO_4$ and crystallised from water.

Second method. A solution of the perchlorate salts of the mixture of diastereoisomers (2 g) in water (2000 ml) was introduced into a SP Sephadex C-25 column (l = 120 cm, $\varnothing$ = 8 cm). Elution with a buffer ($NaHCO_3/Na_2CO_3$ 0.02 M, pH = 10) allowed quantitative separation; the first fraction was identified as *rac*, and the second as *meso*. The fractions were separately acidified with diluted $HClO_4$ and treated as indicated below.

Chiral resolution of *rac*-[Cu(bpp)(H_2O)]$^{2+}$

A solution of 1.5 g of *rac*-[Cu(bpp)(H_2O)][ClO_4]$_2$ in 2000 ml of water were introduced into a SP Sephadex C-25 column (l = 35 cm, $\varnothing$ = 3 cm) which was then washed with water. The complexes were eluted with a solution of sodium L-(+)-tartrate (0.05 M), the pH of which was fixed to 5.0 with NaOH. The *S*,*S* isomer moves faster than the *R*,*R* isomer, the two bands were collected separately. The solutions of the two enantiomers were again introduced into a small SP Sephadex C-25 column, and the tartrate was washed out with water. The compounds were then eluted with a 0.2 M carbonate buffer and the perchlorate salts isolated as described before. The optical purity of the effluent was checked by measuring the ratio of visible absorption to optical rotation and/or CD intensity. The enantiomeric excess (ee) of the samples (90 > ee > 100%) increased up to constant values by recrystallisation from water. Samples of ee < 90% were submitted to repeated separation. [Cu(*R*,*R*-bpp)(H_2O)][ClO_4]$_2$: $[\alpha]_{589}$ = +689° (c = 0.015 M, H_2O); $\Delta\varepsilon_{650}$ = −1.00, $\Delta\varepsilon_{547}$ = 0; $\Delta\varepsilon_{510}$ = +0.14, $\Delta\varepsilon_{650}$ = 0.

Isolation of the three bpp isomers

The three isomers of bpp are liberated from the corresponding copper complexes by a ligand displacement reaction. To the aqueous solution of [Cu(bpp)(H_2O)]$^{2+}$, 1.5 equivalents of *trans*-1,2-diaminocyclohexane-*N*,*N*,*N*′,*N*′-tetraacetic acid were added, and the pH of the solution adjusted to pH = 7.8 with NaOH. The exchange reaction was monitored by UV/Vis for the *meso* complex and by CD for the optically active complexes. After completion of the reaction, the diluted solution containing not more than 1 g dm^{-3} of the initial compound [Cu(bpp)(H_2O)][ClO_4]$_2$, was introduced into a QAE Sephadex anion-exchange column loaded with ClO_4^-. The column was then eluted with water. The effluent solution was monitored by UV absorption (λ = 262 nm) or by polarimetric measurements. Upon concentration of the solutions using a rotatory evaporator, the perchlorate salts of the protonated bpp isomer was obtained as a crystalline solid. The solid was filtered and dried under vacuum. The purity of the products was checked by comparing the specific rotation of the enantiomers of bpp with data given in the literature.[9] The structure of the isomer *meso*-bpp was solved by X-ray crystal structure analysis.

^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.74 (m, 2H), 1.85 (q, 4H), 2.20 (m, 2H), 2.60 (s, 2H), 3.00 (m, 2H), 3.22 (m, 2H), 4.22 (t, 2H), 7.17 (d, 2H), 7.58 (t, 1H). Specific rotation of (+)bpp [(−)bpp]: $[\alpha]_{365}$ (c = 0.10 M, H_2O) +378° [−340°], $[\alpha]_{589}$ (c = 0.10 M, H_2O) +126° [−113°].

Equilibrium data measurements

For the determination of the equilibrium constants by UV/Vis, a series of eight samples (at constant pH) of [Cu(bpp)(H_2O)]$^{2+}$ (2.5×10^{-3} M) containing a carbonate buffer ([HCO_3^-] = [CO_3^{2-}]) were prepared; the total concentration varying between 5×10^{-3} and 0.1 M. The ionic strength was kept at 0.70 M by addition of the calculated amount of KNO_3. The pH of the solution was adjusted, if necessary, to 9.74 by NaOH. The samples were kept at 25 °C for 24 h, and the pH was controlled prior to measuring the UV/Vis spectra. The measurements were repeated after 24 h in order to ensure the stability of the solutions.

For the measurements at variable pH, the solutions were prepared in a similar way with constant total carbonate buffer concentration (0.05 M) the HCO_3^-/CO_3^{2-} ratio being varied from 40 to 0.02 corresponding to a pH range from 8.0 to 11.2 and a pK_a value of 9.74 (μ = 0.70 M and T = 25 °C).

X-Ray crystallography

Suitable crystals of [*meso*-bppH_2][ClO_4], colourless, rod-like single crystals, were grown from water. Intensity data were collected at 233 K on a Stoe AED2 4-circle diffractometer using Mo-Kα graphite monochromated radiation (λ = 0.71073 Å) with $\omega/2\Theta$ scans in the 2Θ range 5–51° (see Table 1). The structure was solved by direct methods using the program SHELXS-97.[11] The refinement and all further calculations were carried out using SHELXL-97.[11] H atoms were included in calculated positions and treated as riding atoms using SHELXL-97 default parameters, except the water H atoms which were located from difference Fourier maps and refined isotropically with a fixed O–H bond length of 0.90(1) Å. The non-H atoms were refined anisotropically, using weighted full-matrix least-squares on F^2.

CCDC reference number 175425.

See http://www.rsc.org/suppdata/dt/b1/b111501b/ for crystallographic data in CIF or other electronic format.

Table 1 Summary of crystal structure data for [*meso*-bppH$_2$][ClO$_4$]$_2$·2H$_2$O

Empirical formula	$C_{13}H_{25}Cl_2N_3O_{10}$
Formula weight	454.26
Crystal system	Monoclinic
Space group	*C*2/*m*
a/Å	14.313(6)
b/Å	11.416(4)
c/Å	12.481(5)
α/°	90.00(3)
β/°	91.15(3)
γ/°	90.00(3)
V/Å^3	2038.9(14)
Z	4
T/K	233(2)
Wavelength, *λ*(Mo-Kα)/Å	0.71073
μ/cm^{-1}	0.0374
Reflections collected	4231
Unique reflections	2001
R_{int}	0.0289
*R*1, *wR*2 [$I > 2.0\sigma(I)$][a]	0.0575, 0.1545

[a] $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$, $wR2 = [\Sigma(w(F_o^2 - F_c^2)^2)/\Sigma w(F_o^4)]^{1/2}$.

Results and discussion

Carbonate binding by [Cu(bpp)(H$_2$O)]$^{2+}$ in aqueous solution

The isomer mixture of [Cu(bpp)(H$_2$O)]$^{2+}$ is only slowly eluted from a SP Sephadex cation-exchange column by a NaClO$_4$ solution even under basic conditions. However, it can be displaced easily by a moderately concentrated (0.2 M) carbonate buffer at pH = 10, suggesting the formation of carbonato complexes. This hypothesis is supported by the visible absorption spectra shown in Fig. 2.

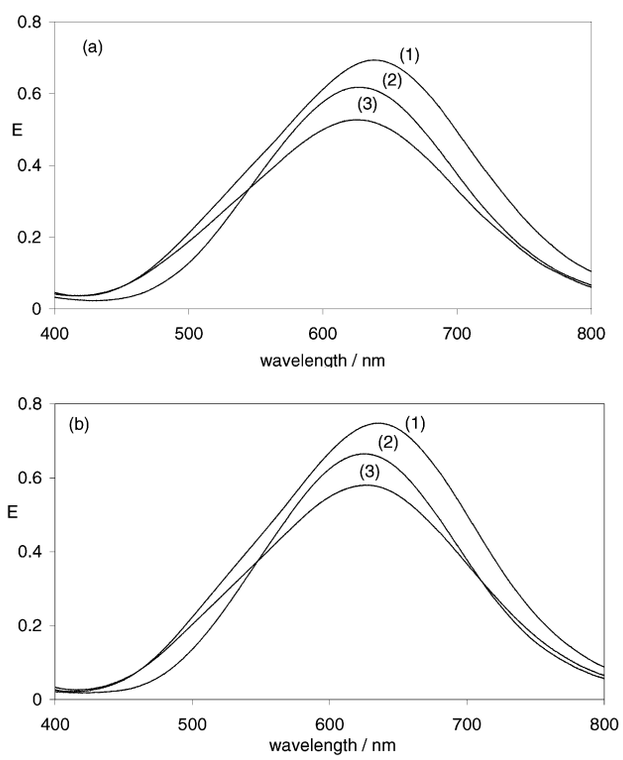

Fig. 2 Visible absorption spectra of [Cu(*meso*-bpp)(H$_2$O)]$^{2+}$ (a) and *rac*-[Cu(bpp)(H$_2$O)]$^{2+}$ (b) in HCO$_3^-$/CO$_3^{2-}$ 0.2 M, pH = 10.3 (1); H$_2$O (2) and NaOH 0.01 M (3).

Even though numerous carbonato complexes are known with their molecular structures,[2] only a few quantitative equilibrium data are known for CO$_3^{2-}$ binding to metal complexes in solution. Thus, Kimura *et al.* have reported a value of log *K* = 2.8 for the formation constant of the carbonato zinc complex, Zn^{II}-aminopropyl-[12]aneN$_3$.[12] The spectral differences between the three species of bpp complexes involved in the two equilibra (1) and (2) allow the determination of the corresponding formation constants using the pK_a of the *meso*- and *rac*-complexes at μ = 0.70 M (8.61 for [Cu(*meso*-bpp)(H$_2$O)]$^{2+}$ and 8.85 for *rac*-[Cu(bpp)(H$_2$O)]$^{2+}$).

$$[Cu(bpp)(H_2O)]^{2+} + OH^- \rightleftharpoons [Cu(bpp)(OH)]^+ + H_2O \quad (1)$$
$$K_{OH} = [\{Cu(bpp)(OH)\}^+]/([\{Cu(bpp)(H_2O)\}^{2+}] \times [OH^-])$$

$$[Cu(bpp)(H_2O)]^{2+} + CO_3^{2-} \rightleftharpoons [Cu(bpp)(CO_3)] + H_2O \quad (2)$$
$$K_{CO_3} = [\{Cu(bpp)(CO_3)\}]/([\{Cu(bpp)(H_2O)\}^{2+}] \times [CO_3^{2-}])$$

Two types of measurements have been performed, one at constant pH with variable concentrations of an equimolar HCO$_3^-$/CO$_3^{2-}$ buffer, and one with a constant total carbonate concentration at variable pH between 8.0 to 11.2. The second type of measurements allow the exclusion of significant binding of HCO$_3^-$. The formation constants reported in Table 2 are calculated from the visible absorption at λ = 639 nm. The acid dissociation constants of the two diasteroisomeric copper complexes at μ = 0.70 M [pK_a(*meso*) = 8.61; pK_a(*rac*) = 8.85] are slightly different compared to the values at μ = 0.10 M, given in the literature.[9]

The values given in Table 2 show that the formation of the hydroxo complex is more favourable with [Cu(*meso*-bpp)(H$_2$O)]$^{2+}$ than with the *racemic* mixture of [Cu(*S*,*S*-bpp)(H$_2$O)]$^{2+}$ and [Cu(*R*,*R*-bpp)(H$_2$O)]$^{2+}$, whereas the opposite is true for the carbonato complexes. If the coordinated water molecule is more strongly bound in [Cu(*meso*-bpp)(H$_2$O)]$^{2+}$, one of the protons is abstracted more easily than in the optically active complexes of the *racemic* mixture. On the other hand, the coordination of the carbonate anion requires the elimination of the whole H$_2$O ligand, which is easier in *rac*-[Cu(bpp)(H$_2$O)]$^{2+}$.

Another possible explanation of the higher stability of *rac*-[Cu(bpp)(CO$_3$)] is based on structural considerations: In the *meso* complex both pyrrolidine rings are located on the same side of the CuN$_3$O plane. This complex therefore offers one favourable and one unfavourable apical position for the coordination of the carbonate anion. In the complex with *rac*-bpp, on the other hand, the pyrrolidine rings are located on opposite sides with respect to the CuN$_3$O plane. The crystallographic analysis of the coordination polymer [Cu(bpp)(SO$_4$)]·2/3H$_2$O·1/3L [L = di-*O*,*O*′-(4-toluyl)-L-tartaric acid][10] shows that both sides are easily accessible in the racemic (or optically active) complex for the coordination of the sulfate oxygen atom. Given the carbonate being a chelating ligand in a pentacoordinate square pyramidal coordination geometry, the carbonate binding in the racemic compound is favoured for statistical reasons. This pentacoordinate pyramidal structure has been found in the above-mentioned coordination polymer. For this reason, we tentatively suggest the structures represented in Fig. 3 for the carbonato-bpp copper(II) complexes in solution.

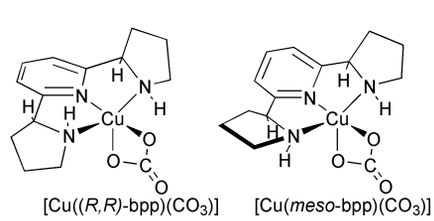

Fig. 3 Suggested structure for [Cu(*R*,*R*-bpp)(CO$_3$)] and [Cu(*meso*-bpp)(CO$_3$)].

The formation of the carbonato complex is in competition with the formation of the hydroxo complex and depends on the pH and on the carbonate buffer concentration. Fig. 4 shows the

Table 2 Molar extinction coefficients and formation constants of the Cu(bpp) complexes

Complex	ε_{636}/cm^{-1} mol^{-1} l		log K (μ = 0.1 M)		log K (μ = 0.7 M)	
	rac	*meso*	*rac*	*meso*	*rac*	*meso*
$[Cu(bpp)(H_2O)]^{2+}$	129.1	128.2				
$[Cu(bpp)(OH)]^{+}$	113.2	109.1	5.51	5.74	5.15	5.39
$[Cu(bpp)(CO_3)]$	147.2	145.6			3.24[a]	3.01[a]

[a] Maximum error ± 0.2 log units.

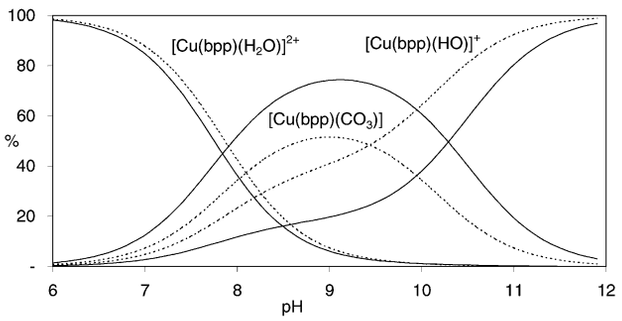

Fig. 4 Calculated distribution of the species for racemic (—) and *meso* (---) complexes; $[HCO_3^-/CO_3^{2-}]_{total}$ = 0.02 M and $[Cu(bpp)]_{total}$ = 10^{-3} M.

distribution of the different species as a function of pH for a constant total carbonate concentration (0.02 M), suggesting the maximum carbonate binding to occur approximately at pH = 9.0 for both, the *meso* isomer and the racemic mixture of the two enantiomers.

Separation of the diasteroisomers

The separation of $[Cu(meso\text{-}bpp)(H_2O)]^{2+}$ and *rac*-$[Cu(bpp)(H_2O)]^{2+}$ can be achieved by two methods. The first method is based on the difference between the pK_a of the two species: (8.25 for $[Cu(meso\text{-}bpp)(H_2O)]^{2+}$ and 8.49 for *rac*-$[Cu(bpp)(H_2O)]^{2+}$, μ = 0.10 M). According to the ratio of the acidity constants $K_{a(meso)}/K_{a(rac)}$ = 1.70, the equilibrium (3) is shifted to the right hand side. At pH = 8.37, corresponding to $1/2[pK_{a(meso)} + pK_{a(rac)}]$, the relative amount of the hydroxo species is 42.2% for the racemic and 55.1% for the *meso*-compound. The latter is therefore eluted first by 0.5% Na_2SO_4 at pH = 8.35, due to the lower affinity of the monocationic hydroxo complex.

$$[Cu(meso\text{-}bpp)(H_2O)]^{2+} + rac\text{-}[Cu(bpp)(OH)]^{+} \underset{5\%\ Na_2SO_4}{\overset{pH = 8.35\ borate\ buffer}{\rightleftharpoons}} [Cu(meso\text{-}bpp)(OH)]^{+} + rac\text{-}[Cu(bpp)(H_2O)]^{2+} \quad (3)$$

The second method takes advantage of the different stabilities of the carbonato complexes. The conditions for the separation are given by two factors: Firstly, the relative difference between the concentrations of the two diastereoisomers, which determines the separation into two bands. Secondly, the sum of the uncharged carbonato species and the charged aqua and hydroxo complexes determine the displacement rate of the two bands in the column. The influence of these two factors are combined to a chromatographic factor f which is given by eqn. (4), in which c represents the identical total concentration of the two diastereoisomers.

$$f = ([rac] - [meso]) \times ([rac] + [meso])/c^2 \quad (4)$$

The calculated value of the chromatographic factor f, which theoretically lies between 0 and 1, is represented in Fig. 5, together with the relative difference of the two diastereoisomeric carbonato complexes for variable carbonate concentrations at pH = 10. The optimum conditions for the separation,

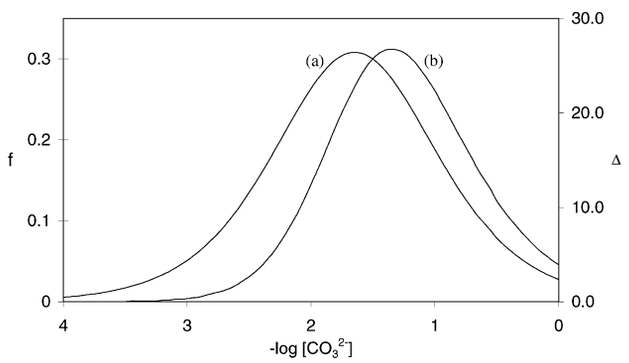

Fig. 5 Relative concentration difference $\Delta = ([rac] - [meso])/c$ (a) and the chromatographic factor f (b) of *meso* and *rac* $[Cu(bpp)(CO_3)]$; pH = 10.0, $[Cu(bpp)]_{total} = 10^{-3}$ M.

defined by f are as seen from Fig. 5, realised by using a carbonate concentration which is roughly twice as high as required to obtain the maximum difference between the concentrations of the two diastereoisomers, *e.g.* c = 0.02–0.04 M for pH = 10.0.

Contrary to the elution as hydroxo complexes with the borate buffer at pH = 8.37 (H_3BO_3 0.1 M, Na_2SO_4 0.5%), the elution as carbonato complexes HCO_3^-/CO_3^{2-} yields the racemic mixture first, due to the higher affinity of the chiral complexes to the carbonate anion, with respect to the *meso* complex.

Chromatographic separation of *rac*-$[Cu(bpp)(H_2O)]^{2+}$ into the enantiomers

The racemic mixture of $[Cu(bpp)(H_2O)]^{2+}$, fixed on a SP Sephadex cation exchanger, can be eluted with a L-(+)-tartrate buffer solution at pH = 5, giving two well separated bands, the ratio of the R_f values being about 1.5 in favour of the *S*,*S* isomer which is eluted first. The quality of the separation depends on both the rate of elution and the concentration of the eluent. Unfortunately, to some extent ligand exchange seems to occur on the column. The separation of the enantiomers might therefore be due to the formation of mixed bpp–tartrato complexes, rather than due to ion pair formation. Best separation is therefore achieved by rapid elution with buffers of low concentration. The optical purity of the separated (*S*,*S*)- and (*R*,*R*)-$[Cu(bpp)(H_2O)]^{2+}$ enantiomers can be checked by comparison of the visible and the CD spectra (Fig. 6). The

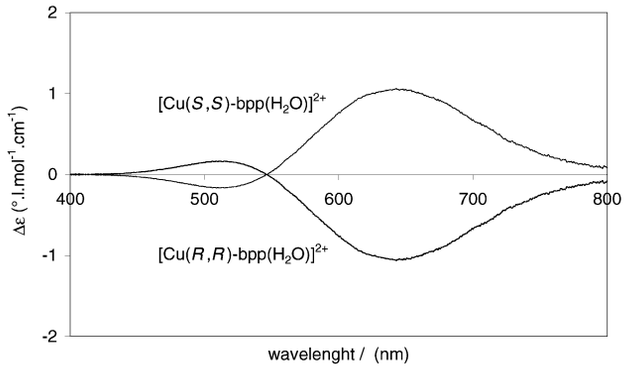

Fig. 6 CD spectra of $[Cu(S,S\text{-}bpp)(H_2O)][ClO_4]_2$ and $[Cu(R,R\text{-}bpp)(H_2O)][ClO_4]_2$; pH = 6.27.

cationic complexes are finally transformed into the perchlorate salts; recrystallisation from water gives the enantiomerically pure perchlorate salts.

Isolation of the free ligands

The three isomers *meso*-bpp, (*R*,*R*)-bpp and (*S*,*S*)-bpp are liberated from the corresponding complexes by ligand displacement with *trans*-1,2-diaminocyclohexane-*N*,*N*,*N*′,*N*′-tetraacetic acid (H_4cdta), the solution being previously adjusted to pH = 7.8 by addition of NaOH [eqn. (5)] followed by anion exchange on a QAE Sephadex C-25 anion exchange column [eqn. (6)].

$$[Cu(bpp)(H_2O)][ClO_4]_2 + H_4cdta + 2\ OH^- \overset{pH=7.8}{\rightleftharpoons} [Cu(cdta)]^{2-} + H_2bpp^{2+} + 2\ ClO_4^- + 3\ H_2O \quad (5)$$

$$[Cu(cdta)]^{2-}{}_{(sol)} + 2\ ClO_{4\,(exch)}^- \overset{QAE}{\rightleftharpoons} [Cu(cdta)]^{2-}{}_{(exch)} + 2\ ClO_{4\,(sol)}^- \quad (6)$$

Concentration of the effluent solution yields the corresponding isomers of bpp in the protonated form as the perchlorate salt. The isolated compounds [*meso*-bppH$_2$][ClO$_4$]$_2$, [(*S*,*S*)-bppH$_2$][ClO$_4$]$_2$ and [(*R*,*R*)-bppH$_2$][ClO$_4$]$_2$ are white, air-stable and water-soluble crystalline materials. The structure of the isolated *meso* isomer was solved by X-ray crystal structure analysis using a single crystal of [*meso*-bppH$_2$][ClO$_4$]·2H$_2$O recrystallised from water.

The molecular structure of the [*meso*-bppH$_2$]$^{2+}$ cation is depicted in Fig. 7. The molecule possesses C_s symmetry, the

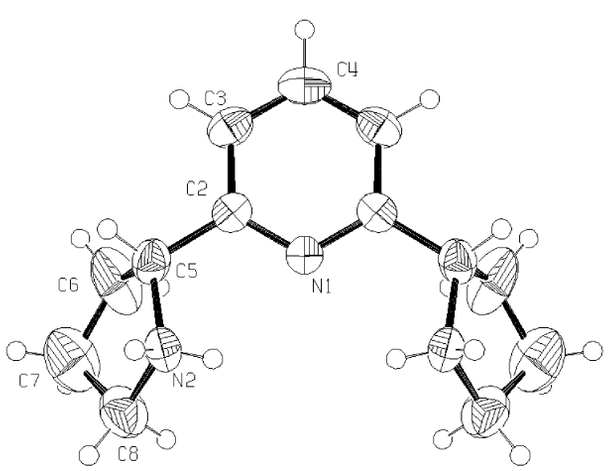

Fig. 7 Molecular structure (ORTEP plot)[13] of [*meso*-bppH$_2$]$^{2+}$. Displacement ellipsoids are drawn at the 50% probability level.

mirror plane passing through C(4) and N(1) being perpendicular with respect to the pyridine ring. The pyridine ring is almost planar (maximum deviation from the plane 0.0004 Å), the ring atoms being formally sp^2 hybridised. In accordance with the aromaticity, the single C–C and C–N bond distances in the pyridine ring are slightly shorter [C(4)–C(3) 1.371(4), C(3)–C(2) 1.383(4), C(2)–N(1) 1.337(4) Å] than those in the two pyrrolidine rings [C(5)–C(6) 1.537(5), C(6)–C(7) 1.482(7), C(7)–C(8) 1.473(7), C(8)–N(2) 1.499(5) Å] (see Table 3). The carbon–carbon bond connecting the pyridine and the pyrrolidine cycles [C(2)–C(5)] measures 1.496(5) Å. The pyrrolidine rings are not planar, the ring atoms being formally sp^3 hybridised. The pyramidalisation of C(5) and C(5′) [C(2)–C(5)–C(6) 114.4(3), C(2)–C(5)–N(2) 111.9(3), C(6)–C(5)–N(2) 102.9(3)°] however, deviates considerably from tetrahedral geometry due to ring restrictions. The torsion angle between the ring systems N(1)–C(2)–C(5)–N(2) measures 15.84(4)°.

Table 3 Selected bond lengths (Å) and angles (°) for [*meso*-bppH$_2$][ClO$_4$]$_2$

C(4)–C(3)	1.371(4)	C(6)–C(7)	1.482(7)
C(3)–C(2)	1.384(4)	C(7)–C(8)	1.473(7)
C(2)–N(1)	1.337(4)	C(8)–N(2)	1.499(5)
C(2)–C(5)	1.496(5)	C(5)–N(2)	1.496(4)
C(5)–C(6)	1.537(5)		
N(1)–C(2)–C(3)	122.4(3)	C(5)–N(2)–C(8)	109.4(3)
N(1)–C(2)–C(5)	117.5(3)	N(2)–C(8)–C(7)	103.7(4)
C(2)–C(5)–N(2)	111.9(3)	C(8)–C(7)–C(6)	105.2(4)
C(2)–C(5)–C(6)	114.4(3)	C(7)–C(6)–C(5)	103.8(3)
C(6)–C(5)–N(2)	102.9(3)		

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