



Cite this: *Dalton Trans.*, 2016, **45**, 8422

Surface functionalization of dinuclear clathrochelates *via* Pd-catalyzed cross-coupling reactions: facile synthesis of polypyridyl metalloligands†

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Dinuclear clathrochelate complexes are easily accessible by reaction of zinc(II) triflate or cobalt(II) nitrate with arylboronic acids and phenoldioximes. The utilization of brominated arylboronic acids and/or brominated phenoldioximes allows preparing clathrochelates with two, three, five or seven bromine atoms on the outside. These clathrochelates can undergo Pd-catalyzed cross-coupling reactions with 3- and 4-pyridylboronic acid to give new metalloligands featuring up to seven pyridyl groups. The pyridyl-capped clathrochelates display characteristics which make them interesting building blocks for structural supramolecular chemistry: they are rigid, large (up to 2.7 nm), luminescent (for M = Zn), and anionic. The pentatopic pyridyl ligands display an unusual trigonal bipyramidal geometry.

Received 4th April 2016,
Accepted 16th April 2016

DOI: 10.1039/c6dt01288d

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Introduction

A metalloligand is a metal complex appended with functional groups capable of binding to other metal ions. Metalloligands have been used extensively in structural supramolecular chemistry.^{1–3} Compared to standard organic ligands, metalloligands have potential advantages. The internal metal ions can add novel functions such as redox-activity, color, magnetism, molecular recognition sites or catalytic activity. In addition, the metal ions can simplify the synthesis of the ligand if metal-templated reactions are employed. Metalloligands featuring two or more pyridyl groups have received particular interest. For example, metalloporphyrin ligands with terminal pyridyl groups have been used extensively for the construction of molecular and polymeric nanostructures.² Pyridyl-functionalized salen-type complexes have also found widespread applications, notably because the salen complexes can be used for catalytic reactions.³

We have recently described the synthesis of metalloligands which feature two pyridyl groups attached to a dinuclear clathrochelate core containing either Zn²⁺ or Co²⁺ ions (Fig. 1).⁴ A special feature of these metalloligands is their negative charge, which can impart an increased stability to metallasupramolecular assemblies. Furthermore, they are very robust compounds, tolerating the rather harsh reaction conditions which are needed for the synthesis of metal-organic frameworks (MOFs). Capitalizing on the inert character of the clathrochelate, we now demonstrate that it is possible to post-functionalize these complexes *via* Pd-catalyzed cross-coupling reactions. This synthetic strategy enabled us to prepare extended metalloligands containing two, three, five or seven pyridyl groups.

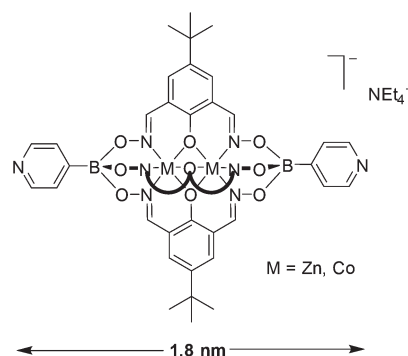


Fig. 1 Dinuclear clathrochelates with terminal 4-pyridyl groups.

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† Electronic supplementary information (ESI) available: Experimental details, analytical data and crystallographic data. CCDC 1453506–1453508. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c6dt01288d



Results and discussion

Ditopic metalloligands

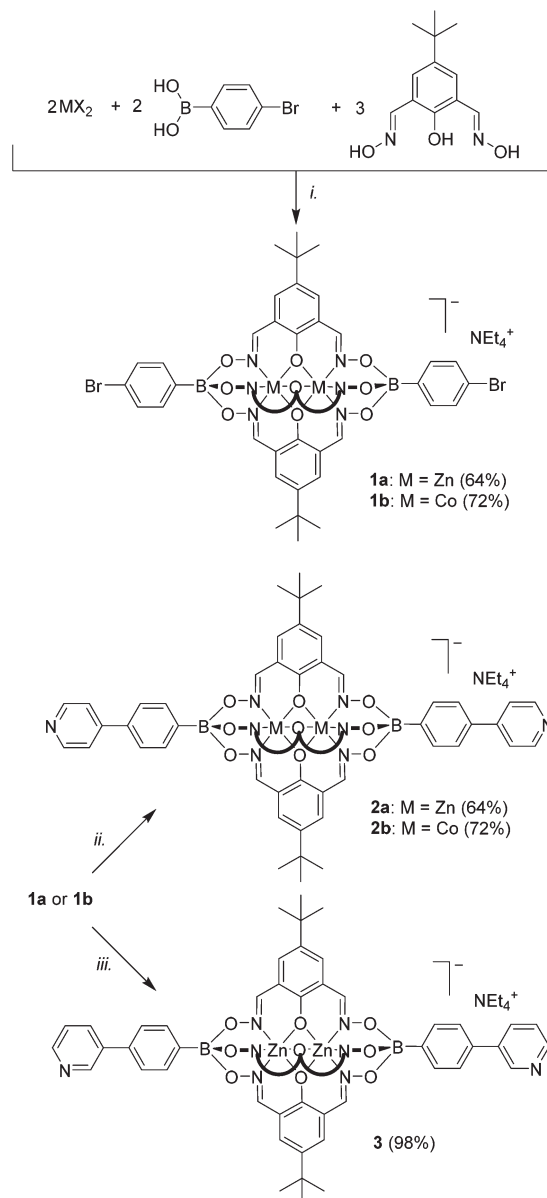
The dipyridyl ligands depicted in Fig. 1 were obtained by reaction of a Zn- or Co-salt with 4-pyridylboronic acid and a phenoldioxime.⁴ The synthesis of clathrochelates with other functional groups (*e.g.* carboxylic acids) in the periphery can be achieved by using different boronic acids and/or phenoldioximes.⁵ For mononuclear clathrochelates based on glyoximate ligands and Fe(II) centers, it had been reported that metal-catalyzed reactions can be used for the post-functionalization of the clathrochelate skeleton.^{6,7} We were wondering if a similar strategy could be employed for the post-modification of dinuclear clathrochelates. To investigate this question, we have prepared the Zn(II) complex **1a** and the Co(II) complex **1b** having two bromine atoms in apical position following a standard protocol (Scheme 1).

The complexes **1a** and **1b** were then used as substrates for a Pd-catalyzed Suzuki–Miyaura cross-coupling reaction with 3- or 4-pyridylboronic acid using Buchwald's ligand SPhos.^{8,9} The reaction was found to give the desired coupling products **2a**, **2b**, and **3** in good to excellent yields (Scheme 1).

Subsequently, we have examined whether coupling reactions in *meta* position with respect to the boronate ester function are possible. We have therefore prepared clathrochelate **4** (Scheme 2) using 3-bromophenylboronic acid (yield: 67%). This complex was then subjected to the Buchwald-type coupling conditions used before. The desired dipyridyl ligand **5** could be isolated in 91% yield (Scheme 2).

The metalloligands **2a/b**, **3**, and **5** are well soluble in polar organic solvents such as DMSO, MeOH, acetonitrile or CH₂Cl₂. In line with the depicted structure, the NMR spectra of the diamagnetic Zn complexes **2a**, **3**, and **5** show one set of signals for the three lateral oximate ligands and one set of signals for the two terminal phenylpyridyl groups. The successful coupling of two pyridyl groups was also confirmed by high-resolution mass spectrometry. As observed for other Zn-based clathrochelates,⁴ solutions of **2a**, **3**, or **5** are luminescent, with an emission maximum of 445 nm (DMF, λ_{ex} = 330 nm). The excitation and the emission spectrum of a representative complex, clathrochelate **3**, are shown in Fig. 2, and additional spectra are depicted in the ESI.†

The molecular structure of complex **2a** in the crystal was determined by single crystal X-ray crystallography (Fig. 3). The two Zn²⁺ ions are coordinated in a trigonal prismatic fashion by three nitrogen (Zn–N_{av.} = 2.13 Å) and three oxygen atoms (Zn–O_{av.} = 2.12 Å). The oxygen atoms bridge the two metal ions resulting in a M...M distance of 2.971(1) Å. The terminal nitrogen atoms of the two pyridyl groups are 2.7 nm apart from each other. This metalloligand is thus substantially longer than the previously reported clathrochelate based on 4-pyridylboronic acid (1.8 nm; Fig. 1),⁴ and it is comparable in size to pyridyl-capped *double* clathrochelates introduced by our group (2.7 nm)⁶ and to bis-(4'-ethynylpyridyl)-functionalized salen ligands (2.4 nm).¹⁰

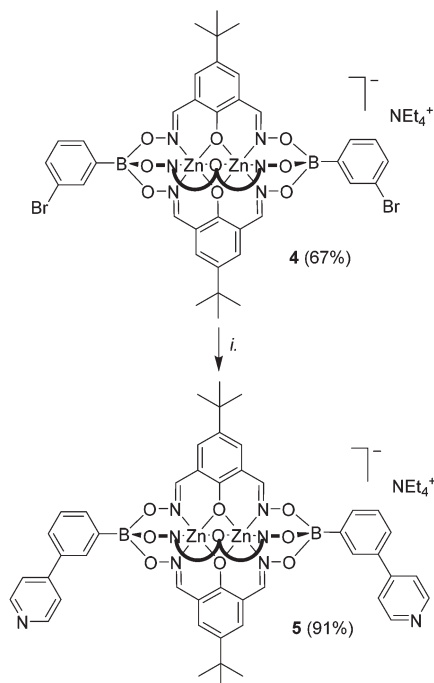


Scheme 1 Synthesis of the clathrochelates **1**–**3**. Reagents and conditions: (i): 4-bromophenylboronic acid, Zn(OTf)₂ or [Co(H₂O)₆](NO₃)₂, MeOH, 70 °C, then NEt₄OH; (ii): **1a** or **1b** (1 eq.), 4-pyridylboronic acid (6 eq.), K₃PO₄ (3 eq.), Pd₂(dba)₃ (5 mol%), SPhos (10 mol%), *n*-BuOH/toluene (1 : 1), 120 °C, 12 h, then NEt₄OH; (iii): **1a** (1 eq.), 3-pyridylboronic acid (6 eq.), K₃PO₄ (3 eq.), Pd₂(dba)₃ (5 mol%), SPhos (10 mol%), *n*-BuOH/toluene (1 : 1), 120 °C, 12 h, then NEt₄OH.

Polytopic metalloligands

Next, we explored the reactivity of clathrochelates having bromo-substituents on the lateral oximate ligands. Reaction of 2,6-diformyl-4-bromophenol dioxime with zinc(II) triflate or cobalt(II) nitrate and the respective boronic acid afforded the complexes **6**–**8** in good yields (Scheme 3). The clathrochelates **6** and **7** have three lateral bromo atoms, whereas complex **8** features a total of five arylbromide groups.





Scheme 2 Synthesis of the bent metalloligand **5**. Reagents and conditions: (i): **4** (1 eq.), 4-pyridylboronic acid (6 eq.), K_3PO_4 (3 eq.), $Pd_2(dba)_3$ (5 mol%), SPhos (10 mol%), *n*-BuOH/toluene (1 : 1), 120 °C, 12 h, then NEt_4OH .

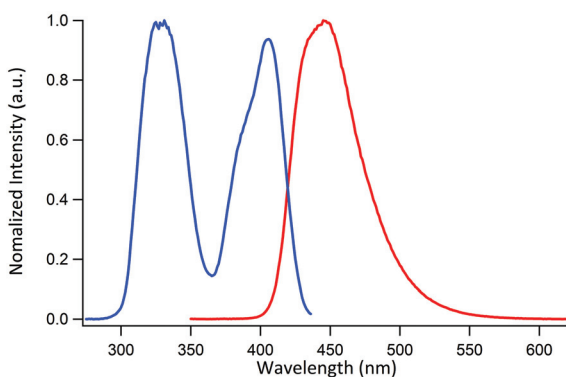


Fig. 2 Excitation spectrum (blue curve, $\lambda_{em} = 445$ nm) and emission spectrum (red curve, $\lambda_{ex} = 330$ nm) of complex **3** in DMF (0.5 mM).

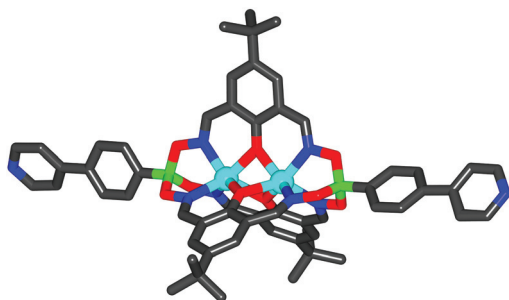
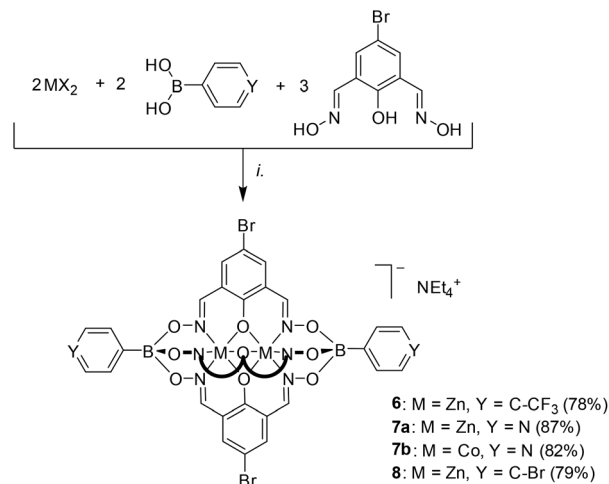
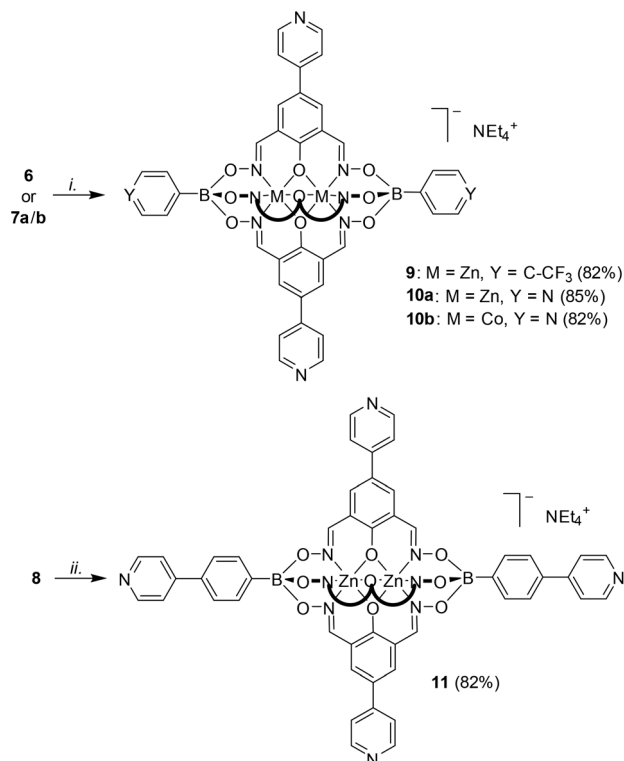


Fig. 3 Molecular structure of **2a** in the crystal. Hydrogen atoms, the counterion (NEt_4^+), and solvent molecules have been omitted for clarity. Color coding: C: grey; O: red; N: blue; B: green; Zn: cyan.



Scheme 3 Synthesis of the polybrominated clathrochelates **6–8**. Reagents and conditions: (i): 4-bromophenylboronic acid, $Zn(OTf)_2$ or $[Co(H_2O)_6](NO_3)_2$, MeOH, 70 °C, then NEt_4OH .

Subsequent Pd-catalyzed cross-coupling with 4-pyridylboronic acid afforded the tripyridyl ligand **9** as well as the pentatopic metalloligands **10a/b** and **11** (Scheme 4).



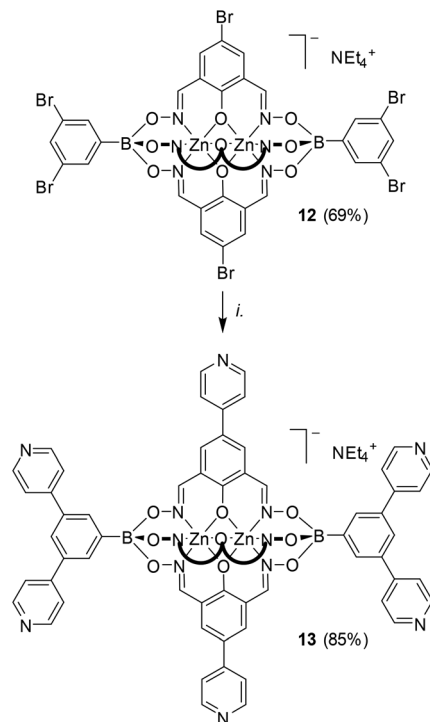
Scheme 4 Synthesis of the tri- and pentatopic metalloligands **9–11**. Reagents and conditions: (i): **6** or **7a/b** (1 eq.), 4-pyridylboronic acid (15 eq.), K_3PO_4 (7.5 eq.), $Pd_2(dba)_3$ (5 mol%), SPhos (10 mol%), *n*-BuOH/toluene (1 : 1), 120 °C, 12 h, then NEt_4OH ; (ii): **8** (1 eq.), 4-pyridylboronic acid (20 eq.), K_3PO_4 (10 eq.), $Pd_2(dba)_3$ (7.5 mol%), SPhos (15 mol%), *n*-BuOH/toluene (1 : 1), 120 °C, 12 h, then NEt_4OH .



The polypyridyl ligands **9–11** are well soluble in DMSO and moderately soluble in CH_2Cl_2 and acetonitrile. The solution-based analysis by NMR spectroscopy and high resolution mass spectrometry confirmed the exhaustive replacement of the bromo atoms with 4-pyridyl groups. The luminescent properties of the Zn complexes **9**, **10a**, and **11** were in line with what was observed previously, with emission maxima at 445 nm (DMF, $\lambda_{\text{ex}} = 330$ nm; Fig. S33†).

Single crystal X-ray structural analyses of **10a** and **11** confirmed the presence of five 4-pyridyl groups with divergent coordinate vectors (Fig. 4). The five peripheral nitrogen atoms are arranged in a distorted trigonal bipyramidal fashion. The distances between the two axial nitrogen atoms are 1.8 nm (**10a**) and 2.7 nm (**11**), and thus similar to what was found for the ditopic metalloligands described above. The average N...N distances for pairs of lateral pyridyl substituents are 1.7 nm (**10a**) and 1.7 nm (**11**) and the angles between the oximate ligands are 117.22° , 117.22° , and 125.57° for **10a**, and 100.15° , 126.60° and 138.25° for **11**. The deviations from the ideal 120° angle is likely due to packing effects in the crystal. The bond lengths and angles observed for the bimetallic core of the clathrochelates are within the expected range.

The good success of the five-fold coupling reactions with precursor **7a/b** prompted us to push the synthetic concept even further. We thus synthesized clathrochelate **12** having seven bromine atoms. The complete surface functionalization of this complex was achieved under slightly more forcing coup-



Scheme 5 Synthesis of the heptatopic metalloligand **13**. Reagents and conditions: (i): **12** (1 eq.), 4-pyridylboronic acid (28 eq.), K_3PO_4 (14 eq.), $\text{Pd}_2(\text{dba})_3$ (10 mol%), SPhos (20 mol%), *n*-BuOH/toluene (1 : 1), 120°C , 12 h, then NEt_4OH .

ling conditions (10 mol% Pd; Scheme 5). The resulting heptapyridyl ligand **13** was characterized by NMR spectroscopy and high resolution mass spectrometry. Attempts to obtain single crystals of **13** were unfortunately not successful. In order to obtain an estimate of the dimensions of this metalloligand, we have performed an exploratory computational study of its geometry using Density Functional Theory (DFT)¹¹ with the PBE0 exchange–correlation functional.¹² The robustness of the method was first evaluated by comparing the XRD structure of clathrochelate **2a** with the computed geometry of **2a**, which

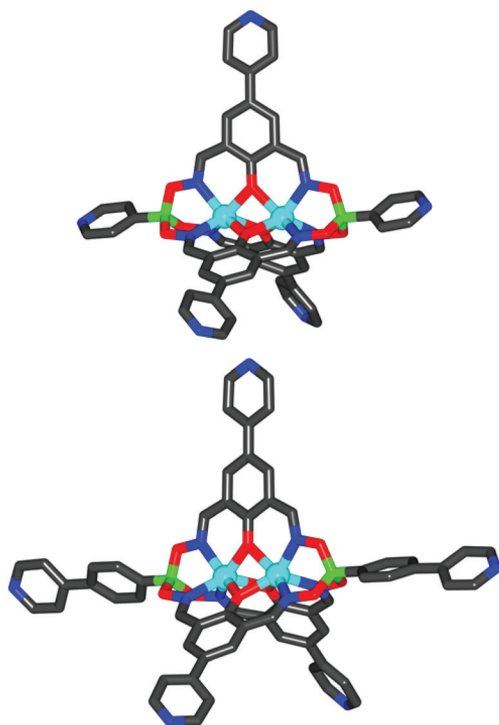


Fig. 4 Molecular structures of the pentatopic metalloligands **10a** (top) and **11** (bottom) in the crystal. Hydrogen atoms, counterions (NEt_4^+), and solvent molecules have been omitted for clarity. Color coding: C: gray; O: red; N: blue; B: green; Zn: cyan.

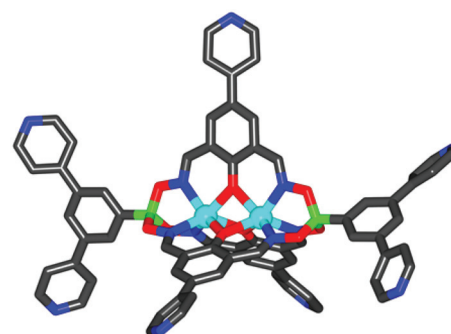


Fig. 5 Minimum-energy structure of the heptatopic metalloligand **13** obtained by DFT/PBE0. Only the anionic clathrochelate was calculated. Hydrogen atoms have been omitted for clarity. Color coding: C: gray; O: red; N: blue; B: green; Zn: cyan.



resulted in a good match. We then calculated the minimum-energy structure of **13**, and the result is shown in Fig. 5.

For clathrochelate **13**, the computed average N...N distance for pairs of lateral pyridyl substituents is 1.7 nm, a value which is in line with the measured values for **10a** and **11**. The maximum N...N distance between opposite pyridyl groups of the terminal 3,5-(dipyridin-4-yl)phenyl moieties is 2.3 nm. These values give an idea about the size of this unusual heptatopic metalloligand.

Conclusions

We have shown that brominated clathrochelate complexes of Zn and Co can be used as substrates for Pd-catalyzed cross-coupling reactions. As nucleophilic reaction partner, we have employed 3- or 4-pyridylboronic acid. The poly-cross-coupling reactions are remarkably efficient and give the desired functionalized clathrochelates in high yields. In view of the characteristics of the new polypyridyl ligands (large, relatively rigid, anionic, and luminescent in case of M = Zn), we expect that they will be of interest as building blocks for supramolecular chemistry and materials science. The ditopic metalloligands **2**, **3**, and **5** could be used for the construction of molecularly defined nanostructures, as already demonstrated for shorter analogues.^{4,5,13} The polytopic metalloligands **9–11** and **13**, on the other hand, appear to be more suited for the construction of polymeric structures such as metal–organic frameworks (MOFs). The penta- and heptatopic ligands **10**, **11**, and **13** are particularly interesting in this context, because MOFs based on ligands with five or seven donor groups have hardly been studied.^{14,15}

For the present investigation, we have focused on the preparation of polypyridyl ligands. However, it appears likely that brominated clathrochelate complexes can be coupled in a similar fashion to boronic acids featuring other functional groups (e.g. cyano groups). We thus predict that brominated clathrochelates should become a versatile and easy-to-access scaffold for the synthesis of novel metalloligands with an unusual trigonal bipyramidal geometry.

Acknowledgements

The work was supported by the Swiss National Science Foundation and by the Ecole Polytechnique Fédérale de Lausanne (EPFL). We are grateful to the Swiss-Norwegian Beamline Consortium for providing access to synchrotron radiation.

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