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Facile, divergent route to bis-Zn(II)dipicolylamine type chemosensors for pyrophosphate

L. Gayathri Pathberiya [a], Nicholas Barlow [b], Tran Nguyen [a], Bim Graham [b], Kellie L. Tuck [a,*]

[a] School of Chemistry, Monash University, Clayton, VIC 3800, Australia
[b] Medicinal Chemistry, Monash Institute of Pharmaceutical Sciences, Parkville, VIC 3052, Australia

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ABSTRACT

A new, two-step synthesis has been developed for a series of bis-DPA-type ligands whose dinuclear Zn(II) complexes function as fluorescent anion sensors. The Zn(II) complexes exhibit good selectivity for PP_i over other anions in aqueous medium (pH 7.5) and may be used to monitor the extent of enzyme-catalysed reactions, in which PP_i is produced or consumed.

1. Introduction

The development of chemosensors to detect anions has been a growing area of research in recent years.[1–8] Of particular interest is the selective detection of pyrophosphate (PP_i, $P_2O_7^{2-}$) over other anions of biological relevance, principally adenosine triphosphate (ATP), adenosine monophosphate (AMP) and phosphate (P_i, PO_4^{2-}).[2,3] Pyrophosphate is extremely important in a number of biological process—for example, as a substrate or product of various enzymes, and as a product of the cellular hydrolysis of ATP.[9] Its quantification can be used for real-time DNA sequencing, thereby obviating of the need for electrophoresis.[10]

The di-(2-picolyl)amine (DPA) unit has been widely exploited as a motif within metal complex-based anion sensor designs, particularly for pyrophosphate detection.[2,8,11–19] Most notably, the Zn(II) complex of DPA exhibits a high affinity for phosphate-bearing moieties, which can lead to either an increase in fluorescence or quenching of a tethered fluorophore, depending on the nature of the fluorophore and the binding mode adopted by the interacting anion. Selectivity for PP_i is achievable using sensor designs that feature two DPA–Zn(II) units appropriately positioned to interact favourably with the PP_i anion. Hong et al., for example, recently reported a 2-naphthalene-bearing bis-DPA ligand **1** (Fig. 1) the dinuclear Zn(II) complex of which, **1**-$\mathbf{Zn_2}$, is able to selectively detect PP_i in the presence of a range of other anions.[15] This sensor has been used to monitor the extent of DNA amplification in PCR,[20] and, in combination with a boronic acid, to distinguish PP_i from nucleoside triphosphates.[21]

Hong et al.'s synthesis of compound **1** requires four steps and proceeds in 35% overall yield, beginning from a precursor that is not commonly available (6-bromo-2,2-dimethyl-4*H*-1,3-benzodioxin-8-methanol).[15] Apart from the number of steps involved, the major drawback of this synthetic route is that it does not allow for the divergent production of analogues featuring other fluorescent moieties in place of the 2-naphthyl group. In this paper we therefore present an alternate two-step synthesis of the 2-naphthalene ligand **1**, in which the fluorophore is introduced in the final step. We also report the ready adaptation of this synthesis to the production of two new, structurally-related ligands, **2** and **3**, featuring 1-naphthyl and 9-anthracenyl moieties, respectively (Fig. 1). It was hypothesised that the 1-naphthyl analogue might have different fluorescent properties due to the different point of attachment to the fluorophore, whilst anthracene is known to have a higher quantum yield than naphthalene.[22,23]

This work was carried out as part of a program directed towards the development of inhibitors of enzymes, which use or produce PP_i, for which we required a reliable means of assaying activity in real-time. As such, we also report an exploration of the sensitivity and selectivity of the Zn(II) complexes of **1**–**3** as chemosensors for PP_i under *pseudo*-biological conditions, and the use of one of the chemosensors in monitoring the activity of inorganic pyrophosphatase as an example of a PP_i-utilising enzyme.

* Corresponding author. E-mail address: Kellie.Tuck@monash.edu (K.L. Tuck).

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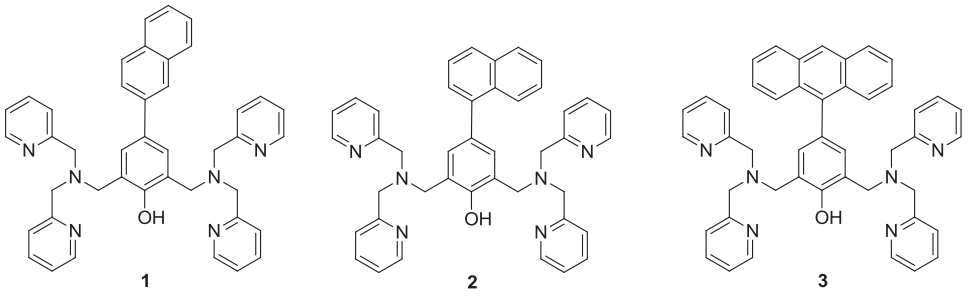
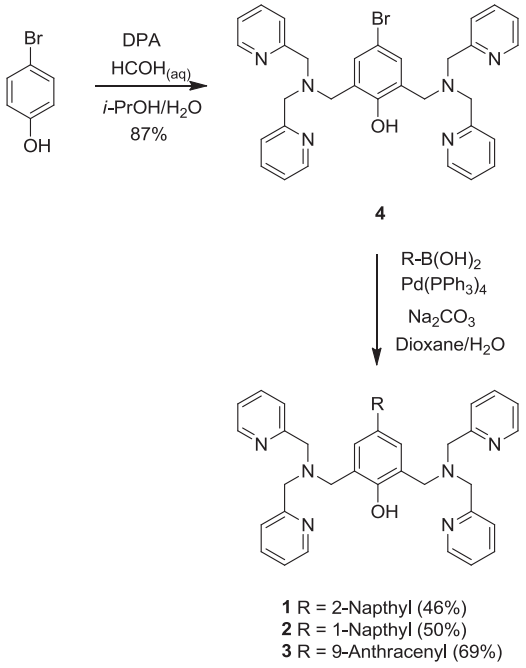


Fig. 1. Structures of Hong et al.'s ligand **1**[15] and the 1-naphthyl and 9-anthracenyl analogues, **2** and **3**, whose dinuclear Zn(II) complexes function as fluorescent pyrophosphate sensors.

2. Results and discussion

The new synthetic route (Scheme 1) involved, firstly, a Mannich reaction between *p*-bromophenol, DPA and formaldehyde to produce the bis-DPA intermediate **4** in good yield (87%). Ligands **1**–**3** were then furnished directly via a Suzuki reaction between **4** and the boronic acid derivatives of the corresponding fluorophores (46–69%). By this novel route, the desired chemosensor precursor ligands were obtained in only two steps from readily available starting materials. The dinuclear Zn(II) complexes, **1**-$\mathbf{Zn_2}$, **2**-$\mathbf{Zn_2}$ and **3**-$\mathbf{Zn_2}$ were then formed by addition of an aqueous solution of $Zn(NO_3)_2$ (2 M equiv) to the respective ligands.



Scheme 1. Synthesis of ligands **1**–**3**.

In our hands, **1**-$\mathbf{Zn_2}$ showed similar fluorescence changes, and selectivity for PP_i over a number of biologically important anions (ATP, AMP and P_i), to those previously described by Hong et al.[15] (Fig. 2). The 1-naphthyl analogue, **2**-$\mathbf{Zn_2}$, showed a similar dose-dependent response to the addition of PP_i as **1**-$\mathbf{Zn_2}$, with the fluorescence output increasing by a factor of ca. 7-fold upon the addition of 1 equiv of PP_i (Fig. 3). However, in this case the increase in fluorescence was also accompanied by a bathochromic shift in the wavelength of maximum emission intensity (λ_{em}) from 450 nm to 464 nm; no further changes in λ_{em} were observed after addition of 1.5 equiv of PP_i. The apparent association constant (K_a), determined from the fluorimetric titration curve, was about 7.2×10^5 M^{-1}. Upon

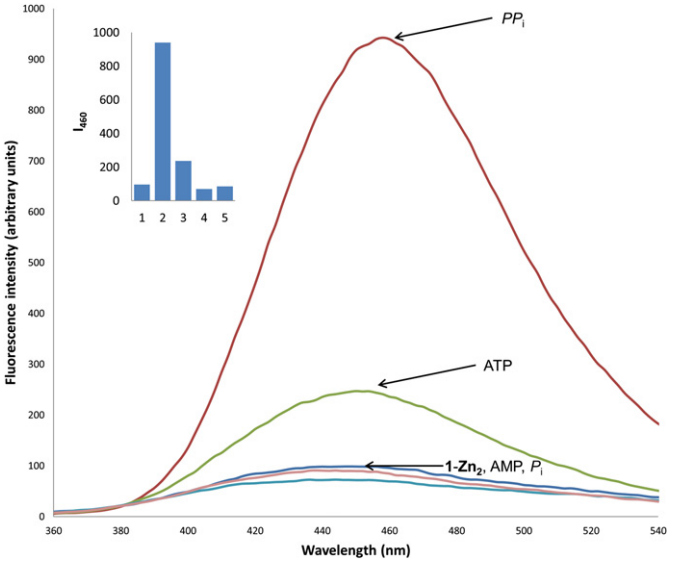


Fig. 2. Changes in fluorescence observed upon the addition of various anions (3 equiv) to **1**-$\mathbf{Zn_2}$ (25 μM, Tris buffer (10 mM, pH 7.5)) (λ_{ex}=310 nm). *Inset*: fluorescence intensity measured at 460 nm, (1) **1**-$\mathbf{Zn_2}$ only, (2) +PP_i, (3) +ATP, (4) +AMP, (5) +P_i.

the addition of a number of biologically and analytically important anions (AMP, Cl^-, P_i, $CH_3CO_2^-$, and HCO_3; 3 equiv), negligible emission changes were observed (Fig. 4), whilst the addition of ATP, GTP and ADP produced much less dramatic increase in fluorescent intensity than PP_i (addition of 3 equiv of ATP resulted in a ca. 2-fold increase in fluorescence). For each of the latter anions, a bathochromic shift of ca. 8 nm in λ_{em} was observed. These results are also similar to those found for **1**-$\mathbf{Zn_2}$[15] and indicate that **2**-$\mathbf{Zn_2}$ is

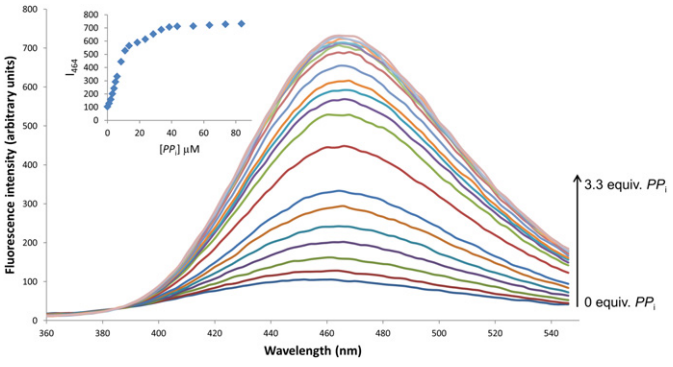


Fig. 3. Change in fluorescence observed upon addition of PP_i to **2**-$\mathbf{Zn_2}$ (25 μM, Tris buffer (10 mM, pH 7.5)) (λ_{ex}=310 nm). *Inset*: fluorescence intensity measured at 464 nm as a function of [PP_i].

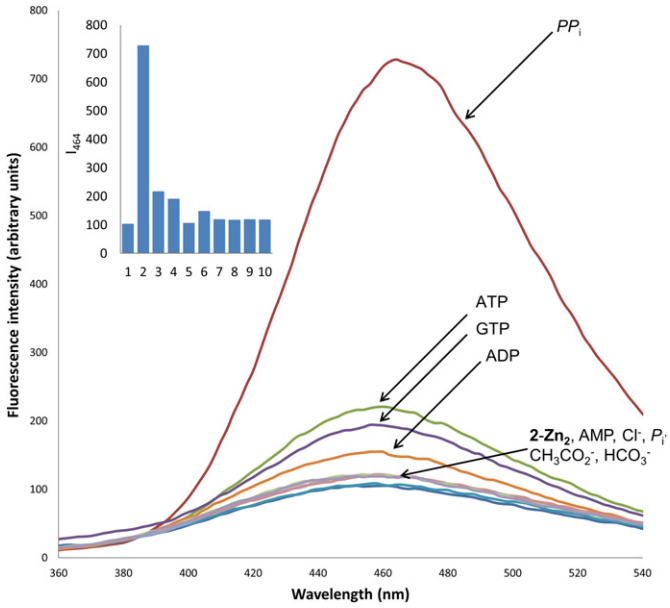


Fig. 4. Changes in fluorescence intensity observed upon addition of various anions (3 equiv) to **2-Zn$_2$** (25 μM, Tris buffer (10 mM, pH 7.5)) (λ_{ex}=310 nm). *Inset*: fluorescence intensity measured at 464 nm, (1) **2-Zn$_2$** only, (2) +PP_i, (3) +ATP, (4) +GTP, (5) +AMP, (6) +ADP, (7) +Cl^-, (8) +P_i, (9) +$CH_3CO_2^-$, (10) +HCO_3^-.

a comparably selective chemosensor for PP_i. The increase in fluorescence observed upon the addition of PP_i to either **1-Zn$_2$** or **2-Zn$_2$** can be attributed to a weakening of the bond between the Zn(II) centres and the bridging phenolate oxygen upon PP_i binding, resulting in increased charge density on the phenolate oxygen and an enhanced fluorescent output due to induced charge transfer.[15]

To further probe the selectivity of **2-Zn$_2$** as a chemosensor for PP_i, we measured its fluorescence response to PP_i in the presence of ATP (the anion, which gave the greatest fluorescence response other than PP_i). Titration of PP_i into a solution that contained **2-Zn$_2$** and 3 equiv of ATP resulted in a dose-dependent increase in fluorescence, with saturation occurring after the addition of 3 equiv of PP_i (Fig. 5). This is indicative of a substantially higher binding affinity for PP_i and indicates that **2-Zn$_2$** may be used to monitor PP_i in the presence of competing anions.

We initially hypothesised that replacement of the 2-naphthyl moiety with a 9-anthracenyl group might result in an increased fluorescent output upon complexation to PP_i. However, addition of 3 equiv of PP_i to **3-Zn$_2$** (10 μM) was instead found to result in near complete *quenching* of the native fluorescence of **3-Zn$_2$**, and a bathochromic shift in λ_{max} of 38 nm (Fig. 6). In contrast, addition of 3 equiv of either AMP, Cl^-, $CH_3CO_2^-$, and HCO_3^-. resulted in only a slight decrease in fluorescence, with no significant change to λ_{em} (Fig. 6). The addition of 3 equiv ADP and ATP produced bathochromic shifts in λ_{max} of 8 nm and 20 nm, with significant quenching occurring in both cases (Fig. 6). P_i addition (3 equiv) yielded a less dramatic decrease in fluorescence and a bathochromic shift of 16 nm.

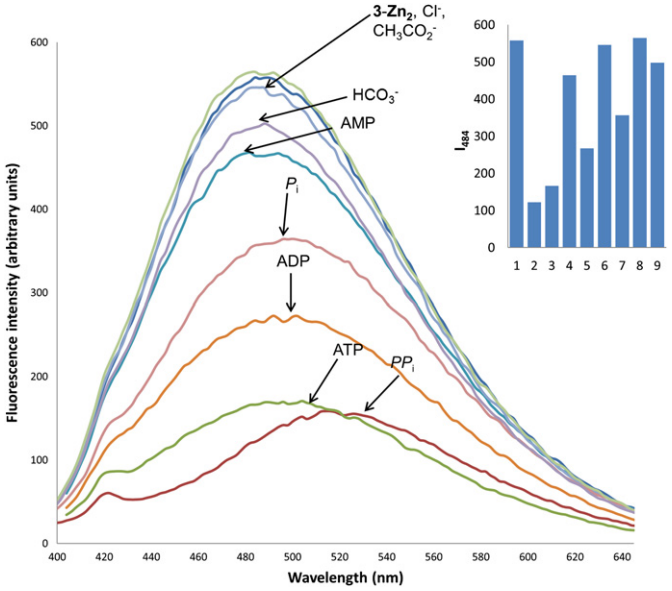


Fig. 6. Changes in fluorescence observed upon addition of various anions (3 equiv) to **3-Zn$_2$** (10 μM, Tris buffer (10 mM, pH 7.5)) (λ_{ex}=370 nm). *Inset*: fluorescence intensity measured at 484 nm, (1) **3-Zn$_2$** only, (2) +PP_i, (3) +ATP, (4) +AMP, (5) +ADP, (6) +Cl^-, (7) +P_i, (9) +$CH_3CO_2^-$, (9) +HCO_3^-.

The addition of increasing amounts of PP_i to **3-Zn$_2$** resulted in a dose-dependent decrease in the fluorescent output, with minimal fluorescence observed after the addition of a single equivalent of PP_i (Fig. 7). The apparent association constant (K_a), determined from the fluorimetric titration curve, was about 1.2×10^6 M^{-1}.

The quenching effect observed upon addition of PP_i to **3-Zn$_2$** contrasts starkly with the fluorescence increase observed for **1-Zn$_2$** or **2-Zn$_2$**, however similar quenching effects have been observed previously with sensors **5**[24] and **6**[17] (Fig. 8), which possess pyrenyl and acridinyl fluorescent moieties, respectively. This may reflect an

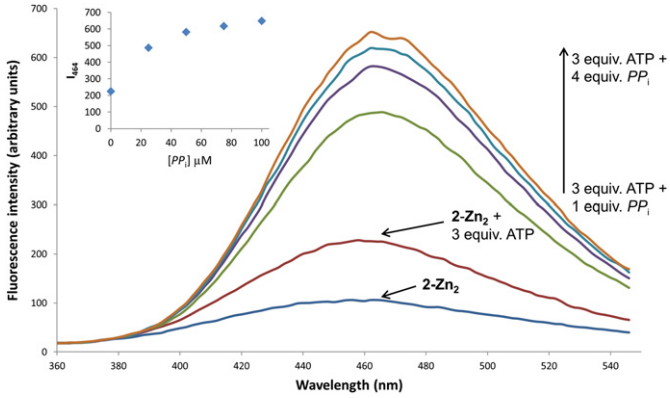


Fig. 5. Change in fluorescence observed upon addition of PP_i to **2-Zn$_2$** complex (25 μM, Tris buffer (10 mM, pH 7.5)) in the presence of ATP (3 equiv) (λ_{ex}=310 nm). *Inset*: fluorescence measured at 464 nm as a function of [PP_i].

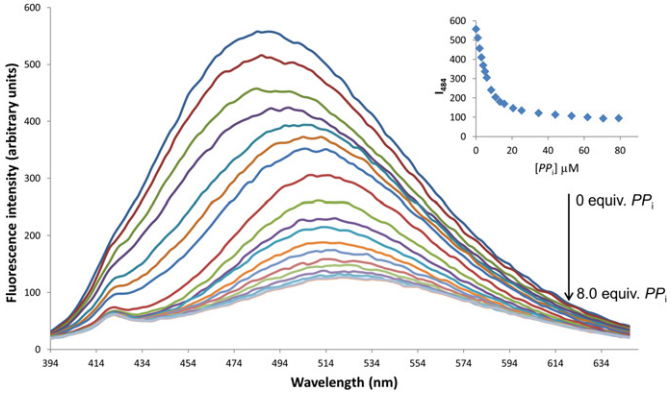


Fig. 7. Change in fluorescence observed upon addition of PP_i to **3-Zn$_2$** (10 μM, Tris buffer (10 mM, pH 7.5)) (λ_{ex}=370 nm). *Inset*: fluorescence intensity measured at 484 nm as a function of [PP_i].

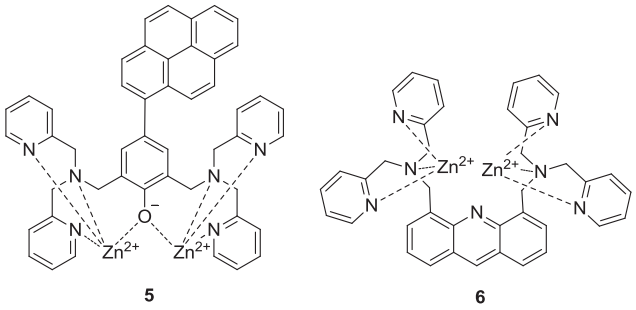


Fig. 8. Previously reported chemosensors whose fluorescence is quenched upon addition of PP_i.

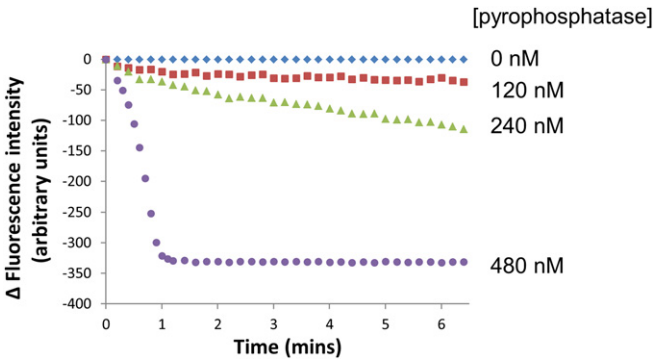


Fig. 9. Assay of pyrophosphatase activity using **2-Zn$_2$**. *Conditions*: 25 μM complex, 10 mM Tris buffer (pH 7.5), 10 mM $MgCl_2$ and 4 equiv PP_i (λ_{ex}=310 nm, λ_{em}=460 nm).

enhanced degree of photoinduced electron transfer (PET) from the amines of the DPA units to the anthracene upon PP_i binding, leading to deactivation of the excited state. Charge transfer-derived fluorescence, observed upon binding of PP_i to **1-Zn$_2$** or **2-Zn$_2$**, may in this instance be prevented by the anthracene lying orthogonal to the phenolate moiety, disrupting the π-conjugation pathway between these groups.

To demonstrate the utility of the chemosensors for monitoring enzymatic processes involving PP_i, we tested one of them (**2-Zn$_2$**) in conjunction with inorganic pyrophosphatase, which catalyses the cleavage of pyrophosphate into two phosphate groups. Chemosensor **2-Zn$_2$** (25 μM), Tris buffer (10 mM, pH 7.5), $MgCl_2$ (10 mM) and PP_i (4 equiv) were incubated at 30 °C for 5 min, then pyrophosphatase added and the emission intensity at 460 nm monitored as a function of time. As expected, the fluorescence intensity decreased with time, accompanying consumption of the PP_i substrate (Fig. 9). The rate of reaction was also confirmed to increase with increasing enzyme concentration.

3. Conclusion

In conclusion, a facile route has been developed for the synthesis of bis-DPA-type anion sensors, in which the fluorescent moiety is introduced in the final step. This route has provided two new ligands, **2** and **3**, featuring 1-naphthyl and 9-anthracenyl moieties, respectively. The corresponding dinuclear Zn(II) complexes, like that of the previously reported ligand **1**,[15] exhibit good-to-high selectivity for PP_i over other anions in aqueous medium (pH 7.5). Fluorescence from the naphthyl moiety increases upon PP_i binding, whilst that from the anthracene group is diminished. We have successfully employed **2-Zn$_2$** for monitoring inorganic phosphatase activity and are now exploring the utility of the chemosensors for assaying a range of other enzymes that feature PP_i as a substrate or product.

4. Experimental section

4.1. General

All reagents and inorganic pyrophosphatase from baker's yeast (*Saccharomyces cerevisiae*), were purchased from Sigma Aldrich and used without further purification. ATP, GTP, ADP, AMP, PP_i P_i, Cl^-, $CH_3CO_2^-$, and HCO_3^- were used as the sodium salts. Organic solutions were dried over $MgSO_4$. The progress of reactions was monitored by thin layer chromatography (TLC) on Merck 60 F240 precoated silica gel polyester plates. Flash chromatography was performed with Davisil LC60A, 40–63 μm silica media. Proton (^{1}H) and carbon (^{13}C) NMR spectra were recorded on either a Bruker AV400 or NMR spectra were recorded on a Bruker Ultrashield 400 Plus spectrometer operating 400 MHz, respectively, for proton nuclei, and 100 MHz for carbon nuclei. Chemical shifts (δ) are expressed in parts per million (ppm) and referenced to residual solvent signal as the internal standard. Low resolution mass spectrometry was performed on an Agilent 6120 single quadrapole LCMS system using electron spray ionization. High resolution electrospray ionisation mass spectra were acquired using a Micromass Platform II single quadrupole mass spectrometer equipped with an atmospheric pressure (ESI/APCI) ion source. Analytical HPLC was performed on a Waters Alliance 2690 fitted with a Waters 5996 PDA detector and a Phenomenex Luna C_8 column (5 μm, 100 Å, 150×4.60 mm). Analyses were conducted using a gradient of 100% buffer A to 80% buffer B over 10 min where buffer A was 0.1% trifluoroacetic acid in water and buffer B was 0.1% trifluoroacetic acid, 80.0% acetonitrile and 19.9% water. Fluorescence spectra were recorded on a Cary Eclipse fluorescence spectrophotometer and analysed with Cary WinUV software.

*4.1.1. 2,6-Bis((bis(2-pyridinylmethyl)amino)methyl)-4-bromo-phenol (**4**).* To a solution of *p*-bromophenol (509 mg, 2.94 mmol) in *iso*-propanol (3 mL) and water (5 mL) was added di-(2-picolyl)amine (2.0 mL, 11.1 mmol) and a 37% formaldehyde solution (1.6 mL, 19 mmol). The resulting solution was refluxed for 15 h. The *iso*-propanol was removed from the reaction mixture in vacuo and water (10 mL) was then added. The reaction mixture was extracted with EtOAc (3×20 mL), the combined organic phases washed with satd $NaHCO_{3(aq)}$ (20 mL), dried and the solvent removed in vacuo. Flash column chromatography (95% $CHCl_3$: 5% MeOH: 5% $NH_{3(aq)}$) afforded the title compound as an oil (1.52 g, 87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (m, 4H), 7.66 (m, 4H), 7.50 (d, J=7.8 Hz, 4H), 7.40 (s, 2H), 7.18 (m, 4H), 3.86 (s, 8H), 3.76 (s, 4H). ^{13}C NMR (100 MHz, acetone-d_6) δ 160.0, 156.5, 149.7, 137.5, 127.9, 123.8, 123.0, 110.6, 60.2, 54.7. LCMS (ESI): m/z: 597.1 (100%), 595.2 (100%).

*4.1.2. 2,6-Bis((bis(Pyridin-2-ylmethyl)amino)methyl)-4-(naphthalen-2-yl)phenol (**1**).* A suspension of 2,6-bis((bis(pyridin-2-ylmethyl)amino)methyl)-4-bromophenol (200 mg, 0.33 mmol), naphthalene-2-boronic acid (70 mg, 0.40 mmol) and potassium carbonate (70 mg) in water (1 mL) and dioxane (5 mL) was saturated with nitrogen. To this mixture was added tetrakis(-triphenylphosphine)palladium (10 mg, 0.0087 mmol) and the suspension refluxed under nitrogen for 15 h. The solvent was removed in vacuo and a third of the residue was purified by reverse phase prep HPLC (0–30 % acetonitrile in water over 30 min, 0.1% TFA throughout) to provide the title compound as a white solid (30 mg, 46%). ^{1}H NMR (400 MHz, DMSO) δ 8.60 (dd, J=0.7, 5.0 Hz, 4H), 8.08 (bs, 1H), 7.87–8.01 (complex, 7H), 7.79 (dd, J=1.8, 8.6 Hz, 1H), 7.73 (s, 2H), 7.50–7.58 (complex, 6H), 7.45 (m, 4H), 4.37 (s, 8H), 4.28 (s, 4H). HPLC: 95% pure. LCMS (ESI): m/z: 643.1(M+H, 100%).

*4.1.3. 2,6-Bis((bis(pyridin-2-ylmethyl)amino)methyl)-4-(naphthalen-1-yl)phenol (**2**).* A suspension of 2,6-bis((bis(pyridin-2-ylmethyl)amino)methyl)-4-bromophenol (200 mg, 0.33 mmol),

naphthalene-1-boronic acid (74 mg, 0.40 mmol) and potassium carbonate (70 mg) in water (1 mL) and dioxane (5 mL) was saturated with nitrogen. To this mixture was added tetrakis(-triphenylphosphine)palladium (10 mg, 0.0087 mmol) and the suspension refluxed under nitrogen for 15 h. The solvent was removed in vacuo and a third of the residue was purified by reverse phase prep HPLC (0–30 % acetonitrile in water over 30 min, 0.1% TFA throughout) to provide the title compound as a white solid (35 mg, 50%). ^{1}H NMR (400 MHz, MeOD) δ 8.44 (d, J=4.9 Hz, 4H, *pyridinyl H6*), 7.88 (d, J=8.1 Hz, 1H, *naphthalenyl H8*), 7.81 (d, J=8.1 Hz, 1H, *naphthalenyl H2*), 7.75 (d, J=8.6 Hz, 1H, *naphthalenyl H5*), 7.69 (t, J=7.6 Hz, 4H, *pyridinyl H4*), 7.55 (d, J=7.6 Hz, 4H, *pyridinyl H4*), 7.50–7.42 (m, 3H, *naphthalenyl H3*, *H6* and *H7*), 7.30 (d, J=7.4 Hz, 2H, *naphthalenyl H4*), 7.27–7.21 (m, 6H, *pyridinyl H5* and *phenolic H3*), 3.92 (s, 8H, NCH_2Py), 3.88 (s, 4H, *2-methylphenol* CH_2). ^{13}C NMR (100 MHz, MeOD) δ 159.9, 156.5, 149.5, 138.6, 135.5, 133.1, 132.5, 132.4, 129.3, 128.2, 127.9, 127.0, 126.8, 126.7, 126.4, 125.0, 124.7, 124.7, 123.8, 60.8, 56.1. HPLC: 95% pure. LRMS (ESI): m/z: 643.2 (M+H, 55%). HRMS (ESI): m/z: calcd for $[M+H]^+$ $C_{42}H_{39}N_6O$: 643.3180, found: 643.3203.

*4.1.4. 4-(Anthracen-9-yl)-2,6-bis((bis(pyridin-2-ylmethyl)amino) methyl)phenol (**3**).* A suspension of 2,6-bis((bis(pyridin-2-ylmethyl) amino)methyl)-4-bromophenol (50 mg, 0.084 mmol), anthracene-9-boronic acid (25 mg, 0.072 mmol) and potassium carbonate (2.0 g) in water (10 mL) and dioxane (20 mL) was saturated with nitrogen. To this mixture was added tetrakis(triphenylphosphine)palladium (5 mg, 0.0043 mmol) and the suspension refluxed under nitrogen for 15 h. The solution was acidified by dropwise addition of 2 M HCl and washed with dichloromethane. The aqueous layer was then freeze-dried and the residue purified by reverse phase prep HPLC (0–30% acetonitrile in water over 30 min, 0.1% TFA throughout) to provide the title compound as a white solid (40 mg, 69%). ^{1}H NMR (400 MHz, MeOD) δ 8.66 (d, J=7.8 Hz, 4H, *pyridinyl H6*), 8.55 (s, 1H, *anthracenyl H10*), 8.08 (d, J=8.5 Hz, 2H, *anthracenyl H4*), 7.99 (d, J=7.8 Hz, 4H, *pyridinyl H4*), 7.59 (d, J=7.8 Hz, 4H, *pyridinyl H3*), 7.54 (t, J=7.8 Hz, 4H, *pyridinyl H5*), 7.47 (t, J=8.5 Hz, 2H, *anthracenyl H3*), 7.43 (d, J=8.5 Hz, 2H, *anthracenyl H1*), 7.35 (s, J=8.5 Hz, 2H *anthracenyl H2*), 7.29 (s, 2H, *phenolic H3*), 4.48 (s, 8H, NCH_2Py), 4.36 (s, 4H, *2-methylphenol* CH_2). ^{13}C NMR (100 MHz, MeOD) δ 157.1, 154.5, 148.4, 141.2, 136.3, 132.9, 131.6, 131.3, 129.7, 128.0, 127.3, 126.7, 126.2, 125.7, 125.6, 122.1, 59.0, 57.0. HPLC: 95% pure. MS (ESI): m/z: 693.1 (M+H, 100%). HRMS (ESI): m/z: calcd for $[M+H]^+$ $C_{46}H_{41}N_6O$: 693.3336, found: 693.3348.

4.2. Formation of zinc(II) complexes

To a solution of ligand **1**, **2** or **3** (0.35 mg) in DMSO (40 μL) was added Tris buffer (1 mL, 10 mM, pH 7.5) and an aqueous solution of $Zn(NO_3)_2 \cdot 6H_2O$ (2 equiv). After 30 min, this stock solution was then diluted to the required concentration with Tris buffer (10 mM, pH 7.5) and the solution utilised for fluorescence experiments.

4.3. Pyrophosphatase assay

To a solution of the complex (25 μM, **2-Zn$_2$**) in Tris buffer (10 mM, pH 7.5), $MgCl_2$ (10 mM) was added PP_i (4 equiv). After 5 min at 30 °C, pyrophosphatase (7 μM stock in 10 mM Tris buffer) was added to the solutions such that the final enzyme concentration was 120, 240, or 480 nM. The fluorescence spectrum was periodically measured to monitor consumption of PP_i by the enzyme.

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References and notes

1. Gunnlaugsson, T.; Glynn, M.; Tocci, G. M.; Kruger, P. E.; Pfeffer, F. M. *Coord. Chem. Rev.* **2006**, *250*, 3094–3117.
2. Sakamoto, T.; Ojida, A.; Hamachi, I. *Chem. Commun.* **2009**, 141–152.
3. Kim, S. K.; Lee, D. H.; Hong, J.-I.; Yoon, J. *Acc. Chem. Res.* **2009**, *42*, 23–31.
4. Martínez-Máñez, R.; Sancenón, F. *Chem. Rev.* **2003**, *103*, 4419–4476.
5. Zhou, Y.; Xu, Z.; Yoon, J. *Chem. Soc. Rev.* **2011**, *40*, 2222–2235.
6. Hargrove, A. E.; Nieto, S.; Zhang, T.; Sessler, J. L.; Anslyn, E. V. *Chem. Rev.* **2011**, *111*, 6603–6782.
7. O'Neil, E. J.; Smith, B. D. *Coord. Chem. Rev.* **2006**, *250*, 3068–3080.
8. Ngo, H. T.; Liu, X.; Jolliffe, K. A. *Chem. Soc. Rev.* **2012**, *41*, 4928–4965.
9. Lipscomb, W. N.; Sträter, N. *Chem. Rev.* **1996**, *96*, 2375–2434.
10. Ronaghi, M.; Karamohamed, S.; Pettersson, B.; Uhlén, M.; Nyrén, P. *Anal. Biochem.* **1996**, *242*, 84–89.
11. Roy, B.; Rao, A. S.; Ahn, K. H. *Org. Biomol. Chem.* **2011**, *9*, 7774–7779.
12. Zhang, J. F.; Kim, S.; Han, J. H.; Lee, S.-J.; Pradhan, T.; Cao, Q. Y.; Lee, S. J.; Kang, C.; Kim, J. S. *Org. Lett.* **2011**, *13*, 5294–5297.
13. (a) Carolan, J. V.; Butler, S. J.; Jolliffe, K. A. *J. Org. Chem.* **2009**, *74*, 2992–2996; (b) DiVittorio, K. M.; Johnson, J. R.; Johansson, E.; Reynolds, A. J.; Jolliffe, K. A.; Smith, B. D. *Org. Biomol. Chem.* **2006**, *4*, 1966–1976; (c) Butler, S. J.; Jolliffe, K. A. *Org. Biomol. Chem.* **2011**, *9*, 3471–3483.
14. Kim, H. J.; Lee, J. H.; Hong, J.-I. *Tetrahedron Lett.* **2011**, *52*, 4944–4946.
15. Lee, D. H.; Kim, S. Y.; Hong, J.-I. *Angew. Chem., Int. Ed.* **2004**, *43*, 4777–4780.
16. Ravikumar, I.; Ghosh, P. *Inorg. Chem.* **2011**, *50*, 4229–4231.
17. Lee, H. N.; Swamy, K. M. K.; Kim, S. K.; Kwon, J.-Y.; Kim, Y.; Kim, S.-J.; Yoon, Y. J.; Yoon, J. *Org. Lett.* **2006**, *9*, 243–246.
18. Lee, H. N.; Xu, Z.; Kim, S. K.; Swamy, K. M. K.; Kim, Y.; Kim, S.-J.; Yoon, J. *J. Am. Chem. Soc.* **2007**, *129*, 3828–3829.
19. Das, P.; Bhattacharya, S.; Mishra, S.; Das, A. *Chem. Commun.* **2011**, 8118–8120.
20. Lee, D.-H.; Hong, J.-I. *Bull. Korean Chem. Soc.* **2008**, *29*, 497–498.
21. Lee, J. H.; Jeong, A. R.; Jung, J.-H.; Park, C.-M.; Hong, J.-I. *J. Org. Chem.* **2011**, *76*, 417–423.
22. Schwarz, F. P.; Wasik, S. P. *Anal. Chem.* **1976**, *48*, 524–528.
23. Weber, G.; Teale, F. W. J. *Trans. Faraday Soc.* **1957**, *53*, 646–655.
24. Kim, S. Y.; Hong, J.-I. *Bull. Korean Chem. Soc.* **2010**, *31*, 716–719.