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**Article:**
Halcrow, MA (2014) Recent advances in the synthesis and applications of 2,6-dipyrrozolylpyridine derivatives and their complexes. New Journal of Chemistry, 38 (5). 1868 - 1882. ISSN 1144-0546

http://dx.doi.org/10.1039/c3nj00835e
Recent Advances in the Synthesis and Applications of 2,6-Dipyrazolylpyridine Derivatives and their Complexes

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Developments in the chemistry of 2,6-di(pyrazol-1-yl)pyridine (1-bpp) and 2,6-di(pyrazol-3-yl)pyridine (3-bpp), their derivatives and their complexes are surveyed, with emphasis on the last eight years. Particular advances include the synthesis of multi-functional spin-crossover switches; the incorporation of emissive f-element podand centres into biomedical sensors; the self-assembly of a variety of functional soft materials and surface structures; and, the use of 3-bpp complexes in catalysis.

Introduction

Tris-heterocyclic ligands continue to be very widely used in transition metal chemistry, because of their synthetic flexibility, strong metal binding properties, and their ability to impart properties like luminescence or spin-crossover onto a coordinated metal ion. 2,2':6',2''-Terpyridine (terpy) and its derivatives are still the most widely used ligand of this type, and are important in supramolecular chemistry, soft materials chemistry and nanoscience among other fields of research. However, other classes of tris-heterocycle such as 2,6-di(benzimidazol-2-yl)pyridines and the 2,6-di(pyrazolyl)pyridines have certain advantages over the terpyridines for some applications and are also well-studied in their own right. The coordination chemistry of 2,6-di(pyrazol-1-yl)pyridine (1-bpp) and 2,6-di(pyrazol-3-yl)pyridine (3-bpp, Scheme 1) was first developed in two particular areas: their iron(II) complexes which can show unusual, and useful, spin-crossover switching properties; and, a class of podands based on the 1-bpp skeleton which form strongly emissive lanthanide complexes. While those areas have continued to expand, more recently the use of bpp derivatives in other areas of research has also been explored, including catalysis, solar cell photosensitisation and soft materials.

The synthesis and coordination chemistry of 1-bpp, 3-bpp and some related ligand classes were surveyed eight years ago, and two more recent articles have reviewed spin-crossover iron(II) complexes of the same ligand types. This article updates these earlier reviews, and emphasises results published since 2005. After a description of current developments in the syntheses of these ligands, the discussion is then grouped according to their different applications. The types of tris-heterocycle to be considered, and their abbreviations, are shown in Scheme 1.

Synthesis of 1-bpp derivatives and related ligands

The first-reported method for synthesising 1-bpp derivatives is still the most commonly used one, namely the nucleophilic coupling of pyrazolide anions with 2,6-dihalopyridines (eq 1, Scheme 2). 2,6-Dibromopyridine precursors (X = Br) are usually used but dichloro- and difluoropyridines (X = Cl or F) can also work well, especially if the pyridine ring has additional electron-withdrawing ‘Y’ substituents (Scheme 2). The yield of the reaction can depend strongly on the presence of other substituents on the pyridine ring, and can be increased if required by using an excess of pyrazole reagent. The process is quite forgiving in other ways, however. For example, 1-bpp derivatives bearing protic...
pyridine substituents \((Y = \text{CO}_2\text{H})\) can be made by eq 1 without prior protection of the acidic function. Since attack by the second pyrazole equivalent requires more forcing conditions, preparation of unsymmetric 1-bpp derivatives by stepwise addition of two different pyrazoles is straightforward and works well (eq 2, Scheme 2). No such unsymmetric ligand with \(Y \neq \text{H}\) has yet been reported, but the method should also work in that case. Only one study of catalysis of eq 1 has been published, reporting that palladium catalysts increase the rate of reaction, but do not give higher yields. Although 1H-pyrazoles can be N-arylated under Ullmann conditions, for example, that has not yet been applied to the synthesis of 1-bpp derivatives.

Where substituents are present on the pyrazole C3 positions, the less hindered 3',3''-disubstituted-1-bpp isomer is the major product of eqs 1 and 2 although small amounts of the 3',5''-disubstituted-1-bpp isomer(s) are also sometimes observed (Scheme 2). If the pyrazole 'R' substituents are small and non-polar (e.g. methyl), the subsequent chromatographic purification of the desired 3',3''-disubstituted isomer can be challenging. A number of 1-bpp derivatives bearing simple alkyl or aryl substituents have been prepared in this way, including chiral derivatives produced using optically pure pyrazole reagents. An exception to this generalisation is where indazole reagents are used, when eq 1 yields the more hindered 2,6-di(indazol-1-yl)pyridine products (1-bip, Scheme 1) in moderate yield. That reflects the usual reactivity pattern for deprotonated indazoles, which prefer electrophilic attack at N1. A small number of 1-bpp ligands substituted at the pyridine ring can be accessed directly by eq 1, but these can be converted into a wider range of 4-substituted-1-bpp products by subsequent functional group transformations (see below). Finally, eq 1 can also be extended to 1-bppyz analogues (Scheme 1), using 2,6-dichloropyrazine as starting material. Much milder reaction conditions are employed in that case, because of the greater reactivity of the dichloropyrazine reagent. However, this also means that unsymmetric 1-bppyz derivatives cannot be produced cleanly (c.f. eq 2).

An alternative route to 1-bpp derivatives substituted at the pyrazole ring has been published by Garner et al., by treatment of 2,6-di(hydrazino)pyridine with β-diketones (Scheme 2, eq 3). This route has a potential advantage in giving the opposite regioselectivity to eq 1, since bulkier or more electron-donating pyrazole substituents tend to adopt the 5',5''-positions in the 1-bpp products (eq 3, Scheme 2). When applied to the 2,6-di(indazol-1-yl)pyridine system, the same 1-bpp products afforded by eq 1 are also obtained by this route (Scheme 1). The methods in eq 1 and eq 3 have also been used to prepare 1-bppym derivatives (Scheme 1), starting from the appropriate 2,6-dihalo- or 2,6-di(hydrazino)-pyrimidine.

Chemical modification of 1-bpp itself can be achieved by halogenation (Scheme 3). Mild electrophilic chlorination, bromination or iodination reagents lead to selective dihalogeneration at the pyrazole C4 positions. Selective monoiodination at just one pyrazole ring has also been achieved by monitoring the reaction carefully, while more forcing conditions lead to multiple halogenerations of 1-bpp, at the pyrazole and pyridine rings. Comparable halogenerations of 1-bppyz were less successful, and 4',4''-dihalo-1-bppyz derivatives are more easily obtained by eq 1, using preformed 4-halopyrazole reagents. 4',4''-Diiodo-1-bpp and -1-bppyz derivatives are good reagents for Sonogashira couplings, affording 4',4''-di(alkynyl)-1-bpp and -1-bppyz products. There is also one report of a Stille coupling from the same precursor, yielding a 4',4''-di(thienyl)-1-bpp derivative, but attempted Heck reactions were reportedly unsuccessful. Attempted nitration of 1-bpp using HNO\(_3\)/\(\text{H}_2\text{SO}_4\) led to a mixture of products, involving partial nitration of the pyridyl as well as the pyrazolyl rings. Dinitro-1-bppyz was prepared by eq 1, however, starting from preformed 4-nitropyrazole. 4',4''-Dinitro-1-bpp cannot be made by that route, because the more forcing conditions required leads to decomposition of the nitropyrazole reagents.
Preformed 1-bpp and 1-bppyz derivatives bearing chemically modifiable pyrazole substituents can be subsequently transformed into more complex structures. One important example here is 3',3''-di(ethylcarboxy)-1-bpp (eq 1, R = CO₂Et), which can transformed into a series of podand derivatives for F-element complexation in three further steps. These podands are described in more detail below.

Most syntheses of 4-substituted-1-bpp ligands (eq 1, Y ≠ H, Scheme 2) begin from commercially available 2,6-diacetylpyridine using dihydroxyisonicotinic acid. After a halogenation step, this is readily converted to 2,6-di(pyrazol-1-yl)pyridine-4-carboxylic acid by eq 1 (Y = CO₂H). From there, a variety of functional group transformations are available, as shown in Scheme 4. This is the most common route for attaching additional functionality to the 1-bpp pyridine ring.

Recently, however, 4-bromo-2,6-difluoropyridine has been identified as an alternative starting material for 4-substituted 1-bpp derivatives. The fluoro groups of this precursor are selectively displaced in eq 1 (X = F, Y = Br), yielding a 4-bromo-1-bpp product that can be further modified by Sonogashira cross-coupling or substitution reactions.

### Synthesis of 3-bpp and 1,3-bpp derivatives

The only known synthetic route to 3-bpp derivatives is to construct the pyrazole rings about a pyridyl precursor, via Claisen condensation or a comparable acetylation reaction followed by hydrazinolysis (Scheme 5). Compound 3-bpp itself is most conveniently prepared from 2,6-diacetylpyridine using dimethylformamide dimethylacetel as formyilating agent, but 3-bpp derivatives substituted at the pyrazole C₅ positions can also be accessed by more conventional Claisen condensations or other acetylation procedures. A number of new derivatives of this type have been prepared in the last eight years, and incorporation of electron-withdrawing substituents at the pyrazole C₄ positions is also achievable by this method.

Preformed 3-bpp can be cleanly dialkylated at the pyrazole

### 1-Bpp and related ligands in spin-crossover

Iron(II) complexes of 1-bpp derivatives continue to be heavily investigated by the spin-crossover community. Results on this topic published since 2009 are discussed here, and the reader is directed to ref. 7 for a discussion of earlier work.

The synthetic versatility of the 1-bpp pyridyl group (Scheme 4), and the tendency for [Fe(1-bpp)]²⁺ derivatives to exhibit spin-crossover near room temperature, has led several groups to pursue multifunctional spin-crossover switches based on the [Fe(1-bpp)]²⁺ framework. Thus, [Fe(L)₂]²⁺ contains two pendant electron-acceptor tetrafluorovanadate (TTF) moieties, which was crystallised with electron-donor anions in the double salt [Fe(L)₂][Ni(nmtt)₂]BF₃·PhCN. Partial electron transfer from the anions to the TTF pendant groups, which is evident in the crystal structure, afforded a semiconducting crystal whose resistivity
Scheme 4. Important methods for the production of 4-substituted-1-bpp derivatives. The procedures are referenced in ref. 7 unless otherwise stated. Typical conditions used: (i) COCl₂, thf; NaN₃, acetone/water; CF₃CO₂H, benzene; K₂CO₃, MeOH. (ii) NaNO₂, KI, HCl. (iii) RCCH, CuI, [Pd(PPh₃)₄] (cat), NEt₃, thf. (iv) H₂, Pd/C (cat), ethyl acetate. (v) RN₃, CuSO₄, Na[ascorbate], dmf. (vi) ArB(OH)₂, [Pd(PPh₃)₄] (cat), toluene or dioxane, Na₂CO₃. (vii) ROH, H₂SO₄ (cat). (viii) LiOH, thf then dil. HCl. (ix) NaBH₄, EtOH. (x) HBr, reflux or Br₂, PPh₃, CH₃CN, rt. (xi) NaX, CH₃CN, reflux or dmf, warm. (xii) R₂NH, Na₂CO₃, KI (cat) or NBu₄Br (cat), CH₃CN, reflux or dmf. (xiii) C₂O₂Cl₂, dmso, CH₂Cl₂, −78 ºC, then NEt₃, rt. (xiv) [RCH₂PPh₃]Br, BuLi or KOtBu, thf.

Scheme 5. Procedures for the synthesis of 3-bpp derivatives. Typical conditions used: (i) Me₂NC(O)R, reflux. (ii) RC(O)Me (2 equiv), NaH or NaOMe (2 equiv), MeOH, dme or CH₂Cl₂, reflux. (iii) N₂H₄·H₂O or N₂H₄·HCl (2-10 equiv), MeOH or EtOH, H⁺ (cat) if required, reflux. (iv) MeCN, NaH (2 equiv), THF, reflux. (v) NaH or LiH (2 equiv), R’X (2 equiv), THF. (vi) R’N₂H₂ (2-10 equiv), MeOH or EtOH, reflux.
shows a distinct discontinuity in the region of the iron spin-transition. Similarly, $L^2$ and $L^3$ are 1-bpp derivatives bearing fluorescent pyrenyl substituents. A solvate of $[\text{Fe}(L^3)_2][\text{ClO}_4]_2$, did exhibit spin-crossover and fluorescence, but no dependence between the iron spin state and the emission profile was observable in that case. Mixed-metal complexes $[\text{Fe}(L^4)_2][\text{BF}_4]_2$ and $[\text{Fe}(L^5)_2][\text{BF}_4]_2$ were also prepared with fluorescence in mind, but no emission from pendant platinum centres was observed from the latter compound in the solid state.

Styryl derivatives $[\text{Fe}(L^6)_2][\text{BF}_4]_2$ and $[\text{Fe}(L^7)_2][\text{BF}_4]_2$ were synthesised for studies of the ligand driven, light-induced spin-crossover (LD-LISC) effect, where $\text{cis}$/$\text{trans}$ photoisomerism of the pendant styryl pendant groups induces a change in spin-state at the coordination iron centres. Both complexes are effective in that regard, undergoing irreversible $\text{cis} \rightarrow \text{trans}$ isomerisation under visible light in solution and, unusually, in the solid state. Notably, while the $\text{trans}$ isomers of both complexes have similarly gradual spin-crossover profiles in the solid state, the $\text{cis}$-isomers are different; solid $\text{cis}$-$[\text{Fe}(L^6)_2][\text{BF}_4]_2$ is high-spin at room temperature, but $\text{cis}$-$[\text{Fe}(L^7)_2][\text{BF}_4]_2$ is predominantly low-spin. Thus, the LD-LISC effect in the two solids has an opposite effect on their iron spin-states.

The compounds $[\text{Fe}(L^8)_2]^2+$ and $[\text{Fe}(L^9)_2]^2+$ have been introduced into single-molecule junctions, to investigate the relationship between conductivity through a single molecule and the spin-state at the central iron atom. Although interpretation of the data is complicated by noise, it was proposed that injecting two electrons onto the ligand-based LUMOs of $[\text{Fe}(L^7)_2]^2$ triggers a low-spin $\rightarrow$ high-spin transition at the iron centre under the conditions of the experiment. That might explain a splitting of the Kondo peak in the I/V response across the molecular junction. Interestingly, an opposing effect has since been reported in other studies, where single-electron charging of a ligand LUMO orbital induces a high-spin $\rightarrow$ low-spin state change in single molecules absorbed on a surface. While low-spin $\rightarrow$ high-spin switching could also be effected in those experiments, that was ascribed to the effect of local heating of the sample rather than to reduction of the molecule.

The salt $[\text{Fe}(L^9)(L^9\text{H})][\text{ClO}_4]_3\cdot\text{MeOH}$ has also been drop cast into polycrystalline thin films, which were subsequently manipulated into 200 nm striped patterns by wet lithography. Raman spectra at 393 and 170 K indicated that these films undergo spin-crossover at a comparable temperature to the bulk material. Drop-casting $[\text{Fe}(L^{10})_2][\text{BF}_4]_2$ onto HOPG (graphite) surfaces instead yielded unusual patterns of bead nanostructures. Each bead was 2.5-4 nm in diameter, implying it contains approximately 5-10 molecules. Individual beads gave different responses under current image tunnelling spectroscopy, which may imply they may contain molecules in different spin states.

Thin electroluminescent films containing $[\text{Fe}(1\text{-bpp})_2][\text{BF}_4]_2$ and chlorophyll have been incorporated into organic LED (OLED) devices, although modulation of the OLED emission by spin-crossover in the film was not observed. Solid solutions of $[\text{Fe}(1\text{-bpp})_2][\text{BF}_4]_2$ doped with $[\text{Cu}(1\text{-bpp})_2][\text{BF}_4]_2$, $[\text{Ru}(\text{terpy})_2][\text{BF}_4]_2$, and $[\text{Co}(\text{terpy})_2][\text{BF}_4]_2$ have been prepared, to investigate how the spin-transition of the $[\text{Fe}(1\text{-bpp})_2][\text{BF}_4]_2$ host lattice at 260 K perturbs the electronic structure of the guest dopant. The materials
[Fe(1-bpp)$_2$][Co(terpy)$_2$][BF$_4$] ($x = 0.95-0.75$) are of particular note, in that spin-crossover of the iron centres in the materials induces an allosteric spin-state switching in the cobalt dopant.\textsuperscript{83,84} Other 1-bpp derivatives whose iron(II) complexes have been investigated for spin-crossover behaviour since 2009 include L$_{11}$\textsuperscript{30}, L$_{12}$\textsuperscript{40}, L$_{13}$\textsuperscript{85} the 1-bppym ligand L$_{14}$\textsuperscript{25} and the series of 1-bppyz derivatives collected as L$_{15}$\textsuperscript{21}. Spin-crossover was observed in most of these examples, although some of them were complicated by polymorphism and solvate formation.\textsuperscript{39,85} Light-induced spin-state trapping (LIEST) effect\textsuperscript{86} studies were also performed in some cases,\textsuperscript{21,40} which mostly followed the established behaviour of the [Fe(1-bpp)$_2$]\textsuperscript{2+} series of complexes.\textsuperscript{7} Finally, the use of [Fe(L$_{18}$)$_2$]\textsuperscript{2+} as a temperature-sensitive probe for magnetic resonance imaging (MRI) has been patented.\textsuperscript{87}

Solid [Co(NO$_3$)$_2$(1-bppyz)] undergoes an unusual hysteretic magnetic discontinuity at 235 K. Rather than being spin-crossover, this reflects a change in zero-field splitting at the high-spin cobalt ion induced by a crystallographic phase transition.\textsuperscript{88}

\textbf{3-Bpp and related ligands in spin-crossover}

Salts of [Fe(3-bpp)$_2$]$^{2+}$ have been heavily studied since the late 1980s.\textsuperscript{63,89} That compound exhibits very variable spin-state behaviour that is highly dependent on the water content of the samples, the presence of lattice water tending to favour the low-spin state of the complex. Its utility is also enhanced because [Fe(3-bpp)$_2$]$^{2+}$ is stable in aqueous solution, in contrast to [Fe(1-bpp)$_2$]$^{2+}$ which decomposes in water. Those observations have been explained by solution-phase measurements, which showed that spin-crossover in [Fe(3-bpp)$_2$]$^{2+}$ shifts to ca. 60 K higher temperature in water compared to organic solvents.\textsuperscript{90} That probably reflects increased polarisation of the N\textsuperscript{6}–H\textsuperscript{86} groups in the molecule by strong N–H...O hydrogen bonding between the complex and the solvent. That would lead to more electron-rich 3-bpp ligands, which in turn would exert a larger ligand field at the iron atom. Similarly spin-crossover of different salts of [Fe(3-bpp)$_2$]$^{2+}$ in solution depends on the anion present, in that more associating halide ions increase the midpoint temperature by up to 20 K in acetone/water mixtures.\textsuperscript{91}

Despite the recent wider availability of substituted 3-bpp derivatives (see above), few of them have investigated in spin-crossover research so far. N,N’-Dialkylolation of 3-bpp suppresses spin-crossover in complexes such as [Fe(L$_{18}$)$_2$][BF$_4$]$_2$ and [Fe(L$_{16}$)$_2$][BF$_4$]$_2$, probably on steric grounds.\textsuperscript{67} However, iron(II) complexes of two NH-pyrazolyl 3-bpp ligands show more interesting behaviour. Hydrated and anhydrous forms of [Fe(L$_{18}$)$_2$][BF$_4$] and [Fe(L$_{10}$)$_2$][ClO$_4$] are isostructural under ambient conditions, but exhibit complicated and contrasting spin-crossover properties. The anhydrous BF$_4^-$ salt exhibits a highly cooperative spin-transition near 205 K with a wide hysteresis loop,\textsuperscript{92} but the ClO$_4^-$ salt is simply high-spin.\textsuperscript{93} Conversely, [Fe(L$_{18}$)$_2$][ClO$_4$]$_2$:2H$_2$O is spin-crossover active, but the hydrated BF$_4^-$ salt is not. X-ray powder diffraction revealed that these differences reflect different sequences of phase changes that take place in the materials upon cooling.\textsuperscript{92,93} Solvates of [Fe(L$_{19}$)$_2$][ClO$_4$]$_2$ have also proven fruitful. The acetone solvate of this salt exhibits a spin-transition around 150 K, with a 40 K hysteresis loop.\textsuperscript{94} The wide hysteresis does not involve a crystallographic phase change, but may be mediated by changes to anion disorder and ligand conformation. Spin-state trapping experiments by laser irradiation (LIEST\textsuperscript{88}) or thermal quenching allow access to two different metastable high-spin states of the compound at low temperatures. The thermally quenched material resembles the thermodynamic high-spin phase, while following LIEST irradiation the ligand conformation is closer to that found in the low-spin phase. This has therefore allowed the spin-state change, and the accompanying conformational rearrangement, to be decoupled in this system.\textsuperscript{95} The thf solvate of the same salt is isostructural with the acetone one, but only undergoes complete spin-crossover following solvent loss on exposure to air.\textsuperscript{96} Other solvates of the same complex salt show more variable spin-state behaviour.\textsuperscript{97} Salts of [Fe(3-bppyz)$_2$]$^{2+}$ (Scheme 1) are low-spin in the solid state.\textsuperscript{70}

The dinuclear complex [[Fe(NCS)$_2$(3-bpp)$_2$]$^{2-}$($\mu$-4,4’-bipy)$_2$] undergoes spin-crossover in just one of its iron centres on cooling under ambient conditions,\textsuperscript{98} which is preceded by the higher temperature loss of a crystallographic centre of symmetry.\textsuperscript{99} This crystallographic phase change is not reversed during LIEST irradiation, so the thermodynamic and kinetically trapped high-spin states of the compound are crystallographically distinct.\textsuperscript{99} Under hydrostatic pressure, however, both iron atoms are gradually converted to the low-spin state as the pressure is increased.\textsuperscript{100} That dimeric complex with this ligand set, [[Fe(NCS)$_2$(3-bpp)$_2$]$^{2-}$($\mu$-4,4’-bipy)$_2$], has also been crystallised but is not spin-crossover active.\textsuperscript{101}

\textbf{f-Block complexes}

The other aspect of bpp research that has been heavily studied is their f-element chemistry.\textsuperscript{6} Tetra-carboxylate podands of type L$_{20}$ were first investigated in 1993.\textsuperscript{32} They encapsulate lanthanide ions in aqueous solution (log $K = 14-16$) with hydration numbers $\leq 0.5$, and are good sensitisers for several f-elements yielding emissions with ms lifetimes.\textsuperscript{6,19,102} Functionalisation of the pyridyl $R'$ group allows a range of targeting groups and receptors to be appended to the podand skeleton, such as streptavidin and biologically labelled silica particles.\textsuperscript{6,19,47} The emission quantum yields of [Ln(L$_{20}$)]
complexes depend strongly on the nature of R, making them responsive to the binding of substrates or changes in their environment. These conjugates have yielded fluorescent sensors for protein:protein interactions and DNA hybridisation, with sensitivities up to the pg range.6

More recent studies have developed these designs into sophisticated time-resolved sensors, for small molecule and biological analytes. Two [Ln(L\textsuperscript{20})] podands bearing oxidisable ‘R’ substituents have been developed, where degradation of the side-chain leads to enhancement of the emission. One of these was employed as a “switch-on” sensor for H\textsubscript{2}O\textsubscript{2}, with ms time resolution and a nM detection limit. This allowed the monitoring of H\textsubscript{2}O\textsubscript{2} production by biological saccharide degradation in leaf cells by fluorescence microscopy.103 Another, slightly different design afforded an analogous fluorescent sensor for monitoring the OH\textsuperscript{•} radical in live cells.104 Two different [Tb(L\textsuperscript{20})] complexes bearing pendant chelate ‘R’ groups have been designed as fluorescent sensors for Zn\textsuperscript{2+} and Hg\textsuperscript{2+} ions.42,43

Silica particles coated with a [Ln(L\textsuperscript{20})] podand were further modified with antibodies or binding proteins for the hepatitis B virus. The resultant particles had good chemical stability and were able to detect hepatitis B antigens at sub-μM limits, with improved hit rates compared to a commercial diagnosis method.105 In another study, [Ln(L\textsuperscript{20})] podands were tethered to polymer beads, which were subsequently labelled with another antibody. The resultant beads were able to detect a cancer antigen with improved sensitivity over a commercial kit.106 A [Tb(L\textsuperscript{20})] derivative bearing a targeting substituent at a podand side-arm, rather than the pyridine ring, was used as a reporter group in a protein/antibody conjugate sensor for trace pesticides.106

Analogous phosphonate (L\textsuperscript{21}) and mixed phosphonate/carboxylate podands (L\textsuperscript{22}) have also recently been reported.107,109 The [Ln(L\textsuperscript{21})] and [Ln(L\textsuperscript{22})] complexes have comparable solution structures and emission properties to their [Ln(L\textsuperscript{20})] analogues, but have improved chemical stability. For example, [Eu(L\textsuperscript{21})] exhibits logK = 20.4 in aqueous solution.107 Two groups have patented the use of these phosphonated podands in biological imaging,110 and in medical diagnostics and phototherapy.111

The tridentate 1-bpp framework itself is also an efficient antenna for lanthanide ions, which has been exploited to make fluorescent materials. The back-to-back derivative L\textsuperscript{23} self-assembles into hollow nanotubes in water:thf mixtures. The nanotubes are blue-emissive, and doping their surfaces with [Eu(tta)\textsubscript{3}] (Htta = 1-thienyl-3-trifluoromethylpropane-1,3-dione) introduces a second red-emissive centre. The resultant hybrid nanostructures exhibit three colour red/blue/purple emission under a fluorescence microscope.112 In a comparable approach, a green-emitting benzothiadiazole dye was decorated with blue-emitting 1-bpp fragments using Click chemistry. The product forms 500 nm vesicles in water:thf, which were doped with red-emitting [Eu(tta)\textsubscript{3}]. The resultant assembly exhibits combined red/blue/green/yellow emission.113 Finally, a 1-bpp/fluorene copolymer that was assembled through multiple Sonogashira couplings (Scheme 3), spin-coated onto quartz then doped with [Eu(tta)\textsubscript{3}] as before, yields an almost perfect white-emitting polymer film.114

An [Eu(L\textsuperscript{24})] derivative bearing a branched R substituent forms a fluorescent gel in dodecane.115 The adduct [Eu(hfac)\textsubscript{3}(L\textsuperscript{25})] is emissive in solution,116 and has been electropolymerised into luminescent conducting thin films.117 Lastly, polymeric catena-[Pr(1-bpp)Ag(SCN)\textsubscript{3}(H\textsubscript{2}O)\textsubscript{11}(x = 0 or 1)] exhibit a strong prasodymium-based emission in the solid state.118

The 3-bpp fragment is also an antenna for europium and terbium emission,119,120 but has not been exploited to the same extent as the 1-bpp series. However, one recent study introduced L\textsuperscript{25} as a reagent for the fractional separation of lanthanide/actinide mixtures. The ligand showed a strong selectivity for americium in liquid/liquid extraction experiments from nitric acid, with a superior selectivity over 4f ions compared to other tris-heterocycle extractants.121

**Emissive d-block complexes**

While [Ru(1-bpp)\textsubscript{2}]\textsuperscript{2+} \textsuperscript{17} and [Ru(3-bpp)\textsubscript{2}]\textsuperscript{2+} \textsuperscript{118} are not emissive, luminescent centres of type [Ru(bpp)(terpy)]\textsuperscript{2+} \textsuperscript{119} and [RuX(bpp)(bipy)]\textsuperscript{+} (X = Cl\textsuperscript{–} or NCS\textsuperscript{–}) have been reported for the 1-bpp,120,119,120 and 3-bpp121 ligand series. Some of these have been investigated as dyes for dye-sensitised solar cells (DSCs).122

The most successful has been achieved with complexes related to I, bearing thienyl substituents at either the 3-bpp ligand (R\textsuperscript{2}) or the terpy derivative (R\textsuperscript{3}).53,121 Conjugation of the acceptor ligand to the thienyl group red-shifts the complexes’ absorption across the full visible spectrum. Using I, DSCs with photoconversion efficiencies of up to 10.7 \% have been prepared, comparable to those using [Ru(NCS)\textsubscript{3}(terpy)] or [Ru(NCS)\textsubscript{3}(bipy)\textsubscript{2}] derivatives.
polymer crystallinity, and by interacting with the TiO
however, L
employed as a dopant in a DSC polymer electrolyte. In this case,
comparable to \([\text{RuCl(dcbpy)(1-bpp)}]\)Cl.
dicarboxylic acid) is moderately effective in DSCs,
the use of \([\text{Co(1-bpp)}]\)
has also been published.

Interestingly, \(L^{18-20H}^{2+}\) are strongly emissive in the solid state. The emissions are
metal-centred, and mediated by \(d^{10-18}\) interactions.\(^{52,132}\)
Another emissive silver complex has also been reported, based on a hybrid 3-bpp/N-heterocyclic carbene ligand.\(^{64}\)

### Dipyrazolylpyridines in self-assembly

Spin-crossover thin films and nanostructures,\(^{78,79}\) luminescent assemblies\(^{31,34,36}\) and soft materials\(^{30,47,113,130}\) formed from 1-bpp
derivatives have been described above. Other 1-bpp moieties have been reported to self-assemble in the absence of a metal ion. Thus, \(L^{31}\) and \(L^{32}\) \((R = H)\) assemble into nanoscale structures when drop-cast from CH\(_3\)Cl\(_2\) solutions, with tape and tubular morphologies respectively. Both assemblies yield the same violet emission exhibited by the crystalline compounds.\(^{35}\)

The corresponding \(L^{31}\) derivative with \(R = n\)-octyl yields a soluble, emissive coordination polymer when treated with Zn[ClO\(_4\)]\(_2\). The polymer has a molecular weight \(ca. 9600\ \text{g mol}^{-1}\), corresponding to 8-9 \([\text{Zn(\(\mu-L^{31})\})]\)\(^{2+}\) repeat units, and was drop-cast into patterns on a silica surface.\(^{33}\) The thiocarboxylate \(L^{33}\) forms monolayers when dropcast onto Au(111) in which the 1-bpp skeleton lies flat on the gold surface in a regular 2D array.\(^{133}\) \(L^{34}\) adsorbs onto steel surfaces with a Langmuir-Blodgett film, and is an efficient inhibitor against acid corrosion.\(^{134}\)

Alternatively, 3-bpp and its derivatives are useful scaffolds for polymetallic complexes, by bridging between metal ions through

![Chemical structures](image-url)
deprotonated pyrazolate groups. For example, treatment of L with silver salts in the presence of base affords clusters of formula [Ag(µ-µ-L-H)]X, whose topology varies depending on the anion X. Reaction of L or L with Cu affords octanuclear [Cu(µ-L-L-H)]4 (L = L or L), with four di-copper fragments arranged in a ladder-type array. 112 Both these cluster types are strongly emissive in the solid state. The following have also been prepared: a hexanuclear iron(III) complex [Fe(µ-µ-L-3-bpp-2H)](µ-O)(µ-Me)(µ-OH)Cl][116] copper(II) adducts [M(µ-L-3-bpp-2H)] and [M(µ-L-3-bpp-2H)] (M = Ni55 57 or Cu137,138); a related dimer [Cu2(NO3)2(µ-µ-L-3-bpp-H)],119 the sulphate complexes [M2(µ-L-2H)](µ-SO4)] (M2 = Co24 58; L = L or L) and [Zn2(µ-L-35-2H)](µ-SO4)][OH]140 and, dinuclear [Ru2(µ-L-35-H)](µ-Cl)(P(C6H4CF3)]2Cl.141 Other polymetallic complexes where a 1-bpp or 3-bpp derivative acts as a simple capping ligand are also known.52,101,142-149

Appending extra donor groups onto the 3-bpp skeleton gives further scope for high-nuclearity complex formation. Thus, the dinaphthoxo derivative L has afforded Ni55 150, Mn4 151 and Al4 clusters in which deprotonated [L-3H]+ or [L-4H]+ ligands exhibit a variety of coordination modes. Treatment of the dipyridyl chloride of L with Co[BF4]2 yields cyclic [Co3((µ-µ-L-38-2H)](µ-OH)2[Mn(CO)]BF4]4; and, the mixed-valent 3x3 grid [Co6Co6(µ-µ-L-38-2H)]4(BF4)4, containing a central cobalt(III) site surrounded by a square of alternating high-spin and low-spin cobalt(II) ions.152 A similar complexation using a 1:1 mixture of iron(II) and cobalt(II) reagents led to an alternative 3x3 structure [FeFeII2CoII2(µ-L-38-2H)](µ-OH)2[Mn(CO)]BF4]4, where iron(II) sites occupy the corners of the grid and the iron(III) ion is at the centre.153 The two grid motifs differ, in that the metal ions are directly linked by [L-3H-2H]2 ligands in the all-cobalt example. In contrast, the L ligands in the mixed-metal grid are protonated, and the metal ions are bridged by hydroxo groups. An intermediate [FeFeII2CoII2(µ-µ-OH)2(µ-µ-L-38-2H)](µ-OH)2[Mn(CO)]BF4]4 was also isolated from the mixed-metal complexation, and its conversion to the grid product was monitored by ES mass spectrometry.154

The corresponding copper complex can be isolated in two different oxidation levels, [Cu2(µ-µ-L-38-2H)]4(BF4)4 and [Cu2(µ-µ-L-38-2H)]4(PF6)4. The copper(I) sites in the latter compound occupy opposite corners of the 3x3 grid, while the central copper(II) site in both structures has an unusual Jahn-Teller-compressed octahedral configuration.154 A hydrogen-bonded grid-like assembly {[Co(L)]2(µ-L)]4(BF4)4} has also been reported, in which the mononuclear complex cation associates with four additional L ligands through N—H…N interactions.155 Copper(I) and silver(I) complexes of 1-bpp, 1-bppyz and 3-bpp exist as dimeric molecules or coordination polymers, in which the ligands adopt a helical conformation.20,62,156-158 Several bpp derivatives bearing pendant pyridyl groups, including L and L, have been used to make extended helicate complexes.6,63,159-161

**Dipyrazolylpyridines in catalysis and small molecule activation**

When ref. 6 was written in 2005, only a handful of catalysis studies involving a bpp derivative had been published. There have been several new investigations since then, particularly involving cross-coupling reactions,17,69,162 transfer hydrogenation66,72,141,163-165 and alkene polymerisation.14,56,139,158,169,170 Individual reports of 1-bpp complexes as oxime dehydrogenation171 and alkane photooxidation catalysts have also been published.172 The most notable results from this list are two reports of nickel/1-bpp catalysts for sp3/sp4 Negishi couplings,171,162 and the consistently high catalytic activity shown by complexes of type [RuCl2(bpp)(Ph3P)] towards transfer hydrogenation.66,72,163-165 None of these studies used a chiral bpp derivative as co-ligand, although those are easily accessible for the 1-bpp series.6

Bubbling O2 or N2 through a solution of [RuL3-2H)(Ph3P)](HMe) rapidly affords [Ru(L)](2H)(Ph3P)]2(N2)] or [Ru(L)](2H)(Ph3P)]2(O2)], containing end-on bound N2 and side-on O2.55 The iron analogue [Fe(L)](PMe3)2(NCMe)](CF3SO3) catalyses the disproportionation of hydrazine into ammonia and dinitrogen, with almost complete conversion after 18 hrs. The reaction can be partially arrested using phenylhydrazine as substrate, allowing [Fe(L)](PMe3)2(NH-NPh)](CF3SO3)] to be isolated from the mixture. The ability of L to act as a proton shuttle during the reaction may be important to the catalytic mechanism.173 A theoretical study investigated the efficacy of rhodium complexes of L, among several other tridentate ligands, for the insertion of CO2 into Rh—C bonds. Neutral chelates like L14 were predicted to be less effective for this step than pincer ligands with negatively charged central atoms, however.174
Other complexes
In addition to those already discussed, many other complexes of 1-bpp and 3-bpp derivatives have been characterised since 2005. Most of these are adducts of 1-bpp derivatives with divalent metal salts from groups 8, 14, 16, 17, 19, 20, 21, and 12. Although individual titanium(IV), iron(III), and rhenium(I) examples are also included. An IR study showed that L forms adducts in methanol solution with CuCl₂, NiCl₂ and CoCl₂, but not with MgCl₂ or CaCl₂. The number of miscellaneous complexes of 3-bpp derivatives is much smaller but more varied, and includes manganese(II), samarium(III) and gold(III) compounds.

Conclusion
The coordination chemistry of bpp and terpy derivatives is complementary in many ways. The weaker ligand field exerted on a metal ion by bpp makes its complexes more labile in solution than corresponding complexes of terpy derivatives. For this reason, terpy derivatives are still more widely used in metal/organic materials chemistry and self-assembly, because their complexes are more robust. However, introducing additional metal-donor groups into the bpp ligand skeleton, which is synthetically facile, overcomes that disadvantage. That has allowed lanthanide complexes of the podands L to find use in bioanalytical chemistry and fluorescent materials. Lanthanide complexes of bpp derivatives can be more emissive that their terpy counterparts, reflecting an improved match between the f-orbital energies and the bpp π-acceptor levels.

The importance of [Fe(bpp)₂]²⁺ derivatives in spin-crossover research also reflects the balance of heterocyclic donor groups in the bpp framework. Corresponding [Fe(terpy)₂]²⁺ complexes are nearly always low-spin. Thus, although a wider range of terpy ligands bearing pendant functionality is available than for the bpp series, functionalised [Fe(bpp)₂]²⁺ complexes can afford switchable multifunctional materials and nanoscale devices that are not accessible with terpy ligands. Lastly, the 3-bpp framework in its iron complexes, or elsewhere, has additional possibilities for supramolecular chemistry and self-assembly that are not possessed by 1-bpp, or by terpy.

In conclusion, recent studies have further developed the established uses of bpp derivatives in spin-crossover and lanthanide chemistry. They have also introduced new directions for bpp research, particularly in self-assembly and nanoscience.

Acknowledgements
The author thanks Drs. Nayan Solanki, Ruth Pritchard, Clare Tovee, Rufeida Mohammed and Laurence Kernshaw, and Tom Roberts, Grant Sherborne and Martin Fallows, who carried out work from our laboratory that is described in this article. Assistance from other collaborators and co-workers is also gratefully acknowledged, who are listed in the references. Our research was funded by the EPSRC and the University of Leeds.

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