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Luminescent Atropisomeric N,N-Chelating Ligands from Copper-Catalyzed One-Pot C–N and C–C Coupling Reactions

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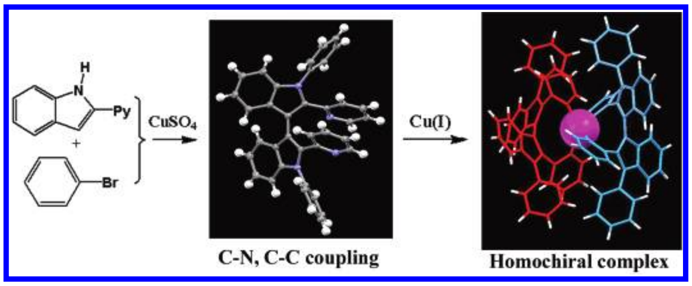
ABSTRACT



New atropisomeric N,N-chelating ligands with a 3,3′-bis[2-(2′-py)-indolyl] unit have been achieved via one-pot reactions that involve the formation of multiple C–N bonds between an indolyl and a brominated benzene and the indolyl 3,3′-C–C coupling. The new ligands display distinct blue intramolecular excimer emission ($\lambda_{max} = 445$ nm). Cu(I) ions bind to the new N,N-chelate ligands with a homochiral selectivity. The complex [Cu(bpib)$_2$][BF$_4$] (bpib = bis{3,3′-[*N*-phenyl-2-(2′-py)-indolyl]}) crystallizes as chiral crystals, thus allowing enantiomeric separation.

Atropisomeric chelate ligands such as BINAP (2,2′-bis-(diphenylphosphino)-1,1′-binaphthyl) are well-known for their important roles in asymmetric catalysis involving transition metals.[1] The majority of previously known atropisomeric ligands are based on 1,1′-binaphthyl with phosphine binding sites.[1] Atropisomeric ligands based on 3,3′-bi-indolyl are rare, but some examples with phosphine donors have been reported.[2] Compared to phosphine ligands, pyridyl and polypyridyl ligands are in general harder donors, are more stable toward oxidation, and can have rich photophysical/photochemical properties when bound to metal ions. Hence, atropisomeric chelate ligands based on pyridine or polypyridine are attractive not only for their potential use in certain asymmetric reactions but also for their applications in chiral supramolecular assembly and chiral recognition.[1,3] In spite of these, examples of atropisomeric ligands involving pyridyls as donors are scarce, and only a few examples are known in the literature.[4] We report herein new atropisomeric ligands that have a 3,3′-bis[2-(2′-py)indolyl] backbone with multiple 2-pyridyl binding sites.

As shown in Figure 1, structurally the new atropisomeric molecules, bpib, bbip, and btib (right column), can be considered as the corresponding 3,3′-C−C coupled dimer of pib, bib, and tib (left column), respectively. In fact, the "dimer" ligands were isolated as a minor product from the Ullmann condensation reaction of 2-(2′-pyridyl)indole with bromobenzene, 1,4-bromobenzene, and 1,3,5-tribromobenzene, respectively, using $CuSO_4$ as the catalyst and K_2CO_3 as the base, with the "monomer" pib, bib, and tib as the

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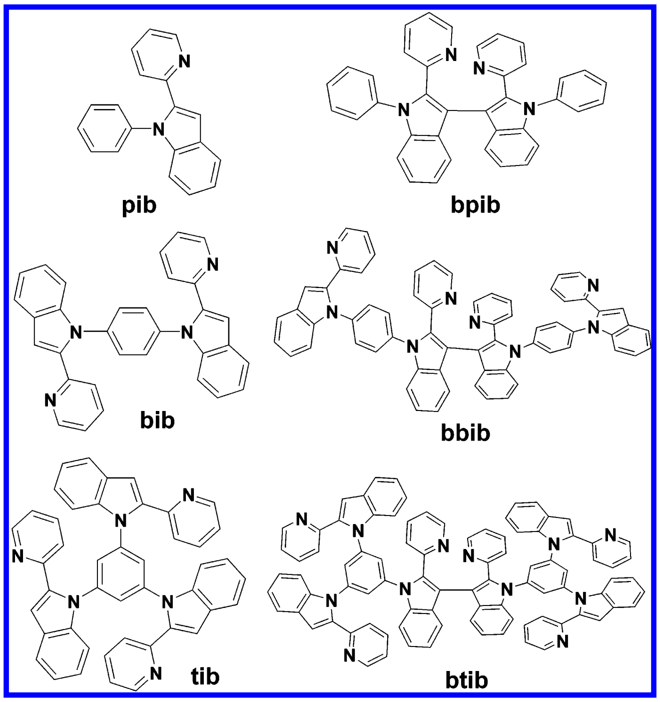
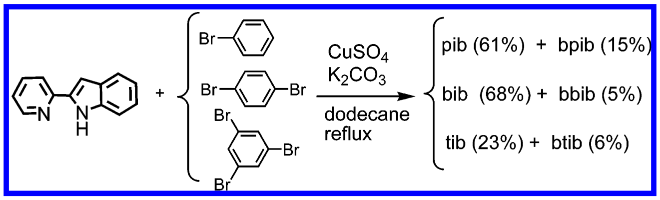


Figure 1. Structures of the monomers (left) and the atropisomeric dimers (right).

Scheme 1



intended targets. The isolated yields (not optimized) of the monomer and the corresponding dimer from each reaction are shown in Scheme 1. Copper-catalyzed Ullmann condensation reactions are commonly known for C−N bond formation but not direct C−C bond coupling.[5] The isolation of the 3,3′-bi-indolyl products from these reactions is therefore surprising. The isolated yield of the small dimer bpib is modest. The isolated yields of the larger dimers bbip and btib are low, which are caused mainly by their poor solubility (slightly soluble in CH_2Cl_2) and the formation of mono- and disubstituted (in the case of 1,3,5-tribromobenzene) C−N coupling side products. In addition, C−C coupling involving the mono- and disubstituted monomers can also occur. C−C homocoupling at the 3 position of the terminal 2-(2′-py)indolyl in bpib and btib is also possible, which can result in the formation of larger oligomeric species and contribute to the low yield of the dimer. Indeed, insoluble organic products were observed from the reaction mixtures for bbip or btib synthesis. However, the insolubility has prevented us from fully characterizing these high molecular weight species.

Examples of one-pot or tandem reactions to form both C−C and C−N in the product are known previously (with Pd catalysts in most instances).[6] However, simultaneous aryl C−C coupling and the formation of multiple aryl C−N bonds catalyzed by copper as shown in Scheme 1 are rare. Because of the apparent monomer−dimer structural relationship between pib and bpib, one possible explanation for the formation of bpib is that pib is the precursor which undergoes direct C−C coupling at the 3 position of indolyl to form the dimer. To confirm this, direct coupling of pib to form bpib was attempted using base and a copper catalyst at elevated temperatures as in the original reaction, but no reaction was observed. Li and co-workers have demonstrated copper-catalyzed C−C coupling reactions at unfunctionalized sp^2 carbon centers with the aid of an oxidant.[7] Unfunctionalized C−C bond formation for biaryl and bipyrroles has also been reported using a hypervalent iodine radical source such as phenyliodine bis(trifluoroactate) (PIFA).[8] Our attempts to use PIFA and other oxidants with or without copper using the reaction conditions reported in the literature failed to convert pib to bpib. However, if the reaction was carried out at high temperature (210 °C) in the presence of PIFA (with or without copper), some conversion of pib to bpib (∼15% by NMR) along with a large amount of decomposition products was observed. Our original one-pot reaction is therefore still the simplest and the best way to produce bpib.

Direct C−C coupling of indole via either a potassium salt or a lithium salt intermediate and the subsequent oxidation by oxidants such as I_2 was known to produce 3,3′-bi-indole in low yield.[9] In our reactions, brominated benzenes are likely the source of radical oxidants generated under the high-temperature reaction conditions. The 2-py group on the indole ring likely functions as a directing group that binds to the Cu ion initially, facilitating the activation of the C−H bond and the subsequent 3,3′-C−C coupling. Similar *ortho*-assisted 1,1′-C−C coupling of naphthalene[1a,5] and C−C coupling in other molecules are well documented.[10]

The new ligands listed in Figure 1 are fully characterized by NMR, elemental analyses, or HRMS. The crystal structures of the dimer bpib and bbib have been determined by X-ray diffraction analyses and are shown in Figure 2. Both bpib and bbib have an approximate C_2 symmetry. The dihedral angle between the indolyl rings is 125.1° for bpib

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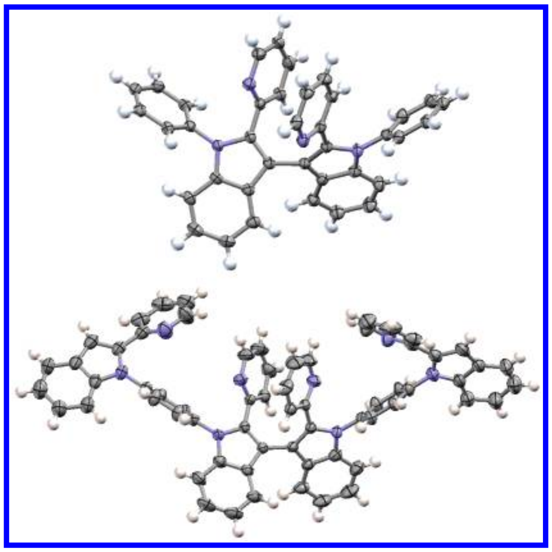

Figure 2. Crystal structures of bpib (top) and bbib (bottom).

and 128.5° for bbib. There are significant $\pi-\pi$ interactions between the two central pyridyl rings with the atomic separation distances being 3.57−4.00 Å for bpib and 3.50−3.90 Å for bbib. Consistent with the $\pi-\pi$ interactions between the two py rings in solution is the distinct upfield shift (~0.4 ppm) by the $C_{(6)}$-H proton of py in the ^{1}H NMR spectra, from monomer to dimer. DFT calculations performed on bpib indicate that the rotation barrier around the 3,3′-C−C bond is ~92 kJ/mol, which, compared to the rotation barriers reported for previously known axially chiral molecules,[4,11] indicates that the enantiomers of bpib may be resolvable at ambient temperature. However, despite numerous attempts, our efforts to resolve the enantiomers of the new ligands by repeated cocrystallization with optically pure tartaric acid using procedures[4] reported for 1,1′-bis(2-py-naphthyl) resolution have not been successful, possibly due to similar solubilities of the diastereomer salts.

The ability of the new 2-py functionalized 3,3′-bi-indolyls to act as ligands for metal ions is demonstrated by the formation and isolation of an orange Cu(I) complex $[Cu^I(bpib)_2]BF_4$ (**1**), isolated initially from the reaction of bpib with $[Cu^I(PPh_3)_2(CH_3CN)_2]BF_4$ in a 1:1 ratio in good yield (the 1:1 complex $[Cu^I(bpib)(PPh_3)_2]BF_4$ was not observed at all). Complex **1** was also obtained by the stoichiometric reaction of pbib with $[Cu^I(CH_3CN)_4]BF_4$. **1** is stable toward air in the solid state. It has a weak MLCT absorption band at 380−450 nm in the UV−vis spectrum, responsbile for its distinct orange color. The crystal structure of **1** is shown in Figure 3.

The crystals of **1** belong to the tetragonal chiral space group *I*422. The Cu(I) center in **1** has a distorted tetrahedral geometry with the N−Cu−N chelate bite angle being 137.1°.

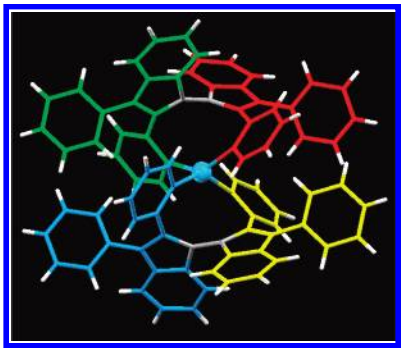

Figure 3. Crystal structure of $[Cu(bpib)_2]^+$. The D_2 symmetry related four subunits are shown in different colors. The two 3,3′ C−C bonds are shown in gray.

The $[Cu(bpib)_2]^+$ cation has a crystallographically imposed D_2 symmetry, which is a consequence of chelation by two identical enantiomers of bpib to the Cu(I) center. The crystal structure shows that the preferential "picking" by the Cu(I) ion for the same enantiomer is due to the favorable intraligand interactions. Despite the formation of the large nine-membered chelate ring, the fact that the bpib ligand can replace PPh_3 ligands on the Cu(I) center is an indication that the bpib ligand can act as a very effective chelate. In solution, ^{1}H NMR spectra showed that the phenyl groups in **1** display hindered rotation around the phenyl−indolyl C−C bond due to *ortho*-H interactions, similar to hindered rotations around C−N bonds of aryl−benzimidazolyl ligands in Cu(I) complexes.[12] In addition, one of the *ortho*-H atoms on the phenyl ring has an ~3 ppm upfield shift due to its interaction with the py "π-cloud"[13] from the second bpib ligand.

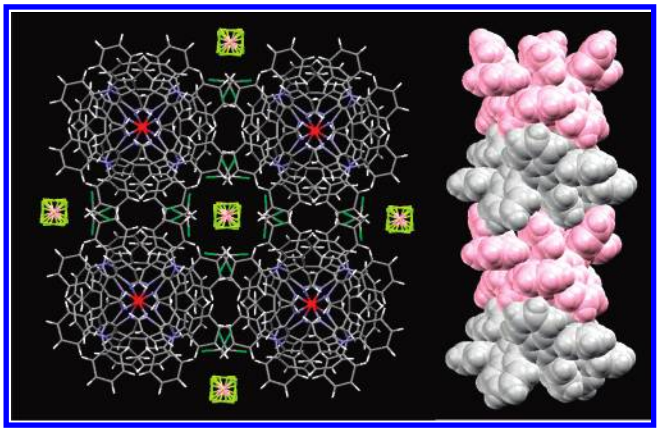

Figure 4. Left: lattice packing diagram of **1** projected down the *c*-axis. Cu, red; N, light blue; F, yellow; Cl, green; B, pink. Right: space-filling diagram showing four stacked cations.

Most interestingly, in the crystal lattice (Figure 4) **1** stacks along the *c*-axis to form homochiral columns, and the

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resulting channels are occupied by the BF_4^- anions and CH_2Cl_2 solvent molecules. The homochiral crystallization of **1** from a racemic solution mixture is interesting due to the relatively rare occurrence of such an event.[14] More important is that it allows us to separate the enantiomers by the Pasteur method, namely, hand picking the crystals.

The CD spectra of two hand-picked crystals of **1** with opposite chirality recorded in CH_2Cl_2 are shown in Figure 5. The spectra were monitored with time to determine the stability of **1** in solution at ambient temperature. We observed that in the absence of air the CD spectrum does not change for weeks, indicating that **1** retains its chiral structure in solution. Our attempts to free the ligand from the copper center by the addition of $[N(C_2H_5)_4]CN$ were unsuccessful. Ligands bbib and btib contain more pyridyl binding sites than bpib, thus more interesting and complex structures with metal ions are anticipated, which are being investigated. The results will be reported in due course.

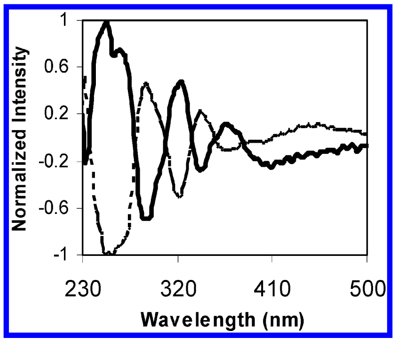

Figure 5. CD spectra of two crystals of **1** with opposite chirality recorded in CH_2Cl_2 at 298 K.

The impact of the 3,3′-C−C coupling on the electronic properties of the ligands was investigated by UV−vis and fluorescent spectroscopic methods. Compared to the corresponding monomer, the bi-indolyl molecules have a shoulder peak at ∼350 nm in the UV−vis spectra, which most likely originated from $\pi-\pi$ interactions of the two central pyridyl rings in the dimer, as revealed by the crystal structures of bpib and bbib. The most significant difference between the monomer and the dimer is observed in the fluorescent spectra. As shown in Figure 6, all monomers emit in the UV region with $\lambda_{max} = 385-389$ nm ($\Phi = 0.45$ for pib). In contrast, all dimers emit in the visible region with $\lambda_{max} = \sim 445$ nm ($\Phi = 0.22$ for bpib). This dramatic spectral red shift and the identical emission spectra by all dimers are consistent with intramolecular excimer formation between the two central py rings in the dimer, a phenomenon similar to the recently reported intramolecular excimer emission involving two carbazole rings[15] or two pyrene rings in a sterically constrained environment.[16] The restricted rotation around the 3,3′-C−C bond in the "dimer" molecules is believed to facilitate the intramolecular py−py interaction and the excimer formation.

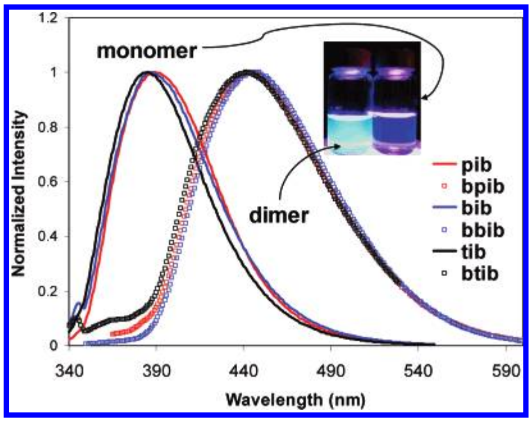

Figure 6. Emission spectra of the ligands in CH_2Cl_2 ($\sim 1 \times 10^{-5}$ M). Inset: photograph of pib (right) and bpib (left) under UV light.

In summary, we have shown that new atropisomeric ligands with py binding sites and a 3,3′-bi-indolyl backbone along with the corresponding monomers can be obtained by one-pot reactions catalyzed by copper ions. These reactions involve the formation of multiple C−N and C−C bonds and likely complex mechanisms that are not fully understood. In addition, we have shown that the new "dimer" ligands display intramolecular excimer emission and are capable of forming chiral chelate metal complexes, which may find applications in asymmetric catalysis and chiral sensing.

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Supporting Information Available: Synthetic procedures, crystallographic tables, figures and cif files, NMR data, molecular orbital details, UV−vis spectra, and low-temperature emission spectra of pib and bpib. This material is available free of charge via the Internet at http://pubs.acs.org.

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