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Improved synthesis of functionalized mesogenic 2,6-bisbenzimidazolylpyridine ligands

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ABSTRACT

A versatile one-pot synthetic platform for the preparation of a range of functionalized 2,6-bisbenzimidazolylpyridine (Bip) derivatives is presented. This protocol significantly reduces the cost and time of previous synthetic routes, while facilitating scale up to multi-gram quantities in good yields (63–90%). The previous synthetic methodology was improved through judicious choice of the reducing agent and solvent in the reduction/ring-closing step. Via this platform, we also successfully accessed a mesogenic Bip ligand and herein report initial liquid crystalline properties of this derivative.

1. Introduction

Over the years, the development of aromatic aza-heterocycles as ligands has provided a valuable resource for researchers working in the field of metal–ligand coordination.[1] Aromatic terdentate ligands are one important class of such aza-ligands, of which terpyridine (Terpy, Fig. 1a) is the most widely utilized and studied.[2] An alternative terdentate aza-ligand, which has garnered much less attention, is the 2,6-bisbenzimidazolylpyridine (Bip, Fig. 1b) core. Nonetheless, this molecular framework has been shown by a number of groups to be versatile and useful in a variety of areas. For example, Piguet and co-workers have used Bip derivatives extensively in several studies of liquid crystalline complexes containing lanthanides,[3,4] to access triple helicates,[5] and to study the communication between lanthanides and transition metals.[6] Benicewicz and co-workers[7] have prepared a polymeric analog of Bip and studied its potential as a material for fuel cell membranes, while Haga and co-workers have studied Bip derivatives in multilayered structures[8] and prepared ruthenium complexes with Bip derivatives with the goal of developing pH-sensitive molecular switches.[9] A number of other groups have studied the physical properties of Bip derivative complexes[10] and investigated these ligands in areas such as urea recognition,[11] DNA binding,[12] nanoparticle preparation,[13] and catalysis.[14] We have been investigating Bip derivatives for use in a number of related areas, including chemical sensors[15] and in a variety of metallo-supramolecular polymers,[16] ranging from thermoplastic elastomers[17] and gels[18] to processable poly(*p*-xylylene)[19] and poly(*p*-phenylene ethynylene).[20]

The most common route[10c,21] to simple Bip derivatives is the reaction of *o*-diaminobenzene derivatives with 2,6-pyridine dicarboxylic acid using 85% phosphoric acid at temperatures exceeding 200 °C, in which the key step is the formation of the benzimidazole rings. However, the harsh conditions of this reaction limit its utility to access a wide variety of highly substituted Bip materials in good yield.

With the goal of expanding the repertoire of Bip ligands that can be incorporated into macromolecular assemblies, an efficient and

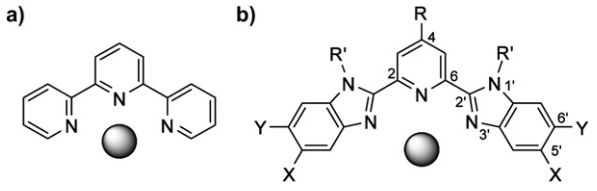

Figure 1. Metal-binding conformation of the terdentate ligands (a) terpyridine (Terpy) and (b) 2,6-bisbenzimidazolylpyridine (Bip) with labeled functional sites: R, R′, X, and Y. The gray spheres represent metal ions.

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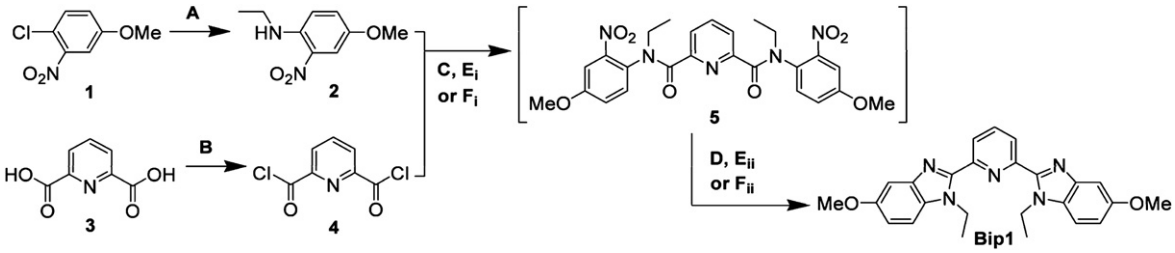


Scheme 1. Synthesis of 2,6-bis(1′-ethyl-5′-methoxybenzimidazol-2′-yl)pyridine (**Bip1**). (A) NH_2Et, high pressure flask, 105 °C, 24 h, 92%; (B) $SOCl_2$, DMF, 75 °C, 2 h, quantitative; (C) $CHCl_3$, NEt_3, reflux, 8 h, 60% (Ref. 22); (D) activated iron, EtOH, H_2O, HCl, reflux, 12 h, 75% (Ref. 22); (E) (i) NMP, 50 °C, 8 h; (ii) activated iron, NMP, HCl, 90 °C, 12 h, EDTA in H_2O, 90%; (F) (i) DMF, rt, 18 h; (ii) $Na_2S_2O_4$, DMF, EtOH, H_2O, 85 °C, 18 h, 70%.

robust synthetic approach to highly functionalized Bip derivatives is necessary. Herein we report a versatile synthetic platform, which allows facile access to such compounds in high yields and multi-gram quantities. We go on to describe how such ligands can be readily functionalized to access monomers suitable for polymerization and that these simple derivatives possess mesogenic properties.

2. Results and discussion

2.1. Previous Bip derivative syntheses

Piguet and co-workers[22] published an elegant solution to the synthesis of functionalized Bip derivatives from an *N*-alkyl-*o*-nitroaniline derivative and 2,6-pyridine dicarboxylic acid chloride. An example of this is shown in Scheme 1. Targeting **Bip1**, ethylamine was reacted with the commercially available 4-chloro-3-nitroanisole (**1**) yielding the desired *N*-ethyl-2-nitroaniline (**2**). 2,6-Pyridine dicarboxylic acid (**3**) was then activated with thionyl chloride to produce 2,6-pyridine dicarboxylic acid chloride (**4**), which was subsequently reacted with **2** in the presence of triethyl amine in chloroform to yield **5** in 60% yield after purification via column chromatography. The desired Bip derivative could then be accessed under relatively milder conditions compared to the previously described method by reduction of the nitro group and subsequent ring-closing with activated iron and hydrochloric acid in aqueous ethanol at 80 °C. Excess iron was removed using a saturated aqueous ethylenediaminetetraacetic acid (EDTA) solution and the crude reaction mixture was neutralized using aqueous ammonium hydroxide. The derivative **Bip1** was isolated in 75% yield after purification by column chromatography. Thus, the overall yield of **Bip1** from **2** and **4** was 45%. We have also followed this synthetic protocol and have accessed **Bip1** in similar overall yields (45%, Table 1) in a process that required 3–4 days to complete from **2** and **4**.

With the goal of being able to quickly obtain multi-gram quantities of Bip derivatives we sought ways to streamline this protocol and improve its yield while maintaining the ability to access a range of functionalized Bip ligands.

Table 1
Bip derivatives, preparation methodology, and isolated yield

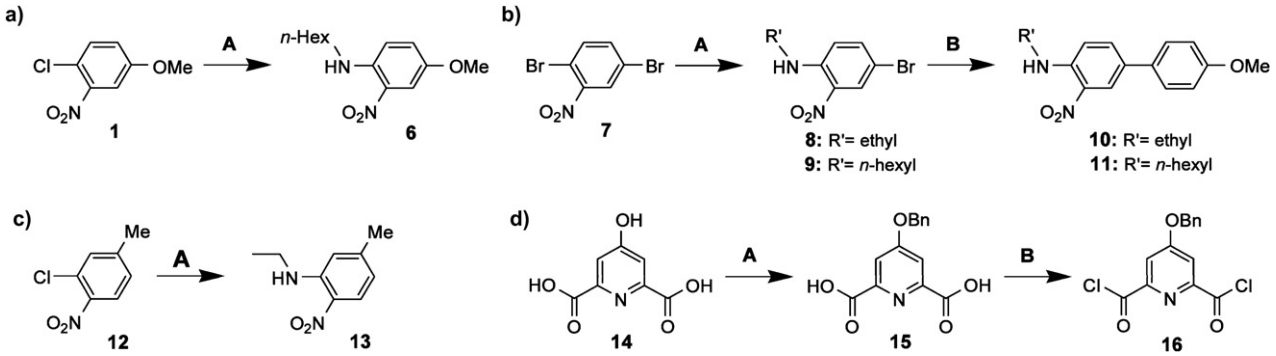
	Bip derivative substitution pattern (Fig. 1b)				Method[a]	Isolated yield[b] (%)
	R	R′	X			
Bip1	H	Et	OMe	H	Two step[c]	45 (lit.: 45[22])[d]
					Fe	90
					$Na_2S_2O_4$	70
Bip2	H	*n*-Hex	OMe	H	Fe	63
					$Na_2S_2O_4$	65
Bip3	H	Et	PhOMe	H	Fe	83
					$Na_2S_2O_4$	72
Bip4	H	*n*-Hex	PhOMe	H	Fe	72
					$Na_2S_2O_4$	69
Bip5	H	Et	H	Me	Fe	84
Bip6	OBn	Et	OMe	H	Fe	72
					$Na_2S_2O_4$	70
Bip7	OMe	Et	OBn	H	$Na_2S_2O_4$	81

[a] Unless otherwise stated, these reactions were performed using either activated iron/HCl ('Fe') or sodium dithionite in aqueous ethanol ('$Na_2S_2O_4$').
[b] Starting from the appropriate *o*-nitroaniline and dicarboxylic acid chloride.
[c] Two-step synthesis following the protocol published by Piguet and co-workers.
[d] Combined yield from the two-step reaction.

2.2. Modification of the Bip protocol: one-pot synthesis with NMP as the solvent

Work by Korshak and co-workers[23] showed that polybenzimidazoles can be accessed by reacting aromatic ditopic *o*-nitroamines and aryl diacid chlorides. The major difference in this approach as compared to the Piguet method described above was the use of *N*-methyl-2-pyrrolidinone (NMP) as the solvent in a one-pot reaction. NMP was chosen to increase solubility of the polymer and thus enhance the propensity for complete reduction and ring-closing. Thus, our first modification to the procedure utilized by Piguet and co-workers was to directly synthesize **Bip1** from **2** and **4** in one-pot using NMP as a common solvent for both reactions (Scheme 1, E_i and E_{ii}). Upon addition of saturated aqueous EDTA and sodium bicarbonate to the reaction mixture, **Bip1** precipitated in 90% yield (pure by ^1H NMR), removing the need for chromatography. Thus, not only does this procedure double the yield of the reaction, it also reduces the preparation time for **Bip1**, from the starting materials **2** and **4**, from ca. four days to one day.

To further examine the versatility of this synthetic protocol, we targeted a range of substituted Bip derivatives (Table 1). With a view to accessing soluble macromolecular architectures we wanted to pursue Bip ligands, which showed enhanced solubility. We, therefore, decided to synthesize Bip ligands, which have solubilizing groups (*n*-hexyl) at the 1′-positions (R′ sites, Fig. 1b). To achieve this, hexylamine was reacted with **1** at 85 °C producing the oily product **6** (Scheme 2a), which was then reacted with **4** under the same modified conditions using NMP as the reaction medium. On account of the 'desired' increased solubility of **Bip2**, it did not precipitate and required column chromatography, which might help to explain the slightly lower yield (63%) compared to **Bip1**. We were also interested in Bip ligands with extended 'arms', so we investigated the synthesis of ligands, which have an aryl substituent in the 5′-positions (X sites, Fig. 1b). Addition of either ethylamine or hexylamine to 2,4-dibromonitrobenzene (**7**) yielded *N*-ethyl-4-bromo-2-nitroaniline (**8**) and *N*-hexyl-4-bromo-2-nitroaniline (**9**), respectively. Suzuki coupling[24] of **8** or **9** with 4-methoxyphenyl boronic acid in the presence of a palladium(0) catalyst yielded the extended *o*-nitro-4-(4′-methoxy)phenylanilines **10** and **11** (Scheme 2b), respectively. Gratifyingly, subsequent reaction of **10** or **11** with **4**, using our modified conditions allowed access to **Bip3** and **Bip4**, respectively, in good yield. Like **Bip1**, the



Scheme 2. (a) (A) NH_2(*n*-hex), 85 °C, 24 h, 90%. (b) (A) NH_2Et, high pressure flask, 105 °C, 24 h, 93% or NH_2(*n*-hex), 85 °C, 24 h, 94%; (B) 4-methoxphenyl boronic acid, K_2CO_3, THF, H_2O, $Pd(PPh_3)_4$, 75 °C, 18 h, 96–98%. (c) (A) NH_2Et, high pressure flask, 105 °C, 24 h, 95%. (d) (A) (i) MeOH, H_2SO_4, 80 °C, 4 h; (ii) BnBr, K_2CO_3, acetonitrile, 70 °C, 22 h; (iii) precipitate from hot EtOH with KOH; (iv) precipitate from H_2O with HCl, quantitative; (B) $SOCl_2$, DMF, 75 °C, 2 h, quantitative.

R′=ethyl derivative, **Bip3**, precipitated from the saturated aqueous EDTA/base solution and was shown to be pure by ^{1}H NMR (83% yield). However, the *n*-hexyl derivative, **Bip4** required column chromatography to yield, in 72%, the pure product. Using this methodology, we also synthesized **Bip5**, which has methyl substituents at the 6′-positions (Y sites, Fig. 1b). As before, the substitution on the benzimidazole moiety was determined by the nature of the *o*-nitroaniline (Scheme 2c, **13**) starting material.

In a number of our previous studies,[15–20] we have utilized a functional group on the 4-position to access Bip end-capped macromonomers. Therefore, we went on to study the potential of this synthetic methodology to access highly functionalized Bip derivatives where one of the substituents was in the 4-position. Thus, we started by protecting chelidamic acid (**14**) with a benzoxy moiety to yield **15** (Scheme 2d).[25] Following activation with thionyl chloride, **16** can be reacted with an appropriate *N*-alkyl-*o*-nitroaniline derivative, e.g., **2**, using our modified protocol to access **Bip6**. As before for the R′=ethyl derivative no column was required to purify **Bip6** (it precipitated from the saturated aqueous EDTA/base solution). However, removal of the Fe^{II} did appear more difficult than for previous ligands, possibly on account of the electron donating properties of the alkoxy group on the 4 position (Fig. 1b) enhancing metal binding. Thus, extensive washing with multiple batches of aqueous EDTA was required to extract the Fe^{II} from **Bip6**.

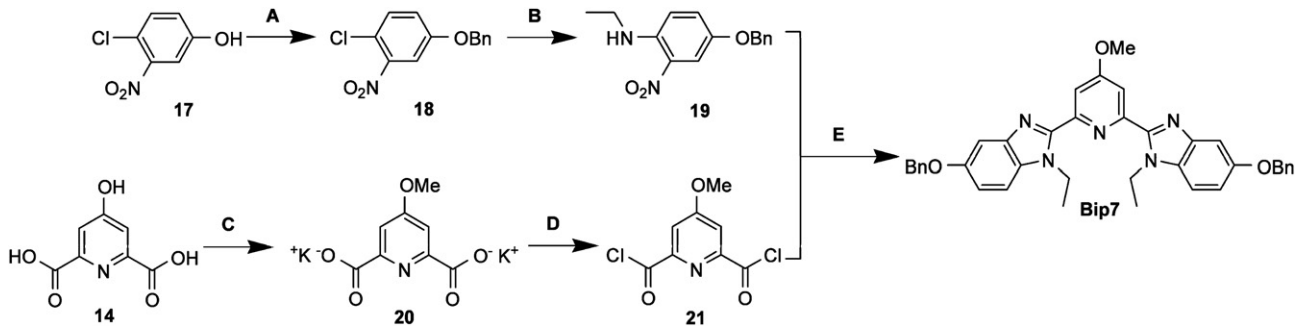
Using this modified NMP/one-pot strategy, six derivatives (**Bip1**–**Bip6**) were successfully synthesized in good to excellent overall yields ranging from 63–90% (Table 1).

2.3. Use of sodium dithionite and aqueous ethanol as the reducing agent in the one-pot synthesis of Bip derivatives

While the above new one-pot procedure works effectively, the use of activated iron in the reduction/ring-closing step has two major disadvantages. First, the oxidized Fe^{II} binds strongly within the Bip cavity and needs to be removed by thorough washing with aqueous EDTA. An additional issue that becomes a significant problem for large-scale synthesis is the cost of the activated iron; currently approximately $40 for 5 g, which produces ca. 3 g of Bip derivative.

Work by Fokas and co-workers[26] showed that benzimidazoles can be accessed in one step by reacting *o*-nitroanilines and aryl aldehydes in the presence of the reducing agent sodium dithionite ($Na_2S_2O_4$) in a dimethyl sulfoxide/ethanol/water mixture at 70–80 °C. Inspired by this, we hypothesized that $Na_2S_2O_4$ could replace activated iron in the reduction/ring-closing step in our one-pot Bip synthesis. If successful, this procedure would eliminate the need for activated iron and therefore washing the product with EDTA. Furthermore, with an eye toward scaling up, $Na_2S_2O_4$ is approximately 20 times less expensive than activated iron.

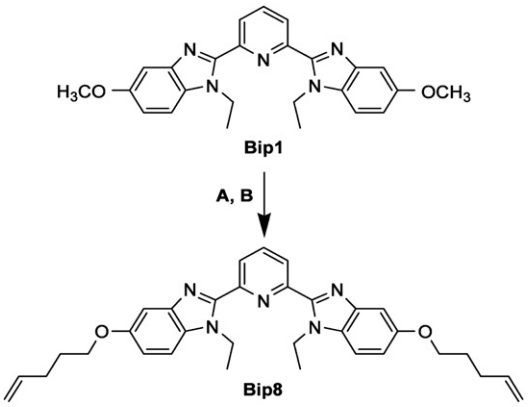
Gratifyingly, following in situ formation of **5**, simple addition of an aqueous ethanolic solution of $Na_2S_2O_4$ results in the formation of **Bip1** from **2** and **4** (Scheme 1, F_i and F_{ii}). Addition of saturated aqueous sodium bicarbonate solution to the reaction mixture resulted in the precipitation of crude **Bip1**. Extraction of this solid with dichloromethane (DCM) yielded the desired product in 70% yield, which was confirmed by ^{1}H NMR. While this purification methodology was efficient for **Bip1**, as before, the *n*-hexyl derivatives (**Bip2** and **Bip4**) did not precipitate from the basic aqueous solution. Therefore, to facilitate a more efficient workup of these ligands, we replaced NMP with a lower boiling aprotic solvent, *N*,*N*-dimethylformamide (DMF). Using this DMF-based protocol we were able to access **Bip1**–**Bip4** and **Bip6** (Table 1) in yields similar to the one-pot activated iron/HCl method (65–81%). An additional derivative with benzoxy substituents in the 5′-positions (X sites, Fig. 1b) and a methoxy substituent in the 4-position (Scheme 3) was also prepared via these reaction conditions, yielding **Bip7** in 81% yield (Table 1).



Scheme 3. (A) BnBr, K_2CO_3, acetonitrile, 70 °C, 22 h, quantitative; (B) NH_2Et, high pressure flask, 105 °C, 24 h, 95%; (C) (i) MeOH, H_2SO_4, 80 °C, 4 h; (ii) CH_3I, K_2CO_3, acetonitrile, 70 °C, 22 h; (iii) precipitate from hot EtOH with KOH, 90%; (D) $SOCl_2$, DMF, 75 °C, 2 h, quantitative; (E) (i) DMF, rt, 18 h; (ii) $Na_2S_2O_4$, DMF, EtOH, H_2O, 85 °C, 18 h, 81%.

2.4. Synthesis and liquid crystalline properties of Bip8

To demonstrate the facile conversion of these Bip derivatives into monomers suitable for polymerization, we converted **Bip1** into the alkene-functionalized **Bip8** (Scheme 4) via a two-step process adapted from the literature.[22,27] The methoxy groups were deprotected with boron tribromide (BBr_3) in DCM and the resulting phenolic groups were reacted with 5-bromopentene to access **Bip8** in good yield (75% from **Bip1**). Interestingly, these simple ligands display thermotropic liquid crystalline properties upon cooling (I 97.7 N ~2 °C g). The differential scanning calorimetry (DSC) cooling (top) trace in Figure 2 reveals, upon cooling from 200 °C, a small exotherm at 97.7 °C. Polarized light optical microscopy (POM) images taken during a similar thermal program show a transition from an isotropic state to a birefringent Schlieren texture indicative of nematic liquid crystalline order (Fig. 2). The temperature of this phase transition (~100 °C) corresponds to the exotherm in the DSC cooling trace. Further cooling reveals a T_g of approximately 2 °C in the DSC, while POM reveals that the liquid crystallinity remains intact throughout the cooling. This transition appears to be monotropic, as, upon heating, no liquid crystalline transitions are apparent via DSC or POM. Upon heating, the monomer does exhibit a T_g (~9 °C) before it recrystallizes at 42.5 °C and subsequently melts at 106.5 °C.



Scheme 4. Synthesis of **Bip8**. (A) BBr_3, rt, 4 h, quantitative; (B) $Br(CH_2)_3CH{=}CH_2$, K_2CO_3, 4:1 THF/methanol, 75 °C, 12 h, 75%.

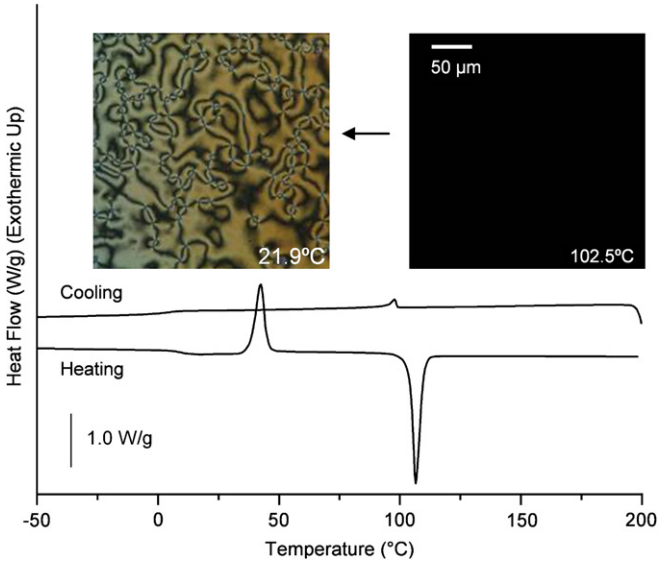


Figure 2. DSC thermogram and POM images of **Bip8** showing the transition from an isotropic to a liquid crystalline state upon cooling. DSC thermal program: equilibrate at −90 °C, heat to 200 °C at 10 °C/min, hold 1 min, cool to −90 °C at 10 °C/min, hold 1 min, heat to 200 °C at 10 °C/min, hold 1 min, cool to −90 °C at 10 °C/min. POM thermal program: heat to 200 °C at 10 °C/min, hold 10 min, cool to −10 °C at 10 °C/min, hold 1 min, heat to 25 °C at 10 °C/min, heat to 200 °C at 10 °C/min, hold 1 min, cool to −10 °C at 10 °C/min. Trace and images are from second cools.

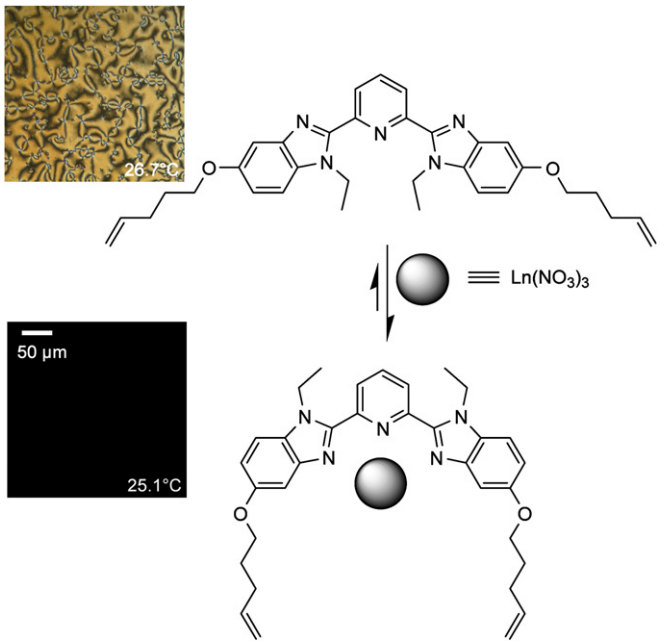


Figure 3. Bip8 binding with a lanthanide nitrate and POM images showing the resulting transition from a liquid crystalline to an isotropic state (POM: **Bip8**/$Eu(NO_3)_3$=1:1).

Piguet and co-workers have designed a variety of mesogenic Bip derivatives and have observed liquid crystalline behavior of such ligands in 1:1 lanthanide complexes.[3,4] We hypothesized that with our 'simple' mesogens the addition of metals would disrupt liquid crystallinity, in part, on account of the smaller aspect ratio and generally less stable mesogenic phases relative to many of the Piguet systems. As a simple demonstration of the chemo-responsive nature of **Bip8**, we examined the POM of the free ligand and its 1:1 complex with $Eu(NO_3)_3$. Figure 3 shows that the **Bip8**·$Eu(NO_3)_3$ complex shows no birefringence, indicative of a 'switching off' of the ligand's liquid crystalline behavior upon complexation with $Eu(NO_3)_3$ at room temperature. Since the binding of such metal ions to Bip is reversible, this could provide a facile route to interesting chemo-responsive liquid crystalline materials.

3. Conclusion

Using a one-pot procedure, we successfully synthesized highly functionalized Bip derivatives (**Bip1**–**Bip7**) with increased yields (63–90% vs 45% for the two-step protocol) and subsequently reduced preparation time from approximately four days to one day. In addition, the R′=ethyl derivatives were determined pure by ^1H NMR and did not require column chromatography. Substituting $Na_2S_2O_4$ for activated iron in the reduction/ring-closing step significantly reduced the cost of the synthesis and eliminated the need to decomplex Fe^{II} from the Bip cavity, further simplifying workup. Overall, the modifications to this protocol proved to be versatile for a range of substituents on the Bip core and allowed access to these ligands on a multi-gram scale. We are currently investigating incorporating these derivatives into a range of macromolecular architectures.

4. Experimental

4.1. General

4-Hydroxypyridine-2,6-dicarboxylic acid (chelidamic acid) was purchased from TCI America and tetrakis(triphenylphosphine) palladium(0) catalyst was purchased from Strem, Inc. All solvents, ammonium chloride, potassium carbonate, potassium hydroxide, sodium dicarbonate, and sodium hydroxide were purchased from Fisher Scientific. Ethylenediaminetetraacetic acid was purchased from Acros. All other chemicals including activated iron were purchased from Aldrich. Solvents were dried accordingly via distillation.

4.1.1. Infrared spectra

IR spectra were recorded as potassium bromide disks on a ABB Bomem MB104 FT-IR spectrometer.

4.1.2. NMR spectra

NMR spectra were recorded on either a Varian Inova 600 MHz NMR spectrometer (^{13}C NMR=150.8 MHz) or a Varian Mercury 300 MHz NMR spectrometer (^{13}C NMR=75.5 MHz) using the deuterated solvents chloroform-*d*, deuterium oxide, or dimethyl sulfoxide-d_6, purchased from Norell, Inc., USA.

4.1.3. Mass spectra

Mass spectra were recorded on a Bruker AutoFlex III MALDI-TOF MS instrument using the matrix 2-(4-hydroxyphenylazo)benzoic acid (HABA) and potassium iodide (KI), if necessary.

High resolution mass spectra were carried out on a Kratos MS25RFA GC/mass spectrometer using the fast atom bombardment (FAB) capability.

4.1.4. High pressure liquid chromatography

All high pressure liquid chromatography (HPLC) experiments were run on a Varian ProStar with reverse-phase C_{18} silica analytical column using the following procedures: flow rate=1 mL/min, solvent A=H_2O (0.10% trifluoroacetic acid, TFA), solvent B=acetonitrile (MeCN, 0.08% TFA). Solvent program: 98%, A 2% B. Ramp to 2% A, 98% B, over 20 min, hold for 10 min. Elution time was reported at 365 nm wavelength, unless otherwise noted.

4.1.5. Differential scanning calorimetry

Differential scanning calorimetry (DSC) experiments were performed on a TA Instruments Q100 DSC equipped with a refrigerated cooling system (RCS). The DSC cell resistance and capacitance were calibrated using the Tzero calibration procedure (TA Instruments-Waters LLC), and the cell constant and temperature were calibrated using an indium standard. All samples were run under flowing nitrogen atmosphere and were heated and cooled at rate of 10 °C/min through the temperature range of −90 to 200 °C. This temperature range proved sufficient to analyze the glass, melting, and isotropization (clearing) transitions in this study. The glass transition temperatures were determined by taking the midpoints of the stepwise change in the heat flow signal from the second heating and second cooling traces. Recrystallization, melting, and clearing temperatures of these monomers were determined from either the peak maximum (for exotherm) or minimum (for endotherm) on the second heating or cooling traces.

4.1.6. Polarized light optical microscopy

Polarized light optical microscopy (POM) studies were performed using an Olympus BX51 microscope equipped with 90° crossed polarizers, a HCS402 hot stage from Instec Inc., and a digital camera (14.2 Color Mosaic Model from Diagnostic Instruments, Inc.). Images were acquired from the camera at selected temperatures using Spot software (Diagnostic Instruments, Inc.). Spatial dimensions were calibrated using a stage micrometer with 10 μm line spacing. Either a 50×/0.5 NA or a 20×/0.4 NA achromat long working-distance objective lens (Olympus LMPlanFI) was employed. The Instec hotstage was equipped with a liquid nitrogen LN2-P cooling accessory for accurate temperature control during heating and cooling runs. The ligand POM sample was dissolved in chloroform to give a 0.5 wt % solution. For the metal-binding experiment, the ligand and one molar equivalent of $Eu(NO_3)_3$ were weighed into a vial, dissolved in acetonitrile, and dried in vacuo. This complex was then dissolved in acetonitrile to give a 0.5 wt % solution. Microscopy slides were prepared by dropping these solutions onto clean microscope slides, which were covered to slow evaporation until this was complete. To clear thermal history, the samples were heated to 200 °C, held at 200 °C for 1 min, cooled to −10 °C at 10 °C/min, held at −10 °C for 1 min, and finally heated to 25 °C at 10 °C/min. The samples were then heated to 200 °C at 10 °C/min, held at 200 °C for 1 min, and cooled to −10 °C at 10 °C/min. Optical micrographs were collected during these second heating and cooling steps.

4.2. Synthesis

N-Ethyl-4-methoxy-2-nitroaniline (**2**)[22] was synthesized according to the literature procedures.

4.2.1. General N-ethyl-2-nitroaniline synthesis

Using a heavy wall glass pressure vessel, the halogenated nitrobenzene compound (10 g) was dissolved in 60–80 mL ethylamine (70 wt %) in water solution. The reaction vessel was sealed, placed in an oil bath heated to 105 °C, and stirred for at least 24 h. The reaction was allowed to cool, poured into dichloromethane (DCM, 50 mL), and washed with half saturated ammonium chloride (3×, 100 mL). The organic solvent was removed in vacuo.

*4.2.1.1. 4-Bromo-N-ethyl-2-nitroaniline (**8**).*[28] Purified via column chromatography on silica (chloroform, $CHCl_3$). Red/orange solid, yield: 93%, mp: 86–89 °C, TLC: 50:50 hexanes/$CDCl_3$ R_f=0.50. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.31 (d, 1H, *J*=2.4 Hz, ArH), 7.95 (br s, 1H, ArH), 7.48 (m, 1H, ArH), 6.75 (d, 1H, *J*=9.6 Hz, ArH), 3.33 (m, 2H, CH_2CH_3), 1.36 (t, 3H, *J*=6.0 Hz, CH_2CH_3). ^{13}C NMR (150.8 MHz, $CDCl_3$) δ (ppm): 144.3, 138.8, 128.8, 115.4, 106.1, 37.8, 14.2. IR (KBr): 3376, 3319, 2981, 2909, 2863, 1614, 1562, 1505, 1474, 1426, 1348, 1264, 1233, 1158, 1137, 1073, 1031 cm^{-1}. HPLC: 20.5 min. HRMS (FAB, M^+) calcd for $C_8H_9N_2O_2Br$ 243.9847, found 243.9841.

*4.2.1.2. N-Ethyl-5-methyl-2-nitroaniline (**13**).* Purified via column chromatography on silica (hexanes/DCM=100:0–0:100). Orange solid, yield: 95%, mp: 53–56 °C, TLC: 50:50 hexanes/$CDCl_3$ R_f=0.37. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.00 (d, 1H, *J*=1.5 Hz, ArH), 7.97 (br s, 1H, NH), 6.57 (s, 1H, ArH), 6.39 (dd, 1H, *J*=0.9, 1.5 Hz, ArH), 3.29 (m, 2H, CH_2), 2.31 (s, 3H, ArCH_3), 1.33 (t, 3H, *J*=3.6 Hz, CH_2CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm): 147.9, 145.6, 129.8, 126.8, 117.0, 113.5, 37.9, 22.5, 14.7. IR (KBr): 3373, 3352, 2966, 2921, 2875, 1629, 1580, 1497, 1475, 1342, 1318, 1263, 1182, 1150, 1076, 1013 cm^{-1}. HPLC: 18.9 min. HRMS (FAB, MH^+) calcd for $C_9H_{13}N_2O_2$ 181.0977, found 181.0985.

*4.2.1.3. 4-Benzoxy-N-ethyl-2-nitroaniline (**19**).* 4-Chloro-3-nitrophenol (1.00 g, 5.76 mmol), distilled acetonitrile (30 mL), K_2CO_3 (4.00 g), and benzyl bromide (1.032 g, 6.036 mmol) were reacted at 75 °C for 24 h under an Ar atmosphere. Solvent was removed in vacuo leaving yellow orange crystals. The crude product was dissolved in chloroform and washed with water. The solvent was removed in vacuo yielding yellow orange crystals that melted at 36–38 °C, which were used without further purification. TLC: 50:50

DCM/hexanes R_f=0.33. This product was used following the procedures for *N*-ethyl-2-nitroaniline synthesis, above. The product was purified via column chromatography on silica (hexanes/DCM=100:0–0:100), which also separated out the byproducts from reactions with benzyl bromide. Bright red crystals, overall yield: 95%, mp: 83–86 °C, TLC: 50:50 DCM/hexanes R_f=0.21. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.98 (s, 2H, PyrH), 7.39 (m, 4H, ArH), 7.05 (dd, 2H, *J*=9.3, 3.0 Hz, ArH), 4.85 (q, 2H, *J*=7.2 Hz, CH_2CH_3), 3.90 (s, 3H, OCH_3), 1.37 (t, 3H, *J*=7.2 Hz, CH_3). ^{13}C NMR (150.8 MHz, $CDCl_3$) δ (ppm): 156.0, 150.7, 150.3, 142.8, 130.1, 114.2, 110.8, 101.1, 55.8, 39.9, 15.5. IR (KBr): 3379, 3358, 3044, 2963, 2927, 2848, 1635, 1574, 1529, 1511, 1384, 1345, 1278, 1218, 1155, 1055, 1010 cm^{-1}. HPLC: 21.4 min. MALDI-MS (*m*/*z*, matrix: none): $[M+K]^+$ 312.

4.2.2. General N-hexyl-2-nitroaniline synthesis

The appropriate halogenated nitrobenzene (43 mmol) was added to a round bottom flask followed by 70 mL of hexyl amine. The flask was stirred at 75 °C for 12 h. The reaction volume was diluted with DCM and extracted with half saturated ammonium chloride (3×100 mL) and water (1×200 mL). The organic phase was dried over Na_2SO_4 and the solvent was removed in vacuo.

*4.2.2.1. N-Hexyl-4-methoxy-2-nitroaniline (**6**).* Purified via column chromatography on silica (hexanes/DCM=100:0–0:100). Red oil, yield: 90%, TLC: 50:50 hexanes/$CDCl_3$ R_f=0.21. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.02 (br s, 1H, NH), 7.58 (d, 1H, *J*=3.0 Hz, ArH), 7.13 (dd, 1H, *J*=3.0, 9.6 Hz, ArH), 6.81 (d, 1H, *J*=9.6 Hz, ArH), 3.78 (s, 3H, OCH_3), 3.27 (q, 2H, *J*=5.4 Hz, NCH_2), 1.70 (p, 2H, *J*=7.2 Hz, NCH_2CH_2), 1.42 (p, 2H, *J*=7.2 Hz, $NCH_2CH_2CH_2$), 1.32 (m, 4H, $CH_2CH_2CH_3$), 0.89 (t, 3H, *J*=7.2 Hz, CH_2CH_3). ^{13}C NMR (150.8 MHz, $CDCl_3$) δ (ppm): 149.1, 141.5, 130.2, 127.3, 115.1, 106.6, 55.7, 43.2, 31.4, 29.0, 26.7, 22.5, 14.0. IR (KBr): 3376, 2957, 2933, 2857, 1574, 1523, 1493, 1443, 1348, 1273, 1231, 1149, 1061, 1043 cm^{-1}. HPLC: 22.3 min (λ=280 nm). HRMS (FAB, M^+) calcd for $C_{13}H_{20}N_2O_3$ 252.1474, found 252.1466.

*4.2.2.2. 4-Bromo-N-hexyl-2-nitroaniline (**9**).* Purified via column chromatography on silica ($CHCl_3$). Red crystals, yield: 94%, mp: 25 °C, TLC: 50:50 hexanes/$CDCl_3$ R_f=0.52. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.28 (d, 1H, *J*=2.4 Hz, ArH), 8.02 (br s, 1H, NH), 7.46 (dd, 1H, *J*=2.4, 9.0 Hz, ArH), 6.74 (d, 1H, *J*=9.0 Hz, ArH), 3.26 (m, 2H, NCH_2), 1.70 (tt, 2H, *J*=7.2 Hz, NCH_2CH_2), 1.42 (m, 2H, $NCH_2CH_2CH_2$), 1.32 (m, 4H, $CH_2CH_2CH_3$), 0.89 (m, 3H, CH_2CH_3); ^{13}C NMR (150.8 MHz, $CDCl_3$) δ (ppm): 144.5, 138.8, 128.8, 115.5, 106.1, 43.1, 31.4, 28.8, 26.6, 22.5, 14.0. IR (KBr): 3449, 3386, 2957, 2927, 2857, 1623, 1565, 1505, 1478, 1402, 1351, 1260, 1236, 1155, 1067 cm^{-1}. HRMS (FAB, M^+) calcd for $C_{12}H_{17}N_2O_2Br$ 300.0473, found 300.0476.

4.2.3. General Suzuki coupling reaction

The appropriate 4-bromo-2-nitrobenzeneamine (12.24 mmol), 4-methoxphenyl boronic acid (1.86 g, 12.2 mmol), and K_2CO_3 (3.21 g) were added to a round bottom flask. THF (86 mL) and water (34 mL) were combined and added to the flask, which was subsequently flushed with Ar. Tetrakis(triphenylphosphine)palladium(0) catalyst (0.78 g, 0.67 mmol) was then added. The round bottom was again flushed with Ar and heated to 75 °C for 18 h, stirring rapidly. The organic layer was removed in vacuo and the resulting dispersion extracted with chloroform (3×100 mL).

*4.2.3.1. N-Ethyl-2-nitro-4-(4′-methoxy)phenylaniline (**10**).* Purified via column chromatography on silica ($CHCl_3$/hexanes=70:30–100:0). Red/orange solid, yield: 98%, mp: 104–107 °C, TLC: 50:50 hexanes/$CDCl_3$ R_f=0.21. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.37 (d, *J*=2.4 Hz, 1H, ArH), 8.00 (br s, 1H, NH), 7.67 (m, 1H, ArH), 7.48 (d, *J*=9.0 Hz, 2H, ArH), 6.96 (d, 2H, *J*=9.0 Hz, ArH), 6.91 (d, 1H, *J*=9.0 Hz, ArH), 3.84 (s, 3H, OCH_3), 3.39 (m, 2H, NCH_2), 1.39 (t, 3H, *J*=7.2 Hz, CH_2CH_3). ^{13}C NMR (150.8 MHz, $CDCl_3$) δ (ppm): 158.9, 144.3, 134.8, 131.4, 128.1, 127.2, 123.8, 114.3, 55.3, 37.8, 14.4. IR (KBr): 3455, 3367, 2975, 2938, 2887, 2857, 1628, 1607, 1559, 1505, 1474, 1424, 1351, 1248, 1173, 1052, 1028 cm^{-1}. HPLC: 21.3 min (λ=310 nm). HRMS (FAB, M^+) calcd for $C_{15}H_{16}N_2O_3$ 272.1168, found 272.1161.

*4.2.3.2. N-Hexyl-2-nitro-4-(4′-methoxy)phenylaniline (**11**).* Purified via column chromatography on silica ($CHCl_3$/hexanes=70:30–100:0). Yield: 96%, mp: 79–81 °C, TLC: 50:50 hexanes/$CDCl_3$ R_f=0.26. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.36 (s, 1H, ArH), 8.07 (br s, 1H, ArH), 7.66 (dd, 1H, ArH), 7.47 (d, 2H, *J*=8.4 Hz, ArH), 6.95 (d, 2H, *J*=8.4 Hz, ArH), 6.90 (d, 1H, *J*=9.0 Hz, ArH), 3.83 (s, 3H, OCH_3), 3.32 (q, 2H, *J*=6.6 Hz, NCH_2), 1.73 (p, 2H, *J*=7.2 Hz, NCH_2CH_2), 1.45 (m, 2H, $NCH_2CH_2CH_2$), 1.34 (m, 4H, $CH_2CH_2CH_3$), 0.90 (m, 3H, CH_2CH_3). ^{13}C NMR (150.8 MHz, $CDCl_3$) δ (ppm): 144.5, 138.8, 128.8, 115.5, 106.1, 43.1, 31.4, 28.8, 26.6, 22.5, 14.0. IR (KBr): 3352, 2954, 2933, 2854, 1631, 1607, 1562, 1505, 1360, 1245, 1185, 1158, 1049, 1025 cm^{-1}. HPLC: 24.3 min (λ=310 nm). HRMS (FAB, M^+) calcd for $C_{19}H_{24}N_2O_3$ 328.1787, found 328.1787.

4.2.4. Addition of alkoxy substituent to 4-hydroxypyridine-2,6-dicarboxylic acid

*4.2.4.1. 4-Benzoxypyridine-2,6-dicarboxylic acid (**15**).* 4-Benzoxypyridine-2,6-dicarboxylic dipotassium salt was prepared according to the literature procedure[25] and dissolved in 20 mL deionized water. Hydrochloric acid was added dropwise until the solution reached a pH of 1 and a white precipitate formed. Yield: quantitative, mp: 120–122 °C. ^{1}H NMR (600 MHz, DMSO-d_6, 40 °C) δ (ppm): 7.95 (s, 2H, PyrH), 7.45 (d, *J*=7.64 Hz, ArH), 7.39 (t, *J*=7.36 Hz, ArH), 7.34 (d, *J*=7.36 Hz, 5H, PhH), 5.33 (s, 2H, OCH_2). ^{13}C NMR (150.8 MHz, DMSO-d_6, 40 °C) δ (ppm): 167.1, 166.0, 150.5, 136.3, 129.3, 129.0, 128.6, 114.6, 70.8.

*4.2.4.2. 4-Methoxypyridine-2,6-dicarboxylic dipotassium salt (**20**).* Chelidamic acid (**14**, 2.00 g, 10.9 mmol), degassed methanol (100 ml), and concentrated sulfuric acid (H_2SO_4, 20 drops) were combined and refluxed at 80 °C for 4 h. After cooling, the mixture was neutralized with a saturated solution of sodium bicarbonate ($NaHCO_3$) in water. The solvent was removed in vacuo, producing a yellow to white solid. Distilled acetonitrile (120 mL), K_2CO_3 (16 g), and iodomethane (2.28 g, 16.1 mmol) were added to the flask and refluxed at 70 °C for 22 h. Solvent was removed in vacuo. The resulting product was extracted with DCM (3×75 mL) from water. The organic layer was dried in vacuo. In a large beaker, ethanol (100 mL) and potassium hydroxide (KOH, 4.00 g) were stirred and heated until the KOH was fully dissolved. The product was dissolved in additional hot ethanol (150 mL). The hot ethanol/product mixture was slowly added to the hot ethanol/KOH mixture and a white precipitate immediately formed. The mixture stirred for 45 min. The white precipitate was filtered off and washed with 50 mL of hot ethanol to remove excess KOH. Yield: 2.68 g (90%), mp: decomposes above 330 °C. ^{1}H NMR (600 MHz, D_2O) δ (ppm): 7.31 (s, 2H, PyrH), 4.63 (s, 3H, OCH_3). ^{13}C NMR (150.8 MHz, D_2O/DMSO-d_6) δ (ppm): 173.0, 167.5, 154.9, 111.1, 55.8. IR (KBr): 2948, 1628, 1589, 1435, 1396, 1354, 1299, 1263, 1115, 1046, 995, 943, 886, 811, 792 cm^{-1}. HPLC: 14.5 min (λ=280 nm). HRMS (FAB, MK^+) calcd for $C_8H_5NO_5K_3$ 311.9079, found 311.9078.

*4.2.5. General synthesis of 2,6-pyridine dicarboxylic acid chloride (**4**, **16**, **21**)*

In a dry 250 mL round bottom flask, 6.0 mmol dry 2,6-pyridine carboxylic acid, 20 mL thionyl chloride, and 0.5 mL anhydrous *N*,*N*-dimethylformamide (DMF) were stirred for 2 h in an oil bath heated to 75 °C under an Ar atmosphere. The excess thionyl chloride was removed in vacuo. These products were used without further purification assuming quantitative yields.

4.2.6. General synthesis of 2,6-bisbenzimidazolylpyridine derivatives using activated iron in mineral oil

Procedure A. This procedure was modified from the literature.[23] The appropriate *N*-alkyl-*o*-nitroaniline derivative (12.0 mmol) dissolved in *N*-methyl pyrrolidinone (NMP, 12 mL) was added into the reaction vessel with the appropriate diacid chloride and stirred under an Ar atmosphere at 50 °C. After 8 h, activated iron in mineral oil (5 g), NMP (38 mL), and hydrochloric acid (10 mL) were slowly added to the reaction flask. The reaction was stirred for 12 h in a 90 °C oil bath under an Ar atmosphere. The contents of the reaction were poured into saturated aqueous EDTA solution (500 mL) and neutralized with sodium bicarbonate.

4.2.7. General synthesis of 2,6-bisbenzimidazolylpyridine derivatives using sodium dithionite

Procedure B. The appropriate *N*-alkyl-*o*-nitroaniline derivative (12.0 mmol) dissolved in anhydrous DMF (5 mL) was added to the reaction vessel with the appropriate diacid chloride and stirred under an Ar atmosphere at room temperature for 18 h. Pure $Na_2S_2O_4$ (85%) added in a 4 molar excess, additional DMF (20 mL), and EtOH (20 mL) were added to the solution and the temperature was increased to 85 °C. Deionized water (20 mL) was added and the reaction was heated to reflux for 18 h under an Ar atmosphere. The reaction was allowed to cool to room temperature and 4 M NaOH was added to the solution. Solvents were removed in vacuo. The crude product was dissolved in DCM (50 mL) and was washed with water (3×100 mL). DCM was removed in vacuo.

*4.2.7.1. 2,6-Bis(1′-ethyl-5′-methoxybenzimidazol-2′-yl)pyridine (**Bip1**). Procedure A*. Precipitated from neutralized aqueous EDTA solution described above. White solid, yield: 90%. *Procedure B*. Recrystallized from DCM/methanol (MeOH). Yield: 70%, mp: 202–204 °C, TLC: 98:2 DCM/MeOH R_f=0.21. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.32 (d, 2H, *J*=9.0 Hz, PyrH), 8.02 (t, 1H, *J*=8.2 Hz, PyrH), 7.35 (d, 2H, *J*=11.6 Hz, ArH), 7.34 (d, 2H, *J*=3.1 Hz, ArH), 7.02 (dd, 2H, *J*=8.7, 3.2 Hz, ArH), 4.78 (q, 4H, *J*=8 Hz, CH_2), 3.90 (s, 6H, OCH_3), 1.36 (t, 6H, *J*=8.0 Hz, CH_2CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm): 156.6, 150.0, 149.9, 143.6, 138.0, 130.6, 125.3, 114.0, 110.7, 101.8, 55.8, 39.8, 15.5. IR (KBr): 3044, 2975, 2938, 2893, 2836, 1619, 1586, 1497, 1490, 1432, 1345, 1279, 1200, 1155, 1115, 1034, 947, 886, 800 cm^{-1}. HPLC: 18.5 min. HRMS (FAB, MH^+) calcd for $C_{25}H_{26}N_5O_2$ 428.2086, found 428.2089.

*4.2.7.2. 2,6-Bis(1′-hexyl-5′-methoxybenzimidazol-2′-yl)pyridine (**Bip2**). Procedure A*. Purified via column chromatography on silica (DCM/MeOH=100:0, 98:2,…90:10). Yellow oil, yield: 63%. *Procedure B*. Purified with column chromatography on silica (DCM/MeOH=100:0, 98:2,…90:10). Yield: 65%, TLC: 98:2 DCM/MeOH R_f=0.35. ^{1}H NMR (600 MHz, CDCl3) δ (ppm): 8.27 (d, 2H, *J*=7.8 Hz, PyrH), 8.03 (t, 1H, *J*=7.8 Hz, PyrH), 7.33 (d, 2H, *J*=9.0 Hz, ArH), 7.32 (s, 2H, ArH), 7.01 (dd, 2H, *J*=2.4, 8.9 Hz, ArH), 4.68 (t, 4H, *J*=7.2 Hz, NCH_2), 3.90 (s, 6H, OCH_3), 1.71 (p, 4H *J*=7.2 Hz, NCH_2CH_2), 1.05 (m, 12H, $CH_2CH_2CH_2CH_3$), 0.65 (t, 6H, *J*=7.2 Hz, CH_2CH_3). ^{13}C NMR (150.8 MHz, $CDCl_3$) δ (ppm): 156.7, 150.0, 149.9, 144.1, 138.2, 130.9, 125.3, 114.1, 110.9, 101.7, 55.8, 44.9, 31.1, 30.0, 26.2, 22.2, 13.6. IR (KBr): 2951, 2922, 2909, 2854, 1689, 1657, 1580, 1498, 1435, 1278, 1200, 1158, 1106, 1031, 953, 826, 804 cm^{-1}. HPLC: 21.1 min. HRMS (FAB, MH^+) calcd for $C_{33}H_{42}N_5O_2$ 540.3338, found 540.3355.

*4.2.7.3. 2,6-Bis(1′-ethyl-5′-(4″-methoxy)phenylbenzimidazol-2′-yl)-pyridine (**Bip3**). Procedure A*. Precipitated from neutralized aqueous EDTA solution described above. Off-white solid, yield: 83%. *Procedure B*. Recrystallized from DCM/MeOH. Yield: 72%, mp: 222–227 °C. TLC: 97:3 DCM/MeOH R_f=0.35. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.38 (d, 2H, *J*=7.2 Hz, PyrH), 8.08 (t, 1H, *J*=7.8 Hz, PyrH), 8.04 (s, 2H, ArH), 7.63 (d, 4H, *J*=9.0 Hz, ArH), 7.59 (d, 2H, *J*=8.4 Hz, ArH), 7.53 (br d, 2H, *J*=8.4 Hz, ArH), 7.03 (d, 4H, *J*=8.4 Hz, ArH), 4.83 (q, 4H, *J*=7.2 Hz, NCH_2), 3.88 (s, 6H, OCH_3), 1.41 (t, 6H, *J*=7.2 Hz, CH_2CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm): 158.9, 150.4, 149.9, 143.5, 138.1, 136.2, 135.4, 134.3, 128.4, 125.7, 123.2, 118.1, 114.3, 110.3, 55.4, 39.9, 15.5. IR (KBr): 2972, 2902, 1607, 1568, 1517, 1474, 1426, 1337, 1278, 1241, 1176, 1154, 1100, 1031, 991, 904, 810, 735 cm^{-1}. HPLC: 21.3 min. HRMS (FAB, MH^+) calcd for $C_{37}H_{34}N_5O_2$ 580.2712, found 580.2712.

*4.2.7.4. 2,6-Bis(1′-n-hexyl-5′-(4″-methoxy)phenylbenzimidazol-2′-yl)pyridine (**Bip4**). Procedure A*. Purified via column chromatography on silica ($CHCl_3$/MeOH=97:3). Off-white solid, yield: 72%. *Procedure B*. Purified via column chromatography on silica ($CHCl_3$/MeOH=97:3). Yield: 69%, mp: 200 °C. TLC: 97:3 DCM/MeOH R_f=0.49. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.34 (d, 2H, *J*=7.8 Hz, PyrH), 8.08 (t, 1H, *J*=8.4, 7.8 Hz, PyrH), 8.03 (s, 2H, ArH), 7.63 (d, 4H, *J*=9 Hz, ArH), 7.58 (dd, 2H, *J*=8.4 Hz, ArH), 7.50 (d, 2H, *J*=8.4 Hz, ArH), 7.03 (d, 4H, *J*=8.4 Hz, ArH), 4.73 (t, 4H, *J*=7.2, 7.8 Hz, NCH_2), 3.88 (s, 6H, OCH_3), 1.76 (tt, 4H, *J*=7.2 Hz, NCH_2CH_2), 1.08 (m, 12H, $CH_2CH_2CH_2CH_3$), 0.66 (m, 6H, CH_2CH_3). ^{13}C NMR (150.8 MHz, $CDCl_3$) δ (ppm): 158.6, 150.4, 149.7, 143.0, 138.0, 135.9, 135.2, 134.0, 128.1, 125.2, 122.9, 117.8, 114.0, 110.2, 55.1, 44.8, 30.9, 29.8, 26.1, 22.1, 13.5. IR (KBr): 2972, 2957, 2924, 2987, 2860, 1650, 1607, 1562, 1465, 1435, 1260, 1179, 1091, 1031, 1016, 910, 841, 816, 798 cm^{-1}. HPLC: 23.3 min. HRMS (FAB, MH^+) calcd for $C_{45}H_{50}N_5O_2$ 692.3964, found 692.3960.

*4.2.7.5. 2,6-Bis(1′-ethyl-6′-methylbenzimidazol-2′-yl)pyridine (**Bip5**). Procedure A*. Purified via column chromatography on silica (DCM/MeOH=100:0, 98:2,…90:10). Off-white solid, yield: 84%, mp: 175–178 °C, TLC: 98:2 DCM/MeOH R_f=0.18. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.30 (d, 2H, *J*=7.5 Hz, PyrH), 8.01 (t, 1H, *J*=7.5 Hz, PyrH), 7.74 (d, 2H, *J*=6.0 Hz, ArH), 7.25 (s, 2H, ArH), 7.17 (dd, 2H, *J*=0.15, 6.0 Hz, ArH), 4.76 (q, 4H, *J*=6.0 Hz, NCH_2), 2.55 (s, 6H, $ArCH_3$), 1.35 (t, 6H, *J*=6.0 Hz, CH_2CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ (ppm): 150.1, 149.5, 141.1, 137.9, 136.2, 133.6, 125.3, 124.4, 119.8, 110.0, 39.7, 22.0, 15.4. IR (KBr): 2972, 2921, 2048, 1596, 1590, 1565, 1436, 1406, 1336, 1327, 1287, 1179, 1061, 814, 750 cm^{-1}. HPLC: 18.7 min (λ=310 nm). HRMS (FAB, MH^+) calcd for $C_{25}H_{26}N_5$ 396.2188, found 396.2205.

*4.2.7.6. 4-Benzoxy-2,6-bis(1′-ethyl-5′-methoxybenzimidazol-2′-yl)-pyridine (**Bip6**). Procedure A*. Precipitated from neutralized aqueous EDTA solution described above. Washed with EDTA (3×100 mL). Off-white solid, yield: 72%. *Procedure B*. Washed with MeOH. Yield: 70%, mp: 206–208 °C, TLC: 97:3 DCM/MeOH R_f=0.30. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.94 (s, 2H, PyrH), 7.45 (d, 2H, *J*=6.4 Hz, ArH), 7.40 (t, 2H, *J*=6.4 Hz, ArH), 7.33 (m, 5H, ArH), 7.05 (dd, 2H, *J*=0.2, 8.3 Hz, ArH), 5.27 (s, 2H, OCH_2), 4.70 (q, 4H, *J*=6.3 Hz, NCH_2), 3.89 (s, 6H, OCH_3), 1.37 (t, 3H, *J*=6.2 Hz, CH_3). ^{13}C NMR (150.8 MHz, $CDCl_3$) δ (ppm): 166.3, 156.8, 151.8, 150.2, 143.7, 135.7, 130.9, 129.0, 128.6, 127.7, 114.2, 112.3, 110.9, 102.0, 70.5, 56.1, 40.1, 15.8. IR (KBr): 3081, 2954, 2933, 2858, 2842, 1620, 1586, 1568, 1490, 1430, 1276, 1197, 1152, 1107, 1028, 1010, 829, 789 cm^{-1}. HPLC: 19.4 min. HRMS (FAB, MH^+) calcd for $C_{32}H_{32}N_5O_3$ 534.2505, found 534.2510.

*4.2.7.7. 2,6-Bis(5′-benzoxy-1′-ethylbenzimidazol-2′-yl)-4-methoxy-pyridine (**Bip7**). Procedure B*. Washed with MeOH. Off-white solid, yield: 81%, mp: 160–162 °C, TLC: 97:3 DCM/MeOH R_f=0.27. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.84 (s, 2H, PyrH), 7.34–7.50 (m, 14H, PhH), 7.09 (dd, 2H, ArH), 5.17 (s, 4H, OCH_2), 4.76 (q, 4H, NCH_2), 4.03 (s, 3H, OCH_3), 1.35 (t, 3H, CH_3). ^{13}C NMR (150.8 MHz, $CDCl_3$) δ (ppm): 155.9, 151.8, 150.3, 142.8, 137.5, 131.9, 131.1, 128.1, 127.7, 114.9, 111.7, 110.8, 103.8, 71.0, 56.0, 40.1, 15.7. IR (KBr): 3075, 2972, 2927, 2897, 2866, 1623, 1590, 1571, 1490, 1472, 1423, 1378, 1345, 1309, 1279, 1173, 1115, 1040, 1013, 971, 919, 829, 796, 735 cm^{-1}.

HPLC: 20.8 min. HRMS (FAB, MH^+) calcd for $C_{38}H_{36}N_5O_3$ 610.2818, found 610.2828.

4.2.8. Alkylation of ***Bip1*** ligand

*4.2.8.1. 2,6-Bis(1′-ethyl-5′-(n-penten-4″-yl-1-oxy)benzimidazol-2′-yl)pyridine (**Bip8**).* **Bip1** was converted from the methoxy derivative into the analogous phenolic derivative via the literature procedures.[20] In a dry 50 mL round bottom flask with a water condenser attached, dry phenolic derivative (0.30 g, 0.75 mmol), 5-bromopentene (0.47 g, 3.0 mmol), K_2CO_3 (0.55 g), and 4:1 tetrahydrofuran/MeOH mixture (10 mL) were stirred for 12 h in an oil bath heated to 75 °C under an Ar gas. All solvents were removed in vacuo until completely dry. The dried compound was dissolved in DCM (100 mL) and washed with water three times. The organic layers were combined and solvent was removed in vacuo. Purified via column chromatography on silica ($CHCl_3$/MeOH=100:0, 98:2,…90:10). White solid, yield: 75%, mp: 106.5 °C from DSC, TLC: 98:2 DCM/MeOH R_f=0.24. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.30 (d, 2H, J=7.8 Hz, PyrH), 8.02 (t, 1H, J=8.1 Hz, PyrH), 7.34 (d, 2H, J=8.4 Hz, ArH), 7.31 (2H, J=1.2 Hz, ArH), 5.87 (m, 2H, H_2C=C*H*), 5.04 (dd, 4H, J=10.2, 40.2 Hz, H_2C=CH), 4.77 (q, 4H, J=7.2 Hz, NCH_2), 4.06 (t, 4H, J=6.6 Hz, OCH_2), 2.28 (q, 4H, J=6.6 Hz, $OCH_2CH_2CH_2$), 1.94 (p, 4H, J=7.2 Hz, OCH_2CH_2), 1.35 (t, 6H, J=7.2 Hz, CH_3). ^{13}C NMR (150.8 MHz, $CDCl_3$) δ (ppm): 156.1, 150.1, 150.0, 143.7, 138.1, 138.0, 130.8, 125.5, 115.4, 114.7, 110.8, 102.9, 68.1, 40.1, 30.5, 28.7, 15.9. IR (KBr): 3068, 2972, 2938, 2899, 2863, 1622, 1577, 1423, 1272, 1192, 1176, 1106, 1064, 965, 907, 810 cm^{-1}. HPLC: 21.0 min (λ=310 nm). HRMS (FAB, MH^+) calcd for $C_{33}H_{38}N_5O_2$ 536.3025, found 536.3034.

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