New Synthetic Approach to Polyaryl Strands Containing Pyridine and Pyrimidine Units

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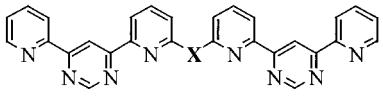
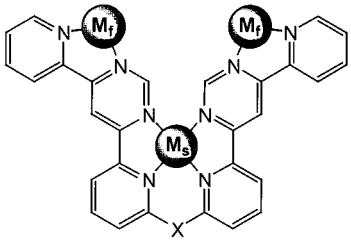
The synthesis of hexaaromatic strand **4** in which pyridyl and pyrimidyl units are linked both directly and by a one-atom spacer is reported. The C-linkage is introduced by double nucleophilic substitution reaction of a carbanion at the bromopyridyl moiety of building block **2a**.

Introduction

Polyaromatic compounds containing alternating pyridine and pyrimidine rings have been extensively studied during the last five years. Interest in this class of molecules is mostly due to their wide use in supramolecular chemistry, particularly in the creation of helical structures based on polyaromatic strand molecules,[1] and as building blocks for self-assembled polynuclear coordination arrays.[1e,2] Our specific interest is in trinucleating ligands containing two triaromatic halves linked by mono- or polyatomic spacer group **X** (Scheme 1). The corresponding trinuclear complexes (Scheme 2) are expected to show interesting "allosteric" behavior: a structural metal $\mathbf{M_s}$ bound by the tetradentate (allosteric) site controls the conformation of the catalytic site in which two functional metals $\mathbf{M_f}$ cooperate in substrate binding and catalysis.[3] Variation of both the $\mathbf{M_s}$ and the spacer group **X** should allow for straightforward fine-tuning of the $\mathbf{M_f}$–$\mathbf{M_f}$ distance.



Scheme 1. General formulae of target trinucleating strand ligands



Scheme 2. Expected structure of trinuclear complexes

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Synthetic approaches to polyheterocyclic pyridine–pyrimidine strands are based on tin-mediated cross-coupling reactions involving 4,6-dichloropyrimidine,[1] generation of internal pyridine rings by interaction of ene-1,5-diones with ammonium acetate,[1] and of internal pyrimidine ring with the help of ring-closure reactions of bis-heteroaryl-β-diketones with formamide[2c,2e] or enaminones with carboxamidines.[2h] Even large pyridyl–pyrimidyl strands with direct aryl–aryl bonds have been generated by such methods.[1] In contrast, versatile methods to link pyridyl–pyrimidyl building blocks by mono- or polyatomic spacing groups are not well established. Here we report an approach for the preparation of molecules shown in Scheme 1, based on a nucleophilic aromatic substitution to the bromopyridine moiety in triaromatic building block **2a**. We include a brief description of other attempts which seemed promising but were inappropriate for the preparation of the target molecule.

Results and Discussion

Synthesis and Reactivity

4-(2-Pyridyl)pyrimidine (**1**) reacts smoothly with 6-lithio-2-bromopyridine in diethyl ether giving a mixture of two isomeric addition products **2a** and **2b** (Scheme 3). A standard aqueous methanol workup of the reaction mixture is accompanied by facile and complete oxidation of initially formed dihydropyrimidines (the ^{1}H NMR spectrum of the crude mixture of products indicates only aromatic resonances). Such behavior, quite usual for addition reactions to pyridazines[4a] and pyrazines,[4b] is not typical for pyrimidines. Normally, the 3,4- or 3,6-dihydropyrimidines obtained are stable enough, and an additional step (oxidation with $KMnO_4$ in acetone,[5] with nitrobenzene[5d] or with substituted benzoquinones[6]) is required to convert them into pyrimidines. However, there are reports about the sensitivity of dihydropyrimidines to atmospheric oxygen which cause difficulties with their isolation.[4b]

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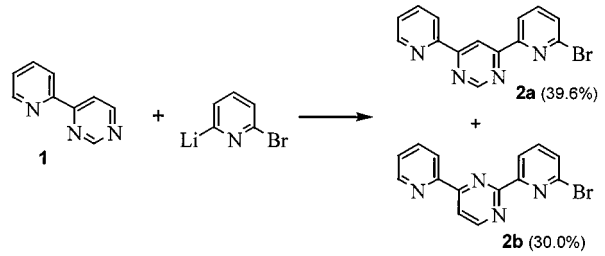


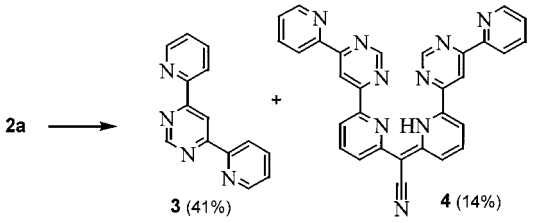
Scheme 3. (a) Diethyl ether, − 70 °C; (b) methanol, H_2O, O_2, 0 °C

As a rule, addition of organolithium compounds to 4-substituted pyrimidines leads to the formation of both 2,4- and 4,6-substitution products.[7] In the reported cases, the 4,6-isomer is clearly favored,[4,8] although the ratio of 2,4- and 4,6-isomers can, to a great extent, depend on the nature of the solvent and on the presence of a complexing agent (e.g., TMEDA).[4a,9] The latter factor can lead to an enrichment of the 2,4-isomer in the resulting product mixture. In our particular case, we found that both isomers are formed in approximately equal ratio, possibly owing to the chelation of lithium with the dipyridyl-like bidentate pocket of **1**. The desired isomer **2a** can be easily isolated by chromatography in sufficient quantities. Products **2a** and **2b** are easily distinguished by the markedly different values of the coupling constants of the pyrimidine protons ($J_{2,5}$ = 1.2 Hz and $J_{5,6}$ = 5.2 Hz).[10] The FD-MS for both **2a** and **2b** indicate a pattern with major peaks at *m*/*z* = 312.0 and 314.0 (ca. 10:9 ratio, ^{79}Br and ^{81}Br isotopes).

Compound **2a** is an important intermediate for the construction of polynucleating ligands. A reasonable approach to enhance the growth of the polyaromatic strand could involve lithiation of **2a** followed by electrophilic addition. However, in spite of numerous attempts to prepare the lithiated derivative of **2a**, we failed to obtain it. The most probable reason is that lithium coordination by the bidentate dipyridyl-like pocket could inhibit lithiation. Quenched reaction mixtures containing 1:1 *n*BuLi/**2a** and prepared at different temperatures (−80 to 0 °C) indicated the presence of only unchanged **2a**. Addition of a second equiv. of *n*BuLi causes no effect between −80 and −50 °C; further warming leads to mixtures of products which could not be characterized.

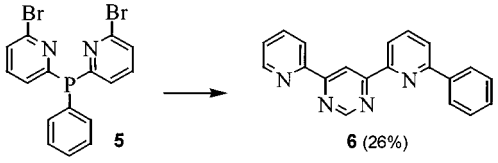
An alternative way to grow the strand is by nucleophilic substitution of the bromine atom. The preparation of various compounds of the type (2-pyridyl)$_2$**X** (**X** = CR_2, NR, S, Se) by nucleophilic addition to 2-bromopyridines has been reported.[11−14] In principle, the same reactions should be possible with **2a** as the bromoaryl component.

Treatment of **2a** with sodium cyanoacetamide in anhydrous DMF at 115 °C for four hours, analogous to the Borror and Haeberer method for 2-quinolyl-2(1*H*)-quinolylideneacetonitrile,[11] produces the formation of **4**, which can be isolated as a red crystalline material (yield 14%) after chromatographic separation (Scheme 4). Note that in the course of this reaction Br−H exchange in **2a** occurs to a great extent, yielding the known compound[2c,2e] **3** (41%). Similar approaches (use of 2-picolyllithium[14a] or lithium acetonitrile in toluene in the presence of TMEDA[12]) for the preparation of **4** were unsuccessful.



Scheme 4. (a) DMF, 2-cyanoacetamide, NaH, 115 °C; (b) H_2O, 80 °C

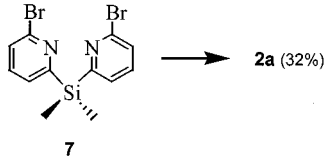
We also attempted to construct the molecular systems of Scheme 1 using preformed (6-bromo-2-pyridyl)$_2$**X** units {**X** = monoatomic spacer: **5** [**X** = −P(C_6H_5)−], **7** [**X** = −Si(CH_3)$_2$−] and **8** [**X** = −C(OCH_2CH_2O)−]}. Although for compounds **7** and **8** lithiation and successful reactions with electrophiles were reported,[15,16] we failed to obtain the desired hexaaromatic compounds by the reaction of dilithiated **5**, **7**, **8** with two equivalents of **1**. Upon reaction of dilithiated **5** with **1**, a tetraaromatic compound **6** (yield 26%) containing an interannular pyridyl−phenyl bond (Scheme 5) was obtained. Product **6** was identified by elemental analysis (no phosphorus is present), FD-MS (only one major peak − molecular ion at *m*/*z* = 310.3) and NMR spectroscopy. The ^{1}H NMR spectrum of **6**, apart from a set of signals characteristic of the Py−Pym−Py moiety, contains also resonances for the phenyl group. No ^{31}P NMR signals are detectable for **6**. In the case of the silicon-containing substrate (Scheme 6), compound **2a** forms unexpectedly (yield 32%), suggesting that Si−Li exchange resulting in 6-bromo-2-lithiopyridine formation takes place on addition of *n*BuLi to **7** (in spite of the reported smooth lithiation of **7** giving rise to the successful preparation of several products).[15] Analogously to the reaction of **5**, this is followed by electrophilic addition to the pyrimidine ring with consequent oxidation in the course of workup. It should be noted that in all considered reactions, the dihydropyrimidine compounds formed appear not to be stable and are easily oxidized. Remarkably, in the case of the phosphorus and silicon reactions, only products corresponding to C-4 addition were isolated. In the case of **8**, we were unable to separate the resulting reaction mixture which contained at least five substances with very similar polarities, according to TLC.



Scheme 5. (a) Diethyl ether, *n*BuLi, − 70 °C; (b) **1**; (c) Methanol, H_2O, O_2, 0 °C

Spectral Properties and Molecular Structure of 4

According to the single-crystal X-ray data, compound **4** exists in a fully conjugated form with a proton localized at



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Scheme 6. (a) Diethyl ether, *n*BuLi, − 70 °C; (b) **1**; (c) methanol, H_2O, O_2, 0 °C

the nitrogen atom of one of the internal pyridine rings. This is also confirmed by the ν(C≡N) stretching mode at 2179 cm^{-1} in the IR spectrum which is characteristic of conjugated nitriles.[12] The ^1H NMR spectrum ($CDCl_3$) reveals a resonance at δ = 16.186 owing to the strongly hydrogen-bonded NH proton[13] which forms a bifurcate H-bond with the internal pyridine and pyrimidine nitrogen atoms. This resonance in the H,H-COSY spectrum is cross-coupled with the overlapped signals of the H-5′ and H-3′ protons of the internal pyridine ring. A broad absorption in the IR spectrum observable at $\tilde{\nu}$ = 3448 cm^{-1} owing to the N−H stretching mode is also indicative of strong hydrogen bonding.

Both the ^1H and ^{13}C NMR spectra of **4** contain a number of signals expected for a molecule with C_2 symmetry (9 signals for aromatic protons in the ^1H and 16 signals in the ^{13}C NMR spectra), indicating rapid intramolecular transfer of the NH-proton between internal pyridines. All the signals in the ^1H and most of the signals in the ^{13}C spectra were assigned unambiguously with the help of H,H- and H,C-COSY experiments. In the ^{13}C NMR spectrum, the position of the resonance corresponding to the bridging sp^2 methine carbon (δ = 70.88) is close to the data reported for other bis(2-pyridyl)acetonitriles.[12,13b,17]

The molecular structure and the numbering scheme for **4** is shown in Figure 1, and selected bond lengths, angles and torsion angles are listed in Table 1. The unit cell is centrosymmetric and contains two enantiomeric conformers of **4** possessing an asymmetric helical structure. In spite of the formal intrinsic C_{2v} symmetry for the non-hydrogen frame, the molecule **4** in the crystal adopts no symmetric conformation. The two central pyridine rings are not equivalent: while the interatomic distances within the non-protonated ring (**D**) are typical for aromatic pyridine rings (no noticeable difference in C−C bond lengths), in the protonated ring **C** the C−N bonds are longer [1.367(3) and 1.375(3) Å] and there is a significant difference in C−C bonds: C(33)−C(34) = 1.395(4), C(35)−C(36) = 1.423(3) Å and C(32)−C(33) = 1.356(3), C(34)−C(35) = 1.343(3) Å which corresponds to the alternating single and double bonds in the pyridylidene system. The corresponding bond angles at the nitrogen atoms of rings **C** and **D** are also significantly different: C(36)−N(31)−C(32) = 124.4(2)° and C(42)−N(41)−C(46) = 117.5(2)° (Figure 1). Essentially, the bonds between sp^2-carbon C(2) and the two pyridyl C atoms are non-equivalent: C(2)−C(36) = 1.396(3) and C(2)−C(42) = 1.454(3) Å. The angle C(36)−C(2)−C(42) is increased to 127.3(2)°. The observed geometrical parameters are similar to those reported for other molecules containing the dipyridylmethine unit.[12,13b,17] Within the

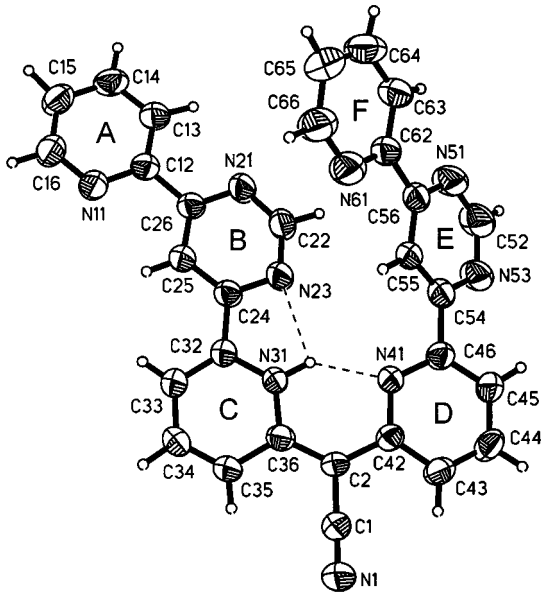

Figure 1. Molecular structure of **4**

rings **A**, **B**, **E**, **F**, the bond lengths are normal for pyridine and pyrimidine, and the interannular bond lengths are typical for alternating pyridine and pyrimidine rings[1] and lie between 1.469(3) and 1.487(3) Å.

The planar conformation of the central moiety of the molecule is stabilized by the short bifurcate intramolecular hydrogen bond formed by the NH group with the pyridine and pyrimidine nitrogen atoms N(31)−H(1)···N(41) = 1.93(3), N(31)−H(1) = 0.95(3), N(31)···N(41a) = 2.712(3) Å, the angle = 138(2)° and N(31)−H(1)···N(23) = 2.29(3), N(31)···N(23) = 2.649(3) Å, the angle = 102(2)°. One of the important consequences of this hydrogen bond is the deviation of the polyaromatic strand from the energetically favored *transoid* orientation about the interannular bonds: the rings **B** and **C** found themselves in a *cis*-conformation with respect to each other owing to the necessity for the N(23) atom to participate in the hydrogen bond.

There are two almost planar fragments in the molecule: one of them is comprised of the **A**, **B**, **C**, **D** rings and involves the central −C(CN)− unit, the second one includes the **E** and **F** rings. The terminal pyridine and pyrimidine rings are nearly coplanar (the dihedral angles between the rings **A** and **B** = 1.3°, between **E** and **F** = 3.9°). The dihedral angle between the central pyridine rings **C** and **D** is 12.0° owing to their non-equivalence discussed above, so that the dipyridylmethine unit is somewhat deviated from planarity: the torsion angles are C(1)−C(2)−C(36)−N(31) = 178.3(2)° and C(1)−C(2)−C(42)−N(41) = 170.9(3)°. In other reported structures of bis(2-pyridyl) *meso*-cyano compounds[12,13b,17] this fragment is perfectly planar. Torsion of the **B** ring with respect to **C** is quite small (interannular torsion angles are less than 9°), so that the **A**, **B**, **C**, **D** rings and the −C(CN)− group form a more or less planar moiety [with maximum deviation from the mean plane of 0.202(2) Å for C(46) and of 0.234(2) Å for N(41)].

In the crystal packing (Figure 2), the stacking interactions between pyridine rings [**A**···**A** (3 − *x*, 1 − *y*, −*z*) =

Table 1. Selected bond lengths [Å], bond angles, and torsion angles [°] for **4**

N(1)−C(1)	1.145(3)
N(31)−C(36)	1.367(3)
N(31)−C(32)	1.375(3)
N(41)−C(42)	1.353(3)
N(41)−C(46)	1.350(3)
C(1)−C(2)	1.424(3)
C(2)−C(36)	1.396(3)
C(2)−C(42)	1.454(3)
C(36)−C(35)	1.423(3)
C(35)−C(34)	1.343(4)
C(34)−C(33)	1.395(4)
C(33)−C(32)	1.356(3)
C(32)−C(24)	1.469(3)
C(42)−C(43)	1.392(3)
C(43)−C(44)	1.365(4)
C(36)−N(31)−C(32)	124.4(2)
C(42)−N(41)−C(46)	117.5(2)
N(1)−C(1)−C(2)	178.3(3)
C(36)−C(2)−C(1)	116.1(2)
C(36)−C(2)−C(42)	127.3(2)
C(1)−C(2)−C(42)	116.6(2)
N(31)−C(36)−C(2)	121.2(2)
N(31)−C(36)−C(35)	115.3(2)
C(2)−C(36)−C(35)	123.4(2)
C(33)−C(32)−N(31)	118.8(2)
N(31)−C(32)−C(24)	115.4(2)
N(41)−C(42)−C(43)	121.6(2)
N(41)−C(42)−C(2)	117.5(2)
C(43)−C(42)−C(2)	120.9(2)
C(44)−C(43)−C(42)	119.8(3)
N(41)−C(46)−C(45)	122.9(2)
N(41)−C(46)−C(54)	117.3(2)
C(1)−C(2)−C(36)−C(35)	−3.3(4)
C(1)−C(2)−C(42)−C(43)	8.7(4)
C(1)−C(2)−C(36)−N(31)	178.3(2)
C(1)−C(2)−C(42)−N(41)	170.9(3)
N(31)−C(32)−C(24)−N(23)	8.9(3)
C(33)−C(32)−C(24)−C(25)	8.6(4)
C(25)−C(26)−C(12)−N(11)	−0.4(4)
N(21)−C(26)−C(12)−C(13)	−1.6(4)
C(36)−C(2)−C(42)−N(41)	11.6(4)
C(45)−C(46)−C(54)−N(53)	31.2(4)
N(41)−C(46)−C(54)−C(55)	32.4(4)
C(55)−C(56)−C(62)−N(61)	−2.5(4)
N(51)−C(56)−C(62)−C(63)	−2.3(4)

3.622 Å centroid-to-centroid separation] and pyrimidine−pyridine rings [**E**···**F** (2 − *x*, 2 − *y*, −*z*) = 3.699 Å] are significant. There are several van der Waal's contacts between the atoms of the −C(CN)− moiety [N(1), C(1), C(2)] and the aromatic rings (3.344−3.716 Å) of a translational molecule **4** which can be interpreted as π−π interaction.

Conclusion

We have developed a new synthetic route for preparation of polyheteroaryl strand molecules containing pyridine and pyrimidine rings. While methods for such polyaryl strands with direct aryl−aryl bonds have been established, our approach also allows for the incorporation of monoatomic spacers between heteryl units. This will enable a more flexible design of oligo(pyridylpyrimidines) for the assembly of polynuclear coordination compounds.

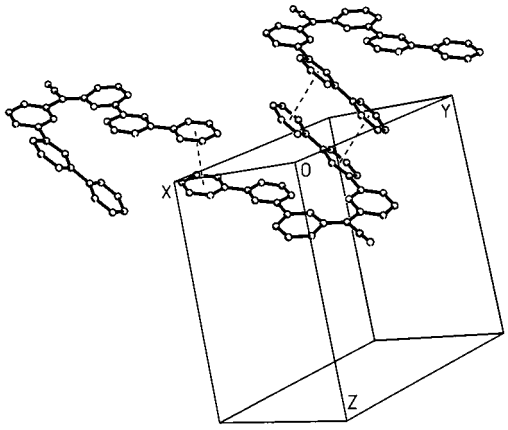

Figure 2. Fragment of crystal packing of **4**

Experimental Section

All reactions were carried out under nitrogen in dry solvents using standard Schlenk techniques. Workup was carried out under air, using solvents of technical quality. Organic extracts were dried with anhydrous $MgSO_4$. − Chromatography was carried out on Merck 60 silica gel (0.040−0.063 mm). Retention factors (R_f) were determined using Macherey−Nagel alumina TLC plates. − Compounds **1**, **7**, **8** were obtained according to literature methods.[15,18,19] − ^1H and ^{13}C nuclear magnetic resonance spectra were recorded on Bruker AC-300 (300.13 MHz) and Bruker AC-400 (400.13 MHz) spectrometers, chemical shifts are reported in ppm downfield from Me_4Si. − IR spectra were obtained on a Perkin−Elmer 983 G spectrometer (as KBr or CsI pellets). − FD mass spectra were recorded on a Finnigan MAT 8230 instrument. − Elemental analyses were performed by the Microanalytisches Laboratorium des Organisch-Chemischen Instituts der Universität Heidelberg.

4-(6-Bromo-2-pyridyl)-6-(2-pyridyl)pyrimidine (2a) and 2-(6-Bromo-2-pyridyl)-4-(2-pyridyl)pyrimidine (2b): To a stirred solution of 2-lithio-6-bromopyridine [prepared from *n*BuLi (32 mL of 1.6 M solution in hexane) and 2,6-dibrompyridine (11.85 g, 50 mmol) in anhydrous ether (150 mL) according to ref.[20]] at −70 °C was added 4-(2-pyridyl)-pyrimidine (**1**) (7.86 g, 50 mmol) in diethyl ether (130 mL). The resulting mixture was stirred for 20 min, then warmed to 0 °C, poured into a mixture of methanol (200 mL) and crushed ice (150 g) and stirred vigorously in air for 2 hours. After evaporation at room temperature of the ether phase (ca. 24 h) a light yellow precipitate formed (a mixture of **2a** and **2b**) which was filtered off, redissolved in dichloromethane (25 mL) and subjected to column chromatography (eluent: acetone/hexane 1:9). The aqueous filtrate was extracted with chloroform (3 × 200 mL), and the solvent evaporated. The residual oil containing **2a**, **2b** and insignificant amounts of both starting reagents was subjected to chromatographic separation as well. First fraction: **2a**, yield 6.2 g (39.6%), R_f = 0.7 (acetone/hexane 3:7); second fraction: **2b**, yield 4.7 g (30.0%), R_f = 0.6 (acetone/hexane 3:7).

2a: ^1H NMR ($CDCl_3$, 400.13 MHz): δ = 7.44 (ddd, $J_{3,5}$ = 1.2 Hz, $J_{4,5}$ = 7.7 Hz, $J_{5,6}$ = 4.8 Hz, 1 H, Py-5), 7.61 (dd, $J_{3,5}$ = 0.8 Hz, $J_{4,5}$ = 7.7 Hz, 1 H, Py′-5), 7.74 (t, $J_{3,4}$ = 7.7 Hz, 1 H, Py′-4), 7.89 (td, $J_{3,4}$ = 7.7 Hz, $J_{4,6}$ = 1.8 Hz, 1 H, Py-4), 8.49 (dd, Py′-3), 8.50 (dt, $J_{3,6}$ = 0.8 Hz, 1 H, Py-3), 8.81 (ddd, 1 H, Py-6), 9.32 (d, $J_{2,5}$ = 1.2 Hz, 1 H, Pym-5), 9.35 (d, 1 H, Pym-2). − $C_{14}H_9N_4Br$ (313.16): calcd. C 53.70, H 2.90, N 17.89, Br 25.52; found C 53.42, H 3.11,

N 17.80, Br 25.61. − MS (FD); *m/z* (%): 312.0 (100) [M^+ (^{79}Br)], 314.0 (89) [M^+ (^{81}Br)].

2b: ^{1}H NMR ($CDCl_3$, 400.13 MHz): δ = 7.46 (ddd, $J_{3,5}$ = 1.2 Hz, $J_{4,5}$ = 7.7 Hz, $J_{5,6}$ = 4.8 Hz, 1 H, Py-5), 7.61 (dd, $J_{3,5}$ = 1.1 Hz, $J_{4,5}$ = 7.7 Hz, 1 H, Py′-5), 7.75 (t, $J_{3,4}$ = 7.7 Hz, 1 H, Py′-4), 7.79 (td, $J_{3,4}$ = 7.7 Hz, $J_{4,6}$ = 1.8 Hz, 1 H, Py-4), 8.41 (d, $J_{5,6}$ = 5.2 Hz, 1 H, Pym-5), 8.61 (dd, $J_{3,6}$ = 1.1 Hz, Py′-3,), 8.69 (dt, 1 H, Py-3), 8.75 (ddd, 1 H, Py-6), 9.09 (d, 1 H, Pym-6). − $C_{14}H_9N_4Br$ (313.16): calcd. C 53.70, H 2.90, N 17.89, Br 25.52; found C 53.63, H 3.05, N 17.95, Br 25.37. − MS (FD); *m/z* (%): 312.0 (100) [M^+ (^{79}Br)]), 314.0 (88) [M^+ (^{81}Br)].

2,4-Di-(2-pyridyl)pyrimidine (3) and [2-Pyridyl-6-(6-{2-pyridyl}-4-pyrimidyl)][6-(6-{2-pyridyl}-4-pyrimidyl)-1*H*-2-pyridylidene]-acetonitrile (4): Sodium hydride (50% dispersion in mineral oil, 0.53 g, 11 mmol) was placed in a 125 mL Schlenk flask, washed with hexane (3 × 15 mL), and then dried under vacuum. Anhydrous DMF (10 mL) and then cyanacetamide (0.84 g, 10 mmol) dissolved in DMF (5 mL) were added dropwise with a syringe with stirring. Upon completion of the addition, the flask was placed in an oil bath and heated to 50 °C, and **1** (1.25 g, 4 mmol) in DMF (5 mL) was added dropwise. The reaction temperature was raised slowly to 110−115 °C and maintained at this temperature with continuous stirring. After 4 h, the mixture was slowly cooled to 80 °C, and water (3 mL) was added. The mixture was then cooled to room temperature, water (50 mL) was added, and extracted with chloroform (3 × 150 mL), the combined extracts were washed with saturated aqueous NaCl, and the solvent distilled. A red solid residue was purified chromatographically with chloroform. First fraction: **3**, yield 0.38 g (41%), R_f = 0.6 (acetone/hexane 3:7); second fraction: **4**, yield 0.14 g (14%), R_f = 0.25 (acetone/hexane 3:7).

3: ^{1}H NMR ([D_6]DMSO, 300.13 MHz): δ = 7.43 (ddd, $J_{3,5}$ = 1.1 Hz, $J_{4,5}$ = 7.8 Hz, $J_{5,6}$ = 4.8 Hz, 2 H, Py-5), 7.89 (td, $J_{3,4}$ = 7.8 Hz, $J_{4,6}$ = 1.2 Hz, 2 H, Py-4), 8.51 (dt, 2 H, Py-3), 8.79 (ddd, 2 H, Py-6), 9.36 (d, $J_{2,5}$ = 1.1 Hz, 2 H, Pym-5), 9.39 (d, 2 H, Pym-2). − $C_{14}H_{10}N_4$ (234.26): calcd. C 71.78, H 4.30, N 23.92; found: C 71.83, H 4.31, N 23.70. − MS (FD); *m/z* (%): 234.3 (100) [M^+]. The data are identical to those reported in the literature.[2c]

4: ^{1}H NMR ([D_6]DMSO, 300.13 MHz): δ = 7.57 (ddd, $J_{3,5}$ = 1.1 Hz, $J_{4,5}$ = 7.7 Hz, $J_{5,6}$ = 4.8 Hz, 2 H, Py-5), 7.84 (d, $J_{4,5}$ = 7.8 Hz, 2 H, Py′-5), 8.01 (td, $J_{3,4}$ = 7.7 Hz, $J_{4,6}$ = 1.2 Hz, 2 H, Py-4), 8.11 (t, $J_{3,4}$ = 7.8 Hz, 2 H, Py′-4), 8.29 (m, 2 H, Py-3), 8.40 (d, 2 H, Py′-3), 8.73 (d, 2 H, Py-6), 8.75 (d, $J_{2,5}$ = 1.1 Hz, 2 H, Pym-2), 9.24 (d, 2 H, Pym-5), 16.02 (s, 1 H, NH). − ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ = 7.15 (ddd, $J_{3,5}$ = 1.1 Hz, $J_{4,5}$ = 7.7 Hz, $J_{5,6}$ = 4.8 Hz, 2 H, Py-5), 7.55−7.60 (m, 4 H, Py′-3 + Py′-5), 7.64 (m, $J_{3,4}$ = 7.7 Hz, $J_{4,5}$ = 1.1 Hz, 2 H, Py′-4), 7.75 (td, $J_{3,4}$ = 7.7 Hz, $J_{4,6}$ = 1.1 Hz, 2 H, Py-4), 8.21 (d, 2 H, Py-3), 8.33 (d, 2 H, Py-6), 8.81 (d, 2 H, $J_{2,5}$ = 1.1 Hz, Pym-2), 8.85 (d, 2 H, Pym-5), 16.17 (s, 1 H, NH). − ^{13}C NMR ($CDCl_3$, 75.47 MHz,), δ = 70.9 [*C*(C≡N)], 113.28 (Py′-5), 113.6 (Pym-5), 121.7 (Py-3), 122.0 (C≡N), 122.7 (Py′-3), 125.3 (Py-5), 136.89 (Py′-4), 137.00 (Py-4), 146.7 (Py′-6), 149.1 (Py-6), 152.9 (Py-2/2′), 155.1 (Py-2/2′), 158.4 (Pym-2), 160.6 (Pym-4/6), 163.0 (Pym-4/6). − IR (KBr: $\tilde{\nu}$ = 2179 (C≡N), 3448br (N−H) cm^{-1}. − $C_{30}H_{19}N_9$ (505.53): calcd. C 71.28, H 3.79, N 24.94; found C 71.15, H 3.92, N 24.66. − UV/Vis (DMSO): λ_{max} (ε) = 382 (14600), 499 (4040) nm. − MS (FD); *m/z* (%): 505.5 (1009 [M^+]).

Bis(6-bromo-2-pyridyl)phenylphosphane (5): Dichlorophenylphosphane (1.79 g, 10 mmol) in diethyl ether (30 mL) was slowly added to a diethyl ether solution (50 mL) of 6-bromo-2-lithiopyridine [from 4.74 g (20 mmol) of 2,6-dibromopyridine and 13 mL of 1.6 M *n*BuLi] at −70 °C. The blood-red mixture were stirred at −60 °C for 30 min, then warmed to 0 °C and quenched with hydrochloric acid (2 N, 100 mL). The white precipitate formed was filtered, dried, and recrystallized from methanol. Yield 3.29 g (78%). − ^{1}H NMR ([D_6]DMSO, 400.13 MHz): δ = 7.21 (dt, *J* = 7.7 and 1.2 Hz, 2 H), 7.42−7.52 (m, 5 H), 7.63 (dt, *J* = 7.7 and 1.2 Hz, 2 H), 7.737 (td, *J* = 7.7 and 2.0 Hz, 2 H). − ^{31}P NMR ([D_6]DMSO, 400.13 MHz): δ = 0.04. − $C_{16}H_{11}Br_2N_2P$ (422.06): calcd. C 45.53, H 2.63, N 6.64, Br 37.86; found C 45.55, H 2.80, N 6.67, Br 37.74. − MS (FD); *m/z* (%): 420.0 (46.5) [M^+ (2 × ^{79}Br)], 422.0 (100) [M^+ (^{79}Br^{81}Br)], 424.0 (44) [M^+ (2 × ^{81}Br)].

4-(6-Phenyl-2-pyridyl)-6-(2-pyridyl)pyrimidine (6): A solution of **5** (0.844 g, 2 mmol) in diethyl ether (20 mL) was treated at −80 °C subsequently with *n*BuLi (1.6 M in hexane, 2.7 mL) and **1** (0.628 g, 4 mmol) in diethyl ether (30 mL). The reaction mixture was allowed to warm to room temperature and poured into methanol (40 mL) with crushed ice (25 g) and stirred for 2 h exposed to air. Then the organic solvents were removed, the aqueous phase was extracted with chloroform (3 × 50 mL), and the solvent removed in vacuum. The oily residue obtained (containing, according to TLC, both the product and significant amounts of both starting reagents) was treated with hot toluene and filtered. After 2 h, the filtrate produced a crystalline material which was recrystallized from methanol, and **6** was obtained as white needle-shaped crystals. Yield 0.16 g (26%). − ^{1}H NMR ([D_6]DMSO, 400.13 MHz): δ = 7.44 (ddd, $J_{3,5}$ = 1.1 Hz, $J_{4,5}$ = 7.9 Hz, $J_{5,6}$ = 4.8 Hz, 1 H, Py-5), 7.48 (tt, 2 H, *m*-C_6H_5), 7.55 (m, 2 H, Py-5′ + *o*-C_6H_5), 7.90 (td, $J_{3,4}$ = 7.9 Hz, $J_{4,6}$ = 1.1 Hz, 1 H, Py-4), 7.96 (t, $J_{3,4}$ = $J_{4,5}$ = 7.8 Hz, 1 H, Py′-4), 8.22 (m, 2 H, *o*-C_6H_5), 8.48 (m, 1 H, Py-3′), 8.53 (dd, 1 H, Py-3), 8.83 (ddd, 1 H, Py-6), 9.38 (d, $J_{2,5}$ = 1.1 Hz, 1 H, Pym-5), 9.52 (d, 1 H, Pym-2). − $C_{20}H_{14}N_4$ (310.36): calcd. C 77.40, H 4.55, N 18.05; found C 77.30, H 4.70, N 17.98. − MS (FD); *m/z* (%): 310.3 (100) [M^+].

Reaction of 1 with Dimethylbis(6-lithio-2-pyridyl)silane (7): Compound **7** (1.12 g, 3 mmol) in diethyl ether (150 mL) was treated at −70 °C with *n*BuLi (1.6 M in hexane, 3.9 mL) and then compound **1** (0.94 g, 6 mmol) in diethyl ether (50 mL). The reaction mixture was allowed to warm to room temperature, quenched with methanol (200 mL) and crushed ice (150 g) and then stirred for 2 h with exposure to air. The organic solvents were removed, the residual aqueous phase was extracted with chloroform (3 × 75 mL), and the solvent distilled. The residual oil was treated with boiling hexane (4 × 50 mL). On cooling, the combined extracts produced a microcrystalline precipitate that was identified as **2a**. Yield 0.30 g (32%).

X-ray Crystallographic Study: Details of the X-ray data collection and refinement for **4** are given in Table 2.[21] The accurate unit cell parameters and the orientation matrices were calculated using 23 reflections collected within a 2θ range from 6 to 38° by the least-squares technique. Intensities were collected with a P_4 Bruker diffractometer in the θ−2θ scan mode at 293(2) K. The intensities of three standard reflections, monitored every 100 intensity scans showed no evidence of crystal decay. Corrections for Lorentz polarization effects but not for absorption were applied. The structure was solved by direct methods using SHELXS-97[22] and refined by full-matrix, least-squares on all F_0^2 using SHELXL-97.[23] The non-hydrogen atoms were refined anisotropically. All the hydrogen atoms were found on the Fourier-difference map, and their positional and isotropic thermal parameters were included in the refinement.

Table 2. Crystal data and structure refinement for **4**

Empirical formula	$C_{30}H_{19}N_9$
M	505.54
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	$P\bar{1}$
a [Å]	8.635(1)
b [Å]	11.581(3)
c [Å]	13.850(2)
α [°]	104.14(1)
β [°]	96.83(1)
γ [°]	111.29(1)
U [Å^3]	1217.9(5)
Z	2
D_c [Mg m^{-3}]	1.379
μ [cm^{-1}]	0.88
F(000) [a]	524
Crystal size [mm]	0.18 × 0.20 × 0.25
θ range [°]	2.11 to 27.00
Range *h*, *k*, *l*	0 to 10, −13 to 13, −17 to 17
Reflections collected	5572
Data / parameters	5213 / 429
Final *R* indices [$I > 2\sigma(I)$]	$R1$[b] = 0.0396, $wR2$[c] = 0.0798
Final *R* indices (all data)	$R1$[b] = 0.1545, $wR2$[c] = 0.1049
Max., min. electron density [e Å^{-3}]	0.160, −0.158

[a] Weighting scheme applied $w = 1/\sigma^2(F_0^2) + (0.0429\ P)^2$ [where P is defined as $(F_0^2 + 2\ F_c^2)/3$]. – [b] $R1 = \Sigma(F_o - F_c)/\Sigma F_o$. – [c] $wR2 = \{\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$.

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