Preparation of a New Friedländer Synthon, 2,3-Diaminobenzene-1,4-dicarbaldehyde, and Its Application towards Synthesis of 1,10-Phenanthrolines and Related Cyclophane

Yang Lu and Yurngdong Jahng*

College of Pharmacy, Yeungnam University, Gyeongsan 38541, Korea

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A new Friedländer synthon, 2,3-diaminobenzene-1,4-dicarbaldehyde, was prepared from p-xylene in 4 steps, of which the Friedländer reaction with acetaldehyde and acetone in a Schulenk bottle afforded 1,10-phenathroline and neocuprine in 44% and 82% yield, respectively. The scope of the Friedländer reactions of 2,3-diaminobenzene-1,4-dicarbaldehyde, including the synthesis of hexaazacyclic cyclophane with 1,10-phenanthroline and pyridine units, was described.

Accepted Article

Background and Originality Content

The importance of 1,10-phenanthroline (**1a**, phen) and its analogues stems from their metal chelating properties, and such ability has been applied widely in analytical chemistry for the analysis of metal cationic species.[1, 2] The utility of 1,10-phenanthroline not only as a single molecule, but also as a part of macrocyclic ligand systems, has been expanded to molecular recognition,[3, 4] cleavage of nucleic acids,[5] sensing agents,[6] catalysis for chemical reactions,[7] and photolysis,[8] as well as for therapeutic and bioanalytical applications,[9] which have been compiled in several reviews,[10-15]

Synthesis of the parent phen, was somewhat limited to a double Skraup reaction of 1,2-diaminobenzene,[16] until the same author reported a procedure using 8-aminoquinoline.[17] On the other hand, many reports claimed that such methods led to unsatisfactory results,[18, 19] Hodel and Gysin reported a procedure, in which the yield was improved up to 30%, by carrying out the synthesis in the presence of a cupric salt, isolating phen as a Cu complex, and liberating it from the complex with H_2S.[20] Such Skraup reaction has been modified by Döbner and Miller using acrolein instead of glycerine.[21] which has also been substituted by acrolein diethyl acetal to lead to improvement of chemical yield. [22]

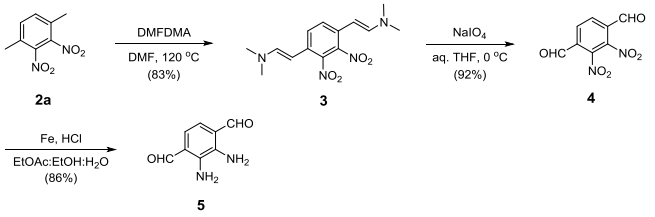
The Friedländer reaction,[23-26] a condensation reaction between enolizable ketones and β-amino-α,β-unsaturated aldehydes or ortho-aminoacetophenones to produce a quinoline nucleus and its derivatives, has long been used as one of the most facile and efficient methods for introducing quinoline and related moieties in a variety of intriguing molecules, particularly in polydentate ligands.[27, 28] The Friedländer reaction has also been employed for the preparation of phen derivatives,[27] but not for phen itself.

As a part of ongoing studies on azaaromatics and their metal complexes,[29-31] we herein described the preparation of a new Friedländer synthon, 2,3-diaminobenzene-1,4-dicarbaldehyde and its potential uses for the synthesis of phen and its derivatives, particularly cyclic ones.

Results and Discussion

To apply the Friedländer reaction to the synthesis of phen and its derivatives, especially cyclic derivatives, diaminodicarbaldehydes such as 2,3-diaminobenzene-1,4-dicarbaldehyde can be assigned as a key starting compound. One of the practical and efficient methods for the synthesis of *o*-aminoarenecarbaldehyde has been Thummel's three-step procedure[28] from *o*-nitromethylarene, i.e., converting a methyl to a *N*,*N*-dimethylaminoethenyl group by *N*,*N*-dimethylformamide dimethyl acetal (DMFDMA)[32] $NaIO_4$ oxidation of ethenyl moiety, followed by reduction of the nitro group.

Thus, the nitration of *p*-xylene can be a good starting point for the reaction sequence. The literature study showed that the products of the nitration of *p*-xylene have been of interest and remained unclear until Kobe and Hudson's decisive experiment[33] of which the structures were further confirmed by a spectral speculation [34] and X-ray analysis.[35] Nölting and Geissmann's nitration procedure[36] of *p*-xylene was modified slightly for the current protocol. The nitration of *p*-xylene with a 1:3.1 mixture of 98% sulfuric acid and nitric acid (73%, *d* = 1.42) at 80 °C afforded a mixture of three isomers in 84% yield. The ratio of the three isomers, 2,3-dinitro-*p*-xylene (**2a**), 2,5-dinitro-*p*-xylene (**2b**), and 2,6-dinitro-*p*-xylene (**2c**), was determined by 400 MHz ^{1}H NMR spectroscopy to be in a ratio of 5.4:1:2.7 for **2a**:**2b**:**2c**, of which **2a** can be separated by either column chromatography on silica gel[37,38] or recrystallization from EtOH to hand-pick the prismatic crystals.[33] The ^{1}H NMR spectrum of **2a** showed a two-proton singlet at δ 7.43 and a six-proton singlet at δ 2.37 and ^{13}C NMR revealed resonances at δ 143.7 (C^2 & C^3), 134.2 (C^5 & C^6) 130.7 (C^1 & C^4), and 18.0. Condensation of **2a** with *N*,*N*-dimethylformamide dimethyl acetal (DMFDMA) gave the corresponding *trans*,*trans*-bis-enamine (**3**)[39] in 83% yield, of which the ^{1}H NMR spectrum showed one two-proton singlet at □ 7.63 for H5 and H6, two doublets at δ 7.38 and δ 4.96 for two vinylic protons with a coupling constant 13.4 Hz, and a 12-proton singlet at □ 2.80 for N-CH_3. Oxidation of the enamine **3** with $NaIO_4$ afforded **4** in 92% yield, of which the NO_2 group was then reduced with Fe in HCl to give the desired aminoaldehyde **5** in 86% yield.



Scheme 1 Synthesis of 2,3-diaminobenzene-1,4-dicarbaldehyde

Although some of the *ortho*-aminoarenealdehydes were somewhat unstable and underwent self-condensation to form cyclic trimers as well as higher oligomers[40, 41] the aminoaldehyde

*E-mail: sunjw@ust.hk
‡These authors contributed equally to this work.

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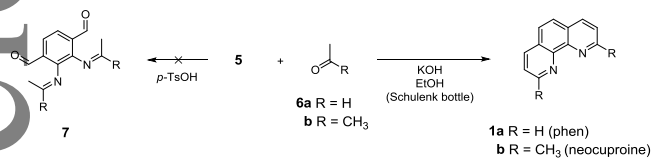
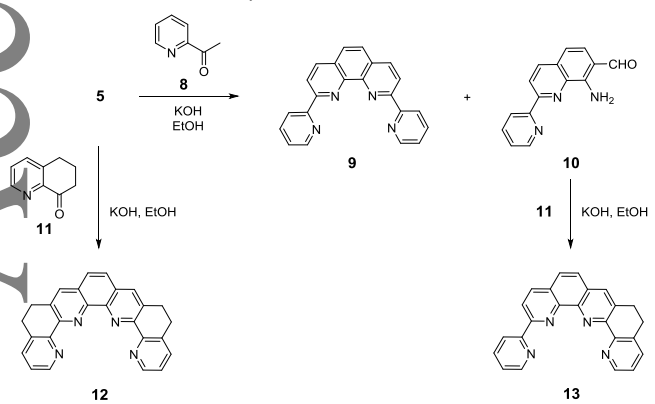
5 was stable enough to be stored at room temperature for more than a month.

The novel Friedländer reaction of **5** with either acetaldehyde (**6a**) or acetone (**6b**) did not afford the desired products, but instead produced disordered mixtures with most of the starting **5** remaining unreacted. In addition, the reactions *via* the acid (*p*-TsOH)-catalyzed Friedländer reaction or acid catalyzed imine (**7**) formation failed to afford desired products. On the other hand, the Friedländer reaction of **5** with **6** in a pressure bottle (Schulenk bottle) afforded phen (**1a**) and neocuprine (**1b**) as bidentates in 44 and 82%, respectively.



Scheme 2 Synthesis of 1,10-penanthroline and neocuprine

The Friedländer reaction of **5** with an equimolar 2-acetylpyridine (**8**) afforded the mono-condensed product **10** in 51% yield and the corresponding doubly condensed tetraaza compound **9**[42] in 22% yield. On the other hand, a reaction with 2 equivalents of 6,7-dihydroquinolin-8(5*H*)-one (**11**)[43, 44] gave the compound **12** in 83% yield along with a trace (4.6%) of 11-amino-5,6-dihydrobenzo[*b*]-1,10-phenanthroline-10-carbaldehyde as a mono-condensed product. Reaction of **10** with **11** afforded an unsymmetrical tetradentate **13** in 79% yield. It should be noted that ^{1}H NMR spectrum of **12** is somewhat abnormal as shown in Figure 1. The most characteristic three protons H^2 (H^{15}) as a broad singlet, H^3 (H^{14}) as a doublet of doublet, and H^4 (H^{13}) as a multiplet, are resonated at δ 7.96, 6.84, and 7.38, respectively, which are normally resonated in the region δ 8.70-9.00, δ 7.0-7.40, and 7.70-8.00,[45, 46] respectively, as three doublets of doublet with a characteristic ^3J values for H^2 (4-5 Hz). Therefore, we took a ^{1}H NMR spectrum at the elevated temperature: At 50 °C, the shape of the spectrum has been changed dramatically to give the spectrum matching to those of 2,3-disubstituted pyridines as shown in Figure 1. We reasoned that the flexibility of the dimethylene bridges is somewhat slow enough to disturb NMR recognition time scale between the two conformational isomers at room temperature while such effect can be neglected at the elevated temperature thus averaging two conformational isomers to lead normal ^{1}H NMR spectrum.



Scheme 3 Synthesis of tetradenates **9**, **12**, and **13**

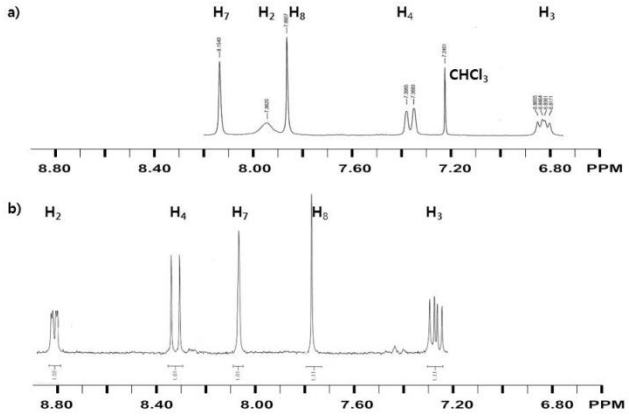
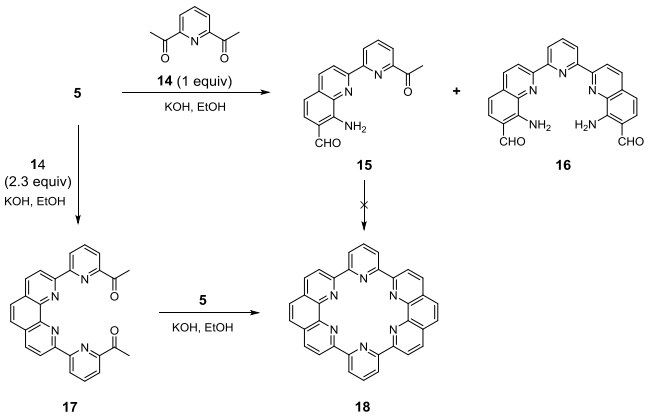


Figure 1 250 MHz ^{1}H NMR spectrum of **12** (aromatic region only). a) at room temperature, b) at 50 °C

It is quite interesting that the reaction of **5** with 2,6-diacetylpyridine (**14**) is strongly dependent on the ratio between **5** and **14**: The reaction of **5** with an equivalent amount of **14** afforded a half mono- (**15**) and a half double-condensed product (**16**) in 35% and 45% yield, respectively, while the reaction with 2.3 equivalents of **14** afforded **17** in 86% yield. Although intermediate **16** was poorly soluble in most organic solvents particularly EtOH and $CDCl_3$, not allowing to 2nd Friedländer reaction, the compound **17** showed good solubility sufficient to give ^{1}H and ^{13}C NMR spectra in $CDCl_3$ affording all the required ^{1}H and ^{13}C resonances. The 2nd Friedländer reaction of **17** with **5** afforded a hexaazacyclobutaphan (**18**) in 84% yield. The ^{1}H NMR spectrum taken from DMSO-d_6 gave one 2 proton triplet (J = 7.8 Hz) at δ 8.23 for two H^4's of two pyridine moieties, three 4 proton resonances at δ 8.68 (J = 8.0 Hz) for two H^4's and two H_7's of two 1,10-phenanthroline moieties, at δ 8.49 (J = 8.0 Hz) for two $H^{3'}$s and two $H^{8'}$s of two phens, at δ 8.35 (J = 7.8 Hz) for two $H^{3'}$s and two $H^{5'}$s of two pyridines, and one 4 proton singlet at δ 8.01 for two H^5s and two H^6s of two phens, respectively. Poor solubility in most of organic solvents did not allow us to take ^{13}C NMR spectrum. The high resolution FAB mass of **18**, however, showed *m/z* 511.1668 as an exact mass for $[C_{34}H_{19}N_6]^+$ (theoretical value comes to 511.1666) and the relative intensity of [M+1] is 36.3% (theoretical value comes 36.8%) compared to [M] supporting for the compound **18**. All attempts to convert **11** to **17** by self-condensation failed while the poor solubility of **15** in most of the organic solvents would not allow us to run the Friedländer reaction with **14**.



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Scheme 4 Synthesis of cyclophane **18**.

Conclusions

A new Friedländer synthon, 2,3-diaminobenzene-1,4-dicarbaldehyde, was prepared in 4 steps from *p*-xylene. A double Friedländer reaction of 2,3-diaminobenzene-1,4-dicarbaldehyde with 2,5-diacetylpyridine afforded 1,3(2,9)-diphenanthrolina-2,4(2,6)-dipyridinacyclobutaphane as the first cyclophan with two 1,10-phenanthrolines and two pyridines. Impressed with the results from the literature for **9** to form metal complexes with various metals [42, 47, 48], studies on the formation of their metal complexes are currently under way.

Experimental

Melting points were determined using a Fischer-Jones melting points apparatus and are not corrected. IR spectra were obtained using a Perkin-Elmer 1330 spectrophotometer. NMR spectra were obtained using a Bruker-250 spectrometer 250 MHz or JEOL 400 MHz for ^{1}H NMR and 62.5 MHz or 100 MHz for ^{13}C NMR and are reported as parts per million (ppm) from the internal standard TMS. Chemicals and solvents were commercial reagent grade and used without further purification. Electrospray ionization (ESI) mass spectrometry (MS) experiments were performed on a LCQ advantage-trap mass spectrometer (Thermo Finnigan, San Jose, USA). Elemental analyses were taken on a Hewlett-Packard Model 185B elemental analyzer.

(1*E*,1'*E*)-2,2'-(2,3-Dinitro-1,4-phenylene)bis(*N*,*N*-dimethylethen-1-amine) (3)

To a solution of 2,3-dinitro-*p*-xylene (2.0 g, 10.2 mmol) in dry DMF (10 mL) was added DMFDMA (7.1 g, 59.7 mmol). The resulting reaction mixture was heated under nitrogen at 140 °C for overnight. Evaporation of the solvent under reduced pressure afforded a crude product, which was flash chromatographed on silica gel eluting with CH_2Cl_2 to afford **3** (R_f = 0.1) as dark pink needles (3.0 g, 96%): mp > 200 °C (lit.[38] mp 237 °C, decomposed). ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.84 (s, 6H), 5.11 (d, J = 13.4 Hz, 1H), 6.80 (d, J = 13.4 Hz, 1H), 7.26 (d, J = 7.8 Hz, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 40.89, 88.27, 125.78, 129.26, 140.05, 144.27.

2,3-Dinitrobenzene-1,4-dicarbaldehyde (4)

To a solution of **3** (7.0 g, 22.9 mmol) in a mixture of water (50 mL) and THF (50 mL) was added $NaIO_4$ (24.6 g, 115 mmol) at 0 °C. Resulting mixture was stirred for 24 h and filtered. The filtrate was extracted with EtOAc (50 mL x 3) and organic layers were dried over $MgSO_4$. Evaporation of the solvent provided red crystalline solid, which was flash chromatographed on silica gel eluting with CH_2Cl_2 to give the desired product (R_f = 0.4) as orange red needles (4.72 g, 92%): mp 64-66 °C. ^{1}H NMR ($CDCl_6$, 250 MHz) δ 10.1 (s, 2H, CHO), 8.31 (s, 2H, C^5 & C^6). ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 184.2, 143.7, 133.2, 132.4. MS (ESI) m/z: 224.01 [M^+, 100.0 %], 225.01 [M + H^+, 8.9%].

2,3-Diaminobenzene-1,4-dicarbaldehyde (5)

To a solution of 2,3-dinitrobenzene-1,3-dicarbaldehyde (**4**, 200 mg, 0.89 mmol) in EtOAc:EtOH:H_2O (2:2:1, 37 mL) was added Fe powder (1.0 g, 1.8 mmol, 20 equiv.) and HCl (0.25 mL). Resulting mixture was refluxed for 3 h and filtered. The filtrate was diluted with water (30 mL) and extracted with EtOAc (30 mL x 3). The organic layers were dried over $MgSO_4$. Evaporation of the solvent provided a solid, which was flash chromatographed on silica gel eluting with CH_2Cl_2 to give the desired product (R_f = 0.4) as orange red needles (126 mg, 86%): mp > 200 °C. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 9.97 (s, 2H, CHO), 7.09 (s, 2H, H^5 & H^6), 5.94 (br. s, NH_2). ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 195.1, 139.6, 122.6, 120.7. MS (ESI) m/z 164.06 [M^+, 100%]. 165.06 [M + H^+, 8.7%). Anal. Calcd for $C_8H_8N_2O_2$: C, 58.53; H, 4.91; N, 17.06. Found C, 58.46; H, 4.92; N, 17.10.

1,10-Phenanthroline (1a)

To a solution of 2,3-diaminobenzene-1,4-dicarbaldehyde (328.0 mg, 2.0 mmol) and acetaldehyde (8.0 mL, 142.8 mmol, 7.0 equiv) in EtOH (30 mL) in Schulenk bottle (100 mL), was added saturated KOH in EtOH (1 mL). Resulting mixture was heated at 80 °C for 8 ht. Evaporation of the solvent and the residue was chromatographed on silica gel eluting with EtOAc. The latter fractions afforded compound **1a** (R_f = 0.1) as pale yellow solid (170 mg, 47%): mp 115-117 °C (lit.[17] mp 117 °C). ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.18 (dd, J = 4.3, 1.7 Hz, 2H, H^2 & H^9), 8.24 (dd, J = 8.1, 1.8 Hz, 2H, H^4 & H^7), 7.79 (s, 2H, H^5 & H^6), 7.62 (dd, J = 8.1, 4.3 Hz, 2H, H^3 & H^8). ^{13}C and IR spectral data were identical to those reported previously.

2,9-Dimethyl-1,10-phenanthroline (1b)

The same procedure described for **1a** was applied to a mixture of 2,3-diaminobenzene-1,4-dicarbaldehyde (170 mg, 1.04 mmol), acetone (70 mL, excess) and 4 drops (1.6 mL) of saturated KOH in EtOH to provide **1b** (170 mg, 79%) as pale yellow solid: mp 164−165 °C (lit.[49] mp 159-160 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.11 (d, J = 8.2 Hz, 2H, H^4 & H^7), 7.69 (s, 2H, H^5 & H^6), 7.47 (d, J = 8.2 Hz, 2H, H^3 & H^8), 2.93 (s, 6H),. ^{13}C and IR spectral data were identical to those reported previously.

2,9-Di(pyridin-2-yl)-1,10-phenanthroline (9) and 8-amino-2-(pyridin-2-yl)quinoline-7-carbaldehyde (10)

Method A: To a solution of the 2,3-diaminobenzene-1,4-dicarbaldehyde (90 mg, 0.55 mmol) and 1-(pyridine-2-yl)ethanone (66 mg, 0.55 mmol) in EtOH (30 mL), was added 2 drops (0.8 mL) of saturated KOH in EtOH. Reaction mixture was refluxed for 10 h. Evaporation of the solvent and the residue was chromatographed on silica gel eluting with CH_2Cl_2 to afford compound **10** (R_f = 0.4) as a yellow solid (75 mg, 51%): mp > 250 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.99 (s, 1H, CHO), 8.71 (ddd, J = 4.8, 1.7, 0.9 Hz, H_6 of pyridine), 8.65 (d, J = 8.6 Hz, H_3), 8.57 (dt, J = 8.0 Hz, J = 1.0 Hz, H_3 of pyridine), 8.13 (d, J = 8.6 Hz, H_4), 7.86 (td, J = 7.6 Hz, 1.8 Hz, H_4 of pyridine), 7.52 (d, J = 8.6 Hz, H_6/H_5), 7.35 (ddd, J = 8.6, 4.8, 1.2 Hz, H_5 of pyridine), 7.02 (d, J = 8.6 Hz, H_5/H_6). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 199.4, 155.9, 153.9, 149.47, 149.40, 137.9, 137.13, 136.94, 131.5, 130.9, 124.33, 122.40, 121.7, 113.9, 113.5. MS (ESI) m/z 249.09 [M^+, 100%], 250.09 [M + H^+, 16.2%]. And the latter fraction from eluent EtOAc afforded compound **9** (R_f = 0.1) as a brown solid (40 mg, 22%): mp 205-206 °C (lit.[41] mp 205-206 °C). Spectral data were identical to those reported previously in the literature.

Method B: A mixture of 2,3-diaminobenzene-1,4-dicarbaldehyde (198 mg, 1.20 mmol), 1-(pyridine-2-yl)ethanone (66 mg, 0.55 mmol), and saturated KOH in EtOH (1.0 mL) in EtOH (30 mL) was refluxed for 10 h. Evaporation of the solvent and recrystallized from EtOH to afford **9** (158 mg, 86%) as a yellow solid, of which physical and spectral properties are same as those described above.

5,6,11,12-Tetrahydrobenzo[2,1-*b*:3,4-*b'*]bis([1,10]phenanthroline) (12)

To a solution of 2,3-diaminobenzene-1,4-dicarbaldehyde (60 mg, 0.37 mmol) and 6,7-dihydroquinolin-8(5*H*)-one (265 mg, 1.80 mmol, 2.5 equiv.) in EtOH (30 mL), was added 2 drops (0.8 mL) of saturated KOH in EtOH solution. Resulting reaction mixture was refluxed for 10 h. Evaporation of the solvent and the residue was chromatographed on silica gel eluting with EtOAc. The early fractions afforded 11-amino-5,6-dihydrobenzo[*b*]-1,10-phenanthroline-10-carbaldehyde (R_f = 0.4) as a yellow crystalline solid (5.52 mg, 4.6%): mp 88-90 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.86 (s, 1H, CHO), 8.62 (d, J = 4.8 Hz, H^2), 8.49 (br. s, 2H, NH_2), 7.70 (s, H^7), 7.52 (d, 1H, J = 7.5 Hz,

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H^4), 7.37 (d, J = 8.5 Hz, H^8/H^9), 7.20 (dd, J = 7.4 Hz, 4.6 Hz, H^3), 6.79 (d, J = 8.5 Hz, H^9/H^8), 2.95-2.96 (m, 2H), 3.02-3.05 (m, 2H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 192.8, 151.1, 150.6, 149.4, 148.6, 138.2, 135.06, 135.03, 134.2, 131.5, 131.4, 124.2, 113.1, 112.2, 28.1, 27.6. The latter fractions eluting with EtOAc:CH_3OH (9:1) afforded the compound **12** (R_f = 0.1) as a yellow solid (119 mg, 83%): mp >200 °C. ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C) δ 8.15 (s, 2H, H^7 & H^{10}), 7.96 (br. s, 2H, H^2 & H^{15}), 7.88 (s, 2H, H^8 & H^9), 7.38 (d, 2H, H^4 & H^9), 6.84 (dd, 2H, H^3 & H^{14}), 3.18 (t, 4H, J = 5.8 Hz), 2.96 (t, 4H, J = 5.8 Hz). ^{1}H NMR (250 MHz, $CDCl_3$, 50 °C) δ 8.84 (d, 2H, J = 4.8 Hz, H^2 & H^{15}), 7.98 (s, 2H, H^7 & H^{10}), 7.88 (s, 2H, H^8 & H^9), 7.38 (dd, 2H, J = 7.8, 1.8 Hz, H^4 & H^{13}), 7.20 (dd, J = 7.8, 4.8 Hz, H^3 & H^{14}), 3.24 (t, 4H, J = 6.8 Hz), 3.08 (t, 4H, J = 6.8 Hz). ^{13}C NMR (62.5 MHz, $CDCl_3$, 25 °C) δ 152.0, 151.5, 148.8, 145.9, 136.1, 135.2, 134.5, 133.8, 129.0, 126.9, 124.1, 28.0, 27.6. MS (ESI) m/z 386.15 [M^+, 100%], 387.16 [M + H^+, 28.1%].

12-(Pyridin-2-yl)-5,6-dihydroquinolino[8,7-*b*][1,10]phenanthroline (**13**).

To a solution of 8-amino-2-(pyridine-2-yl)quinoline-7-carbaldehyde (**10**, 60.0 mg, 0.24 mmol) and 2-acetylpyridine (35.4 mg, 0.2 mmol) in EtOH (30 mL), was added 2 drops (0.8 mL) of saturated KOH in EtOH solution. The resulting reaction mixture was refluxed for 10 h. Evaporation of the solvent and the residue was chromatographed on silica gel eluting with ethyl acetate to afford compound **13** (86.7 mg, 79%, R_f = 0.1) as a yellow solid: mp > 200 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.15 (d, 1H, J = 8.0 Hz, 1.0 Hz, H^3 of pyridine), 8.85 (dd, 1H, J = 4.8, 1.5 Hz, H^2), 8.80 (d, J = 8.5 Hz, H^{11}), 8.72 (ddd, 59 (d, 1H, J = 4.8, 1.8, 0.8 Hz, H^6 of pyridine), 8.35 (d, J = 8.5 Hz, H^{10}), 8.09 (s, 1H, H^7), 7.97 (dt, J = 8.0, 1.0 Hz, H^4 of pyridine), 7.82 (d, 1H, J = 8.8 Hz, H^8/H^9), 7.76 (d, H, J = 8.8 Hz, H^9/H^8), 7.63 (dd, 1H, J = 7.8, 1.5 Hz, H^5), 7.36 (ddd, 1H, J = 7.8, 4.8, 1.5 Hz, H^5 of pyridine), 7.31 (dd, J = 7.8, 4.8 Hz, H^3), 3.32-3.20 (m, 2H), 3.12-3.05 (m, 2H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 156.7, 155.9, 151.9, 151.8, 149.0, 148.9, 146.2, 145.7, 137.2, 137.1, 136.1, 134.93, 134.87, 133.6, 129.2, 128.8, 127.1, 126.2, 124.13, 124.09, 123.4, 121.1, 28.0, 27.7. MS (ESI) m/z 360.14 [M^+, 100%], 361.14 [M + H^+, 26.0%]. Anal. Calcd for $C_{24}H_{16}N_4$: C, 79.98; H, 4.47; N, 15.55. Found C, 81.08; H, 4.56; N, 14.36.

2-(6-Acetylpyridin-2-yl)-8-aminoquinoline-7-carbaldehyde (15) and 2,2'-(pyridine-2,6-diyl)bis(8-amino-quinoline-7-carbaldehyde) (16)

A mixture of 2,3-diaminobenzene-1,4-dicarbaldehyde (100.0 mg, 0.61 mmol), 2,6-diacetylpyridine (100.0 mg, 0.61 mmol, 1.0 equiv.) and saturated KOH in EtOH (2 mL) in EtOH (30 mL) was refluxed for 9 h. The reaction mixture was filtered to afford the compound **16** as a brown solid (61 mg, 23%): mp > 200 °C. ^{1}H NMR (250 MHz, DMSO-d_3) δ 10.04 (s, 2H, CHO), 9.04 (d, 2H, J = 7.8 Hz, H^3), 8.97 (d, 2H, J = 8.5 Hz, H^3 and H^5 of pyridine), 8.45 (dm, 1H, J = 8.6 Hz, H^4 of pyridine, overlapped with NH_2), 8.40 (d, 2H, J = 7.7 Hz, H^4), 7.71 (d, 2H, J = 8.6 Hz, H^5), 7.17 (d, 1H, J = 8.6 Hz, H_6),. The filtrate was evaporated and the residue was chromatographed on silica gel eluting with CH_2Cl_2 to afford **15** (R_f = 0.1) as a yellow solid (90 mg, 51%): mp > 250 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ 10.00 (s, 1H, -CHO), 8.75 (dd, 1H, J = 8.0, 1.4 Hz, H^2 of pyridine), 8.73 (d, 1H, J = 8.0 Hz, H^3), 8.20 (d, 1H, J = 8.0 Hz, H^5 of pyridine), 8.09 (dd, 1H, J = 8.0, 1.3 Hz, H^5 of pyridine), 8.01 (t, 1H, J = 7.8 Hz, H^4 of pyridine), 7.54 (d, 1H, J = 8.5 Hz, H^5), 7.04 (d, 1H, J = 8.5 Hz, H^5), 2.85 (s, 3H, CH_3). MS (ESI) m/z 291.10 [M^+, 100%], 292.10 [M + H^+, 18.4%].

2,9-Di(6-acetylpyridin-2-yl)-1,10-phenanthroline (**17**)

A mixture of 2,3-diaminobenzene-1,4-dicarbaldehyde (110.0 mg, 0.67 mmol), 2,6-diacetylpyridine (250.0 mg, 1.53 mmol, 2.3 equiv.), and saturated KOH in EtOH (2 mL) in EtOH (70 mL) was refluxed for 9 h. Reaction mixture was evaporated and the residue was chromatographed on alumina (Al_2O_3) eluting with CH_2Cl_2 (R_f = 0.7) to afford the desired compound **17** as a white crystalline solid (227.0 mg, 81%): mp > 200 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.27 (dd, J = 8.0, 1.8 Hz, 2H, H^3 and H^8), 8.96 (d, J = 8.5 Hz, 2H, H^3 of pyridine), 8.43 (d, J = 8.3 Hz, 2H, H^5 of pyridine), 8.14-8.11 (m, 4H, H^4, H^6, H^4 of pyridine), 7.89 (s, 2H, H^5 and H^6), 2.90 (s, 6H, CH_3). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 200.5, 155.6, 155.4, 153.2, 145.8, 138.2, 137.5, 129.6, 127.2, 125.5, 122.3, 120.85, 26.1. MS (ESI) m/z 418.14 [M^+, 100%], 419.15 [M + H^+, 28.1%].

1,3(2,9)-Diphenanthrolina-2,4(2,6)-dipyridinacyclobutaphane (**18**)

To a solution of 2,3-diaminoterephthalaldehyde (110 mg, 0.67 mmol) and 2,9-di(6-acetylpyridin-2-yl)-1,10-phenanthroline (280 mg, 0.67 mmol) in EtOH (30 mL) was added 2 drops (0.8 mL) of saturated KOH in EtOH. Resulting reaction mixture was refluxed for 12 h and filtered while hot. The filter cake was washed with CH_2Cl_2, CH_3OH, and CH_3CN to afford the compound **18** as a brown solid (321 mg, 94%): mp >200 °C. ^{1}H NMR (250 MHz, DMSO-d_6) δ 8.68 (d, J = 8.0 Hz, 4H, H^4 and H^7 of phen), 8.49 (d, J = 8.0 Hz, 4H, H^3 and H^8 of phen), 8.35 (d, J = 7.8 Hz, 4H, H^3 and H^5 of pyridine), 8.23 (t, J =7.8 Hz, 2H, H^4 of pyridine), 8.01 (AB quartet, 4H, H^5 and H^6 of phen). Not soluble enough to give ^{13}C NMR spectrum. MS (ESI) *m/z* 510.16 [M^+, 100%], 511.16 [M + H^+, 36.8%]. HRFAB *m/z* 511.1668 Calcd for $[C_{34}H_{19}N_6]^+$: 511.1666. Anal. Calcd for $C_{34}H_{18}N_6$-$2H_2O$: C, 74.71; H, 4.06; N, 15.38; O, 5.85. Found C, 74.82; H, 4.05; N, 15.34.

Supporting Information

The supporting information for this article is available on the WWW under https://doi.org/10.1002/cjoc.2018xxxxx.

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Entry for the Table of Contents

Page No.

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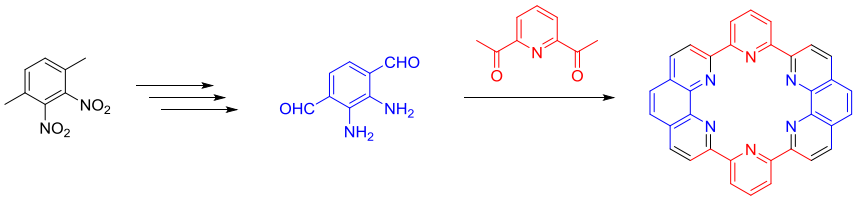

Yang Lu, Yurngdong Jahng*

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