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SYNTHESIS OF 2,4,5-TRIARYL-5*H*-CHROMENO[4,3-*b*]PYRIDINES IN IONIC LIQUID

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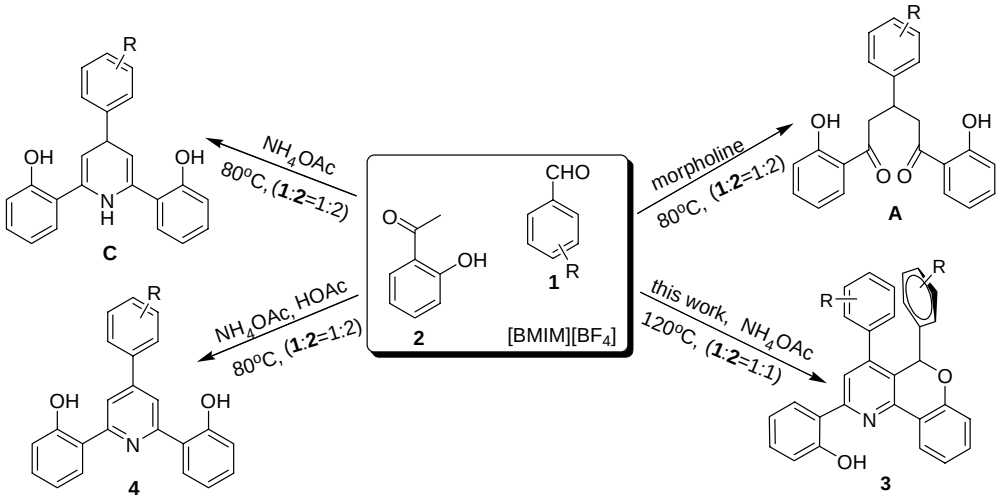
Abstract – The synthesis of 2,4,5-triaryl-5*H*-chromeno[4,3-*b*]pyridines via a three-component one-pot cascade reaction of 2-hydroxyacetophenone, aromatic aldehyde and ammonium acetate in ionic liquid [BMIM][BF_4] was reported.

INTRODUCTION

5*H*-chromeno[4,3-*b*]pyridines have some important biological activities such as analgesic, anti-inflammation and antibacterial.[1,2] Accordingly, the development of efficient synthetic strategies for the construction of this molecular architecture is of considerable importance from the standpoint of the material and organic chemistry. By far, for its complex structure, few approaches for obtaining 5*H*-chromeno[4,3-*b*]pyridines have been reported. The usually used one was mainly based on the multi-step intramolecular oxaza- or diaza-Diels-Alder cycloadditions1 with some shortcomings such as low yields, high reaction temperature (180-200 ˚C), long reaction time (48h[2]) and requirement of toxic solvents. Moreover, unavailable starting material such as 3-benzylidenechroman-4-one, or neutral 2-azadienes or 2-[2-(prop-2-ynyloxy)phenyl]pyridine[2] was required. In other approaches,[3] it is the product of the primary 1,4-addition followed by the pyrone ring-opening, attack of the NH_2 group to the carbonyl bound with the aromatic cycle, and ring-closure involving the phenolic hydroxyl and aldehyde group.

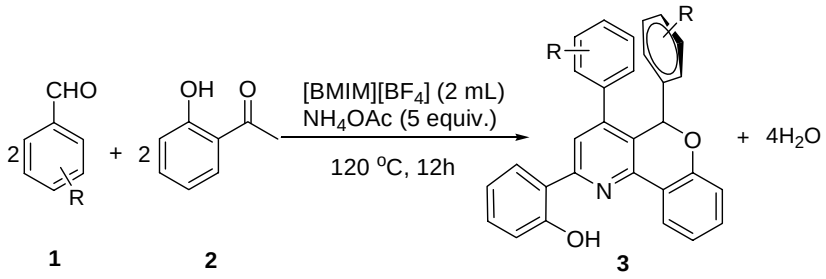
During the past decade, ionic liquids have gained increasing attention for performing all types of reaction with sometimes remarkable results.[4,5]

The reaction of aromatic aldehyde (**1**) and 2-hydroxyacetophenone (**2**) under different reaction conditions can give interesting different products (Scheme 1). In our previous work,[6] **1** and **2** (mol ratio = 1:2) reacted at 80 ˚C catalyzed by morpholine (pK_b=5.51) in ionic liquid [BMIM][BF_4] afford 1,3,5-triaryl-1,5-diketones (**A,** 58-80%). But when morpholine was replaced with ammonium acetate (pK_b $[OAc]^-$= 9.25), which can not catalyze the same reaction and so act as reagent, we could obtain 2,4,6-triaryl-1,4-dihydropyridines (**C,** 44-78%) selectively under the same conditions.[7] Moreover, when acetic acid (HOAc) was used as catalyst, 2,4,6-triarylpyridine (**4**) could be given at 80°C in ionic liquid [BMIM][BF_4][8] (Scheme 1).



Scheme 1

In the present work, the one-pot three-component cascade reaction of equivalent of **1** and **2** with 5 equiv. of ammonium acetate (1:1:5) in ionic liquid [BMIM][BF_4] at 120 ˚C without any catalyst afforded 2,4,5-triaryl-5*H*-chromeno[4,3-*b*]pyridines (Scheme 2). Up to nine new bonds and two new rings were formed in one-pot with water as the only one by-product in this reaction. Bogner and co-workers[9] have ever synthesized **3a** (R=H) with troublesome procedure, but their work can obtain only one compound of this series.



Scheme 2. Synthesis of triaryl-5*H*-chromeno[4,3-*b*]pyridines

RESULTS AND DISCUSSION

Initially, we screened various reaction conditions for the reaction of 4-cyanobenzaldehyde (2.0 mmol), 2-hydroxyacetophenone (2.0 mmol) and ammonium acetate and the results were summarized in Table 1. It was shown that when common organic solvents and water were used as solvent, no desired product was checked (Table 1, entries 1-5). It may be because those classical organic solvents, such as acetone which has no catalysis on this reaction, could only give some cross aldol condensations products, and meanwhile water derived the equilibrium toward reactants. And these low-boiling solvents can not offer enough energy to afford desired product which may be a thermodynamic controlled ones. However, when using ionic liquid [BMIM][Br][10] as reaction medium (Table 1, entry 6), the desired product triaryl-5*H*-chromeno[4,3-*b*]pyridines **3** was isolated in 32% yield, which indicated the significant role in controlling this multi-component reaction as solvent and catalyst of ionic liquids. The best result was

Table 1. Optimization of the reaction of 4-cyanobenzaldehyde, 2-hydroxyacetophenone and ammonium acetate.[a]

Entry	Temp. (^{o}C)	Solvent	Time (h)	Isolated yield (%)
1	120	neat	12	no reaction
2	refluxing temp.	acetone	12	no product **3**
3	refluxing temp.	EtOH	12	no product **3**
4	120	DMF	12	no product **3**
5	refluxing temp.	H_2O	12	no reaction
6	120	[BMIM][Br]	12	32
7	120	[BMIM][BF_4]	12	59
8	120	[BMIM][ClO_4]	12	43
9	120	[BPY][Br][b]	12	34
10	120	[BPY][BF4]	12	29
11	120	[BPY][ClO_4]	12	28
12	80	[BMIM][BF_4]	12	35
13	100	[BMIM][BF_4]	12	45
14	140	[BMIM][BF_4]	12	54
15	160	[BMIM][BF_4]	12	52
16	120	[BMIM][BF_4]	9	33
17	120	[BMIM][BF_4]	10	45
18	120	[BMIM][BF_4]	11	55
19	120	[BMIM][BF_4]	13	54

[a]All reactions were carried out on a 2.0 mmol of aromatic aldehyde, 2.0 mmol of 2-hydroxyacetophenone, 5 equiv. of ammonium acetate in 2 mL of ionic liquid. [b][BPY]=1-n-butylpridinum.

obtained in [BMIM][BF_4], which may be attribute to its strongest basicity among these six kinds of ionic liquid (pKa[ClO_4]$^-$= -11, pKa[Br]$^-$ = -9, pKa[BF_4]$^-$ = 0.5). It was also realized that the process was efficiently facilitated at 120 ^oC. When reaction temperature was 80 ^oC, the yield of desired 2,4,5-triaryl-5*H*-chromeno[4,3-*b*]pyridine decreased (35%).

We applied this condition to other substrates and the results were summaried in Table 2. It showed the electronic nature and steric effect of substituted group in aromatic aldehyde had some influenced on the yield, electron donating substituents could enhance the yields, which implied the nucleophilic procedure of the reaction.

Table 2. Synthesis of triaryl-5*H*-chromeno[4,3-*b*]pyridines.[a]

Entry	R	Time (h)	Product	Isolated yield (%)
1	H	12	**3a**	75
2	4-Me	10	**3b**	78
3	4-MeO	10	**3c**	81
4	4-Br	13	**3d**	52
5	2,3-$(MeO)_2$	12	**3e**	68
6	4-CN	15	**3f**	59
7	4-Cl	14	**3g**	62
8	2-MeO	13	**3h**	70
9	3,4,5-$(MeO)_3$	12	**3i**	73
10	2-Cl	13	**3j**	60
11	3-Br	14	**3k**	63
12	3,4-OCH_2O	11	**3l**	66
13	3-NO_2	13	**3m**	64
14	4-F	11	**3n**	64

[a]All reactions were carried out on a 2.0 mmol of aromatic aldehyde, 2.0 mmol of 2-hydroxyacetophenone, 5 equiv. of ammonium acetate in 2 mL of ionic liquid.

The X-ray structure of **3e** was shown in Figure 1.[11]

On the basis of our previous works, [6-8] a reasonable mechanism for the formation of the products 3 were outlined in Scheme 3. The reaction resembles to the synthesis of dihydropyridines or pyridines according to Hantzsch.[12] Firstly, 2-hydroxyacetophenones react with arylaldehyde to generate A, which further undergoes nucleophilic addition-elimination (Adn-E) reaction of ammonia (deriving from ammonium acetate) to give B then to C, which subsequently convert to D via Adn-E reaction of the second arylaldehyde, D was easily etherified and dehydrogenated to the final product **3**.

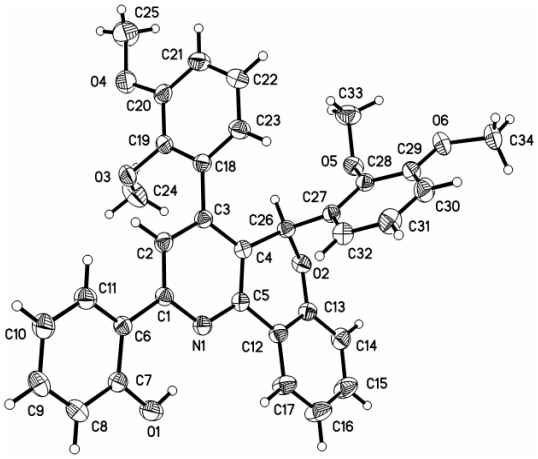
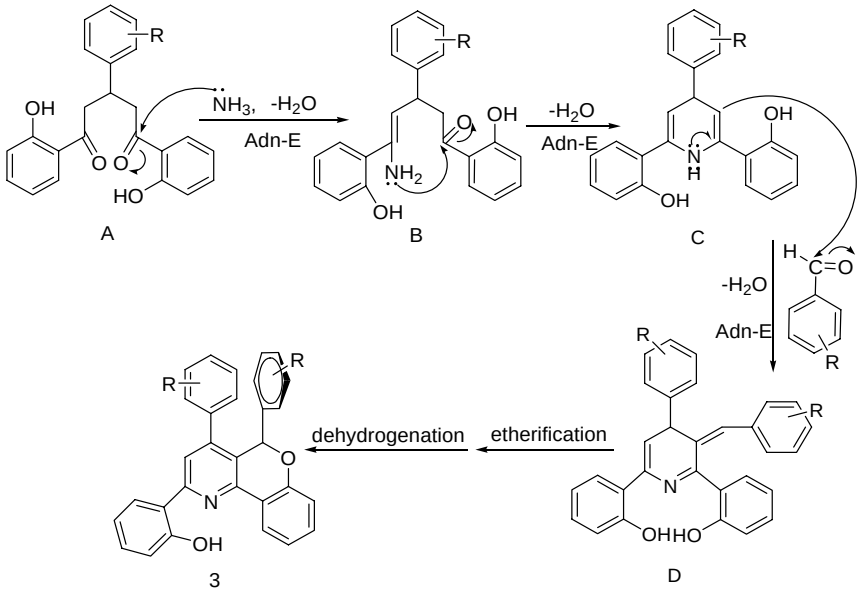


Figure 1. Molecular structure (X-ray diffraction data) of **3e**.



Scheme 3. A possible mechanism for the formation of **3**.

In summary, we have developed a novel simple, effective and catalysis free process for the preparation of 2,4,5-triaryl-5*H*-chromeno[4,3-*b*]pyridines in [BMIM][BF_4]. Besides the advantages that all the reagents were added at the beginning and the same reaction conditions were maintained throughout, the features of this process include: (1) the starting materials are available; (2) the reaction has good atom-economy and environmental friendliness: nine new bonds (three C-N bonds, one C-O bond, three C-C single bonds, two C-C double bonds) and two new rings were formed in one-pot with water as the only one by-product during the whole process. Indeed, the present protocol provides a straightforward and effective pathway to afford triaryl-5*H*-chromeno[4,3-*b*]pyridines.

EXPERIMENTAL

Infrared spectra were obtained on a Bruker FT-IR spectrometer. ^{1}H NMR spectra were recorded at 400

MHz on a Bruker DPX 400 or AV 400 spectrometer. ^{13}C NMR spectra were recorded at 100.6 MHz. Mass spectra was determined by using a TOF-MS high resolution mass spectrometer. Thin layer chromatography analysis was carried out on aluminium sheets of silica gel GF_{254}. All reagents were obtained from commercial suppliers and used without further purification unless otherwise stated. Organic solvents were dried and/or distilled prior to use. The X-ray structure determination for complex **3e** was given by Smartapex Bruke diffractometer.

Typical procedure for the preparation of triaryl-5H-chromeno[4,3-b]pyridines

A mixture of aromatic aldehyde **1** (2.0 mmol), 2-hydroxyacetophenone **2** (0.27 g, 2.0 mmol), ammonium acetate (0.77 g, 10 mmol, 5 equiv.), and ionic liquid 1-butyl-3-methylimidazolium tetrafluoroborate ([BMIM][BF_4]) (2.0 mL) was placed in a 25 mL flask and then heated at 120 °C with stirring for 10-15 h. After completion of the reaction, as indicated by thin layer chromatography (TLC). The reaction mixture was then quenched with water and the product **3** was isolated by filtration followed by purification through simple recrystallization with DMF. Ionic liquids were prepared according to the literature.[10]

Spectra data of products:

2-(4,5-Diphenyl-5H-chromeno[4,3-b]pyridin-2-yl)phenol (3a).

Yellow crystals, mp. 194.1-195.3 ˚C, (75%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.80 (1H, s), 8.20 (1H, d, *J*=8.4 Hz), 8.14 (1H, s), 8.01 (1H, d, *J*=8.0 Hz), 7.46 (3H, m), 7.36 (4H, m), 7.24 (3H, m), 7.11 (1H, t), 7.04 (2H, t), 7.02 (1H, d, *J*=9.6 Hz), 6.97 (2H, t), 6.50 (1H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.50, 159.20, 156.51, 153.21, 148.00, 141.20, 139.20, 135.02, 134.50, 131.50, 131.39, 131.35, 131.24, 131.05, 130.80, 130.33, 126.40, 125.50, 125.31, 124.50, 123.40, 122.91, 122.82, 120.90, 120.50. IR (cm^{-1}): 3310 (w), 3030 (s), 1600 (s), 1580 (m), 1031 (m). HRMS (ESI): m/z calcd. for $C_{30}H_{21}NO_2$, 427.4932; found, 427.1554.

2-(4,5-Bis(4-methylphenyl)-5H-chromeno[4,3-b]pyridin-2-yl)phenol (3b).

Yellow crystals, mp. 207.7-208.7 ˚C, (78%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 14.70 (1H, s), 8.11 (1H, dd, J_1=1.6 Hz, J_2=7.6 Hz), 7.85 (1H, dd, J_1=1.6 Hz, J_2=7.6 Hz), 7.80 (1H, s), 7.33-7.37 (1H, t), 7.24-7.28 (1H, t), 7.18 (2H, d, *J*=7.6 Hz), 7.11-7.04 (4H, m), 7.02 (4H, s), 6.91-6.95 (1H, t), 6.88-6.85 (1H, dd, J_1=1.6 Hz, J_2=7.6 Hz), 6.38 (1H, s,), 2.39 (3H, s,), 2.25 (3H, s,). ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.98, 156.91, 154.25, 149.80, 145.99, 138.72, 138.24, 136.17, 134.16, 131.98, 131.64, 129.27, 129.10, 128.26, 127.92, 126.38, 124.28, 123.34, 122.29, 122.12, 119.25, 118.92, 118.81, 118.50, 118.10, 21.19, 21.07. IR (cm^{-1}): 3310 (w), 3030 (s), 2985 (s), 1600 (s), 1550 (m), 1030 (m). HRMS (ESI): m/z calcd. for $C_{32}H_{25}NO_2$, 455.5464; found, 455.1871.

2-(4,5-Bis(4-methoxyphenyl)-5H-chromeno[4,3-b]pyridin-2-yl)phenol (3c).

Brown crystals, mp. 191.2-192.4 ˚C, (81%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.91 (1H, s), 8.18 (1H, dd, J_1=1.6 Hz, J_2=7.6 Hz), 8.09 (1H, s), 8.00 (1H, dd, J_1=1.6 Hz, J_2=7.6 Hz), 7.39-7.32 (2H, m), 7.26 (2H, d, J=7.6 Hz), 7.12-7.17 (1H, t), 6.90-7.07 (7H, m), 6.79-6.81 (2H, d, J=7.6 Hz), 6.45 (1H, s), 3.78 (3H, s), 3.65 (3H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.99, 159.57, 156.92, 154.16, 149.44, 145.97, 132.00, 131.67, 131.35, 129.72, 129.47, 129.32, 126.39, 124.29, 123.53, 122.32, 122.16, 119.33, 118.95, 118.83, 118.54, 118.14, 114.02, 113.80, 55.34, 55.12. IR (cm^{-1}): 3310 (w), 3030 (s), 2985 (s), 1610 (s), 1540 (m), 1020 (m). HRMS (ESI): m/z calcd. for $C_{32}H_{25}NO_4$, 487.5452; found, 487.1771.

2-(4,5-Bis(4-bromophenyl)-5H-chromeno[4,3-b]pyridin-2-yl)phenol (3d).

Yellow crystals, mp. 221.5-222.5 ˚C, (52%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.65 (1H, s), 8.21 (1H, d, J=9.6 Hz), 8.15 (1H, s), 8.06 (1H, d, J=9.6 Hz), 7.67 (2H, d, J=8.0 Hz), 7.44 (2H, d, J=9.6 Hz), 7.33-7.41 (2H, m), 7.29 (2H, d, J=8.0 Hz), 7.14-7.21 (1H, t), 6.94-7.09 (5H, m), 6.47 (1H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ 155.27, 152.83, 149.14, 143.88, 141.46, 138.00, 135.09, 133.12, 131.01, 127.71, 127.33, 127.27, 127.07, 125.13, 124.90, 121.74, 119.68, 118.72, 118.30, 118.05, 117.63, 117.00, 114.40, 114.29, 113.93, 113.80, 113.44. IR (cm^{-1}): 3310 (w), 3030 (s), 2980 (s), 1600 (s), 1550 (m), 1010 (m). HRMS (ESI): m/z calcd. for $C_{30}H_{19}Br_2NO_2$, 585.2854; found, 584.9760.

2-(4,5-Bis(2,3-dimethoxyphenyl)-5H-chromeno[4,3-b]pyridin-2-yl)phenol (3e).

Yellow crystals, mp. 223.7-225.2 ˚C, (68%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.95 (1H, s), 8.23 (1H, d, J=8.0 Hz), 8.15 (1H, s), 8.00 (1H, d, J =8.0 Hz), 7.33-7.41 (2H, m), 7.13-7.18 (1H, t), 6.10-7.08 (6H, m), 6.84 (1H, s), 6.77 (1H, d, J=8.0 Hz), 6.46 (1H, d, J=8.0 Hz), 6.44 (1H, s), 3.79 (3H, s), 3.67 (3H, s), 3.65 (3H, s), 3.52 (3H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.00, 155.37, 154.30, 153.00, 152.90, 147.00, 145.50, 145.00, 132.80, 132.35, 131.80, 131.00, 128.30, 124.80, 123.90, 122.90, 121.90, 121.60, 120.90, 119.90, 119.50, 118.54, 118.00, 61.00, 60.50, 56.50, 56.00. IR (cm^{-1}): 3310 (w), 3030 (s), 2986 (s), 1600 (s), 1560 (m), 1030 (m). HRMS (ESI): *m/z* calcd. for $C_{34}H_{35}NO_6$, 547.5972; found, 547.1975.

2-(4,5-Bis(4-cyanophenyl)-5H-chromeno[4,3-b]pyridin-2-yl)phenol (3f).

Yellow crystals, mp. >300 ˚C, (59%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.50 (1H, s), 8.21 (1H, d, J=8.0 Hz), 8.19 (1H, s), 8.03 (1H, d, J=7.6 Hz), 7.94 (2H, d, J=8.0 Hz), 7.71 (2H, d, J=8.0 Hz), 7.54 (2H, d, J=8.0 Hz), 7.37-7.41 (2H, t), 7.30 (2H, d, J=8.0 Hz), 7.17-7.21 (1H, t), 6.96-7.04 (3H, t), 6.57 (1H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.20, 156.85, 154.05, 149.55, 148.32, 148.05, 147.95, 147.90, 145.75, 133.05, 132.90, 132.30, 130.30, 128.50, 124.00, 123.30, 123.00, 122.90, 122.20, 122.10, 121.90, 119.90, 119.80, 118.80, 118.20, 109.40, 109.00, 108.40, 101.90. IR (cm^{-1}): 3320 (w), 3030 (s), 2980(s),

2250 (s), 1600 (s), 1560 (m), 1030 (m). HRMS (ESI): *m/z* calcd. for $C_{32}H_{19}N_3O_2$, 477.5122; found, 477.1455.

2-(4,5-Bis(4-chlorophenyl)-5H-chromeno[4,3-b]pyridin-2-yl)phenol (3g).

Yellow crystals, mp. 208.3-209.4 ˚C, (62%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.62 (1H, s), 8.20 (1H, d, *J*=8.0 Hz), 8.13 (1H, s), 8.01 (1H, d, *J*=8.0 Hz), 7.52 (2H, d, *J*=8.0 Hz), 7.29-7.35 (6H, m), 7.11-7.20 (3H, m), 6.94-7.04 (3H, m), 6.48 (1H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.10, 157.00, 153.90, 148.90, 145.92, 137.90, 135.80, 134.20, 134.00, 133.00, 132.80, 130.90, 130.00, 129.50, 129.00, 128.60, 124.00, 123.20, 123.00, 121.90, 121.00, 119.00, 118.90, 118.30. IR (cm^{-1}): 3350 (w), 3030 (s), 2980 (s), 1640 (s), 1580 (m), 1050 (m). HRMS (ESI): *m/z* calcd. for $C_{30}H_{19}Cl_2NO_2$, 496.3834; found, 495.0775.

2-(4,5-Bis(2-methoxyphenyl)-5H-chromeno[4,3-b]pyridin-2-yl)phenol (3h).

Yellow crystals, mp. 244.5-245.5 ˚C, (70%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 14.70 (1H, s), 8.11 (1H, dd, J_1=1.2 Hz, J_2=1.6 Hz), 7.81 (1H, dd, J_1=1.6 Hz, J_2=1.6 Hz), 7.81 (1H, s), 7.56 (1H, t), 7.31-7.33 (1H, t), 7.08-7.18 (6H, m), 6.78-6.98 (4H, m), 6.75-6.79 (2H, m), 6.39 (1H, s), 3.88 (3H, s), 3.74 (3H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ 160.19, 159.72, 159.32, 156.98, 154.10, 149.80, 145.90, 132.90, 132.15, 131.12, 130.30, 129.69, 129.10, 128.05, 124.10, 123.60, 123.00, 122.53, 121.00, 119.93, 119.90, 118.85, 118.82, 114.80, 114.70. IR (cm^{-1}): 3310 (w), 3030 (s), 2985 (s), 1600 (s), 1550 (m), 1050 (m). HRMS (ESI): *m/z* calcd. for $C_{32}H_{25}NO_4$, 487.5452; found, 487.1768.

2-(4,5-Bis(3,4,5-trimethoxyphenyl)-5H-chromeno[4,3-b]pyridin-2-yl)phenol (3i).

Brown crystals, mp. 236.1-237.9 ˚C, (73%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.95 (1H, s), 8.22 (1H, d, *J*=8.0 Hz), 8.17 (1H, s), 8.02 (1H, d, *J*=8.0 Hz), 7.53-7.59 (1H, t), 7.34-7.44 (1H, m), 6.94-7.22 (4H, m), 6.60 (2H, s), 6.46 (3H, d, *J*=11.2 Hz), 3.56-3.61 (18H, m). ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.40, 156.96, 154.46, 153.96, 150.10, 147.68, 145.67, 138.23, 135.21, 132.82, 132.38, 131.62, 128.49, 127.76, 123.57, 123.60, 122.33, 121.09, 120.00, 119.66, 119.61, 118.61, 118.25, 106.62, 106.560,106.15, 60.69, 60.51, 60.39, 56.97, 56.42, 56.05. IR (cm^{-1}): 3300 (w), 3030 (s), 2980 (s), 1600 (s), 1550 (m), 1050 (m). HRMS (ESI): *m/z* calcd. for $C_{36}H_{33}NO_4$, 607.6491; found, 607.2217.

2-(4,5-Bis(2-chlorophenyl)-5H-chromeno[4,3-b]pyridin-2-yl)phenol (3j).

Yellow crystals, mp. 196.9-197.7 ˚C, (60%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.62 (1H, s), 8.16-8.21 (1H, t), 8.13 (1H, s), 8.09 (1H, d, *J*=8.0 Hz), 7.67-7.75 (1H, m), 6.81-7.49 (12H, m), 6.60 (1H, d, *J*=9.6 Hz), 6.58 (1H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.21, 157.72, 153.82, 153.73, 147.20, 145.65, 135.21, 135.16, 133.45, 133.11, 132.42, 131.35, 131.20, 131.18, 131.10, 130.78, 130.35, 130.29, 130.07,

128.65, 127.93, 123.59, 119.77, 118.27. IR (cm^{-1}): 3350 (w), 3010 (s), 2990 (s), 1630 (s), 1580 (m), 1010 (m). HRMS (ESI): *m/z* calcd. for $C_{30}H_{19}Cl_2NO_2$, 496.3834; found, 495.0769.

2-(4,5-Bis(3-bromophenyl)-5H-chromeno[4,3-b]pyridin-2-yl)phenol (3k).

Brown crystals, mp. 187.1-188.6 ˚C, (63%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 14.70 (1H, s), 8.10 (1H, dd, J_1=1.6 Hz, J_2=7.6 Hz), 7.85 (1H, dd, J_1=1.6 Hz, J_2=7.6 Hz), 7.79 (1H, s), 7.33-7.37 (1H, t), 7.23-7.27 (1H, t), 7.18 (2H, d, *J*=7.6 Hz), 7.01-7.11 (8H, m), 6.90-6.94 (1H, t), 6.82 (1H, dd, J_1=1.6 Hz, J_2=7.6 Hz), 6.38 (1H, t). ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.25, 157.00, 154.21, 149.98, 145.78, 139.03, 137.00, 132.21, 129.70, 129.35, 129.18, 129.09, 129.03, 128.84, 128.53, 128.12, 124.10, 123.28, 123.07, 122.17, 121.17, 121.16, 119.81, 119.71, 118.66, 118.23. IR (cm^{-1}): 3320 (w), 3020 (s), 2980 (s), 1620 (s), 1580 (m), 1020 (m). HRMS (ESI): *m/z* calcd. for $C_{30}H_{19}Br_2NO_2$, 585.2854; found, 584.9753.

2-(4-(Benzo[d][1,3]dioxol-5-yl)-5-(benzo[d][1,3]dioxol-6-yl)-5H-chromeno[4,3-b]pyridin-2-yl)phenol (3l).

Yellow crystals, mp. 234.1-235.0 ˚C, (66%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.85 (1H, s), 8.19 (1H, d, *J*=8.0 Hz), 8.09 (1H, s), 7.81 (1H, d, *J*=8.0 Hz), 7.37 (2H, t), 7.17 (1H, t), 6.95-7.02 (5H, m), 6.73-6.81 (3H, m), 6.46 (1H, d, *J*=8.0 Hz), 6.43 (1H, s), 6.09 (2H, s), 5.97 (2H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.20, 156.92, 154.00, 152.93, 149.30, 148.25, 148.00, 147.90, 133.95, 123.61, 122.12, 120.00, 118.90, 109.3, 109.00, 108.00. IR (cm^{-1}): 3320 (w), 3020 (s), 2995 (s), 1600 (s), 1500 (m), 1010 (m). HRMS (ESI): *m/z* calcd. for $C_{30}H_{17}Cl_4NO_2$, 515.5122; found, 515.1360.

2-(4,5-Bis(3-nitrophenyl)-5H-chromeno[4,3-b]pyridin-2-yl)phenol (3m).

Yellow crystals, mp. 186.2-197.7 ˚C, (64%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 14.35 (1H, s), 8.50 (1H, m), 8.25-8.35 (3H, m), 8.17 (1H, s), 8.00 (1H, dd, J_1=1.6 Hz, J_2=7.6 Hz), 7.50-7.67 (2H, m), 7.10-7.49 (9H, m), 6.55 (1H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ 155.31, 153.66, 148.82, 141.79, 135.89, 133.57, 129.33, 128.70, 128.19, 127.77, 125.55, 125.17, 121.86, 119.92, 119.31, 119.23, 118.55, 117.98, 116.72, 116.62, 114.59, 114.36, 114.06, 113.50. IR (cm^{-1}): 3350 (w), 3010 (s), 2995 (s), 1600 (s), 1530 (m), 1040 (m). HRMS (ESI): *m/z* calcd. for $C_{30}H_{19}N_3O_6$, 517.4884; found, 517.1360.

2-(4,5-Bis(4-fluorophenyl)-5H-chromeno[4,3-b]pyridin-2-yl)phenol (3n).

Yellow crystals, mp. 197.6-198.1 ˚C, (64%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.70 (1H, s), 8.19 (1H, d, *J*=8.0 Hz), 8.13 (1H, s), 7.43 (1H, s), 8.02 (1H, d, *J*=8.0 Hz), 7.27-7.38 (7H, m), 7.13-7.19 (3H, m), 6.94-7.10 (4H, m), 6.49 (1H, s). ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.3, 156. 7, 152.8, 147.7, 147.6, 146.5, 145.8, 139.9, 137.6, 133.3, 132.7, 132.2, 127.8, 125.6, 125.2, 121.9, 119.9, 119.32 119.2, 118.6,

118.0, 116.7, 116.6, 114.6, 114.4, 114.1, 113.5, 70.6. IR (cm^{-1}): 3350 (w), 3010 (s), 2995 (s), 1600 (s), 1530 (m), 1040 (m). HRMS (ESI): *m/z* calcd. for $C_{30}H_{19}F_2NO_2$, 463.4742; found,463.1228.

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11. The single crystal growth was carried out in DMF at room temperature. Crystal data for **3e**: Empirical formula $C_{32}H_{25}NO_6$, yellow, crystal dimension 0.28 × 0.26 × 0.20 mm, monoclinic, space group P 2(1)/c, a=12.2594(18) Å, b=16.619(2) Å, c=14.727(2) Å, α=90.00º, β=113.610(2)º, γ=90.00º, V=2749.3(7) $Å^3$, Mr=547.58, Z=4, Dc=1.323 Mg/m^3, λ=0.71073 Å, μ (MoKα)=0.091 mm^{-1}, F(000)=1152, S=1.017, R_1=0.0418, *w*R_2=0.1013. Crystallographic data for the structures of **3e** reported in this letter have been deposited with the Cambridge Crystallographic Date Centre as supplementary publication No. CCDC-655834.
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