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Acid-controlled multicomponent selective synthesis of 2,4,6-triaryl pyridines and pyrimidines by using hexamethyldisilazane as a nitrogen source under microwave irradiation†

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An efficient and general protocol for the synthesis of functionalized 2,4,6-triaryl pyridines and pyrimidines was developed from commercially available aromatic ketones, aldehydes and hexamethyldisilazane (HMDS) as a nitrogen source under microwave irradiation. In this multicomponent synthetic route, Lewis acids play an important role in selectively synthesizing six-membered heterocycles, including pyridines (1N) and pyrimidines (2N), by involving [2 + 1 + 2 + 1] or [2 + 1 + 1 + 1 + 1] annulated processes.

Over the past decade, multicomponent reactions (MCRs) have been recognized as a powerful synthetic tool for the establishment of diverse and complicated skeletons. By definition, these components have been assembled in protocols to form desired compound frameworks without adding any reagents, catalysts, solvents, or substrates.[1] MCRs started from simple and readily available synthons to achieve facile execution, generate high productivities, increase transformation efficiency, and reduce lengthy pathways.[2] The benefits of these combinatorial approaches are not only the systematic distribution in arrays of reactions to construct iterations but also the utilization of the natural characteristics of the chemical building blocks to connect chemical bonds on the common MCR-product skeletons.[3] Some name reactions have been developed by Biginelli,[4] Hantzsch,[5] Mannich,[6] Passerini,[7] Povarov,[8] Strecker[9] and Ugi.[10] These reactions are also broadly applied for synthetic and biological interests.

Nitrogen-containing heterocyclic compounds are identified as one of the privileged structural motifs in organic chemistry.[11] Among them, the six-membered heterocyclic compounds such as pyridines and pyrimidines are representative compounds for their broad natural existence in natural products, synthetic intermediates, bioactive compounds, and functional materials.[12] Furthermore, these heterocycles have also been applied in the pharmaceutical industry for their anticancer, antimycobacterial, antibacterial, antimalarial, anti-inflammatory, anticonvulsant, and antimicrobial activities.[13] Since the first pyrimidine synthesis by Brugnatelli and later on by Kolbe, and the initial discovery of pyridine by Thomas Anderson, the various synthetic approaches of these two families have been an area of continuous active research and innovative methodologies and are frequently reported.[14] As a consequence, providing a facile and efficient protocol for the controllable construction of these two azaaromaric skeletons is highly desired. In a comparison of the reported studies on pyridine synthesis,[15] the synthetic protocols of the pyrimidine motif are relatively rarely developed.

Based on the reported literature, a variety of synthetic routes toward the preparation of substituted pyrimidines have been developed.[16] The nitrogen source on the pyrimidine scaffold is an important issue in these methodologies, as shown in Scheme 1. Numerous commonly used protocols apply a nitrogen-fixed substrate as a starting material, including amidines,[17] nitriles,[18,19] and enamidines (enamidine)[20] to construct the pyrimidine skeletons. Among them, substituted amidines are frequently applied as versatile nitrogen-containing blocks to react with various cyclization partners to form a pyrimidine ring to utilize the inherent nitrogen on the substrate.[21] The MCRs for the preparation of pyrimidines from amidines have also been recognized as an efficient strategy.[22] Some other synthetic routes utilized the extrinsic nitrogen-containing reagents, including ammonium acetate,[23] ammonium iodide,[24] hydroxylamine,[25] and urea[26] to generate *in situ* ammonia surrogate and condensed with carbonyl synthons to construct pyrimidine structures.

Although many remarkable protocols have been reported for the construction of pyrimidines, the development of a facile synthetic protocol from simple and readily available starting materials under the MCRs strategy is of great interest.[27] Recently, Li and Huang developed a concise and efficient protocol by controlling the carbon source to obtain diverse substituted pyridines and pyrimidines with high selectivity.

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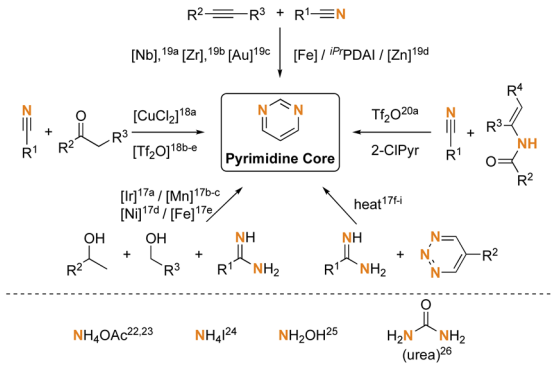
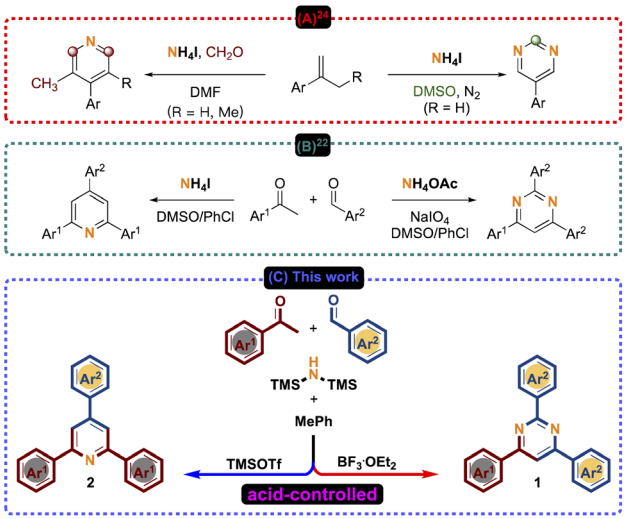
† Electronic supplementary information (ESI) available: Experimental procedures, characterisation data, copies of ^{1}H and ^{13}C NMR spectra data. See https://doi.org/10.1039/d2ra04739j



Scheme 1 Synthesis of 2,4,6-triarylpyrimidines.

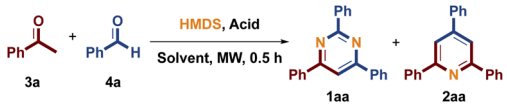


Scheme 2 Selective synthesis of pyridines and pyrimidines.

This reaction was conducted from isopropene derivatives and the involvement of NH_4I as the "N" source (Scheme 2A).[24] In 2019, Deng and Zhang reported a synthetic route to selectively construct pyridines and pyrimidines by varying "N" sources in ammonium salts (NH_4I and NH_4OAc) under the DMSO/PhCl co-solvent system (Scheme 2B).[22] Continuing our investigation of HMDS as a nitrogen source for the synthesis of N-heterocyclic compounds under a MW system,[28] herein, we present a synthetic route to construct 1N or 2N six-membered ring pyrimidines 1 and pyridines 2 controlled by Lewis acids (BF_3-$\cdot OEt_2$ and TMSOTf) from commercially available acetophenones 3 and benzaldehydes 4 (Scheme 2C).

We started our investigation with commercially available acetophenone **3a**, benzaldehyde **4a**, hexamethyldisilazane (HMDS), and acids under microwave irradiation (MW) to explore the viability of controlling the selective formation of pyrimidine **3** and pyridine **4**, as shown in Table 1. Based on our previous report, we first examined TMSOTf as Lewis acid for the synthesis of nitrogen-containing compounds. In entry 1, the reaction of **3a** with **4a** can provide **2aa** in 92% yield in the presence of HMDS and toluene under MW at 150 °C in 0.5 h.[28] Various metal triflates conducted the reaction well to obtain

Table 1 Optimization of the reaction conditions[a]



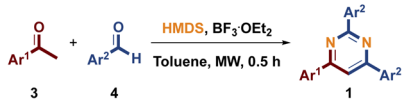
Entry	Acid	Solvent	Yields[b] (%) 1aa	2aa
1	TMSOTf	Toluene	0	92
2	$In(OTf)_3$	Toluene	0	80
3	$Fe(OTf)_3$	Toluene	0	80
4	$Bi(OTf)_3$	Toluene	0	81
5	$Sc(OTf)_3$	Toluene	0	82
6	$Cu(OTf)_2$	Toluene	0	76
7	$AlCl_3$	Toluene	0	91
8	$InCl_3$	Toluene	0	80
9	TfOH	Toluene	0	82
10	AcOH	Toluene	N.R.	N.R.
11	*p*-TsOH	Toluene	N.R.	N.R.
12	$BF_3 \cdot OEt_2$	Toluene	58	0
13[c]	$BF_3 \cdot OEt_2$	Toluene	68	0
14[c]	TMSOTf	Toluene	0	92
15[c]	$BF_3 \cdot OEt_2$	DCM	55	0
16[c]	$BF_3 \cdot OEt_2$	THF	62	0
17[c]	$BF_3 \cdot OEt_2$	MeCN	63	0

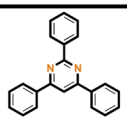
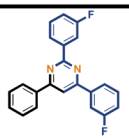
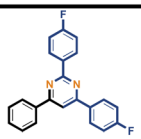
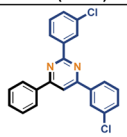
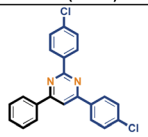
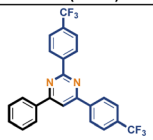
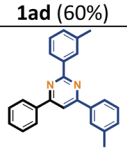
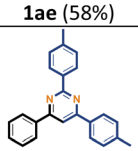
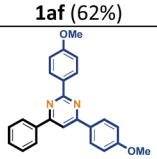
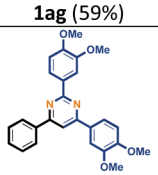
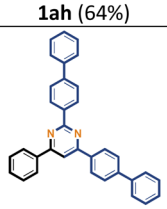
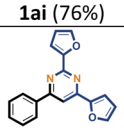
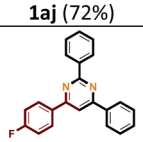
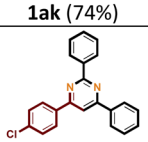
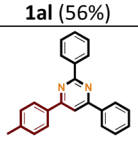
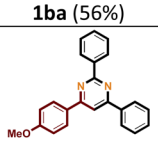
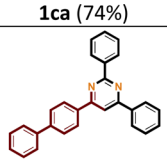
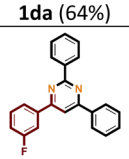
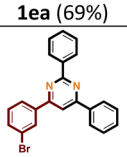
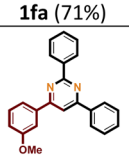
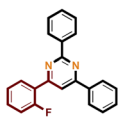
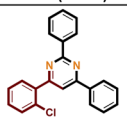
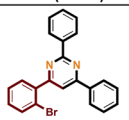
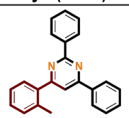
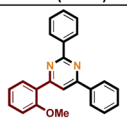
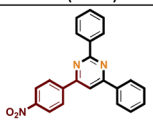
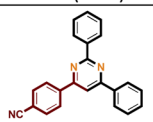
[a] Reaction conditions: **3a** (4.0 mmol), **4a** (4.0 mmol), HMDS (3.0 mL, 14.4 mmol), acid (0.5 mmol), solvent (2 mL), MW (150 °C), 0.5 h. [b] Isolated yields. [c] Reaction time: 2 h.

compound **2aa** in approximate 80% yields (entries 2–6). Other Lewis acids, including $AlCl_3$ and $InCl_3$, give good to excellent yields of compound **2aa** (entries 7 and 8). Brønsted acids were also investigated in this reaction, TfOH promotes the formation of **2aa** in 82% yield but AcOH and *p*-TsOH did not (entries 9–11). Interestingly, $BF_3 \cdot OEt_2$ catalyzed the reaction of **3a** and **4a** in the presence of HMDS to obtain corresponding pyrimidine **1aa** with 58% yield without the formation of pyridine **2aa** (entry 12). When the reaction time was extended from 0.5 to 2 h, the yield of **1aa** was increased, that of **2aa** did not change (entries 13–14). The reaction proceeded well by changing reaction solvents such as DCM, THF and MeCN with lower isolated yields (entries 15–17). Therefore, an acid-controlled synthesis of pyrimidines and pyridines from commercially available **3a** and **4a** by using HMDS as a nitrogen source was established.

After screening the reaction conditions in Table 1, we examined various acetophenones **3** and benzaldehydes **4** for the synthesis of triaryl-substituted pyrimidines **1** by involving of the conditions mentioned in Table 1, entry 14. As shown in Table 2, the model reaction of **3a** with **4a** and HMDS in the presence of $BF_3 \cdot OEt_2$ provided **1aa** in 78% yield. We first investigated the scope of the reaction with **3a** and substituted benzaldehydes **4b–4k** (**4b**, 3FPh; **4c**, 4FPh; **4d**, 3ClPh; **4e**, 4ClPh; **4f**, $4CF_3Ph$; **4g**, 3MePh; **4h**, 4MePh; **4i**, 4OMePh; **4j**, 34OMePh; **4k**, 4PhPh, and **4l**, furfural), coupling by HMDS/$BF_3 \cdot OEt_2$ system as nitrogen source under MW to provide the corresponding **1ab–1ak**, with a yield between 58% and 74%. A lower yield of **1al** was obtained

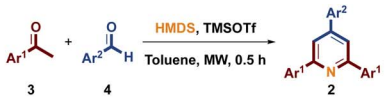
Table 2 Synthesis of triaryl-substituted pyrimidines 1[ab]

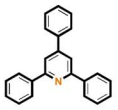
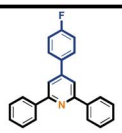
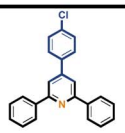
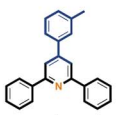
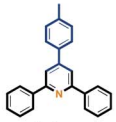
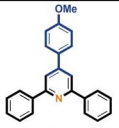
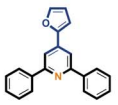
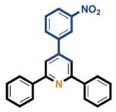
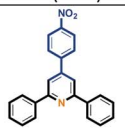
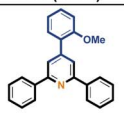
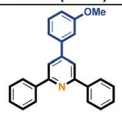


 1aa (78%)	 1ab (65%)	 1ac (70%)
 1ad (60%)	 1ae (58%)	 1af (62%)
 1ag (59%)	 1ah (64%)	 1ai (76%)
 1aj (72%)	 1ak (74%)	 1al (56%)
 1ba (56%)	 1ca (74%)	 1da (64%)
 1ea (69%)	 1fa (71%)	 1ga (65%)
 1ha (66%)	 1ia (69%)	 1ja (64%)
 1ka (61%)	 1la (56%)	 1ma (54%)
 1na (58%)	 1oa (71%)	 1pa (65%)

[a] Reaction conditions: 3 (4.0 mmol), 4 (4.0 mmol), HMDS (3.0 mL, 14.4 mmol), $BF_3 \cdot OEt_2$ (0.5 mmol), toluene (2 mL), MW (150 °C), 0.5 h. [b] Isolated yields.

Table 3 Synthesis of triaryl-substituted pyridines 2[a,b]



 2aa (88%)	 2ac (76%)	 2ae (83%)
 2ag (80%)	 2ah (93%)	 2ai (81%)
 2al (81%)	 2am (81%)	 2an (87%)
 2ao (83%)	 2ap (89%)	2aq (79%)
2ar (87%)	2as (62%)	2at (83%)
2au (84%)	2ba (89%)	2ca (91%)
2da (88%)	2ea (92%)	2fa (72%)
2ga (92%)	2ia (82%)	2la (81%)
2ma (81%)	2na (77%)	2qa (85%)
2ra (70%)	2sa (76%)	2ta (80%)

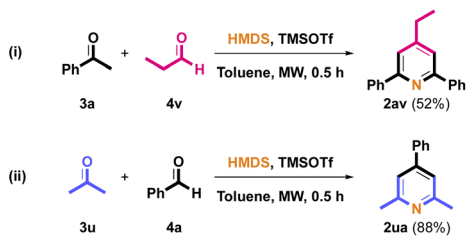
[a] Reaction conditions: 3 (4.0 mmol), 4 (4.0 mmol), HMDS (3.0 mL, 14.4 mmol), TMSOTf (0.5 mmol), toluene (2 mL), MW (150 °C), 0.5 h. [b] Isolated yields.

when heterocyclic furfural **4l** as aldehyde partner. We next screened the functionalized acetophenones **3b–3p** (**3b**, 4FPh; **3c**, 4FPh; **3d**, 4MePh; **3e**, 4OMePh; **3f**, 4PhPh; **3g**, 3FPh; **3h**, 3BrPh; **3i**, 3OMePh; **3j**, 2FPh; **3j**, 2ClPh; **3k**, 2BrPh; **3m**, 2MePh; **3n**, 2OMePh; **3o**, 4NO_2Ph and **3p**, 4CNPh) with **4a** under optimized reaction conditions to afford corresponding pyrimidines **1ba–1pa** in modest yields (see Table 3).

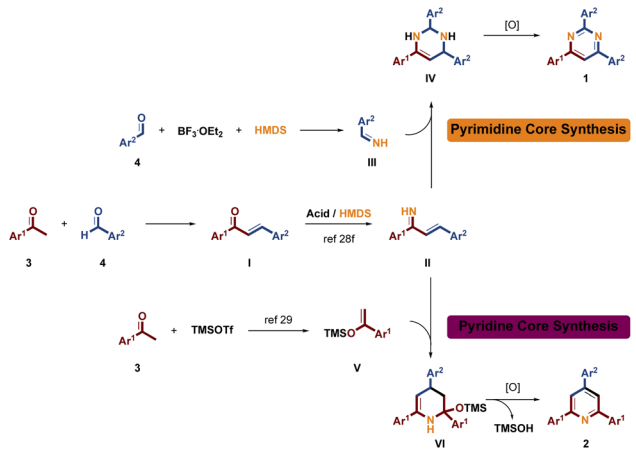
On the other hand, substituted pyrimidines are recognized as an important scaffold in pharmaceuticals.[29] Among them, 2,4,6-triarlpyridines (TAPs) skeleton are also a practical synthon in the synthesis of drugs.[30] In our previous work, we conducted the synthesis of TAPs by using HMDS/TMSOTf catalytic system under MW condition.[28f] Herein, we also describe a synthetic route to yield TAPs from the easily available acetophenones **3** and benzaldehydes **4** in the optimized reaction condition (Table 1, entry x1x). As shown in Scheme 2, we selected non-substituted **3a** with some functionalized benzaldehydes **4c** (4-FPh), **4e** (4-ClPh), **4g** (3-MePh), **4h** (4-MePh), **4i** (4-OMePh), **4l** (2-furan), **4m** (3-NO_2Ph), **4n** (4-NO_2Ph), **4o** (2-OMePh), **4p** (3-OMePh), **4q** (3,5-OMePh), **4r** (3,5-CH_2O_2Ph), **4s** (anthracene), **4t** (2-naphthalene) and **4r** (2-thiophene) under the optimized conditions to give desired pyridines **2ac–2au** in 62–93% yields. Further investigation of **4a** with diversified acetophenones **3b** (4-FPh), **3c** (4-ClPh), **3d** (4-MePh), **3e** (4-OMePh), **3f** (4-PhPh), **3g** (3-FPh), **3i** (3-OMePh), **3l** (2-BrPh), **3m** (2-MePh), **3n** (2-OMePh), **3q** (4-CF_3Ph), **3r** (3-MePh), **3s** (2-furan) and **3t** (3-thiophene) in the optimized condition provided corresponding TAPs **2ba–2ta** between 70% and 92% yields.

As shown in Scheme 3, non-aromatic benzaldehyde propionaldehyde **4v** was also examined with **3a** in this transformation to afford the desired pyridine **2av**. It is possible that due to the low boiling point of **4v**, only a 52% isolated yield of **2av** was observed. Acetone **3u** was also selected as aliphatic ketone with **4a** to investigate this pathway to prepare desired pyridine **2ua** in 88% yield.

On the basis of the above experimental results and the reported literature, a proposed reaction pathway is shown in Scheme 4. Claisen–Schmidt condensation of acetophenone **3** and benzaldehyde **4** occurred to give chalcone synthon **I**, which further reacts with HMDS to provide intermediate **II** under acidic conditions.[28f] Possibly, benzaldehyde **4** is transformed to intermediate **III** in $BF_3\cdot OEt_2$/HMDS system, which then reacted with intermediate **II** to provide intermediate **IV**, and further aromatically converted to pyrimidine **1** under MW condition. Differently, TMSOTf acts not only as an acidic catalyst in the formation of **II** but also as a silylating agent to catalyze the



Scheme 3 Synthesis of compound **2av** and **2ua**.



Scheme 4 Plausible reaction pathway.

conversion of acetophenone **3** to provide intermediate **V**. After the condensation of **II** with **V**, the intermediate **VI** was obtained, which further underwent aromatic cyclization to give corresponding pyridine **2**. Therefore, we presume that the selective synthesis of skeletons **1** and **2** is based on the alternative pathway by involving $BF_3\cdot OEt_2$ or TMSOTf.

Conclusions

In summary, we developed a strategy for the selective synthesis of six-membered heterocyclic compounds pyrimidines, and pyridines from commercially available acetophenones and benzaldehydes. In this protocol, same amounts of acetophenone and benzaldehyde were involved by using HMDS as a nitrogen source and control of Lewis acids under microwave irradiation. Acid catalysts TMSOTf and $BF_3\cdot OEt_2$ played an important role in this selective transformation of corresponding pyrimidines and pyridines obtained in modest yields in this MCR method.

Experimental section

General information

All reagents and solvents were commercially available and used without further purification. Reactions were routinely performed using the discover SP system (CEM) in the sealed reaction vessels in standard mode with the temperature monitored using a vertically focused IR sensor. All reactions were monitored by thin-layer chromatography on silica gel 60 F254 (Merck) with detection by UV light. Column chromatography was performed using silica gel (200–300 mesh). Products in organic solvents were dried with anhydrous magnesium sulfate before concentration *in vacuo*. Melting points were determined with an MP-2D melting apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AVIII 500 spectrometer operating at 500 and 125 MHz, respectively. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad), coupling constants (Hz) and integration. HRMS were obtained on a Waters LCT Premier XE

(Waters Corp., Manchester, UK) instrument equipped with an electrospray source. The X-ray intensity data were measured at a low temperature of 100 K using a Mo Kα radiation diffractometer equipped with a kappa geometry goniometer and corrected for absorption effects using the numerical method (SADABS).

General procedure for the synthesis of skeleton 1

A mixture of acetophenone **3** (4.0 mmol), benzaldehyde **4** (4.0 mmol), HMDS (14.4 mmol), $BF_3 \cdot OEt_2$ (0.5 mmol) and toluene (2 mL) in a dried 35 mL microwave vial at 25 °C. The mixture was subjected to a microwave irradiation instrument and stirred at 150 °C for 0.5 h. The consumption of the starting materials was confirmed by TLC. The reaction was cooled to 25 °C, the mixture of crude product was transferred to a 100 mL round bottom flask, and the solvent was concentrated. The residue was diluted with water (10 mL) and the mixture was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product under reduced pressure. Purification on silica gel (hexanes/EtOAc = 8/1–3/1) afforded compounds **1aa–1pa**.

2,4,6-Triphenylpyrimidine (1aa).[22] Yield = 78% (481 mg); colorless solid; mp = 191–192 °C; HRMS (ESI, M^+ + H) calcd for $C_{22}H_{17}N_2$ 309.1386, found 309.1395; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.76 (d, J = 8.0 Hz, 2H), 8.33–8.27 (m, 4H), 8.02 (s, 1H), 7.62–7.51 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.70 (2x), 164.46, 138.13, 137.50 (2x), 130.74 (2x), 130.60, 128.87 (4x), 128.45 (2x), 128.41 (2x), 127.25 (4x), 110.25.

2,4-Bis(3-fluorophenyl)-6-phenylpyrimidine (1ab). Yield = 65% (447 mg); colorless solid; mp = 217–218 °C; HRMS (ESI, M^+ + H) calcd for $C_{22}H_{15}F_2N_2$ 345.1198, found 345.1200; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.49 (d, J = 7.5 Hz, 1H), 8.38 (d, J = 10.0 Hz, 1H), 8.29–8.22 (m, 2H), 8.04–7.97 (m, 2H), 7.95 (s, 1H), 7.59–7.47 (m, 5H), 7.27–7.19 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.04, 163.30 (d, J = 244.875 Hz), 163.17 (d, J = 243.125 Hz), 139.92 (d, J = 94.125 Hz), 139.86 (d, J = 93.875 Hz), 136.94, 131.05, 130.43 (d, J = 8.0 Hz), 129.89 (d, J = 7.875 Hz), 128.95 (2x), 127.23 (2x), 124.05 (d, J = 2.25 Hz), 122.74 (d, J = 2.375 Hz), 117.75 (d, J = 21.25 Hz, 2x), 117.58 (d, J = 21.25 Hz, 2x), 115.21 (d, J = 23.0 Hz), 114.19 (d, J = 22.75 Hz), 110.53.

2,4-Bis(4-fluorophenyl)-6-phenylpyrimidine (1ac).[30a] Yield = 70% (482 mg); colorless solid; mp = 212–213 °C; HRMS (ESI, M^+ + H) calcd for $C_{22}H_{15}F_2N_2$ 345.1198, found 345.1196; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.71 (t, J = 7.5 Hz, 2H), 8.31–8.22 (m, 4H), 7.93 (s, 1H), 7.60–7.53 (m, 3H), 7.28–7.16 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.73 (d, J = 248.75 Hz), 164.59 (d, J = 254.875 Hz), 164.85, 163.62, 137.28, 134.18 (d, J = 2.5125 Hz), 133.51 (d, J = 2.875 Hz), 130.89, 130.53 (d, J = 8.625 Hz, 2x), 129.25 (d, J = 8.625 Hz, 2x), 128.92 (2x), 128.70, 127.22 (2x), 115.93 (d, J = 21.625 Hz, 2x), 115.35 (d, J = 21.375 Hz, 2x), 109.72.

2,4-Bis(3-chlorophenyl)-6-phenylpyrimidine (1ad). Yield = 60% (451 mg); white solid; mp = 173–174 °C; HRMS (ESI, M^+ + H) calcd for $C_{22}H_{15}Cl_2N_2$ 377.0612, found 377.0608; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.66–8.62 (m, 1H), 8.56 (d, J = 7.5 Hz, 1H), 8.26–8.20 (m, 3H), 8.10 (d, J = 7.5 Hz, 1H), 7.92 (s, 1H), 7.58–7.53 (m, 3H), 7.52–7.43 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.03, 163.31, 163.23, 139.66, 138.97, 136.86, 135.08, 134.57, 131.08, 130.81, 130.68, 130.14, 129.67, 128.94 (2x), 128.44, 127.31, 127.24 (2x), 126.57, 125.31, 110.55.

2,4-Bis(4-chlorophenyl)-6-phenylpyrimidine (1ae).[23c] Yield = 58% (436 mg); white solid; mp = 200–201 °C; HRMS (ESI, M^+ + H) calcd for $C_{22}H_{15}Cl_2N_2$ 377.0612, found 377.0606; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.64 (d, J = 7.0 Hz, 2H), 8.26 (d, J = 2.5 Hz, 2H), 8.20 (d, J = 7.0 Hz, 2H), 7.97 (s, 1H), 7.57–7.50 (m, 7H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.05, 163.62, 163.60, 137.15, 137.12, 136.94, 136.43, 135.73, 131.02, 129.79 (2x), 129.18 (2x), 128.98 (2x), 128.68 (2x), 128.53 (2x), 127.26, (2x) 110.13.

4-Phenyl-2,6-bis(4-(trifluoromethyl)phenyl)pyrimidine (1af).[30a] Yield = 62% (551 mg); white solid; mp = 179–180 °C; HRMS (ESI, M^+ + H) calcd for $C_{24}H_{15}F_6N_2$ 445.1139, found 445.1137; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.80 (d, J = 8.0 Hz, 2H), 8.37 (d, J = 8.0 Hz, 2H), 8.31–8.26 (m, 2H), 8.07 (s, 1H), 7.83 (d, J = 8.0 Hz, 2H), 7.79 (d, J = 8.0 Hz, 2H), 7.62–7.56 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.43, 163.48, 163.39, 141.03, 140.51, 136.78, 132.66 (q, J = 30.35 Hz, 2x), 136.42 (q, J = 30.35 Hz, 2x), 131.30, 129.07 (2x), 128.73 (2x), 127.62 (2x), 127.30 (2x), 125.93 (q, J = 3.65 Hz), 125.42 (q, J = 3.65 Hz), 124.17 (d, J = 272.30 Hz), 123.91 (d, J = 272.30 Hz), 111.20.

4-Phenyl-2,6-di-*m*-tolylpyrimidine (1ag). Yield = 59% (397 mg); white solid; mp = 107–108 °C; HRMS (ESI, M^+ + H) calcd for $C_{24}H_{21}N_2$ 337.1699, found 337.1703; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.56–8.50 (m, 2H), 8.35 (dd, J = 1.5, 8.0 Hz, 2H), 8.10 (s, 1H), 8.08 (d, J = 7.5 Hz, 1H), 8.00 (s, 1H), 7.60–7.53 (m, 3H), 7.49–7.41 (m, 2H), 7.39–7.32 (m, 2H), 2.52 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.97, 164.65 (2x), 138.61, 138.12, 138.02, 137.63, 137.58, 131.51, 131.40, 130.69, 128.97, 128.89 (2x), 128.81, 128.35, 127.89, 127.29 (2x), 125.70, 124.47, 110.40, 21.60 (2x).

4-Phenyl-2,6-di-*p*-tolylpyrimidine (1ah).[25] Yield = 64% (430 mg); colorless solid; mp = 167–168 °C; HRMS (ESI, M^+ + H) calcd for $C_{24}H_{21}N_2$ 337.1699, found 337.1696; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.63 (d, J = 8.0 Hz, 2H), 8.29 (dd, J = 1.5, 8.5 Hz, 2H), 8.20 (d, J = 8.0 Hz, 2H), 7.96 (s, 1H), 7.59–7.52 (m, 3H), 7.34 (t, J = 8.0 Hz, 4H), 2.47 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.58, 164.50 (2x), 141.01, 140.69, 137.76, 135.58, 134.83, 130.58, 129.59 (2x), 129.15 (2x), 128.83 (2x), 128.41 (2x), 127.24 (2x), 127.15 (2x), 109.66, 21.52, 21.45.

2,4-Bis(4-methoxyphenyl)-6-phenylpyrimidine (1ai).[25] Yield = 76% (560 mg); yellow solid; mp = 126–127 °C; HRMS (ESI, M^+ + H) calcd for $C_{24}H_{21}N_2O_2$ 369.1598, found 369.1598; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.68 (d, J = 8.5 Hz, 2H), 8.29–8.23 (m, 4H), 7.89 (s, 1H), 7.59–7.49 (m, 3H), 7.09–7.02 (m, 4H), 3.90 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.34, 164.11, 164.06, 161.82, 161.72, 137.84, 131.04, 130.52, 130.09, 130.03 (2x), 128.81 (2x), 128.72 (2x), 127.20 (2x), 114.19 (2x), 113.69 (2x), 108.76, 55.41, 55.35.

2,4-Bis(3,4-dimethoxyphenyl)-6-phenylpyrimidine (1aj). Yield = 72% (617 mg); white solid; mp = 184–185 °C; HRMS (ESI, M^+ + H) calcd for $C_{26}H_{25}N_2O_4$ 429.1809, found 429.1811; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.32 (d, J = 8.5 Hz, 1H), 8.26 (s, 1H), 8.25–8.21 (m, 2H), 7.90 (s, 1H), 7.85–7.81 (m, 1H), 7.80–7.75 (m, 1H), 7.57–7.49 (m, 3H), 7.02–6.94 (m, 2H), 4.04 (s, 3H), 4.02 (s, 3H), 3.96 (s, 3H), 3.94 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$):

δ 164.20, 163.81 (2x), 151.31, 151.19, 149.14, 148.69, 137.61, 131.04, 130.49, 130.16, 128.72 (2x), 127.10 (2x), 121.67, 120.15, 111.03, 110.89, 110.62, 109.91, 108.84, 55.89, 55.84 (2x), 55.78.

2,4-Di([1,1′-biphenyl]-4-yl)-6-phenylpyrimidine (1ak). Yield = 74% (681 mg); white solid; mp = 215–216 °C; HRMS (ESI, M^+ + H) calcd for $C_{34}H_{25}N_2$ 461.2012, found 461.2002; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.82 (d, J = 8.0 Hz, 2H), 8.40 (d, J = 8.0 Hz, 2H), 8.33 (d, J = 8.0 Hz, 2H), 8.07 (s, 1H), 7.80 (t, J = 8.0 Hz, 4H), 7.71 (t, J = 8.0 Hz, 4H), 7.63–7.56 (m, 3H), 7.53–7.48 (m, 4H), 7.44–7.37 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.78, 164.34, 164.32, 143.57, 143.27, 140.76, 140.33, 137.57, 137.15, 136.37, 130.79, 128.93 (8x), 128.83, 127.85, 127.73, 127.60 (2x), 127.30, 127.20 (4x), 127.18 (4x), 110.12.

2,4-Di(furan-2-yl)-6-phenylpyrimidine (1al). Yield = 56% (323 mg); white solid; mp = 108–109 °C; HRMS (ESI, M^+ + H) calcd for $C_{18}H_{13}N_2O_2$ 289.0972, found 289.0966; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.24–8.21 (m, 2H), 7.87 (s, 1H), 7.68 (s, 1H), 7.64 (s, 1H), 7.55–7.46 (m, 3H), 7.47 (d, J = 3.0 Hz, 1H), 7.42 (d, J = 3.0 Hz, 1H), 6.65–6.55 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.88, 157.93, 156.30, 152.53, 152.05, 144.95 (2x), 136.93, 130.92, 128.87 (2x), 127.24 (2x), 113.63, 112.50, 112.48, 112.05, 107.88.

4-(4-Fluorophenyl)-2,6-diphenylpyrimidine (1ba).[22] Yield = 56% (365 mg); white solid; mp = 162–163 °C; HRMS (ESI, M^+ + H) calcd for $C_{22}H_{16}FN_2$ 327.1292, found 327.1294; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.71 (d, J = 7.5 Hz, 2H), 8.31–8.28 (m, 4H), 7.97 (s, 1H), 7.60–7.51 (m, 6H), 7.27–7.23 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.86, 164.59 (d, J = 249.475 Hz), 164.51, 163.63, 138.01, 137.43, 133.65 (d, J = 2.75 Hz), 130.84, 130.71, 129.29 (d, J = 8.5 Hz, 2x), 128.93 (2x), 128.46 (2x), 128.44 (2x), 127.26 (2x), 115.93 (d, J = 21.5 Hz, 2x), 109.89.

4-(4-Chlorophenyl)-2,6-diphenylpyrimidine (1ca).[22] Yield = 74% (506 mg); white solid; mp = 158–159 °C; HRMS (ESI, M^+ + H) calcd for $C_{22}H_{16}ClN_2$ 343.0997, found 343.0987; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.71 (d, J = 7.5 Hz, 2H), 8.29 (d, J = 7.5 Hz, 2H), 8.25 (d, J = 7.0 Hz, 2H), 7.98 (s, 1H), 7.59–7.53 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.98, 164.58, 163.52, 137.95, 137.36, 136.97, 135.95, 130.90, 130.75, 129.14 (2x), 128.94 (2x), 128.55 (2x), 128.47 (2x), 128.45 (2x), 127.28 (2x), 109.98.

2,4-Diphenyl-6-(*p*-tolyl)pyrimidine (1da).[22] Yield = 64% (412 mg); colorless solid; mp = 146–147 °C; HRMS (ESI, M^+ + H) calcd for $C_{23}H_{19}N_2$ 323.1543, found 323.1534; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.73 (d, J = 6.5 Hz, 2H), 8.29 (d, J = 6.5 Hz, 2H), 8.21 (d, J = 7.0 Hz, 2H), 8.00 (s, 1H), 7.57–7.52 (m, 6H), 7.37 (d, J = 8.0 Hz, 2H), 2.47 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.67, 164.60, 164.42, 141.13, 138.24, 137.64, 134.71, 130.67, 130.54, 129.63 (2x), 128.87 (2x), 128.44 (2x), 128.40 (2x), 127.25 (2x), 127.17 (2x), 109.93, 21.47.

4-(4-Methoxyphenyl)-2,6-diphenylpyrimidine (1ea).[22] Yield = 69% (467 mg); colorless solid; mp = 136–137 °C; HRMS (ESI, M^+ + H) calcd for $C_{23}H_{19}N_2O$ 339.1492, found 339.1494; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.72 (d, J = 8.0 Hz, 2H), 8.29 (d, J = 7.5 Hz, 4H), 7.96 (s, 1H), 7.57–7.51 (m, 6H), 7.07 (d, J = 8.5 Hz, 2H), 3.91 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.49, 164.35, 164.21, 161.92, 138.28, 137.71, 130.63, 130.52, 129.96, 128.87 (2x), 128.78 (2x), 128.42 (2x), 128.40 (2x), 127.24 (2x), 114.25 (2x), 109.42, 55.44.

4-([1,1′-Biphenyl]-4-yl)-2,6-diphenylpyrimidine (1fa).[22] Yield = 71% (546 mg); colorless solid; mp = 174–175 °C; HRMS (ESI, M^+ + H) calcd for $C_{28}H_{21}N_2$ 385.1699, found 385.1705; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.76 (d, J = 8.5 Hz, 2H), 8.39 (d, J = 8.5 Hz, 2H), 8.32 (d, J = 8.0 Hz, 2H), 8.06 (s, 1H), 7.80 (d, J = 8.0 Hz, 2H), 7.70 (d, J = 7.5 Hz, 2H), 7.61–7.53 (m, 6H), 7.52–7.48 (m, 2H), 7.44–7.39 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.75, 164.52, 164.31, 143.55, 140.32, 138.16, 137.55, 136.36, 130.76, 130.63, 128.91 (3x), 128.47 (2x), 128.44 (2x), 127.84, 127.71 (2x), 127.58 (2x), 127.28 (2x), 127.17 (2x), 127.12, 110.13.

4-(3-Fluorophenyl)-2,6-diphenylpyrimidine (1ga).[27] Yield = 65% (424 mg); white solid; mp = 184–185 °C; HRMS (ESI, M^+ + H) calcd for $C_{22}H_{16}FN_2$ 327.1292, found 327.1293; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.72 (d, J = 7.5 Hz, 2H), 8.30 (d, J = 7.5 Hz, 2H), 8.05 (d, J = 8.5 Hz, 2H), 7.99 (s, 1H), 7.59–751 (m, 7H), 7.24–7.22 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.06, 164.60, 163.39 (d, J = 2.5 Hz), 163.34 (d, J = 244.75 Hz), 139.88 (d, J = 7.375 Hz), 137.88, 137.30, 130.85 (d, J = 17.875 Hz, 2x), 130.42 (d, J = 8.0 Hz), 128.95 (2x), 128.48 (2x), 128.47 (2x), 127.28 (2x), 122.77 (d, J = 2.375 Hz), 117.62 (d, J = 21.125 Hz), 114.26 (d, J = 22.875 Hz), 110.27.

4-(3-Bromophenyl)-2,6-diphenylpyrimidine (1ha).[30b] Yield = 66% (510 mg); white solid; mp = 128–129 °C; HRMS (ESI, M^+ + H) calcd for $C_{22}H_{16}BrN_2$ 387.0491, found 387.0491; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.72 (d, J = 8.5 Hz, 2H), 8.44 (s, 1H), 8.29 (d, J = 8.0 Hz, 2H), 8.20 (d, J = 8.0 Hz, 1H), 7.97 (s, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.61–7.52 (m, 6H), 7.43 (t, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.04, 164.61, 163.21, 139.60, 137.85, 137.24, 133.61, 130.95, 130.80, 130.40, 130.31, 128.94 (2x), 128.48 (4x), 127.29 (2x), 125.80, 123.20, 110.25.

4-(3-Methoxyphenyl)-2,6-diphenylpyrimidine (1ia).[30c] Yield = 69% (467 mg); white solid; mp = 124–125 °C; HRMS (ESI, M^+ + H) calcd for $C_{23}H_{19}N_2O$ 339.1492, found 339.1489; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.74 (d, J = 6.5 Hz, 2H), 8.30 (d, J = 6.0 Hz, 2H), 8.00 (s, 1H), 7.90 (s, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.60–7.50 (m, 6H), 7.48 (t, J = 8.0 Hz, 1H), 7.09 (dd, J = 1.5, 8.0 Hz, 1H), 3.95 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.71, 164.48, 164.41, 160.12, 138.98, 138.08, 137.46, 130.75, 130.61, 129.87, 128.87 (2x), 128.44, (2x) 128.41 (2x), 127.25 (2x), 119.59, 116.29, 112.77, 110.40, 55.43.

4-(2-Fluorophenyl)-2,6-diphenylpyrimidine (1ja).[30d] Yield = 64% (417 mg); white solid; mp = 143–144 °C; HRMS (ESI, M^+ + H) calcd for $C_{22}H_{16}FN_2$ 327.1292, found 327.1293; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.74–8.68 (m, 2H), 8.44–8.38 (m, 1H), 8.32–8.27 (m, 2H), 8.17 (d, J = 1.5 Hz, 1H), 7.60–7.47 (m, 7H), 7.40–7.34 (m, 1H), 7.25–7.22 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.54 (d, J = 23.125 Hz), 161.51 (d, J = 250.5 Hz), 160.90, 160.87, 138.04, 137.39, 132.05 (d, J = 8.875 Hz), 131.10 (d, J = 2.0 Hz), 130.82, 130.66, 128.90 (2x), 128.46 (2x), 128.38 (2x), 127.38 (2x), 125.63 (d, J = 10.375 Hz), 124.70 (d, J = 3.25 Hz), 116.54 (d, J = 0.375 Hz), 114.53 (d, J = 0.375 Hz).

4-(2-Chlorophenyl)-2,6-diphenylpyrimidine (1ka).[22] Yield = 61% (417 mg); white solid; mp = 118–119 °C; HRMS (ESI, M^+ + H) calcd for $C_{22}H_{16}ClN_2$ 343.0997, found 343.0996; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.69–8.66 (m, 2H), 8.30–8.27 (m, 2H), 8.03 (s, 1H), 7.89–7.82 (m, 1H), 7.59–7.50 (m, 7H), 7.49–7.41 (m, 2H);

^{13}C NMR (125 MHz, $CDCl_3$): δ 164.69, 164.64, 163.89, 137.95, 137.58, 137.27, 132.44, 131.70, 130.89, 130.69, 130.66, 130.50, 128.94 (2x), 128.47 (4x), 127.38 (2x), 127.22, 115.16.

4-(2-Bromophenyl)-2,6-diphenylpyrimidine (1la).[22] Yield = 56% (432 mg); white solid; mp = 130–131 °C; HRMS (ESI, M^+ + H) calcd for $C_{22}H_{16}ClN_2$ 387.0491, found 387.0498; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.68 (d, J = 7.5 Hz, 2H), 8.29 (d, J = 7.0 Hz, 2H), 7.97 (s, 1H), 7.80–7.73 (m, 2H), 7.60–7.47 (m, 7H), 7.35 (t, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.09, 164.55, 163.82, 139.59, 137.91, 137.22, 133.75, 131.57, 130.90, 130.72, 130.70, 128.94 (2x), 128.49 (2x), 128.47 (2x), 127.76, 127.36 (2x), 121.65, 115.07.

2,4-Diphenyl-6-(*o*-tolyl)pyrimidine (1ma).[22] Yield = 54% (348 mg); white solid; mp = 59–60 °C; HRMS (ESI, M^+ + H) calcd for $C_{23}H_{19}N_2$ 323.1543, found 323.1551; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.73–8.66 (m, 2H), 8.32–8.30 (m, 2H), 7.77 (s, 1H), 7.66–7.50 (m, 7H), 7.46–7.35 (m, 3H), 2.61 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.19, 164.16, 164.04, 138.65, 138.12, 137.37, 136.50, 131.27, 130.81, 130.61, 129.63, 129.41, 128.93 (2x), 128.46 (4x), 127.26 (2x), 126.15, 114.36, 20.71.

4-(2-Methoxyphenyl)-2,6-diphenylpyrimidine (1na).[27] Yield = 58% (392 mg); white solid; mp = 67–68 °C; HRMS (ESI, M^+ + H) calcd for $C_{23}H_{19}N_2O$ 339.1492, found 339.1500; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.70 (d, J = 7.0 Hz, 2H), 8.30 (s, 1H), 8.29–8.24 (m, 3H), 7.56–7.49 (m, 7H), 7.18 (t, J = 8.0 Hz, 1H), 7.08 (d, J = 8.0 Hz, 1H), 3.96 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.20, 163.60, 163.40, 158.06, 138.39, 137.91, 131.49, 131.33, 130.46, 130.36, 128.81 (2x), 128.36 (2x), 128.33 (2x), 127.34, 126.98 (2x), 121.17, 115.39, 111.60, 55.76.

4-(4-Nitrophenyl)-2,6-diphenylpyrimidine (1oa).[22] Yield = 71% (501 mg); yellow solid; mp = 216–217 °C; HRMS (ESI, M^+ + H) calcd for $C_{22}H_{16}ClN_2$ 354.1237, found 354.1231; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.71 (d, J = 5.0 Hz, 2H), 8.46 (d, J = 8.5 Hz, 2H), 8.41 (d, J = 9.0 Hz, 2H), 8.30 (d, J = 3.5 Hz, 2H), 8.06 (s, 1H), 7.59–7.56 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.49, 164.86, 162.30, 149.17, 143.42, 137.53, 136.92, 131.24, 131.07, 129.05 (2x), 128.58 (2x), 128.48 (2x), 128.20 (2x), 127.32 (2x), 124.10 (2x), 110.84.

4-(2,6-Diphenylpyrimidin-4-yl)benzonitrile (1pa).[22] Yield = 65% (433 mg); yellow solid; mp = 185–186 °C; HRMS (ESI, M^+ + H) calcd for $C_{23}H_{16}N_3$ 334.1339, found 334.1334; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.71–8.64 (m, 2H), 8.33 (d, J = 8.5 Hz, 2H), 8.28–8.22 (m, 2H), 7.94 (s, 1H), 7.80 (d, J = 8.5 Hz, 2H), 7.60–7.51 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.18, 164.59, 162.40, 141.46, 137.48, 136.82, 132.55 (2x), 131.12, 130.95, 128.94 (2x), 128.48 (2x), 128.37 (2x), 127.69 (2x), 127.20 (2x), 1218.47, 113.98, 110.40.

General procedure for the synthesis of skeleton 2

A mixture of acetophenone **3** (4.0 mmol), benzaldehyde **4** (4.0 mmol), HMDS (14.4 mmol), TMSOTf (0.5 mmol) and toluene (2 mL) in a dried 35 mL microwave vial at 25 °C. The mixture was subjected to a microwave irradiation instrument and stirred at 150 °C for 0.5 h. The consumption of the starting materials was confirmed by TLC. The reaction was cooled to 25 °C, the mixture of crude product was transferred to a 100 mL round bottom flask, and the solvent was concentrated. The residue was diluted with water (10 mL) and the mixture was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product under reduced pressure. Purification on silica gel (hexanes/EtOAc = 8/1–3/1) afforded compounds **2aa–2av.**

2,4,6-Triphenylpyridine (2aa).[22] Yield = 92% (565 mg); colorless solid; mp = 138–139 °C; HRMS (ESI, M^+ + H) calcd for $C_{23}H_{18}N$ 308.1439, found 308.1447; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.35–8.31 (m, 4H), 7.96 (s, 2H), 7.82–7.80 (m, 2H), 7.66–7.57 (m, 6H), 7.57–7.51 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.32 (2x), 149.99, 139.45 (2x), 138.87, 128.96 (2x), 128.93 (2x), 128.83, 128.58 (4x), 127.03 (6x), 116.93 (2x).

4-(4-Fluorophenyl)-2,6-diphenylpyridine (2ac).[28f] Yield = 76% (535 mg); colorless solid; mp = 141–142 °C; HRMS (ESI, M^+ + H) calcd for $C_{23}H_{17}FN$ 326.1340, found 326.1337; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.22 (d, J = 8.0 Hz, 4H), 7.84 (s, 2H), 7.74–7.71 (m, 2H), 7.54 (t, J = 8.0 Hz, 4H), 7.49–7.46 (m, 2H), 7.23 (t, J = 8.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.31 (d, J = 247.25 Hz), 157.49 (2x), 149.04, 139.36 (2x), 135.03 (d, J = 3.0 Hz), 129.08 (2x), 128.87 (d, J = 8.25 Hz, 2x), 128.68 (4x), 127.06 (4x), 116.83 (2x), 116.06 (d, J = 21.375 Hz, 2x).

4-(4-Chlorophenyl)-2,6-diphenylpyridine (2ae).[28f] Yield = 83% (566 mg); yellow solid; mp = 119–120 °C; HRMS (ESI, M^+ + H) calcd for $C_{23}H_{17}ClN$ 342.1044, found 342.1048; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.20 (d, J = 8.0 Hz, 4H), 7.84 (s, 2H), 7.68 (d, J = 8.5 Hz, 2H), 7.56–7.49 (m, 6H), 7.48–7.44 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.66 (2x), 148.92, 139.38 (2x), 137.46, 135.17, 139.31 (2x), 129.15 (2x), 128.72 (4x), 128.43 (2x), 127.10 (4x), 116.79 (2x).

2,6-Diphenyl-4-(*m*-tolyl)pyridine (2ag).[28f] Yield = 80% (514 mg); yellow solid; mp = 84–85 °C; HRMS (ESI, M^+ + H) calcd for $C_{24}H_{20}N$ 322.1590, found 322.1588; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.26–8.20 (m, 4H), 7.90 (s, 2H), 7.5–7.51 (m, 6H), 7.49–7.41 (m, 3H), 7.31 (d, J = 7.5 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.42, 150.30, 139.61, 139.02, 138.80, 129.70, 128.99, 128.67, 127.86, 127.11, 124.27, 117.13, 21.52.

2,6-Diphenyl-4-(*p*-tolyl)pyridine (2ah).[28f] Yield = 93% (597 mg); white solid; mp = 117–118 °C; HRMS (ESI, M^+ + H) calcd for $C_{24}H_{20}N$ 322.1590, found 322.1588; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.23 (d, J = 8.5 Hz, 4H), 7.90 (s, 2H), 7.68 (d, J = 8.5 Hz, 2H), 7.54 (t, J = 8.0 Hz, 4H), 7.47 (t, J = 7.5 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 2.46 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.42 (2x), 150.00, 139.64 (2x), 139.03, 136.03, 129.79 (2x), 128.95 (2x), 128.65 (4x), 127.10 (4x), 126.96 (2x), 116.85 (2x), 21.22.

4-(4-Methoxyphenyl)-2,6-diphenylpyridine (2ai).[28f] Yield = 81% (546 mg); white solid; mp = 101–102 °C; HRMS (ESI, M^+ + H) calcd for $C_{24}H_{20}NO$ 338.1545, found 338.1541; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.22 (d, J = 7.5 Hz, 4H), 7.87 (s, 2H), 7.72 (d, J = 9.0 Hz, 2H), 7.57–7.50 (m, 4H), 7.49–7.43 (m, 2H), 7.06 (d, J = 9.0 Hz, 2H), 3.89 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.43, 157.41 (2x), 149.59, 139.68 (2x), 131.24, 128.93 (2x), 128.64 (4x), 128.28 (2x), 127.09 (4x), 116.57 (2x), 114.49 (2x), 55.38.

4-(Furan-2-yl)-2,6-diphenylpyridine (2al).[28f] Yield = 81% (481 mg); brown solid; mp = 154–155 °C; HRMS (ESI, M^+ + H) calcd for $C_{21}H_{16}NO$ 298.1226, found 298.1236; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.26–8.18 (m, 4H), 7.95 (s, 2H), 7.61–7.46 (m, 7H), 6.99 (d, J = 3.0 Hz, 1H), 6.62–6.54 (m, 1H); ^{13}C NMR (125 MHz,

$CDCl_3$): δ 157.48 (2x), 151.95, 143.58, 139.44 (2x), 139.03, 129.05 (2x), 128.64 (4x), 127.04 (4x), 112.97 (2x), 112.08, 108.45.

4-(3-Nitrophenyl)-2,6-diphenylpyridine (2am).[30e] Yield = 81% (570 mg); colorless solid; mp = 140–141 °C; HRMS (ESI, M^+ + H) calcd for $C_{23}H_{17}N_2O_2$ 353.1285, found 353.1280; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.59 (s, 1H), 8.33 (d, J = 8.0 Hz, 1H), 8.21 (d, J = 8.0 Hz, 4H), 8.05 (d, J = 7.5 Hz, 1H), 7.88 (s, 2H), 7.71 (t, J = 8.0 Hz, 1H), 7.57–7.51 (m, 4H), 7.50–7.44 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.92 (2x), 148.81, 147.60, 140.72, 138.98 (2x), 133.06, 130.14, 129.37 (2x), 128.77 (4x), 127.09 (4x), 123.61, 122.07, 116.70 (2x).

4-(4-Nitrophenyl)-2,6-diphenylpyridine (2an).[28f] Yield = 87% (612 mg); white solid; mp = 174–175 °C; HRMS (ESI, M^+ + H) calcd for $C_{23}H_{17}N_2O_2$ 353.1290, found 353.1290; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.39 (d, J = 8.5 Hz, 2H), 8.24–8.18 (m, 4H), 7.90 (d, J = 8.5 Hz, 2H), 7.88 (s, 2H), 7.56–7.51 (m, 4H), 7.51–7.45 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.96 (2x), 148.14, 147.83, 145.44, 139.00 (2x), 129.42 (2x), 128.81 (4x), 128.16 (2x), 127.11 (4x), 124.35 (2x), 116.93 (2x).

4-(2-Methoxyphenyl)-2,6-diphenylpyridine (2ao).[28f] Yield = 83% (560 mg); yellow gum; HRMS (ESI, M^+ + H) calcd for $C_{24}H_{20}NO$ 338.1545, found 338.1541; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.20 (d, J = 7.5 Hz, 4H), 7.88 (s, 2H), 7.55–7.49 (m, 4H), 7.48–7.41 (m, 4H), 7.14–7.09 (m, 1H), 7.07 (d, J = 8.5 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.74, 156.60, 147.87, 139.85, 130.50, 130.02, 128.78, 128.60, 128.46, 127.13, 121.06, 119.70, 111.44, 55.67.

4-(3-Methoxyphenyl)-2,6-diphenylpyridine (2ap).[28f] Yield = 89% (600 mg); white solid; mp = 124–125 °C; HRMS (ESI, M^+ + H) calcd for $C_{24}H_{20}NO$ 338.1539, found 338.1538; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.23 (d, J = 7.5 Hz, 4H), 7.90 (s, 2H), 7.54 (t, J = 7.5 Hz, 4H), 7.50–7.43 (m, 3H), 7.35 (d, J = 7.5 Hz, 1H), 7.28 (t, J = 2.0 Hz, 1H), 7.03 (dd, J = 2.0, 8.0 Hz, 1H), 3.92 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.14 157.46 (2x), 150.06, 140.53, 139.53 (2x), 130.14, 129.02 (2x), 128.67 (4x), 127.10 (4x), 119.57, 117.13 (2x), 114.17, 112.99, 55.40.

4-(3,5-Dimethoxyphenyl)-2,6-diphenylpyridine (2aq). Yield = 79% (580 mg); colorless solid; mp = 101–102 °C; HRMS (ESI, M^+ + H) calcd for $C_{25}H_{22}NO_2$ 368.1645, found 368.1644; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.26 (d, J = 7.0 Hz, 4H), 7.89 (s, 2H), 7.56 (t, J = 7.0 Hz, 4H), 7.49 (t, J = 7.0 Hz, 2H), 6.91 (s, 2H), 6.61 (s, 1H), 3.90 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.42 (2x), 157.51 (2x), 150.28, 141.32, 139.61 (2x), 129.14 (2x), 128.78 (4x), 127.21 (4x), 117.21 (2x), 105.57 (2x), 100.67, 55.57 (2x).

4-(Benzo[*d*][1,3]dioxol-5-yl)-2,6-diphenylpyridine (2ar).[28f] Yield = 87% (611 mg); white solid; mp = 152–153 °C; HRMS (ESI, M^+ + H) calcd for $C_{24}H_{18}NO_2$ 352.1332, found 352.1333; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.20–8.18 (m, 4H), 7.82 (s, 2H), 7.55–7.48 (m, 4H), 7.47–7.42 (m, 2H), 7.28–7.21 (m, 2H), 6.96 (d, J = 8.0 Hz, 1H), 6.06 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.46 (2x), 149.71, 148.47, 148.44, 139.55 (2x), 133.12, 129.02 (2x), 128.69 (4x), 127.09 (4x), 121.06, 116.76 (2x), 108.86, 107.45, 101.49. Single-crystal X-ray diagram: crystal of **2q** was grown by slow diffusion of EtOAc into a solution of **2q** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group $P2_1/n$, a = 6.4058(2) Å, b = 12.1092(3) Å, c = 21.6453(7) Å, V = 1677.71(9) Å^3, Z = 4, d_{calcd} = 1.391 mg m^{-3}, $F(000)$ = 736, 2θ range 1.927–27.102, R indices (all data) $R1$ = 0.0412, w$R2$ = 0.0956. CCDC number is 2085356.†

4-(Anthracen-9-yl)-2,6-diphenylpyridine (2as).[28f] Yield = 62% (505 mg); yellow solid; mp = 222–223 °C; HRMS (ESI, M^+ + H) calcd for $C_{31}H_{22}N$ 408.1747, found 408.1745; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.58 (s, 1H), 8.28–8.22 (m, 4H), 8.10 (d, J = 8.5 Hz, 2H), 7.84 (s, 2H), 7.75 (d, J = 9.0 Hz, 2H), 7.54–7.48 (m, 6H), 7.47–7.43 (m, 2H), 7.42–7.37 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.03 (2x), 148.90, 139.23 (2x), 134.30, 131.29 (2x), 129.53 (2x), 129.20 (2x), 128.74 (4x), 128.53 (2x), 127.48, 127.13 (4x), 126.15 (2x), 126.07 (2x), 125.35 (2x), 121.39 (2x).

4-(Naphthalen-2-yl)-2,6-diphenylpyridine (2at).[28f] Yield = 83% (593 mg); white solid; mp = 128–129 °C; HRMS (ESI, M^+ + H) calcd for $C_{27}H_{20}N$ 358.1590, found 358.1590; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.30–8.21 (m, 5H), 8.05–7.96 (m, 4H), 7.95–7.90 (m, 1H), 7.87 (dd, J = 1.5, 8.0 Hz, 1H), 7.60–7.52 (m, 6H), 7.51–7.45 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.56 (2x), 150.07, 139.59 (2x), 136.27, 133.49, 133.40, 129.05 (2x), 128.91, 128.70 (4x), 128.42, 127.74, 127.15 (4x), 126.74, 126.68, 126.45, 124.81, 117.28 (2x).

2,6-Diphenyl-4-(thiophen-2-yl)pyridine (2au).[30e] Yield = 84% (526 mg); white solid; mp = 161–162 °C; HRMS (ESI, M^+ + H) calcd for $C_{21}H_{16}NS$ 314.0998, found 314.1006; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.25–8.19 (m, 4H), 7.89 (s, 2H), 7.64–7.61 (m, 1H), 7.55 (t, J = 7.5 Hz, 4H), 7.51–7.46 (m, 2H), 7.45 (dd, J = 1.0, 5.0 Hz, 1H), 7.19 (dd, J = 3.5, 5.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.64 (2x), 142.92, 141.88, 139.33 (2x), 129.09 (2x), 128.65 (4x), 128.32, 127.06 (4x), 126.85, 125.19, 115.25 (2x).

4-Ethyl-2,6-diphenylpyridine (2av).[30h] Yield = 52% (270 mg); yellow gum; HRMS (ESI, M^+ + H) calcd for $C_{19}H_{18}N$ 260.1434, found 260.1430; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.06 (d, J = 8.0 Hz, 2H), 7.74 (s, 1H), 7.69 (d, J = 8.0 Hz, 2H), 7.55–7.38 (m, 6H), 7.32 (s, 1H), 2.97 (q, J = 8.0 Hz, 2H), 1.43 (t, J = 8.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.94, 157.47, 149.57, 139.96, 139.08, 129.01 (2x), 128.78, 128.73, 128.67 (2x), 127.12 (4x), 118.58, 116.23, 31.66, 13.98.

2,6-Bis(4-fluorophenyl)-4-phenylpyridine (2ba).[28f] Yield = 89% (611 mg); white solid; mp = 175–176 °C; HRMS (ESI, M^+ + H) calcd for $C_{23}H_{16}F_2N$ 344.1245, found 344.1242; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.20–8.16 (m, 4H), 7.82 (d, J = 6.0 Hz, 2H), 7.73 (d, J = 8.0 Hz, 2H), 7.57–7.52 (m, 2H), 7.51–7.47 (m, 1H), 7.20 (t, J = 8.5 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.64 (d, J = 247.125 Hz, 2x), 156.46 (2x), 150.44, 138.84 (2x), 135.57 (d, J = 2.75 Hz, 2x), 129.15 (2x), 129.11, 128.89 (d, J = 8.2 Hz, 4x), 127.14 (2x), 116.67, 115.62 (d, J = 21.3625 Hz, 4x).

2,6-Bis(4-chlorophenyl)-4-phenylpyridine (2ca).[28f] Yield = 91% (683 mg); colorless solid; mp = 186–187 °C; HRMS (ESI, M^+ + H) calcd for $C_{23}H_{16}Cl_2N$ 376.0654, found 376.0654; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.12 (d, J = 8.5 Hz, 4H), 7.84 (s, 2H), 7.73–7.71 (m, 2H), 7.56–7.49 (m, 7H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.31 (2x), 150.54, 138.67, 137.75 (2x), 135.27 (2x), 129.17 (2x), 128.90 (4x), 128.33 (4x), 127.14 (2x), 117.06 (2x).

4-Phenyl-2,6-di-*p*-tolylpyridine (2da).[28f] Yield = 88% (590 mg); colorless solid; mp = 159–160 °C; HRMS (ESI, M^+ + H) calcd for $C_{25}H_{22}N$ 336.1747, found 336.1744; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.12 (d, J = 8.0 Hz, 4H), 7.85 (s, 2H), 7.76–7.74 (m, 2H), 7.55–7.52 (m, 2H), 7.49–7.47 (m, 1H), 7.33 (d, J = 8.0 Hz, 4H),

2.45 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.38 (2x), 149.99, 139.26, 138.93 (2x), 136.88 (2x), 129.38 (4x), 129.04 (2x), 128.83, 127.16 (2x), 126.97 (4x), 116.49 (2x), 21.30 (2x).

2,6-Bis(4-methoxyphenyl)-4-phenylpyridine (2ea).[28f] Yield = 92% (676 mg); white solid; mp = 131–132 °C; HRMS (ESI, M^+ + H) calcd for $C_{25}H_{22}NO_2$ 368.1645, found 368.1645; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.20 (d, J = 9.0 Hz, 4H), 7.79 (s, 2H), 7.75 (d, J = 7.5 Hz, 2H), 7.58.7.52 (m, 2H), 7.51–7.46 (m, 1H), 7.07 (d, J = 8.0 Hz, 4H), 3.89 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.40 (2x), 156.81 (2x), 149.84, 139.21, 132.23 (2x), 128.94 (2x), 128.72, 128.27 (4x), 127.05 (2x), 115.53 (2x), 113.93 (4x), 55.24 (2x)

2,6-Di([1,1′-biphenyl]-4-yl)-4-phenylpyridine (2fa).[28f] Yield = 72% (661 mg); white solid; mp = 180–181 °C; HRMS (ESI, M^+ + H) calcd for $C_{35}H_{26}N$ 460.2060, found 460.2058; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.32 (d, J = 8.0 Hz, 4H), 7.95 (s, 2H), 7.82–7.75 (m, 6H), 7.70 (d, J = 8.0 Hz, 4H), 7.59–7.53 (m, 2H), 7.53–7.46 (m, 5H), 7.43–7.37 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.12 (2x), 150.23 (2x), 141.81 (2x), 140.68 (2x), 139.06, 138.47 (2x), 129.13 (2x), 129.00 (2x), 128.83 (4x), 127.52 (4x), 127.43 (4x), 127.20 (2x), 127.12 (4x), 117.04 (2x).

2,6-Bis(3-fluorophenyl)-4-phenylpyridine (2ga).[28f] Yield = 92% (631 mg); white solid; mp = 147–148 °C; HRMS (ESI, M^+ + H) calcd for $C_{23}H_{16}F_2N$ 344.1245, found 344.1254; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.98–7.92 (m, 4H), 7.89 (s, 2H), 7.77–7.72 (m, 2H), 7.58–7.53 (m, 2H), 7.52–7.45 (m, 3H), 7.18–7.13 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.35 (d, J = 243.75 Hz, 2x), 156.19 (d, J = 2.25 Hz, 2x), 150.62, 141.62 (d, J = 7.375 Hz, 2x), 138.59, 130.20 (d, J = 8.125 Hz, 2x), 129.22, 129.20 (2x), 127.15 (2x), 122.56 (d, J = 2.375 Hz, 2x), 117.62 (2x), 116.00 (d, J = 21.125 Hz, 2x), 114.06 (d, J = 22.75 Hz, 2x).

2,6-Bis(3-methoxyphenyl)-4-phenylpyridine (2ia).[30f] Yield = 82% (602 mg); colorless gum; HRMS (ESI, M^+ + H) calcd for $C_{25}H_{22}NO_2$ 368.1645, found 368.1640; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89 (s, 2H), 7.82–7.81 (m, 2H), 7.79–7.73 (m, 4H), 7.57–7.52 (m, 2H), 7.51–7.46 (m, 1H), 7.44 (t, J = 8.0 Hz, 2H), 7.01 (dd, J = 2.5, 8.0 Hz, 2H), 3.93 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.03 (2x), 157.18 (2x), 150.17, 141.03 (2x), 138.98, 129.66 (2x), 129.10 (2x), 128.98, 127.16 (2x), 119.53 (2x), 117.39 (2x), 114.71 (2x), 112.66 (2x), 55.38, 55.36.

2,6-Bis(2-bromophenyl)-4-phenylpyridine (2la).[28f] Yield = 61% (565 mg); white solid; mp = 150–151 °C; HRMS (ESI, M^+ + H) calcd for $C_{23}H_{16}Br_2N$ 463.9644, found 463.9644; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 (s, 2H), 7.78–7.75 (m, 2H), 7.74–7.70 (m, 4H), 7.55–7.50 (m, 2H), 7.49–7.46 (m, 1H), 7.45–7.41 (m, 2H), 7.27 (td, J = 2.0, 8.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.39 (2x), 148.20, 141.18 (2x), 138.11 (2x), 133.29 (2x), 131.75 (2x), 129.76 (2x), 129.13 (2x), 127.58 (2x), 127.21 (2x), 121.94 (2x), 121.41 (2x).

4-Phenyl-2,6-di-*o*-tolylpyridine (2ma).[28f] Yield = 81% (543 mg); white solid; mp = 133–134 °C; HRMS (ESI, M^+ + H) calcd for $C_{25}H_{22}N$ 336.1747, found 336.1747; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74–7.72 (m, 2H), 7.60 (s, 2H), 7.54–7.49 (m, 4H), 7.48–7.43 (m, 1H), 7.34–7.27 (m, 6H), 2.49 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.09 (2x), 148.79, 140.72 (2x), 138.49, 135.90 (2x), 130.68 (2x), 129.83 (2x), 129.13 (2x), 129.02, 128.24 (2x), 127.12 (2x), 125.83 (2x), 120.11 (2x), 20.62 (2x).

2,6-Bis(2-methoxyphenyl)-4-phenylpyridine (2na).[28f] Yield = 77% (565 mg); white solid; mp = 133–134 °C; HRMS (ESI, M^+ + H) calcd for $C_{25}H_{22}NO_2$ 368.1651, found 368.1642; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.00 (s, 2H), 7.96 (dd, J = 1.5, 7.5 Hz, 2H), 7.76–7.72 (m, 2H), 7.54–7.49 (m, 2H), 7.47–7.42 (m, 1H), 7.42–7.36 (m, 2H), 7.14–7.09 (m, 2H), 7.04 (d, J = 8.5 Hz, 2H), 3.90 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.08 (2x), 155.97 (2x), 147.66 (2x), 139.48, 131.56 (2x), 129.72 (2x), 129.62, 128.91 (2x), 128.51, 127.34 (2x), 121.41 (2x), 121.05 (2x), 111.41 (2x), 55.72 (2x).

4-Phenyl-2,6-bis(4-(trifluoromethyl)phenyl)pyridine (2qa).[30f] Yield = 85% (753 mg); white solid; mp = 156–157 °C; HRMS (ESI, M^+ + H) calcd for $C_{25}H_{16}F_6N$ 444.1182, found 444.1180; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.30 (d, J = 8.0 Hz, 4H), 7.99–7.92 (m, 2H), 7.78 (d, J = 8.0 Hz, 4H), 7.75 (d, J = 7.0 Hz, 2H), 7.60–7.50 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.24, 150.87, 142.50 (2x), 138.34, 131.07 (q, J = 32.7 Hz, 2x), 129.40 (2x), 129.28 (2x), 127.38 (4x), 127.16 (2x), 125.71 (d, J = 3.5 Hz, 4x), 124.23 (q, J = 273.62 Hz, 2x), 118.18 (2x).

4-Phenyl-2,6-di-*m*-tolylpyridine (2ra).[30g] Yield = 70% (469 mg); yellow solid; mp = 162–163 °C; (ESI, M^+ + H) calcd for $C_{25}H_{22}N$ 336.1747, found 336.1742; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.04 (s, 2H), 8.00 (d, J = 7.5 Hz, 2H), 7.89 (s, 2H), 7.77 (d, J = 7.5 Hz, 2H), 7.55 (t, J = 8.0 Hz, 2H), 7.50 (d, J = 7.5 Hz, 1H), 7.43 (t, J = 7.5 Hz, 2H), 7.29 (d, J = 7.5 Hz, 2H), 2.51 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.71 (2x), 150.02, 139.64 (2x), 139.11, 138.27 (2x), 129.75 (2x), 129.06 (2x), 128.89, 128.58 (2x), 127.83 (2x), 127.17 (2x), 124.30 (2x), 117.15 (2x), 21.59 (2x).

2,6-Di(furan-2-yl)-4-phenylpyridine (2sa).[28f] Yield = 76% (436 mg); bown solid; mp = 118–119 °C; HRMS (ESI, M^+ + H) calcd for $C_{19}H_{14}NO_2$ 288.1025, found 288.1033; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81 (s, 2H), 7.78–7.74 (m, 2H), 7.58–7.55 (m, 2H), 7.54–7.50 (m, 2H), 7.49–7.44 (m, 1H), 7.20 (dd, J = 1.0, 3.0 Hz, 2H), 6.58–6.55 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 153.77 (2x), 149.77, 149.69 (2x), 143.28 (2x), 138.38, 129.11, 129.04 (2x), 127.03 (2x), 114.80 (2x), 112.05 (2x), 109.09 (2x).

4-Phenyl-2,6-di(thiophen-3-yl)pyridine (2ta).[28f] Yield = 80% (510 mg); yellow solid; mp = 135–136 °C; HRMS (ESI, M^+ + H) calcd for $C_{19}H_{14}NS_2$ 320.0562, found 320.0561; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.08 (dd, J = 1.5, 3.0 Hz, 2H), 7.84 (dd, J = 1.5, 5.0 Hz, 2H), 7.76–7.72 (m, 4H), 7.59–7.54 (m, 2H), 7.52–7.48 (m, 1H), 7.45 (dd, J = 3.0, 5.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 153.64 (2x), 150.15, 142.44 (2x), 138.90, 129.09 (2x), 128.98, 127.10 (2x), 126.45 (2x), 126.14 (2x), 123.78 (2x), 116.60 (2x).

2,6-Dimethyl-4-phenylpyridine (2ua).[31] Yield = 88% (322 mg); white solid; mp = 58–59 °C; HRMS (FAB, M^+ + H) calcd for $C_{13}H_{14}N$ 184.1126, found 184.1126; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73–7.54 (m, 2H), 7.51–7.39 (m, 3H), 7.19 (s, 2H), 2.60 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.01, 149.35, 138.61, 128.99 (2x), 128.85 (2x), 127.05 (2x), 118.53 (2x), 24.41 (2x).

Conflicts of interest

The authors declare no conflicts of interest.

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Notes and references

1 J. Zhu and H. Bienaymé, *Multicomponent Reactions*, Wiley-VCH, Weinheim, Germany, 2005.

2 (*a*) C. Allais, J.-M. Grassot, J. Rodriguez and T. Constantieux, *Chem. Rev.*, 2014, **114**, 10829–10868; (*b*) W. Guo, J. Liao, D. Liu, J. Li, F. Ji, W. Wu and H. Jiang, *Angew. Chem., Int. Ed.*, 2017, **56**, 1289–1293; (*c*) R. Echemendía, A. F. de La Torre, J. L. Monteiro, M. Pila, A. G. Corrêa, B. Westermann, D. G. Rivera and M. W. Paixão, *Angew. Chem., Int. Ed.*, 2015, **54**, 7621–7625; (*d*) L. Reguera and D. G. Rivera, *Chem. Rev.*, 2019, **119**, 9836–9860; (*e*) P. Wu, M. Givskov and T. E. Nielsen, *Chem. Rev.*, 2019, **119**, 11245–11290.

3 (*a*) B. H. Rotstein, S. Zaretsky, V. Rai and A. K. Yudin, *Chem. Rev.*, 2014, **114**, 8323–8359; (*b*) R. C. Cioc, E. Ruijter and R. V. A. Orru, *Green Chem.*, 2014, **16**, 2958–2975.

4 P. Biginelli, *Ber. Dtsch. Chem. Ges.*, 1891, **24**, 1317–1319.

5 A. Hantzsch, *Ber. Dtsch. Chem. Ges.*, 1881, **14**, 1637–1638.

6 C. Mannich and W. Krösche, *Arch. Pharm.*, 1912, **250**, 647–667.

7 M. Passerini and L. Simone, *Gazz. Chim. Ital.*, 1921, **51**, 126–129.

8 L. S. Povarov, *Russ. Chem. Rev.*, 1967, **36**, 656–670.

9 A. Strecker, *Justus Liebigs Ann. Chem.*, 1854, **91**, 349–351.

10 (*a*) I. Ugi, R. Meyr, U. Fetzer and C. Steinbrückner, *Angew. Chem.*, 1959, **71**, 386; (*b*) A. Dömling and I. Ugi, *Angew. Chem., Int. Ed.*, 2000, **39**, 3168–3210.

11 (*a*) A. R. Katrizky and C. W. Rees, *Comprehensive Heterocyclic Chemistry*, Pergamon Press, 1984; (*b*) J. A. Joule and K. Mills, *Heterocyclic Chemistry*, Wiley-Blackwell, Oxford, 5th edn, 2010; (*c*) E. Vitaku, D. T. Smith and J. T. Njardarson, *J. Med. Chem.*, 2014, **57**, 10257–10274.

12 (*a*) I. M. Lagoja, *Chem. Biodiversity*, 2005, **2**, 1–50; (*b*) A. Basnet, P. Thapa, R. Karki, Y. Na, Y. Jahng, B.-S. Jeong, T. C. Jeong, C.-S. Lee and E.-S. Lee, *Bioorg. Med. Chem.*, 2007, **15**, 4351–4359; (*c*) S. R. Walker, E. J. Carter, B. C. Huff and J. C. Morris, *Chem. Rev.*, 2009, **109**, 3080–3098; (*d*) E. P. Aparna and K. S. Devaky, *ACS Comb. Sci.*, 2019, **21**, 35–68.

13 (*a*) T. P. Selvam, C. R. James, P. V. Dniandev and S. K. Valzita, *Res. Pharm.*, 2012, **2**, 1–9; (*b*) S. P. Chan, K. Han, R. Qu, L. J. Tong, Y. J. Li, Z. Zhang, H. M. Cheng, X. J. Lu, A. Patterson, J. Smaill, X. M. Ren, J. Ding, H. Xie and K. Ding, *Bioorg. Med. Chem. Lett.*, 2015, **25**, 4277–4281; (*c*) O. S. Reddy, C. V. Suryanarayana, K. J. P. Narayana, V. Anuradha and B. H. Babu, *Med. Chem. Res.*, 2015, **24**, 1777–1788; (*d*) R. M. Okasha, F. F. Albalawi, T. H. Afifi, A. M. Fouda, A. A. M. Al-Dies and A. M. El-Agrody, *Molecules*, 2016, **21**, 1450; (*e*) M. Erra, J. Taltavull, A. Gréco, F. J. Bernal, J. F. Caturla, J. Gràcia, M. Domínguez, M. Sabaté, S. Paris, S. Soria, B. Hernández, C. Armengol, J. Cabedo, M. Bravo, E. Calama, M. Miralpeix and M. D. Lehner, *ACS Med. Chem. Lett.*, 2017, **8**, 118–123; (*f*) Z. Fang, S. Zheng, K.-F. Chan, W. Yuan, Q. Guo, W. Wu, H.-K. Lui, Y. Lu, Y.-C. Leung, T. H. Chan, K.-Y. Wong and N. Sun, *Eur. J. Med. Chem.*, 2019, **161**, 141–153.

14 (*a*) G. Brugnatelli, *Ann. Chim. Phys.*, 1818, **8**, 201–206; (*b*) E. Frankland and H. Kolbe, *Justus Liebigs Ann. Chem.*, 1848, **65**, 269–287.

15 (*a*) G. Domínguez and J. Perez-Castells, *Chem. Soc. Rev.*, 2011, **133**, 12285–12292; (*b*) J. A. Bull, J. J. Mousseau, G. Pelletier and A. B. Charette, *Chem. Rev.*, 2012, **112**, 2642–2713; (*c*) D. A. Shabalin, *Org. Biomol. Chem.*, 2021, **19**, 8184–8204.

16 (*a*) W. Guo, J. Liao, D. Liu, J. Li, F. Ji, W. Wu and H. Jiang, *Angew. Chem., Int. Ed.*, 2017, **56**, 1289–1293; (*b*) M. Mahfoudh, R. Abderrahim, E. Leclerc and J.-M. Campagne, *Eur. J. Org. Chem.*, 2017, **2017**, 2856–2865.

17 (*a*) N. Deibl, K. Ament and R. Kempe, *J. Am. Soc. Chem.*, 2015, **137**, 12804–12807; (*b*) M. Mastalir, M. Glatz, E. Pittenauer, G. Allmaier and K. Kirchner, *J. Am. Soc. Chem.*, 2016, **138**, 15543–15546; (*c*) N. Deibl and R. Kempe, *Angew. Chem., Int. Ed.*, 2017, **56**, 1663–1666; (*d*) G. Chakraborty, R. Sikari, R. Mondal, S. Mandal and N. D. Paul, *Asian J. Org. Chem.*, 2020, **9**, 431–436; (*e*) R. Mondal, S. Sinha, S. Das, G. Chakraborty and N. D. Paul, *Adv. Synth. Catal.*, 2020, **362**, 594–600; (*f*) E. D. Anderson and D. L. Boger, *J. Am. Soc. Chem.*, 2011, **133**, 12285–12292; (*g*) E. D. Anderson and D. L. Boger, *Org. Lett.*, 2011, **13**, 2492–2494; (*h*) E. D. Anderson and D. L. Boger, *J. Am. Soc. Chem.*, 2011, **133**, 12285–12292; (*i*) C. M. Glinkerman and D. L. Boger, *Org. Lett.*, 2015, **17**, 4002–4005.

18 (*a*) L. Su, K. Sun, N. Pan, L. Liu, M. Sun, J. Dong, Y. Zhou and S.-F. Yin, *Org. Lett.*, 2018, **20**, 3399–3402; (*b*) A. Herrera, R. Martínez-Álvarez, P. Ramiro, M. Chioua and R. Torres, *Tetrahedron*, 2002, **58**, 3755–3764; (*c*) A. Herrera, R. Martínez-Álvarez, M. Chioua, R. Chioua and Á. Sánchez, *Tetrahedron*, 2002, **58**, 10053–10058; (*d*) Z. D. Pardo, G. L. Olsen, M. E. Fernández-Valle, L. Frydman, R. Martínez-Álvarez and A. Herrera, *J. Am. Soc. Chem.*, 2012, **134**, 2706–2715; (*e*) M. E. Fernández-Valle, R. Martínez-Álvarez, D. Molero-Vílchez, Z. D. Pardo, E. Sáez-Barajas and A. Herrera, *J. Org. Chem.*, 2015, **80**, 799–805.

19 (*a*) Y. Satoh, K. Yasuda and Y. Obora, *Organometallics*, 2012, **31**, 5235–5238; (*b*) X. You, S. Yu and Y. Liu, *Organometallics*, 2013, **32**, 5273–5276; (*c*) S. N. Karad and R.-S. Liu, *Angew. Chem., Int. Ed.*, 2014, **53**, 9072–9076; (*d*) T. K. Lane, M. H. Nguyen, B. R. D'Souza, N. A. Spahn and J. Louie, *Chem. Commun.*, 2013, **49**, 7735–7737.

20 (*a*) M. Movassaghi and M. D. Hill, *J. Am. Chem. Soc.*, 2006, **128**, 14254–14255; (*b*) O. K. Ahmad, M. D. Hill and M. Movassaghi, *J. Org. Chem.*, 2009, **74**, 8460–8463; (*c*) M. Movassaghi and M. D. Hill, *Nat. Protoc.*, 2007, **2**, 2018–2023; (*d*) H. B. Jalani, W. Cai and H. Lu, *Adv. Synth. Catal.*, 2017, **359**, 2509–2513.

21 (*a*) X.-Q. Chu, W.-B. Cao, X.-P. Xu and S.-J. Ji, *J. Org. Chem.*, 2017, **82**, 1145–1154; (*b*) L.-Y. Zheng, W. Guo and X.-L. Fan, *Asian J. Org. Chem.*, 2017, **6**, 837–840; (*c*) C. Xu, S.-F. Jiang,

X.-H. Wen, Q. Zhang, Z.-W. Zhou, Y.-D. Wu, F.-C. Jia and A.-X. Wu, *Adv. Synth. Catal.*, 2018, **360**, 2267–2271; (*d*) Q. Gao, M. Wu, K. Zhang, N. Yang, M. Liu, J. Li, L. Fang, S. Bai and Y. Xu, *Org. Lett.*, 2020, **22**, 5645–5649; (*e*) A. R. Romanov, A. Y. Rulev, A. V. Popov, E. V. Kondrashov and S. V. Zinchenko, *Synthesis*, 2020, **52**, 1512–1522; (*f*) J. L. Zhan, M. W. Wu, F. Chen and B. Han, *J. Org. Chem.*, 2016, **81**, 11994–12000; (*g*) Y. Zhou, Z. H. Tang and Q. L. Song, *Adv. Synth. Catal.*, 2017, **359**, 952–958.

22 J. Chen, H. Meng, F. Zhang, F. Xiao and G.-J. Deng, *Green Chem.*, 2019, **21**, 5201–5206.

23 (*a*) T. Sasada, F. Kobayashi, N. Sakai and T. Konakahara, *Org. Lett.*, 2009, **11**, 2161–2164; (*b*) P. Wang, X. Zhang, Y. Liu and B. Chen, *Asian J. Org. Chem.*, 2019, **8**, 1122–1127; (*c*) P. Wu, X.-M. Cai, Q.-F. Wang and C.-G. Yan, *Synth. Commun.*, 2007, **37**, 223–229; (*d*) Y. Ding, R. Ma, R. C. Hider and Y. Ma, *Asian J. Org. Chem.*, 2020, **9**, 242–246; (*e*) C. Rakhi, K. Ramesh, M. P. Darbem, T. A. Branquinho, A. R. de Oliveira, P. S. Manjari and N. L. C. Domingues, *Tetrahedron Lett.*, 2016, **57**, 1656–1660.

24 J. Li, J. Li, R. He, J. Liu, Y. Liu, L. Chen, Y. Huang and Y. Li, *Org. Lett.*, 2022, **24**, 1620–1625.

25 M. Adib, N. Mahmoodi, M. Mahdavi and H. R. Bijanzadeh, *Tetrahedron Lett.*, 2006, **47**, 9365–9368.

26 Z. Hassani, *Lett. Org. Chem.*, 2014, **11**, 546–549.

27 D. Liu, W. Guo, W. Wu and H. Jiang, *J. Org. Chem.*, 2017, **82**, 13609–13616.

28 (*a*) C.-K. Chan, C.-Y. Lai, W.-C. Lo, Y.-T. Cheng, M.-Y. Chang and C.-C. Wang, *Org. Biomol. Chem.*, 2020, **18**, 305–315; (*b*) C.-K. Chan, C.-Y. Lai and C.-C. Wang, *Org. Biomol. Chem.*, 2020, **18**, 7201–7212; (*c*) K. H. Asressu, C.-K. Chan and C.-C. Wang, *RSC Adv.*, 2021, **11**, 28061–28071; (*d*) C.-K. Chan, C.-Y. Lai and C.-C. Wang, *Synthesis*, 2020, **18**, 1779–1794; (*e*) C.-K. Chan, C.-Y. Lai and C.-C. Wang, *Catalyst*, 2021, **11**, 877; (*f*) C.-K. Chan, Y.-H. Chung and C.-C. Wang, *RSC Adv.*, 2022, **12**, 8263–8273.

29 D. Cantillo, O. de Frutos, J. A. Rincón, C. Mateos and C. O. Kappe, *Org. Lett.*, 2014, **16**, 896–899.

30 (*a*) C. H. Low, J. N. Rosenberg, M. A. Lopez and T. Agapie, *J. Am. Soc. Chem.*, 2018, **140**, 11906–11910; (*b*) Y. Hiraga, R. Kuwahara and T. Hatta, *Tetrahedron*, 2021, **94**, 132317; (*c*) R. Mondal and D. E. Herbert, *Organometallics*, 2020, **39**, 1310–1317; (*d*) A. K. Bains and D. Adhikari, *Catal. Sci. Technol.*, 2020, **10**, 6309–6318; (*e*) S. Forouzandehdel, M. Meskini and R. Rami, *J. Mol. Struct.*, 2020, **1214**, 128142; (*f*) Y. Yi, M.-N. Zhao, Z.-H. Ren, Y.-Y. Wang and Z.-H. Guan, *Green Chem.*, 2017, **19**, 1023–1027; (*g*) Q. Yang, Y. Zhang, W. Zeng, Z.-C. Duan, X. Sang and D. Wang, *Green Chem.*, 2019, **21**, 5683–5690; (*h*) J.-C. Xiang, M. Wang, Y. Cheng and A.-X. Wu, *Org. Lett.*, 2016, **18**, 24–27.

31 L. A. Lumangtad, E. Claeys, S. Hamal, A. Intasiri, C. Basrai, E. Yen-Pon, D. Beenfeldt, K. Vermeire and T. W. Bell, *Bioorg. Med. Chem.*, 2020, **28**, 115816.