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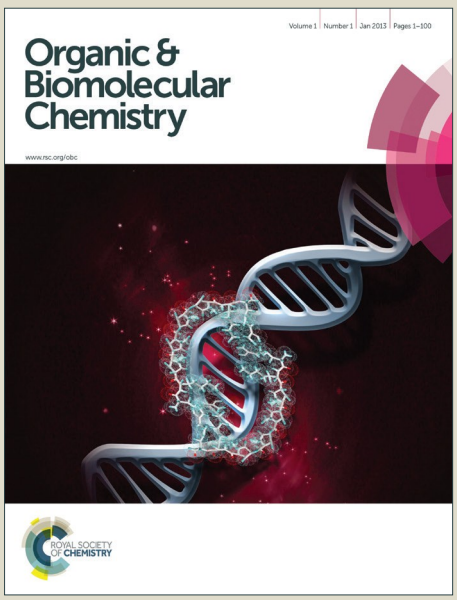

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ARTICLE

Synthesis of Quinazolinimines and Quinazolinamines from 2-Fluorobenzonitriles under Catalyst-free Conditions

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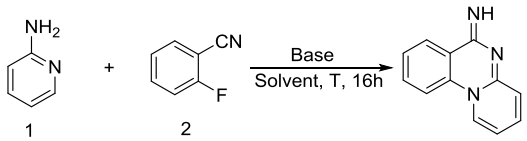
Dedicated to Professor Wen-Jing Xiao on the occasion of his 50th birthday!

A convenient procedure for the synthesis of quinazolinimines and quinazolinamines from 2-fluorobenzontriles has been developed. By using KO^{t}Bu as the promotor and with 2-aminopyridines or amidines as the reaction partner, the desired heterocycles were produced in moderate to good yields under catalyst-free conditions.

The development of new procedures for heterocyclic compounds synthesis is one of the main branches in organic chemistry.[1] As heterocycles are presenting wildly in naturally occurring compounds and also hold numerous important applications in pharmaceuticals and so on. In the past centuries, countless methodologies have been established as the realized importance of heterocycles, such as the name reactions,[2] and recently C-H activation procedures.[3] However, from the point view of pharmaceutical industrials, the requirement of Novel metal catalysts of these methods limited their application in industrial scale. Mainly for two reasons: 1) the using of Nobel metal catalysts increase the cost of the procedure; 2) the biological activity of heterocycles is sensitive to the residual amount of metal catalyst in the final compounds, and hence special attention has to be paid to the product purification and impurity detection which further increase the cost. Hence, the developing of synthetic procedures without requires a metal catalyst or additive become the target of synthetic community.[4] Gratifying many transition metal-free procedures have been achieved, for example, hypervalent iodine-catalyzed methods,[5] iodide-catalyzed oxidative pathways and etc.[6] Here, we wish to report our new results on the development of new transition metal-free procedure for heterocycles synthesis.[7] By using KO^{t}Bu as the promotor, with 2-fluorobenzontriles and 2-aminopyridines or amidines as the substrates *via* SNAr reactions,[4] biological active quinazolinimines and quinazolinamines were produced in moderate to good yields.[8]

Initially, 2-fluorobenzonitrile and 2-aminopyridine were chosen as the model system to test the effects of solvents (Table 1, entries 1-6). In the presence of KO^{t}Bu at 100 ^{o}C, moderate to good yields can be achieved in all the tested cases. To our delight, 88% of 6*H*-pyrido[1,2-*a*]quinazolin-6-imine can be isolated from DMAc (Table´1, entry 2). Then we choose DMAc as the solvent to check out the effect of bases, surprisingly, no desired product was detected in the reactions with the other tested bases (Table 1, entries 1-13). Some tiny modifications were performed subsequently, however, decreased yields were observed when shorten the reaction time, decrease reaction temperature, lower the amount of promoter and even change the concertation (Table 1, entries 2, 14-18).

Table 1. Optimization for the synthesis of quinazolinimine.[a]



1 2

Entry	Base	Solvent	Temp.	Yield (%)[b]
1	^{t}BuOK	DMF	100	62
2	^{t}BuOK	DMAc	100	88 64[c]
3	^{t}BuOK	DMSO	100	53
4	^{t}BuOK	Toluene	100	41
5	^{t}BuOK	1,4-Dioxane	100	44
6	^{t}BuOK	*o*-xylene	100	43
7	^{t}BuONa	DMAc	100	0
8	K_2CO_3	DMAc	100	1
9	K_3PO_4	DMAc	100	6
10	KOH	DMAc	100	1
11	DBU	DMAc	100	0
12	NEt_3	DMAc	100	0
13	DABCO	DMAc	100	0
14	^{t}BuOK	DMAc	100	15[d]

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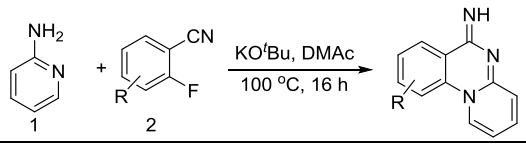
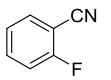
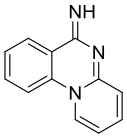
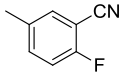
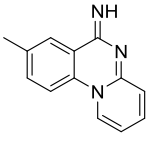
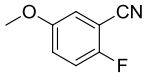
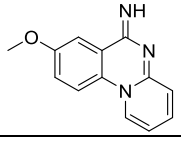
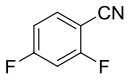
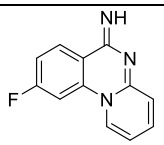
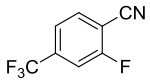
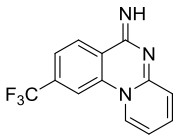
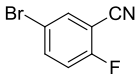
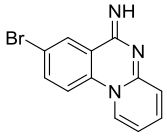
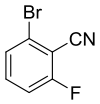
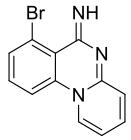
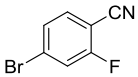
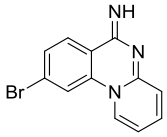
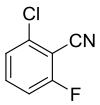
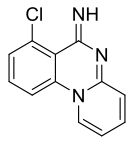
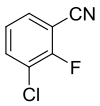
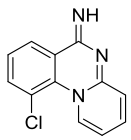
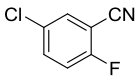
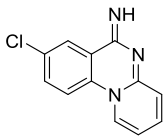
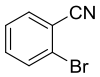
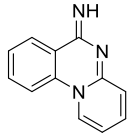
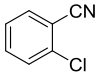
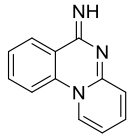
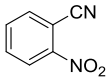
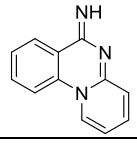
15	^{t}BuOK	DMAc	120	31
16	^{t}BuOK	DMAc	80	61
17	^{t}BuOK	DMAc	100	59[e]
18	^{t}BuOK	DMAc	100	63[f]

a: Reaction condition: 2aminopyridine (1 mmol), 2-fluorobenzonitrile (1.5 mmol), base (3 equiv.), solvent (2 mL), 100 °C, 16 h, air; b: isolated yields; c: 12 h; d: KO^{t}Bu (2 equiv.); e: solvent (4 mL); f: solvent (1 mL).

With the best reaction conditions in hand (KO^{t}Bu (3 equiv.), DMAc (2 mL), 100 °C, 16 h), the generality of limitation testing of this transition metal-free was carried out. Firstly, a various substituted 2-fluorobenzontriles were tested with 2-aminopyridine. As shown in Table 2, moderate to good yields of the desired products can be achieved in all the cases. More specifically, both electron-donating and electron-withdrawing substituents can be tolerated. In addition to interesting fluoro and trifluoromethyl,[9] bromide and chloride can be tolerated as well which are ready for further modification in cross-coupling reactions.[10] Concerning the reaction mechanism, we believe the reaction starts with the deprotonation of 2-aminopyridine with tBuOK. Then the nitrogen atom of the pyridine ring attacks the carbon at which fluorine atom is substituted through S_NAr (Nucleophilic Aromatic Substitution) reaction and followed by attacks of the nitrogen atom of the amino group to the cyano carbon. The final product can be produced after intramolecular rearrangement. In order to confirm that the cyclization proceeds via S_NAr, 2-halobenzonitriles and 2-nitrobenzontrile were tested with 2-aminopyridine instead of 2-fluorobenzonitriles and the desired products could be formed as well (Table 2, entries 12-14). Then 2-aminopyridines were tested successively (Table 3). Moderate yields can be achieved except in the cases of isoquinolinamines (Table 3, entries 5 and 6).

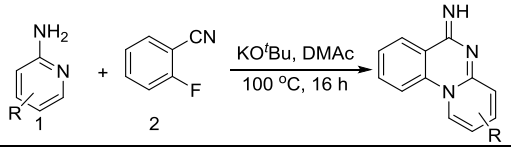
Table 2. Synthesis of quinazolinimines with 2-fluorobenzontriles.[a]



Entry	Substrate	Product	Yield
1			88%
2			79%
3			54%
4			57%
5			61%
6			33%
7			68%
8			48%
9			70%
10			68%
11			71%
12			55%
13			26%
14			8%

a: Reaction condition: 1 (1 mmol), 2 (1.5 mmol), ^{t}BuOK (3 equiv.), DMAc (2 mL), 100 °C, 16 h, air, isolated yield.

Table 3. Synthesis of quinazolinimines with aminopyridines.[a]



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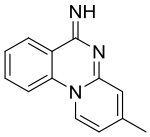
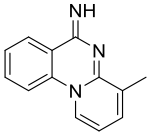
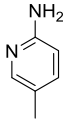
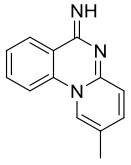
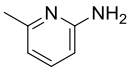
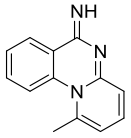
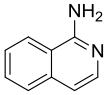
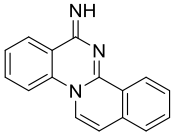
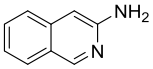
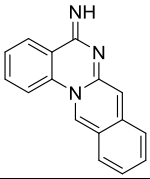
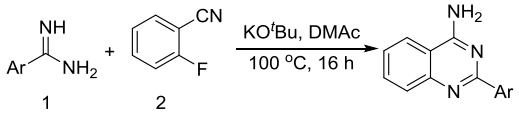
1			78%
2			70%
3			46%
4			63%
5			7% 12%[b]
6			10%

a: Reaction condition: 1 (1 mmol), 2 (1.5 mmol), ^{t}BuOK (3 equiv.), DMAc (2 mL), 100 °C, 16 h, air, isolated yield; b: 140 °C.

From the chemical structure of 2-aminopyridines, amidine is considered to be the same catalogue. As shown in Table 4, amidines were selected to react with 2-fluorobenzontrile. 70% of 2-phenylquinazolin-4-amine was produced from benzamidine under the same reaction conditions (Table 4, entry 1). However, lower yields were obtained in the cases of electron-withdrawing group substituted amidines (Table 4, entries 3-6) which may due to the low stability of these amidines. When 1*H*-pyrazole-1-carboximidamides were tested with 2-fluorobenzonitrile, 2-(1*H*-pyrazol-1-yl)benzonitrile was produced in good yields (Table 4, entries 7-9). We believe 1*H*-pyrazole-1-carboximidamides decomposed in the reaction solution and gave pyrazole which then react with 2-fluorobenzonitrile to give the product obtained. In the case of benzene-1,2-diamine, only 2-((2-aminophenyl)amino)benzonitrile was formed (Table 4, entry 10).

Table 4. Synthesis of quinazolinamines.[a]



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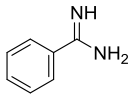
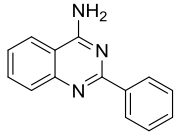
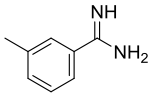
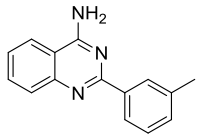
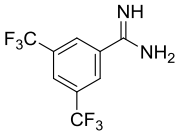
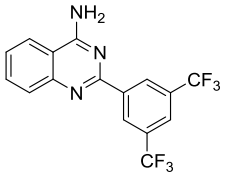
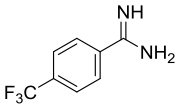
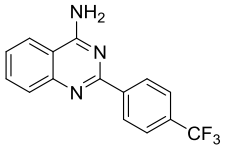
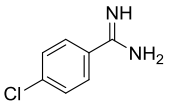
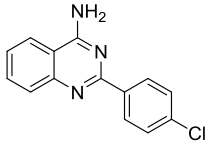
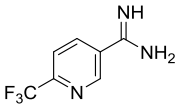
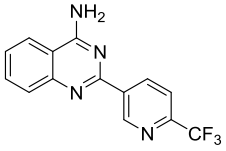
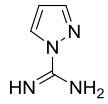
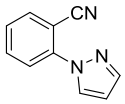
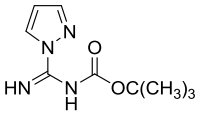
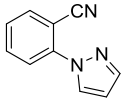
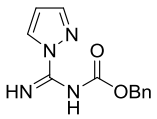
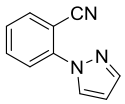
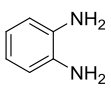
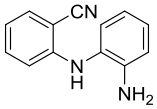
1			70%
2			55%
3			20%
4			52%
5			20%
6			51%
7			36%
8			77%
9			86%
10			31%[b]

a: Reaction condition: 1 (1 mmol), 2 (1.5 mmol), ^{t}BuOK (3 equiv.), DMAc (2 mL), 100 °C, 16 h, air, isolated yield. b: ^{t}BuOK (5 equiv.)

Conclusions

In conclusion, a convenient procedure for the synthesis of quinazolinimines and quinazolinamines from 2-fluorobenzontriles and 2-aminopyridines or amidines has been developed. By using KO^{t}Bu as the promotor, the desired heterocycles were produced in moderate to good yields under catalyst-free conditions.

The authors thank the state of Mecklenburg-Vorpommern, the Bundesministerium für Bildung und Forschung (BMBF), and the Deutsche Forschungsgemeinschaft for financial support. In addition, the research leading to these results has received funding from the Innovative Medicines Initiative Joint Undertaking (CHEM21) under grant agreement no. 115360, resources of which are composed of a financial contribution from the European Union's Seventh Framework Programme (FP7/2007–2013) and EFPIA companies in kind contribution. We also thank Dr. C. Fischer, S. Schareina, and Dr. W. Baumann for their excellent technical and analytical support. We also appreciate the general support from Prof. Matthias Beller.

Experimental section

General procedure: Under air, in a 25 mL reaction tube equipped with a stirring bar, 2-fluorobenzonitrile (1.5 mmol), 2-aminopyridine (1 mmol), ^{t}BuOK (3 equiv.) and DMAc (2 mL) were added. Then close the tube and heat it up to 100 ℃ for 16 h., cool the reaction mixture to room temperature when the reaction completed. The reaction solution was quenched with distilled water and extracted with ethyl acetate three times. The combined organic phases were washed with saturated NaCl solution and dried over Na_2SO_4. The crude product was purified by column chromatography to give the pure product.

6*H*-Pyrido[1,2-*a*]quinazolin-6-imine

148 mg, 76%, yellow solid, 185 ℃; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 9.06 (dt, *J* = 7.5, 1.1 Hz, 1H), 7.89 (dt, *J* = 8.4, 0.9 Hz, 1H), 7.67 – 7.58 (m, 2H), 7.45 – 7.27 (m, 3H), 6.69 (ddd, *J* = 7.7, 6.3, 1.5 Hz, 1H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 155.88, 148.04, 144.61, 134.68, 133.31, 128.15, 127.10, 125.65, 124.91, 124.16, 115.39, 111.53; GC-MS (EI, 70ev): m/z(%) = 194 (M+, 100), 195 (65), 169 (51), 67 (11); HRMS(ESI): calcd. for $[C_{13}H_{11}N_3 + H]^+$: 196.08692; found: 196.08706.

8-Methyl-6*H*-pyrido[1,2-*a*]quinazolin-6-imine

167 mg, 79 %, yellow solid, 147℃; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 9.03 (ddd, *J* = 7.5, 1.6, 0.9 Hz, 1 H), 7.68 (dt, *J* = 1.7, 0.9 Hz, 1 H), 7.50 – 7.47 (m, 1 H), 7.53 (d, *J* = 8.3 Hz, 1 H), 7.55 – 7.51 (m, 1 H), 7.49 (dd, *J* = 1.9, 0.5 Hz, 1 H), 7.35 (ddd, *J* = 9.2, 6.2, 1.6 Hz, 1 H), 7.28 – 7.20 (m, 1 H), 6.65 (ddd, *J* = 7.7, 6.2, 1.6 Hz, 1 H), 2.54 – 2.45 (m, 4 H), 7.71 – 7.64 (m, 1 H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 155.83, 147.43, 142.73, 134.74, 133.81, 127.97, 127.09, 125.78, 123.52, 115.09, 111.11, 21.52; GC-MS (EI, 70ev): m/z(%) = 210 (M+, 100), 211 (17), 209 (43), 181 (39); HRMS(ESI): calcd. for $[C_{13}H_{11}N_3 + H]^+$: 210.10257; found: 210.10269.

7-Bromo-6*H*-pyrido[1,2-*a*]quinazolin-6-imine

188 mg, 68 %, white solid, 177℃; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 8.7, 0.9 Hz, 1 H), 8.30 (ddd, *J* = 5.0, 1.9, 0.9 Hz, 1 H), 7.62 (ddd, *J* = 8.4, 7.3, 1.9 Hz, 1 H), 7.35 (dd, *J* = 8.7, 8.0 Hz, 1 H), 7.19 (dd, *J* = 8.0, 0.9 Hz, 1 H), 7.06 (s, 1 H), 6.93 (ddd, *J* = 7.3, 5.0, 0.9 Hz, 1 H), 6.88 (dt, *J* = 8.3, 0.9 Hz, 1 H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 153.53, 147.98, 145.90, 138.13, 134.28, 124.98, 124.62, 117.61, 116.55, 115.93, 111.99, 103.41; GC-MS (EI, 70ev): m/z(%) = 275 (M+, 100), 276 (54), 273 (56), 272 (96), 249 (33), 247 (34), 193 (23); HRMS(ESI): calcd. for $[C_{12}H_8BrN_3 + H]^+$: 273.99744; found: 273.99791.

10-Chloro-6*H*-pyrido[1,2-*a*]quinazolin-6-imine

156 mg, 68 %, yellow solid, 206 ℃; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 9.06 (dt, *J* = 7.5, 1.2 Hz, 1 H), 8.53 – 8.25 (m, 1 H), 7.79 (ddd, *J* = 14.5, 7.9, 1.3 Hz, 2 H), 7.63 – 7.35 (m, 2 H), 7.39 – 7.12 (m, 1 H), 6.76 (ddd, *J* = 7.6, 5.6, 2.3 Hz, 1 H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 155.30, 148.45, 141.99, 134.86, 133.14, 131.32, 127.98, 126.41, 124.08, 122.84, 116.80, 111.90; GC-MS (EI, 70ev): m/z(%) = 194 (M+, 100), 229 (14), 195 (13); HRMS(ESI): calcd. for $[C_{12}H_8ClN_3 + H]^+$: 230.04795; found: 230.04834.

8-Bromo-6*H*-pyrido[1,2-*a*]quinazolin-6-imine

90 mg, 33%, yellow solid, 185 ℃; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 9.04 (ddd, *J* = 7.5, 1.6, 0.8 Hz, 1 H), 8.00 (d, *J* = 2.2 Hz, 1 H), 7.71 (dd, *J* = 8.8, 2.1 Hz, 1 H), 7.48 (d, *J* = 8.8 Hz, 1 H), 7.42 (ddd, *J* = 9.2, 6.4, 1.6 Hz, 1 H), 7.31 – 7.21 (m, 2 H), 6.71 (ddd, *J* = 7.6, 6.4, 1.5 Hz, 1 H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 154.62, 148.23, 143.86, 136.18, 134.73, 129.08, 128.06, 126.66, 125.81, 117.47, 116.79, 111.66; GC-MS (EI, 70ev): m/z(%) = 272 (M+, 100), 273 (65), 274(75), 274 (72), 249 (39), 247(22), 193 (29), 249 (39); HRMS(ESI): calcd. for $[C_{12}H_8BrN_3 + H]^+$: 273.99744; found: 273.99792.

8-Methoxy-6*H*-pyrido[1,2-*a*]quinazolin-6-imine

122 mg, 54 %, yellow solid, 174 ℃; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.96 (ddd, *J* = 7.5, 1.6, 0.9 Hz, 1 H), 7.53 (d, *J* = 8.9 Hz, 1 H), 7.28 – 7.24 (m, 1 H), 7.24 – 7.21 (m, 1 H), 7.20 – 7.14 (m, 2 H), 6.59 (ddd, *J* = 7.7, 6.2, 1.6 Hz, 1 H), 3.87 (s, 3 H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 157.10, 155.55, 146.43, 139.46, 133.03, 129.03, 127.73, 125.86, 122.83, 115.81, 111.09, 104.64, 55.76; GC-MS (EI, 70ev): m/z(%) = 225 (M+, 100), 226 (16), 224 (51), 210 (98), 211 (18), 199 (20), 182 (15), 182 (42); HRMS(ESI): calcd. for $[C_{13}H_{11}N_3O + H]^+$: 226.09749; found: 226.09768.

7-Chloro-6*H*-pyrido[1,2-*a*]quinazolin-6-imine

160 mg, 70 %, white solid, 156 ℃; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.35 (dd, *J* = 8.6, 0.9 Hz, 1 H), 8.31 (ddd, *J* = 5.0, 2.0, 0.9 Hz, 1 H), 7.63 (ddd, *J* = 8.3, 7.3, 1.9 Hz, 1 H), 7.43 (dd, *J* = 8.7, 8.0 Hz, 1 H), 7.03 (dd, *J* = 8.0, 0.9 Hz, 2 H), 6.94 (ddd, *J* = 7.3, 5.0, 0.9 Hz, 1 H), 6.88 (dt, *J* = 8.3, 0.9 Hz, 1 H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 153.50, 147.98, 145.60, 138.16, 136.73, 134.11, 121.49, 117.61, 116.04, 114.73, 111.96, 99.99; GC-MS (EI, 70ev): m/z(%) = 228 (M+, 100), 229 (55), 230 (39), 231 (18), 205 (10), 203 (37), 193 (10); HRMS(ESI): calcd. for $[C_{12}H_8ClN_3 + H]^+$: 230.04795; found: 230.04827.

8-Chloro-6*H*-pyrido[1,2-*a*]quinazolin-6-imine

163 mg, 71 %, yellow solid, 180 ℃; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 9.05 (ddd, *J* = 7.5, 1.6, 0.8 Hz, 1 H), 7.85 (dd, *J* = 1.8, 0.9 Hz, 1 H), 7.57 (t, *J* = 1.4 Hz, 2 H), 7.43 (ddd, *J* = 9.2, 6.3, 1.6 Hz, 1 H), 7.32 – 7.23 (m, 2 H), 6.72 (ddd, *J* = 7.7, 6.3, 1.5 Hz, 1 H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 154.75, 148.11, 143.43, 134.75, 133.55, 130.06, 128.87, 128.05, 125.74, 123.55, 116.29, 111.73; GC-MS (EI, 70ev): m/z(%) = 228 (M+, 100), 229 (67), 230 (42), 231 (23), 205 (12), 203 (37), 193 (14); HRMS(ESI): calcd. for $[C_{12}H_8ClN_3 + H]^+$: 230.04795; found: 230.04827.

9-Bromo-6*H*-pyrido[1,2-*a*]quinazolin-6-imine

109 mg, 48 %, yellow solid, 167 ℃; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.85 (ddd, *J* = 7.4, 1.5, 0.9 Hz, 1 H), 8.27 (d, *J* = 8.7 Hz, 1 H), 7.95 (d, *J* = 1.8 Hz, 1 H), 7.56 (d, *J* = 1.8 Hz, 1 H), 7.53 (dd, *J* = 2.5, 1.7 Hz, 1 H), 7.49 (ddd, *J* = 9.2, 1.7, 0.9 Hz, 1 H), 6.90 (ddd, *J* = 7.6, 6.1, 1.6 Hz, 1 H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 158.57, 149.31, 148.47, 134.98, 130.14, 129.37, 128.75, 128.64, 126.81, 126.26, 114.89, 112.98; GC-MS (EI, 70ev): m/z(%) = 226 (M+, 100), 227 (15);

HRMS(ESI): calcd. for $[C_{12}H_8BrN_3 + H]^+$: 273.99744; found: 273.99793.

9-(Trifluoromethyl)-6*H*-pyrido[1,2-*a*]quinazolin-6-imine

160 mg, 61 %, yellow solid; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 9.10 (ddd, *J* = 7.5, 1.6, 0.8 Hz, 1H), 8.03 (d, *J* = 8.5 Hz, 1 H), 7.90 (dd, *J* = 1.8, 0.9 Hz, 1 H), 7.62 – 7.41 (m, 2 H), 7.32 (ddd, *J* = 9.2, 1.5, 0.8 Hz, 1 H), 6.78 (ddd, *J* = 7.7, 6.4, 1.5 Hz, 1 H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.04, 148.80, 145.03, 135.25, 135.20 – 134.07 (m, *J* = 33.19 Hz), 128.06, 125.79, 125.20, 124.81 (q, *J* = 4.2 Hz), 122.20, 120.20 (q, *J* = 3.4 Hz), 117.40, 111.96; GC-MS (EI, 70ev): m/z(%) = 262 (M+, 100), 263 (79), 242 (18), 237 (49), 67 (11); HRMS(ESI): calcd. for $[C_{13}H_8F_3N_3 + H]^+$: 264.07431; found: 264.07458.

4-Methyl-6*H*-pyrido[1,2-*a*]quinazolin-6-imine

146 mg, 70 %, yellow solid, 153 °C; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.97 (ddd, *J* = 7.6, 1.7, 0.9 Hz, 1 H), 8.01 – 7.83 (m, 1 H), 7.75 – 7.55 (m, 2 H), 7.33 (ddd, *J* = 8.2, 6.4, 1.9 Hz, 1 H), 7.28 – 7.17 (m, 1 H), 6.59 (t, *J* = 7.0 Hz, 1 H), 2.49 (t, *J* = 0.9 Hz, 3 H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 156.52, 147.74, 144.73, 133.68, 132.79, 132.28, 127.84, 126.10, 124.57, 123.90, 115.24, 110.70, 18.71; GC-MS (EI, 70ev): m/z(%) = 208 (M+, 100), 209 (65), 193 (10), 183 (36); HRMS(ESI): calcd. for $[C_{13}H_{11}N_3 + H]^+$: 210.10257; found: 210.10272.

3-Methyl-6*H*-pyrido[1,2-*a*]quinazolin-6-imine

146 mg, 70 %, yellow solid, 158 °C; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 9.17 (d, *J* = 7.6 Hz, 1 H), 8.08 (ddd, *J* = 8.1, 1.3, 0.6 Hz, 1 H), 7.91 – 7.65 (m, 2 H), 7.61 – 7.44 (m, 1 H), 7.31 – 7.16 (m, 1 H), 6.73 (dd, *J* = 7.6, 2.0 Hz, 1 H), 2.55 (d, *J* = 1.2 Hz, 3 H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 155.87, 148.02, 145.75, 145.23, 132.94, 127.17, 127.01, 124.12, 123.95, 123.18, 115.12, 114.12, 21.24; GC-MS (EI, 70ev): m/z(%) = 208 (M+, 100), 209 (58), 183 (38), 80(10); HRMS(ESI): calcd. for $[C_{13}H_{11}N_3 + H]^+$: 210.10257; found: 210.10272.

1-Methyl-6*H*-pyrido[1,2-*a*]quinazolin-6-imine

132 mg, 63 %, yellow solid, 114 °C; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.47 – 8.08 (m, 1 H), 7.65 – 7.37 (m, 3 H), 7.10 – 6.90 (m, 2 H), 6.74 (ddd, *J* = 15.0, 7.9, 0.9 Hz, 2 H), 2.49 (s, 3 H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 157.31, 153.28, 144.05, 138.33, 133.90, 132.78, 121.08, 118.19, 117.31, 116.44, 108.00, 100.55, 24.28; GC-MS (EI, 70ev): m/z(%) = 208 (M+, 100), 209 (48), 183 (13); HRMS(ESI): calcd. for $[C_{13}H_{11}N_3 + H]^+$: 210.10257; found: 210.10277.

2-Methyl-6*H*-pyrido[1,2-*a*]quinazolin-6-imine

96 mg, 46 %, yellow oil; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.91 – 8.84 (m, 1 H), 7.96 – 7.88 (m, 1 H), 7.68 – 7.61 (m, 2 H), 7.35 (ddd, *J* = 8.2, 6.0, 2.2 Hz, 1 H), 7.30 – 7.25 (m, 2 H), 2.30 (d, *J* = 1.3 Hz, 3 H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 155.94, 147.26, 144.95, 137.65, 132.94, 127.17, 125.33, 124.92, 124.51, 124.03, 121.01, 115.30, 18.18; GC-MS (EI, 70ev): m/z(%) = 208 (M+, 100), 209 (59), 183 (39); HRMS(ESI): calcd. for $[C_{13}H_{11}N_3 + H]^+$: 210.10257; found: 210.10290.

6*H*-Isoquinolino[2,1-*a*]quinazolin-6-imine

29 mg, 12 %, yellow solid, 167°C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.98 (ddt, *J* = 8.1, 1.4, 0.7 Hz, 1 H), 8.84 (d, *J* = 7.9 Hz, 1 H), 7.91 (dd, *J* = 8.1, 1.4 Hz, 1 H), 7.74 (dd, *J* = 8.2, 1.3 Hz, 1 H), 7.68 (ddt, *J* = 8.3, 7.0, 1.4 Hz, 2 H), 7.62 – 7.54 (m, 2 H), 7.39 (ddd, *J* = 8.2, 7.0, 1.3 Hz, 1 H), 6.89 (dd, *J* = 7.9, 0.7 Hz, 1H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.36, 146.32, 144.12, 133.31, 132.89, 131.92, 128.05 (d, *J* = 4.9 Hz), 127.81, 127.46, 127.24, 126.17, 125.34, 123.94, 123.39, 116.88, 111.55; GC-MS (EI, 70ev): m/z(%) = 244 (M+, 100), 246 (15), 245 (93), 219 (32); HRMS(ESI): calcd. for $[C_{16}H_{11}N_3 + H]^+$: 246.10257; found: 246.10285.

5*H*-Isoquinolino[2,3-*a*]quinazolin-5-imine

25 mg, 10 %, yellow solid; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.97 (t, *J* = 0.9 Hz, 1 H), 7.96 – 7.88 (m, 1 H), 7.83 (dq, *J* = 8.3, 1.0 Hz, 1 H), 7.65 – 7.58 (m, 1 H), 7.57 – 7.40 (m, 3 H), 7.35 (ddd, *J* = 8.1, 6.6, 1.4 Hz, 1 H), 7.22 – 7.16 (m, 1 H), 7.01 (s, 1 H), 6.93 (td, *J* = 7.6, 1.0 Hz, 1 H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 151.97, 149.43, 144.59, 138.16, 133.93, 133.08, 130.94, 127.80, 125.55, 125.06, 124.98, 121.03, 117.32, 117.29, 103.81, 100.72; GC-MS (EI, 70ev): m/z(%) = 245 (M+, 100), 246 (20), 244 (69), 205 (29), 219 (29), 213 (26), 117 (57); HRMS(ESI): calcd. for $[C_{16}H_{11}N_3 + H]^+$: 246.10257; found: 246.10278.

2-Phenylquinazolin-4-amine

155 mg, 70 %, white solid, 138 °C; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.55 – 8.39 (m, 2 H), 7.96 (ddd, *J* = 8.4, 1.2, 0.6 Hz, 1 H), 7.79 – 7.65 (m, 2 H), 7.54 – 7.43 (m, 3 H), 7.39 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1 H), 6.03 (s, 2 H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 161.67, 161.00, 150.93, 138.61, 133.33, 130.21, 128.56 – 128.21 (m), 128.69, 128.46, 128.43, 125.78, 121.73, 113.07; GC-MS (EI, 70ev): m/z(%) = 221 (M+, 100), 222 (17), 220 (16), 205 (29), 118 (21); HRMS(ESI): calcd. for $[C_{16}H_{11}N_3 + H]^+$: 222.10257; found: 222.1028.

2-(4-Chlorophenyl)quinazolin-4-amine

52 mg, 20 %, white solid, 149 °C; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.50 – 8.41 (m, 2 H), 7.94 (ddd, *J* = 8.5, 1.2, 0.6 Hz, 1 H), 7.83 – 7.69 (m, 2 H), 7.52 – 7.40 (m, 3 H), 5.71 (s, 2 H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 161.38, 159.76, 150.86, 136.92, 136.34, 133.41, 129.71, 128.80, 128.54, 125.97, 121.58, 112.99; GC-MS (EI, 70ev): m/z(%) = 255 (M+, 100), 257 (38), 256 (17), 239 (29), 207 (18), 118 (19), 103 (10); HRMS(ESI): calcd. for $[C_{14}H_{10}ClN_3 + H]^+$: 256.0636; found: 256.06383.

2-(3,5-Bis(trifluoromethyl)phenyl)quinazolin-4-amine

71 mg, 20 %, yellow solid, 197 °C; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 9.27 – 8.73 (m, 2 H), 8.11 – 7.90 (m, 2 H), 7.90 – 7.70 (m, 2 H), 7.54 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1 H), 5.75 (s, 2 H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 161.49, 157.60, 150.66, 140.50, 133.69, 131.58 (q, *J* = 33.4 Hz), 129.06, 128.97, 128.43 (d, *J* = 4.2 Hz), 126.67, 125.35, 123.84 – 123.17 (m), 121.74, 121.63, 118.13, 113.28; GC-MS (EI, 70ev): m/z(%) = 357 (M+, 100), 358 (12), 356 (18), 341 (22), 338 (14); HRMS(ESI): calcd. for $[C_{16}H_9F_6N_3 + H]^+$: 358.07734; found: 358.07789.

2-(6-(Trifluoromethyl)pyridin-3-yl)quinazolin-4-amine

148 mg, 51 %, white solid, 205 °C; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 9.85 – 9.74 (m, 1 H), 8.96 (ddd, *J* = 8.3, 1.9, 0.8 Hz, 1 H), 7.98 (dt, *J* = 8.4, 1.0 Hz, 1 H), 7.90 – 7.71 (m, 3 H), 7.54 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1 H), 5.81 (s, 2 H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 161.50, 157.50, 150.71, 150.29, 136.98, 136.62, 133.68, 132.86, 129.10, 126.75, 121.66, 119.99 (q, *J* = 2.6 Hz), 113.35; GC-MS (EI, 70ev): m/z(%) = 290 (M+, 100), 291(17), 221(32); HRMS(ESI): calcd. for $[C_{15}H_{10}F_3N_3 + H]^+$: 291.08521; found: 291.08566.

2-(4-(Trifluoromethyl)phenyl)quinazolin-4-amine

150 mg, 52 %, white solid, 170 °C; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.70 – 8.51 (m, 2 H), 8.02 – 7.91 (m, 1 H), 7.85 – 7.66 (m, 4 H), 7.49 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1 H), 5.86 (s, 2 H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 161.57, 159.42, 150.88, 141.84, 133.68, 132.11, 131.68, 129.10, 128.76, 126.50, 126.22, 125.40 (q, *J* = 3.8 Hz), 122.61, 121.77, 113.28; GC-MS (EI, 70ev): m/z(%) = 289 (M+, 100), 290(18), 288 (18), 273 (26), 118 (10); HRMS(ESI): calcd. for $[C_{15}H_{10}F_3N_3 + H]^+$: 290.08996; found: 290.09042.

2-(*o*-Tolyl)quinazolin-4-amine

129 mg, 55 %, white solid, 134 °C; ^{1}H NMR (300 MHz, Chloroform-d) δ 8.39 – 8.22 (m, 2 H), 7.96 (ddd, *J* = 8.5, 1.2, 0.6 Hz, 1 H), 7.80 – 7.61 (m, 2 H), 7.38 (ddd, *J* = 8.3, 7.1, 1.4 Hz, 2 H), 7.27 (ddt, *J* = 7.6, 1.6, 0.9 Hz, 1H), 6.01 (s, 2 H), 2.44 (d, *J* = 0.9 Hz, 3 H); ^{13}C NMR (75 MHz, Chloroform-d) δ 161.61, 161.13, 150.94, 138.55, 138.00,

133.23, 130.97, 128.96, 128.66, 128.35, 125.6, 125.58, 121.71, 113.05, 21.55; GC-MS (EI, 70ev): m/z(%) = 235 (M+, 100), 236 (17), 234 (19), 219 (20), 207(10), 118 (17); HRMS(ESI): calcd. for $[C_{15}H_{13}N_3 + H]^+$: 236.11822; found: 236.11853.

2-(1*H*-Pyrazol-1-yl)benzonitrile

145 mg, 86 %, yellow oil; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.09 (t, *J* = 2.3 Hz, 1 H), 7.81 – 7.69 (m, 3 H), 7.69 – 7.59 (m, 1 H), 7.38 (ddt, *J* = 9.2, 7.2, 1.7 Hz, 1 H), 6.50 (q, *J* = 2.2 Hz, 1 H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 142.19, 141.92, 134.46, 134.02, 129.53, 127.28, 124.19, 117.02, 108.47, 105.32; GC-MS (EI, 70ev): m/z(%) = 169 (M+, 100), 170 (12), 168 (10), 142 (47), 129(15), 115 (23), 102(27), 75 (14); HRMS(ESI): calcd. for $[C_{10}H_7N_3 + H]^+$: 170.07127; found: 170.07124.

2-((2-Aminophenyl)amino)benzonitrile

65 mg, 31 %, yellow oil; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.47 (ddd, *J* = 7.8, 1.6, 0.5 Hz, 1H), 7.36 – 7.27 (m, 1H), 7.21 – 7.05 (m, 2H), 6.96 – 6.64 (m, 3H), 6.57 (dt, *J* = 8.5, 0.7 Hz, 1H), 6.19 – 5.68 (m, 1H), 3.41 (s, 2H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 148.77, 143.15, 134.14, 132.64, 128.02, 127.64, 124.81, 119.21, 118.32, 117.70, 116.34, 113.40, 96.80; GC-MS (EI, 70ev): m/z(%) = 209 (M+, 100), 210 (15), 208 (17), 182 (15), 181(13).

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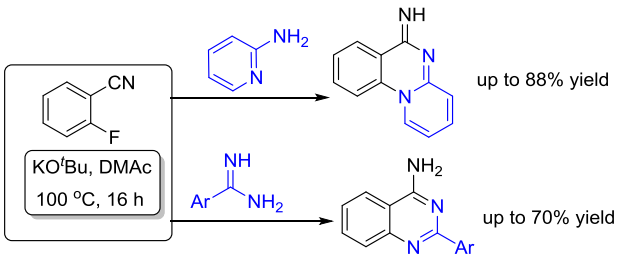

A convenient procedure for the synthesis of quinazolinimines and quinazolinamines from 2-fluorobenzontriles and 2-aminopyridines or amidines with KO^{t}Bu as the promotor has been developed.