Microwave-Assisted Three-Component Reaction for the Synthesis of Pyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-ones

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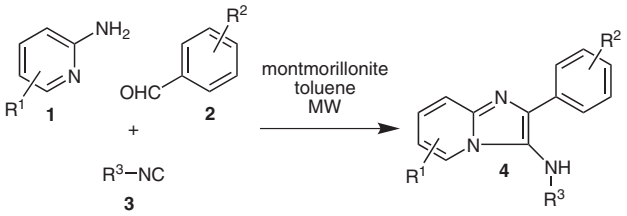
Abstract: Pyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-ones can be obtained by a microwave-assisted three-component reaction between 2-aminopyridines, isocyanides, and 2-carboxybenzaldehydes under acidic conditions.

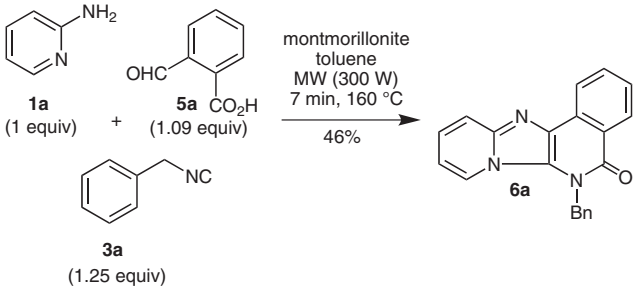
Key words: heterocycles, lactams, multicomponent reaction, Ugi reaction, isocyanides

There is no doubt that multicomponent reactions (MCRs) are of central importance to the rapid assembly of large arrays of compounds with diverse substitution patterns.[1] A particularly efficient variant of the Ugi reaction,[2] the so-called Groebke reaction, makes use of the conversion of 2-aminoazines, aldehydes, and isocyanides in the presence of a Brønsted acid for the synthesis of fused 3-aminoimidazoles, such as imidazo[1,2-*a*]pyridines, imidazo[1,2-*a*]pyrimidines, and imidazo[1,2-*a*]pyrazines.[3] As these types of heterocycles have proven to be successful in the field of medicinal chemistry,[4] different reaction conditions have been developed that allow this three-component reaction (3CR) to be carried out efficiently.[3,5]



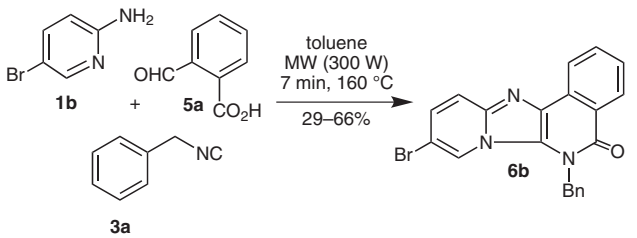
Scheme 1 Microwave-assisted synthesis of imidazo[1,2-*a*]pyridines **4**

When we performed experiments towards the microwave-assisted synthesis of imidazo[1,2-*a*]pyridines **4** by reaction of different substituted 2-aminopyridines **1**, benzaldehydes **2**, and isocyanides **3**, it was found that these transformations can be effectively conducted with montmorillonite as the reagent and toluene as the solvent. Under these conditions the corresponding imidazo[1,2-*a*]pyridines **4** could be synthesized successfully (Scheme 1).[6] Analysis of the studies published so far revealed that the scope of this reaction can be expanded considerably when the nucleophilicity of the amino group in the 3-position of the imidazole moiety is employed for further transformations. Here we report on experiments to try out this approach. The reaction between 2-carboxy-substituted benzaldehydes, 2-aminopyridines, and isocyanides was chosen as an example. The spatial proximity of the amino nitrogen of the imidazole moiety and the carboxy group of the aryl moiety should allow the formation of a lactam and, hence, provide a new access to pyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-ones in a single synthetic operation.[7]



Scheme 2 Microwave-assisted synthesis of pyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one **6a**

The model reaction between 2-aminopyridine (**1a**), benzyl isocyanide (**3a**), and 2-carboxybenzaldehyde (**5a**) was performed under the conditions that had proven successful for the synthesis of **4**; compound **6a**, with a pyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one skeleton, was isolated in 46% yield (Scheme 2). Obviously, this three-component reaction allows the formation of two heterocyclic rings and four new bonds in a single operation. The positive outcome of the model reaction prompted detailed studies on the scope of the new reaction.



Scheme 3 Optimization of the reaction conditions using the synthesis of **6b** as an example

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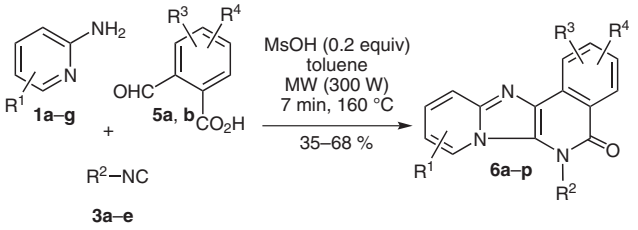
To start with, the reaction conditions were optimized using the example of the transformation of the aminopyridine **1b** with **3a** and **5a**. It was found that not only montmorillonite, but also several Brønsted acids, like 4-toluenesulfonic acid, methanesulfonic acid, and trifluoromethanesulfonic acid (Scheme 3, Table 1), can be used as a reagent. By varying the amount of methanesulfonic acid, it could be established that the highest yield of **6b** was obtained with 0.2 equivalents of this acid (Table 1, entry 5). A further increase in the yield of **6b** from 54% to 66% was achieved by using the isocyanide **3a** in excess (2.25 equiv) (Table 1, entry 7). It was also possible to run the reaction of **1b**, **3a**, and **5a** in different imidazolium and guanidinium salts as ionic liquids in the presence or in the absence of montmorillonite and methanesulfonic acid, respectively. It should be noted that the synthesis of **6b** from **1b**, **3a** and **5a** can also be achieved in the absence of any reagent and solvent. However, in no case did the yield of **6b** exceed that obtained under the conditions given in Table 1, entry 7.

Table 1 Optimizing the Reaction Conditions for the Reaction of **1b** with **3a** and **5a**

Entry	Equiv of **1b**	Equiv of **3a**	Equiv of **5a**	Reagent	Equiv	Yield[a] (%) of **6b**
1	1	1.25	1.09	clay[b]	76 mg	29
2	1	1.25	1.09	TsOH	0.1	46
3	1	1.25	1.09	TfOH	0.1	42
4	1	1.25	1.09	$MeSO_3H$	0.1	52
5	1	1.25	1.09	$MeSO_3H$	0.2	54
6	1	1.25	1.09	$MeSO_3H$	0.7	52
7	1	2.25	1.09	$MeSO_3H$	0.2	66

[a] Isolated yield of product.
[b] Montmorillonite was used as clay.

After optimizing the reaction conditions we focused on the question of whether this domino process could be used for the generation of libraries of pyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-ones. For this purpose reactions with different substituted 2-aminopyridines **1**, isocyanides **3**, and 2-carboxybenzaldehydes **5** were performed under our optimized reaction conditions (Scheme 4).



Scheme 4 Microwave-assisted synthesis of pyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-ones **6** under optimized reaction conditions

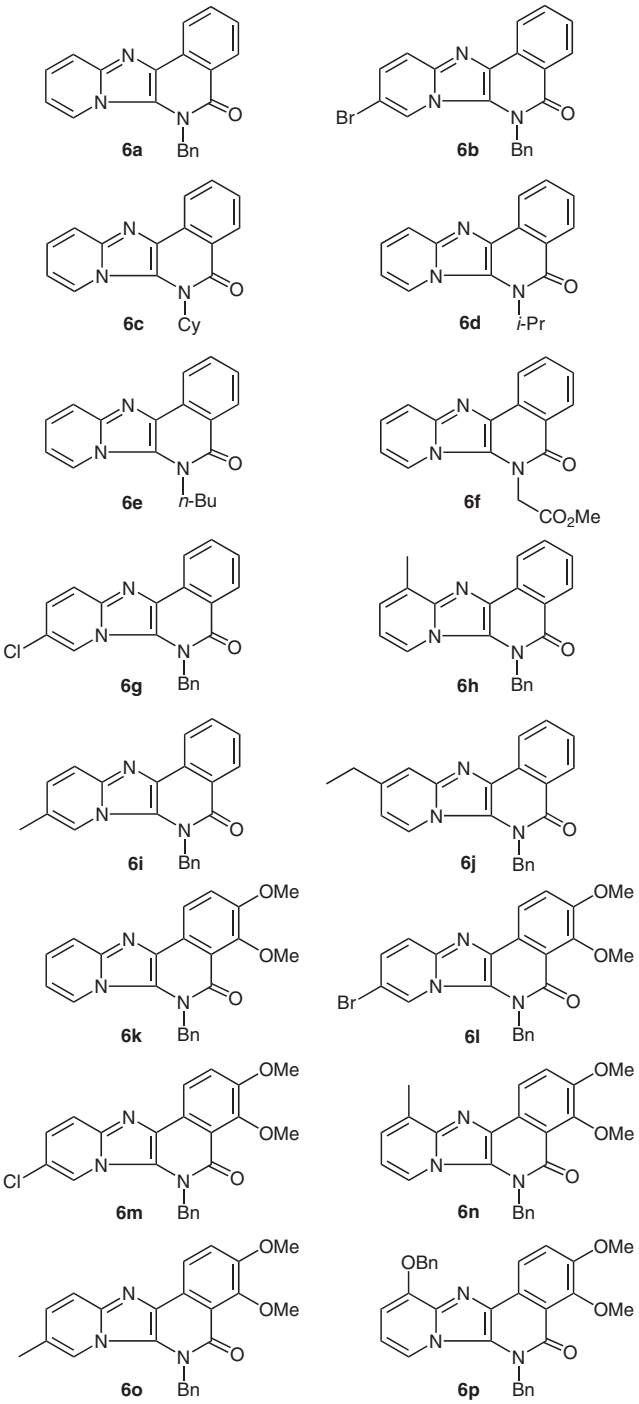
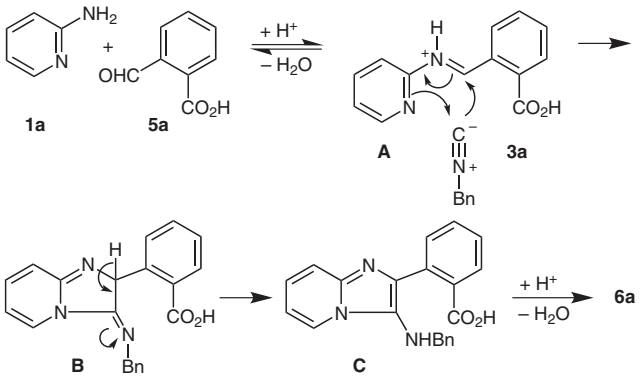


Figure 1 Structures of pyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-ones **6a–p**

To start with, reactions of **1a** and **5a** with different isocyanides **3a–e** were conducted. We found that apart from benzyl isocyanide (**3a**), cyclohexyl isocyanide (**3b**), isopropyl isocyanide (**3c**), butyl isocyanide (**3d**), and methyl isocyanoacetate (**3e**) could be successfully employed. The yields of the tetracycles **6a**,**c–f** isolated ranged between 46% and 56% (Figure 1, Table 2, entries 1, 3–6). The variation of the aminopyridines also met with success. In the reactions of **3a** and **5a** with the differently substituted aminopyridines **1b–f**, the heterocycles **6b**,**g–j** were isolat-

ed as single products in analytically pure form with yields ranging from 50% to 66% (Figure 1, Table 2, entries 2, 7–10). In addition to the parent 2-aminopyridine (**1a**) the halogen-substituted compounds **1b**,**c**, the alkyl-substituted derivatives **1d–f**, and the benzyl ether **1g** could also be reacted. Finally, the reactions of differently substituted aminopyridines **1** with benzyl isocyanide (**3a**), and 2-carboxy-3,4-dimethoxybenzaldehyde (**5b**) were performed. Here, the products **6k–p** were obtained in analytically pure form as single products in 35–68% yields (Figure 1, Table 2, entries 11–16).

It is assumed that the reaction proceeds according to the mechanism depicted in Scheme 5. The key step of the sequence is the nonconcerted [4+1] cycloaddition between the protonated Schiff base **A** and the isocyanide **3a** with formation of **B**, which then undergoes a proton shift to yield **C**; after elimination of water, the lactam **6a** is formed.



Scheme 5 Proposed mechanism for the formation of pyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-ones **6a**

The structures of all the pyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-ones **6** described here have been elucidated by MS, ^{1}H, ^{13}C, COSY, HSQC, HMBC, and INADEQUATE spectroscopic methods. The complete ^{1}H, ^{13}C NMR spectral assignment, especially of quaternary carbons C11a, C11b, and C6a of compound **6n**, is shown in Figure 2. In the HMBC spectra long-range correlations between the protons H1 ($^{3}J_{CH}$), H2 ($^{4}J_{CH}$), H9 ($^{5}J_{CH}$) and the carbon signal at δ = 123.66 along with correlations between H7 ($^{3}J_{CH}$), H8 ($^{4}J_{CH}$), H2 ($^{5}J_{CH}$) and the carbon at δ = 123.62 unambiguously established the C11a and C6a positions, respectively. Furthermore, the signal at δ = 126.39 was definitely assigned to the carbon C11b because of its HMBC correlation to H2 and its ^{13}C connectivity to C1 in the INADEQUATE spectrum. Unfortunately, strong signal overlap between the aromatic protons H2′, H4′, and H6′ prevents the ^{13}C assignment by HMBC methods. Nevertheless, it was possible to deduce the missing assignment by evaluating the ^{13}C-^{13}C INADEQUATE (Figure 2).

The structural assignments based on NMR spectroscopic methods were unambiguously confirmed by the results of the X-ray crystal structure analysis of **6n** (Figure 3).[8–13]

Table 2 Synthesis of Pyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-ones **6** from Different 2-Aminopyridines **1**, Isocyanides **3**, and 2-Carboxybenzaldehydes **5**

Entry	Pyridine	R^1	Isocyanide	R^2	Benzaldehyde	R^3	R^4	Product	Yield (%)
1	**1a**	H	**3a**	Bn	**5a**	H	H	**6a**	56
2	**1b**	5-Br	**3a**	Bn	**5a**	H	H	**6b**	66
3	**1a**	H	**3b**	Cy	**5a**	H	H	**6c**	46
4	**1a**	H	**3c**	*i*-Pr	**5a**	H	H	**6d**	48
5	**1a**	H	**3d**	Bu	**5a**	H	H	**6e**	51
6	**1a**	H	**3e**	CH_2CO_2Me	**5a**	H	H	**6f**	46
7	**1c**	5-Cl	**3a**	Bn	**5a**	H	H	**6g**	64
8	**1d**	3-Me	**3a**	Bn	**5a**	H	H	**6h**	53
9	**1e**	5-Me	**3a**	Bn	**5a**	H	H	**6i**	60
10	**1f**	4-Et	**3a**	Bn	**5a**	H	H	**6j**	50
11	**1a**	H	**3a**	Bn	**5b**	3-OMe	4-OMe	**6k**	35
12	**1b**	5-Br	**3a**	Bn	**5b**	3-OMe	4-OMe	**6l**	43
13	**1c**	5-Cl	**3a**	Bn	**5b**	3-OMe	4-OMe	**6m**	42
14	**1d**	3-Me	**3a**	Bn	**5b**	3-OMe	4-OMe	**6n**	68
15	**1e**	5-Me	**3a**	Bn	**5b**	3-OMe	4-OMe	**6o**	38
16	**1g**	3-OBn	**3a**	Bn	**5b**	3-OMe	4-OMe	**6p**	50

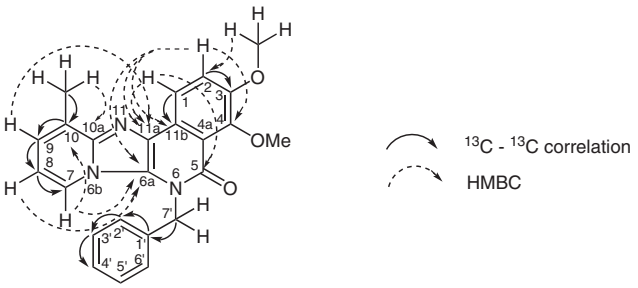


Figure 2 Important ^{3}J, ^{4}J, and ^{5}J ^{1}H-^{13}C HMBC and ^{13}C-^{13}C correlations in compound **6n**

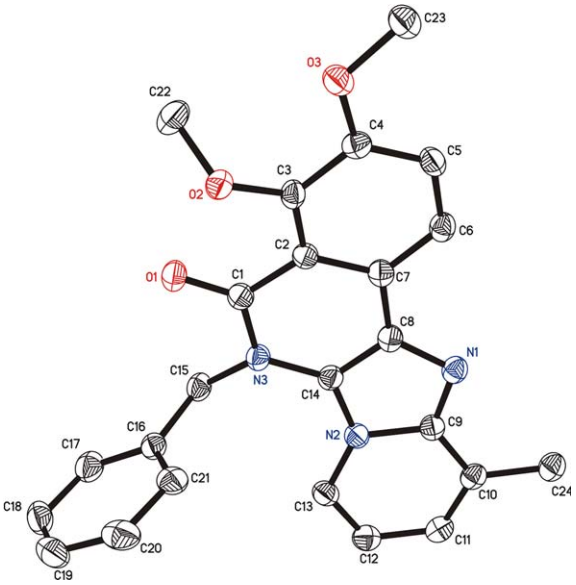


Figure 3 Solid state structure of compound **6n**; anisotropic displacement parameters are depicted at the 50% probability level; the second molecule of the asymmetric unit and H atoms are omitted for reasons of clarity.

To summarize, pyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-ones can be obtained in a few minutes with yields ranging from 35% to 68% by means of a microwave-assisted three-component reaction between 2-aminopyridines, isocyanides, and 2-carboxybenzaldehydes. The transformation is easy to perform, robust, and highly efficient, as this process allows the formation of two heterocyclic rings and four new bonds in a single synthetic operation.

Starting materials were purchased from chemical companies and used without purification. Reactions were performed using a Discover Explorer microwave synthesizer (CEM Corp.), producing continuous irradiation at 2450 MHz. All experiments were conducted under argon. Anhyd toluene was distilled from Na. TLC was performed on TLC aluminum roll silica gel 60 F_{254} (MERCK). Compounds were visualized with UV light (λ = 254 nm) and/or immersion in $KMnO_4$ soln followed by heating. NMR spectra were recorded in $CDCl_3$ on 300 MHz and 500 MHz spectrometers. The ^{1}H and ^{13}C chemical shifts were referenced to residual solvent signals at δ_H = 7.26 and δ_C = 77 relative to TMS. ^{1}H, ^{13}C{^{1}H}, gDQFCOSY, gHSQC, INADEQUATE (300 MHz, 90 mg of **6n**, 5 mm Shigemi tube) spectra were measured with standard Varian pulse sequences. Adiabatic broadband and band selective gHMBC spectra were recorded using CHEMPACK 4.0 pulse sequences. Melting points were determined on a Kofler melting point apparatus (Reichert, Austria) and are uncorrected. Mass spectra were recorded on a MAT95 with 70 eV ionization energy. IR spectra were taken on a Spectrum One FT-IR spectrophotometer. UV spectra were measured using a CARY 4E UV-Visible spectrophotometer. Elemental analyses were carried out by F. Hambloch, Institute of Organic and Biomolecular Chemistry, University of Göttingen.

Microwave-Assisted 3CR of 2-Aminopyridines 1, Isocyanides 3, and Carboxybenzaldehydes 5; General Procedure

Compounds **1** (1 mmol), **3** (2.25 mmol), and **5** (1.09 mmol) were suspended in toluene (2 mL) and placed in a 10-mL reaction vial that had been heated and cooled under argon. After the addition of $MeSO_3H$ (0.2 mmol), the vial was sealed with a septum and irradiated with microwaves (Discover by CEM; 2450 MHz; 300 W) at 160 °C for 7 min. The mixture was allowed to cool to r.t., diluted with CH_2Cl_2 (100 mL), and then washed with $NaHCO_3$ soln (2 × 100 mL). The residue obtained after drying the organic phase ($MgSO_4$) and concentration in vacuo was purified by column chromatography (silica gel, EtOAc or EtOAc–CH_2Cl_2) to yield **6**.

6-Benzylpyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one (6a)

Pale brown solid; yield: 56%; mp 234–236 °C (Lit.[7d] mp 228–229 °C).

IR (ATR): 1642, 1618, 1559, 1495, 1425, 1385, 1300, 1258, 1153, 1128, 979, 772, 730, 710, 702, 681 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.91 (s, 2 H, 7′-CH_2), 6.57 (ddd, *J* = 1.3 Hz, *J* = 6.7 Hz, *J* = 7.2 Hz, 1 H, H8), 7.05 (ddd, *J* = 1.1 Hz, *J* = 6.8 Hz, *J* = 9.4 Hz, 1 H, H9), 7.20–7.27 (m, 2 H, H2′, H6′), 7.27–7.31 (m, 1 H, H4′), 7.31–7.39 (m, 2 H, H3′, H5′), 7.62 (ddd, *J* = 1.4 Hz, *J* = 7.3 Hz, *J* = 8.1 Hz, 1 H, H3), 7.67 (dt, *J* = 1.3 Hz, *J* = 9.3 Hz, 1 H, H10), 7.84 (ddd, *J* = 1.3 Hz, *J* = 7.2 Hz, *J* = 8.1 Hz, 1 H, H2), 8.13 (dt, *J* = 1.1 Hz, *J* = 7.3 Hz 1 H, H7), 8.44 (ddd, *J* = 0.7 Hz, *J* = 1.3 Hz, *J* = 8.0 Hz, 1 H, H1), 8.55 (ddd, *J* = 0.6 Hz, *J* = 1.3 Hz, *J* = 8.1 Hz, 1 H, H4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 46.8 (C7′), 112.5 (C8), 118.7 (C10), 121.9 (C1), 123.1 (C7), 123.7 (C9), 123.9 (C4a), 124.7 (C11a), 125.1 (C6a), 125.4 (C2′, C6′), 127.2 (C3), 127.8 (C4′), 129.4 (C3′, C5′), 129.5 (C4), 131.9 (C11b), 133.3 (C2), 135.9 (C1′), 143.0 (C10a), 161.7 (C5).

MS (EI, 70 eV): *m*/*z* (%) = 325 (37) [M^{+}], 234 (100), 130 (15), 78 (12), 51 (2).

UV/Vis (MeCN): λ_{max} (log ε) = 377 (4.15), 309 (3.61), 259 (4.57), 240 (4.47), 227 nm (4.58).

6-Benzyl-8-bromopyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one (6b)

Yellow solid; yield: 66%; mp 270–272 °C.

IR (ATR): 3055, 1640, 1618, 1524, 1405, 1340, 1316, 1303, 1267, 933, 796, 765, 732, 713, 698, 660 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.88 (s, 2 H, 7′-CH_2), 7.08 (dd, *J* = 1.3 Hz, *J* = 9.6 Hz, 1 H, H9), 7.22–7.29 (m, 2 H, H2′, H6′), 7.29–7.34 (m, 1 H, H4′), 7.34–7.42 (m, 2 H, H3′, H5′), 7.48 (dd, *J* = 0.9 Hz, *J* = 9.7 Hz, 1 H, H10), 7.60 (ddd, *J* = 1.2 Hz, *J* = 7.3 Hz, *J* = 8.1 Hz, 1 H, H3), 7.84 (ddd, *J* = 1.3 Hz, *J* = 7.2 Hz, *J* = 8.5 Hz, 1 H, H2), 8.32 (dd, *J* = 0.9 Hz, *J* = 1.7 Hz, 1 H, H7), 8.40 (ddd, *J* = 0.6 Hz, *J* = 1.2 Hz, *J* = 8.0 Hz, 1 H, H1), 8.55 (ddd, *J* = 0.6 Hz, *J* = 1.3 Hz, *J* = 8.1 Hz, 1 H, H4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 46.7 (C7′), 107.2 (C8), 119.0 (C10), 121.9 (C1), 123.2 (C7), 124.1 (C4a), 124.7 (C11a), 125.5 (C2′, C6′), 125.8 (C6a), 126.9 (C9), 127.6 (C3), 128.1 (C4′), 129.5

(C3′, C5′), 129.7 (C4), 131.6 (C11b), 133.4 (C2), 135.7 (C1′), 141.2 (C10a), 161.7 (C5).

MS (EI, 70 eV): *m*/*z* (%) = 403 (55) [M$^+$], 312 (100), 233 (5), 204 (3), 156 (13), 130 (47), 91 (16), 76 (6), 65 (3).

UV/Vis (MeCN): λ_{max} (log ε) = 403 (4.02), 383 (4.17), 318 (3.70), 266 (4.52), 245 (4.50), 231 (4.60), 208 nm (4.56).

Anal. Calcd for $C_{21}H_{14}BrN_3O$: C, 62.39; H, 3.49; N, 10.39. Found: C, 62.65; H, 3.70; N, 10.16.

6-Cyclohexylpyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one (6c)

Yellow solid; yield: 46%; mp 224–226 °C.

IR (ATR): 2935, 2850, 1645, 1617, 1298, 1268, 1131, 772, 746, 724, 704, 689 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27–2.14 (m, 8 H, H2′$_b$, 2 H3′, 2 H4′, 2 H5′, H6′$_b$), 2.81–3.09 (m, 2 H, H2′$_a$, H6′$_a$), 4.43 (tt, *J* = 3.6 Hz, *J* = 11.9 Hz, 1 H, H1′), 6.87 (dt, *J* = 1.2 Hz, *J* = 7.1 Hz, 1 H, H8), 7.17 (ddd, *J* = 1.2 Hz, *J* = 6.7 Hz, *J* = 9.2 Hz, 1 H, H9), 7.53 (ddd, *J* = 1.3 Hz, *J* = 7.3 Hz, *J* = 8.1 Hz, 1 H, H3), 7.71 (dt, *J* = 1.2 Hz, *J* = 9.2 Hz, 1 H, H10), 7.78 (ddd, *J* = 1.3 Hz, *J* = 7.2 Hz, *J* = 8.1 Hz, 1 H, H2), 8.14 (br d, *J* = 7.4 Hz, 1 H, H7), 8.36 (ddd, *J* = 0.6 Hz, *J* = 1.2 Hz, *J* = 7.8 Hz, 1 H, H1), 8.43 (ddd, *J* = 0.6 Hz, *J* = 1.3 Hz, *J* = 8.1 Hz, 1 H, H4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.0 (C4′), 26.4 (C3′, C5′), 29.8 (C2′, C6′), 60.3 (C1′), 112.8 (C8), 119.1 (C10), 121.8 (C1), 123.3 (C7), 123.4 (C9), 125.3 (C6a), 125.7 (C11a), 125.9 (C4a), 127.1 (C3), 128.8 (C4), 131.6 (C11b), 132.8 (C2), 142.8 (C10a), 162.8 (C5).

MS (EI, 70 eV): *m*/*z* (%) = 317 (22) [M$^+$], 235 (100), 206 (7), 130 (2), 78 (6).

UV/Vis (MeCN): λ_{max} (log ε) = 381 (4.06), 309 (3.52), 261 (4.52), 229 (4.49), 207 nm (4.46).

Anal. Calcd for $C_{20}H_{19}N_3O$: C, 75.69; H, 6.03; N, 13.24. Found: C, 75.43; H, 5.85; N, 13.01.

6-Isopropylpyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one (6d)

Pale green solid; yield: 48%; mp 180–182 °C.

IR (ATR): 1628, 1617, 1574, 1556, 1403, 1302, 1272, 1096, 763, 731, 711, 698, 683 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.86 [d, *J* = 6.8 Hz, 6 H, 1′-$(CH_3)_2$], 5.01 (hept, *J* = 6.8 Hz, 1 H, H1′), 6.85 (dt, *J* = 1.3 Hz, *J* = 6.9 Hz, 1 H, H8), 7.17 (ddd, *J* = 1.2 Hz, *J* = 6.6 Hz, *J* = 9.2 Hz, 1 H, H9), 7.53 (ddd, *J* = 1.2 Hz, *J* = 7.1 Hz, *J* = 8.2 Hz, 1 H, H3), 7.71 (dt, *J* = 1.2 Hz, *J* = 9.2 Hz, 1 H, H10), 7.77 (ddd, *J* = 1.3 Hz, *J* = 7.2 Hz, *J* = 8.2 Hz, 1 H, H2), 8.26 (br d, *J* = 7.3 Hz, 1 H, H7), 8.37 (ddd, *J* = 0.6 Hz, *J* = 1.0 Hz, *J* = 7.9 Hz, 1 H, H1), 8.43 (dd, *J* = 1.7 Hz, *J* = 8.1 Hz, 1 H, H4).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.7 (1′-CH_3), 51.3 (C1′), 112.8 (C8), 119.0 (C10), 121.9 (C1), 123.5 (C7), 123.6 (C9), 125.2 (C6a), 125.6 (C11a), 125.8 (C4a), 127.2 (C3), 128.8 (C4), 131.6 (C11b), 132.9 (C2), 142.8 (C10a), 162.7 (C5).

MS (El, 70 eV): *m*/*z* (%) = 277 (34) [M$^+$], 235 (100), 206 (14), 130 (10), 78 (13), 51 (3).

UV/Vis (MeCN): λ_{max} (log ε) = 380 (4.05), 309 (3.51), 260 (4.50), 228 (4.48), 205 nm (4.44).

Anal. Calcd for $C_{17}H_{15}N_3O$: C, 73.63; H, 5.45; N, 15.15. Found: C, 73.65; H, 5.16; N, 15.03.

6-Butylpyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one (6e)

Yellow solid; yield: 51%; mp 134–135 °C.

IR (ATR): 2950, 2868, 1639, 1617, 1574, 1558, 1498, 1387, 1303, 1262, 773, 734, 703, 682 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.02 (t, *J* = 7.4 Hz, 3 H, 4′-CH_3), 1.49–1.64 (m, 2 H, 3′-CH_2), 1.80–1.96 (m, 2 H, 2′-CH_2), 4.56–4.68 (m, 2 H, 1′-CH_2), 6.84 (ddd, *J* = 1.3 Hz, *J* = 6.7 Hz, *J* = 7.3 Hz, 1 H, H8), 7.15 (ddd, *J* = 1.1 Hz, *J* = 6.6 Hz, *J* = 9.2 Hz, 1 H, H9), 7.53 (ddd, *J* = 1.3 Hz, *J* = 7.2 Hz, *J* = 8.1 Hz, 1 H, H3), 7.68 (dt, *J* = 1.2 Hz, *J* = 9.2 Hz, 1 H, H10), 7.77 (ddd, *J* = 1.3 Hz, *J* = 7.2 Hz, *J* = 8.1 Hz, 1 H, H2), 8.31 (dt, *J* = 1.1 Hz, *J* = 7.3 Hz, 1 H, H7), 8.38 (ddd, *J* = 0.7 Hz, *J* = 1.3 Hz, *J* = 8.1 Hz, 1 H, H1), 8.46 (ddd, *J* = 0.7 Hz, *J* = 1.3 Hz, *J* = 8.1 Hz, 1 H, H4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8 (C4′), 19.9 (C3′), 32.1 (C2′), 42.7 (C1′), 112.9 (C8), 118.9 (C10), 121.9 (C1), 122.8 (C7), 123.6 (C9), 124.0 (C4a), 124.5 (C6a), 124.8 (C11a), 127.1 (C3), 129.2 (C4), 131.3 (C11b), 132.9 (C2), 142.8 (C10a), 161.2 (C5).

MS (EI, 70 eV): *m*/*z* (%) = 291 (95) [M$^+$], 235 (100), 206 (15), 130 (23), 78 (27), 51 (6).

UV/Vis (MeCN): λ_{max} (log ε) = 379 (4.12), 309 (3.54), 260 (4.53), 241 (4.40), 227 (4.50), 205 nm (4.46).

Anal. Calcd for $C_{18}H_{17}N_3O$: C, 74.20; H, 5.88; N, 14.42. Found: C, 76.16; H, 5.76; N, 13.89.

6-[(Methoxycarbonyl)methyl]pyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one (6f)

Yellow solid; yield: 46%; mp 221–223 °C.

IR (ATR): 1748, 1736, 1644, 1619, 1558, 1388, 1365, 1318, 1227, 1145, 967, 770, 739, 728, 702 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.81 (s, 3 H, OCH_3), 5.46 (s, 2 H, 2′-CH_2), 6.78 (ddd, *J* = 1.3 Hz, *J* = 6.7 Hz, *J* = 7.2 Hz, 1 H, H8), 7.13 (ddd, *J* = 1.2 Hz, *J* = 6.7 Hz, *J* = 9.2 Hz, 1 H, H9), 7.55 (ddd, *J* = 1.3 Hz, *J* = 7.3 Hz, *J* = 8.1 Hz, 1 H, H3), 7.67 (dt, *J* = 1.2 Hz, *J* = 9.2 Hz, 1 H, H10), 7.81 (ddd, *J* = 1.3 Hz, *J* = 7.2 Hz, *J* = 8.0 Hz, 1 H, H2), 8.13 (dt, *J* = 1.0 Hz, *J* = 7.3 Hz, 1 H, H7), 8.39 (ddd, *J* = 0.6 Hz, *J* = 1.2 Hz, *J* = 8.0 Hz, 1 H, H1), 8.46 (ddd, *J* = 0.7 Hz, *J* = 1.3 Hz, *J* = 8.1 Hz, 1 H, H4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 44.7 (C2′), 53.2 (OCH_3), 113.0 (C8), 119.0 (C10), 121.9 (C1), 121.9 (C7), 123.5 (C4a), 123.7 (C9), 123.9 (C6a), 125.0 (C11a), 127.3 (C3), 129.4 (C4), 131.9 (C11b), 133.5 (C2), 142.9 (C10a), 161.3 (C5), 168.7 (C1′).

MS (EI, 70 eV): *m*/*z* (%) = 307 (100) [M$^+$], 275 (4), 248 (61), 234 (72), 220 (16), 130 (17), 78 (21), 51 (4).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{13}N_3O_3$: 308.1035; found: 308.1030.

UV/Vis (MeCN): λ_{max} (log ε) = 376 (4.09), 309 (3.57), 258 (4.52), 240 (4.41), 228 nm (4.51).

6-Benzyl-8-chloropyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one (6g)

Yellow solid; yield: 64%; mp 273–274 °C.

IR (ATR): 3057, 1642, 1618, 1515, 1493, 1302, 1266, 1066, 941, 811, 765, 732, 724, 696, 681 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.89 (s, 2 H, 7′-CH_2), 7.00 (dd, *J* = 1.7 Hz, *J* = 9.6 Hz, 1 H, H9), 7.22–7.29 (m, 2 H, H2′, H6′), 7.29–7.34 (m, 1 H, H4′), 7.34–7.42 (m, 2 H, H3′, H5′), 7.55 (dd, *J* = 1.0 Hz, *J* = 9.7 Hz, 1 H, H10), 7.62 (ddd, *J* = 1.3 Hz, *J* = 7.2 Hz, *J* = 8.2 Hz, 1 H, H3), 7.84 (ddd, *J* = 1.3 Hz, *J* = 7.2 Hz, *J* = 8.1 Hz, 1 H, H2), 8.21 (br dd, *J* = 0.8 Hz, *J* = 2.0 Hz, 1 H, H7), 8.41 (ddd, *J* = 0.7 Hz, *J* = 1.3 Hz, *J* = 8.0 Hz, 1 H, H1), 8.55 (ddd, *J* = 0.6 Hz, *J* = 1.3 Hz, *J* = 8.1 Hz, 1 H, H4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 46.7 (C7′), 118.8 (C10), 120.7 (C8), 121.0 (C7), 121.9 (C1), 124.0 (C4a), 124.9 (C6a), 124.9 (C9), 125.5 (C2′, C6′), 126.0 (C11a), 127.6 (C3), 128.1 (C4′), 129.5 (C3′,

C5′), 129.7 (C4), 131.6 (C11b), 133.4 (C2), 135.7 (C1′), 141.2 (C10a), 161.7 (C5).

MS (EI, 70 eV): *m*/*z* (%) = 359 (31) [M$^+$], 268 (100), 130 (21), 112 (9), 91 (9), 76 (4), 65 (2).

UV/Vis (MeCN): λ_{max} (log ε) = 403 (3.98), 383 (4.13), 317 (3.67), 265 (4.51), 244 (4.45), 230 (4.57), 206 nm (4.55).

Anal. Calcd for $C_{21}H_{14}ClN_3O$: C, 70.10; H, 3.92; N, 11.68. Found: C, 69.85; H, 3.79; N, 11.50.

6-Benzyl-10-methylpyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one (6h)

Yellow solid; yield: 53%; mp 242–244 °C.

IR (ATR): 1647, 1621, 1557, 1387, 1306, 1269, 1157, 1132, 983, 772, 732, 707, 700, 682 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.68 (s, 3 H, 10-CH_3), 5.92 (s, 2 H, 7′-CH_2), 6.53 (t, *J* = 7.0 Hz, 1 H, H8), 6.91 (d, *J* = 6.7 Hz, 1 H, H9), 7.22–7.27 (m, 2 H, H2′, H6′), 7.27–7.31 (m, 1 H, H4′), 7.31–7.39 (m, 2 H, H3′, H5′), 7.59 (ddd, *J* = 1.2 Hz, *J* = 7.2 Hz, *J* = 8.1 Hz, 1 H, H3), 7.85 (ddd, *J* = 1.4 Hz, *J* = 7.2 Hz, *J* = 7.9 Hz, 1 H, H2), 8.06 (br d, *J* = 7.1 Hz, 1 H, H7), 8.56 (dd, *J* = 1.5 Hz, *J* = 8.2 Hz, 1 H, H4), 8.59 (dd, *J* = 1.1 Hz, *J* = 8.1 Hz, 1 H, H1).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.3 (10-CH_3), 46.7 (C7′), 112.6 (C8), 121.1 (C7), 122.2 (C1), 122.6 (C9), 123.9 (C4a), 124.5 (C11a), 125.1 (C6a), 125.5 (C2′, C6′), 127.1 (C3), 127.8 (C4′), 128.5 (C10), 129.3 (C3′, C5′), 129.5 (C4), 131.9 (C11b), 133.1 (C2), 136.0 (C1′), 143.4 (C10a), 161.8 (C5).

MS (EI, 70 eV): *m*/*z* (%) = 339 (29) [M$^+$], 248 (100), 130 (12), 92 (12), 65 (6).

UV/Vis (MeCN): λ_{max} (log ε) = 373 (4.07), 260 (4.56), 243 (4.42), 229 (4.48), 205 nm (4.60).

Anal. Calcd for $C_{22}H_{17}N_3O$: C, 77.86; H, 5.05; N, 12.38. Found: C, 77.51; H, 4.82; N, 12.62.

6-Benzyl-8-methylpyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one (6i)

Pale yellow solid; yield: 60%; mp 257–259 °C.

IR (ATR): 1646, 1616, 1557, 1451, 1407, 1300, 1263, 973, 783, 773, 736, 704 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.14 (d, *J* = 1.1 Hz, 3 H, 8-CH_3), 5.93 (br s, 2 H, 7′-CH_2), 7.01 (dd, *J* = 1.5 Hz, *J* = 9.3 Hz, 1 H, H9), 7.21–7.30 (m, 3 H, H2′, H4′, H6′), 7.30–7.39 (m, 2 H, H3′, H5′), 7.61 (dd, *J* = 1.0 Hz, *J* = 9.2 Hz, 1 H, H10), 7.64 (ddd, *J* = 1.3 Hz, *J* = 7.1 Hz, *J* = 8.2 Hz, 1 H, H3), 7.87 (ddd, *J* = 1.4 Hz, *J* = 7.2 Hz, *J* = 8.2 Hz, 1 H, H2), 8.02 (q, *J* = 1.3 Hz, 1 H, H7), 8.51 (ddd, *J* = 0.7 Hz, *J* = 1.3 Hz, *J* = 8.0 Hz, 1 H, H1), 8.57 (ddd, *J* = 0.7 Hz, *J* = 1.3 Hz, *J* = 8.1 Hz, 1 H, H4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.5 (8-CH_3), 46.9 (C7′), 117.7 (C10), 120.7 (C7), 121.9 (C1), 122.1 (C8), 123.8 (C4a), 124.4 (C6a), 124.8 (C11a), 125.5 (C2′, C6′), 127.1 (C9), 127.2 (C3), 127.8 (C4′), 129.3 (C3′, C5′), 129.5 (C4), 131.8 (C11b), 133.2 (C2), 136.2 (C1′), 142.1 (C10a), 161.8 (C5).

MS (EI, 70 eV): *m*/*z* (%) = 339 (27) [M$^+$], 248 (100), 130 (13), 92 (9), 65 (6).

UV/Vis (MeCN): λ_{max} (log ε) = 377 (4.11), 315 (3.68), 261 (4.54), 244 (4.44), 228 (4.54), 205 nm (4.56).

Anal. Calcd for $C_{22}H_{17}N_3O$: C, 77.86; H, 5.05; N, 12.38. Found: C, 77.62; H, 4.75; N, 12.10.

6-Benzyl-9-ethylpyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one (6j)

Yellow solid; yield: 50%; mp 222–224 °C.

IR (ATR): 1639, 1623, 1561, 1496, 1448, 1427, 1386, 1307, 1267, 1150, 980, 861, 772, 728, 703, 682 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.23 (t, *J* = 7.5 Hz, 3 H, 1″-CH_3), 2.61 (q, *J* = 7.5 Hz, 2 H, 1″-CH_2), 5.89 (s, 2 H, 7′-CH_2), 6.43 (dd, *J* = 1.4 Hz, *J* = 7.3 Hz, 1 H, H8), 7.19–7.26 (m, 2 H, H2′, H6′), 7.26–7.30 (m, 1 H, H4′), 7.30–7.38 (m, 2 H, H3′, H5′), 7.39 (br s, 1 H, H10), 7.56 (ddd, *J* = 1.4 Hz, *J* = 7.1 Hz, *J* = 8.1 Hz, 1 H, H3), 7.82 (ddd, *J* = 1.4 Hz, *J* = 7.2 Hz, *J* = 8.3 Hz, 1 H, H2), 8.02 (dd, *J* = 0.8 Hz, *J* = 7.3 Hz, 1 H, H7), 8.42 (ddd, *J* = 0.6 Hz, *J* = 1.2 Hz, *J* = 8.0 Hz, 1 H, H1), 8.54 (ddd, *J* = 0.6 Hz, *J* = 1.3 Hz, *J* = 8.1 Hz, 1 H, H4).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8 (1″-CH_3), 28.1 (C1″), 46.8 (C7′), 114.3 (C8), 115.3 (C10), 121.8 (C1), 122.5 (C7), 123.8 (C4a), 124.4 (C6a), 124.9 (C11a), 125.5 (C2′, C6′), 126.9 (C3), 127.8 (C4′), 129.4 (C3′, C5′), 129.5 (C4), 132.1 (C11b), 133.2 (C2), 135.9 (C1′), 140.8 (C9), 143.8 (C10a), 161.6 (C5).

MS (EI, 70 eV): *m*/*z* (%) = 353 (23) [M$^+$], 262 (100), 130 (10), 106 (7).

UV/Vis (MeCN): λ_{max} (log ε) = 378 (4.09), 261 (4.57), 240 (4.43), 227 (4.53), 206 nm (4.60).

Anal. Calcd for $C_{23}H_{19}N_3O$: C, 78.16; H, 5.42; N, 11.89. Found: C, 77.97; H, 5.19; N, 12.13.

6-Benzyl-3,4-dimethoxypyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one (6k)

Yellow solid; yield: 35%; mp 281–286 °C.

IR (ATR): 1641, 1615, 1577, 1385, 1294, 1252, 1232, 1080, 1072, 1043, 1030, 988, 943, 852, 811, 732, 718, 691 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.99 (s, 3 H, 3-OCH_3), 4.01 (s, 3 H, 4-OCH_3), 5.86 (s, 2 H, 1′-CH_2), 6.59 (t, *J* = 6.8 Hz, 1 H, H8), 7.08 (dd, *J* = 6.9 Hz, *J* = 8.8 Hz, 1 H, H9), 7.22–7.31 (m, 3 H, H2′, H4′, H6′), 7.31–7.40 (m, 2 H, H3′, H5′), 7.51 (d, *J* = 8.9 Hz, 1 H, H2), 7.65 (br d, *J* = 9.1 Hz, 1 H, H10), 8.10 (br d, *J* = 7.2 Hz, 1 H, H7), 8.25 (d, *J* = 8.9 Hz, 1 H, H1).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 46.4 (C7′), 56.7 (3-OCH_3), 61.5 (4-OCH_3), 112.7 (C8), 118.1 (C10), 118.2 (C1), 118.6 (C4a), 119.1 (C2), 123.1 (C7), 123.7 (C6a), 123.9 (C9), 124.1 (C11a), 125.5 (C2′, C6′), 126.1 (C11b), 127.8 (C4′), 129.3 (C3′, C5′), 136.1 (C1′), 142.5 (C10a), 150.9 (C4), 152.9 (C3), 159.5 (C5).

MS (EI, 70 eV): *m*/*z* (%) = 385 (56) [M$^+$], 294 (100), 279 (18), 251 (14), 190 (7), 91 (6), 78 (18).

UV/Vis (MeCN): λ_{max} (log ε) = 389 (4.13), 266 (4.36), 229 nm (4.61).

Anal. Calcd for $C_{23}H_{19}N_3O_3$: C, 71.67; H, 4.97; N, 10.90. Found: C, 71.39; H, 4.70; N, 11.18.

6-Benzyl-8-bromo-3,4-dimethoxypyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one (6l)

Yellow solid; yield: 43%; mp 262–264 °C.

IR (ATR): 1651, 1399, 1274, 1258, 1246, 1083, 1074, 1031, 990, 976, 810, 798, 786, 780, 747, 697 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.99 (s, 3 H, 3-OCH_3), 4.02 (s, 3 H, 4-OCH_3), 5.83 (s, 2 H, 7′-CH_2), 7.08 (dd, *J* = 1.3 Hz, *J* = 9.5 Hz, 1 H, H9), 7.23–7.29 (m, 2 H, H2′, H6′), 7.29–7.33 (m, 1 H, H4′), 7.33–7.42 (m, 2 H, H3′, H5′), 7.48 (dd, *J* = 0.8 Hz, *J* = 9.6 Hz, 1 H, H10), 7.51 (d, *J* = 8.8 Hz, 1 H, H2), 8.19 (d, *J* = 8.7 Hz, 1 H, H1), 8.27 (dd, *J* = 0.9 Hz, *J* = 1.8 Hz, 1 H, H7).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 46.3 (C7′), 56.7 (3-OCH_3), 61.5 (4-OCH_3), 107.2 (C8), 118.2 (C1), 118.5 (C10), 118.7 (C4a), 119.1 (C2), 123.1 (C7), 123.7 (C6a), 125.1 (C11a), 125.6 (C2′, C6′), 125.8 (C11b), 126.8 (C9), 127.9 (C4′), 129.5 (C3′, C5′), 135.9 (C1′), 140.8 (C10a), 150.9 (C4), 153.2 (C3), 159.5 (C5).

MS (EI, 70 eV): *m*/*z* (%) = 463 (51) [M+], 372 (100), 357 (28), 344 (22), 329 (18), 190 (11), 158 (17), 91 (24), 76 (9), 65 (6).

UV/Vis (MeCN): λ_{max} (log ε) = 416 (4.14), 394 (4.25), 274 (4.39), 234 nm (4.69).

Anal. Calcd for $C_{23}H_{18}BrN_3O_3$: C, 59.50; H, 3.91; N, 9.05. Found: C, 59.35; H, 3.94; N, 8.75.

6-Benzyl-8-chloro-3,4-dimethoxypyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one (6m)

Yellow solid; yield: 42%; mp 278–279 °C.

IR (ATR): 3082, 1652, 1462, 1400, 1291, 1276, 1259, 1247, 1083, 1053, 1035, 991, 976, 953, 810, 799, 787, 748, 698 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 4.00 (s, 3 H, 3-OCH_3), 4.02 (s, 3 H, 4-OCH_3), 5.83 (s, 2 H, 7′-CH_2), 7.01 (dd, *J* = 1.5 Hz, *J* = 9.6 Hz, 1 H, H9), 7.23–7.29 (m, 2 H, H2′, H6′), 7.29–7.33 (m, 1 H, H4′), 7.33–7.42 (m, 2 H, H3′, H5′), 7.50 (d, *J* = 8.7 Hz, 1 H, H2), 7.56 (br d, *J* = 9.8 Hz, 1 H, H10), 8.17 (br d, *J* = 2.1 Hz, 1 H, H7), 8.21 (d, *J* = 8.7 Hz, 1 H, H1).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 46.3 (C7′), 56.7 (3-OCH_3), 61.6 (4-OCH_3), 118.2 (C10), 118.3 (C1), 118.7 (C4a), 119.1 (C2), 120.8 (C8), 120.9 (C7), 123.9 (C6a), 124.9 (C9), 125.2 (C11a), 125.5 (C2′, C6′), 125.8 (C11b), 128.0 (C4′), 129.5 (C3′, C5′), 135.9 (C1′), 140.8 (C10a), 150.9 (C4), 153.2 (C3), 159.5 (C5).

MS (EI, 70 eV): *m*/*z* (%) = 419 (54) [M+], 328 (100), 312 (29), 285 (21), 190 (7), 112 (19), 91 (16), 76 (7), 65 (4).

UV/Vis (MeCN): λ_{max} (log ε) = 415 (4.13), 394 (4.25), 273 (4.39), 234 nm (4.69).

Anal. Calcd for $C_{23}H_{18}ClN_3O_3$: C, 65.79; H, 4.32; N, 10.01. Found: C, 65.44; H, 4.18; N, 9.85.

6-Benzyl-3,4-dimethoxy-10-methylpyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one (6n)

Yellow solid; yield: 68%; mp 202–204 °C.

IR (ATR): 1650, 1470, 1418, 1385, 1297, 1271, 1249, 1077, 1046, 999, 828, 722, 715, 696 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.67 (s, 3 H, 10-CH_3), 3.99 (s, 3 H, 3-OCH_3), 4.02 (s, 3 H, 4-OCH_3), 5.85 (s, 2 H, 7′-CH_2), 6.50 (t, *J* = 7.0 Hz, 1 H, H8), 6.87 (d, *J* = 6.7 Hz, 1 H, H9), 7.21–7.29 (m, 3 H, H2′, H4′, H6′), 7.29–7.38 (m, 2 H, H3′, H5′), 7.50 (d, *J* = 8.7 Hz, 1 H, H2), 7.98 (d, *J* = 7.2 Hz, 1 H, H7), 8.34 (d, *J* = 8.8 Hz, 1 H, H1).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 16.9 (10-CH_3), 45.9 (C7′), 56.3 (3-OCH_3), 61.1 (4-OCH_3), 111.8 (C8), 117.7 (C1), 118.0 (C4a), 118.4 (C2), 120.5 (C7), 121.8 (C9), 123.6 (C6a), 123.7 (C11a), 125.2 (C2′, C6′), 126.4 (C11b), 127.2 (C4′), 127.6 (C10), 128.8 (C3′, C5′), 136.1 (C1′), 142.7 (C10a), 150.3 (C4), 152.1 (C3), 159.0 (C5).

MS (El, 70 eV): *m*/*z* (%) = 399 (47) [M+], 308 (100), 293 (14), 265 (12), 190 (6), 92 (15), 65 (8).

UV/Vis (MeCN): λ_{max} (log ε) = 386 (4.13), 266 (4.44), 230 (4.59), 219 nm (4.60).

Anal. Calcd for $C_{24}H_{21}N_3O_3$: C, 72.16; H, 5.30; N, 10.52. Found: C, 71.85; H, 4.97; N, 10.39.

6-Benzyl-3,4-dimethoxy-8-methylpyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one (6o)

Dark yellow solid; yield: 38%; mp 241–245 °C.

IR (ATR): 1639, 1578, 1400, 1292, 1263, 1240, 1070, 1040, 1029, 985, 850, 813, 788, 712, 693 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.07 (d, *J* = 1.0 Hz, 3 H, 8-CH_3), 3.98 (s, 3 H, 3-OCH_3), 4.01 (s, 3 H, 4-OCH_3), 5.84 (s, 2 H, 7′-CH_2), 6.88 (dd, *J* = 1.5 Hz, *J* = 9.3 Hz, 1 H, H9), 7.22–7.30 (m, 3 H, H2′, H4′, H6′), 7.30–7.40 (m, 2 H, H3′, H5′), 7.47 (d, *J* = 8.8 Hz, 1 H, H2), 7.50 (d, *J* = 9.3 Hz, 1 H, H10), 7.85–7.92 (m, 1 H, H7), 8.19 (d, *J* = 8.6 Hz, 1 H, H1).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.5 (8-CH_3), 46.5 (C7′), 56.7 (3-OCH_3), 61.5 (4-OCH_3), 117.3 (C2), 117.9 (C1), 118.5 (C4a), 119.1 (C10), 120.7 (C7), 121.9 (C8), 123.5 (C6a), 124.3 (C11a), 125.6 (C2′, C6′), 126.5 (C11b), 126.9 (C9), 127.7 (C4′), 129.2 (C3′, C5′), 136.5 (C1′), 141.8 (C10a), 150.9 (C4), 152.7 (C3), 159.6 (C5).

MS (EI, 70 eV): *m*/*z* (%) = 399 (45) [M+], 308 (100), 393 (13), 265 (13), 190 (6), 92 (13), 65 (9).

UV/Vis (MeCN): λ_{max} (log ε) = 389 (4.17), 267 (4.40), 253 (4.40), 230 nm (4.65).

Anal. Calcd for $C_{24}H_{21}N_3O_3$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.06; H, 5.57; N, 10.30.

6-Benzyl-10-(benzyloxy)-3,4-dimethoxypyrido[2′,1′:2,3]imidazo[4,5-*c*]isoquinolin-5(6*H*)-one (6p)

Yellow solid; yield: 50%; mp 215–217 °C.

IR (ATR): 1647, 1545, 1535, 1394, 1268, 1254, 1236, 1195, 1068, 1049, 999, 970, 818, 752, 725, 699 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.98 (s, 3 H, 3-OCH_3), 4.00 (s, 3 H, 4-OCH_3), 5.38 (s, 2 H, 7″-CH_2), 5.81 (br s, 2 H, 7′-CH_2), 6.32 (dd, *J* = 1.3 Hz, *J* = 7.6 Hz, 1 H, H9), 6.37 (dd, *J* = 6.6 Hz, *J* = 7.5 Hz, 1 H, H8), 7.19–7.25 (m, 2 H, H2′, H6′), 7.28–7.41 (m, 6 H, H3′, H4′, H5′, H3″, H4″, H5″), 7.48 (d, *J* = 8.9 Hz, 1 H, H2), 7.47–7.52 (m, 2 H, H2″, H6″), 7.70 (dd, *J* = 1.3 Hz, *J* = 6.7 Hz, 1 H, H7), 8.40 (d, *J* = 8.6 Hz, 1 H, H1).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 46.4 (C7′), 56.7 (3-OCH_3), 61.5 (4-OCH_3), 70.8 (C7″), 101.9 (C9), 112.2 (C8), 116.2 (C7), 118.5 (C4a), 118.6 (C1), 118.9 (C2), 123.8 (C11a), 124.5 (C6a), 125.5 (C2′, C6′), 126.5 (C11b), 127.1 (C2″, C6″), 127.6 (C4′), 128.1 (C4″), 128.6 and 129.2 (C3′, C5′; C3″, C5″), 136.0 and 136.2 (C1′, C1″), 137.3 (C10a), 147.9 (C10), 150.7 (C4), 152.6 (C3), 159.6 (C5).

UV/Vis (MeCN): λ_{max} (log ε) = 381 (4.09), 269 (4.52), 219 (4.64), 210 nm (4.65).

Anal. Calcd for $C_{30}H_{25}N_3O_4$: C, 73.30; H, 5.13; N, 8.55. Found: C, 73.03; H, 4.90; N, 8.32.

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(8) (a) X-ray crystal structure analysis for **6n**: formula $C_{24}H_{21}N_3O_3$, M = 399.44, orange crystal 0.10 × 0.03 × 0.02 mm^3, monoclinic, space group $P2_1/n$, a = 22.673(2), b = 7.2566(7), c = 24.348(2) Å, β = 107.4740(10)°, V = 3821.1(6) Å^3, ρ_{calcd} = 1.389 μg/m^3, absorption coefficient μ = 0.093 mm^{-1}, Z = 8, reflections collected 41880, θ_{max} = 28.49°, independent reflections 9106 [R_{int} = 0.0678], final $R1$ [$I > 2\sigma(I)$] = 0.0454, $wR2$ [$I > 2\sigma(I)$] = 0.0977, $R1$ (all data) = 0.1016, $wR2$ (all data) = 0.1172, GOF = 1.016, extinction parameter = 0.0012(2), largest diff. peak and hole 0.252 and –0.249 eÅ^{-3}. (b) X-ray data were collected at 100(2) K on an INCOATEC Microsource device with mirror-monochromated Mo-Kα radiation (λ = 0.71073 Å). The device is equipped with a SMART APEX II area detector. The data were integrated with SAINT[9] and an empirical absorption correction (SADABS)[10] was applied. The structure was solved by using direct methods with SHELXS-97 and refined by full-matrix least-squares on F^2 for all data with SHELXL-97.[11–13] All non-hydrogen atoms were refined with anisotropic displacement parameters. A riding model with idealized geometry was employed for all hydrogen atoms. CCDC-674626 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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