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SYNTHESIS OF 5-AMINOBENZIMIDAZO[1,2-*a*]QUINOLINE DERIVATIVES THROUGH ONE-POT TWO-STEP CASCADE REACTION

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Dedicated with respect to Professor Dr. Lutz F. Tietze on occasion of his 75th birthday.

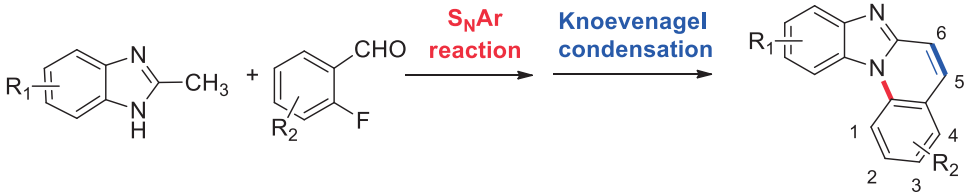
Abstract – An efficient method for the synthesis of 5-aminobenzimidazo[1,2-*a*]quinolines with high diversity has been developed through a cascade reaction involving sequential aromatic nucleophilic substitution and the Dieckmann–Thorpe cyclization. This method is applicable to the synthesis of a wide range of 5-aminobenzimidazo[1,2-*a*]quinoline derivatives from readily available 2-fluoroarylnitriles and benzimidazole substrates. Moderate light emission was observed for some 5-aminobenzimidazo[1,2-*a*]quinolines.

INTRODUCTION

Fused benzimidazoles represent a class of important compounds that display a broad spectrum of biological functions.[1] Among fused benzimidazoles, some benzimidazo[1,2-*a*]quinolines have been recently reported to show the powerful activity of DNA-intercalation as well as the inhibition of topoisomerase II activity.[2] In addition, benzimidazo[1,2-*a*]quinolines are utilized as an important skeletal component as luminophores for use in organic light-emitting diodes.[3]

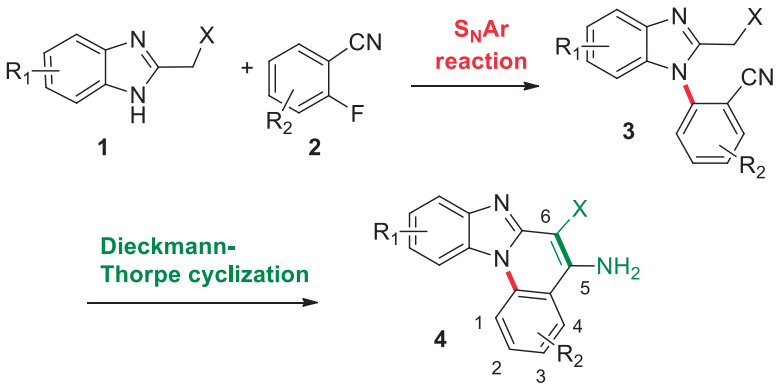
Although a variety of methods has been developed for the synthesis of substituted benzimidazo[1,2-*a*]quinolines, these methods require an inconvenient multi-step synthesis for the required substrates, and do not meet the demands in the study of structure-activity relationships.[4-9] In our recent efforts to develop more facile methods for the synthesis of substituted poly-fused heterocycles,[10] we recently disclosed a one-pot, two-step cascade synthesis of benzimidazo[1,2-*a*]quinolines.[11] This cascade reaction involves sequential intermolecular aromatic nucleophilic substitution (S_NAr) and intramolecular

Knoevenagel condensation (S_NAr/Knoevenagel cascade reaction). By using the cascade reaction, substituted benzimidazo[1,2-*a*]quinoline derivatives having a variety of substituents at varied positions could be synthesized, upon selecting two readily available substrates (**Scheme 1**).



Scheme 1. Cascade reaction for substituted benzimidazo[1,2-*a*]quinolines[11]

However, there is still in a possibility of extending this methodology to applying the facile introduction of substituents to the 5- and 6-positions. Meanwhile the group of David-Cordonnier and Hranjec have reported 5-aminobenzimidazo[1,2-*a*]quinoline derivatives having a functional group at the 6-position exhibiting powerful anti-proliferative activities through intercalation to DNAs.[12] This report prompted us to develop a facile method introducing an amino-functionality at the 5-position of benzimidazo[1,2-*a*]quinolones having a variety of substituents at the 6-position as an extension of the previous work.[11] In this paper, we disclose a new cascade reaction for the synthesis of the target 5-aminobenzimidazo[1,5-*a*]quinoline derivatives from two readily available components through sequential S_NAr reaction and Dieckmann-Thorpe cyclization (S_NAr/Dieckmann–Thorpe cyclization cascade) (**Scheme 2**). In addition to these results, we will also describe the photophysical properties of the synthesized compounds.



Scheme 2. New cascade reaction for the synthesis of 5-aminobenzimidazo[1,2-*a*]quinoline derivatives

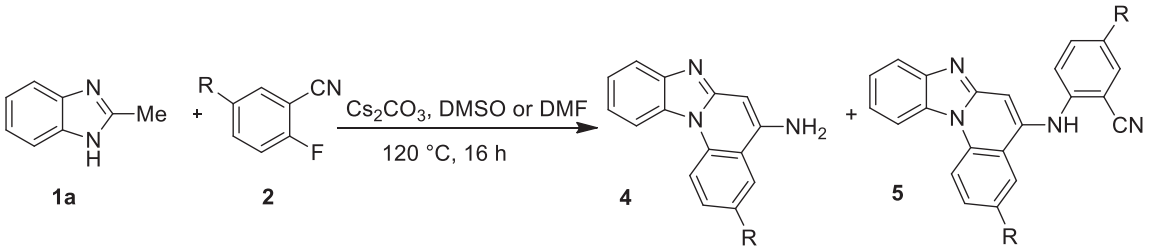
RESULTS AND DISCUSSION

Reaction of 2-methyl-1*H*-benzo[*d*]imidazole (1a) and fluoroarylnitriles

To verify the validity of the proposed cascade reaction for the synthesis of 5-aminobenzimidazo[1,2-*a*]quinoline, first, we chose 2-fluoroarynitriles **2a–2f** as one of the substrates in

our cascade reaction from 2-methyl-1*H*-benzo[*d*]imidazole (**1a**). In our previous studies on S_NAr/Dieckmann–Thorpe cyclization cascade reaction from 2-fluoroarylnitriles and 3,5-disubstituted 1*H*-pyrazoles, Cs_2CO_3 was found to be the best base promoting this reaction in DMF or DMSO at 120 °C.[10a,] With these findings in mind, the reaction of **1a** with 2-fluoroarylnitriles **2a–2f** was examined under the two representative conditions. The results are summarized in Table 1.

Table 1. The cascade reaction of 2-methyl-1*H*-benzo[*d*]imidazole (**1a**) with 2-fluorobenzolnitriles **2**[a]



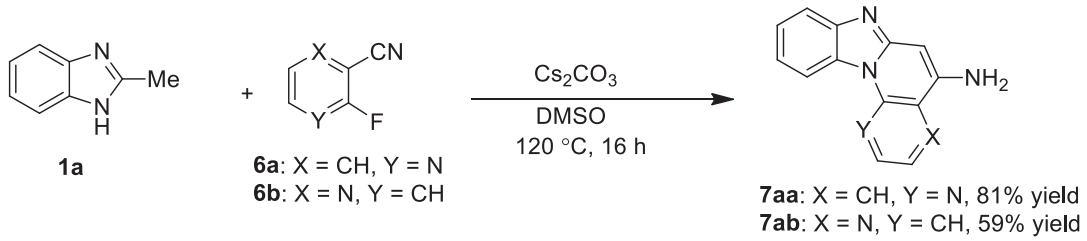
Entry	Benzonitrile		Product **4**		By-product **5**	
	2	R	Yield %		Yield %	
1	**2a**	H	**4aa**	63 (7)[b]	**5aa**	26
2	**2b**	CF_3	**4ab**	68	**5ab**	trace
3	**2c**	Br	**4ac**	52	**5ac**	trace
4	**2d**	Cl	**4ad**	47	**5ad**	trace
5	**2e**	Me	**4ae**	43	**5ae**	trace
6	**2f**	MeO	**4af**	36	**5af**	trace

[a] All reactions were carried out in the presence of 1*H*-benzimidazole **1a** (1.0 mmol), 2-fluorobenzonitrile **2** (1.2 mmol), and Cs_2CO_3 (3.0 mmol) in DMSO (5 mL) at 120 ºC for 16 h unless stated otherwise. [b] Yield in parentheses refer to the reaction in DMF instead of DMSO.

Initially, a mixture of 2-fluorobenzonitrile (**2a**) and 2-methyl-1*H*-benzo[*d*]imidazole (**1a**) was heated at 120 °C in DMF in the presence of Cs_2CO_3 for 16 h as a model reaction (entry 1). This reaction gave the expected cascade product **4aa** in a very low yield (7%). In this reaction, a large amount of unidentified products were produced though the starting two substrates were almost consumed. Resubmission of the isolated **4aa** to the same conditions (Cs_2CO_3, DMF, 120 °C, 16 h) gave an insoluble unidentified compound. This suggested to us that DMF may react with the amino group of the cascade product **4aa** under the conditions to suppress a good yield.[13] The yield significantly increased to 63%, upon switching the solvent to DMSO (entry 1). In this reaction, by-product **5aa**, which was produced by concomitant S_NAr reaction between **4a** and **2a** under the conditions, was isolated in a 26% yield. In an effort to survey the scope of the present cascade reaction, several 2-fluorobenzonitriles **2b–2f** were reacted with **1a** in the presence of Cs_2CO_3 in DMSO. As expected, almost all of the tested combinations successfully produced the desired cascade products **4ab**–**4af**, though the yields varied depending on the electron nature of the substituents. 2-Fluorobenzonitriles **2b–2d** bearing an electron-withdrawing group were found to be the

better substrate than 2-fluorobenzonitriels **2e** and **2f** having an electron-donating group (entries 2, 3, 4 vs. 5, 6). In these reactions, trace amounts of by-products **5ab–5af** were detected in the crude NMR spectrum

Fluoropyridinylnitriles were also available to the S_NAr/Dieckmann–Thorpe cyclization cascade reaction. As shown in Scheme 3, 2-fluoronicotinonitrile (**6a**) reacted with **1a** to give naphthyridine derivative **7aa** in an 81% yield, while a modest yield (59%) was observed with 3-fluoropicolinonitrile (**6b**) under the same conditions (Cs_2CO_3, DMSO, 120 °C).

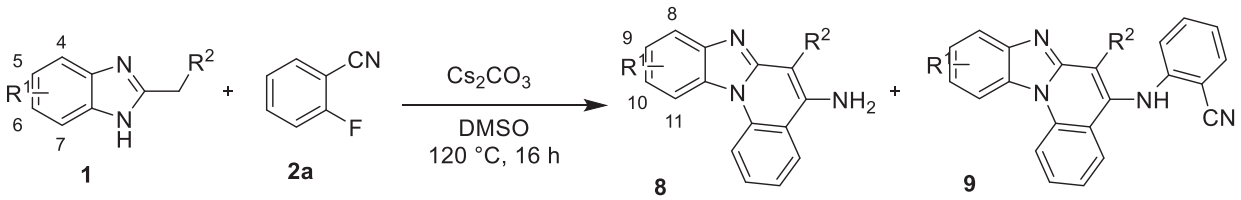


Scheme 3. The cascade reaction with fluoropyridinylnitriles

Scope of 2-methyl-1*H*-benzo[*d*]imidazoles

To extend the scope of the 2-methyl-1*H*-benzimidazole substrates for our cascade reaction, we next examined the reaction of 2-fluorobenzonitrile (**2a**) with a variety of 2-methyl-1*H*-benzimidazole derivatives **1** under the conditions (Cs_2CO_3, DMSO, 120 ºC). The results are shown in Table 2.

Table 2. Cascade reaction of 1*H*-benzo[*d*]imidazoles **1** with 2-fluorobenzonitrile (**2a**)[a]



Entry	1*H*-benzimidazole			Product				Yield (%) of **9**[b]	
	1	R^1	R^2	**8**	R^1	R^2	Yield (%)[b]		
1	**1a**	H	H	**8aa(4aa)**	H	H	63	**9aa(5aa)**	26
2	**1b**	5-Me	H	**8ba**	9- & 10-Me	H	89[c]	**9ba**	14[d]
3	**1c**	5,6-$(Me)_2$	H	**8ca**	9,10-$(Me)_2$	H	72	**9ca**	10
4	**1d**	5,6-$(Cl)_2$	H	**8da**	5,6-$(Cl)_2$	H	43	**9da**	19
5	**1e**	4-Me	H	**8ea**	8-Me	H	61	**9ea**	5
6	**1f**	4-MeO	H	**8fa**	8-MeO	H	60	**9fa**	10
7	**1g**	4-Br	H	**8ga**	8-Br	H	18	**9ga**	6
8	**1h**	H	Me	**8ha**	H	Me	77	**9ha**	10
9	**1i**	H	MeO	**8ia**	H	MeO	61	**9ia**	21
10	**1j**	H	MeS	**8ja**	H	MeS	39	**9ja**	28
11	**1k**	H	CN	**8ka**	H	CN	49 (73)[e]	**9ka**	ND[f]
12	**1l**	H	CO_2Et	**8la**	H	CO_2Et	ND[f] (52)[e]	**9la**	ND[f]

[a] All reactions were carried out in the presence of 1*H*-benzimidazole **1a–1l** (1.0 mmol), 2-fluorobenzaldehyde (**2a**) (1.2 mmol), and Cs_2CO_3 (3.0 mmol) in DMSO (5 mL) at 120 ºC for 16 h unless state othewise. [b] Isolated yield. [c] For an 1:1 mixture of regioisomers. [d] For an 1:1.4 mixture of regioisomers. [e] Yield in parentheses refer to the reaction using K_2CO_3 instead of Cs_2CO_3. [f] Not detected.

As shown in Table 2, almost all of the tested combinations successfully produced the desired benzimidazo[1,2-*a*]quinolines **8ba–8la** with moderate to good isolated yields, though an undeniable amount of overreaction product **9** was isolated in most entries. Unsymmetrical 1*H*-benzo[*d*]imidazoles such as **1b**, **1e**, **1f** and **1g** exist as an equilibrium mixture of their tautomers. Therefore, the S_NAr sequence of our cascade reaction with these substrates theoretically provides a regioisomeric mixture of the corresponding adducts. Our survey revealed that the regiochemical outcome is highly controlled upon utilizing **1e**, **1f** and **1g** having a substituent at the 4-position to give **8ea**, **8fa** and **8ga** without detecting their regioisomers (entries 5–7). However, no reigioselectivity was observed with the cascade reaction with **1b** bearing methyl substituent at the 5-position (entry 2). These results suggest to us that the less sterically congested nitrogen atom of 1*H*-benzo[*d*]imidazoles preferably reacted with 2-fluorobenzonitrile (**2a**) in the S_NAr reaction. 2-Methyl-1*H*-benzimidazole derivatives **1h**, **1i**, and **1j**, having an electron donating group (–CH_3, –OCH_3, –SCH_3), reacted with **2a** to give **8ha**, **8ia**, and **8ja** in modest yields under the conditions, respectively (entries 8–10). When the benzimidazoles **1k** and **1l** possessing an electron withdrawing group (–CN, –CO_2Et) at the 2-methyl group were treated with **2a** under the conditions, a large amount of insoluble unidentified product was produced. In these reactions, the desired cascade product **8la** was not detected while the cascade product **8ka** was isolated in a modest yield (entries 11 and 12). The cascade products **8ka** and **8la** were obtained in good yields upon replacing Cs_2CO_3 with K_2CO_3. (entries 11 and 12). In our S_NAr/Knoevenagel cascade reaction with **1k** and **1l**, we found the Knoevenagel condensation between aldehydes and the active methylene of **1k** and **1l** occured preferably to the S_NAr reaction in the first step, and the desired cascade adducts could not be obtained.[14] These comparative results indicate that the S_NAr reaction occured preferably to the Dieckmann–Thorpe type reaction in the present cascade reaction upon fine-tuning the base used.

Photophysical properties of the synthesized compounds

Recently, biarylic benzimidazole quinoline derivatives have been developed as a fluorescence dye, and applied to bioimaging probes.[15] That report prompted us to determine the photochemical properties of benzimidazo[1,2-*a*]quinolines as the fused analogues of biarylic benzimidazole quinolines. The UV-vis absorption and emission spectra of representative compounds (0.1 μM solution in CH_2Cl_2) were collected. 5-Aminobenzimidazo[1,2-*a*]quinoline (**4aa)** has a maximum absorption at 343 nm and a maximum emission at 392 nm, respectively. Larger Stork's shifts were observed for **8fa** ($\lambda_{ab/max}$ = 345 nm, $\lambda_{em/max}$ = 413 nm) having a methoxy group at the 8-position and **8ia** ($\lambda_{ab/max}$ = 351 nm, $\lambda_{em/max}$ = 416 nm) possessing a methoxy group at the 6-position as an electron donating group.

CONCLUSIONS

In summary, a concise and general method for the synthesis of 5-aminobenzimidazo[1,2-*a*]quinolines and related heterocycles has been developed. The method is based upon a novel cascade reaction through an aromatic nucleophilic substitution of 2-methyl-1*H*-benzimidazoles with 2-fluorobenznitriles, followed by Dieckmann–Thorpe cyclization of the resulting adducts. Our method potentially provides a variety of substituted 5-aminobenzimidazo[1,2-*a*]quinolines without using any transition metal catalysts upon fine-tuning a combination of two readily available substrates.

EXPERIMENTAL

All reagents and solvents were pure analytical-grade materials purchased from commercial sources and were used without further purification. All melting points were taken on a Yanagimoto micromelting point apparatus and were uncorrected. IR spectra were recorded on a JASCO FTIR-620. Mass spectra were measured on JEOL GCmate by electron ionization and Micromass Autospec by electrospray ionization. Elemental analysis was performed on an Elemental Vavio EL. NMR spectra were obtained on a JEOL JNM-ECP400 NMR Spectrometer (^{1}H NMR: 400 MHz), Bruker DPX400 NMR Spectrometer (^{1}H NMR: 400 MHz) or Bruker AVANCE III NMR spectrometer (^{1}H NMR: 400 MHz and ^{13}C NMR: 100 MHz). The chemical shift data for each signal on ^{1}H NMR are given in units of δ relative to $CHCl_3$ (δ = 7.26 ppm) for $CDCl_3$ solution and to DMSO (δ = 2.50 ppm) for d_6-DMSO solution. For ^{13}C NMR spectra, the chemical shifts for $CDCl_3$ and d_6-DMSO solutions were relative to $CDCl_3$ (δ = 77.0) and d_6-DMSO (δ =39.5) resonances, respectively. UV-vis absorption and emission spectra were obtained on a Shimadzu RF-5300pc spectrometer. Column chromatography was carried out using 63–210 μm silica gel 60N (Kanto Chemical Co., Inc.). Analytical TLC was carried out with Merck plates precoated with silica gel 60F_{254} plates (0.25 mm).

5-Aminobenzimidazo[1,2-*a*]quinoline (4aa) and 2-{(benzo[4,5]imidazo[1,2-*a*]quinolin-5-yl)amino}benzonitrile (5aa) (representative procedure)

Condition A: A mixture of 2-fluorobenzonitrile (**2a**, 138 mg, 1.20 mmol), 2-methlbenzimidazole **1a** (132 mg, 1.00 mmol), and Cs_2CO_3 (977 mg, 3.00 mmol) in DMSO (5.0 mL) was stirred at 120 °C. After being stirred for 16 h, the mixture was cooled to room temperature and diluted with water. The resulting mixture was extracted with ethyl acetate (50 mL) twice. The combined organic layers were washed with water (50 mL) twice, dried over $MgSO_4$ and the solvent was removed *in vacuo* to afford a residue. The residue was purified by flash column chromatography ($CHCl_3$:MeOH = 50:1) on silica gel to afford **5aa** (61.0 mg, 26%) as orange solid. Successive elution with the same eluent gave **4aa** (146 mg, 63% yield) as

pale yellow solid. **Condition B**: The reaction was carried out in DMF instead of DMSO under the same conditions as that of condition A to afford **4aa** (18.0 mg, 7% yield). The physical data of **4aa** and **5aa** are described as follows: **4aa**: mp 217–219 °C (EtOAc–ether), mp 271–273 °C (for the hydrochloride, EtOH–$CHCl_3$). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.53 (d, J = 8.4 Hz, 1H), 8.21 (d, J = 8.3 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.84 (d, J = 8.0 Hz 1H), 7.76 (t, J = 8.3 Hz 1H), 7.52–7.43 (m, 2H), 7.35 (t, J = 8.3 Hz 1H), 6.84(s, 1H), 5.29 (br s, 2H). ^{13}C-NMR (d_6-DMSO, 100 MHz) δ 150.76, 146.86, 145.22, 135.07, 130.45, 124.09, 123.51, 123.44, 120.03, 117.48, 117.39, 115.74, 113.40, 90.10, 48.59. HR-MS (ESI) calcd for $C_{15}H_{12}N_3$ $(M+H)^+$ requires 234.1031, found 234.1037. Anal. Calcd for $C_{15}H_{12}N_3$•HCl•1.75H_2O: C, 59.80; H, 5.19; N, 13.95. Found: C, 59.71; H, 5.20; N, 13.74. **5aa**: mp 189–191 °C, IR (neat): ν_{max} / cm^{-1} 2223, 1633, 1595, 1544, 1482, 1453, 1389, 752, ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.63 (d, J = 8.4 Hz, 1H), 8.33 (d, J = 8.2 Hz, 1H), 8.08 (d, J = 8.1 Hz, 1H), 7.93 (d, J = 7.8 Hz, 1H), 7.83 (t, J = 8.4 Hz, 1H), 7.66 (dd, J = 7.8, 1.3 Hz, 1H), 7.57–7.43 (m, 6H), 7.10 (t, J = 8.1 Hz, 1H), 6.84 (brs, 1H), ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 148.80, 145.29, 145.02, 139.04, 136.14, 134.17, 133.30, 130.96, 130.64, 124.47, 124.31, 123.05, 122.26, 122.01, 119.94, 119.21, 118.53, 117.00, 116.01, 113.62, 103.20, 101.84, HR-MS (ESI) calcd for $C_{22}H_{15}N_4$ $(M+H)^+$ requires 335.1297, found 335.1291.

5-Amino-3-(trifluoromethyl)benzimidazo[1,2-*a*]quinoline (4ab)

Prepared from **1a** and **2b** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 68%. Pale yellow solid. Mp 282–284 °C (EtOAc–ether). ^{1}H-NMR (d_6-DMSO, 400 MHz) δ 8.86 (d, J = 8.8 Hz, 1H), 8.69 (s, 1H), 8.42 (d, J = 8.0 Hz, 1H), 8.07 (d, J = 8.8 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.39 (t, J = 7.6 Hz, 1H), 7.29 (t, J = 7.2 Hz, 1H), 6.83 (br s, 2H), 6.57 (s, 1H). ^{13}C-NMR (d_6-DMSO, 100 MHz) δ 150.81, 146.17, 145.58, 137.16, 130.35, 126.35, 124.25 (q, $^1J_{CF}$ = 270.0 Hz), 123.95, 123.59 (t, $^2J_{CF}$ = 32.0 Hz), 121.71 (d, $^3J_{CF}$ = 4.0 Hz), 120.47, 117.92, 117.58, 116.66, 113.45, 91.35. HR-MS (ESI) calcd for $C_{16}H_{11}N_3F_3$ $(M+H)^+$ requires 302.0903, found 302.0903.

5-Amino-3-bromobenzimidazo[1,2-*a*]quinoline (4ac)

Prepared from **1a** and **2c** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 52%. Yellow solid. Mp 284–286 °C (EtOAc–ether). ^{1}H-NMR (d_6-DMSO, 400 MHz) δ 8.63 (d, J = 9.2 Hz, 1H), 8.49 (d, J = 2.4 Hz, 1H), 8.37 (d, J = 8.4 Hz, 1H), 7.93 (dd, J = 9.2 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.36(t, J = 7.6 Hz, 1H), 7.26 (t, J = 7.6 Hz 1H), 6.68 (s, 2H), 6.53(s, 1H). ^{13}C-NMR (d_6-DMSO, 100 MHz) δ 150.50, 145.70, 145.40, 134.30, 132.65, 130.30, 126.47, 123.64, 120.25, 119.36, 117.84, 117.80, 115.95, 113.33, 91.20. HR-MS (ESI) calcd for $C_{15}H_{11}N_3Br$ $(M+H)^+$ requires 312.0136, found 312.0136. Anal. Calcd for $C_{15}H_{10}N_3Br$: C, 57.71; H, 3.23; N, 13.46. Found: C, 57.49; H, 3.49; N, 13.17.

5-Amino-3-chlorobenzimidazo[1,2-*a*]quinoline (4ad)

Prepared from **1a** and **2d** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 47%. Pale yellow solid. Mp 280–281 °C (EtOAc–ether). ^{1}H-NMR (d_6-DMSO, 400 MHz) δ 8.70 (d, J = 9.0 Hz, 1H), 8.38 (d, J = 8.1 Hz, 1H), 8.37 (s, 1H), 7.81 (dd, J = 8.8, 2.2 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.37 (t, J = 7.6 Hz 1H), 7.26 (t, J = 7.6 Hz 1H), 6.67 (s, 2H), 6.54 (br s, 1H). ^{13}C-NMR (d_6-DMSO, 100 MHz) δ 150.54, 145.74, 145.44, 133.70, 130.31, 129.85, 127.94, 123.62, 123.56, 120.24, 119.05, 117.82, 117.62, 113.29, 91.24. HR-MS (ESI) calcd for $C_{15}H_{11}N_3Cl$ $(M+H)^+$ requires 268.0641, found 268.0642.

5-Amino-3-methylbenzimidazo[1,2-*a*]quinoline (4ae)

Prepared from **1a** and **2e** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 43%. Pale yellow solid. Mp 222–224 °C (EtOAc–ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.44 (d, J = 8.8 Hz, 1H), 8.21 (d, J = 8.4 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H), 7.63 (s, 1H), 7.57 (d, J = 8.8 Hz, 1H), 7.44 (t, J = 7.2 Hz, 1H), 7.34 (t, J = 7.2 Hz, 1H), 6.79 (s, 1H), 4.67 (br s, 2H), 2.56 (s, 3H). ^{13}C-NMR (d_6-DMSO, 100 MHz) δ 149.71, 147.89, 142.61, 133.25, 132.83, 131.72, 129.95, 124.00, 123.76, 120.48, 117.15, 116.45, 115.84, 113.56, 88.75, 20.68. HR-MS (ESI) calcd for $C_{16}H_{14}N_3$ $(M+H)^+$ requires 248.1188, found 248.1188.

5-Amino-3-methoxybenzimidazo[1,2-*a*]quinoline (4af)

Prepared from **1a** and **2f** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 36%. Pale yellow solid. Mp 271–272 °C (EtOAc–ether). ^{1}H-NMR (d_6-DMSO, 400 MHz) δ 8.62 (d, J = 8.5 Hz, 1H), 8.37 (d, J = 8.4 Hz, 1H), 7.76 (d, J = 2.8 Hz, 1H), 7.60 (d, J = 7.6 Hz, 1H), 7.41 (dd, J = 9.2, 2.8 Hz, 1H), 7.33 (t, J = 7.6 Hz, 1H), 7.23 (t, J = 7.2 Hz, 1H), 6.62 (br s, 2H), 6.51 (s, 1H), 3.93 (s, 3H). ^{13}C-NMR (d_6-DMSO, 100 MHz) δ 155.31, 150.31, 146.45, 145.16, 130.31, 129.43, 123.09, 119.76, 118.62, 117.83, 117.48, 117.03, 112.97, 107.14, 90.48, 55.78. HR-MS (ESI) calcd for $C_{16}H_{14}N_3O$ $(M+H)^+$ requires 264.1137, found 264.1133.

5-Aminobenzimidazo[1,2-*a*][1,8]naphthyridine—methanol (1/1) (7aa)

Prepared from **1a** and **6a** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 81%. Yellow solid. Mp 264–266 °C (EtOAc–ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.99 (d, J = 8.5 Hz, 1H), 8.81 (d, J = 3.9 Hz, 1H), 8.07 (d, J = 3.9 Hz, 1H), 7.81 (d, J = 7.9 Hz, 1H), 7.52–7.26 (m, 3H), 6.74 (s, 1H), 4.50 (s, 2H), 3.49 (s, 3H). ^{13}C-NMR (d_6-DMSO, 100 MHz) δ 150.81, 149.37, 146.28, 146.24, 144.98, 132.76, 130.22, 123.86, 120.41, 119.49, 117.19, 115.54, 112.57, 91.35, 48.60. HR-MS (ESI)

calcd for $C_{14}H_{11}N_4$ $(M+H)^+$ requires 235.0984, found 235.0991. Anal. Calcd for $C_{15}H_{13}N_4O$: C, 67.65; H, 5.30; N, 21.04. Found: C, 67.20; H, 5.04; N, 21.04.

5-Aminobenzimidazo[1,2-*a*][1,5]naphthyridine (7ab)

Prepared from **1a** and **6b** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 59%. Yellow solid. Mp 253–254 °C (EtOAc–ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.79 (dd, J = 8.6, 1.1 Hz, 1H), 8.73 (dd, J = 4.4, 1.1 Hz, 1H), 8.12 (d, J = 8.2 Hz, 1H), 7.86 (d, J = 8.0 Hz 1H), 7.70 (dd, J = 8.5, 4.5 Hz, 1H), 7.46 (t, J = 7.3 Hz, 1H), 7.35 (t, J = 7.3 Hz, 1H), 6.84 (s, 1H), 5.47 (br s, 2H). ^{13}C-NMR (d_6-DMSO, 100 MHz) δ 150.10, 146.25, 145.49, 144.46, 133.93, 131.21, 130.69, 124.81, 123.68, 123.42, 120.37, 117.89, 113.07, 91.03. HR-MS (ESI) calcd for $C_{14}H_{10}N_4$ $(M+H)^+$ requires 235.0984, found 235.0986.

A mixture of 5-amino-9-methylbenzimidazo[1,2-a]quinoline and 5-amino-10-methyl-benzo-imidazo[1,2-*a*]quinoline (8ba)

Prepared from **1b** and **2a** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 89%. Pale yellow solid. Mp 210–220 °C (EtOAc–ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.51 (d, J = 8.4 Hz, 0.5H), 8.46 (d, J = 8.4 Hz, 0.5H), 8.04 (d, J = 8.4 Hz, 0.5H), 8.00 (s, 0.5H), 7.87 (d, J = 6.8 Hz, 0.5H), 7.85 (d, J = 7.6 Hz, 0.5H), 7.75 (t, J = 8.3 Hz, 0.5H), 7.73 (d, J = 8.8 Hz, 0.5H), 7.71 (d, J = 8.2 Hz, 0.5H), 7.52 (s, 0.5H), 7.47 (td, J = 7.3, 3.2 Hz, 1H), 7.25 (s, 0.5H), 7.14 (d, J = 8.4 Hz, 0.5H), 6.79 (d, J = 7.2 Hz, 1H), 4.89 (brs, 1H), 4.78 (brs, 1H), 2.61 (s, 1.5H), 2.53(s, 1.5H). ^{13}C-NMR (d_6-DMSO, 100 MHz) δ 150.68, 150.31, 146.48, 145.30, 142.96, 135.11, 134.98, 132.66, 130.60, 130.42, 130.33, 129.45, 128.46, 124.69, 124.06, 124.01, 123.43, 123.37, 121.29, 117.44, 117.38, 117.24, 116.98, 115.79, 115.65, 113.52, 112.94, 90.21, 90.11, 21.51, 21.16. HR-MS (ESI) calcd for $C_{16}H_{14}N_3$ $(M+H)^+$ requires 248.1188, found 248.1184.

A mixture of 2-{(9-methylbenzo[4,5]imidazo[1,2-*a*]quinolin-5-yl)amino}benzonitrile and 2-{(10-methylbenzo[4,5]imidazo[1,2-*a*]quinolin-5-yl)amino}benzonitrile (9ba)

Prepared from **1b** and **2a** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 14%. Yellow solid. Mp 230–242 °C (EtOAc–ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.63 (d, J = 8.3 Hz, 0.4H), 8.59 (d, J = 8.5 Hz, 0.6H), 8.19 (d, J = 8.5 Hz, 0.6H), 8.13 (s, 0.6H), 8.07–8.04 (m, 1H), 7.86–7.77 (m, 2H), 7.71 (s, 0.6H), 7.65 (d, J = 7.8 Hz, 1H), 7.56–7.49 (m, 2H), 7.44–7.40 (m, 2H), 7.34 (d, J = 8.2 Hz, 0.4H), 7.29 (s, 0.4H), 7.09 (d, J = 7.3 Hz, 0.4H), 7.07 (t, J = 7.3 Hz, 0.6H), 6.80–6.74 (m, 0.6H), 2.64 (s, 1.2H), 2.56 (s, 1.8H). HR-MS (ESI) calcd for $C_{23}H_{17}N_4$ $(M+H)^+$ requires 349.1453, found 349.1462.

5-Amino-9,10-dimethylbenzimidazo[1,2-*a*]quinoline (8ca)

Prepared from **1c** and **2a** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 72%. Pale yellow solid. Mp 264–266 °C (EtOAc–ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.53 (d, J = 8.4 Hz, 1H), 7.99 (s, 1H), 7.80 (d, J = 8.1 Hz, 1H), 7.76 (t, J = 8.1 Hz, 1H), 7.60 (s, 1H), 7.46 (t, J = 7.5 Hz, 1H), 6.74 (s, 1H), 4.51 (br s, 2H), 2.5 (s, 3H), 2.44 (s, 3H). ^{13}C-NMR (d_6-DMSO, 100 MHz) δ 150.00, 146.25, 143.45, 135.04, 131.69, 130.21, 128.81, 128.52, 123.95, 123.21, 117.76, 117.30, 115.66, 113.71, 90.37, 20.06, 19.90. HR-MS (ESI) calcd for $C_{17}H_{16}N_3$ $(M+H)^+$ requires 262.1344, found 262.1337.

2-{(9,10-Dimethylbenzo[4,5]imidazo[1,2-*a*]quinolin-5-yl)amino}benzonitrile (9ca)

Prepared from **1c** and **2a** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 10%. Yellow solid. Mp 233–235 °C (EtOAc–ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.61 (d, J = 8.5 Hz, 1H), 8.09 (s, 1H), 8.06 (d, J = 8.1 Hz, 1H), 7.83 (t, J = 7.8 Hz, 1H), 7.70 (s, 1H), 7.65 (d, J = 7.8 Hz, 1H), 7.54 (t, J = 7.5 Hz, 1H), 7.50 (d, J = 7.3 Hz, 1H), 7.43–7.42 (m, 2H), 7.08 (t, J = 7.5 Hz, H), 6.83 (br s, 1H), 2.56 (s, 3H), 2.48 (s, 3H). HR-MS (ESI) calcd for $C_{24}H_{19}N_4$ $(M+H)^+$ requires 363.1610, found 363.1611.

5-Amino-9,10-dichrolobenzimidazo[1,2-*a*]quinoline (8da)

Prepared from **1d** and **2a** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 43%. Pale yellow solid. Mp >300 °C (sublime) (EtOAc–ether). ^{1}H-NMR (d_6-DMSO, 400 MHz) δ 8.69 (s, 1H), 8.66 (d, J = 8.6 Hz, 1H), 8.27 (d, J = 8.0 Hz, 1H), 7.84 (t, J = 7.8 Hz, 1H), 7.79 (s, 1H), 7.58 (t, J = 7.7 Hz, 1H), 6.85 (br s, 1H), 6.47 (s, 1H). ^{13}C-NMR (d_6-DMSO, 100 MHz) δ 152.84, 147.96, 145.37, 134.45, 130.86, 129.87, 125.82, 124.10 (2C), 121.38, 117.71, 117.24, 116.19, 114.47, 89.39. HR-MS (ESI) calcd for $C_{15}H_{10}N_3Cl_2$ $(M+H)^+$ requires 302.0252, found 302.0246.

2-{(9,10-Dichlorobenzo[4,5]imidazo[1,2-*a*]quinolin-5-yl)amino}benzonitrile (9da)

Prepared from **1d** and **2a** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 21%. Pale yellow solid. Mp >300 °C (sublime) (EtOAc–ether). ^{1}H-NMR (d_6-DMSO, 400 MHz) δ 9.21 (s, 1H), 8.85 (s, 1H), 8.80 (d, J = 8.4 Hz, 1H), 8.45 (d, J = 7.0 Hz, 1H), 7.97–7.92 (m, 3H), 7.80 (dt, J = 8.0, 1.6 Hz, 3H), 7.70 (t, J = 8.0 Hz, 1H), 7.54 (d, J = 7.6 Hz, 1H), 7.44 (dt, J = 7.6, 0.8 Hz,1H), 6.53 (s, 1H). HR-MS (ESI) calcd for $C_{22}H_{13}N_4Cl_2$ $(M+H)^+$ requires 403.0517, found 403.0510.

5-Amino-8-methylbenzimidazo[1,2-*a*]quinoline (8ea)

Prepared from **1e** and **2a** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 61%. Pale yellow solid. Mp 250 °C (EtOAc–ether). ^{1}H-NMR (d_6-DMSO, 400 MHz) δ 8.67 (d, J = 8.4 Hz, 1H), 8.25 (d, J = 7.1 Hz, 1H), 7.82 (t, J = 7.2 Hz, 1H), 7.55 (t, J = 7.4 Hz, 1H), 7.20–7.14 (m, 2H), 6.63 (br s, 2H), 6.54 (s, 1H), 2.59 (s, 3H). ^{13}C-NMR (d_6-DMSO, 100 MHz) δ 149.93, 146.50, 144.01, 135.06, 130.27, 129.81, 126.77, 123.98, 123.73, 123.38, 119.92, 117.72, 115.58, 110.92, 90.31, 16.79. HR-MS (ESI) calcd for $C_{16}H_{14}N_3$ $(M+H)^+$ requires 248.1188, found 248.1185.

2-{(8-Methylbenzo[4,5]imidazo[1,2-*a*]quinolin-5-yl)amino}benzonitrile (9ea)

Prepared from **1e** and **2a** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 5%. Brown solid. Mp 238–240 °C (EtOAc-ether). ^{1}H-NMR (d_6-DMSO, 400 MHz) δ 9.02 (s, 1H), 8.80 (d, J = 8.5 Hz, 1H), 8.41~8.34 (m, 2H), 7.93 (d, J = 7.2 Hz, 1H), 7.92 (t, J = 7.3 Hz, 1H), 7.75 (dt, J = 8.1, 1.6 Hz, 1H), 7.65 (t, J = 7.4 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.37 (dt, J = 7.6, 0.9 Hz, 1H), 7.28 (q, J = 7.3 Hz, 1H), 7.28 (s, 1H), 6.60 (s, 1H), 2.60 (s, 3H). HR-MS (ESI) calcd for $C_{23}H_{17}N_4$ $(M+H)^+$ requires 349.1453, found 349.1456.

5-Amino-8-methoxylbenzimidazo[1,2-*a*]quinoline (8fa)

Prepared from **1f** and **2a** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 60%. Pale yellow solid. Mp 213–215 °C (EtOAc–ether). ^{1}H-NMR (d_6-DMSO, 400 MHz) δ 8.66 (d, J = 8.4 Hz, 1H), 8.23 (d, J = 8.4 Hz, 1H), 8.02 (d, J = 8.4 Hz, 1H), 7.82 (t, J = 7.6 Hz, 1H), 7.55 (t, J = 8.0 Hz 1H), 7.19 (t, J = 8.0 Hz, 1H), 6.93 (d, J = 8.0 Hz, 1H), 6.55 (br s, 2H), 6.51 (s, 1H), 3.96 (s, 3H). ^{13}C-NMR (d_6-DMSO, 100 MHz) δ 150.01, 149.45, 146.22, 135.29, 134.94, 131.58, 130.21, 123.95, 123.52, 120.71, 117.58, 115.67, 106.46, 105.32, 90.60, 55.61. HR-MS (ESI) calcd for $C_{16}H_{14}N_3O$ $(M+H)^+$ requires 264.1137, found 264.1144

2-{(8-Methoxybenzo[4,5]imidazo[1,2-*a*]quinolin-5-yl)amino)}benzonitrile (9fa)

Prepared from **1f** and **2a** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 10%. Reddish brown solid. Mp 229–239 °C (EtOAc–ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.62 (d, J = 8.4 Hz, 1H), 8.04 (d, J = 8.0 Hz, 1H), 7.93 (d, J = 8.4 Hz, 1H), 7.82 (t, J = 8.4 Hz, 1H), 7.64 (dd, J = 7.6, 1.2 Hz, 1H), 7.57–7.46 (m, 3H), 7.39 (d, J = 8.0 Hz, 1H), 7.41-7.37 (m, 2H), 7.05 (t, J = 7.6 Hz, 1H), 6.95 (d, J = 8.0 Hz, 3H), 6.71 (s, 1H), 4.09 (s, 3H). ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 151.63, 147.65, 145.49, 138.88, 136.07, 135.60, 134.28, 133.43, 132.09, 130.54, 124.51, 123.31, 123.21, 121.96, 119.64, 118.50, 117.27, 116.12, 106.13, 104.89, 104.09, 101.81, 56.01. HR-MS (ESI) calcd for $C_{23}H_{17}N_4O$ $(M+H)^+$ requires 365.1402, found 365.1404.

5-Amino-8-bromobenzimidazo[1,2-*a*]quinoline (8ga)

Prepared from **1g** and **2a** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 18%. Pale yellow solid. Mp 268–270 °C (EtOAc–ether). ^{1}H-NMR (d_6-DMSO, 400 MHz) δ 8.69 (d, J = 8.4 Hz, 1H), 8.45 (d, J = 8.0 Hz, 1H), 8.29 (d, J = 8.0 Hz, 1H), 7.85 (t, J = 8.4 Hz, 1H), 7.59 (t, J = 7.6 Hz, 1H), 7.60–7.57 (m, 2H), 7.17 (t, J = 8.0 Hz, 1H), 6.79 (br s, 2H), 6.51 (s, 1H). ^{13}C-NMR (d_6-DMSO, 100 MHz) δ 151.31, 147.45, 143.76, 134.89, 131.07, 130.57, 126.08, 124.11, 123.87, 120.71, 117.38, 115.80, 112.74, 110.30, 89.86. HR-MS (ESI) calcd for $C_{15}H_{11}N_3Br$ $(M+H)^+$ requires 312.0136, found 312.0145.

2-{(8-Bromobenzo[4,5]imidazo[1,2-*a*]quinolin-5-yl)amino}benzonitrile (9ga)

Prepared from **1g** and **2a** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 6%. Pale yellow solid. Mp 274–276 °C (EtOAc–ether). ^{1}H-NMR (d_6-DMSO, 400 MHz) δ 9.19 (s, 1H), 8.82(d, J = 8.4 Hz, 1H), 8.61 (d, J = 8.2 Hz, 1H), 8.46 (dd, J = 8.2, 1.2 Hz, 1H), 7.96–7.93 (m, 2H), 7.79 (dt, J = 8.0, 1.5 Hz, 1H), 7.70 (t, J = 7.5 Hz 1H), 7.67 (d, J = 7.7 Hz, 1H), 7.53 (d, J = 7.9 Hz, 1H), 7.43 (dt, J = 7.7, 1.0 Hz, 1H), 7.29 (t, J = 8.1 Hz, 1H), 6.53 (s, 1H). HR-MS (ESI) calcd for $C_{22}H_{14}N_4Br$ $(M+H)^+$ requires 413.0402, found 413.0414.

5-Amino-6-methylbenzimidazo[1,2-*a*]quinoline (8ha)

Prepared from **1h** and **2a** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 77%. Pale yellow solid. Mp 266–267 °C (EtOAc–ether). ^{1}H-NMR (d_6-DMSO, 400 MHz) δ 8.68 (d, J = 8.4 Hz, 1H), 8.44 (d, J = 8.2 Hz, 1H), 8.31 (d, J = 8.1 Hz, 1H), 7.78 (t, J = 7.8 Hz, 1H), 7.69 (d, J = 7.9 Hz, 1H), 7.53 (t, J = 7.7 Hz 1H), 7.37 (t, J = 7.5 Hz, 1H), 7.26 (t, J = 8.0 Hz, 1H), 6.24 (br s, 2H), 2.41 (s, 3H). ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 151.19, 145.14, 141.96, 133.71, 131.09, 129.24, 123.68, 123.38, 123.32, 120.08, 117.82, 117.36, 115.36, 113.51, 97.56, 11.34. HR-MS (ESI) calcd for $C_{16}H_{14}N_3$ $(M+H)^+$ requires 248.1188, found 248.1190. Anal. Cacd for $C_{16}H_{13}N_3$: C, 77.71; H, 5.30; N, 16.99. Found: C, 77.50; H, 5.42; N, 16.84.

2-{(6-Methylbenzo[4,5]imidazo[1,2-*a*]quinolin-5-yl)amino}benzonitrile (9ha)

Prepared from **1h** and **2a** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 10%. Pale yellow solid. Mp 240–241 °C (EtOAc–ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.65 (d, J = 8.4 Hz, 1H), 8.42 (d, J = 8.0 Hz, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.94 (d, J = 8.0, 1.2 Hz, 1H), 7.77 (t, J = 8.0 Hz, 1H), 7.60–7.46 (m, 4H), 6.85 (t, J = 7.5 Hz, 1H), 6.39 (d, J = 8.5 Hz, 1H), 6.33 (s, 1H), 2.66 (s, 3H). HR-MS (ESI) calcd for $C_{23}H_{17}N_4$ $(M+H)^+$ requires 349.1453, found 349.1454.

5-Amino-6-methoxybenzimidazo[1,2-*a*]quinoline (8ia)

Prepared from **1i** and **2a** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 61%. Yellow solid. Mp 200–202 °C (EtOAc–ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.57 (d, *J* = 8.4 Hz, 1H), 8.28 (d, *J* = 8.4 Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.84 (d, *J* = 7.6 Hz, 1H), 7.73 (t, *J* = 8.4 Hz 1H), 7.54–7.46 (m, 2H), 7.39 (t, *J* = 7.2 Hz, 1H), 4.66 (s, 2H), 4.21 (s, 3H). ^{13}C-NMR (d_6-DMSO, 100 MHz) δ 146.37, 145.37, 135.86, 132.59, 130.72, 128.88, 125.28, 124.13, 123.54(2C), 120.49, 118.20, 117.59, 115.35, 113.64, 59.13. HR-MS (ESI) calcd for $C_{16}H_{14}N_3O$ $(M+H)^+$ requires 264.1137, found 264.1141. Anal. Calcd for $C_{16}H_{13}N_3O$: C, 72.99; H, 4.98; N, 15.96. Found: C, 72.84; H, 5.10; N, 15.69.

2-{(6-Methoxybenzo[4,5]imidazo[1,2-*a*]quinolin-5-yl)amino}benzonitrile (9ia)

Prepared from **1i** and **2a** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 21%. Yellow solid. Mp 119–200 °C (EtOAc–ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.64 (d, *J* = 8.4 Hz, 1H), 8.42 (d, *J* = 8.0 Hz, 1H), 8.09 (d, *J* = 7.6 Hz, 1H), 7.85 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.73 (t, *J* = 7.2 Hz, 1H), 7.62–7.51 (m, 3H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.29 (t, *J* = 7.2 Hz, 1H), 6.92 (t, *J* = 8.0 Hz, 1H), 6.56 (s, 1H), 6.53 (s, 1H), 4.24 (s, 3H). ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 148.30, 144.91, 144.77, 141.48, 134.07, 133.39, 133.00, 131.29, 128.67, 125.96, 125.28, 124.84, 124.50, 123.22, 120.99, 120.95, 120.02, 117.56, 115.48, 115.45, 114.04, 99.01, 61.51. HR-MS (ESI) calcd for $C_{23}H_{17}N_4O$ $(M+H)^+$ requires 365.1402, found 365.1398.

5-Amino-6-methylthiobenzimidazo[1,2-*a*]quinoline (8ja)

Prepared from **1j** and **2a** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 39%. Yellow solid. Mp 182–184 °C (EtOAc–ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.55 (d, *J* = 8.4 Hz, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 8.00 (d, *J* = 8.0 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.77 (t, *J* = 8.4 Hz, 1H), 7.49 (t, *J* = 8.0 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.36 (t, *J* = 8.0 Hz, 1H), 5.56 (s, 2H), 2.50 (s, 3H). ^{13}C-NMR (d_6-DMSO, 100 MHz) δ 150.18, 148.06, 145.10, 134.64, 131.11, 130.94, 124.93, 123.72, 123.48, 120.53, 118.21, 116.30, 115.66, 113.61, 93.92, 16.41. HR-MS (ESI) calcd for $C_{16}H_{14}N_3S$ $(M+H)^+$ requires 280.0908, found 280.0913. Anal. Cacd for $C_{16}H_{13}N_3S$: C, 68.79; H, 4.69; N, 15.04. Found: C, 68.61; H, 4.89; N, 14.94.

2-{(6-(Methylthio)benzo[4,5]imidazo[1,2-*a*]quinolin-5-yl)amino}benzonitrile (9ja)

Prepared from **1j** and **2a** in an analogous manner for the preparation of **4aa** under the condition A. Yield: 28%. Pale yellow solid. Mp 232–233 °C (EtOAc–ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.65 (d, *J* = 8.4 Hz, 1H), 8.39 (d, *J* = 8.2 Hz, 1H), 8.15 (d, *J* = 7.9 Hz, 1H), 7.82 (d, *J* = 8.4 Hz, 1H), 7.79 (t, *J* = 7.6 Hz,

1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.57 (t, *J* = 7.2 Hz, 1H), 7.52 (t, *J* = 7.2 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.31–7.20 (m, 2H), 7.28 (s, 1H), 7.00 (t, *J* = 7.6 Hz, 1H), 6.50 (d, *J* = 8.4 Hz, 1H) 2.68 (s, 3H). ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 148.13, 148.05, 145.06, 140.87, 135.61, 133.97, 133.37, 131.45, 130.59, 126.90, 124.79, 124.32, 123.13, 121.15, 121.02, 119.59, 118.82, 117.27, 116.75, 115.76, 114.03, 100.70, 18.32. HR-MS (ESI) calcd for $C_{23}H_{17}N_4S$ $(M+H)^+$ requires 381.1174, found 381.1179.

5-Aminobenzo[4,4]imidazo[1,2-*a*]quinoline-6-carbonitrile (8ka)

Prepared from **1k** and **2a** in an analogous manner for the preparation of **4aa** under the condition A except the substitution of K_2CO_3 for Cs_2CO_3 as a base. Yield: 49%. Yellow solid. Mp 297–299 °C (EtOAc–ether). ^{1}H-NMR (*d*$_6$-DMSO, 400 MHz) δ 8.69 (d, *J* = 8.4 Hz, 1H), 8.50 (d, *J* = 8.2 Hz, 1H), 8.45 (d, *J* = 8.2 Hz, 1H), 7.96-7.93 (m, 3H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.36 (t, *J* = 7.8 Hz, 1H), 7.34 (t, *J* = 7.3 Hz, 2H). ^{13}C-NMR (*d*$_6$-DMSO, 100 MHz) δ 153.04, 147.95, 144.76, 135.61, 133.35, 130.77, 125.26, 124.28, 123.92, 121.17, 118.28, 116.22, 116.08, 115.30, 113.65, 72.96. HR-MS (ESI) calcd for $C_{16}H_{11}N_4$ $(M+H)^+$ requires 259.0984, found 259.0995.

Ethyl 5-Aminobenzo[4,5]imidazo[1,2-*a*]quinoline-6-carboxylate (8la)

Prepared from **1l** and **2a** in an analogues manner for preparation of **4aa** under the condition A except the substitution of K_2CO_3 for Cs_2CO_3 as a base. Yield: 52%. Pale yellow solid. Mp 269–271 °C (EtOAc–ether). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.54 (d, *J* = 8.4 Hz, 1H), 8.17 (d, *J* = 8.2 Hz, 1H), 7.93 (d, *J* = 7.7 Hz, 2H), 7.83 (t, *J* = 8.0 Hz, 1H), 7.64 (s, 2H), 7.51 (t, *J* = 8.0 Hz, 1H), 7.45 (t, *J* = 7.4 Hz, 1H), 7.34 (t, *J* = 7.4 Hz, 1H), 4.61 (q, *J* = 7.1 Hz, 2H), 1.54 (t, *J* = 7.1 Hz, 3H). ^{13}C-NMR (*d*$_6$-DMSO, 100 MHz) δ 167.82, 151.03, 147.57, 144.75, 135.43, 132.77, 130.08, 125.17, 123.95, 123.50, 120.94, 118.31, 116.29, 115.85, 113.44, 90.5, 60.16, 14.39. HR-MS (ESI) calcd for $C_{18}H_{16}N_3O_2$ $(M+H)^+$ requires 306.1243, found 306.1245.

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