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Synthesis of Aminoalkyl-Functionalized 4-Arylquinolines from 2-(3,4-Dihydroisoquinolin-1-yl)anilines via the Friedländer Reaction

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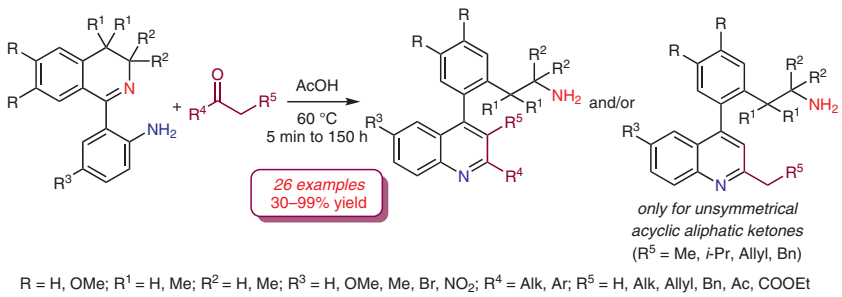


Received: 12.04.2020
Accepted after revision: 27.07.2020
Published online: 01.09.2020
DOI: 10.1055/s-0040-1706424; Art ID: ss-2020-t0376-op

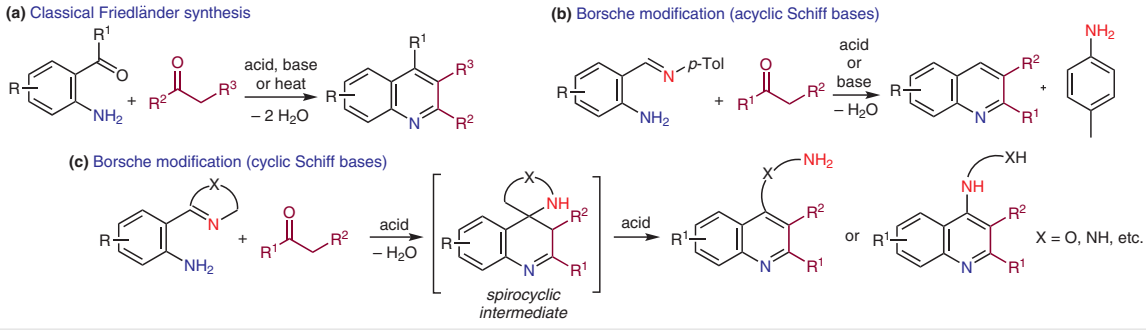
Abstract A new approach for the efficient and convenient synthesis of novel aminoalkyl-functionalized 4-arylquinolines via the Friedländer reaction of differently substituted 2-(3,4-dihydroisoquinolin-1-yl)anilines with various α-methylene ketones in acetic acid was developed. The reaction allows easy access to a diversity of 4-arylquinoline derivatives in moderate to excellent yields under mild conditions.

Key words Friedländer reaction, Schiff bases, 2-(3,4-dihydroisoquinolin-1-yl)anilines, ketones, acetic acid, 4-arylquinolines

The quinoline ring system is the core structure of many natural and synthetic compounds known for exhibiting a wide variety of biological activities.[1] Many synthetic approaches to various quinoline derivatives have already been developed. However, the diversity of pharmacological properties of these compounds and their exceptional importance for medicinal chemistry inspire research aimed at improving classical approaches to quinoline synthesis and developing new synthetic routes to novel, variously functionalized, quinoline derivatives.[2]

One of the oldest methods for the construction of a quinoline cycle is the Friedländer reaction which in its classical form involves the acid-, base- or heat-promoted condensation of aromatic 2-amino carbonyl derivatives with carbonyl compounds that have an α-methylene group, followed by cyclodehydration (Scheme 1a).[3] The Friedländer reaction provides a convenient access to a rich diversity of quinoline derivatives because of the wide substrate scope of both of its reagents, the applicability of many acid and base catalysts under various conditions, and the tolerance of many functional groups.[2,4,5]

The Borsche modification is one of the synthetically useful variations of the Friedländer reaction, where Schiff bases, usually 2-[(*p*-tolylimino)methyl]anilines, are used as substrates instead of the prone to self-condensation *o*-aminobenzaldehydes (Scheme 1b).[6] The Borsche modification allows the effective synthesis of 4-unsubstituted quinolines[6,7] and has been successfully used for the construction of various quinoline-based polyannelated aza-hetero-

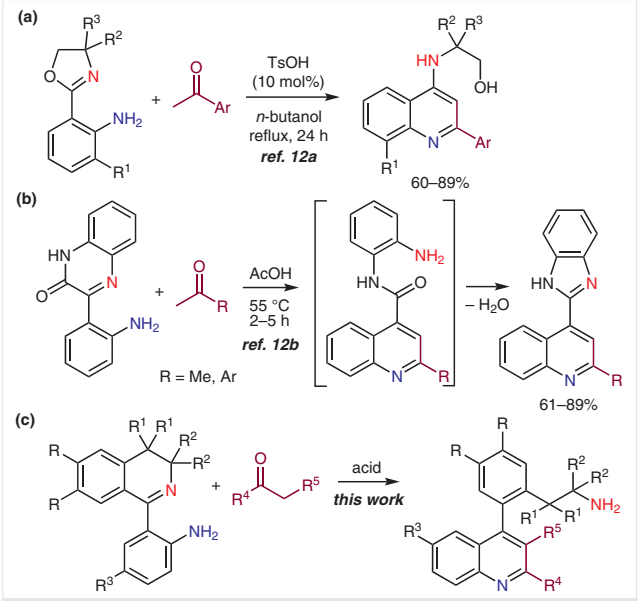


Scheme 1 The Friedländer synthesis of quinolines

cycles,[7a,d,8] including camptothecin[9] and luotonine A[7a,10] alkaloids and related compounds.[10b,11]

Intriguing synthetic possibilities of the Friedländer reaction (Borsche modification) appeared with the use of cyclic Schiff bases containing a 2-aminophenyl fragment attached to the carbon atom of the imine unit (Scheme 1c). While the reaction with acyclic imines as substrates releases amine (*p*-toluidine) to give 4-unsubstituted quinolines, in the case of cyclic Schiff bases, the amine comes to be tethered to the C-4 atom of the formed quinoline, and the type of amino fragment (for example, primary or secondary amino group) depends on the direction of the spirocyclic intermediate ring opening which, in turn, is influenced by the structure of the starting cyclic Schiff base. It should be noted that, even though the scope of the Friedländer reaction with respect to both reagents has been very well studied during the 137 years since its discovery, the use of cyclic Schiff bases as substrates for this reaction remains surprisingly poorly developed, and we found only two reports that describe the Friedländer synthesis with cyclic Schiff bases as reagents.[12] In 2006, Luo and co-workers reported the synthesis of 4-amino-substituted quinolines via the acid-catalyzed reaction of 2-(4,5-dihydrooxazol-2-yl)anilines with ketones (Scheme 2a).[12a] More recently, the Mamedov group developed an original approach to 4-(benzimidazol-2-yl)quinolines which involves the condensation of 3-(2-aminophenyl)quinoxalin-2(1*H*)-ones with various ketones via the Friedländer reaction, followed by intramolecular cyclization of the intermediate *N*-(2-aminophenyl)quinoline-4-carboxamides (Scheme 2b).[12b]

The above examples demonstrate that the use of cyclic Schiff bases as substrates for the Friedländer reaction offers excellent opportunities to access unique functionalized quinoline derivatives, and studies directed toward extending the scope of the Friedländer reaction with respect to the various cyclic Schiff bases have a great potential for the development of new, effective protocols for quinoline synthesis.

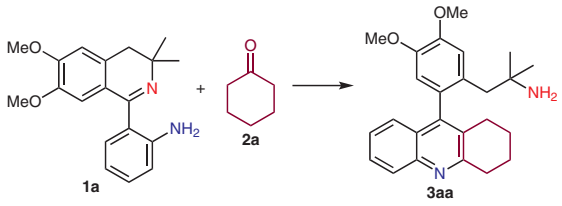


Scheme 2 Cyclic Schiff bases as substrates for the Friedländer reaction

In an attempt to contribute toward the development of new approaches to quinoline synthesis based on Friedländer annulation, herein, we report for the first time the use of 2-(3,4-dihydroisoquinolin-1-yl)anilines as new substrates for the Friedländer reaction and their application in the synthesis of novel amino-functionalized 4-arylquinoline derivatives (Scheme 2c).

In order to test that 3,4-dihydroisoquinolines with a 2-aminophenyl substituent at the C-1 atom could serve as substrates for the Friedländer reaction, we first examined the model reaction of 3,4-dihydroisoquinoline **1a** with cyclohexanone (**2a**) under acidic conditions (Table 1).

Table 1 Optimization of the Reaction Conditions[a]



Entry	Acid (equiv)	Solvent	Temp (°C)	Time	Yield (%)[b] of **3aa**
1	–	CH_2Cl_2	rt	5 d	trace
2	MsOH (1)	CH_2Cl_2	rt	20 h	65
3	TsOH (1)	CH_2Cl_2	rt	20 h	61
4	TfOH (1)	CH_2Cl_2	rt	20 h	58
5	TFA (1)	CH_2Cl_2	rt	20 h	63
6	AcOH (1)	CH_2Cl_2	rt	40 h	40[c]
7	MsOH (1)	DCE	rt	20 h	62
8	MsOH (0.1)	DCE	rt	5 d	22[c]
9	MsOH (5)	DCE	rt	4 d	30[c]
10	MsOH (1)	DCE	reflux	1.5 h	54
11	MsOH (1)	MeOH	reflux	1.5 h	60
12	MsOH (1)	MeCN	reflux	6 h	59
13	MsOH (1)	toluene	reflux	7 h	51[c]
14	AcOH[d]		rt	1 h	60
15	**AcOH[d]**		**60**	**30 min**	**80**
16	AcOH[d]		90	15 min	54
17	AcOH[d,e]		60	30 min	72

[a] Reaction conditions: **1a** (0.35 mmol, 1 equiv), **2a** (0.42 mmol, 1.2 equiv), solvent (0.6 mL).
[b] Isolated yield after recrystallization.
[c] Incomplete conversion was observed.
[d] AcOH (1.5 mL) was used.
[e] **2a** (1 equiv) was used.

Only trace amounts of quinoline **3aa** were detected in a control experiment carried out in CH_2Cl_2 at room temperature without catalyst (Table 1, entry 1). Performing the reaction in the presence of 1 equivalent of MsOH in CH_2Cl_2 at room temperature led to the formation of the desired quinoline **3aa** in 65% yield within 20 hours (entry 2). The structure of compound **3aa** was unambiguously confirmed by X-ray crystallography (Figure 1; see the Supporting Information for details).[13] Under the same conditions, TsOH, TfOH or TFA gave a yield of product **3aa** which was comparable with that obtained with MsOH (entries 3–5), whereas the use of AcOH resulted in a lower yield of **3aa** (40%) with incomplete conversion even after 40 hours (entry 6). Next, in order to find the optimal reaction conditions in terms of improvement of the product yield and shortening of the reaction time, we tested different reaction parameters using MsOH (entries 7–13). Although the experiments performed allowed us to determine the effect of acid loading, temperature and solvent on the reaction rate and yield of product **3aa** and significantly reduced the reaction time (entry 2 vs entries 10, 11), unfortunately they were not successful in terms of increasing the yield of quinoline **3aa**.

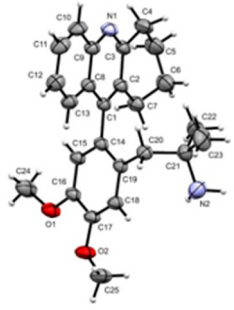


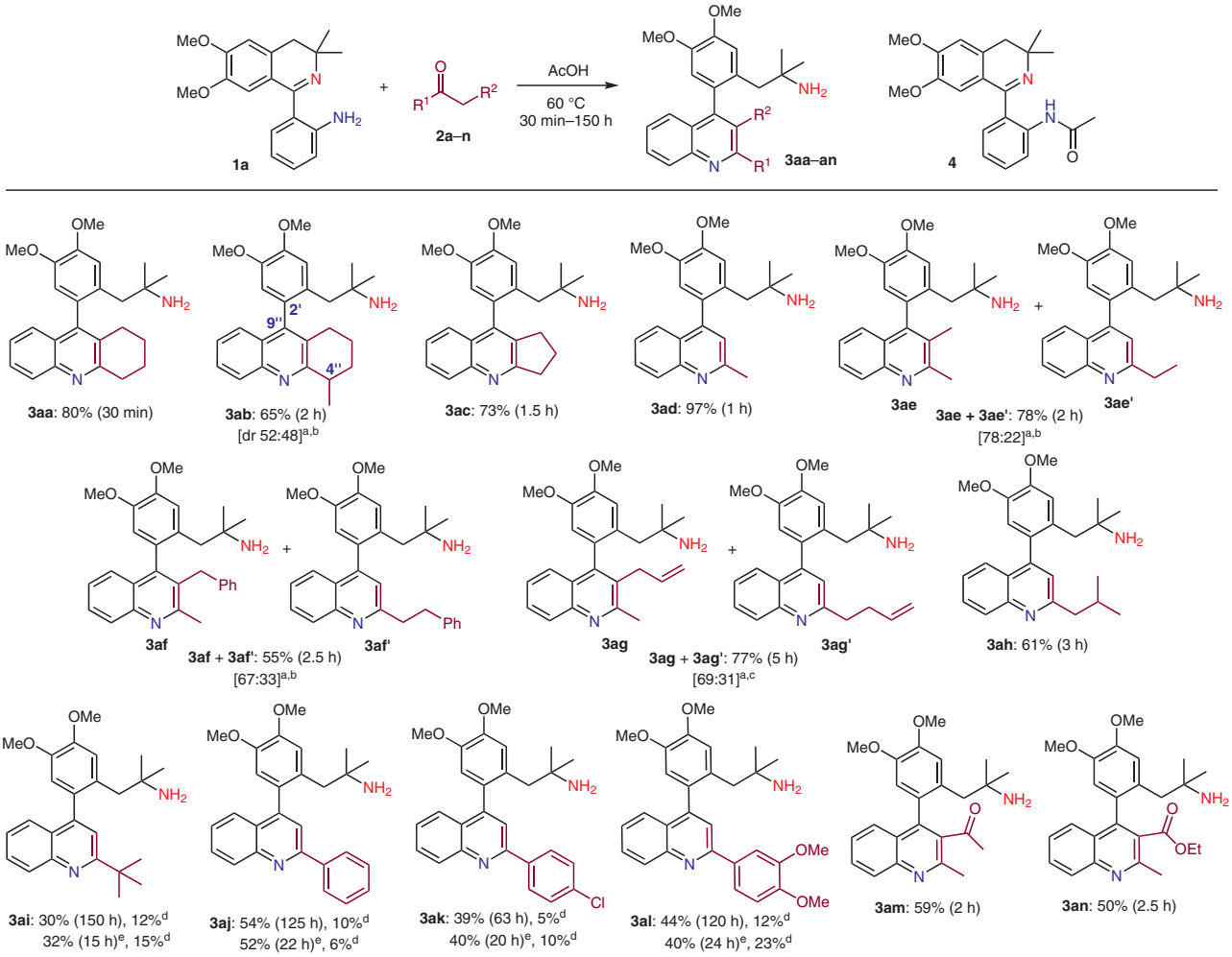
Figure 1 Molecular structure of **3aa** according to XRD data with thermal ellipsoids at the 40% probability level [only the (R_a)-atropisomer is shown]

Further continuing our efforts to improve the yield of **3aa**, we examined the reaction in excess acetic acid. These conditions were chosen because performing the Friedländer reaction (Borsche modification) in acetic acid proved to be successful in several cases.[7c,11b,e,12b] Accordingly, condensation of 3,4-dihydroisoquinoline **1a** with cyclohexanone (**2a**) in acetic acid at room temperature gave **3aa** in 60% yield within 1 hour (Table 1, entry 14). To our delight, significant improvement was observed when the reaction was performed at 60 °C (entry 15). In this case, the reaction was completed within 30 minutes to afford quinoline **3aa** in 80% yield. Further increase of the reaction temperature to 90 °C led to a significant decrease in the product yield (entry 16). Finally, we found that performing the reaction in acetic acid at 60 °C with 1 equivalent of **2a** provided quinoline **3aa** in 72% yield (entry 17). Thus, based on the results obtained, the optimal reaction conditions were determined as carrying out the reaction in acetic acid at 60 °C with a 1:1.2 ratio of **1a**/**2a**.

With the optimized conditions identified, the reaction of 3,4-dihydroisoquinoline **1a** with a range of ketones **2a–n** was further explored (Scheme 3). Reaction of **1a** with the cyclic aliphatic ketones 2-methylcyclohexanone (**2b**) and cyclopentanone (**2c**) occurred smoothly to give the corresponding quinolines **3ab** and **3ac** in 65% and 73% yield, respectively.

The ^{1}H and ^{13}C NMR spectra of compound **3ab** revealed doubling of some of the signals and, in the gas chromatogram of the substance (see Figure S74 in the Supporting Information), there were two poorly separated peaks with the same mass spectrum, which was attributed to the presence of two atropdiastereomers. In fact, molecule **3ab** possesses two chirality elements including a chirality center at the C-4″ atom and a chirality axis lying along the C-2′$_{(aryl)}$–C-9″$_{(het-aryl)}$ bond with restricted rotation around it (the chirality axis is present in all compounds **3**, as discussed below). According to ^{1}H NMR spectra, the diastereomeric ratio was determined to be nearly 52:48, both in $CDCl_3$ and DMSO-d_6 at 30 °C. Variable temperature ^{1}H NMR experiments showed that upon heating **3ab** in DMSO-d_6 up to 120 °C broadening of the signals did not occur, which indicates a high rotational barrier for the atropisomers of compound **3ab** (see Figures S71–S73 in the Supporting Information).

Acetone (**2d**) successfully afforded quinoline **3ad** in 97% yield. The structure of compound **3ad** was unambiguously confirmed by X-ray crystallography (see Figure S76 in the Supporting Information).[13] Unsymmetrical ketones such as methyl ethyl ketone (**2e**), benzylacetone (**2f**) and allylacetone (**2g**) gave regioisomeric mixtures of 2,3-disubstituted/2-monosubstituted quinolines **3ae**/**3ae′**–**3ag**/**3ag′** with predominance of the 2,3-disubstituted products, in good combined yields. The reaction of 3,4-dihydroisoquinoline **1a** with methyl isobutyl ketone (**2h**) occurred regioselectively to afford only 2-monosubstituted quinoline **3ah** in 61% yield. Regioselectivity of this reaction is caused by steric hindrance in methyl isobutyl ketone (**2h**) provided by the isopropyl group. Sterically hindered pinacolone (**2i**) required a considerably longer reaction time relative to the other aliphatic ketones (150 h vs 30 min to 5 h) to afford product **3ai** in only 30% yield along with amide **4** (12%). Compound **4** apparently arises from NH_2 acylation of the starting 2-(3,4-dihydroisoquinolin-1-yl)aniline **1a** with acetic acid in the course of the reaction. As with pinacolone (**2i**), acetophenones **2j–l** reacted with isoquinoline **1a** sluggishly and required long reaction times (63–125 h) to give quinolines **3aj–al** in 39–54% yield together with side product **4** (5–12%). Performing the reactions of **1a** with pinacolone (**2i**) or acetophenones **2j–l** at 90 °C led to highly shortened reaction times (15–24 h vs 63–150 h), but did not have a significant effect on the product yields, with only a slight increase or decrease in the yield of quinolines **3ai**,



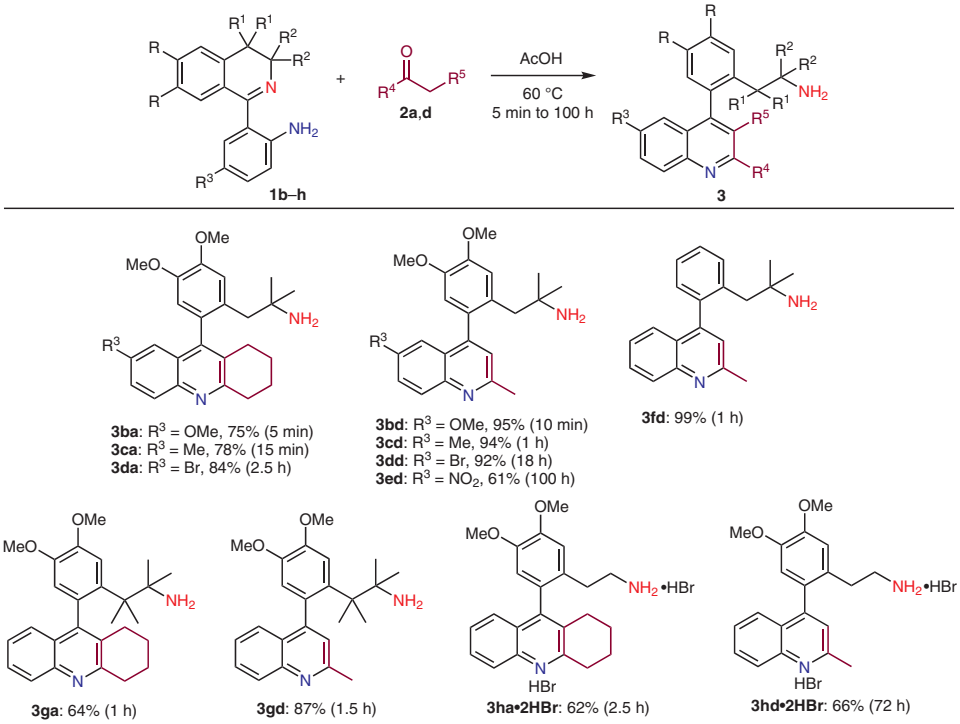
Scheme 3 Reaction of 3,4-dihydroisoquinoline **1a** with ketones **2a–n**. *Reagents and conditions*: **1a** (0.35 mmol), **2a–n** (0.42 mmol), AcOH (1.5 mL), 60 °C. Isolated yields are reported. [a] Ratio was determined by ^{1}H NMR analysis of the crude reaction mixture. [b] Inseparable mixture. [c] Major regioisomer **3ag** was isolated in 29% yield. [d] Amide **4** was also isolated. [e] Reaction was performed at 90 °C.

3ak and **3aj**, **3al**, respectively. In these cases, along with products **3ai–al**, amide **4** was also isolated in 6–23% yield. Further, the reaction was shown to be also applicable to acetylacetone (**2m**) and ethyl acetoacetate (**2n**), providing quinolines **3am** and **3an** in 59% and 50% yield, respectively.

To further demonstrate the substrate scope of the reaction, we explored the condensation of differently substituted 2-(3,4-dihydroisoquinolin-1-yl)anilines **1b–h** with cyclohexanone (**2a**) or acetone (**2d**) (Scheme 4).

Condensation of ketones **2a**, **2d** with isoquinolines **1b–e** containing an electron-donating (OMe, **1b**; Me, **1c**) or electron-withdrawing substituent (Br, **1d**; NO_2, **1e**) in the 2-aminophenyl moiety provided the expected quinolines **3ba–da**, **3bd–ed** in good to excellent yields (61–95%), but the reaction times differed significantly. Electron-donating substituents in the 2-aminophenyl moiety of isoquinolines **1b–e**, especially the OMe group, strongly increase the rate of the reaction whereas electron-withdrawing substituents slow the process down. Reaction of acetone (**2d**) with 3,4-dihydroisoquinoline **1f** unsubstituted on the benzene ring afforded quinoline **3fd** in nearly quantitative yield (99%). Next, we found that 3,3,4,4-tetramethyl-3,4-dihydroisoquinoline **1g** readily underwent condensation with cyclohexanone (**2a**) or acetone (**2d**) to give quinolines **3ga** and **3gd** in 64% and 87% yield, respectively. 3,4-Unsubstituted 3,4-dihydroisoquinoline **1h** is also a suitable substrate for the Friedländer reaction with ketones **2a**, **2d** to afford products **3ha** and **3hd**, respectively, in good yields (Scheme 4).

The ^{1}H NMR spectra of almost all compounds **3** demonstrated nonequivalency of some groups. For example, the CH_2 protons and/or Me groups in the $CH_2C(Me_2)NH_2$ fragment of quinolines **3aa**, **3ac–an**, **3ba–ed** appear as two doublets (AB system) and as two singlets, respectively. Also, ^{1}H NMR spectra clearly indicated the nonequivalency of protons of both methylene groups in the $CH_2CH_2NH_2$ fragment of compound **3hd** and methyl groups in the

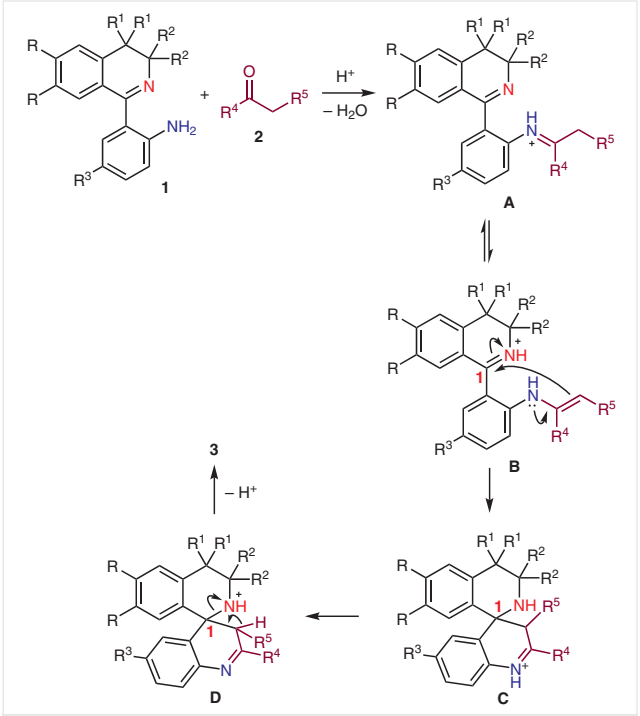


Scheme 4 Reaction of 3,4-dihydroisoquinolines **1b–h** with ketones **2a**, **2d**. *Reagents and conditions*: **1b–h** (0.35 mmol), **2a**, **2d** (0.42 mmol), AcOH (1.5 mL), 60 °C.

$C(Me_2)C(Me_2)NH_2$ fragment of quinolines **3ga**, **3gd**. The only explanation for this is hindered rotation around the bond connecting the aryl and quinoline moieties of the molecules, also in the case of quinoline **3ab**, the stereoisomerism of which is discussed above.

The proposed reaction mechanism is described in Scheme 5. The reaction begins with the formation of iminium ion **A**, which tautomerizes to enamine **B**. Next, intramolecular nucleophilic attack of the enamine fragment on the electron-deficient azomethine carbon (C-1) of the isoquinoline cycle results in the formation of spiro intermediate **C**. Finally, acid-promoted isoquinoline ring opening with cleavage of the C1–N bond affords quinoline **3**. This mechanism corresponds well to the observed influence of substituent R^3 on the reaction rate: electron-donating substituents at the *para* position to the amino group in the 2-aminophenyl moiety should increase the electron density on the amino group of starting isoquinolines and on the β-carbon of the enamine fragment of intermediate **B** and promote the nucleophilic attack on carbonyl and intramolecular cyclization of intermediate **B**, respectively; electron-withdrawing groups should act in the opposite direction.

In summary, for the first time we have successfully employed 2-(3,4-dihydroisoquinolin-1-yl)anilines as substrates for the Friedländer reaction. Condensation of differently substituted 2-(3,4-dihydroisoquinolin-1-yl)anilines with various α-methylene ketones in acetic acid afforded



Scheme 5 Proposed reaction mechanism

novel aminoalkyl-functionalized 4-arylquinolines in moderate to excellent yields. We demonstrated that this protocol is very attractive for the construction of unique amino-functionalized quinoline derivatives which are of significant interest for medicinal chemistry. Further studies to extend the scope of the reaction to various 3,4-dihydroisoquinolines and related compounds, and investigation of both synthetic transformations and atropisomerism of the quinolines obtained, are in progress in our laboratory.

TLC was performed on commercially available Sorbfil silica gel plates, which were visualized under UV light (254 nm). Column chromatography was performed on silica gel 60 (0.063–0.200 mm, Macherey-Nagel); flash chromatography was performed on silica gel 60 (0.040–0.063 mm, Merck). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance III HD 400 spectrometer using $CDCl_3$, DMSO-d_6 or D_2O as solvent. ^{1}H chemical shifts were measured relative to internal HMDS (δ_H 0.055 ppm) for $CDCl_3$ and DMSO-d_6, or residual HDO (δ_H 4.79 ppm) for D_2O. ^{13}C chemical shifts were measured relative to the solvent signal (δ_C 77.00 ppm for $CDCl_3$, δ_C 39.50 ppm for DMSO-d_6), or internal dioxane (δ_C 67.19 ppm) for D_2O. The assignment of primary (CH_3), secondary (CH_2), tertiary (CH) and quaternary (C) carbon nuclei was made by using DEPT-135 spectra. The signals in the ^{1}H and ^{13}C NMR spectra of compound **3ab** were assigned on the basis of 2D ^{1}H–^{1}H COSY, ^{1}H–^{1}H NOESY, ^{1}H–^{13}C HSQC and ^{1}H–^{13}C HMBC experiments. Chromatograms and low-resolution mass spectra were obtained with an Agilent 6890N/5975B GC-MS system [HP-5ms column (30 m × 0.25 mm, 0.25 μm), helium as carrier gas, 1 mL/min, electron impact ionization mode (230 °C, 70 eV)]. To improve the GC separation or to obtain a mass spectrum with an intensive M^+ peak, some substances were derivatized by adding a slight excess of $(CF_3CO)_2O$ to the solution before injection. High-resolution mass spectra were recorded with a Bruker maXis HD UHR-QTOF mass spectrometer equipped with an electrospray ionization ion source. IR spectra were recorded on a Bruker IFS 66 FT-IR spectrometer. Elemental analysis was carried out on a Vario EL Cube analyzer. Melting points were determined using a PTP apparatus and are uncorrected. For the synthesis of 2-(3,4-dihydroisoquinolin-1-yl)anilines **1**, see the Supporting Information.

Quinolines 3; General Procedure

A mixture of 2-(3,4-dihydroisoquinolin-1-yl)aniline **1** (0.35 mmol, 1 equiv) and ketone **2** (0.42 mmol, 1.2 equiv) in AcOH (1.5 mL) was heated with stirring at 60 °C until the starting aniline **1** disappeared (5 min to 150 h, monitored by TLC). Then, the reaction mixture was cooled to room temperature, poured into a mixture of crushed ice (5–7 g) and 25% aq NH_3 (2.6 mL), and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with water, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The resulting crude product was analyzed by ^{1}H NMR spectroscopy and purified further if necessary.

1-(4,5-Dimethoxy-2-(1,2,3,4-tetrahydroacridin-9-yl)phenyl)-2-methylpropan-2-amine (3aa)

Prepared using **1a** (109 mg, 0.35 mmol) and cyclohexanone (**2a**; 0.044 mL, 0.42 mmol); reaction time: 30 min. The crude product was purified by recrystallization from acetone/hexane to give pure **3aa**.

Yield: 109 mg (80%); white solid; mp 150–164 °C.

IR (thin film): 3356, 3286, 3062, 2936, 2863, 1605, 1571, 1516, 1493, 1464, 1395, 1371, 1354, 1336, 1290, 1249, 1215, 1166, 1095, 758 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (d, *J* = 8.0 Hz, 1 H), 7.56 (ddd, *J* = 8.3, 6.7, 1.5 Hz, 1 H), 7.34 (dd, *J* = 8.4, 1.0 Hz, 1 H), 7.29 (ddd, *J* = 8.2, 6.7, 1.2 Hz, 1 H), 7.09 (s, 1 H), 6.58 (s, 1 H), 3.94 (s, 3 H), 3.78 (s, 3 H), 3.17 (t, *J* = 6.7 Hz, 2 H), 2.64–2.46 (m, 2 H), 2.38 (d, *J* = 13.7 Hz, 1 H), 2.29 (d, *J* = 13.7 Hz, 1 H), 2.01–1.89 (m, 2 H), 1.83–1.68 (m, 2 H), 1.28 (br s, 2 H), 0.85 (s, 3 H), 0.81 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.2 (C), 148.1 (C), 147.6 (C), 146.5 (C), 145.8 (C), 129.6 (C), 129.2 (C), 129.1 (C), 128.6 (CH), 128.3 (CH), 126.7 (C), 126.0 (CH), 125.4 (CH), 114.4 (CH), 112.8 (CH), 55.9 (2 OCH_3), 51.00 (C), 46.7 (CH_2), 34.1 (CH_2), 30.8 (CH_3), 30.7 (CH_3), 28.0 (CH_2), 22.9 (CH_2), 22.8 (CH_2).

MS (EI, 70 eV): *m*/*z* (%) = 390.1 (0.1) $[M]^+$, 389.1 (0.2) $[M - H]^+$, 375.2 (2) $[M - CH_3]^+$, 333.2 (72) $[M - (CH_3)_2C{=}NH]^+$, 332.2 (55) $[M - (CH_3)_2CNH_2]^+$, 318.2 (100) $[M - CH_2C(CH_3)_2NH_2]^+$, 316.1 (10) $[M - (CH_3)_2CHNH_2 - CH_3]^+$, 302.1 (6) $[M - (CH_3)_2C{=}NH - OCH_3]^+$, 58.1 (37) $[(CH_3)_2C{=}NH_2]^+$.

Anal. Calcd for $C_{25}H_{30}N_2O_2$: C, 76.89; H, 7.74; N, 7.17. Found: C, 77.21; H, 7.96; N, 7.12.

1-(4,5-Dimethoxy-2-(4-methyl-1,2,3,4-tetrahydroacridin-9-yl)phenyl)-2-methylpropan-2-amine (3ab) (Mixture of Atropdiastereomers)

Prepared using **1a** (109 mg, 0.35 mmol) and 2-methylcyclohexanone (**2b**; 0.051 mL, 0.42 mmol); reaction time: 2 h. ^{1}H NMR analysis of the crude product in $CDCl_3$ or DMSO-d_6 indicated the ratio of atropdiastereomers A/B to be ~52:48. The crude product was purified by trituration with hexane to give pure **3ab** as a mixture of atropdiastereomers A/B in a ratio of ~52:48, according to ^{1}H NMR analysis. The chromatogram of a solution of substance **3ab** in CH_2Cl_2 displayed two poorly resolved peaks with retention times t_{R1} ≈13.86 and t_{R2} = 13.91 min, while the mass spectrum from the beginning of the 1st peak to the end of the 2nd apparently did not change [temperature program: 100 °C, rate 30 °C/min, 260 °C, rate 5 °C/min, 300 °C (2 min); inlet: 300 °C]. Under the same temperature program, the trifluoroacetyl derivatives of the stereoisomers showed a better separation, with peak resolution R_s = 1.2 (ratio of peak areas approx. 1:1); retention times were 13.96 and 14.07 min. Mass spectra of the trifluoroacetyl derivatives differed significantly only in intensity of the signal at *m*/*z* 332 (the spectra below were averaged across 6 scans).

Yield: 92 mg (65%); white solid.

Data refer to the inseparable mixture of atropdiastereomers.

IR (thin film): 3359, 3060, 2956, 2934, 2865, 1605, 1570, 1515, 1492, 1464, 1454, 1372, 1356, 1249, 1215, 1189, 1100, 1021, 757 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, *J* = 8.4 Hz, 1 H, 5″-H, both), 7.56 (br t, *J* = 7.6 Hz, 1 H, 6″-H, both), 7.37 (br d, *J* = 8.0 Hz, 1 H, 8″-H, both), 7.33–7.27 (m, 1 H, 7″-H, both), 7.09 (s, 1 H, 6′-H, A), 7.08 (s, 1 H, 6′-H, B), 6.60 (s, 1 H, 3′-H, A), 6.58 (s, 1 H, 3′-H, B), 3.96 (s, 3 H, 5′-OCH_3, both), 3.80 (s, 3 H, 4′-OCH_3, A), 3.79 (s, 3 H, 4′-OCH_3, B), 3.30–3.20 (m, 1 H, 4″-H, both), 2.64–2.47 (m, 2 H, 1″-H^a and 1″-H^b, both), 2.38 (d, *J* = 13.6 Hz, 1 H, 1-H^b, B), 2.36 (d, *J* = 13.6 Hz, 1 H, 1-H^b, A), 2.31 (d, *J* = 13.6 Hz, 1 H, 1-H^a, B), 2.26 (d, *J* = 13.6 Hz, 1 H, 1-H^a, A), 2.17–2.05 (m, 1 H, 3″-H^b, both), 1.83–1.78 (m, 1 H, 2″-H^b, both), 1.76–1.64 (m, 2 H, 2″-H^a and 3″-H^a, both), 1.53 (d, *J* = 7.2 Hz, 3 H, 4″-CH_3, A), 1.51 (d, *J* = 7.2 Hz, 3 H, 4″-CH_3, B), 1.08 (br s, 2 H, NH_2, both), 0.87 (s, 3 H, $C(CH_3)_2$, B), 0.85 (s, 3 H, $C(CH_3)_2$, A), 0.82 (s, 3 H, $C(CH_3)_2$, B), 0.81 (s, 3 H, $C(CH_3)_2$, A).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.1 and 163.0 (C4a″), 148.1 (C5′), 147.6 (C4′), 146.7 and 146.6 (C10a″), 145.6 and 145.5 (C9″), 129.8 and 129.7 (C1′), 129.4 (C2′), 129.0 and 128.89 (C5″), 128.93 and 128.8 (C9a″), 128.14 and 128.12 (C6″), 126.6 (C8a″), 126.0 (C8″), 125.44 and

125.41 (C7″), 114.5 and 114.4 (C6′), 113.0 and 112.9 (C3′), 56.00 (2 OCH_3), 55.98 (2 OCH_3), 50.9 (C2), 46.93 and 46.86 (C1), 37.2 and 37.1 (C4″), 31.2 and 31.0 (C3″), 31.03, 31.01, 30.86 and 30.84 [$C(CH_3)_2$], 28.6 and 28.4 (C1″), 21.9 and 21.4 (4″-CH_3), 20.4 and 20.0 (C2″).

MS (EI, 70 eV): *m*/*z* (%) = 404.1 (0.1) $[M]^+$, 403.1 (0.2) $[M - H]^+$, 389.1 (1) $[M - CH_3]^+$, 347.1 (63) $[M - (CH_3)_2C{=}NH]^+$, 346.1 (42) $[M - (CH_3)_2CNH_2]^+$, 332.1 (100) $[M - CH_2C(CH_3)_2NH_2]^+$, 330.1 (11) $[M - (CH_3)_2CHNH_2 - CH_3]^+$, 316.1 (7) $[M - (CH_3)_2C{=}NH - OCH_3]^+$, 58.1 (46) $[(CH_3)_2C{=}NH_2]^+$.

MS of trifluoroacetyl derivative with t_R 13.96 min (EI, 70 eV): *m*/*z* (%) = 500.1 (25) $[M]^+$, 387.1 (10) $[M - CF_3CONH_2]^+$, 347.0 (46) $[M - CH_2{=}C(CH_3)NHCOCF_3]^+$, 346.0 (100) $[M - (CH_3)_2CNHCOCF_3]^+$, 332.0 (52) $[M - CH_2C(CH_3)_2NHCOCF_3]^+$, 330.0 (19), 153.9 (13) $[(CH_3)_2C{=}NHCOCF_3]^+$.

MS of trifluoroacetyl derivative with t_R 14.07 min (EI, 70 eV): *m*/*z* (%) = 500.1 (26) $[M]^+$, 387.1 (10) $[M - CF_3CONH_2]^+$, 347.0 (47) M – $CH_2{=}C(CH_3)NHCOCF_3]^+$, 346.0 (100) $[M - (CH_3)_2CNHCOCF_3]^+$, 332.0 (47) $[M - CH_2C(CH_3)_2NHCOCF_3]^+$, 330.0 (20), 153.9 (12) $[(CH_3)_2C{=}NHCOCF_3]^+$.

Anal. Calcd for $C_{26}H_{32}N_2O_2$: C, 77.19; H, 7.97; N, 6.92. Found: C, 77.10; H, 8.38; N, 6.82.

1-(2-(2,3-Dihydro-1*H*-cyclopenta[*b*]quinolin-9-yl)-4,5-dimethoxyphenyl)-2-methylpropan-2-amine (3ac)

Prepared using **1a** (109 mg, 0.35 mmol) and cyclopentanone (**2c**; 0.037 mL, 0.42 mmol); reaction time: 1.5 h. The crude product was purified by recrystallization from acetone to give pure **3ac**.

Yield: 96 mg (73%); white solid; mp 215–224 °C.

IR (thin film): 3366, 3294, 3061, 2999, 2956, 2932, 2846, 2834, 1605, 1573, 1517, 1500, 1461, 1441, 1407, 1380, 1352, 1331, 1294, 1268, 1245, 1211, 1152, 1104, 1071, 1001, 781, 767 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.04 (br d, *J* = 8.4 Hz, 1 H), 7.61–7.55 (m, 1 H), 7.50 (br d, *J* = 8.4 Hz, 1 H), 7.38–7.31 (m, 1 H), 7.03 (s, 1 H), 6.65 (s, 1 H), 3.95 (s, 3 H), 3.80 (s, 3 H), 3.28–3.14 (m, 2 H), 2.90–2.72 (m, 2 H), 2.41 (s, 2 H), 2.20–2.06 (m, 2 H), 0.88 (br s, 2 H), 0.82 (s, 3 H), 0.80 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.4 (C), 148.2 (C), 148.0 (C), 147.5 (C), 142.7 (C), 134.5 (C), 129.6 (C), 129.0 (C), 128.9 (CH), 128.2 (CH), 126.5 (C), 125.8 (CH), 125.5 (CH), 114.5 (CH), 112.9 (CH), 56.0 (2 OCH_3), 50.7 (C), 47.1 (CH_2), 35.2 (CH_2), 30.8 (CH_3), 30.7 (CH_2), 30.6 (CH_3), 23.4 (CH_2).

MS (EI, 70 eV): *m*/*z* (%) = 376.1 (0.02) $[M]^+$, 375.2 (0.08) $[M - H]^+$, 361.2 (1) $[M - CH_3]^+$, 319.1 (61) $[M - (CH_3)_2C{=}NH]^+$, 318.1 (100) $[M - (CH_3)_2CNH_2]^+$, 302.1 (8) $[M - (CH_3)_2CHNH_2 - CH_3]^+$, 58.1 (28) $[(CH_3)_2C{=}NH_2]^+$.

Anal. Calcd for $C_{24}H_{28}N_2O_2$: C, 76.56; H, 7.50; N, 7.44. Found: C, 76.34; H, 7.76; N, 7.09.

1-(4,5-Dimethoxy-2-(2-methylquinolin-4-yl)phenyl)-2-methylpropan-2-amine (3ad)

Prepared using **1a** (109 mg, 0.35 mmol) and acetone (**2d**; 0.031 mL, 0.42 mmol); reaction time: 1 h. ^1H NMR analysis of the crude product revealed that no further purification was required.

Yield: 119 mg (97%); white solid; mp 142–158 °C.

IR (thin film): 3357, 3288, 3060, 2959, 2935, 2866, 2845, 1598, 1560, 1517, 1504, 1464, 1410, 1391, 1355, 1256, 1231, 1215, 1192, 1178, 1149, 1096, 763, 754 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 7.96 (br d, *J* = 8.4 Hz, 1 H), 7.70–7.65 (m, 1 H), 7.46–7.40 (m, 2 H), 7.29 (s, 1 H), 7.14 (s, 1 H), 6.75 (s, 1 H), 3.84 (s, 3 H), 3.70 (s, 3 H), 2.68 (s, 3 H), 2.54 (d, *J* = 13.3 Hz, 1 H), 2.21 (d, *J* = 13.3 Hz, 1 H), 1.12 (br s, 2 H), 0.70 (s, 3 H), 0.67 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.0 (C), 148.0 (C), 147.8 (C), 147.5 (C), 146.8 (C), 129.7 (C), 129.4 (C), 129.0 (CH), 128.6 (CH), 125.6 (CH), 125.6 (CH), 125.5 (C), 123.6 (CH), 114.9 (CH), 113.5 (CH), 55.52 (OCH_3), 55.48 (OCH_3), 50.3 (C), 46.3 (CH_2), 30.7 (CH_3), 30.4 (CH_3), 24.8 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 350.1 (0.03) $[M]^+$, 349.1 (0.08) $[M - H]^+$, 335.1 (1) $[M - CH_3]^+$, 293.1 (52) $[M - (CH_3)_2C{=}NH]^+$, 292.1 (100) $[M - (CH_3)_2CNH_2]^+$, 278.0 (9) $[M - CH_2C(CH_3)_2NH_2]^+$, 276.0 (8) $[M - (CH_3)_2CHNH_2 - CH_3]^+$, 58.1 (30) $[(CH_3)_2C{=}NH_2]^+$.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{22}H_{27}N_2O_2$: 351.2067; found: 351.2072.

1-(2-(2,3-Dimethylquinolin-4-yl)-4,5-dimethoxyphenyl)-2-methylpropan-2-amine (3ae) and 1-(2-(2-Ethylquinolin-4-yl)-4,5-dimethoxyphenyl)-2-methylpropan-2-amine (3ae′)

Prepared using **1a** (109 mg, 0.35 mmol) and methyl ethyl ketone (**2e**; 0.038 mL, 0.42 mmol); reaction time 2 h. ^1H NMR analysis of the crude product indicated the ratio of regioisomers **3ae**/**3ae′** to be 78:22; no further purification was required.

Combined yield of both regioisomers **3ae** and **3ae′**: 100 mg (78%); white solid.

Data refer to the inseparable mixture of regioisomers **3ae** and **3ae′**.

IR (thin film): 3361, 2998, 2960, 2932, 2861, 2837, 1603, 1586, 1515, 1494, 1455, 1397, 1368, 1327, 1290, 1263, 1244, 1215, 1102, 1074, 1026, 996, 897, 863, 839, 777 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ (**3ae**) = 7.91 (dd, *J* = 8.4, 0.8 Hz, 1 H), 7.59 (ddd, *J* = 8.4, 6.8, 1.6 Hz, 1 H), 7.37 (ddd, *J* = 8.4, 6.8, 1.2 Hz, 1 H), 7.27–7.25 (m, 1 H), 7.26 (s, 1 H), 6.61 (s, 1 H), 3.844 (s, 3 H), 3.68 (s, 3 H), 2.67 (s, 3 H), 2.25 (d, *J* = 13.6 Hz, 1 H), 2.20 (d, *J* = 13.6 Hz, 1 H), 2.14 (s, 3 H), 1.15 (br s, 2 H), 0.71 (s, 3 H), 0.67 (s, 3 H); δ (**3ae′**) = 7.98 (dt, *J* = 8.4, 0.8 Hz, 1 H), 7.70–7.65 (m, 1 H), 7.44–7.43 (m, 2 H), 7.30 (s, 1 H), 7.13 (s, 1 H), 6.76 (s, 1 H), 3.840 (s, 3 H), 3.71 (s, 3 H), 2.96 (qd, *J* = 7.6, 2.0 Hz, 2 H), 2.54 (d, *J* = 13.2 Hz, 1 H), 2.20 (d, *J* = 13.6 Hz, 1 H), 1.33 (t, *J* = 7.8 Hz, 3 H), 0.70 (s, 3 H), 0.67 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ (**3ae**) = 158.7 (C), 147.6 (C), 147.0 (C), 145.6 (C), 145.1 (C), 130.1 (C), 128.6 (C), 128.3 (CH), 128.1 (C), 127.8 (CH), 126.5 (C), 126.0 (CH), 125.4 (CH), 114.7 (CH), 113.1 (CH), 55.50 (OCH_3), 55.4 (OCH_3), 50.4 (C), 46.2 (CH_2), 30.70 (2 CH_3), 24.2 (CH_3), 16.9 (CH_3); δ (**3ae′**) = 162.7 (C), 148.1 (C), 147.8 (C), 147.5 (C), 146.9 (C), 129.8 (C), 129.4 (C), 129.0 (CH), 128.8 (CH), 125.8 (C), 125.7 (CH), 125.5 (CH), 122.7 (CH), 115.0 (CH), 113.5 (CH), 55.53 (OCH_3), 50.3 (C), 46.3 (CH_2), 31.3 (CH_2), 30.66 (CH_3), 30.3 (CH_3), 13.5 (CH_3); the missing signal for one of the OCH_3 groups is overlapped.

MS (EI, 70 eV): **3ae** *m*/*z* (%) = 364.3 (0.05) $[M]^+$, 363.1 (0.2) $[M - H]^+$, 349.2 (2) $[M - CH_3]^+$, 307.1 (71) $[M - (CH_3)_2C{=}NH]^+$, 306.1 (67) $[M - (CH_3)_2CNH_2]^+$, 292.1 (100) $[M - CH_2C(CH_3)_2NH_2]^+$, 290.1 (6) $[M - (CH_3)_2CHNH_2 - CH_3]^+$, 276.1 (9) $[M - (CH_3)_2C{=}NH - OCH_3]^+$, 58.1 (34) $[(CH_3)_2C{=}NH_2]^+$; MS of trifluoroacetyl derivative (EI, 70 eV): *m*/*z* (%) = 460.2 (25) $[M]^+$, 347.1 (21) $[M - CF_3CONH_2]^+$, 307.1 (52) $[M - CF_3CONC(CH_3)_2]^+$, 306.1 (100) $[M - CF_3CONHC(CH_3)_2]^+$, 292.1 (67) $[M - CF_3CONHC(CH_3)_2CH_2]^+$, 291.1 (23), 290.1 (16), 276.1 (12), 260.0 (19), 154.0 (16) $[CF_3CONHC(CH_3)_2]^+$; **3ae′** *m*/*z* (%) = $[M]^+$ not detected, 363.1 (0.1) $[M - H]^+$, 349.2 (1) $[M - CH_3]^+$, 307.1 (51) $[M - (CH_3)_2C{=}NH]^+$, 306.1 (100) $[M - (CH_3)_2CNH_2]^+$, 290.1 (7) $[M - (CH_3)_2CHNH_2 - CH_3]^+$, 278.1 (7) $[M - (CH_3)_2C{=}NH - C_2H_5]^+$, 58.1 (31) $[(CH_3)_2C{=}NH_2]^+$; MS of

trifluoroacetyl derivative: *m*/*z* (%) = 460.2 (25) [M]$^+$, 306.1 (100) [M – $CF_3CONHC(CH_3)_2$]$^+$, 292.1 (67) [M – $CF_3CONHC(CH_3)_2CH_2$]$^+$, 290.1 (17), 154.0 (16) [$CF_3CONHC(CH_3)_2$]$^+$.

Anal. Calcd for $C_{23}H_{28}N_2O_2$: C, 75.79; H, 7.74; N, 7.69. Found: C, 76.02; H, 7.88; N, 7.27.

1-(2-(3-Benzyl-2-methylquinolin-4-yl)-4,5-dimethoxyphenyl)-2-methylpropan-2-amine (3af) and 1-(4,5-Dimethoxy-2-(2-phenethylquinolin-4-yl)phenyl)-2-methylpropan-2-amine (3af′)

Prepared using **1a** (109 mg, 0.35 mmol) and benzylacetone (**2f**; 0.063 mL, 0.42 mmol); reaction time: 2.5 h. ^{1}H NMR analysis of the crude product indicated the ratio of regioisomers **3af**/**3af′** to be 67:33. The crude product was recrystallized from acetone/hexane to give a pure regioisomeric mixture of **3af**/**3af′** in a ratio of 79:21, according to ^{1}H NMR analysis.

Combined yield of both regioisomers **3af** and **3af′**: 85 mg (55%); white solid.

Data refer to the inseparable mixture of regioisomers **3af** and **3af′**.

IR (thin film): 3359, 3291, 3061, 3025, 3000, 2958, 2935, 2845, 1604, 1582, 1516, 1494, 1465, 1452, 1407, 1392, 1372, 1351, 1253, 1215, 1190, 1159, 1106, 1085, 870, 772, 753, 723, 697 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (**3af**) = 8.06 (d, *J* = 8.4 Hz, 1 H), 7.65–7.61 (m, 1 H), 7.40–7.33 (m, 2 H), 7.20–7.08 (m, 3 H), 7.07 (s, 1 H), 6.88 (br d, *J* = 7.1 Hz, 2 H), 6.45 (s, 1 H), 4.03 (s, 2 H), 3.92 (s, 3 H), 3.36 (s, 3 H), 2.65 (s, 3 H), 2.39 (d, *J* = 13.6 Hz, 1 H), 2.30 (d, *J* = 13.8 Hz, 1 H), 1.46 (br s, 2 H), 0.87 (s, 3 H), 0.85 (s, 3 H); δ (**3af′**) = 8.11 (d, *J* = 8.4 Hz, 1 H), 7.69–7.64 (m, 1 H), 7.50 (br d, *J* = 8.0 Hz, 1 H), 7.40–7.33 (m, 1 H), 7.27–7.22 (m, 3 H), 7.20–7.08 (m, 3 H), 6.99 (s, 1 H), 6.65 (s, 1 H), 3.95 (s, 3 H), 3.81 (s, 3 H), 3.36–3.13 (m, 4 H), 2.59 (d, *J* = 13.6 Hz, 1 H), 2.31 (d, *J* = 13.6 Hz, 1 H), 1.46 (br s, 2 H), 0.81 (br s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (**3af**) = 159.6 (C), 148.2 (C), 147.20 (C), 147.15 (C), 146.8 (C), 139.8 (C), 130.0 (C), 129.2 (C), 129.1 (C), 128.8 (CH), 128.7 (CH), 128.4 (2 CH), 127.9 (2 CH), 126.9 (C), 126.5 (CH), 126.0 (CH), 125.8 (CH), 114.3 (CH), 113.0 (CH), 56.0 (OCH_3), 55.4 (OCH_3), 51.4 (C), 46.4 (CH_2), 36.5 (CH_2), 30.5 (CH_3), 30.4 (CH_3), 24.4 (CH_3); δ (**3af′**) = 161.1 (C), 148.6 (C), 148.4 (C), 148.3 (C), 147.5 (C), 141.4 (C), 130.7 (C), 129.31 (CH), 129.27 (CH), 129.0 (C), 128.5 (2 CH), 126.2 (C), 125.9 (CH), 123.3 (CH), 114.5 (CH), 113.7 (CH), 56.1 (OCH_3), 51.2 (C), 40.8 (CH_2), 35.8 (CH_2), 30.8 (CH_3), 30.2 (CH_3); the missing signals for one of the OCH_3 and CH_2 groups, as well as for four aromatic CH carbons, are overlapped.

MS (EI, 70 eV): **3af** *m*/*z* (%) = 440.2 (0.02) [M]$^+$, 439.0 (0.07) [M – H]$^+$, 425.1 (0.8) [M – CH_3]$^+$, 383.2 (18) [M – $(CH_3)_2C{=}NH$]$^+$, 382.1 (6) [M – $(CH_3)_2CNH_2$]$^+$, 368.2 (100) [M – $CH_2C(CH_3)_2NH_2$]$^+$, 352.1 (5) [M – $(CH_3)_2C{=}NH$ – OCH_3]$^+$, 292.1 (5) [M – $(CH_3)_2C{=}NH$ – $PhCH_2$]$^+$, 91.1 (5) [$PhCH_2$]$^+$, 58.1 (23) [$(CH_3)_2C{=}NH_2$]$^+$; **3af′** *m*/*z* (%) = 440.0 (0.05) [M]$^+$, 439.0 (0.1) [M – H]$^+$, 425.1 (1) [M – CH_3]$^+$, 383.1 (62) [M – $(CH_3)_2C{=}NH$]$^+$, 382.1 (100) [M – $(CH_3)_2CNH_2$]$^+$, 368.1 (5) [M – $CH_2C(CH_3)_2NH_2$]$^+$, 366.0 (6) [M – $(CH_3)_2CHNH_2$ – CH_3]$^+$, 278 (10) [M – $(CH_3)_2C{=}NH$ – CH_2CH_2Ph and/or M – $(CH_3)_2CNH_2$ – $CH_2{=}CHPh$]$^+$, 58.1 (31) [$(CH_3)_2C{=}NH_2$]$^+$.

Anal. Calcd for $C_{29}H_{32}N_2O_2$: C, 79.06; H, 7.32; N, 6.36. Found: C, 79.36; H, 7.49; N, 6.07.

1-(2-(3-Allyl-2-methylquinolin-4-yl)-4,5-dimethoxyphenyl)-2-methylpropan-2-amine (3ag) and 1-(2-(2-(But-3-en-1-yl)quinolin-4-yl)-4,5-dimethoxyphenyl)-2-methylpropan-2-amine (3ag′)

Prepared using **1a** (109 mg, 0.35 mmol) and allylacetone (**2g**; 0.049 mL, 0.42 mmol); reaction time 5 h. ^{1}H NMR analysis of the crude product indicated the ratio of regioisomers **3ag**/**3ag′** to be 69:31. The crude residue was purified by silica gel flash chromatography (EtOAc/MeOH, 4:1 → 1:1) to afford (in order of elution) **3ag** (40 mg, 29%), a mixture of **3ag** and **3ag′** (46 mg, **3ag**/**3ag′** = 78:22) and a mixture of **3ag** and **3ag′** (20 mg, **3ag**/**3ag′** = 13:87).

Combined yield of both regioisomers **3ag** and **3ag′**: 106 mg (77%).

3ag: white solid; mp 130–134 °C (acetone/hexane); R_f = 0.10 (EtOAc/MeOH, 4:1).

IR (thin film): 3359, 3290, 3077, 3061, 2999, 2958, 2934, 2846, 1636, 1606, 1581, 1516, 1493, 1465, 1445, 1393, 1372, 1351, 1252, 1215, 1190, 1160, 1106, 1089, 1014, 999, 916, 870, 772, 761 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03 (br d, *J* = 8.4 Hz, 1 H), 7.64–7.57 (m, 1 H), 7.34–7.32 (m, 2 H), 7.10 (s, 1 H), 6.65 (s, 1 H), 5.91–5.81 (m, 1 H), 5.03 (dq, *J* = 10.2, 1.7 Hz, 1 H), 4.78 (dq, *J* = 17.1, 1.9 Hz, 1 H), 3.96 (s, 3 H), 3.77 (s, 3 H), 3.37–3.34 (m, 2 H), 2.77 (s, 3 H), 2.33 (d, *J* = 13.6 Hz, 1 H), 2.27 (d, *J* = 13.6 Hz, 1 H), 1.22 (br s, 2 H), 0.85 (s, 3 H), 0.82 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.3 (C), 148.3 (C), 147.2 (C), 146.7 (C), 146.6 (C), 135.9 (CH), 129.6 (C), 129.5 (C), 129.2 (C), 128.7 (CH), 128.6 (CH), 127.0 (C), 126.5 (CH), 125.7 (CH), 116.0 (CH_2), 114.2 (CH), 113.3 (CH), 56.0 (OCH_3), 55.9 (OCH_3), 50.8 (C), 46.9 (CH_2), 35.0 (CH_2), 31.0 (CH_3), 30.9 (CH_3), 24.0 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 390.2 (0.04) [M]$^+$, 333.1 (35) [M – $(CH_3)_2C{=}NH$]$^+$, 332.1 (16) [M – $(CH_3)_2CNH_2$]$^+$, 318.1 (100) [M – $CH_2C(CH_3)_2NH_2$]$^+$, 305.1 (55) [M – $(CH_3)_2CNH_2$ – $CH{=}CH_2$]$^+$, 304.1 (67) [M – $(CH_3)_2CNH_2$ – $CH_2{=}CH_2$]$^+$, 302.1 (11) [M – $(CH_3)_2C{=}NH$ – OCH_3]$^+$, 182.1 (34) [$C_9H_4N(CH_3)(CH_2CH{=}CH_2)$]$^+$, 58.1 (64) [$(CH_3)_2C{=}NH_2$]$^+$.

Anal. Calcd for $C_{25}H_{30}N_2O_2$: C, 76.89; H, 7.74; N, 7.17. Found: C, 77.12; H, 7.63; N, 7.12.

3ag′: R_f = 0.14 (EtOAc/MeOH, 4:1).

Data refer to the inseparable mixture of regioisomers **3ag** and **3ag′** (**3ag**/**3ag′** = 13:87).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08 (br d, *J* = 8.4 Hz, 1 H), 7.65 (ddd, *J* = 8.4, 6.8, 1.4 Hz, 1 H), 7.51 (br d, *J* = 8.2 Hz, 1 H), 7.37 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1 H), 7.20 (s, 1 H), 7.00 (s, 1 H), 6.72 (s, 1 H), 5.98–5.87 (m, 1 H), 5.07 (dq, *J* = 17.2, 1.6 Hz, 1 H), 4.99–4.96 (m, 1 H), 3.96 (s, 3 H), 3.82 (s, 3 H), 3.12–3.07 (m, 2 H), 2.66 (d, *J* = 13.6 Hz, 1 H), 2.64–2.58 (m, 2 H), 2.35 (d, *J* = 13.6 Hz, 1 H), 2.00 (br s, 2 H), 0.84 (s, 3 H), 0.82 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.4 (C), 148.6 (C), 148.5 (C), 148.3 (C), 147.5 (C), 137.7 (CH), 130.7 (C), 129.7 (2 CH), 129.2 (C), 126.2 (C), 125.9 (CH), 125.8 (CH), 123.1 (CH), 115.3 (CH_2), 114.5 (CH), 113.7 (CH), 56.1 (OCH_3), 56.0 (OCH_3), 51.0 (C), 46.6 (CH_2), 38.5 (CH_2), 33.7 (CH_2), 30.44 (CH_3), 30.39 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 390.1 (0.05) [M]$^+$, 333.1 (56) [M – $(CH_3)_2C{=}NH$]$^+$, 332.1 (100) [M – $(CH_3)_2CNH_2$]$^+$, 58.1 (32) [$(CH_3)_2C{=}NH_2$]$^+$.

1-(2-(2-Isobutylquinolin-4-yl)-4,5-dimethoxyphenyl)-2-methylpropan-2-amine (3ah)

Prepared using **1a** (109 mg, 0.35 mmol) and methyl isobutyl ketone (**2h**; 0.053 mL, 0.42 mmol); reaction time: 3 h. The crude product was purified by recrystallization from hexane to give pure **3ah**.

Yield: 84 mg (61%); white solid; mp 113–115 °C.

IR (thin film): 3360, 3060, 2957, 2934, 2868, 2845, 1597, 1556, 1517, 1501, 1465, 1411, 1365, 1255, 1230, 1214, 1178, 1150, 1098, 1085, 1009, 756 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.09 (br d, *J* = 8.4 Hz, 1 H), 7.65 (ddd, *J* = 8.4, 6.8, 1.4 Hz, 1 H), 7.52 (dd, *J* = 8.4, 0.8 Hz, 1 H), 7.38 (ddd, *J* = 8.1, 6.8, 1.1 Hz, 1 H), 7.18 (s, 1 H), 7.01 (s, 1 H), 6.73 (s, 1 H), 3.96 (s, 3 H), 3.82 (s, 3 H), 2.92–2.83 (m, 2 H), 2.66 (d, *J* = 13.6 Hz, 1 H), 2.36 (d, *J* = 13.6 Hz, 1 H), 2.31–2.17 (m, 1 H), 1.15 (br s, 2 H), 1.00 (d, *J* = 6.6 Hz, 6 H), 0.84 (s, 3 H), 0.81 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.6 (C), 148.4 (C), 148.3 (C), 148.3 (C), 147.4 (C), 130.7 (C), 129.4 (C), 129.3 (CH), 129.1 (CH), 126.2 (C), 125.8 (2 CH), 123.7 (CH), 114.5 (CH), 113.7 (CH), 56.1 (OCH_3), 56.0 (OCH_3), 50.7 (C), 48.4 (CH_2), 46.9 (CH_2), 30.7 (CH_3), 30.7 (CH_3), 29.4 (CH), 22.6 (CH_3), 22.5 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 392.2 (0.07) $[M]^+$, 391.2 (0.3) $[M - H]^+$, 377.2 (1) $[M - CH_3]^+$, 335.2 (54) $[M - (CH_3)_2C{=}NH]^+$, 334.2 (100) $[M - (CH_3)_2CNH_2]^+$, 318.1 (8) $[M - (CH_3)_2CHNH_2 - CH_3]^+$, 278.1 (10) [M – $(CH_3)_2C{=}NH$ – C_4H_9 and/or M – $(CH_3)_2CNH_2$ – $C_4H_8]^+$, 58.1 (29) $[(CH_3)_2C{=}NH_2]^+$.

Anal. Calcd for $C_{25}H_{32}N_2O_2$: C, 76.49; H, 8.22; N, 7.14. Found: C, 76.90; H, 8.34; N, 6.99.

1-(2-(2-*tert*-Butylquinolin-4-yl)-4,5-dimethoxyphenyl)-2-methylpropan-2-amine (3ai)

Prepared using **1a** (109 mg, 0.35 mmol) and pinacolone (**2i**; 0.052 mL, 0.42 mmol); reaction time: 150 h (60 °C), 15 h (90 °C). The crude residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/TEA, 98.5:1:0.5) to afford crude products **3ai** and **4**, which were further recrystallized from hexane to give pure quinoline **3ai** (60 °C: 41 mg, 30%; 90 °C: 44 mg, 32%) and amide **4** (60 °C: 15 mg, 12%; 90 °C: 18 mg, 15%).

3ai: white solid; mp 122–126 °C; R_f = 0.35 (CH_2Cl_2/MeOH/TEA, 98.5:1:0.5).

IR (thin film): 3361, 3293, 3060, 2959, 2934, 2909, 2866, 1605, 1594, 1555, 1516, 1501, 1465, 1409, 1391, 1357, 1263, 1243, 1233, 1214, 1180, 1149, 1092, 1022, 1008, 869, 785, 763 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.09 (br d, *J* = 8.4 Hz, 1 H), 7.63 (ddd, *J* = 8.4, 6.8, 1.6 Hz, 1 H), 7.48 (dd, *J* = 8.4, 0.8 Hz, 1 H), 7.42 (s, 1 H), 7.36 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1 H), 7.00 (s, 1 H), 6.74 (s, 1 H), 3.96 (s, 3 H), 3.83 (s, 3 H), 2.61 (d, *J* = 13.6 Hz, 1 H), 2.33 (d, *J* = 13.6 Hz, 1 H), 1.48 (s, 9 H), 1.06 (br s, 2 H), 0.84 (s, 3 H), 0.82 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.5 (C), 148.3 (C), 148.2 (C), 147.7 (C), 147.4 (C), 131.3 (C), 129.8 (CH), 129.5 (C), 128.9 (CH), 126.0 (C), 125.8 (CH), 125.5 (CH), 120.2 (CH), 114.5 (CH), 113.7 (CH), 56.1 (OCH_3), 56.0 (OCH_3), 50.7 (C), 46.9 (CH_2), 38.1 (C), 30.8 (CH_3), 30.7 (CH_3), 30.1 (3 CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 392.2 (0.05) $[M]^+$, 391.2 (0.2) $[M - H]^+$, 377.2 (1) $[M - CH_3]^+$, 335.2 (54) $[M - (CH_3)_2C{=}NH]^+$, 334.2 (100) $[M - (CH_3)_2CNH_2]^+$, 318.1 (8) $[M - (CH_3)_2CHNH_2 - CH_3]^+$, 278.1 (7) [M – $(CH_3)_2C{=}NH$ – C_4H_9 and/or M – $(CH_3)_2CNH_2$ – $C_4H_8]^+$, 58.1 (28) $[(CH_3)_2C{=}NH_2]^+$.

Anal. Calcd for $C_{25}H_{32}N_2O_2$: C, 76.49; H, 8.22; N, 7.14. Found: C, 76.54; H, 8.59; N, 7.09.

Characterization data for amide **4** are given below.

1-(4,5-Dimethoxy-2-(2-phenylquinolin-4-yl)phenyl)-2-methylpropan-2-amine (3aj)

Prepared using **1a** (109 mg, 0.35 mmol) and acetophenone (**2j**; 0.049 mL, 0.42 mmol); reaction time: 125 h (60 °C), 22 h (90 °C). The crude residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/TEA, 98.5:1:0.5) to afford crude products **3aj** and **4**, which were further recrystallized from acetone/hexane (for **3aj**) or hexane (for **4**) to give pure quinoline **3aj** (60 °C: 78 mg, 54%; 90 °C: 75 mg, 52%) and amide **4** (60 °C: 12 mg, 10%; 90 °C: 7 mg, 6%).

3aj: white solid; mp 172–174 °C; R_f = 0.30 (CH_2Cl_2/MeOH/TEA, 98.5:1:0.5).

IR (thin film): 3358, 3291, 3060, 3000, 2959, 2934, 2844, 1593, 1546, 1516, 1504, 1494, 1464, 1445, 1409, 1390, 1361, 1262, 1247, 1231, 1213, 1184, 1096, 773, 753, 696 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.31–8.27 (m, 2 H), 8.13 (br d, *J* = 8.4 Hz, 1 H), 8.00 (s, 1 H), 7.79–7.73 (m, 1 H), 7.57–7.48 (m, 5 H), 7.16 (s, 1 H), 6.87 (s, 1 H), 3.86 (s, 3 H), 3.73 (s, 3 H), 2.58 (d, *J* = 13.2 Hz, 1 H), 2.26 (d, *J* = 13.2 Hz, 1 H), 1.14 (br s, 2 H), 0.72 (s, 3 H), 0.70 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 155.4 (C), 149.2 (C), 148.0 (C), 147.8 (C), 147.0 (C), 138.7 (C), 129.9 (C), 129.61 (CH), 129.60 (CH), 129.56 (CH), 129.5 (C), 128.8 (2 CH), 127.2 (2 CH), 126.5 (CH), 126.3 (C), 125.7 (CH), 120.4 (CH), 115.0 (CH), 113.7 (CH), 55.6 (OCH_3), 55.5 (OCH_3), 50.4 (C), 46.5 (CH_2), 30.7 (CH_3), 30.4 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 412.2 (0.03) $[M]^+$, 411.1 (0.08) $[M - H]^+$, 397.1 (0.9) $[M - CH_3]^+$, 355.1 (58) $[M - (CH_3)_2C{=}NH]^+$, 354.1 (100) $[M - (CH_3)_2CNH_2]^+$, 338.1 (10) $[M - (CH_3)_2CHNH_2 - CH_3]^+$, 278.1 (6) [M – $(CH_3)_2C{=}NH$ – Ph]$^+$, 58.1 (28) $[(CH_3)_2C{=}NH_2]^+$.

Anal. Calcd for $C_{27}H_{28}N_2O_2$: C, 78.61; H, 6.84; N, 6.79. Found: C, 78.50; H, 6.86; N, 6.73.

Characterization data for amide **4** are given below.

1-(2-(2-(4-Chlorophenyl)quinolin-4-yl)-4,5-dimethoxyphenyl)-2-methylpropan-2-amine (3ak)

Prepared using **1a** (109 mg, 0.35 mmol) and 4′-chloroacetophenone (**2k**; 0.054 mL, 0.42 mmol); reaction time: 63 h (60 °C), 20 h (90 °C). The crude residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/TEA, 98.5:1:0.5) to afford crude products **3ak** and **4**, which were further recrystallized from hexane/CH_2Cl_2 (for **3ak**) or hexane (for **4**) to give pure quinoline **3ak** (60 °C: 61 mg, 39%; 90 °C: 63 mg, 40%) and amide **4** (60 °C: 6 mg, 5%; 90 °C: 12 mg, 10%).

3ak: white solid; mp 139–142.5 °C; R_f = 0.35 (CH_2Cl_2/MeOH/TEA, 98.5:1:0.5).

IR (thin film): 3360, 3061, 3002, 2959, 2934, 2848, 1593, 1544, 1516, 1504, 1492, 1464, 1417, 1361, 1261, 1247, 1232, 1213, 1182, 1093, 1012, 866, 835, 754 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19 (br d, *J* = 8.4 Hz, 1 H), 8.15–8.12 (m, 2 H), 7.76 (s, 1 H), 7.70 (ddd, *J* = 8.4, 6.8, 1.4 Hz, 1 H), 7.56 (dd, *J* = 8.4, 0.9 Hz, 1 H), 7.50–7.46 (m, 2 H), 7.43 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1 H), 7.04 (s, 1 H), 6.77 (s, 1 H), 3.97 (s, 3 H), 3.83 (s, 3 H), 2.66 (d, *J* = 13.6 Hz, 1 H), 2.39 (d, *J* = 13.6 Hz, 1 H), 1.32 (br s, 2 H), 0.86 (s, 3 H), 0.85 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.3 (C), 149.6 (C), 148.60 (C), 148.55 (C), 147.5 (C), 138.0 (C), 135.7 (C), 130.7 (C), 130.1 (CH), 129.7 (CH), 129.5 (C), 129.1 (2 CH), 128.8 (2 CH), 126.8 (C), 126.6 (CH), 125.9 (CH), 120.3 (CH), 114.5 (CH), 113.6 (CH), 56.1 (OCH_3), 56.0 (OCH_3), 50.8 (C), 46.9 (CH_2), 30.9 (CH_3), 30.8 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 446.1 (0.03) $[M]^+$, 445.1 (0.07) $[M - H]^+$, 431.1 (0.9) $[M - CH_3]^+$, 389.1 (59) $[M - (CH_3)_2C{=}NH]^+$, 388.1 (100) $[M - (CH_3)_2CNH_2]^+$, 372.1 (9) $[M - (CH_3)_2CHNH_2 - CH_3]^+$, 278.1 (6) [M – $(CH_3)_2C{=}NH$ – $ClC_6H_4]^+$, 58.1 (45) $[(CH_3)_2C{=}NH_2]^+$.

Anal. Calcd for $C_{27}H_{27}ClN_2O_2$: C, 72.55; H, 6.09; N, 6.27. Found: C, 72.17; H, 6.38; N, 6.11.

Characterization data for amide **4** are given below.

1-(2-(2-(3,4-Dimethoxyphenyl)quinolin-4-yl)-4,5-dimethoxyphenyl)-2-methylpropan-2-amine (3al)

Prepared using **1a** (109 mg, 0.35 mmol) and 3′,4′-dimethoxyacetophenone (**2l**; 76 mg, 0.42 mmol); reaction time: 120 h (60 °C), 24 h (90 °C). The crude residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/TEA, 98.5:1:0.5) to afford crude products **3al** and **4**, which were further recrystallized from hexane/CH_2Cl_2 (for **3al**) or hexane (for **4**) to give pure quinoline **3al** (60 °C: 73 mg, 44%; 90 °C: 66 mg, 40%) and amide **4** (60 °C: 15 mg, 12%; 90 °C: 25 mg, 23%).

3al: white solid; mp 112–113.5 °C; R_f = 0.35 (CH_2Cl_2/MeOH/TEA, 98.5:1:0.5).

IR (thin film): 3359, 3061, 3002, 2959, 2935, 2838, 1673, 1593, 1546, 1517, 1500, 1464, 1423, 1348, 1263, 1242, 1214, 1172, 1147, 1132, 1096, 1026, 872, 753 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.19 (dd, *J* = 8.4, 0.5 Hz, 1 H), 7.92 (d, *J* = 2.0 Hz, 1 H), 7.77 (s, 1 H), 7.71–7.65 (m, 2 H), 7.53 (dd, *J* = 8.4, 1.0 Hz, 1 H), 7.40 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1 H), 7.04 (s, 1 H), 6.98 (d, *J* = 8.4 Hz, 1 H), 6.79 (s, 1 H), 4.04 (s, 3 H), 3.98 (s, 3 H), 3.95 (s, 3 H), 3.84 (s, 3 H), 2.67 (d, *J* = 13.6 Hz, 1 H), 2.40 (d, *J* = 13.6 Hz, 1 H), 1.05 (br s, 2 H), 0.87 (s, 3 H), 0.85 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.1 (C), 150.6 (C), 149.6 (C), 149.1 (C), 148.6 (C), 148.5 (C), 147.5 (C), 132.5 (C), 130.9 (C), 130.0 (CH), 129.53 (C), 129.49 (CH), 126.6 (C), 126.1 (CH), 125.8 (CH), 120.3 (CH), 120.3 (CH), 114.5 (CH), 113.7 (CH), 111.2 (CH), 110.6 (CH), 56.1 (2 OCH_3), 56.0 (2 OCH_3), 50.8 (C), 46.9 (CH_2), 30.9 (CH_3), 30.8 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 472.1 (0.06) $[M]^+$, 471.1 (0.1) $[M - H]^+$, 457.1 (0.6) $[M - CH_3]^+$, 415.1 (57) $[M - (CH_3)_2C{=}NH]^+$, 414.1 (100) $[M - (CH_3)_2CNH_2]^+$, 398.1 (10) $[M - (CH_3)_2CHNH_2 - CH_3]^+$, 278.1 (5) $[M - (CH_3)_2C{=}NH - Ar]^+$, 58.1 (31) $[(CH_3)_2C{=}NH_2]^+$.

Anal. Calcd for $C_{29}H_{32}N_2O_4{\cdot}0.75\ CH_2Cl_2$: C, 66.63; H, 6.30; N, 5.22. Found: C, 66.78; H, 6.66; N, 5.07.

Characterization data for amide **4** are given below.

1-(4-(2-(2-Amino-2-methylpropyl)-4,5-dimethoxyphenyl)-2-methylquinolin-3-yl)ethanone (3am)

Prepared using **1a** (109 mg, 0.35 mmol) and acetylacetone (**2m**; 0.043 mL, 0.42 mmol); reaction time: 2 h. The crude product was purified by recrystallization from MeOH to give pure **3am**.

Yield: 85 mg (59%); white solid; mp 147–154 °C.

IR (thin film): 3360, 3298, 3063, 3001, 2961, 2936, 2848, 1697, 1605, 1564, 1545, 1517, 1492, 1465, 1444, 1404, 1393, 1369, 1354, 1252, 1220, 1209, 1180, 1150, 1098, 761 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 7.99 (br d, *J* = 8.4 Hz, 1 H), 7.75 (ddd, *J* = 8.4, 6.8, 1.5 Hz, 1 H), 7.60 (dd, *J* = 8.4, 0.8 Hz, 1 H), 7.50 (ddd, *J* = 8.4, 6.8, 1.2 Hz, 1 H), 7.31 (s, 1 H), 6.82 (s, 1 H), 3.84 (s, 3 H), 3.72 (s, 3 H), 2.59 (s, 3 H), 2.26 (d, *J* = 14.0 Hz, 1 H), 2.22 (d, *J* = 14.0 Hz, 1 H), 2.01 (s, 3 H), 1.08 (br s, 2 H), 0.71 (s, 3 H), 0.64 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 204.7 (C), 153.0 (C), 148.4 (C), 147.0 (C), 146.6 (C), 143.2 (C), 135.0 (C), 130.9 (C), 129.9 (CH), 128.4 (CH), 126.7 (CH), 126.6 (C), 126.2 (CH), 125.3 (C), 114.9 (CH), 113.4 (CH), 55.6 (OCH_3), 55.4 (OCH_3), 50.2 (C), 46.3 (CH_2), 31.6 (CH_3), 31.2 (CH_3), 30.3 (CH_3), 23.4 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = $[M]^+$ not detected, 391.1 (0.04) $[M - H]^+$, 377.1 (1) $[M - CH_3]^+$, 335.1 (85) $[M - (CH_3)_2C{=}NH]^+$, 334.1 (82) $[M - (CH_3)_2CNH_2]^+$, 320.1 (100) $[M - CH_2C(CH_3)_2NH_2]^+$, 318.1 (14) $[M - (CH_3)_2CHNH_2 - CH_3]^+$, 304.1 (6) $[M - (CH_3)_2C{=}NH - OCH_3]$, 292.1 (53) $[M - (CH_3)_2C{=}NH - CH_3CO]$, 276.1 (15) $[M - (CH_3)_3CNH_2 - CH_3CO]^+$, 58.1 (82) $[(CH_3)_2C{=}NH_2]^+$, 43.0 (5) $[CH_3CO]^+$.

MS of trifluoroacetyl derivative (EI, 70 eV): *m*/*z* (%) = 488.2 (12) $[M]^+$, 375.1 (100) $[M - CF_3CONH_2]^+$, 335.1 (100) $[M - CF_3CONC(CH_3)_2]^+$, 334.1 (55) $[M - CF_3CONHC(CH_3)_2]^+$, 332.1 (17) 320.1 (100) $[M - CF_3CONHC(CH_3)_2CH_2]^+$, 318.1 (37), 316.1 (11), 292.1 (93), 276.1 (35), 248.1 (11), 218.0 (10), 154.0 (28) $[CF_3CONHC(CH_3)_2]^+$, 114.0 (10), 59.1 (18), 43.1 (19) $[CH_3CO]^+$.

Anal. Calcd for $C_{24}H_{28}N_2O_3{\cdot}H_2O$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.22; H, 7.62; N, 6.63.

Ethyl 4-(2-(2-Amino-2-methylpropyl)-4,5-dimethoxyphenyl)-2-methylquinoline-3-carboxylate (3an)

Prepared using **1a** (109 mg, 0.35 mmol) and ethyl acetoacetate (**2n**; 0.053 mL, 0.42 mmol); reaction time: 2.5 h. The crude product was purified by recrystallization from CH_2Cl_2/hexane to give pure **3an**.

Yield: 74 mg (50%); white solid; mp 101.5–106 °C.

IR (thin film): 3361, 3064, 2962, 2936, 2847, 1725, 1606, 1565, 1517, 1494, 1465, 1406, 1371, 1299, 1249, 1218, 1184, 1098, 1063, 777, 765 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 8.4 Hz, 1 H), 7.67 (ddd, *J* = 8.4, 6.8, 1.4 Hz, 1 H), 7.53 (dd, *J* = 8.4, 0.9 Hz, 1 H), 7.39 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1 H), 7.12 (s, 1 H), 6.74 (s, 1 H), 4.11 (q, *J* = 7.1 Hz, 2 H), 3.93 (s, 3 H), 3.80 (s, 3 H), 2.76 (s, 3 H), 2.46 (d, *J* = 14.0 Hz, 1 H), 2.36 (d, *J* = 14.0 Hz, 1 H), 1.08 (t, *J* = 7.1 Hz, 3 H), 1.02 (br s, 2 H), 0.88 (s, 3 H), 0.86 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.5 (C), 154.9 (C), 148.7 (C), 147.8 (C), 147.3 (C), 145.9 (C), 130.3 (CH), 130.1 (C), 129.1 (CH), 128.1 (C), 127.9 (C), 126.8 (CH), 126.4 (CH), 125.4 (C), 114.6 (CH), 113.5 (CH), 61.4 (CH_2), 56.03 (OCH_3), 55.98 (OCH_3), 51.0 (C), 47.3 (CH_2), 31.1 (CH_3), 30.4 (CH_3), 23.9 (CH_3), 13.9 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = $[M]^+$ not detected, 421.1 (0.02) $[M - H]^+$, 407.1 (0.9) $[M - CH_3]^+$, 365.2 (81) $[M - (CH_3)_2C{=}NH]^+$, 364.2 (100) $[M - (CH_3)_2CNH_2]^+$, 336.1 (6) $[M - (CH_3)_2C{=}NH - C_2H_5]^+$, 318.1 (6) $[M - (CH_3)_2CHNH_2 - C_2H_5O]^+$, 292.1 (63) $[M - (CH_3)_2C{=}NH - C_2H_5OCO]^+$, 276.1 (9) $[M - (CH_3)_3CNH_2 - C_2H_5OCO]^+$, 58.1 (43) $[(CH_3)_2C{=}NH_2]^+$.

MS of trifluoroacetyl derivative (EI, 70 eV): *m*/*z* (%) = 518.2 (12) $[M]^+$, 405.1 (47) $[M - CF_3CONH_2]^+$, 365.1 (100) $[M - CF_3CONC(CH_3)_2]^+$, 364.1 (58) $[M - CF_3CONHC(CH_3)_2]^+$, 320.1 (13) $[M - CF_3CONC(CH_3)_2 - C_2H_5O]^+$, 318.1 (37), 292.1 (40), 291.1 (20), 276.1 (14), 260.0 (15), 154.0 (17) $[CF_3CONHC(CH_3)_2]^+$, 59.1 (18).

Anal. Calcd for $C_{25}H_{30}N_2O_4$: C, 71.07; H, 7.16; N, 6.63. Found: C, 71.38; H, 7.56; N, 6.59.

1-(4,5-Dimethoxy-2-(7-methoxy-1,2,3,4-tetrahydroacridin-9-yl)phenyl)-2-methylpropan-2-amine (3ba)

Prepared using **1b** (119 mg, 0.35 mmol) and cyclohexanone (**2a**; 0.044 mL, 0.42 mmol); reaction time: 5 min. The crude residue was purified by silica gel flash chromatography (EtOAc/MeOH, 3:1 → 1:1) to afford **3ba**.

Yield: 110 mg (75%); white solid; mp 141–143 °C; R_f = 0.21 (EtOAc/MeOH, 3:1).

IR (thin film): 3356, 3291, 3000, 2937, 2864, 1621, 1516, 1496, 1466, 1353, 1248, 1225, 1169, 1093, 835, 755 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, *J* = 9.1 Hz, 1 H), 7.25 (dd, *J* = 9.3, 2.8 Hz, 1 H), 7.11 (s, 1 H), 6.65 (d, *J* = 2.8 Hz, 1 H), 6.59 (s, 1 H), 3.96 (s, 3 H), 3.81 (s, 3 H), 3.67 (s, 3 H), 3.15 (t, *J* = 6.6 Hz, 2 H), 2.59–2.46 (m, 2 H), 2.40 (d, *J* = 13.6 Hz, 1 H), 2.31 (d, *J* = 13.7 Hz, 1 H), 1.98–1.92 (m, 2 H), 1.79–1.72 (m, 2 H), 1.34 (br s, 2 H), 0.88 (s, 3 H), 0.85 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.0 (C), 156.6 (C), 148.1 (C), 147.7 (C), 144.7 (C), 142.7 (C), 130.1 (CH), 129.8 (C), 129.5 (C), 129.4 (C), 127.6 (C), 120.7 (CH), 114.4 (CH), 112.8 (CH), 104.3 (CH), 56.0 (OCH_3), 55.9 (OCH_3), 55.3 (OCH_3), 50.8 (C), 46.8 (CH_2), 33.8 (CH_2), 31.0 (2 CH_3), 28.1 (CH_2), 23.0 (CH_2), 22.9 (CH_2).

MS (EI, 70 eV): *m*/*z* (%) = 420.2 (0.1) $[M]^+$, 419.2 (0.2) $[M - H]^+$, 405.1 (1) $[M - CH_3]^+$, 363.2 (54) $[M - (CH_3)_2C{=}NH]^+$, 362.2 (18) $[M - (CH_3)_2CNH_2]^+$, 348.1 (100) $[M - CH_2C(CH_3)_2NH_2]^+$, 58.1 (42) $[(CH_3)_2C{=}NH_2]^+$.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{26}H_{33}N_2O_3$: 421.2486; found: 421.2488.

1-(4,5-Dimethoxy-2-(6-methoxy-2-methylquinolin-4-yl)phenyl)-2-methylpropan-2-amine (3bd)

Prepared using **1b** (119 mg, 0.35 mmol) and acetone (**2d**; 0.031 mL, 0.42 mmol); reaction time: 10 min. ^{1}H NMR analysis of the crude product revealed that no further purification was required.

Yield: 126 mg (95%); white solid; mp 135–137 °C.

IR (thin film): 3356, 3290, 3001, 2960, 2936, 2845, 1621, 1603, 1561, 1516, 1501, 1465, 1405, 1356, 1267, 1248, 1230, 1215, 1158, 1090, 1034, 1017, 834, 753 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 9.2 Hz, 1 H), 7.30 (dd, *J* = 9.2, 2.8 Hz, 1 H), 7.14 (s, 1 H), 7.00 (s, 1 H), 6.76 (d, *J* = 2.9 Hz, 1 H), 6.72 (s, 1 H), 3.95 (s, 3 H), 3.82 (s, 3 H), 3.70 (s, 3 H), 2.71 (s, 3 H), 2.62 (d, *J* = 13.6 Hz, 1 H), 2.35 (d, *J* = 13.6 Hz, 1 H), 1.14 (br s, 2 H), 0.84 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.4 (C), 155.7 (C), 148.3 (C), 147.51 (C), 147.45 (C), 144.3 (C), 130.9 (C), 130.5 (CH), 129.4 (C), 126.8 (C), 123.8 (CH), 121.5 (CH), 114.5 (CH), 113.5 (CH), 104.0 (CH), 56.03 (OCH_3), 55.99 (OCH_3), 55.4 (OCH_3), 50.7 (C), 46.9 (CH_2), 30.8 (CH_3), 30.7 (CH_3), 25.0 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 380.2 (0.04) $[M]^+$, 365.2 (2) $[M - CH_3]^+$, 323.1 (70) $[M - (CH_3)_2C{=}NH]^+$, 322.1 (62) $[M - (CH_3)_2CNH_2]^+$, 308.1 (100) $[M - CH_2C(CH_3)_2NH_2]^+$, 58.1 (69) $[(CH_3)_2C{=}NH_2]^+$.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{29}N_2O_3$: 381.2173; found: 381.2177.

1-(4,5-Dimethoxy-2-(7-methyl-1,2,3,4-tetrahydroacridin-9-yl)phenyl)-2-methylpropan-2-amine (3ca)

Prepared using **1c** (113 mg, 0.35 mmol) and cyclohexanone (**2a**; 0.044 mL, 0.42 mmol); reaction time: 15 min. The crude product was purified by washing with cold acetone to give pure **3ca**.

Yield: 110 mg (78%); white solid; mp: 210–212 °C (dec; compound began to darken above 206 °C).

IR (thin film): 3367, 3021, 2939, 2862, 1566, 1517, 1496, 1465, 1398, 1253, 1219, 1168, 771, 758 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 8.6 Hz, 1 H), 7.41 (dd, *J* = 8.6, 2.0 Hz, 1 H), 7.11 (m, 2 H), 6.58 (s, 1 H), 3.97 (s, 3 H), 3.81 (s, 3 H), 3.16 (t, *J* = 6.6 Hz, 2 H), 2.59–2.46 (m, 2 H), 2.42–2.35 (m, 4 H), 2.28 (d, *J* = 13.7 Hz, 1 H), 2.01–1.90 (m, 2 H), 1.82–1.69 (m, 2 H), 1.15 (br s, 2 H), 0.88 (s, 3 H), 0.83 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.2 (C), 148.1 (C), 147.6 (C), 145.2 (C), 145.1 (C), 135.1 (C), 130.6 (CH), 129.7 (C), 129.4 (C), 129.2 (C), 128.4 (CH), 126.7 (C), 124.8 (CH), 114.5 (CH), 112.9 (CH), 56.0 (OCH_3), 55.9 (OCH_3), 50.8 (C), 46.9 (CH_2), 34.1 (CH_2), 31.0 (CH_3), 30.9 (CH_3), 28.0 (CH_2), 22.94 (CH_2), 22.88 (CH_2), 21.6 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 404.1 (0.1) $[M]^+$, 403.2 (0.2) $[M - H]^+$, 389.2 (1) $[M - CH_3]^+$, 347.2 (58) $[M - (CH_3)_2C{=}NH]^+$, 346.2 (30) $[M - (CH_3)_2CNH_2]^+$, 332.2 (100) $[M - CH_2C(CH_3)_2NH_2]^+$, 58.1 (44) $[(CH_3)_2C{=}NH_2]^+$.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{26}H_{33}N_2O_2$: 405.2537; found: 405.2541.

1-(2-(2,6-Dimethylquinolin-4-yl)-4,5-dimethoxyphenyl)-2-methylpropan-2-amine (3cd)

Prepared using **1c** (113 mg, 0.35 mmol) and acetone (**2d**; 0.031 mL, 0.42 mmol); reaction time: 1 h. ^{1}H NMR analysis of the crude product revealed that no further purification was required.

Yield: 120 mg (94%); white solid; mp 208–213 °C.

IR (thin film): 3357, 3291, 2960, 2931, 2851, 1596, 1560, 1516, 1465, 1441, 1402, 1385, 1355, 1257, 1215, 1154, 1093, 1018, 828, 753 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 8.6 Hz, 1 H), 7.47 (dd, *J* = 8.6, 1.9 Hz, 1 H), 7.22 (br s, 1 H), 7.13 (s, 1 H), 7.00 (s, 1 H), 6.70 (s, 1 H), 3.96 (s, 3 H), 3.82 (s, 3 H), 2.72 (s, 3 H), 2.60 (d, *J* = 13.6 Hz, 1 H), 2.39 (s, 3 H), 2.33 (d, *J* = 13.6 Hz, 1 H), 1.10 (br s, 2 H), 0.84 (s, 3 H), 0.83 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.2 (C), 148.3 (C), 148.0 (C), 147.4 (C), 146.8 (C), 135.6 (C), 131.5 (CH), 130.9 (C), 129.4 (C), 128.8 (CH), 125.9 (C), 124.6 (CH), 123.6 (CH), 114.5 (CH), 113.7 (CH), 56.04 (OCH_3), 55.99 (OCH_3), 50.7 (C), 46.9 (CH_2), 30.8 (2 CH_3), 25.2 (CH_3), 21.6 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 364.1 (0.03) $[M]^+$, 307.1 (62) $[M - (CH_3)_2C{=}NH]^+$, 306.1 (100) $[M - (CH_3)_2CNH_2]^+$, 292.1 (41) $[M - CH_2C(CH_3)_2NH_2]^+$, 290.1 (13), 58.1 (54) $[(CH_3)_2C{=}NH_2]^+$.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{29}N_2O_2$: 365.2224; found: 365.2222.

1-(2-(7-Bromo-1,2,3,4-tetrahydroacridin-9-yl)-4,5-dimethoxyphenyl)-2-methylpropan-2-amine (3da)

Prepared using **1d** (136 mg, 0.35 mmol) and cyclohexanone (**2a**; 0.044 mL, 0.42 mmol); reaction time: 2.5 h. The crude residue was purified by silica gel flash chromatography (EtOAc/MeOH, 3:1 → 1:1) to afford **3da**.

Yield: 138 mg (84%); white solid; mp: 231–234 °C (dec; compound began to darken above 180 °C); R_f = 0.20 (EtOAc/MeOH, 3:1).

IR (thin film): 3357, 3286, 3064, 2938, 2864, 2845, 1603, 1568, 1516, 1481, 1464, 1368, 1355, 1248, 1217, 1180, 1095, 1008, 834, 758 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 8.9 Hz, 1 H), 7.63 (dd, *J* = 8.9, 2.2 Hz, 1 H), 7.50 (d, *J* = 2.2 Hz, 1 H), 7.13 (s, 1 H), 6.54 (s, 1 H), 3.96 (s, 3 H), 3.81 (s, 3 H), 3.15 (t, *J* = 6.7 Hz, 2 H), 2.61–2.48 (m, 2 H), 2.34 (d, *J* = 13.7 Hz, 1 H), 2.26 (d, *J* = 13.7 Hz, 1 H), 1.99–1.92 (m, 2 H), 1.81–1.70 (m, 2 H), 1.27 (br s, 2 H), 0.86 (s, 3 H), 0.83 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.9 (C), 148.5 (C), 147.8 (C), 145.09 (C), 145.08 (C), 131.8 (CH), 130.5 (CH), 130.4 (C), 129.8 (C), 128.3 (C), 128.2 (CH), 128.1 (C), 119.4 (C), 114.6 (CH), 112.8 (CH), 56.1 (OCH_3), 56.0 (OCH_3), 50.9 (C), 46.7 (CH_2), 34.2 (CH_2), 31.1 (CH_3), 31.0 (CH_3), 28.1 (CH_2), 22.8 (CH_2), 22.7 (CH_2).

MS (EI, 70 eV): *m*/*z* (%) = $[M]^+$ not detected, 453.0 (1) $[M - CH_3]^+$, 411.0 (20) $[M - (CH_3)_2C{=}NH]^+$, 409.9 (10) $[M - (CH_3)_2CNH_2]^+$, 396.0 (23) $[M - CH_2C(CH_3)_2NH_2]^+$, 58.0 (100) $[(CH_3)_2C{=}NH_2]^+$.

MS of trifluoroacetyl derivative (EI, 70 eV): *m*/*z* (%) = 564.2 (14) $[M]^+$, 451.1 (10) $[M - CF_3CONH_2]^+$, 411.1 (44) $[M - (CH_3)_2C{=}NCOCF_3]^+$, 410.1 (24) $[M - (CH_3)_2CNHCOCF_3$, 396.1 (46) $[M - CH_2C(CH_3)_2NHCOCF_3]^+$, 331.1 (100) $[M - Br - (CH_3)_2CNHCOCF_3]^+$, 330.1 (31) $[M - HBr -$

$(CH_3)_2CNHCOCF_3]^+$, 329.1 (15), 316.1 (14) [M – HBr – $CH_2C(CH_3)_2NHCOCF_3]^+$, 300.1 (58) [M – Br – $(CH_3)_2CNHCOCF_3$ – $OCH_3]^+$, 154.0 (56) $[(CH_3)_2CNHCOCF_3]^+$, 114.0 (19), 59.1 (36), 42.1 (13), 41.1 (20).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{30}BrN_2O_2$: 469.1485; found: 469.1491.

1-(2-(6-Bromo-2-methylquinolin-4-yl)-4,5-dimethoxyphenyl)-2-methylpropan-2-amine (3dd)

Prepared using **1d** (136 mg, 0.35 mmol) and acetone (**2d**; 0.031 mL, 0.42 mmol); reaction time: 18 h. ^{1}H NMR analysis of the crude product revealed that no further purification was required.

Yield: 140 mg (92%); white solid; mp 195–196 °C.

IR (thin film): 3356, 3290, 3065, 2961, 2848, 1599, 1516, 1485, 1464, 1376, 1262, 1248, 1222, 1214, 1167, 1098, 1017, 830, 754 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, *J* = 8.9 Hz, 1 H), 7.70 (dd, *J* = 8.9, 2.2 Hz, 1 H), 7.61 (d, *J* = 2.2 Hz, 1 H), 7.20 (s, 1 H), 7.02 (s, 1 H), 6.67 (s, 1 H), 3.96 (s, 3 H), 3.82 (s, 3 H), 2.73 (s, 3 H), 2.60 (d, *J* = 13.6 Hz, 1 H), 2.28 (d, *J* = 13.6 Hz, 1 H), 1.09 (br s, 2 H), 0.84 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.8 (C), 148.6 (C), 148.0 (C), 147.6 (C), 146.8 (C), 132.8 (CH), 130.8 (CH), 129.8 (C), 129.5 (C), 127.9 (CH), 127.4 (C), 124.4 (CH), 119.8 (C), 114.6 (CH), 113.5 (CH), 56.05 (OCH_3), 56.02 (OCH_3), 50.8 (C), 46.8 (CH_2), 30.8 (CH_3), 30.8 (CH_3), 25.3 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = [M]$^+$ not detected, 413.0 (1) [M – $CH_3]^+$, 371.0 (33) [M – $(CH_3)_2C{=}NH]^+$, 369.9 (50) [M – $(CH_3)_2CNH_2]^+$, 260.1 (10), 58.0 (100) $[(CH_3)_2C{=}NH_2]^+$.

MS of trifluoroacetyl derivative (EI, 70 eV): *m*/*z* (%) = 524.2 (14) [M]$^+$, 411.2 (10) [M – $CF_3CONH_2]^+$, 371.1 (42) [M – $(CH_3)_2C{=}NCOCF_3]^+$, 370.1 (58) [M – $(CH_3)_2CNHCOCF_3]^+$, 291.2 (100) [M – Br – $(CH_3)_2CNHCOCF_3]^+$, 290.2 (29) [M – HBr – $(CH_3)_2CNHCOCF_3]^+$, 276.1 (15) [M – HBr – $CH_2C(CH_3)_2NHCOCF_3]^+$, 260.1 (79) [M – Br – $(CH_3)_2CNHCOCF_3$ – $OCH_3]^+$, 246.1 (11) [M – Br – $CH_2C(CH_3)_2NHCOCF_3$ – $OCH_3]^+$, 217.1 (12), 154.1 (56) $[(CH_3)_2CNHCOCF_3]^+$, 114.1 (12), 59.1 (24), 41.1 (11).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{26}BrN_2O_2$: 429.1172; found: 429.1168.

1-(4,5-Dimethoxy-2-(2-methyl-6-nitroquinolin-4-yl)phenyl)-2-methylpropan-2-amine (3ed)

Prepared using **1e** (124 mg, 0.35 mmol) and acetone (**2d**; 0.031 mL, 0.42 mmol); reaction time: 100 h. The crude product was purified by recrystallization from hexane/acetone to give pure **3ed**.

Yield: 84 mg (61%); yellow solid; mp 200–203.5 °C.

IR (thin film): 3361, 3083, 3000, 2961, 2936, 2850, 1619, 1601, 1565, 1532, 1516, 1493, 1465, 1381, 1341, 1262, 1247, 1227, 1215, 1111, 1075, 1017, 841, 799, 755 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.44 (d, *J* = 2.4 Hz, 1 H), 8.40 (dd, *J* = 9.2, 2.4 Hz, 1 H), 8.15 (d, *J* = 9.2 Hz, 1 H), 7.35 (s, 1 H), 7.06 (s, 1 H), 6.68 (s, 1 H), 3.98 (s, 3 H), 3.83 (s, 3 H), 2.81 (s, 3 H), 2.63 (d, *J* = 13.6 Hz, 1 H), 2.27 (d, *J* = 13.6 Hz, 1 H), 0.98 (br s, 2 H), 0.83 (s, 3 H), 0.82 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.5 (C), 150.8 (C), 150.3 (C), 149.0 (C), 147.7 (C), 145.2 (C), 130.8 (CH), 129.5 (C), 128.8 (C), 125.3 (CH), 125.2 (C), 122.9 (CH), 122.8 (CH), 114.7 (CH), 113.5 (CH), 56.1 (2 OCH_3), 50.8 (C), 46.8 (CH_2), 30.9 (CH_3), 30.8 (CH_3), 25.7 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = [M]$^+$ not detected, 380.0 (0.7) [M – $CH_3]^+$, 338.0 (14) [M – $(CH_3)_2C{=}NH]^+$, 337.0 (4) [M – $(CH_3)_2CNH_2]^+$, 321.0 (28) [M – $(CH_3)_2CHNH_2$ – $CH_3]^+$, 260.0 (5), 58.1 (100) $[(CH_3)_2C{=}NH_2]^+$.

MS of trifluoroacetyl derivative (EI, 70 eV): *m*/*z* (%) = 491.2 (11) [M]$^+$, 476.1 (0.4) [M – $CH_3]^+$, 378.1 (21) [M – $CF_3CONH_2]^+$, 338.1 (19) [M – $CF_3CONC(CH_3)_2]^+$, 337.1 (9) [M – $CF_3CONHC(CH_3)_2]^+$, 321.1 (100), 320.1 (10), 304.1 (15), 303.1 (14), 291.1 (40), 290.1 (24), 276.1 (11), 260.0 (55), 154.0 (59) $[CF_3CONHC(CH_3)_2]^+$, 114.0 (10), 59.1 (18).

Anal. Calcd for $C_{22}H_{25}N_3O_4$: C, 66.82; H, 6.37; N, 10.63. Found: C, 67.03; H, 6.15; N, 10.21.

2-Methyl-1-(2-(2-methylquinolin-4-yl)phenyl)propan-2-amine (3fd)

Prepared using **1f** (88 mg, 0.35 mmol) and acetone (**2d**; 0.031 mL, 0.42 mmol); reaction time: 1 h. ^{1}H NMR analysis of the crude product revealed that no further purification was required.

Yield: 100 mg (99%); white solid; mp 92–93 °C.

IR (thin film): 3357, 3278, 3060, 2961, 2922, 2868, 1594, 1559, 1508, 1485, 1466, 1444, 1406, 1381, 1344, 1193, 1150, 870, 844, 769, 743, 722 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06 (br d, *J* = 8.0 Hz, 1 H), 7.64 (ddd, *J* = 8.4, 6.8, 1.6 Hz, 1 H), 7.49–7.33 (m, 5 H), 7.22–7.20 (m, 1 H), 7.20 (s, 1 H), 2.76 (s, 3 H), 2.69 (d, *J* = 13.6 Hz, 1 H), 2.42 (d, *J* = 13.6 Hz, 1 H), 0.93 (br s, 2 H), 0.83 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.2 (C), 148.7 (C), 148.1 (C), 138.4 (C), 137.0 (C), 131.4 (CH), 130.6 (CH), 129.3 (CH), 129.0 (CH), 127.8 (CH), 126.4 (CH), 125.77 (CH), 125.76 (CH), 123.4 (CH), 50.7 (C), 47.3 (CH_2), 30.7 (CH_3), 30.6 (CH_3), 25.4 (CH_3); the missing signal for one of the aromatic carbons is overlapped.

MS (EI, 70 eV): *m*/*z* (%) = 290.0 (0.04) [M]$^+$, 289.1 (0.2) [M – H]$^+$, 275.1 (4) [M – $CH_3]^+$, 233.1 (52) [M – $(CH_3)_2C{=}NH]^+$, 232.1 (100) [M – $(CH_3)_2CNH_2]^+$, 231.1 (17) [M – $(CH_3)_2CHNH_2]^+$, 218.1 (10) [M – $CH_2C(CH_3)_2NH_2]^+$, 58.1 (28) $[(CH_3)_2C{=}NH_2]^+$.

Anal. Calcd for $C_{20}H_{22}N_2$: C, 82.72; H, 7.64; N, 9.65. Found: C, 83.03; H, 8.01; N, 9.32.

3-(4,5-Dimethoxy-2-(1,2,3,4-tetrahydroacridin-9-yl)phenyl)-2,3-dimethylbutan-2-amine (3ga)

Prepared using **1g** (118 mg, 0.35 mmol) and cyclohexanone (**2a**; 0.044 mL, 0.42 mmol); reaction time: 1 h. The crude product was purified by recrystallization from CH_2Cl_2/hexane to give pure **3ga**.

Yield: 94 mg (64%); white solid; mp 198–200 °C.

IR (thin film): 3371, 3061, 2982, 2936, 2867, 2839, 1605, 1570, 1517, 1492, 1464, 1399, 1365, 1349, 1311, 1246, 1216, 1169, 1129, 1063, 1002, 772, 756 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (d, *J* = 8.4 Hz, 1 H), 7.81 (s, 1 H), 7.56 (ddd, *J* = 8.3, 6.7, 1.5 Hz, 1 H), 7.38 (dd, *J* = 8.4, 1.0 Hz, 1 H), 7.29 (ddd, *J* = 8.2, 6.7, 1.2 Hz, 1 H), 6.26 (s, 1 H), 3.96 (s, 3 H), 3.73 (s, 3 H), 3.16 (t, *J* = 6.6 Hz, 2 H), 2.68–2.59 (m, 1 H), 2.53–2.44 (m, 1 H), 2.02–1.87 (m, 2 H), 1.83–1.74 (m, 2 H), 1.10 (br s, 2 H), 1.11 (s, 3 H), 1.01 (s, 3 H), 0.96 (s, 3 H), 0.85 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.0 (C), 150.6 (C), 147.0 (C), 146.9 (C), 146.2 (C), 137.8 (C), 129.3 (C), 128.4 (CH, C), 128.2 (CH), 127.6 (C), 126.9 (CH), 125.0 (CH), 115.8 (CH), 113.5 (CH), 56.1 (C), 55.89 (OCH_3), 55.85 (OCH_3), 47.1 (C), 34.2 (CH_2), 28.9 (CH_3), 28.8 (CH_3), 28.6 (CH_2), 26.7 (CH_3), 25.7 (CH_3), 23.0 (CH_2), 22.8 (CH_2).

MS (EI, 70 eV): *m*/*z* (%) = 418.2 (0.12) [M]$^+$, 417.2 (0.2) [M – H]$^+$, 403.2 (1) [M – $CH_3]^+$, 361.2 (100) [M – $CH_2{=}C(CH_3)NH_2]^+$, 360.2 (39) [M – $(CH_3)_2CNH_2]^+$, 346.2 (58) [M – $(CH_3)_2C{=}NH$ – $CH_3]^+$, 344.2 (12) [M – $(CH_3)_2CHNH_2$ – $CH_3]^+$, 332.2 (54) [M – $(CH_3)_2CNH_2$ – $C_2H_4]^+$, 330.2 (10)

[M – $(CH_3)_2C$=NH – OCH_3]$^+$, 318.2 (89) [M – $(CH_3)_2CC(CH_3)_2NH_2$]$^+$, 302.1 (8) [M – $(CH_3)_2CHC(CH_3)_2NH_2$ – CH_3]$^+$, 286.1 (6), 184.1 (5), 58.1 (48) [$(CH_3)_2C$=NH_2]$^+$.

Anal. Calcd for $C_{27}H_{34}N_2O_2$: C, 77.48; H, 8.19; N, 6.69. Found: C, 77.38; H, 8.57; N, 6.69.

3-(4,5-Dimethoxy-2-(2-methylquinolin-4-yl)phenyl)-2,3-dimethylbutan-2-amine (3gd)

Prepared using **1g** (118 mg, 0.35 mmol) and acetone (**2d**; 0.031 mL, 0.42 mmol); reaction time: 1.5 h. The crude product was purified by recrystallization from acetone/hexane to give pure **3gd**.

Yield: 115 mg (87%); pale yellow solid; mp 161–166 °C.

IR (thin film): 3375, 2967, 2935, 2839, 1596, 1561, 1518, 1503, 1464, 1407, 1377, 1346, 1309, 1248, 1229, 1213, 1192, 1177, 1156, 1067, 782, 754 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.92 (d, J = 8.4 Hz, 1 H), 7.63 (t, J = 7.6 Hz, 1 H), 7.44 (s, 1 H), 7.40 (t, J = 7.6 Hz, 1 H), 7.33 (s, 1 H), 7.30 (d, J = 8.3 Hz, 1 H), 6.38 (s, 1 H), 3.86 (s, 3 H), 3.63 (s, 3 H), 2.66 (s, 3 H), 1.27 (s, 3 H), 1.22 (br s, 2 H), 0.98 (s, 6 H), 0.64 (s, 3 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 157.1 (C), 151.8 (C), 146.9 (C), 146.5 (C), 145.9 (C), 137.0 (C), 129.0 (C), 128.4 (CH), 128.1 (CH), 127.2 (C), 126.1 (CH), 125.1 (CH), 122.6 (CH), 116.0 (CH), 114.9 (CH), 55.6 (OCH_3), 55.3 (OCH_3), 54.4 (C), 46.6 (C), 28.0 (CH_3), 27.4 (CH_3), 27.4 (CH_3), 24.9 (CH_3), 24.5 (CH_3).

MS (EI, 70 eV): m/z (%) = 378.2 (0.3) [M]$^+$, 377.2 (0.4) [M – H]$^+$, 363.2 (0.8) [M – CH_3]$^+$, 321.1 (53) [M – $(CH_3)_2C$=NH]$^+$, 320.1 (61) [M – $(CH_3)_2CNH_2$]$^+$, 306.1 (100) [M – $(CH_3)_2C$=NH – CH_3]$^+$, 305.1 (20) [M – $(CH_3)_2CNH_2$ – CH_3]$^+$, 304.1 (20) [M – $(CH_3)_2CHNH_2$ – CH_3]$^+$, 290.1 (21) [M – $(CH_3)_2C$=NH – OCH_3]$^+$, 58.1 (89) [$(CH_3)_2C$=NH_2]$^+$.

Anal. Calcd for $C_{24}H_{30}N_2O_2$: C, 76.16; H, 7.99; N, 7.40. Found: C, 75.95; H, 8.21; N, 7.03.

2-(4,5-Dimethoxy-2-(1,2,3,4-tetrahydroacridin-9-yl)phenyl)-ethan-1-amine Dihydrobromide (3ha·2 HBr)

Prepared using **1h** (99 mg, 0.35 mmol) and cyclohexanone (**2a**; 0.044 mL, 0.42 mmol); reaction time: 2.5 h. Quinoline **3ha** was isolated as the dihydrobromide salt, obtained by analogy with a literature procedure.[14] The crude product was dissolved in MeOH (2 mL) and 33% HBr in AcOH (0.22 mL) was added. The mixture was stirred at room temperature for 30 min and concentrated *in vacuo*. The residue was dissolved in MeOH (2–3 mL) and concentrated *in vacuo*; this procedure was then repeated three times. After, the crude residue was dissolved in MeOH (1 mL) and *i*-PrOH (2.5 mL) was added. The mixture was left to stand overnight at room temperature. The precipitated dihydrobromide salt was collected by filtration, washed with MeOH/*i*-PrOH (~1:2.5) and dried in a desiccator at room temperature.

Yield: 114 mg (62%); yellow solid; mp: 265–267 °C (dec; compound began to darken above 170 °C).

IR (Vaseline oil): 2726, 2641, 1642, 1594, 1519, 1490, 1461, 1408, 1379, 1362, 1286, 1256, 1220, 1165, 1154, 1106, 1087, 1019, 1003, 851, 761 cm^{-1}.

^{1}H NMR (400 MHz, D_2O): δ = 8.28 (br d, J = 8.5 Hz, 1 H), 8.18 (ddd, J = 8.5, 6.9, 1.3 Hz, 1 H), 7.88 (ddd, J = 8.2, 7.0, 1.2 Hz, 1 H), 7.73 (d, J = 8.1 Hz, 1 H), 7.36 (s, 1 H), 6.99 (s, 1 H), 4.13 (s, 3 H), 3.93 (s, 3 H), 3.55 (t, J = 6.5 Hz, 2 H), 3.14–2.96 (m, 2 H), 2.92–2.58 (m, 4 H), 2.26–2.09 (m, 2 H), 2.07–1.94 (m, 2 H).

^{13}C NMR (100 MHz, D_2O): δ = 158.1 (C), 156.0 (C), 149.9 (C), 148.6 (C), 136.9 (C), 134.4 (CH), 133.0 (C), 129.9 (CH), 128.0 (C), 127.5 (C), 127.1 (CH), 127.0 (C), 120.2 (CH), 114.0 (CH), 112.6 (CH), 56.7 (OCH_3), 56.6 (OCH_3), 40.3 (CH_2), 30.5 (CH_2), 29.5 (CH_2), 27.2 (CH_2), 21.7 (CH_2), 20.9 (CH_2).

MS (EI, 70 eV): free base m/z (%) = 362.1 (7) [M]$^+$, 333.1 (60) [M – CH_2NH]$^+$, 332.1 (64) [M – CH_2NH_2]$^+$, 318.1 (100) [M – $CH_2CH_2NH_2$]$^+$, 316.1 (15) [M – CH_3NH_2 – CH_3]$^+$, 302.0 (9), 30.1 (5) [CH_2=NH_2]$^+$.

HRMS (ESI): m/z [M – 2 HBr + H]$^+$ calcd for $C_{23}H_{27}N_2O_2$: 363.2067; found: 363.2067.

Anal. Calcd for $C_{23}H_{26}N_2O_2$·2 HBr·0.25 H_2O: C, 52.24; H, 5.43; N, 5.30; Br, 30.22. Found: C, 52.61; H, 5.31; N, 5.10; Br, 29.77.

2-(4,5-Dimethoxy-2-(2-methylquinolin-4-yl)phenyl)ethan-1-amine Dihydrobromide (3hd·2 HBr)

Prepared using **1h** (99 mg, 0.35 mmol) and acetone (**2d**; 0.031 mL, 0.42 mmol); reaction time: 72 h. Quinoline **3hd** was isolated as the dihydrobromide salt, obtained by analogy with a literature procedure.[14] The crude product was dissolved in MeOH (2 mL) and 33% HBr in AcOH (0.22 mL) was added. The mixture was stirred at room temperature for 30 min and concentrated *in vacuo*. The residue was dissolved in MeOH (2–3 mL) and concentrated *in vacuo*; this procedure was then repeated three times. After, the crude residue was dissolved in MeOH (1 mL) and Et_2O (~1.5–1.7 mL) was added. The mixture was left to stand overnight at room temperature. The precipitated dihydrobromide salt was collected by filtration, washed with MeOH/Et_2O (~1:2) and dried in a desiccator at room temperature.

Yield: 117 mg (66%); yellow solid; mp: 231–234 °C (dec; compound began to darken above 180 °C).

IR (Vaseline oil): 2724, 2683, 2639, 1643, 1605, 1519, 1494, 1461, 1414, 1379, 1362, 1358, 1257, 1240, 1219, 1179, 1157, 1142, 1106, 1087, 1020, 1006, 985, 855, 766 cm^{-1}.

^{1}H NMR (400 MHz, D_2O): δ = 8.34 (br d, J = 8.5 Hz, 1 H), 8.28–8.22 (m, 1 H), 7.98 (s, 1 H), 7.96–7.89 (m, 2 H), 7.33 (s, 1 H), 7.11 (s, 1 H), 4.13 (s, 3 H), 3.94 (s, 3 H), 3.16 (s, 3 H), 3.15–3.03 (m, 2 H), 3.02–2.92 (m, 1 H), 2.78–2.70 (m, 1 H).

^{13}C NMR (100 MHz, D_2O): δ = 157.8 (C), 157.5 (C), 150.2 (C), 148.0 (C), 138.4 (C), 135.3 (CH), 130.3 (CH), 128.1 (2 C), 127.5 (CH), 127.2 (C), 125.1 (CH), 120.7 (CH), 113.9 (2 CH), 56.7 (OCH_3), 56.6 (OCH_3), 40.7 (CH_2), 30.6 (CH_2), 20.8 (CH_3).

MS (EI, 70 eV): free base m/z (%) = 322.1 (2) [M]$^+$, 293.1 (55) [M – CH_2NH]$^+$, 292.1 (100) [M – CH_2NH_2]$^+$, 278.1 (10) [M – $CH_2CH_2NH_2$]$^+$, 276.1 (15) [M – CH_3NH_2 – CH_3]$^+$, 260.1 (5) [M – CH_3NH_2 – OCH_3]$^+$, 234.1 (5), 218.1 (6), 30.1 [CH_2=NH_2]$^+$ (5).

HRMS (ESI): m/z [M – 2 HBr + H]$^+$ calcd for $C_{20}H_{23}N_2O_2$: 323.1754; found: 323.1754.

Anal. Calcd for $C_{20}H_{22}N_2O_2$·2 HBr·0.7 H_2O·0.15 Et_2O: C, 48.71; H, 5.34; N, 5.51; Br, 31.46. Found: C, 48.62; H, 5.21; N, 5.32; Br, 31.46.

N-(2-(6,7-Dimethoxy-3,3-dimethyl-3,4-dihydroisoquinolin-1-yl)phenyl)acetamide (4)

Pale yellow solid; mp 170–172 °C (hexane); R_f = 0.60 (CH_2Cl_2/MeOH/TEA, 98.5:1:0.5).

IR (thin film): 3246, 3064, 3007, 2965, 2934, 2833, 1690, 1605, 1581, 1559, 1515, 1463, 1446, 1349, 1299, 1273, 1229, 1212, 1170, 1130, 1094, 756 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.05 (br s, 1 H), 8.27 (d, *J* = 8.0 Hz, 1 H), 7.44–7.38 (m, 1 H), 7.32 (dd, *J* = 7.8, 1.5 Hz, 1 H), 7.10 (td, *J* = 7.7, 1.1 Hz, 1 H), 6.76 (s, 1 H), 6.71 (s, 1 H), 3.94 (s, 3 H), 3.70 (s, 3 H), 2.75 (s, 2 H), 2.11 (s, 3 H), 1.33 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.5 (C), 165.0 (C), 152.2 (C), 147.3 (C), 137.6 (C), 131.7 (C), 130.5 (CH), 130.3 (CH), 125.5 (C), 123.3 (CH), 122.9 (CH), 120.0 (C), 112.6 (CH), 111.2 (CH), 56.2 (OCH_3), 56.1 (OCH_3), 54.8 (C), 38.4 (CH_2), 27.6 (2 CH_3), 24.5 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 352.2 (27) $[M]^+$, 337.2 (100) $[M - CH_3]^+$, 321.1 (16), 310.1 (16), 309.1 (42) $[M - C(O)CH_3]^+$, 295.1 (13), 294.1 (20) $[M - NHC(O)CH_3]^+$, 279.1 (11).

Anal. Calcd for $C_{21}H_{24}N_2O_3$: C, 71.57; H, 6.86; N, 7.95. Found: C, 71.20; H, 6.97; N, 7.73.

Funding Information

This work was financially supported by the Russian Foundation for Basic Research (grant 16-03-00561) and the Ministry of Science and Higher Education of the Russian Federation (project AAAA-A18-118033090090-0).

Acknowledgment

The work was carried out using the equipment of The Core Facilities Center 'Research of Materials and Matter' at the PFRC UB RAS.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0040-1706424.

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