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Bismuth(III)-catalyzed regioselective alkylation of tetrahydroquinolines and indolines towards the synthesis of bioactive core-biaryl oxindoles and CYP19 inhibitors†

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Bismuth(III)-catalyzed regioselective functionalization at the C-6 position of tetrahydroquinolines and the C-5 position of indolines has been demonstrated. For the first time, one pot symmetrical and unsymmetrical arylation of isatins with tetrahydroquinolines was accomplished giving a completely new product skeleton in good to excellent yields. Most importantly, this protocol leads to the formation of a highly strained quaternary carbon stereogenic center, which is a challenging task. Benzhydryl and 1-phenylethyl trichloroacetimidates have been used as the alkylating partners to functionalize the C-6 and C-5 positions of tetrahydroquinolines and indolines, respectively. The scope of the developed methodology has been extended for the synthesis of the bioactive CYP19-inhibitor and its analogue.

1. Introduction

Tetrahydroquinoline and indoline skeletons are the common structural motifs present in a wide range of pharmaceuticals and bioactive natural products.[1] As substituted tetrahydroquinolines and indolines show significant effects on biological metabolism[2] and they show pharmaceutical activity towards Alzheimer's disease, obesity, asthma, epilepsy, antitumor, antibiotic, bradykinin antagonist, schistosomicidal, and anti-proliferative activities, the synthesis and functionalization of tetrahydroquinolines and indolines are of immense interest (Fig. 1).

In this context, development of new methodology for the selective C–H functionalization of these molecules can give access to medicinally important scaffolds.[3] Significant efforts have been made over the last decade to develop efficient and practical strategies for the regioselective alkylation on the benzenoid nucleus of indolines[4–7] and tetrahydroquinolines.[8–10]

In this regard, the directing group assisted transition metal (Rh, Ru, Pd, Ir, and Co)-catalyzed activation of the proximal sp^2 C–H bond, *i.e.* C-7 of indolines,[11] and C-8 of tetrahydroquinolines,[12] are well documented. Recently, the Yu group has demonstrated elegant strategies to deliver *meta* functionalization of cyclic amines (indolines and tetrahydroquinolines) by utilizing a U-shaped template.[13] However, template assisted *para*-functionalization of cyclic amines is still underdeveloped as it is associated with certain limitations such as regioselectivity (*ortho* and *para* products) (Fig. 2a), chemoselectivity and reactivity (mono- and di-alkylation) (Fig. 2b).[14,15] Consequently, the development of efficient synthetic methodology to access those molecules overcoming the regio- and chemo-selectivity issues is a challenging task.

Considering the significance of selective functionalization, we have explored the selective C-5 and C-6 alkylation of indolines and tetrahydroquinolines, respectively, through Lewis acid assisted alkylation reaction. The developed alkylation reaction works efficiently in a regioselective manner under transition metal free conditions.

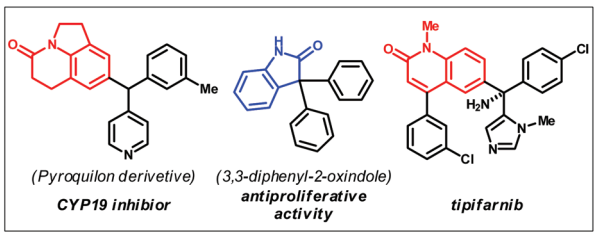

Fig. 1 Selected examples of natural products and bioactive analogs bearing substituted indoline and substituted tetrahydroquinoline scaffolds.

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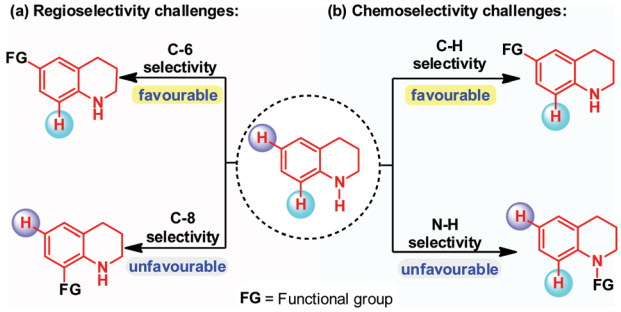


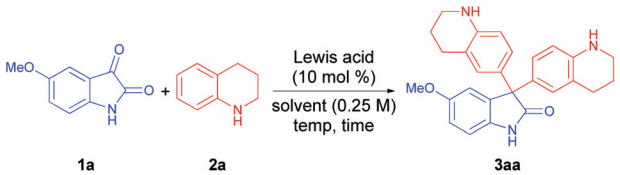
Fig. 2 Regio- and chemo-selectivity challenges between C-6 and C-8 functionalization of tetrahydroquinoline.

2. Results and discussion

We decided to try a new substrate combination which has never been explored before. Hence, we chose 5-methoxyisatin **1a** and tetrahydroquinoline **2a** (Table 1) as the model substrates to test the hypothesis. Accordingly, the reaction of **1a** with **2a** was tested under Lewis acid conditions.

Gratifyingly, under the influence of the catalytic quantity of $In(OTf)_3$ in 1,4-dioxane, at 80 °C for 6 h, the selective C-6 functionalization of tetrahydroquinoline occurred smoothly resulting in the desired product **3aa** in 55% isolated yield (Table 1, entry 1). Next, a series of solvents such as DMSO, DMF, MeOH, DCM and DCE were tested using $In(OTf)_3$ (Table 1, entries 2–6). Among them, DCE produced a better yield of **3aa**, 79%. So, we kept DCE as the optimised solvent and varied other parameters for further optimization. When we screened other Lewis acids such as $ZnCl_2$, $AlCl_3$ and $Bi(OTf)_3$, the yield of **3aa** was improved to 83% with $Bi(OTf)_3$ (Table 1, entries 7–9). Interestingly, further improvement of the product yield to 96% was observed on increasing the reaction time to 8 h (Table 1, entry 10). Then we reduced the catalyst loading from 10 mol% to 5 mol%, but the yield of **3aa** decreased to 55% (Table 1, entry 11). Therefore, we fixed the catalyst loading to 10 mol% and varied the temperature. However, at reduced or increased temperature such as 60 °C, 100 °C and room temperature (Table 1, entries 12–14) the yields of **3aa** dropped to 79%, 48% and 11%, respectively. Moreover, to understand the influence of the number of equivalents of quinolines, we tested the reaction with 2 and 2.8 equivalents of **2a** (for more details see the ESI†) and observed a decrease in the yield of **3aa** (Table 1, entries 15 & 16) in both cases. This indicates that 2.5 equivalents of **2a** are essential for this reaction. Thus, 10 mol% of $Bi(OTf)_3$, with DCE as the solvent at 80 °C for 8 h were found to be the optimized conditions (Table 1, entry 10).

Table 1 Optimization of the reaction conditions[a]



Entry	2a (equiv.)	Lewis acid	Solvent	Temp	Time	Yield[b] (%)
1	2.5	$In(OTf)_3$	1,4-Dioxane	80 °C	6 h	59 (55)[c]
2	2.5	$In(OTf)_3$	DMSO	80 °C	6 h	Nr
3	2.5	$In(OTf)_3$	DMF	80 °C	6 h	56
4	2.5	$In(OTf)_3$	MeOH	80 °C	6 h	67
5	2.5	$In(OTf)_3$	DCM	80 °C	6 h	64
6	2.5	$In(OTf)_3$	DCE	80 °C	6 h	79
7	2.5	$ZnCl_2$	DCE	80 °C	6 h	58
8	2.5	$AlCl_3$	DCE	80 °C	6 h	39
9	2.5	$Bi(OTf)_3$	DCE	80 °C	6 h	83
10	**2.5**	**$Bi(OTf)_3$**	**DCE**	**80 °C**	**8 h**	**96 (92)[c]**
11[d]	2.5	$Bi(OTf)_3$	DCE	80 °C	8 h	55
12	2.5	$Bi(OTf)_3$	DCE	60 °C	6 h	79 (73)
13	2.5	$Bi(OTf)_3$	DCE	100 °C	6 h	48
14	2.5	$Bi(OTf)_3$	DCE	rt	6 h	11
15	2	$Bi(OTf)_3$	DCE	80 °C	8 h	68
16	2.8	$Bi(OTf)_3$	DCE	80 °C	8 h	75

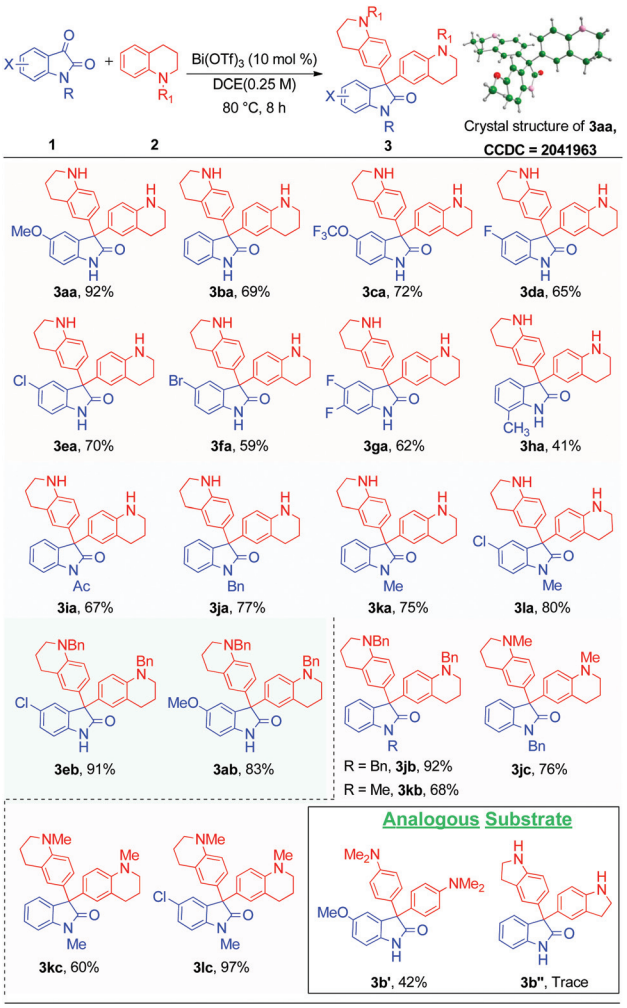
[a] Reaction conditions: **1a** (0.1 mmol), **2a** (2.5 equiv.), Lewis acid (10 mol%), and solvent (0.25 M), rt to 80 °C, 6–8 h. [b] NMR yield. [c] Isolated yields. [d] $Bi(OTf)_3$ (5 mol%).

With the optimized reaction conditions in hand, the viability of the C-6 functionalization of quinoline derivatives **2** was tested with various substituted and unsubstituted isatins **1** in both protected and unprotected forms (Scheme 1).

The C-6 functionalization of **2a** with N–H isatin **1b** gave a 69% isolated yield of the arylated product (Scheme 1, **3ba**). When C5-trifluoromethoxy isatin was used, the yield of the product **3ca** increases to 72%. Then C5-halo substituted oxindoles were used, and 65%, 70% and 59% yields of the respective products were observed (Scheme 1, **3da**, **3ea** & **3fa**). Upon taking the dihalo substituted isatin, good yield of the product **3ga** (62%) was obtained, but when C7-methyl isatin was taken as the substrate, the yield of the product **3ha** decreased to 41%.

Then we decided to check the effect of *N*-protection on isatin. Interestingly, the yield (67%) did not change much with *N*-acetyl isatin (Scheme 1, **3ia**). However, the yields (77% & 75%) of the arylated adduct improved with both *N*-benzyl and *N*-methyl isatins (Scheme 1, **3ja** & **3ka**). Next, we tested the effect of a halo group on *N*-methyl isatin that led to further improvement of yield, 80% (Scheme 1, **3la**). From the above set of experiments, it can be concluded that the reaction works well irrespective of the nature of the substituent present on the benzenoid ring of isatin. Subsequently, the effect of *N*-protection on tetrahydroquinolines was explored while keeping the nitrogen atom of the isatin molecule unprotected. The reaction of **2b** with **1e** and **1a** produced very good yields (91% & 83%) of their respective products (Scheme 1, **3eb** & **3ab**). Furthermore, we have screened the effect of *N*-protection on both tetrahydroquinoline and isatin derivatives.

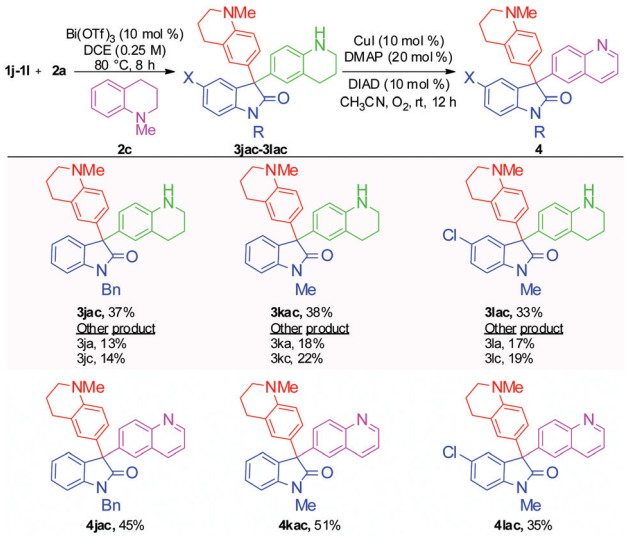
In these cases, we obtained good to excellent yields 60–97% of the products (Scheme 1, **3kc**, **3kb**, **3jc**, **3jb** & **3lc**). Overall, this reaction worked well with a broad range of substrates. Then we applied our developed protocol to other cyclic amine substrates such as aniline and indoline. The *N*-protected



Scheme 1 Scope of the isatins and tetrahydroquinolines in a two-component system. Reaction conditions: **1** (0.1 mmol), **2** (2.5 equiv.), $Bi(OTf)_3$ (10 mol%), and DCE (0.25 M), 80 °C, 8 h.

aniline with 5-methoxy isatin gave the product **3b′** with 42% yield and indoline with isatin gave the product **3b″** in a trace amount. So the above study reveals the broader scope of this developed methodology.

Having successfully demonstrated the utility of this protocol for the synthesis of a variety of symmetrically arylated products, we were interested in examining the scope of this protocol for the synthesis of an unsymmetrically arylated product as well.[16] Accordingly, we tested this protocol with two different tetra-hydroquinolines (**2a** and **2c**) with *N*-benzylisatin. To our delight, we obtained a 37% yield of an unsymmetrically arylated product (Scheme 2, **3jac**) along with the symmetrical products **3ja** (13%) and **3jc** (14%). Also, with *N*-methylisatin and 5-chloro-*N*-methylisatin, 38% and 33% of respective yields of the unsymmetrically arylated products were obtained (Scheme 2, **3kac** & **3lac**) along with symmetrical products **3ka** (18%), **3kc** (22%), **3la** (17%), **3lc** (19%). To further enhance the scope of the products through this methodology, we oxidized the unsymmetrically arylated products following a procedure

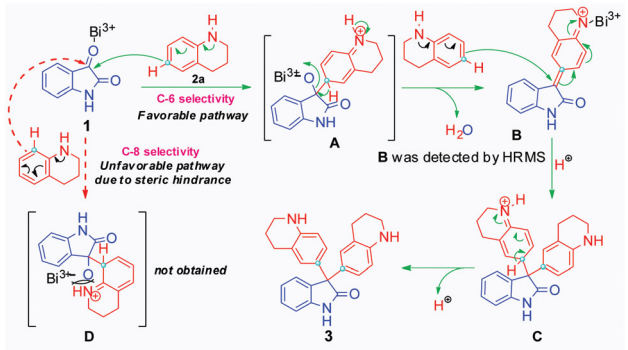


Scheme 2 Scope of the isatins and tetrahydroquinolines in a three-component system and its oxidized product. Reaction conditions for products **3jac**–**3lac**: (a) **1** (0.1 mmol), **2a** (1.2 equiv.), **2c** (1.2 equiv.), Bi $(OTf)_3$ (10 mol%), and DCE (0.25 M), 80 °C, 8 h; Reaction conditions for products **4jac**–**4lac**: (b) **3** (0.1 mmol), CuI (10 mol%), DMAP (20 mol%), DIAD (10 mol%), and MeCN (0.1 M), rt, 12 h.

reported in the literature.[17] A reasonable yield of the respective oxidized products was obtained (Scheme 2, **4jac**, **4kac** & **4lac**).

Synthesis of molecules containing all carbon quaternary centers is always a challenging task in organic synthesis. Indeed, the generation of a quaternary carbon stereo center is even more challenging. Herein, we have successfully synthesized the compounds bearing a quaternary stereo center.[18] In addition, our protocol provides an opportunity to synthesize various analogs of biologically important symmetrical and unsymmetrical 3,3′-bis-heteroaryl-2-oxindoles, which were not accessed before.

Based on the above experiments and literature precedence[19] a plausible mechanism is depicted in Scheme 3. Coordination of bismuth to the keto-carbonyl group of isatin **1** increases the electrophilicity so much so that the C-6 position of tetrahydroquinoline **2** undergoes electrophilic attack by carbonyl carbon



Scheme 3 Plausible mechanism for regioselective C-6 functionalization of tetrahydroquinoline.

of isatin and forms intermediate **A**. Even though the C-8 position of tetrahydroquinoline is also capable of undergoing a similar electrophilic attack, we did not observe any product derived from this mode of attack, possibly due to steric reasons as shown below (intermediate **D**). Deprotonation and elimination of hydroxide from intermediate **A** lead to a quinoid type of intermediate **B** (detected by HRMS; see the ESI†) which reacts with another molecule of tetrahydroquinoline at the C-6 position and forms Sigma complex **C** which then undergoes deprotonation to regain aromaticity giving rise to biarylated product **3**.

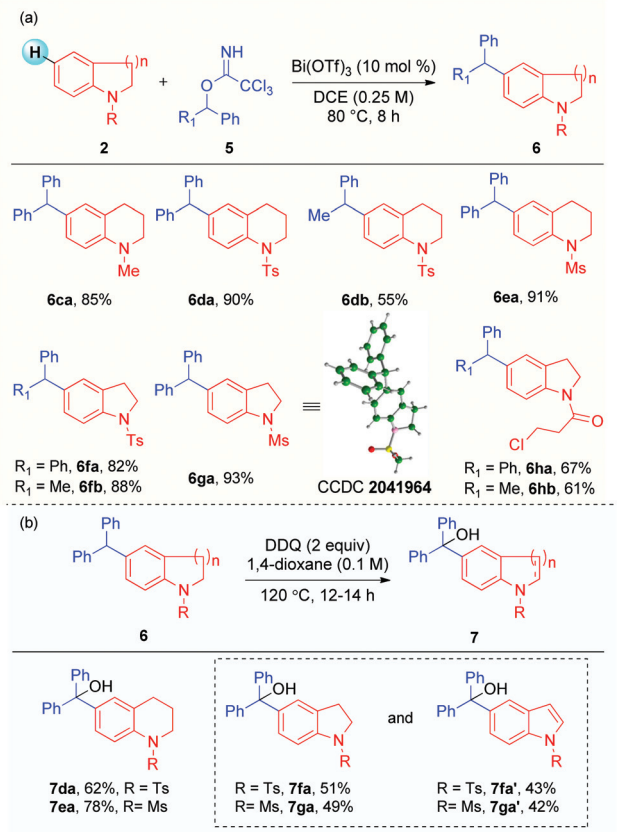
We intended to further demonstrate the scope of this methodology for the synthesis of another biologically important class of molecules such as 5-substituted indoline and 6-substituted tetrahydroquinoline derivatives **6** (Scheme 4a) for which trichloroacetimidate **5** was taken as the alkylating agent.[20] Hence, **2c** and **5a** were subjected to the optimized reaction conditions. As expected, we obtained the C-6 alkylated product in a very good yield of 85% (Scheme 4a, **6ca**).

Also, with *N*-tosyl and *N*-mesyl tetrahydroquinolines **2d** and **2e** the respective alkylated products were obtained in excellent yields of 90% and 91% (Scheme 4a, **6da** & **6ea**). Similarly, *N*-protected indolines **2f** and **2g** also resulted in good yields (82% & 93%) of their respective alkylated products (Scheme 4a, **6fa** & **6ga**). Additionally, when the alkylating agent was changed to 1-phenylethyltrichloroacetimidate, the reaction worked efficiently affording 55% and 88% yields of the respective alkylated products (Scheme 4a, **6db** & **6fb**).

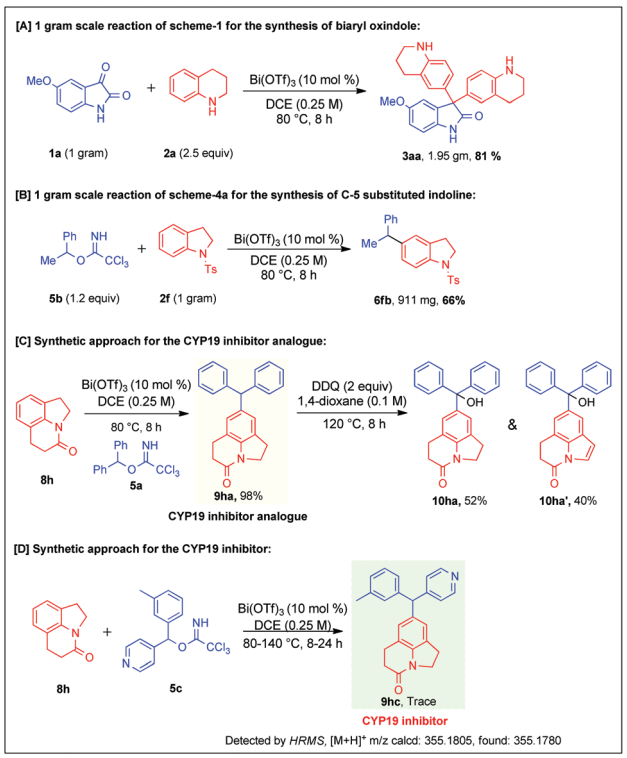
To test the robustness of this methodology we designed a substrate, which could potentially undergo intramolecular Friedel–Crafts alkylation in addition to intermolecular alkylation. When compound **2h** was allowed to react with **5a** and **5b** under the standard conditions, to our delight, it underwent chemoselective alkylation furnishing good yields 67% & 61% of their respective intermolecular alkylation products (Scheme 4a, **6ha** & **6hb**).

In order to diversify the product library, products **6** were oxidized using DDQ. Interestingly, in all cases triarylmethine carbon was oxidized to tertiary alcohol (Scheme 4b, **7da**, **7ea**, **7fa** & **7ga**) and in indoline cases, we obtained both hydroxylation and aromatization products (Scheme 4b, **7fa′** & **7ga′**) with 2 equivalents of DDQ. Apparently, it is clear that the hydroxylation step seems to be faster as compared to the aromatization of indoline to indole.

To show the efficiency of our protocol, we performed gram scale reaction for the synthesis of the biaryl oxindole and distal C–H functionalized product of tetrahydroquinoline and



Scheme 4 Scope of remote C–H functionalization of cyclic amines & DDQ oxidation. Reaction conditions for products **6ca–6hb**: (a) **2** (0.1 mmol), **5** (1.5 equiv.), $Bi(OTf)_3$ (10 mol%), and DCE (0.25 M), 80 °C, 8 h; Reaction conditions for products **7da–7ga′**: (b) **6** (0.1 mmol), DDQ (2 equiv.), and 1,4-dioxane (0.1 M), 120 °C, 12–14 h.



Scheme 5 Application of this methodology. Reaction conditions: (A) 1 g scale reaction for biaryloxindole synthesis; (B) 1 g scale reaction for the synthesis of C-5 substituted indoline; (C) 1st step = **8h** (0.1 mmol), **5a** (1.5 equiv.), $Bi(OTf)_3$ (10 mol%), and DCE (0.25 M), 80 °C, 8 h; 2nd step = **9ha** (0.1 mmol), DDQ (2 equiv.), and 1,4-dioxane (0.1 M), 120 °C, 8 h; (D) **8h** (0.1 mmol), **5c** (1.5 equiv.), $Bi(OTf)_3$ (10 mol%), DCE (0.25 M), 80–140 °C, 8–24 h.

indoline. When 1 g 5-methoxy isatin **1a** was reacted with **2a**, it gave the product **3aa** with 81% yield (1.95 g) (Scheme 5a). The *N*-tosyl indoline **2f** (1 g) on reaction with **5b** gave the product **6fb** with 66% yield (911 mg) (Scheme 5b). Hence the methodology is very much efficient in a large scale. Then to show more applications of this methodology we have synthesized molecules with close similarity to potent drug candidates such as the CYP19 inhibitor. Intramolecular alkylation of **2h** in the presence of $AlCl_3$ at 140 °C gave the intramolecular alkylation product **8h**, which under the standard conditions along with **5a** resulted in the C-5 alkylated product in 98% yield (Scheme 5c, **9ha**). The molecule **9ha** is analogous to the drug candidate, CYP19 inhibitor. Oxidation of **9ha** with 2 equivalents of DDQ led to the formation of two products (Scheme 5c, **10ha** & **10ha′**). With further interest, we tried to synthesize the CYP19 inhibitor molecule by reacting pyridin-4-yl(*m*-tolyl) methyl 2,2,2-trichloroacetimidate **5c** with **8h**, where a trace amount of product was found which was detected by HRMS.

3. Conclusions

In summary, we have developed bismuth catalyzed regioselective C-6 alkylation of tetrahydroquinolines with isatin derivatives. Both symmetrical and unsymmetrically arylated product of isatin derivatives were prepared in good to excellent yields. Bismuth is found to be the best catalyst choice because it is less toxic, works under low catalyst loading and allows hydrocompatibility (substrates with free OH/NH bonds). We have also developed C-6 and C-5 alkylation of tetrahydroquinolines and indolines, respectively, using trichloroacetimidates for the first time, where we attempted to synthesize the CYP-19 inhibitor and its analogues. We have demonstrated numerous applications of this methodology for the synthesis of drug-like molecules.

4. Experimental section

4.1 General information

Reactions were performed using oven dried Borosil seal-tube glass vials with Teflon-coated magnetic stirring bars under a N_2 atmosphere. A syringe was used to transfer the solvents and liquid reagents. Dioxane, DMF, MeOH, DCM, DCE, and CH_3CN were distilled and dried over calcium hydride. All other solvents such as hexane, EtOAc, DMSO, THF, diethyl ether, and acetone was used as received. Column chromatography was performed by using 100–200 and 230–400 mesh size silica gel from Acme Synthetic Chemicals Company. A gradient elution was performed by using distilled petroleum ether and ethyl acetate. TLC plates were detected under UV light at 254 nm. ^{1}H NMR and ^{13}CNMR spectra were recorded on Bruker AV 400 and 700 MHz spectrometers and a JEOL 400 MHz spectrometer using $CDCl_3$ as the deuterated solvent.[21] Chemical shifts (δ) are reported in ppm relative to the residual solvent ($CHCl_3$) signal (δ = 7.26 for ^{1}H NMR and δ = 77.36 for ^{13}C NMR). Data for ^{1}H NMR spectra are reported as follows: chemical shift (multiplicity, coupling constants, and number of hydrogen). Abbreviations are as follows: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet), dd (double doublet), br (broad signal), and *J* (coupling constants) in Hz (hertz). High-resolution mass spectrometry (HRMS) data were recorded using a micro-TOF Q-II mass spectrometer using methanol as solvent. IR spectra were recorded on a FTIR system and values are reported in frequency of absorption (cm^{-1}). Digital melting point apparatus is used to record the melting points. Reagents and starting materials were purchased from Sigma Aldrich, Alfa Aesar, TCI, Avra, Spectrochem and other commercially available sources and were used without further purification unless otherwise noted.

4.2 Experimental procedures

General procedure for the synthesis of *N*-acetyl isatin (1i). 1-Acetylindoline-2,3-dione was prepared according to a previously reported procedure.[29] Isatin (1.7 mmol) was suspended in acetic anhydride (10 mL) in a round bottom flask with a stir bar. Then 1 drop of H_2SO_4 was added to it and the reaction mixture was heated at reflux for 5 minutes at 140 °C. After the completion of reaction determined by TLC analysis, the reaction mixture was diluted with H_2O and saturated aqueous $NaHCO_3$ and worked up with EtOAc and the organic layer was washed with brine solution and dried over Na_2SO_4 and evaporated. Column chromatography gave the pure product as a yellow solid (82% yield).

General procedure for the synthesis of *N*-alkyl isatin (1j–1l). *N*-Protected isatins were prepared according to a previously reported procedure.[22–28] Isatin (1 equiv., 3.4 mmol) was dissolved in DMF (5 mL) solvent under a N_2 atmosphere and the mixture was taken in an oven-dried round-bottom flask equipped with a magnetic stir bar at room temperature. To this reaction mixture NaH (1.2 equiv., 4.1 mmol) was added portion-wise at 0 °C. Then alkyl halide (1.2 equiv., 4.1 mmol) was added to the solution in a dropwise manner through a syringe. The reaction mixture was allowed to stir for 2 h at 0 °C and then it was stirred at rt for 12 h. After the completion of reaction as monitored by TLC analysis, the reaction mixture was quenched with slow addition of water and then diluted with 10 mL of DCM. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated in a rotary evaporator under vacuum. The crude products were purified by flash chromatography on silica gel (30% EtOAc/petroleum ether) to afford the desired product.

General procedure for the synthesis of *N*-alkyl tetrahydroquinolines (2b and 2c). *N*-Protected tetrahydroquinolines were prepared according to a previously reported procedure.[30] Tetrahydroquinoline (1 equiv., 7.5 mmol) was dissolved in THF (10 mL) solvent under a N_2 atmosphere and the mixture was taken in an oven-dried round-bottom flask equipped with a magnetic stir bar at rt. To the reaction mixture, NaH (1.2 equiv., 9.0 mmol) was added portion-wise at 0 °C. Then alkyl halide (1.2 equiv., 9.0 mmol) was added to the solution in a

dropwise manner through a syringe. The reaction mixture was allowed to stir for 16 h at rt. It was quenched with slow addition of water and then diluted with 10 mL of EtOAc upon completion of reaction. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated in the rotary evaporator under vacuum. The crude products were purified by column chromatography to give the pure product as a colorless liquid.

General procedure for the synthesis of *N*-tosyl tetrahydroquinoline (2d). *N*-Tosyl tetrahydroquinoline was prepared according to a previously reported procedure.[31] To a solution of tetrahydroquinoline (1 equiv.) in pyridine was added TsCl (1.2 equiv.). It was stirred at rt for 2 h. When the reaction was complete as monitored by TLC, the pyridine was evaporated under reduced pressure. To the obtained crude product, H_2O was added followed by DCM solvent. After the separation of the organic layer, the water layer was extracted with 30 mL DCM. The combined organic layer was dried over anhydrous Na_2SO_4, filtered, evaporated and the evaporation residue was purified *via* column chromatography on silica gel (eluent: petroleum ether/ethyl acetate) to give the desired product as a white solid (84% yield).

General procedure for the synthesis of *N*-mesyl tetrahydroquinoline (2e). *N*-Mesyl tetrahydroquinoline was prepared according to a previously reported procedure.[32] Tetrahydroquinoline (1000 mg, 7.5 mmol) was dissolved in 5 mL dry pyridine and methanesulfonyl chloride (1.2 equiv., 9.0 mmol) was dropped in 2 portions under N_2. The reaction mixture was stirred for 2 h at room temperature and an intense red colour developed. When the reaction was complete as determined by TLC, the crude reaction mixture was poured into 100 mL of cold 0.5 M HCl and extracted twice with 50 mL DCM. The organic phase was evaporated and the evaporation residue was purified by passing through a silica plug. The product eluted in 7/3 PE/EtOAc, while all of the pink polar by-product was retained on silica. The product was obtained as a brown solid (85% yield).

General procedure for the synthesis of *N*-tosyl indoline (2f). *N*-Tosyl indoline was prepared according to a previously reported procedure.[33] To a solution of the indoline (1.0 equiv.) in DCM (0.1 M) were added pyridine (3.0 equiv.) and *p*-toluenesulfonyl chloride (1.1 equiv.) and the resulting solution was stirred at room temperature for 16 h. Upon completion of reaction confirmed by TLC check, H_2O was added. The phases were separated and the aqueous layer was extracted with DCM (3 × 10 mL). The combined organic layers were washed with 1 M HCl and brine. Then the organic solvent was dried over anhydrous Na_2SO_4 and filtered and evaporated under reduced pressure. The evaporation residue was purified on silica gel to give the product as a white solid (76% yield).

General procedure for the synthesis of *N*-mesyl indoline (2g). *N*-Mesyl indoline was prepared according to a previously reported procedure.[34] In a 100 mL two-neck round bottom flask, NaH (1.3 equiv.) was taken under a N_2-atmosphere and to it dry hexane was added, so that it dissolved the grease present in NaH and then hexane was decanted through a syringe. Then indoline (1 equiv.) in diethyl ether (5 mL) was added slowly after the addition of dry ether (3 mL) (under ice cold conditions). Then it was washed with 2 mL dry ether and left for stirring for 30 minutes. Then methane sulfonyl chloride in diethyl ether was added to it and washed with 5 mL ether under ice cold conditions. After being stirred at room temperature for 14 h, the reaction was quenched with saturated aqueous NH_4Cl (10 mL), and extracted with DCM (3 × 10 mL). The combined organic phases were washed with brine (10 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by column chromatography on silica gel (hexane : ethyl acetate = 3 : 1) afforded the pure product (67% yield) as a light brown solid, R_f = 0.3 (20% EtOAc in hexane).

General procedure for *N*-acylation of indoline (2h). 3-Chloro-dihydro-indolyl propanone was prepared according to a previously reported procedure.[35] To a solution of indoline (4.0 g, 0.03 mol) in acetone (100 mL) in a round bottomed flask was added 3-chloro-propionyl chloride (4.7 g, 0.04 mol). After heating the mixture at 70 °C in an oil bath for 3 h, the solvent was removed under vacuum. The resulting residue was dissolved in DCM and washed with water and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated to give the product as a brown solid (7.0 g, 99% yield).

General procedure for the synthesis of pyrroloquinolinone (8h). Tetrahydropyrroloquinolinone was prepared according to a previously reported procedure.[36] A molten mixture of 3-chloro-dihydro-indolyl propanone (44.5 g, 212 mmol) and $AlCl_3$ (149 g, 1.12 mol) was taken in a round bottom flask and refluxed at 140 °C in a preheated oil bath for 4 h. Upon completion of reaction, it was cooled to 0 °C and then a mixture of water/ice (500 g) was added to decompose excess $AlCl_3$. The resulting solution was extracted with EtOAc (3 × 200 ml), followed by drying over $MgSO_4$. Removal of the solvent gave a yellow solid, which was purified by flash chromatography (EtOAc : hexane = 2 : 5, R_f = 0.15) to give the product as a white solid (25.7 g, 70% yield).

General procedure for the synthesis of trichloroacetimidate (5). Trichloroacetimidate was prepared according to a previously reported procedure.[37] Acetophenol or benzophenol (1 equiv.) was taken in a round bottom flask with a stir bar and to that DCM (0.32 M) was added through a syringe. Then DBU (0.02 equiv.) was added to the reaction mixture and kept at 0 °C by putting ice. After stirring for 5 min, trichloroacetonitrile (10 equiv.) was added to the reaction mixture slowly and left to stir for 10 min under cold conditions. Then after bringing it to room temperature, it was allowed to stir for 16 h. After the reaction completion, the reaction mixture was rota-evaporated and column chromatography (5% basified with Et_3N) gave the pure product.

General procedure A for the synthesis of biaryl oxindole *via* 2-component reaction (3). Isatin derivative **1** (1 equiv., 0.3 mmol) was dissolved in DCE (0.25 M) solvent under a N_2 atmosphere in an oven-dried sealed tube equipped with a magnetic stir bar at room temperature. A catalytic amount

of $Bi(OTf)_3$ (10 mol%) was added to the reaction mixture followed by the addition of tetrahydroquinoline derivative **2** (2.5 equiv., 0.6 mmol). The reaction mixture was allowed to stir at 80 °C in a pre-heated aluminum block until the reaction completed. The reaction mixture was quenched with and diluted with EtOAc after the completion of reaction (monitored by TLC). The reaction mixture was then passed through Celite and evaporated. The evaporation residue was purified by column chromatography (200–400 mesh silica, basified with 5% Et_3N) to give the pure product **3**.

Procedure for the synthesis of biaryl oxindole *via* 3-component reaction (3jac–3lac). Isatin derivative **1** (1 equiv., 0.3 mmol) was dissolved in DCE (1 mL) solvent under a N_2 atmosphere in an oven-dried sealed tube flask equipped with a magnetic stir bar at room temperature. A catalytic amount of $Bi(OTf)_3$ (10 mol%) was added to the solution of the starting material and then tetrahydroquinoline **2a** (1.2 equiv., 0.34 mmol) and another derivative of tetrahydroquinoline **2c** (1.2 equiv., 0.34 mmol) were added to the reaction mixture. The reaction mixture was allowed to stir at 80 °C in a pre-heated aluminum block until the reaction completed. It was quenched and diluted with EtOAc after the completion of reaction (monitored by TLC). The reaction mixture was then passed through Celite and the solvent was evaporated. The evaporation residue was purified by column chromatography (200–400 mesh silica, basified with 5% Et_3N) to give the pure product.

General procedure B for the synthesis of oxidized product 4. The oxidised product of biaryl oxindole **3** was prepared according to a previously reported procedure.[38] Biaryl oxindole derivative **3** (1 equiv., 0.1 mmol) was dissolved in CH_3CN (1.5 mL) solvent under an O_2 atmosphere and the mixture was taken in an oven-dried round bottom flask equipped with a magnetic stir bar at room temperature. Then copper iodide (0.1 equiv., 0.01 mmol) and DIAD (0.1 equiv., 0.01 mmol) were added followed by the addition of DMAP (20 mol%) to this reaction mixture. The reaction mixture was allowed to stir at room temperature until the reaction completed. The reaction mixture was quenched and diluted with EtOAc after the completion of reaction (monitored by TLC). The reaction mixture was then passed through Celite and the solvent was evaporated. The crude mixture was purified by column chromatography (200–400 mesh silica, basified by 5% Et_3N) to give the pure product **4**.

General procedure C for the synthesis of the remote C–H functionalized product of tetrahydroquinolines & indolines (6). The compound **2** (1 equiv., 0.43 mmol) was dissolved in DCE (0.2 M) solvent under a N_2 atmosphere in an oven-dried sealed tube flask equipped with a magnetic stir bar at room temperature. Then a catalytic amount of $Bi(OTf)_3$ (10 mol%) was added to the solution of the starting material and then trichloroacetimidate derivative **5** (1.2 equiv.) was added to this reaction mixture. The reaction mixture was allowed to stir at 80 °C in a pre-heated aluminum block until the reaction completed. The reaction mixture was quenched and diluted with EtOAc after the completion of reaction (monitored by TLC). The reaction mixture was then passed through Celite and the solvent was evaporated. The crude products were purified by column chromatography (200–400 mesh silica) to give the pure product **6.**

General procedure D for oxidation of 6 to 7. The oxidized product of **6** was prepared according to a previously reported procedure.[39] The compound **6** (1 equiv.) was dissolved in dioxane (0.1 M) solvent under a N_2 atmosphere and the mixture was taken in an oven-dried sealed tube flask equipped with a magnetic stir bar at room temperature. Then a catalytic amount of DDQ (2 equiv.) was added to the solution of the starting material and then the reaction mixture was allowed to stir at 120 °C in a pre-heated aluminum block until the reaction completed. The reaction mixture was quenched and diluted with EtOAc after the completion of reaction (monitored by TLC). The reaction mixture was then passed through Celite and the solvent was evaporated. The crude products were purified by column chromatography (200–400 mesh silica) to give the pure product **7**.

4.3 Mechanistic studies

Synthesis of 3aa in the presence of BHT. 5-Methoxy isatin (**1a**, 30 mg, 1 equiv.), tetrahydroquinoline (**2a**, 2.5 equiv.), $Bi(OTf)_3$ (10 mol%), BHT (1 equiv.) and DCE (0.25 M) were charged into a Schlenk tube. The reaction mixture was allowed to stir at 80 °C in a pre-heated aluminum block for 8 h. After the completion of reaction as monitored by TLC, the crude reaction mixture was passed through a Celite pad. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using a hexane/ethyl acetate (4 : 6) solvent system to afford compound **3aa** in 92% isolated yield.

Synthesis of 3aa in the presence of TEMPO. 5-Methoxy isatin (**1a**, 30 mg, 1 equiv.), tetrahydroquinoline (**2a**, 2.5 equiv.), $Bi(OTf)_3$ (10 mol%), TEMPO (1 equiv.) and DCE (0.25 M) were charged into a Schlenk tube. The reaction mixture was allowed to stir at 80 °C in a pre-heated aluminum block for 8 h. After the completion of reaction as monitored by TLC, the crude reaction mixture was passed through a Celite pad. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography using a hexane/ethyl acetate (4 : 6) solvent system to afford compound **3aa** in 78% isolated yield.

4.4 Application

General procedure for the synthesis of the CYP19 inhibitor (9hc) & its analogue (9ha). Tetrahydropyrroloquinolinone (**8h**, 40 mg, 0.23 mmol) was dissolved in DCE (0.25 M) under a N_2 atmosphere in an oven-dried sealed tube equipped with a magnetic stir bar at room temperature. An amidate derivative (1.5 equiv., 0.35 mmol) was added to the reaction mixture followed by the addition of a catalytic amount of $Bi(OTf)_3$ (10 mol%). The reaction mixture was allowed to stir at 80 °C in a pre-heated aluminum block until the reaction completed. The reaction mixture was quenched and diluted with EtOAc after the completion of reaction (monitored by TLC) and then it was

passed through Celite and evaporated. The crude products were purified by column chromatography (200–400 mesh silica) to give the pure product.

General procedure for the synthesis of 10ha & 10ha′. The product **9ha** (50 mg, 0.15 mmol) was taken in an oven-dried sealed tube equipped with a magnetic stir bar and subjected to DDQ (2 equiv., 0.3 mmol) in dioxane solvent (0.1 M). The reaction mixture was allowed to stir at 120 °C in a pre-heated aluminum block for 8 h and it was quenched and diluted with EtOAc after the completion of reaction (monitored by TLC) and then it was passed through Celite and evaporated. The crude products were purified by column chromatography (200–400 mesh silica) to give the pure products **10ha** as a white solid (27 mg, 52% yield) and **10ha′** as a brown solid (20 mg, 40% yield).

5. Experimental characterization data for the starting materials, products and post-functionalized adducts

Staring materials used in this study:

Starting materials **1i**,[29] **1j–1k**,[25,26] **1l**,[25,27] **2b–2c**,[30] **2d**,[32] **2e**,[31] **2f**,[33] **2g**,[34] **2h**,[35] **5a–5c**,[37] and **8h**[36] were synthesized according to previously reported procedures and the spectroscopic data were identical to those reported.

5.1 Experimental characterization data for the products 3

*5-Methoxy-3,3-bis(1,2,3,4-tetrahydroquinolin-6-yl)indolin-2-one (**3aa**)* was prepared according to general procedure A. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **3aa** (44.2 mg for 0.11 mmol scale) in 92% yield. Physical state: white solid. M.p.: 118–120 °C. R_f-Value: 0.3 (50% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (s, 1H), 6.86–6.79 (m, 6H), 6.71 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 6.38 (d, J = 8.8 Hz, 2H), 3.73 (s, 3H), 3.26 (t, J = 5.2 Hz, 4H), 2.67 (t, J = 6.0 Hz, 4H), 1.88 (quint, J = 6 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.1, 156.1, 144.1, 136.9, 133.8, 130.5, 129.7, 127.3, 121.6, 114.4, 113.6, 112.5, 110.4, 62.5, 56.1, 42.3, 27.4, 22.4. IR (KBr, cm^{-1}): 3384, 3157, 2925, 1698, 1611, 1508, 1302. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{27}H_{28}N_3O_2$: 426.2176; Found: 426.2173.

*3,3-Bis(1,2,3,4-tetrahydroquinolin-6-yl)indolin-2-one (**3ba**)* was prepared according to general procedure A. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **3ba** (37 mg for 0.14 mmol scale) in 69% yield. Physical state: light yellow solid. M.p.: 190–197 °C. R_f-Value: 0.2 (50% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21 (s, 1H), 7.19–7.16 (m, 2H), 7.01 (t, J = 7.6 Hz, 1H), 6.91–6.84 (m, 5H), 6.38–6.36 (m, 2H), 3.25 (t, J = 5.6 Hz, 4H), 2.66 (t, J = 6.4 Hz, 4H), 1.88 (quint, J = 6.0 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.2, 144.0, 140.3, 135.5, 130.5, 129.7, 127.9, 127.3, 126.5, 122.9, 121.6, 114.4, 110.1, 62.0, 42.3, 27.3, 22.4. IR (KBr, cm^{-1}): 3402, 3022, 2836, 1703, 1653, 1510. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{26}H_{26}N_3O$: 396.2070; Found: 396.2084.

*3,3-Bis(1,2,3,4-tetrahydroquinolin-6-yl)-5-(trifluoromethoxy) indolin-2-one (**3ca**)* was prepared according to general procedure A. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **3ca** (75 mg for 0.22 mmol scale) in 72% yield. Physical state: white solid. M.p.: 157–162 °C. R_f-Value: 0.5 (30% EtOAc/hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.42 (s, 1H), 7.04–7.01 (m, 2H), 6.84–6.81 (m, 5H), 6.37 (d, J = 8.4 Hz, 2H), 3.24 (t, J = 5.6 Hz, 4H), 2.65 (t, J = 6.4 Hz, 4H), 1.87 (quint, J = 6.4 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.1, 144.8, 144.3, 139.4, 137.0, 129.5, 127.1, 122.1, 121.5, 120.45, 119.6, 114.4, 111.0, 62.5, 42.2, 27.3, 22.3.

IR (KBr, cm^{-1}): 3390, 2930, 2843, 1716, 1699, 1615, 1510, 1218, 823. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{27}H_{25}F_3N_3O_2$: 480.1893; Found: 480.1896.

*5-Fluoro-3,3-bis(1,2,3,4-tetrahydroquinolin-6-yl)indolin-2-one (**3da**)* was prepared according to general procedure A. The crude reaction mixture was purified by column chromatography using silica gel (100–200 mesh) giving **3da** (49 mg for 0.18 mmol scale) in 65% yield. Physical state: pale yellow solid. M.p.: 110–120 °C. R_f-Value: 0.3 (50% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.16 (s, 1H), 6.91–6.78 (m, 7H), 6.38–6.36 (m, 2H), 3.25 (t, J = 5.6 Hz, 4H), 2.66 (t, J = 6.4 Hz, 4H), 1.87 (quint, J = 6.4 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.9, 159.3 (d, J_{C-F} = 239.0 Hz), 144.3, 137.1 (d, J_{C-F} = 8 Hz), 136.4 (d, J_{C-F} = 2 Hz), 129.8, 129.5, 127.2, 121.6, 114.4, 114.3 (d, J_{C-F} = 23 Hz), 114.0 (d, J_{C-F} = 25 Hz), 110.9 (d, J_{C-F} = 8 Hz), 62.6, 42.2, 27.3, 22.3. IR (KBr, cm^{-1}): 3402, 2926, 2841, 1702, 1510, 1485, 793. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{26}H_{25}FN_3O$: 414.1976; Found: 414.2010.

*5-Chloro-3,3-bis(1,2,3,4-tetrahydroquinolin-6-yl)indolin-2-one (**3ea**)* was prepared according to general procedure A. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **3ea** (33 mg for 0.11 mmol scale) in 70% yield. Physical state: light yellow solid. M.p.: 138–140 °C. R_f-Value: 0.2 (40% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.70 (s, 1H), 7.13 (s, 2H), 6.82–6.81 (m, 5H), 6.37 (d, J = 8.8 Hz, 2H), 3.26–3.25 (m, 4H), 2.68–2.66 (m, 4H), 1.88–1.87 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.1, 144.4, 139.0, 137.3, 129.7, 129.6, 128.1, 128.0, 127.2, 126.8, 121.6, 114.4, 111.2, 62.3, 42.3, 27.4, 22.4. IR (KBr, cm^{-1}): 3401, 3158, 2925, 1700, 1612, 1508, 732. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{26}H_{25}ClN_3O$: 430.1681; Found: 430.1701.

*5-Bromo-3,3-bis(1,2,3,4-tetrahydroquinolin-6-yl)indolin-2-one (**3fa**)* was prepared according to general procedure A. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **3fa** (62 mg for 0.22 mmol scale) in 59% yield. Physical state: yellow solid. M.p.: 140–145 °C. R_f-Value: 0.2 (40% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.46 (s, 1H), 7.31–7.27 (m, 2H), 6.82–6.77 (m, 5H), 6.39–6.37 (m, 2H), 3.26 (t, J = 5.6 Hz, 4H), 2.67 (t, J = 6.4 Hz, 4H), 1.89 (quint, J = 6.4 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.0, 144.4, 139.4, 137.6, 130.8, 129.6, 129.56, 129.5, 127.2, 121.6, 115.5, 114.4, 111.7, 62.3, 42.3, 27.4, 22.4.

IR (KBr, cm^{-1}): 3380, 3105, 2809, 1704, 1580, 1509, 738. HRMS (ESI) *m*/*z*: $[M + H]^+$ Calcd for $C_{26}H_{25}BrN_3O$: 474.1176; Found: 474.1148.

*5,6-Difluoro-3,3-bis(1,2,3,4-tetrahydroquinolin-6-yl)indolin-2-one (**3ga**)* was prepared according to general procedure A. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **3ga** (71 mg for 0.27 mmol scale) in 62% yield. Physical state: yellow solid. M.p.: 175–180 °C. R_f-Value: 0.1 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.77 (s, 1H), 6.985 (dd, J_1 = 9.6 Hz, J_2 = 7.6 Hz, 1H), 6.82–6.79 (m, 4H), 6.73 (dd, J_1 = 9.6 Hz, J_2 = 6.4 Hz, 1H), 6.38 (d, J = 8.0 Hz, 2H), 3.26 (t, J = 5.6 Hz, 4H), 2.67 (t, J = 6.4 Hz, 4H), 1.89 (quint, J = 6.4 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.3, 171.6, 150.1, 146.9, 144.4, 136.6, 131.0, 129.5, 129.4, 127.1, 121.6, 115.4, 114.4, 100.6, 62.3, 42.2, 27.3, 22.2, (60.7, 21.4, 14.5 = EtOAc peaks). IR (KBr, cm^{-1}): 3399, 2929, 2841, 1716, 1630, 1612, 1503, 1184, 798. HRMS (ESI) *m*/*z*: $[M + H]^+$ Calcd for $C_{26}H_{24}F_2N_3O$: 432.1882; Found: 432.1812.

*7-Methyl-3,3-bis(1,2,3,4-tetrahydroquinolin-6-yl)indolin-2-one (**3ha**)* was prepared according to general procedure A. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **3ha** (52 mg for 0.31 mmol scale) in 41% yield. Physical state: yellow solid. M.p.: 240–245 °C. R_f-Value: 0.2 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.50 (s, 1H), 7.03–6.98 (m, 2H), 6.94–6.90 (m, 1H), 6.86–6.84 (m, 4H), 6.36 (d, J = 8.8 Hz, 2H), 3.25 (t, J = 5.6 Hz, 4H), 2.66 (t, J = 6.4 Hz, 4H), 2.25 (s, 3H), 1.88 (quint, J = 6.4 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.0, 144.0, 139.2, 135.0, 130.6, 129.7, 129.1, 127.3, 123.9, 122.6, 121.4, 119.6, 114.3, 62.4, 42.3, 27.3, 22.4, 16.9. IR (KBr, cm^{-1}): 2957, 2856, 1699, 1611, 1508, 1464, 1301, 810, 732. HRMS (ESI) *m*/*z*: $[M + H]^+$ Calcd for $C_{27}H_{28}N_3O$: 410.2227; Found: 410.2169.

*1-Acetyl-3,3-bis(1,2,3,4-tetrahydroquinolin-6-yl)indolin-2-one (**3ia**)* was prepared according to general procedure A. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **3ia** (31 mg for 0.11 mmol scale) in 67% yield. Physical state: colourless liquid. R_f-Value: 0.2 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (d, J = 8.4 Hz, 1H), 7.32–7.28 (m, 1H), 7.18 (d, J = 4.4 Hz, 2H), 6.80–6.75 (m, 4H), 6.36 (d, J = 8.4 Hz, 2H), 3.26 (t, J = 5.6 Hz, 4H), 2.69–2.64 (m, 7H), 1.89 (quint, J = 6.0 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.1, 171.8, 144.4, 139.5, 134.0, 130.1, 129.7, 128.2, 127.4, 126.1, 125.5, 121.4, 116.9, 114.2, 62.1, 42.2, 27.4, 27.2, 22.3. IR (KBr, cm^{-1}): 3405, 3126, 2928, 1709, 1611, 1511. HRMS (ESI) *m*/*z*: $[M + H]^+$ Calcd for $C_{28}H_{28}N_3O_2$: 438.2176; Found: 438.2166.

*1-Benzyl-3,3-bis(1,2,3,4-tetrahydroquinolin-6-yl)indolin-2-one (**3ja**)* was prepared according to general procedure A. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **3ja** (31.5 mg for 0.08 mmol scale) in 77% yield. Physical state: yellow solid. M.p.: 82–88 °C. R_f-Value: 0.4 (50% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.22 (m, 6H), 7.11–7.09 (m, 1H), 7.01–6.97 (m, 1H), 6.84 (s, 4H), 6.73–6.71 (m, 1H), 6.36 (d, J = 7.2 Hz, 2H), 4.96 (s, 2H), 3.25 (br, 4H), 2.66 (br, 4H), 1.89–1.88 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.1, 144.1, 142.3, 136.5, 134.9, 130.8, 129.7, 129.0, 127.73, 127.72, 127.6, 127.2, 126.1, 122.9, 121.5, 114.3, 109.5, 61.6, 44.2, 42.3, 27.4, 22.4. IR (KBr, cm^{-1}): 3389, 2924, 2838, 1701, 1608, 1509. HRMS (ESI) *m*/*z*: $[M + H]^+$ Calcd for $C_{33}H_{32}N_3O$: 486.2540; Found: 486.2533.

*1-Methyl-3,3-bis(1,2,3,4-tetrahydroquinolin-6-yl)indolin-2-one (**3ka**)* was prepared according to general procedure A. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **3ka** (38 mg for 0.12 mmol scale) in 75% yield. Physical state: pale solid. M.p.: 278–280 °C. R_f-Value: 0.13 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26–7.21 (m, 2H), 7.04 (t, J = 7.2 Hz, 1H), 6.87–6.81 (m, 5H), 6.35–6.33 (m, 2H), 3.76 (br, 2H), 3.25–3.22 (m, 7H), 2.65 (t, J = 6.4 Hz, 4H), 1.87 (p, J_1 = 5.6 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.1, 144.1, 143.3, 134.8, 130.7, 129.6, 127.9, 127.2, 126.2, 122.8, 121.4, 114.2, 108.4, 61.5, 42.3, 27.4, 26.9, 22.4. IR (KBr, cm^{-1}): 3409, 2839, 2925, 1703, 1606, 1511, 1275. HRMS (ESI) *m*/*z*: $[M + H]^+$ Calcd for $C_{27}H_{28}N_3O$: 410.2227; Found: 410.2246.

*5-Chloro-1-methyl-3,3-bis(1,2,3,4-tetrahydroquinolin-6-yl) indolin-2-one (**3la**)* was prepared according to general procedure A. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **3la** (36 mg for 0.10 mmol scale) in 80% yield. Physical state: pink solid. M.p.: 195–200 °C. R_f-Value: 0.3 (40% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 1H), 7.18 (d, J = 2.0 Hz, 1H), 6.79–6.77 (m, 5H), 6.37–6.35 (m, 2H), 3.27–3.24 (m, 7H), 2.67 (t, J = 6.4 Hz, 4H), 1.89 (quint, J = 5.6 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.7, 144.3, 141.9, 136.5, 130.0, 129.5, 128.2, 127.9, 127.2, 126.5, 121.5, 114.3, 109.4, 61.8, 42.3, 27.4, 27.0, 22.4. IR (KBr, cm^{-1}): 3365, 2923, 2836, 1706, 1610, 1514, 811. HRMS (ESI) *m*/*z*: $[M + H]^+$ Calcd for $C_{27}H_{27}ClN_3O$: 444.1837; Found: 444.1780.

*3,3-Bis(1-benzyl-1,2,3,4-tetrahydroquinolin-6-yl)-5-chloro-indolin-2-one (**3eb**)* was prepared according to general procedure A. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **3eb** (61 mg for 0.11 mmol scale) in 91% yield. Physical state: pale green solid. M.p.: 110–120 °C. R_f-Value: 0.5 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.48–9.40 (m, 1H), 7.33–7.18 (m, 10H), 7.10 (s, 1H), 7.04 (d, J = 8.4 Hz, 1H), 6.87 (s, 2H), 6.81–6.80 (m, 2H), 6.72 (d, J = 8.4 Hz, 1H), 6.39 (d, J = 8.4 Hz, 2H), 4.39 (s, 4H), 3.28 (br, 4H), 2.70–2.69 (m, 4H), 1.93–1.92 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.9, 145.2, 139.2, 137.4, 129.1, 128.9, 128.4, 127.9, 127.8, 127.5, 127.1, 127.0, 126.6, 122.5, 111.6, 111.5, 111.1, 62.3, 55.6, 50.1, 28.5, 22.6. IR (KBr, cm^{-1}): 3366, 2923, 2838, 1707, 1610, 1509, 732. HRMS (ESI) *m*/*z*: $[M + H]^+$ Calcd for $C_{40}H_{37}ClN_3O$: 610.2620; Found: 610.2616.

*3,3-Bis(1-benzyl-1,2,3,4-tetrahydroquinolin-6-yl)-5-methoxy indolin-2-one (**3ab**)* was prepared according to general procedure A. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **3ab** (57 mg for 0.11 mmol scale) in 83% yield. Physical state: brown solid. M.p.: 125–130 °C. R_f-Value: 0.5 (30% EtOAc/

hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.47 (s, 1H), 7.29 (t, J = 7.2 Hz, 4H), 7.24–7.19 (m, 6H), 6.90 (d, J = 2 Hz, 2H), 6.84 (d, J = 2 Hz, 1H), 6.82 (d, J = 2.4 Hz, 1H), 6.79 (d, J = 8.4 Hz, 1H), 6.76 (d, J = 2.8 Hz, 1H), 6.68 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 2H), 6.40 (d, J = 8.8 Hz, 2H), 4.41 (s, 4H), 3.71 (s, 3H), 3.30 (t, J = 5.6 Hz, 4H), 2.72 (t, J = 6.4 Hz, 4H), 1.95 (quint, J = 6.4 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.0, 155.9, 145.0, 139.3, 137.0, 134.1, 129.2, 129.1, 128.8, 127.5, 127.0, 126.9, 122.3, 113.5, 112.3, 111.0, 110.6, 62.4, 56.0, 55.6, 50.1, 28.5, 22.6. IR (KBr, cm^{-1}): 3433, 3053, 2985, 1635, 1421, 1247. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{41}H_{40}N_3O_2$: 606.3115; Found: 606.3118.

*1-Benzyl-3,3-bis(1-benzyl-1,2,3,4-tetrahydroquinolin-6-yl) indolin-2-one (**3jb**)* was prepared according to general procedure A. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **3jb** (52 mg for 0.08 mmol scale) in 92% yield. Physical state: maroon solid. M.p.: 105–115 °C. R_f-Value: 0.6 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29–7.23 (m, 16H), 7.10–7.07 (m, 1H), 6.98–6.95 (m, 1H), 6.90 (s, 2H), 6.83 (d, J = 8.4 Hz, 2H), 6.69 (d, J = 7.2 Hz, 1H), 6.39 (d, J = 8.0 Hz, 2H), 4.94 (s, 2H), 4.41 (s, 4H), 3.30 (br, 4H), 2.71 (br, 4H), 1.95 (br, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.2, 145.0, 142.3, 139.4, 136.5, 135.0, 129.4, 129.3, 129.1, 129.0, 128.8, 127.7, 127.6, 127.5, 127.1, 127.0, 126.2, 122.8, 122.3, 110.9, 109.5, 61.4, 55.6, 50.2, 44.2, 28.6, 22.6. IR (KBr, cm^{-1}): 3028, 2925, 1710, 1608, 1510. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{47}H_{44}N_3O$: 666.3479; Found: 666.3480.

*3,3-Bis(1-benzyl-1,2,3,4-tetrahydroquinolin-6-yl)-1-methyl indolin-2-one (**3kb**)* was prepared according to general procedure A. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **3kb** (50 mg for 0.12 mmol scale) in 68% yield. Physical state: brown solid. M.p.: 120–130 °C. R_f-Value: 0.5 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26–7.21 (m, 12H), 7.00 (s, 1H), 6.88–6.79 (m, 5H), 6.36 (d, J = 7.2 Hz, 2H), 4.38 (S, 4H), 3.28–3.22 (m, 7H), 2.70 (br, 4H), 1.92 (br, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.2, 144.9, 143.2, 139.3, 134.8, 129.3, 129.1, 128.8, 127.8, 127.4, 127.0, 126.9, 126.2, 122.7, 122.2, 110.8, 108.3, 61.2, 55.5, 50.1, 28.5, 26.8, 22.6. IR (KBr, cm^{-1}): 3142, 2924, 2851, 1709, 1607, 1509. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{41}H_{40}N_3O$: 590.3166; Found: 590.3161.

*1-Benzyl-3,3-bis(1-methyl-1,2,3,4-tetrahydroquinolin-6-yl) indolin-2-one (**3jc**)* was prepared according to general procedure A. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **3jc** (82 mg for 0.21 mmol scale) in 76% yield. Physical state: white solid. M.p.: 117–122 °C. R_f-Value: 0.5 (20% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.24 (m, 6H), 7.11 (dt, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 1H), 7.00 (dd, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 1H), 6.95 (dd, J_1 = 8.8 Hz, J_2 = 2.4 Hz, 2H), 6.87 (d, J = 2.4 Hz, 2H), 6.71 (d, J = 7.6 Hz, 1H), 6.48 (d, J = 8.4 Hz, 2H), 4.96 (s, 2H), 3.17 (t, J = 6 Hz, 4H), 2.84 (s, 6H), 2.67 (t, J = 6.4 Hz, 4H), 1.92 (quint, J = 6.4 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.1, 146.0, 142.4, 136.6, 135.0, 129.9, 129.1, 129.0, 127.7, 127.6, 127.4, 126.2, 122.9, 122.88, 110.9, 109.5, 61.4, 51.5, 44.2, 39.4, 28.2, 22.7. IR (KBr, cm^{-1}): 2927, 2855, 1713, 1608, 1506, 1323, 1207. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{35}H_{36}N_3O$: 514.2818; Found: 514.2853.

*1-Methyl-3,3-bis(1-methyl-1,2,3,4-tetrahydroquinolin-6-yl) indolin-2-one (**3kc**)* was prepared according to general procedure A. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **3kc** (32.5 mg for 0.12 mmol scale) in 60% yield. Physical state: brown solid. M.p.: 150–165 °C. R_f-Value: 0.6 (30% EtOAc/hexane). ^{1}H NMR (700 MHz, $CDCl_3$): δ 7.18–7.16 (m, 2H), 6.96 (t, J = 7.7 Hz, 1H), 6.84 (d, J = 8.4 Hz, 2H), 6.79–6.77 (m, 3H), 6.39 (d, J = 8.4 Hz, 2H), 3.18 (s, 3H), 3.09 (t, J = 5.6 Hz, 4H), 2.75 (s, 6H), 2.59 (t, J = 7 Hz, 4H), 1.84 (quint, J = 6.3 Hz, 4H). ^{13}C NMR (175 MHz, $CDCl_3$): δ 179.1, 146.0, 143.3, 134.9, 129.8, 129.0, 127.8, 127.4, 126.2, 122.9, 122.8, 110.8, 108.4, 61.4, 51.5, 39.4, 28.2, 26.9, 22.7. IR (KBr, cm^{-1}): 3130, 2927, 1709, 1606, 1510. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{29}H_{32}N_3O$: 438.2540; Found: 438.2511.

*5-Chloro-1-methyl-3,3-bis(1-methyl-1,2,3,4 tetrahydroquinolin-6-yl)indolin-2-one (**3lc**)* was prepared according to general procedure A. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **3lc** (47 mg for 0.10 mmol scale) in 97% yield. Physical state: white solid. M.p.: 110–112 °C. R_f-Value: 0.2 (50% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23–7.19 (m, 2H), 6.89–6.86 (m, 2H), 6.81–6.76 (m, 3H), 6.46 (d, J = 8.4 Hz, 2H), 3.23 (s, 3H), 3.18 (t, J = 6.0 Hz, 4H), 2.84 (s, 6H), 2.67 (t, J = 6.4 Hz, 4H), 1.92 (quint, J = 6.0 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.7, 146.2, 141.9, 136.5, 129.0, 128.9, 128.1, 127.9, 127.3, 126.5, 123.0, 110.8, 109.3, 61.6, 51.5, 39.3, 28.2, 27.0, 22.7. IR (KBr, cm^{-1}): 2928, 2817, 1717, 1608, 1510, 806. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{29}H_{31}ClN_3O$: 472.2150; Found: 472.2167.

*3,3-Bis(4-(dimethylamino)phenyl)-5-methoxyindolin-2-one (**3b′**)* was prepared according to general procedure A. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **3b′** (17 mg for 0.10 mmol scale) in 42% yield. Physical state: yellow solid. M.p.: 247–250 °C. R_f-Value: 0.4 (40% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.90 (s, 1H), 7.15 (d, J = 8.8 Hz, 4H), 6.82 (d, J = 8.4 Hz, 1H), 6.79 (d, J = 2.4 Hz, 1H), 6.70 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 6.65 (J = 8.8 Hz, 4H), 3.78 (s, 3H), 2.90 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.5, 156.0, 149.9, 136.6, 134.1, 130.0, 129.4, 113.4, 112.7, 112.67, 110.7, 62.4, 56.0, 40.9. IR (KBr, cm^{-1}): 2922, 2850, 1717, 1516, 1489, 1288, 1246, 1030. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{28}N_3O_2$: 402.2176; Found: 402.2171.

*2,2″,3,3″-Tetrahydro-1H,1″H-[5,3′:3′,5″-terbenzo[b]pyrrol]-2′(1′H)-one (**3b″**)* was prepared according to general procedure A. The crude reaction mixture was subjected to HRMS and a trace amount of the product **3b″** was observed. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{22}N_3O$: 368.1757; Found: 368.1728.

5.2 Experimental characterization data for the three-component products 3jac–3lac

*1-Benzyl-3-(1-methyl-1,2,3,4-tetrahydroquinolin-6-yl)-3-(1,2,3,4-tetrahydroquinolin-6-yl)indolin-2-one (**3jac**)* was prepared according to general procedure A. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **3jac** (78 mg for 0.42 mmol scale) in 37% yield along with the formation of two 2-component pro-

ducts **3ja** (13% yield) & **3jc** (14% yield). Physical state: pale yellow solid. M.p.: 150–160 °C. R_f-Value: 0.2 (40% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.23 (m, 6H), 7.13–7.09 (m, 1H), 7.01–6.94 (m, 2H), 6.86 (d, J = 6.4 Hz, 3H), 6.72 (d, J = 8.0 Hz, 1H), 6.48 (d, J = 8.8 Hz, 1H), 6.38–6.36 (m, 1H), 4.96 (s, 2H), 3.25 (t, J = 5.6 Hz, 2H), 3.17 (t, J = 5.6 Hz, 2H), 2.84 (s, 3H), 2.66 (t, J = 5.6 Hz, 4H), 1.95–1.85 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.1, 146.0, 144.1, 142.4, 136.6, 135.0, 130.8, 129.9, 129.7, 129.1, 129.0, 128.7, 127.7, 127.6, 127.4, 127.3, 126.2, 122.93, 122.9, 121.5, 114.3, 110.9, 109.5, 61.5, 51.5, 44.2, 42.3, 39.4, 28.2, 27.4, 22.7, 22.5. IR (KBr, cm^{-1}): 3380, 2924, 2836, 1706, 1608, 1511. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{34}H_{34}N_3O$: 500.2696; Found: 500.2667.

*1-Methyl-3-(1-methyl-1,2,3,4-tetrahydroquinolin-6-yl)-3-(1,2,3,4-tetrahydroquinolin-6-yl)indolin-2-one (**3kac**)* was prepared according to general procedure A. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **3kac** (30 mg for 0.19 mmol scale) in 38% yield along with the formation of two 2-component products **3ka** (18% yield) & **3kc** (22% yield). Physical state: pale yellow solid. M.p.: 119–120 °C. R_f-Value: 0.3 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27–7.22 (m, 2H), 7.04 (t, J = 7.6 Hz, 1H), 6.91 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 6.87–6.81 (m, 4H), 6.46 (d, J = 8.4 Hz, 1H), 6.36–6.34 (m, 1H), 3.25–3.23 (m, 5H), 3.16 (t, J = 6.0 Hz, 2H), 2.83 (s, 3H), 2.66 (t, J = 6.4 Hz, 4H), 1.95–1.84 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.1, 146.0, 144.0, 143.3, 134.8, 130.8, 129.8, 129.6, 129.0, 127.8, 127.4, 127.2, 126.2, 122.9, 122.8, 121.4, 114.3, 110.8, 108.4, 61.4, 51.5, 42.3, 39.4, 28.2, 27.3, 26.9, 22.7, 22.4. IR (KBr, cm^{-1}): 2925, 2835, 1707, 1607, 1510. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{28}H_{30}N_3O$: 424.2383; Found: 424.2376.

*5-Chloro-1-methyl-3-(1-methyl-1,2,3,4-tetrahydroquinolin-6-yl)-3-(1,2,3,4-tetrahydroquinolin-6-yl)indolin-2-one (**3lac**)* was prepared according to general procedure A. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **3lac** (16 mg for 0.10 mmol scale) in 33% yield along with the formation of two 2-component products **3la** (17% yield) & **3lc** (19% yield). Physical state: pale yellow solid. M.p.: 118–120 °C. R_f-Value: 0.4 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22 (dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 1H), 7.18 (d, J = 2.0 Hz, 1H), 6.87 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 6.81–6.77 (m, 4H), 6.46 (d, J = 8.4 Hz, 1H), 6.36–6.34 (m, 1H), 3.26–3.23 (m, 5H), 3.18 (t, J = 5.6 Hz, 2H), 2.83 (s, 3H), 2.67 (t, J = 6.4 Hz, 4H), 1.95–1.85 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.7, 146.2, 144.3, 141.9, 136.5, 129.9, 129.5, 128.94, 128.9, 128.1, 127.9, 127.3, 127.1, 126.5, 123.0, 121.5, 114.3, 110.8, 109.3, 61.6, 51.5, 42.2, 39.3, 28.2, 27.4, 27.0, 22.6, 22.4. IR (KBr, cm^{-1}): 3132, 1714, 1638, 1401, 811. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{28}H_{29}ClN_3O$: 458.1994; Found: 458.1998.

5.3 Experimental characterization data for the products 4

*1-Benzyl-3-(1-methyl-1,2,3,4-tetrahydroquinolin-6-yl)-3-(quinolin-6-yl)indolin-2-one (**4jac**)* was prepared according to general procedure B. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **4jac** (13.5 mg for 0.06 mmol scale) in 45% yield. Physical state: pale yellow solid. M.p.: 110–117 °C. R_f-Value: 0.4 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.87 (dd, J_1 = 4.0 Hz, J_2 = 1.2 Hz, 1H), 8.04 (d, J = 8.8 Hz, 2H), 7.74 (dd, J_1 = 8.8 Hz, J_2 = 2.0 Hz, 1H), 7.70 (d, J = 1.6 Hz, 1H), 7.37–7.25 (m, 7H), 7.19 (t, J = 7.6 Hz, 1H), 7.06 (t, J = 7.6 Hz, 1H), 6.95–6.93 (m, 1H), 6.86–6.81 (m, 2H), 6.50 (d, J = 8.8 Hz, 1H), 5.02 (d, J = 2.8 Hz, 2H), 3.20 (t, J = 5.6 Hz, 2H), 2.86 (s, 3H), 2.66 (t, J = 6.4 Hz, 2H), 1.93 (quint, J = 6.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.2, 150.7, 147.8, 146.4, 142.5, 141.1, 136.7, 136.3, 133.6, 131.0, 129.9, 129.12, 129.1, 128.7, 128.4, 128.2, 127.9, 127.6, 127.4, 127.0, 126.3, 123.23, 123.2, 121.5, 111.0, 109.9, 62.0, 51.5, 44.4, 39.3, 28.2, 22.6. IR (KBr, cm^{-1}): 3133, 2924, 1709, 1607, 1511, 1401. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{34}H_{30}N_3O$: 496.2383; Found: 496.2387.

*1-Methyl-3-(1-methyl-1,2,3,4-tetrahydroquinolin-6-yl)-3-(quinolin-6-yl)indolin-2-one (**4kac**)* was prepared according to general procedure B. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **4kac** (20 mg for 0.09 mmol scale) in 51% yield. Physical state: pale yellow solid. M.p.: 105–110 °C. R_f-Value: 0.2 (50% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.86 (d, J = 2.8 Hz, 1H), 8.07–8.01 (m, 2H), 7.72–7.67 (m, 2H), 7.36–7.31 (m, 3H), 7.10 (t, J = 8.0 Hz, 1H), 6.95–6.90 (m, 2H), 6.84 (d, J = 1.6 Hz, 1H), 6.48 (d, J = 8.4 Hz, 1H), 3.32 (s, 3H), 3.19 (t, J = 5.6 Hz, 2H), 2.85 (s, 3H), 2.66 (t, J = 6.4 Hz, 2H), 1.93 (quint, J = 6.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.2, 150.7, 147.8, 146.4, 143.4, 141.1, 136.7, 133.5, 130.9, 129.8, 129.0, 128.6, 128.5, 128.2, 127.4, 127.0, 126.3, 123.2, 123.1, 121.5, 110.9, 108.9, 64.0, 51.5, 39.3, 28.2, 27.0, 22.6. IR (KBr, cm^{-1}): 3160, 2927, 1686, 1608, 1511, 1401. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{28}H_{26}N_3O$: 420.2070; Found: 420.2092.

*5-Chloro-1-methyl-3-(1-methyl-1,2,3,4-tetrahydroquinolin-6-yl)-3-(quinolin-6-yl)indolin-2-one (**4lac**)* was prepared according to general procedure B. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **4lac** (7 mg for 0.04 mmol scale) in 35% yield. Physical state: light orange solid. M.p.: 122–130 °C. R_f-Value: 0.4 (40% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.89–8.88 (m, 1H), 8.08–8.03 (m, 2H), 7.68–7.64 (m, 2H), 7.38–7.35 (m, 1H), 7.31–7.27 (m, 2H), 6.89–6.85 (m, 2H), 6.80 (d, J = 1.6 Hz, 1H), 6.49 (d, J = 8.4 Hz, 1H), 3.30 (s, 3H), 3.21 (t, J = 6.0 Hz, 2H), 2.86 (s, 3H), 2.67 (t, J = 6.4 Hz, 2H), 1.94 (quint, J = 6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.8, 150.9, 147.9, 146.5, 142.0, 140.3, 136.7, 135.2, 130.7, 130.1, 128.9, 128.6, 128.5, 128.2, 127.8, 127.3, 127.0, 126.7, 123.3, 121.6, 110.9, 109.8, 62.2, 51.4, 39.3, 28.2, 27.2, 22.6. IR (KBr, cm^{-1}): 3133, 1716, 1607, 1401, 809. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{28}H_{25}ClN_3O$: 454.168; Found: 454.1660.

5.4 Experimental characterization data for the products 5c & 6

*Pyridin-4-yl(m-tolyl)methyl 2,2,2-trichloroacetimidate (**5c**)* was prepared according to a previously reported procedure. The crude reaction mixture was purified by column chromatography using silica gel (100–200 mesh) giving **5c** (82 mg for 0.25 mmol scale) in 95% yield. Physical state: yellow liquid. R_f-

Value: 0.4 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.60–8.58 (m, 2H), 8.49 (s, 1H), 7.35–7.34 (m, 2H), 7.28–7.21 (m, 3H), 7.15–7.13 (m, 1H), 6.86 (s, 1H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.3, 150.2, 149.0, 138.8, 138.4, 129.8, 128.9, 128.1, 124.5, 121.5, 91.5, 80.2, 21.7. IR (KBr, cm^{-1}): 3028, 2922, 1688, 1599, 1412, 1289, 1068, 795. HRMS (ESI) *m*/*z*: $[M + H]^+$ Calcd for $C_{15}H_{14}Cl_3N_2O$: 343.0166; Found: 343.0160.

*6-Benzhydryl-1-methyl-1,2,3,4-tetrahydroquinoline (**6ca**)* was prepared according to general procedure C. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **6ca** (36 mg for 0.14 mmol scale) in 85% yield. Physical state: colourless solid. M.p.: 108–111 °C. R_f-Value: 0.2 (5% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27–7.22 (m, 4H), 7.19–7.11 (m, 6H), 6.76 (d, J = 8.0 Hz, 1H), 6.71 (s, 1H), 6.50 (d, J = 8.4 Hz, 1H), 5.40 (s, 1H), 3.17 (t, J = 5.6 Hz, 2H), 2.84 (s, 3H), 2.67 (t, J = 6.4 Hz, 2H), 1.94 (quint, J = 6.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.5, 145.1, 131.9, 130.2, 129.8, 128.5, 128.2, 126.3, 123.0, 111.0, 56.4, 51.6, 39.5, 28.1, 22.8. IR (KBr, cm^{-1}): 3134, 1636, 1510, 1401. HRMS (ESI) *m*/*z*: $[M + H]^+$ Calcd for $C_{23}H_{24}N$: 314.1903; Found: 314.1901.

*6-Benzhydryl-1-tosyl-1,2,3,4-tetrahydroquinoline (**6da**)* was prepared according to general procedure C. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **6da** (71 mg for 0.17 mmol scale) in 90% yield. Physical state: white solid. M.p.: 150–160 °C. R_f-Value: 0.2 (20% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, J = 8.4 Hz, 1H), 7.39 (d, J = 8.4 Hz, 2H), 7.21–7.17 (m, 4H), 7.13–7.07 (m, 4H), 7.00 (d, J = 7.2 Hz, 4H), 6.83 (dd, J_1 = 8.8 Hz, J_2 = 1.6 Hz, 1H), 6.66 (s, 1H), 5.38 (s, 1H), 3.68 (t, J = 6.0 Hz, 2H), 2.28–2.25 (m, 5H), 1.52 (quint, J = 6.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.1, 143.7, 140.7, 137.2, 135.5, 130.7, 130.2, 129.8, 129.7, 128.6, 127.8, 127.4, 126.6, 124.8, 56.6, 46.9, 27.0, 21.9, 21.8. IR (KBr, cm^{-1}): 3019, 2922, 1595, 1489, 1357, 1186. HRMS (ESI) *m*/*z*: $[M + H]^+$ Calcd for $C_{29}H_{28}NO_2S$: 454.1835; Found: 454.1837.

*6-(1-Phenylethyl)-1-tosyl-1,2,3,4-tetrahydroquinoline (**6db**)* was prepared according to general procedure C. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **6db** (15 mg for 0.07 mmol scale) in 55% yield. Physical state: white solid. M.p.: 120–130 °C. R_f-Value: 0.3 (20% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, J = 8.4 Hz, 1H), 7.47 (d, J = 8.4 Hz, 2H), 7.31–7.27 (m, 2H), 7.20–7.16 (m, 5H), 7.06–7.04 (m, 1H), 6.83 (s, 1H), 4.07 (q, J = 7.2 Hz, 1H), 3.78–3.75 (m, 2H), 2.41–2.37 (m, 5H), 1.61–1.56 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.7, 143.7, 143.2, 137.3, 135.2, 130.7, 129.9, 128.7, 128.5, 127.9, 127.4, 126.4, 126.1, 125.0, 46.8, 44.5, 27.0, 22.2, 21.92, 21.9. IR (KBr, cm^{-1}): 3025, 2920, 2872, 1598, 1493, 1341, 1163. HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{24}H_{25}NO_2SNa$: 414.1498; found: 414.1488.

*6-Benzhydryl-1-(methylsulfonyl)-1,2,3,4-tetrahydroquinoline (**6ea**)* was prepared according to general procedure C. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **6ea** (44 mg for 0.13 mmol scale) in 91% yield. Physical state: yellow solid. M.p.: 94–96 °C. R_f-Value: 0.4 (20% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, J = 8.8 Hz, 1H), 7.29 (t, J = 7.6 Hz, 4H), 7.21 (t, J = 7.6 Hz, 2H), 7.11 (d, J = 7.2 Hz, 4H), 6.94–6.91 (m, 1H), 6.88 (s, 1H), 5.46 (s, 1H), 3.81–3.78 (m, 2H), 2.90 (s, 3H), 2.76 (t, J = 6.8 Hz, 2H), 1.97 (quint, J = 6.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.9, 140.3, 135.4, 130.8, 129.6, 129.1, 128.6, 128.1, 126.6, 122.6, 56.4, 46.7, 38.9, 27.4, 22.5. IR (KBr, cm^{-1}): 1491, 1344, 1155, 975, 753. HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{23}H_{23}NO_2SNa$: 400.1342; Found: 400.1331.

*5-Benzhydryl-1-tosylindoline (**6fa**)* was prepared according to general procedure C. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **6fa** (40 mg for 0.11 mmol scale) in 82% yield. Physical state: brown solid. M.p.: 106–112 °C. R_f-Value: 0.2 (20% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, J = 8.0 Hz, 2H), 7.52 (d, J = 8.4 Hz, 1H), 7.27–7.17 (m, 8H), 7.06 (d, J = 7.2 Hz, 4H), 6.94 (d, J = 8.4 Hz, 1H), 6.80 (s, 1H), 5.45 (s, 1H), 3.87 (t, J = 8.4 Hz, 2H), 2.77 (t, J = 8.4 Hz, 2H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.3, 144.1, 140.6, 139.9, 134.3, 132.3, 129.9, 129.6, 129.1, 128.6, 127.6, 126.6, 126.3, 114.9, 56.5, 50.4, 28.1, 21.8. IR (KBr, cm^{-1}): 3164, 1596, 1484, 1401, 1354, 1164, 1029. HRMS (ESI) *m*/*z*: $[M + H]^+$ Calcd for $C_{28}H_{26}NO_2S$: 440.1679; Found: 440.1685.

*5-(1-Phenylethyl)-1-tosylindoline (**6fb**)* was prepared according to general procedure C. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **6fb** (36 mg for 0.11 mmol scale) in 88% yield. Physical state: white solid. M.p.: 101–104 °C. R_f-Value: 0.3 (20% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, J = 8.4 Hz, 2H), 7.52 (d, J = 8.4 Hz, 1H), 7.26 (t, J = 7.6 Hz, 2H), 7.21–7.15 (m, 5H), 7.06 (dd, J_1 = 8.0 Hz, J_2 = 0.8 Hz, 1H), 6.90 (s, 1H), 4.06 (q, J = 7.2 Hz, 1H), 3.87 (t, J = 8.4 Hz, 2H), 2.80 (t, J = 8.4 Hz, 2H), 2.35 (s, 3H), 1.57 (d, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.7, 144.3, 142.4, 140.4, 134.3, 132.3, 129.9, 128.7, 127.8, 127.6, 127.2, 126.4, 124.6, 115.0, 50.4, 44.6, 28.2, 22.3, 21.8. IR (KBr, cm^{-1}): 3133, 1636, 1401, 1165, 1106. HRMS (ESI) *m*/*z*: $[M + H]^+$ Calcd for $C_{23}H_{24}NO_2S$: 378.1522; found: 378.1525.

*5-Benzhydryl-1-(methylsulfonyl)indoline (**6ga**)* was prepared according to general procedure C. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **6ga** (47 mg for 0.14 mmol scale) in 93% yield. Physical state: colourless white solid. M.p.: 98–102 °C. R_f-Value: 0.2 (20% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (m, 5H), 7.24–7.19 (m, 2H), 7.10 (d, J = 7.6 Hz, 4H), 6.96–6.94 (m, 2H), 5.49 (s, 1H), 3.95 (t, J = 8.4 Hz, 2H), 3.07 (t, J = 8.4 Hz, 2H), 2.85 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.1, 140.7, 140.0, 131.7, 129.7, 129.5, 128.7, 126.7, 126.6, 113.7, 56.6, 50.9, 34.8, 28.3. IR (KBr, cm^{-1}): 3371, 3023, 2927, 1696, 1485, 1347, 1160. HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{22}H_{21}NO_2SNa$: 386.1185; Found: 386.1185.

*1-(5-Benzhydrylindolin-1-yl)-3-chloropropan-1-one (**6ha**)* was prepared according to general procedure C. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **6ha** (36 mg for 0.14 mmol scale) in 67% yield. Physical state: brown solid. M.p.: 168–172 °C. R_f-Value: 0.4 (20% EtOAc/hexane). ^{1}H NMR (700 MHz, $CDCl_3$): δ 8.05 (d, J = 8.4 Hz, 1H), 7.21–7.17 (m, 4H), 7.14–7.12 (m,

2H),7.02 (d, J = 7.7 Hz, 4H), 6.89 (d, J = 8.4 Hz, 1H), 6.85 (s, 1H), 5.43 (s, 1H), 3.96 (t, J = 8.4 Hz, 2H), 3.81 (t, J = 7.0 Hz, 2H), 3.05 (t, J = 8.4 Hz, 2H), 2.80 (t, J = 7.0 Hz, 2H). ^{13}C NMR (175 MHz, $CDCl_3$): δ 167.9, 144.3, 141.4, 140.2, 131.7, 129.7, 129.1, 128.6, 126.6, 125.8, 117.1, 56.7, 48.5, 39.7, 39.0, 28.3. IR (KBr, cm^{-1}): 3131, 1661, 1487, 1401, 1115. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{23}ClNO$: 376.1463; Found: 376.1464.

3-Chloro-1-(5-(1-phenylethyl)indolin-1-yl)propan-1-one ***(6hb)*** was prepared according to general procedure C. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **6hb** (18 mg for 0.09 mmol scale) in 61% yield. Physical state: light yellow solid. M.p.: 152–156 °C. R_f-Value: 0.3 (20% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (d, J = 8.4 Hz, 1H), 7.29–7.28 (m, 2H), 7.21–7.17 (m, 3H), 7.09 (d, J = 8.4 Hz, 1H), 7.01 (s, 1H), 4.14–4.10 (m, 1H), 4.05 (t, J = 8.4 Hz, 2H), 3.90 (t, J = 6.8 Hz, 2H), 3.16 (t, J = 8.4 Hz, 2H), 2.89 (t, J = 6.8 Hz, 2H), 1.61 (d, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.8, 156.1, 146.8, 142.8, 131.7, 128.7, 127.9, 127.1, 126.4, 124.2, 117.2, 48.5, 44.7, 39.8, 39.0, 28.3, 22.3. IR (KBr, cm^{-1}): 3133, 1650, 1490, 1402, 1287, 1114. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{20}ClNONa$: 336.1126; Found: 336.1117.

5.5 Experimental characterization data for the products 7

Diphenyl(1-tosyl-1,2,3,4-tetrahydroquinolin-6-yl)methanol ***(7da)*** was prepared according to general procedure D. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **7da** (13 mg for 0.04 mmol scale) in 62% yield. Physical state: white solid. M.p.: 172–178 °C. R_f-Value: 0.3 (20% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61–7.59 (m, 1H), 7.42 (d, J = 8.4 Hz, 2H), 7.25–7.16 (m, 10H), 7.11 (d, J = 8.0 Hz, 2H), 6.92–6.91 (m, 2H), 3.71 (t, J = 6.0 Hz, 2H), 2.79 (br, 1H), 2.34–2.30 (m, 5H), 1.56 (quint, J = 6.0 Hz, 2H). ^{13}C NMR (175 MHz, $CDCl_3$): δ 147.0, 143.9, 143.4, 137.1, 136.3, 130.1, 129.9, 128.7, 128.3, 128.2, 127.6, 127.4, 126.6, 124.0, 82.0, 46.9, 27.2, 21.9, 21.87. IR (KBr, cm^{-1}): 3547, 3133, 1493, 1401, 1345, 1160, 1025. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{29}H_{28}NO_3S$: 470.1784; Found: 470.1774.

(1-(Methylsulfonyl)-1,2,3,4-tetrahydroquinolin-6-yl)diphenyl methanol ***(7ea)*** was prepared according to general procedure D. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **7ea** (16 mg for 0.05 mmol scale) in 78% yield. Physical state: white solid. M.p.: 150–160 °C. R_f-Value: 0.2 (30% EtOAc/hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (d, J = 8.8 Hz, 1H), 7.26–7.18 (m, 10H), 7.04 (d, J = 1.2 Hz, 1H), 6.94 (dd, J_1 = 8.8 Hz, J_2 = 2.0 Hz, 1H), 3.72 (t, J = 6.0 Hz, 2H), 2.83 (s, 3H), 2.71 (t, J = 6.4 Hz, 2H), 1.93–1.87 (m, 2H). ^{13}C NMR (175 MHz, $CDCl_3$): δ 147.0, 143.1, 136.2, 129.3, 128.6, 128.3, 128.1, 127.7, 127.0, 121.9, 81.9, 46.8, 39.0, 27.7, 22.5. IR (KBr, cm^{-1}): 3134, 1636, 1492, 1401, 1338, 1151. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{23}NO_3SNa$: 416.1291; Found: 416.1294.

Diphenyl(1-tosylindolin-5-yl)methanol ***(7fa)*** was prepared according to general procedure D. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **7fa** (10 mg for 0.04 mmol scale) in 51% yield. Physical state: white solid. M.p.: 120–130 °C. R_f-Value: 0.3 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, J = 8.4 Hz, 2H), 7.52 (d, J = 8.4 Hz, 1H), 7.32–7.21 (m, 12H), 7.05 (dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 1H), 7.01 (s, 1H), 3.89 (t, J = 8.4 Hz, 2H), 2.85 (br, 1H), 2.83 (t, J = 8.4 Hz, 2H), 2.39 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.1, 144.4, 142.8, 141.4, 134.2, 131.9, 130.0, 128.3, 128.1, 128.0, 127.7, 127.6, 125.1, 114.1, 82.1, 50.4, 28.1, 21.9. IR (KBr, cm^{-1}): 3511, 3135, 1482, 1401, 1345, 1161. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{28}H_{25}NO_3SNa$: 478.1447; Found: 478.1457.

Diphenyl(1-tosyl-1H-indol-5-yl)methanol ***(7fa′)*** was prepared according to general procedure D. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **7fa′** (9 mg for 0.04 mmol scale) in 43% yield. Physical state: light yellow solid. M.p.: 130–133 °C. R_f-Value: 0.4 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (d, J = 8.8 Hz, 1H), 7.77 (d, J = 8.4 Hz, 2H), 7.54 (d, J = 3.6 Hz, 1H), 7.37 (d, J = 1.6 Hz, 1H), 7.30–7.22 (m, 13H), 6.56 (d, J = 4.0 Hz, 1H), 2.86 (s, 1H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.3, 145.3, 142.5, 135.6, 134.1, 130.5, 130.3, 128.3, 128.2, 127.6, 127.2, 127.0, 125.3, 121.2, 113.2, 109.5, 82.4, 21.9. IR (KBr, cm^{-1}): 3543, 3161, 1401, 1364, 1170, 1122. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{28}H_{23}NO_3SNa$: 476.1291; Found: 476.1281.

(1-(Methylsulfonyl)indolin-5-yl)diphenylmethanol ***(7ga)*** was prepared according to general procedure D. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **7ga** (15 mg for 0.08 mmol scale) in 49% yield. Physical state: white solid. M.p.: 155–160 °C. R_f-Value: 0.2 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27–7.18 (m, 11H), 7.10 (s, 1H), 7.00 (d, J = 8.4 Hz, 1H), 3.90 (t, J = 8.4 Hz, 2H), 3.02 (t, J = 8.4 Hz, 2H), 2.80 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.1, 143.0, 141.4, 131.3, 128.32, 128.3, 128.1, 127.7, 125.4, 113.0, 82.1, 50.9, 34.9, 28.3. IR (KBr, cm^{-1}): 3500, 1483, 1443, 1338, 1242, 1151. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{22}H_{21}NO_3SNa$: 402.1134; Found: 402.1131.

(1-(Methylsulfonyl)-1H-indol-5-yl)diphenylmethanol ***(7ga′)*** was prepared according to general procedure D. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **7ga′** (13 mg for 0.08 mmol scale) in 42% yield. Physical state: light yellow solid. M.p.: 90–93 °C. R_f-Value: 0.4 (30%

EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, J = 8.8 Hz, 1H), 7.43 (d, J = 1.2 Hz, 1H), 7.35 (d, J = 3.6 Hz, 1H), 7.28–7.18 (m, 11H), 6.55 (d, J = 3.6 Hz, 1H), 3.02 (s, 3H). ^{13}C NMR (175 MHz, $CDCl_3$): δ 147.3, 142.9, 134.2, 130.5, 128.33, 128.3, 127.7, 126.8, 125.6, 121.3, 112.7, 109.5, 82.4, 41.2. IR (KBr, cm^{-1}): 3516, 3150, 1401, 1360, 1164, 1141. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{22}H_{19}NO_3SNa$: 400.0978; Found: 400.0810.

5.6 Experimental characterization data for the products 9ha, 9hc, 10ha, and 10ha′

8-Benzhydryl-5,6-dihydro-1H-pyrrolo[3,2,1-ij]quinolin-4(2H)-one ***(9ha)*** was prepared according to general procedure C. The crude reaction mixture was purified by column chromato-

graphy using silica gel (230–400 mesh) giving **9ha** (76 mg for 0.23 mmol scale) in 98% yield. Physical state: light yellow solid. M.p.: 105–110 °C. R_f-Value: 0.5 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (t, J = 7.6 Hz, 4H), 7.23–7.18 (m, 2H), 7.11 (d, J = 7.6 Hz, 4H), 6.82 (s, 1H), 6.75 (s, 1H), 5.48 (s, 1H), 4.04 (t, J = 8.8 Hz, 2H), 3.09 (t, J = 8.4 Hz, 2H), 2.86 (t, J = 7.6 Hz, 2H), 2.63 (t, J = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.8, 144.3, 140.0, 139.8, 129.6, 129.2, 128.6, 126.9, 126.6, 124.6, 120.1, 56.9, 45.6, 31.9, 28.0, 24.7. IR (KBr, cm^{-1}): 3056, 2928, 1615, 1490, 1382, 1154. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{22}NO$: 340.1696; Found: 340.1711.

*8-(Pyridin-3-yl(m-tolyl)methyl)-5,6-dihydro-1H-pyrrolo[3,2,1-ij]-quinolin-4(2H)-one (**9hc**)* was prepared according to general procedure C. The crude reaction mixture was subected to HRMS and a trace amount the product **9hc** was observed. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{23}N_2O$: 355.1805; Found: 355.1780.

*8-(Hydroxydiphenylmethyl)-5,6-dihydro-1H-pyrrolo[3,2,1-ij]-quinolin-4(2H)-one (**10ha**)* was prepared according to general procedure D. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **10ha** (27 mg for 0.15 mmol scale) in 52% yield. Physical state: white solid. M.p.: 140–145 °C. R_f-Value: 0.3 (70% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.27 (m, 10H), 6.97 (s, 1H), 6.93 (s, 1H), 4.07 (t, J = 8.8 Hz, 2H), 3.13 (t, J = 8.8 Hz, 2H), 2.90 (t, J = 7.6 Hz, 2H), 2.77 (s, 1H), 2.66 (t, J = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.0, 147.4, 143.0, 140.9, 128.8, 128.4, 128.2, 127.7, 125.7, 123.5, 119.7, 82.4, 45.8, 32.0, 28.1, 24.9. IR (KBr, cm^{-1}): 3134, 1645, 1494, 1400. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{22}NO_2$: 356.1645; Found: 356.1661.

*8-(Hydroxydiphenylmethyl)-5,6-dihydro-4H-pyrrolo[3,2,1-ij]-quinolin-4-one (**10ha′**)* was prepared according to general procedure D. The crude reaction mixture was purified by column chromatography using silica gel (230–400 mesh) giving **10ha′** (20 mg for 0.15 mmol scale) in 40% yield. Physical state: brown solid. M.p.: 138–142 °C. R_f-Value: 0.1 (70% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, J = 3.2 Hz, 1H), 7.35–7.27 (m, 11H), 7.16 (s, 1H), 6.61 (d, J = 3.6 Hz, 1H), 3.21 (t, J = 7.6 Hz, 2H), 2.99 (t, J = 7.6 Hz, 2H), 2.87 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.9, 147.5, 143.5, 134.9, 129.0, 128.5, 128.3, 127.6, 122.3, 122.1, 120.0, 119.2, 110.6, 82.7, 32.9, 24.7. IR (KBr, cm^{-1}): 3406, 3141, 2919, 2850, 1685, 1467, 1399. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{19}NO_2Na$: 376.1308; Found: 376.1314.

5.7 Crystallographic studies

Details of the single crystal X-ray structures have been deposited in the form of crystallographic information files with the Cambridge Crystallographic Data Centre (see Schemes 1 & 4 for specific CCDC numbers) where copies of the data can be downloaded free-of-charge.

Abbreviation

CH_3CN	Acetonitrile
DCE	Dichloroethane
DCM	Dichloromethane
DMF	Dimethyl formamide
Et_2O	Diethyl ether
EtOAc	Ethyl acetate
ETOH	Ethanol
MeOH	Methanol
^{t}BuOH	*tert*-Butanol
TFE	2,2,2-trifluoroethanol
AcOH	Acetic acid
Ac_2O	Acetic anhydride
Et_3N	Triethylamine
DIAD	Diisopropyl azodicarboxylate
DMAP	4-Dimethylaminopyridine,
BHT	Butylated hydroxytoluene
DBU	Diazabicycloundecene
CCl_3CN	Trichloroacetonitrile
NaH	Sodium hydride
$Bi(OTf)_3$	Bismuth triflate
$In(OTf)_3$	Indium triflate
$ZnCl_2$	Zinc chloride
$AlCl_3$	Aluminium chloride
$NaHCO_3$	Sodium bicarbonate
Na_2SO_4	Sodium sulfate
OTf	Trifluoromethanesulfonate
Ts	Tosyl
Ms	Mesyl
Bn	Benzyl
rt	Room temperature

Conflicts of interest

The authors declare no conflict of interest.

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