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Redox-Neutral Cascade Dearomatization of Indoles via Hydride Transfer: Divergent Synthesis of Tetrahydroquinoline-Fused Spiroindolenines

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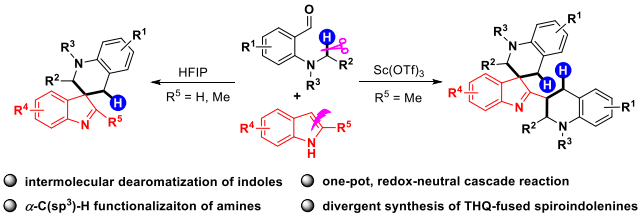
Graphic Abstract



Abstract: The redox-neutral cascade dearomatization of indoles with *o*-aminobenzaldehydes has been realized via hydride transfer strategy, achieving the condition- and substrate-controlled divergent synthesis of tetrahydroquinoline-fused spiroindolenines. The integration of hydride transfer-involved C(sp^3)–H functionalization with dearomatization provides a promising platform for the construction of structurally diverse molecules.

INTRODUCTION

Spiroindolenines are not only the core structures of naturally occurring products and pharmaceutically relevant molecules (Figure 1),[1] but also the versatile synthetic intermediates

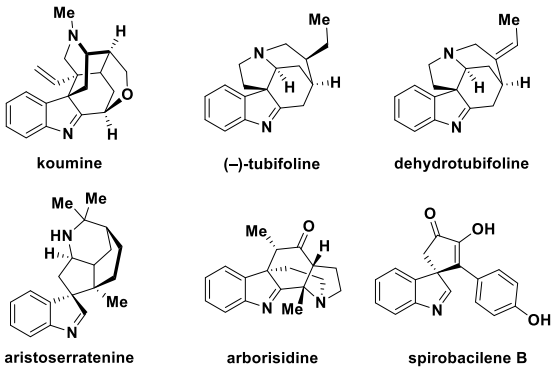


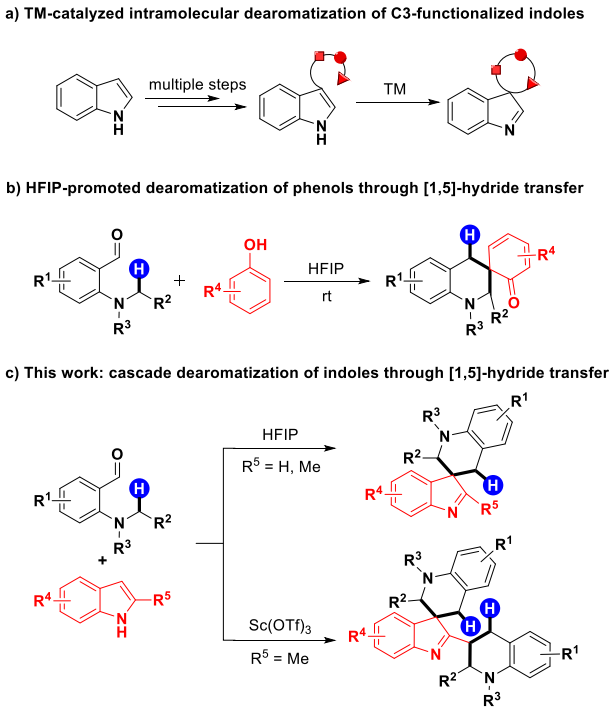
Figure 1. Natural products and bioactive molecules containing spiroindolenine skeleton.

for the syntheses of tetrahydrocarbolines, tetrahydrocarbazoles as well as spiroindolines.[2] Consequently, tremendous efforts have focused on the development of effective strategies to access these attractive scaffolds,[3] wherein the transition-metal (TM)-catalyzed intramolecular dearomatization of indoles have proved to be the robust way (Scheme 1, a).[2, 4–5] Despite the advances, these methods generally suffer from the substrate engineering, namely the complicated pre-preparation of C3-functionalized indole precursors, which contradicts the principle of step-economy. Moreover, this type of reactions has been restrained by the intramolecular versions, and the dearomatization reactions between independent indoles and dearomatizing spiroannulation reagents are underdeveloped. At the same time, the synthesis of tetrahydroquinoline(THQ)-fused spiroindolenines remains elusive, in spite of the vital role of THQ skeletons in pharmaceutical and agrochemical industries.[6] Therefore, it is highly appealing to explore an efficient intermolecular methodology for the rapid, divergent assembly of THQ-fused spiroindolenines from readily accessible indole feedstocks and dearomatizing spiroannulation reagents.

The cascade [1,5]-hydride transfer/cyclization represents a powerful redox-neutral strategy for the direct functionalization of inert C(sp^3)–H bonds, allowing the rapid generation of polycyclic and spirocyclic architectures.[7] Owing to its high efficiency and atom-economy in building molecular complexity, a plethora of protocols have been developed by employing various types of hydride acceptors beforehand or in situ.[8–13] Although great achievements have been made in this area, the reaction modes are still relatively limited. To the best of our knowledge, there are only sporadic reports combining hydride transfer with dearomatization process.[14] In this regard, our group recently disclosed a redox-neutral dearomative cyclization of phenols with

o-aminobenzaldehydes, affording an array of highly functionalized THQ scaffolds (Scheme 1, b).[14a] Inspired by this exciting result, we hypothesized that the dearomatization of simple indoles could also be realized by using readily available *o*-aminobenzaldehydes as the dearomatizing spiroannulation reagents. As our continuing interest in the one-step assembly of biologically important molecules, herein, we reported the redox-neutral cascade dearomatization of simple indoles with *o*-aminobenzaldehydes through hydride transfer strategy, furnishing two kinds of THQ-fused spiroindolenines in good yields with moderate diastereoselectivities (Scheme 1, c).

Scheme 1. Redox-Neutral Cascade Dearomatization of Indoles through [1,5]-Hydride Transfer

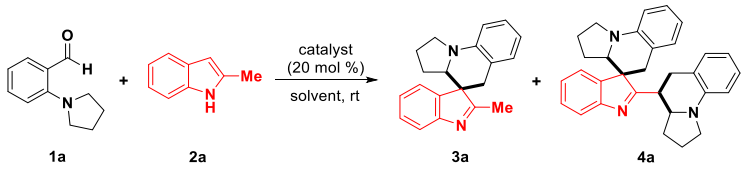


RESULTS AND DISCUSSION

To verify the feasibility of our hypothesis, 2-(pyrrolidin-1-yl)benzaldehyde **1a** and 2-methylindole **2a** were chosen as the model substrates to optimize the reaction conditions (Table 1). Given the unique characteristics of fluorinated alcohols[15] as well as our recent success in HFIP-promoted hydride transfer reactions[9b, 14a], HFIP was initially investigated as both promoter and solvent in the absence of any catalyst (Table 1, entry 1). Gratifyingly, the reaction proceeded efficiently to provide the desired THQ-fused spiroindolenine **3a** in 96% yield with moderate diastereoselectivity (Table 1, entry 1). In comparison, the employment of other alcohols and H_2O

exhibited inferior outcomes (Table 1, entries 2–5). Afterwards, the screening of various Brønsted acids and Lewis acids failed to produce a superior result (Table 1, entries 6–10). However, it was exciting that an intriguing product **4a** was isolated in 12% yield when $Sc(OTf)_3$ was used as a catalyst (Table 1, entry 9). The structure of **4a** has been confirmed undoubtedly by NMR and HRMS analysis. To improve the reaction efficiency, the molar ratio of starting materials was adjusted from 1.2:1 to 2.5:1, which resulted in an enhanced yield of 66%, albeit with low diastereoselectivity (Table 1, entry 11). Further evaluation of other solvents indicated that DCE was the best solvent (Table 1, entries 12–14). Finally, the elevation of temperature led to a lower yield (Table 1, entry 15).

Table 1. Optimization of the Reaction Conditions[a]



1a 2a 3a 4a

				yield (%)[b]/dr[c]	
entry	catalyst	solvent	time (h)	**3a**	**4a**
1	-	HFIP	0.2	96/3.3:1	0
2	-	TFE	24	53/2.6:1	0
3	-	*i*-PrOH	24	0	0
4	-	EtOH	24	0	0
5	-	H_2O	24	0	0
6	TfOH	DCE	24	45/2.8:1	trace
7	$TsOH·H_2O$	DCE	24	52/2.6:1	trace
8	$PhCO_2H$	DCE	24	23/3:1	0
9	$Sc(OTf)_3$	DCE	3	47/2:1	12/1.8:1
10	$Zn(OTf)_2$	DCE	3	30/2.3:1	trace
11[d]	$Sc(OTf)_3$	DCE	72	trace	66/2:1
12[d]	$Sc(OTf)_3$	DCM	72	trace	54/2:1
13[d]	$Sc(OTf)_3$	toluene	72	25/2:1	19/2.2:1
14[d]	$Sc(OTf)_3$	DMF	72	0	0
15[d, e]	$Sc(OTf)_3$	DCE	72	trace	51/1.8:1

[a]Reaction conditions (unless other indicated): **1a** (0.12 mmol), **2a** (0.1 mmol), and catalyst (20 mol %) in 1 mL of solvent at room temperature. [b]Isolated yield. [c]Determined by ^1H NMR analysis. [d]**1a** (0.25 mmol), **2a** (0.1 mmol). [e]At 60 °C.

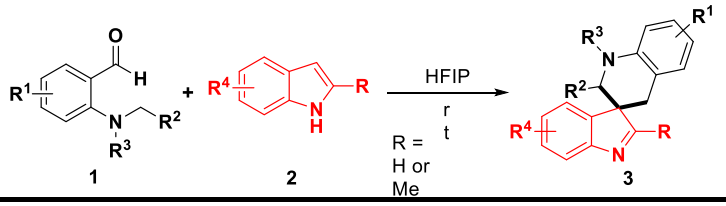
After the optimized reaction conditions established, the substrate scope for the synthesis of THQ-fused spiroindolenines **3** was explored by using a variety of *o*-aminobenzaldehydes and 2-methylindoles (Table 2). Regarding the substituents (R^1) on the phenyl ring of 2-(pyrrolidin-1-yl)benzaldehydes, the electron-donating groups (-MeO and -Me) were fully compatible, giving the corresponding products **3b–d** in 82–93% yields. Satisfyingly, various electron-withdrawing groups ($-CF_3$, -F, -Cl, -Br, -CN, and 4-Ac-Ph) were also well-tolerated to

afford **3e**–**m** in 53–97% yields, which demonstrated the excellent functional group tolerance of this methodology. Notably, the position of substituents on the phenyl rings had little influence on these transformations. When the hydride donors varied from pyrrolidine to octahydroisoindole or seven-membered hexamethyleneimine, the reactions still proceeded smoothly and furnished the desired spiroindolenines **3n** and **3o** in 90% and 79% yields, respectively. Remarkably, the less reactive 2-(dimethylamino)benzaldehyde was also a competent dearomatizing spiroannulation reagent, providing product **3p** in 49% yield. Furthermore, 2-methylindoles bearing electron-donating and electron-withdrawing groups could be readily converted into the corresponding adducts **3q** and **3r** in 90% and 92% yields.

According to the previous reports,[2] it was difficult to synthesize the C2-unsubstituted spiroindolenines under the acidic conditions due to their propensity for rearomatization to undergo intramolecular 1,2-migration to afford C2-alkylated indole derivatives. Thus, the more challenging dearomatization reactions of *o*-aminobenzaldehydes with C2-unsubstituted indoles were investigated. To our delight, an array of indoles incorporating multifarious electron-donating or electron-withdrawing substituents were totally amenable to the reaction and provided THQ-fused spiroindolenines **3s**–**za** in 65–82% yields, albeit with poor diastereoselectivities. Obviously, the electronic effect of substituents had marginal impacts on the transformations. It was worth mentioning that the C4-substituted indole could furnish product **3z** with excellent diastereoselectivity (dr >20:1), which might be attributed to the steric hindrance of the bromo group.

Subsequently, we continue to investigate the substrate scope of the three-component reactions for the assembly of THQ-fused indolenines **4** (Table 3). With respect to *o*-aminobenzaldehydes, the fluro (-F) and bromo (-Br) substituents were well-tolerated, and the corresponding products **4b** and **4c** were delivered in 59% and 63% yields with relatively lower diastereoselectivities. Moreover, 2-methylindoles incorporating methoxy (-MeO) and fluro (-F) groups were proved to be ideal candidates for this reaction, giving adducts **4d** and **4e** in good yields.

Table 2. Scope for Reactions of *o*-Aminobenzaldehydes with 2-Alkylindoles[a]



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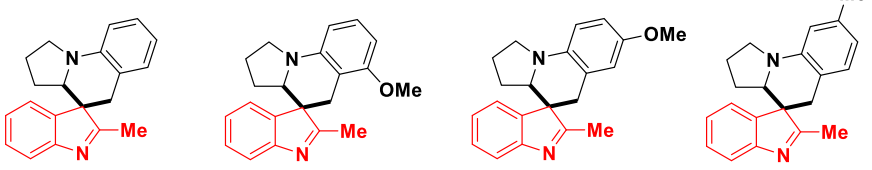
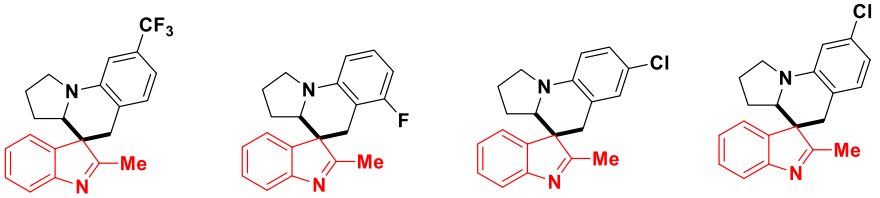
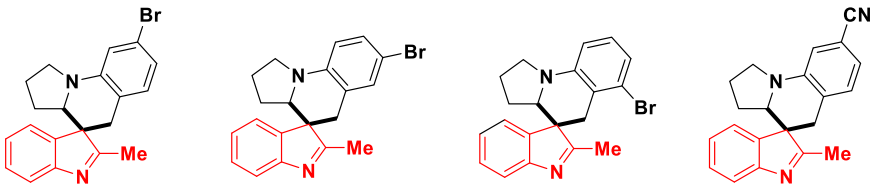


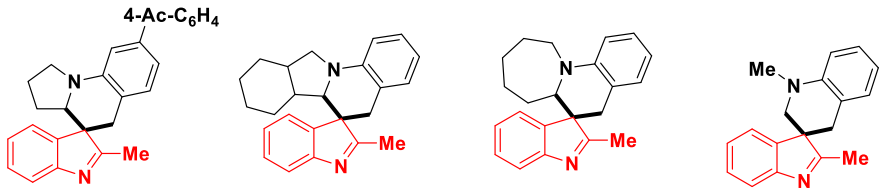
3a, 96%, dr 3.3:1 **3b**, 93%, dr 3.7:1 **3c**, 82%, dr 3.3:1 **3d**, 87%, dr 3.7:1



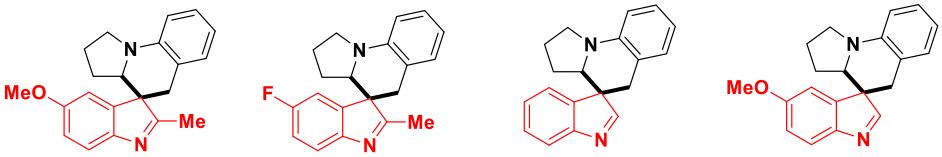
3e, 53%, dr 4:1 **3f**, 93%, dr 4.2:1 **3g**, 90%, dr 3.3:1 **3h**, 95%, dr 4:1



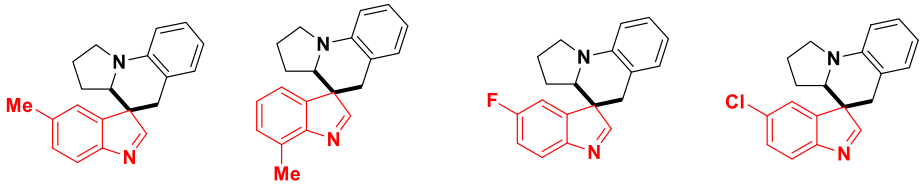
3i, 93%, dr 1.5:1 **3j**, 97%, dr 4:1 **3k**, 94%, dr 3.8:1 **3l**, 90%, dr 4.3:1



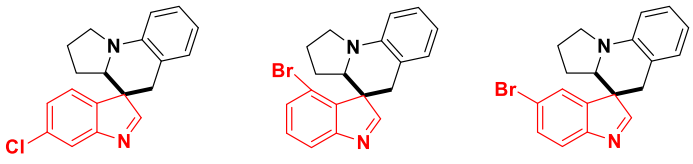
3m, 89%, dr 5:1 **3n**, 90%, dr 3.8:1 **3o**, 79%, dr 4:1 **3p**, 49%



3q, 90%, dr 3.3:1 **3r**, 92%, dr 4:1 **3s**, 74%, dr 1:1 **3t**, 67%, dr 1.1:1



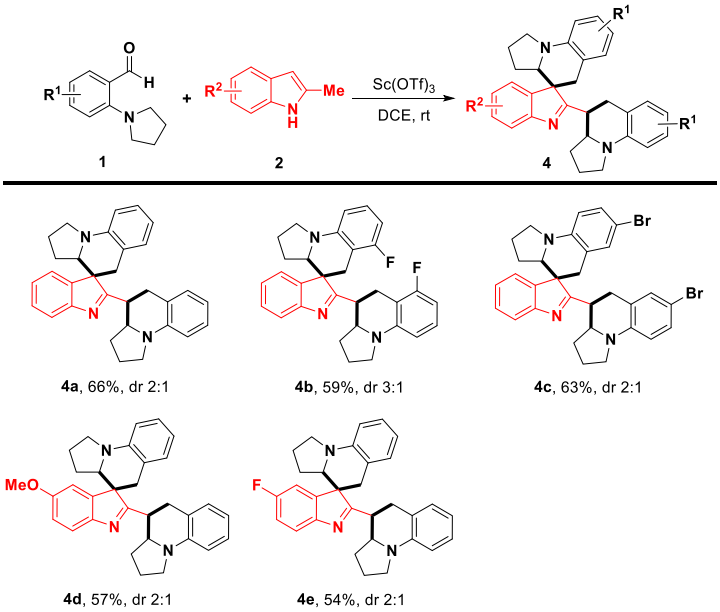
3u, 75%, dr 1.5:1 **3v**, 65%, dr 1:1 **3w**, 82%, dr 1.2:1 **3x**, 71%, dr 1.1:1



3y, 66%, dr 1.2:1 **3z**, 68%, dr >20:1 **3za**, 75%, dr 1.4:1

[a]Reaction conditions: **1** (0.12 mmol) and **2** (0.1 mmol) in 1 mL of HFIP at room temperature. Isolated yields after column chromatography, dr was determined by ^{1}H NMR analysis.

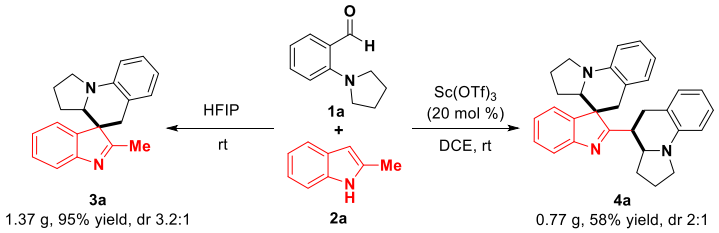
Table 3. Scope for the Three-Component Reactions[a]



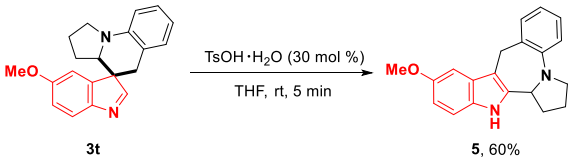
[a]Reaction conditions: **1** (0.25 mmol), **2** (0.1 mmol), and $Sc(OTf)_3$ (20 mol %) in 1 mL of DCE at room temperature for 72 h. Isolated yields after column chromatography, dr was determined by ^{1}H NMR analysis.

To illustrate the practical utility of this protocol, the large-scale reactions of 2-(pyrrolidin-1-yl)benzaldehyde **1a** and 2-methylindole **2a** were conducted (Scheme 2). The reactions proceeded smoothly and furnished products **3a** and **4a** in 95% and 58% yields, respectively. Furthermore, the derivatization of THQ-fused spiroindolenine **3t** was performed under the acidic conditions (Scheme 3).[2a] Delightedly, the acid-catalyzed ring expansion occurred via an 1,2-migration process to afford the indole-fused benzazepine **5** in 60% yield, which was difficult to realize in previous report.[11f]

Scheme 2. Large-Scale Synthesis of Products 3a and 4a.

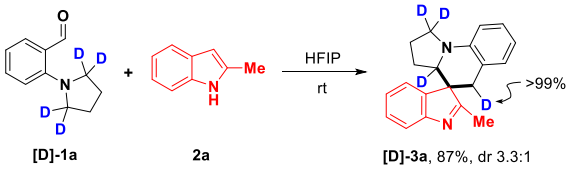


Scheme 3. Transformation of Product 3t.



To get insights into the mechanism, the isotopic experiment between the deuterium substrate **[D]-1a** and 2-methylindole **2a** was performed under the optimized conditions (Scheme 4). The corresponding product **[D]-3a** was isolated in 87% yield and the observation of >99% deuterium at the benzyl position fully demonstrated the intramolecular hydride transfer process.

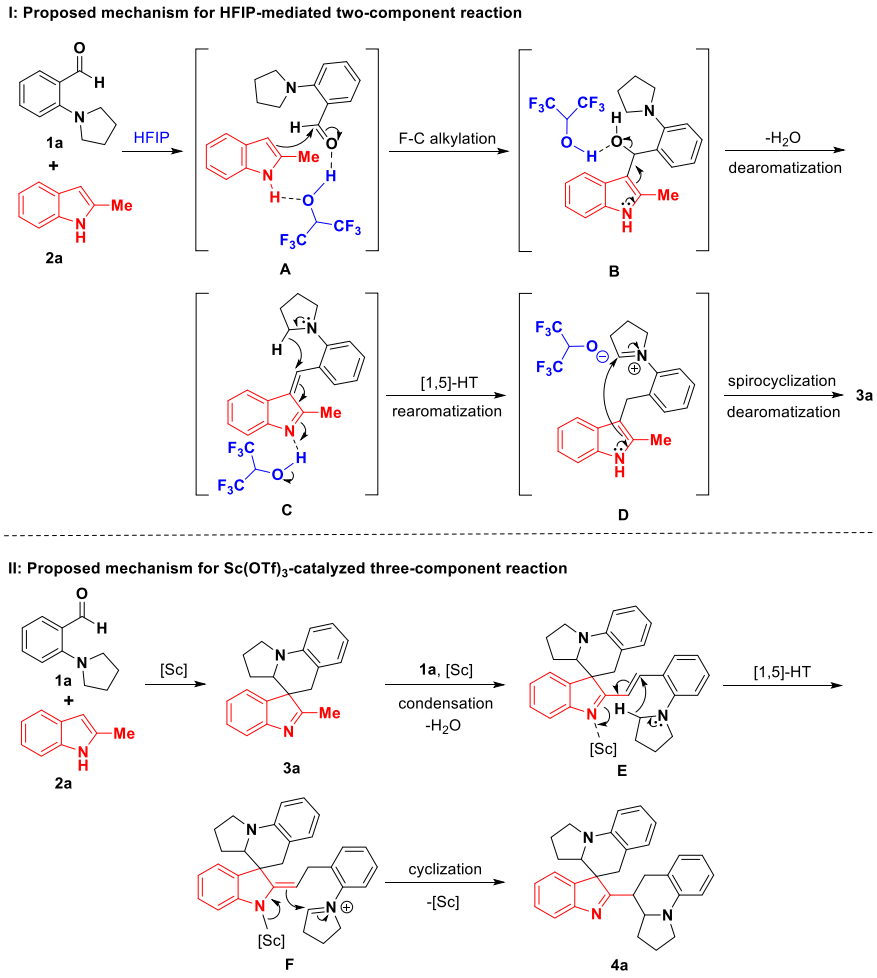
Scheme 4. Deuterium Labeling Experiment.



On the basis of the above experimental results and literature precedents, the plausible mechanisms were proposed as shown in Scheme 5. With respect to the HFIP-mediated two-component reaction, HFIP initially aggregates both substrates **1a** and **2a** via the double hydrogen-bonding activation mode to generate the transition state **A**, which subsequently undergoes the Friedel–Crafts alkylation to form 3-indolylmethanol **B**.[14a] Afterwards, with the assistance of the hydrogen-bonding cluster of HFIP, the dehydration of 3-indolylmethanol **B** affords the dearomatized vinylimine species **C**. Then the rearomatization-driven [1,5]-hydride transfer occurs to give the iminium intermediate **D**, which is stabilized by the HFIP counteranion. Finally, the cascade dearomatization/spirocyclization occurs to provide the THQ-fused spiroindolenine **3a** (Scheme 5, **I**). However, owing to the weak acidity of HFIP, the activation of **3a** to undergo condensation with **1a** is prohibited. In contrast, $Sc(OTf)_3$ could push forward this process, affording the α,β-unsaturated indolenine intermediate **E**.[9e] Then the $Sc(OTf)_3$-catalyzed [1,5]-hydride transfer operates and gives rise to the iminium intermediate **F**, which is followed by the 6-*endo* cyclization to furnish the desired product **4a**. It is worth mentioning that $Sc(OTf)_3$ could produce the product **4a** due to its strong Lewis acidity. Compared with various Brønsted acids and Lewis acids, HFIP exhibits excellent efficiency in the two-component reaction, thanks

to its inherent properties of strong hydrogen bond donor ability and the cationic species stabilization ability.[16]

Scheme 5. Proposed Mechanism



CONCLUSION

In summary, we developed the redox-neutral cascade dearomatization of indoles with *o*-aminobenzaldehydes via hydride transfer strategy, accomplishing the condition- and substrate-controlled divergent synthesis of THQ-fused spiroindolenines. This method featured mild reaction conditions, wide substrate scope, and good functional group tolerance. Mechanistically, the key step of intramolecular [1, 5]-hydride transfer has been fully confirmed by the isotope experiment. We were optimistic that the strategy merging hydride transfer with dearomatization would provide a straightforward avenue for the assembly of bioactive spirocyclic molecules in drug discovery.

Experimental Section

All commercially available reagents, unless otherwise indicated, were used without further purification. All solvents were purified and dried according to standard methods prior to use. Reactions were monitored by thin layer chromatography (TLC) with 0.2 mm silica gel-coated HSGF 254 plates, visualized by UV light at 254 or 365 nm. Products were isolated and purified by column chromatography on 200–300 mesh silica gel. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker AMX 500 (500 MHz for ^{1}H NMR, 125 MHz for ^{13}C NMR and 470 MHz for ^{19}F NMR) spectrometer at room temperature. The chemical shifts (δ) were reported in ppm with respect to an internal standard, tetramethylsilane (0 ppm), and the solvent ($CDCl_3$, ^{1}H: δ = 7.26 ppm, ^{13}C: δ = 77.16 ppm). Coupling constants (*J*) are given in Hertz. Splitting patterns of apparent multiplets associated with an averaged coupling constants were designated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublets) and br (broadened). All ^{13}C spectra were recorded with broadband proton decoupling. HRMS were performed on a Waters XEVO QTOF mass spectrometer.

General Procedure for the Synthesis of *o*-Aminobenzaldehydes 1.[8a, 12c, 13a, 14b]

An oven-dried round-bottomed flask was charged with 2-chloro/fluorobenzaldehydes (1.0 equiv, 10 mmol), secondary amines (1.2 equiv, 12 mmol), K_2CO_3 (2.0 equiv, 20 mmol), and DMF (50 mL). The reaction mixture was stirred vigorously and refluxed in oil bath for 12 h and monitored by TLC. Upon consumption, the mixture was cooled to room temperature and diluted with water (100 mL), and extracted with EtOAc (3 x 100 mL). The combined extracts were washed with brine (3 x 50 mL), dried by anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure and the residue was purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc) to afford *o*-aminobenzaldehydes **1**. 2-Methoxy-6-(pyrrolidin-1-yl)benzaldehyde **1b** was a new compound and characterized as follows.

Procedure for the Synthesis of Deuterated Substrate [D]-1a.

To a solution of pyrrolidine-2,5-dione (3.6 mmol, 357 mg) in THF (15 mL) was added $LiAlD_4$ (18 mmol, 756 mg) in portions in ice bath (0 °C). After stirring at 40 °C in oil bath for 12 h, $Na_2SO_4 \cdot 10H_2O$ was added until no bubbles appeared. Then DMF (15 mL), K_2CO_3 (4.5 mmol, 622 mg), and 2-fluorobenzaldehyde (3 mmol, 372 mg) were added in sequence. The mixture was heated to 120 °C in oil bath and monitored by TLC. After the consumption of 2-fluorobenzaldehyde, the mixture was cooled to room temperature and diluted with water (40 mL), and extracted with EtOAc (3 x 30 mL). The combined extracts were washed with brine (3 x 30 mL), dried by anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure and the residue was purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc) to afford the deuterated substrate **[D]-1a** as colorless oil in 76% yield (408 mg).

General Procedure for the Synthesis of Products 3.

An oven-dried reaction tube was charged with *o*-aminobenzaldehydes **1** (1.2 equiv, 0.12 mmol), indoles **2** (1.0 equiv, 0.1 mmol), and HFIP (1 mL). The reaction mixture was stirred vigorously at room temperature and monitored by TLC. After the consumption of **2**, the reaction mixture was concentrated under reduced pressure and then purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc) to afford products **3**.

General Procedure for the Synthesis of Products 4.

An oven-dried reaction tube was charged with *o*-aminobenzaldehydes **1** (2.5 equiv, 0.25 mmol), 2-methylindoles **2** (1.0 equiv, 0.1 mmol), DCE (1 mL), and $Sc(OTf)_3$ (20 mol %, 9.8 mg). The reaction mixture was stirred vigorously at room temperature for 72 h and monitored by TLC. After the completion of the reaction, the reaction mixture was concentrated under reduced pressure and

then purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc) to afford products **4**.

Procedure for the Large-Scale Synthesis of 3a.

An oven-dried round-bottomed flask was charged with 2-(pyrrolidin-1-yl)benzaldehyde **1a** (6 mmol, 1050 mg), 2-methylindole **2a** (5 mmol, 655 mg), and HFIP (50 mL). The reaction mixture was stirred vigorously at room temperature for 0.2 h and monitored by TLC. After the consumption of **2a**, the reaction mixture was concentrated under reduced pressure and then purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc = 5:1) to afford product **3a** as white solid in 95% yield (1368 mg) with moderate diastereoselectivity (3.2:1 dr).

Procedure for the Large-Scale Synthesis of 4a.

An oven-dried round-bottomed flask was charged with 2-(pyrrolidin-1-yl)benzaldehyde **1a** (7.5 mmol, 1313 mg), 2-methylindole **2a** (3 mmol, 393 mg), DCE (30 mL), and $Sc(OTf)_3$ (0.6 mmol, 295 mg). The reaction mixture was stirred vigorously at room temperature for 72 h and monitored by TLC. After the completion of the reaction, the reaction mixture was concentrated under reduced pressure and then purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc = 20:1) to afford product **4a** as yellow solid in 58% yield (774 mg) with moderate diastereoselectivity (2:1 dr).

Procedure for the Deuterium Labeling Experiment.

An oven-dried reaction tube was charged with **[D]-1a** (0.12 mmol, 21.5 mg), 2-methylindole **2a** (0.1 mmol, 13.1 mg), and HFIP (1 mL). The reaction mixture was stirred vigorously at room temperature for 0.2 h and monitored by TLC. After the consumption of **2a**, the reaction mixture

was concentrated under reduced pressure and then purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc = 5:1) to afford product **[D]-3a** as white solid in 87% yield (25.4 mg) with moderate diastereoselectivity (3.3:1 dr).

Procedure for the Transformation of Product 3t.

An oven-dried reaction tube was charged with **3t** (0.1 mmol, 30.4 mg), $TsOH \cdot H_2O$ (0.03 mmol, 5.7 mg), and THF (1 mL). The reaction mixture was stirred vigorously at room temperature for 5 min and monitored by TLC. After the consumption of **3t**, the reaction mixture was concentrated under reduced pressure and then purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc = 10:1) to afford product **5** as white solid in 60% yield (18.3 mg).

2-methoxy-6-(pyrrolidin-1-yl)benzaldehyde (1b). Yellow solid; 1.78 g, 87% yield; mp 50–52 °C; column chromatography eluent, petroleum ether/EtOAc = 20:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.44 (s, 1H), 7.27 (t, *J* = 8.4 Hz, 1H), 6.46 (d, *J* = 8.7 Hz, 1H), 6.25 (d, *J* = 8.0 Hz, 1H), 3.86 (s, 3H), 3.23–3.16 (m, 4H), 1.97–1.91 (m, 4H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 189.0, 164.0, 150.3, 134.3, 112.3, 107.3, 98.0, 55.8, 52.4 (2C), 25.9 (2C); HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{12}H_{16}NO_2$ 206.1176; found 206.1175.

2-methyl-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (3a). White solid; 27.6 mg, 96% yield, dr 3.3:1; mp 246–248 °C; column chromatography eluent, petroleum ether/EtOAc = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.7 Hz, 1H), 7.28–7.21 (m, 2H), 6.97 (d, *J* = 7.4 Hz, 1H), 6.92 (t, *J* = 7.5 Hz, 1H), 6.64 (t, *J* = 7.2 Hz, 1H), 6.59 (d, *J* = 8.1 Hz, 1H), 6.53 (d, *J* = 7.0 Hz, 1H), 3.95 (dd, *J* = 10.2, 5.8 Hz, 1H), 3.58–3.49 (m, 1H), 3.43 (d, *J* = 15.4 Hz, 1H), 3.23 (dd, *J* = 16.4, 8.9 Hz, 1H), 2.44 (d, *J* = 15.4 Hz, 1H), 2.32 (s, 3H), 1.90–1.82 (m, 1H),

1.82–1.74 (m, 1H), 1.67–1.58 (m, 1H), 0.64 (tdd, *J* = 11.7, 9.9, 7.9 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 184.2, 154.9, 144.0, 139.0, 129.6, 128.1, 127.8, 125.2, 123.9, 119.7, 117.9, 115.8, 110.2, 61.3, 56.5, 47.3, 35.7, 26.8, 23.3, 16.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{21}N_2$ 289.1699; found 289.1697.

6'-methoxy-2-methyl-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline]

(3b). White solid; 29.6 mg, 93% yield, dr 3.7:1; mp 194–196 °C; column chromatography eluent, petroleum ether/EtOAc = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.6 Hz, 1H), 7.27–7.24 (m, 1H), 7.24–7.11 (m, 1H), 6.94 (t, *J* = 7.4 Hz, 1H), 6.65 (d, *J* = 7.4 Hz, 1H), 6.36–6.22 (m, 2H), 3.92–3.82 (m, 1H), 3.72 (s, 3H), 3.49 (td, *J* = 8.8, 2.3 Hz, 1H), 3.27 (dd, *J* = 16.4, 8.5 Hz, 1H), 3.02 (d, *J* = 16.3 Hz, 1H), 2.72 (d, *J* = 16.3 Hz, 1H), 2.33 (s, 3H), 1.90–1.78 (m, 1H), 1.77–1.70 (m, 1H), 1.68–1.58 (m, 1H), 0.68–0.57 (m, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 184.5, 158.1, 155.0, 144.9, 139.6, 127.9, 127.7, 125.1, 123.9, 119.6, 106.0, 104.0, 98.5, 60.6, 56.5, 55.3, 47.5, 29.2, 26.8, 23.3, 16.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{23}N_2O$ 319.1805; found 319.1809.

7'-methoxy-2-methyl-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline]

(3c). White solid; 26.1 mg, 82% yield, dr 3.3:1; mp 238–240 °C; column chromatography eluent, petroleum ether/EtOAc = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.7 Hz, 1H), 7.28–7.25 (m, 1H), 6.94 (t, *J* = 7.5 Hz, 1H), 6.83 (dd, *J* = 8.7, 2.7 Hz, 1H), 6.62 (d, *J* = 2.5 Hz, 1H), 6.58 (d, *J* = 7.4 Hz, 1H), 6.54 (d, *J* = 8.7 Hz, 1H), 3.94–3.86 (m, 1H), 3.74 (s, 3H), 3.51–3.38 (m, 2H), 3.22 (dd, *J* = 16.2, 8.5 Hz, 1H), 2.42 (d, *J* = 15.6 Hz, 1H), 2.31 (s, 3H), 1.91–1.80 (m, 1H), 1.76 (ddd, *J* = 7.3, 6.2, 2.3 Hz, 1H), 1.66–1.58 (m, 1H), 0.69–0.55 (m, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 184.2, 155.0, 150.7, 139.1, 138.8, 127.8, 125.1, 124.1, 119.7, 119.0, 115.7, 113.6, 111.0,

61.4, 56.8, 55.8, 47.7, 35.9, 26.7, 23.3, 16.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{23}N_2O$ 319.1805; found 319.1811.

2,8'-dimethyl-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (3d). Faint yellow solid; 26.3 mg, 87% yield, dr 3.7:1; mp 125–127 °C; column chromatography eluent, petroleum ether/EtOAc = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.7 Hz, 1H), 7.24 (t, *J* = 7.7 Hz, 1H), 6.92 (t, *J* = 7.5 Hz, 1H), 6.85 (d, *J* = 7.5 Hz, 1H), 6.56 (d, *J* = 7.4 Hz, 1H), 6.46 (d, *J* = 7.0 Hz, 1H), 6.40 (s, 1H), 3.91 (dd, *J* = 10.0, 5.5 Hz, 1H), 3.49 (td, *J* = 8.8, 2.2 Hz, 1H), 3.36 (d, *J* = 15.3 Hz, 1H), 3.21 (dd, *J* = 16.4, 8.8 Hz, 1H), 2.39 (d, *J* = 15.3 Hz, 1H), 2.36 (s, 3H), 2.30 (s, 3H), 1.96–1.72 (m, 2H), 1.63–1.57 (m, 1H), 0.67–0.56 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 184.2, 154.9, 143.8, 139.1, 137.7, 129.4, 127.7, 125.1, 123.9, 119.6, 116.7, 115.0, 111.0, 61.3, 56.7, 47.3, 35.4, 26.7, 23.3, 21.7, 16.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{23}N_2$ 303.1856; found 303.1855.

2-methyl-8'-(trifluoromethyl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (3e). Yellow solid; 18.9 mg, 53% yield, dr 4:1; mp 170–172 °C; column chromatography eluent, petroleum ether/EtOAc = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.7 Hz, 1H), 7.28 (t, *J* = 7.5 Hz, 1H), 7.04 (d, *J* = 7.7 Hz, 1H), 6.95 (t, *J* = 7.5 Hz, 1H), 6.88 (d, *J* = 7.5 Hz, 1H), 6.76 (s, 1H), 6.48 (d, *J* = 7.4 Hz, 1H), 3.95 (dd, *J* = 10.0, 6.0 Hz, 1H), 3.62–3.51 (m, 1H), 3.42 (d, *J* = 15.7 Hz, 1H), 3.25 (dd, *J* = 16.5, 9.0 Hz, 1H), 2.49 (d, *J* = 15.7 Hz, 1H), 2.33 (s, 3H), 2.06–1.78 (m, 2H), 1.65 (ddd, *J* = 12.5, 7.2, 1.6 Hz, 1H), 0.73–0.59 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 183.5, 155.0, 144.1, 138.6, 130.4 (q, *J* = 31.5 Hz), 129.7, 128.2, 125.4, 124.6 (q, *J* = 270.6 Hz), 123.6, 121.6 (q, *J* = 1.0 Hz), 120.0, 112.3 (q, *J* = 3.9 Hz), 106.4 (q, *J* = 3.9 Hz), 61.4,

55.8, 47.5, 35.6, 26.8, 23.3, 16.2; ^{19}F NMR (470 MHz, $CDCl_3$) δ –62.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{20}F_3N_2$ 357.1573; found 357.1573.

6'-fluoro-2-methyl-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (3f). White solid; 28.5 mg, 93% yield, dr 4.2:1; mp 156–158 °C; column chromatography eluent, petroleum ether/EtOAc = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.7 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.19–7.09 (m, 1H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.58 (d, *J* = 7.4 Hz, 1H), 6.45–6.34 (m, 2H), 3.90 (dd, *J* = 9.5, 6.0 Hz, 1H), 3.57–3.48 (m, 1H), 3.24 (dd, *J* = 16.5, 8.9 Hz, 1H), 3.12 (d, *J* = 16.1 Hz, 1H), 2.71 (d, *J* = 15.8 Hz, 1H), 2.34 (s, 3H), 2.02–1.74 (m, 2H), 1.68–1.62 (m, 1H), 0.71–0.57 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 183.8, 161.8 (d, *J* = 240.4 Hz), 155.0, 145.4 (d, *J* = 7.6 Hz), 138.9, 128.5 (d, *J* = 10.8 Hz), 128.0, 125.3, 123.6, 119.9, 106.0 (d, *J* = 2.3 Hz), 105.2 (d, *J* = 20.1 Hz), 102.6 (d, *J* = 22.5 Hz), 60.8, 55.8, 47.7, 28.4 (d, *J* = 4.4 Hz), 26.8, 23.3, 16.3; ^{19}F NMR (470 MHz, $CDCl_3$) δ –117.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{20}FN_2$ 307.1605; found 307.1614.

7'-chloro-2-methyl-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (3g). Yellow solid; 29.0 mg, 90% yield, dr 3.3:1; mp 124–126 °C; column chromatography eluent, petroleum ether/EtOAc = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.6 Hz, 1H), 7.29 (td, *J* = 7.6, 1.1 Hz, 1H), 7.17 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.00–6.87 (m, 2H), 6.59–6.46 (m, 2H), 3.99–3.84 (m, 1H), 3.54–3.46 (m, 1H), 3.38 (d, *J* = 15.5 Hz, 1H), 3.19 (dd, *J* = 16.4, 9.0 Hz, 1H), 2.40 (d, *J* = 15.6 Hz, 1H), 2.31 (s, 3H), 2.05–1.84 (m, 1H), 1.83–1.75 (m, 1H), 1.63 (ddd, *J* = 12.8, 7.5, 1.9 Hz, 1H), 0.64 (tdd, *J* = 11.8, 9.9, 7.9 Hz, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 183.7, 154.9, 142.6, 138.6, 129.2, 128.1, 127.9, 125.3, 123.9, 120.3, 119.9, 119.5, 111.2, 61.3, 56.1, 47.6, 35.5, 26.8, 23.3, 16.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{20}ClN_2$ 323.1310; found 323.1316.

8'-chloro-2-methyl-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (3h).

White solid; 30.6 mg, 95% yield, dr 4:1; mp 176–178 °C; column chromatography eluent, petroleum ether/EtOAc = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.7 Hz, 1H), 7.27 (t, *J* = 7.3 Hz, 1H), 6.95 (t, *J* = 7.7 Hz, 1H), 6.86 (d, *J* = 7.9 Hz, 1H), 6.66–6.56 (m, 1H), 6.55 (d, *J* = 1.5 Hz, 1H), 6.51 (d, *J* = 7.5 Hz, 1H), 3.97–3.86 (m, 1H), 3.52–3.45 (m, 1H), 3.33 (d, *J* = 15.4 Hz, 1H), 3.18 (dd, *J* = 16.6, 9.0 Hz, 1H), 2.40 (d, *J* = 15.4 Hz, 1H), 2.31 (s, 3H), 1.94–1.84 (m, 1H), 1.83–1.76 (m, 1H), 1.66–1.58 (m, 1H), 0.69–0.58 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 183.7, 154.9, 144.9, 138.6, 133.5, 130.4, 128.0, 125.3, 123.7, 119.8, 116.4, 115.5, 109.9, 61.2, 56.1, 47.4, 35.2, 26.7, 23.3, 16.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{20}ClN_2$ 323.1310; found 323.1310.

8'-bromo-2-methyl-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (3i).

Yellow solid; 34.0 mg, 93% yield, dr 1.5:1; mp 138–140 °C; column chromatography eluent, petroleum ether/EtOAc = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.6 Hz, 1H), 7.28 (t, *J* = 7.5 Hz, 1H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.81 (d, *J* = 7.9 Hz, 1H), 6.75 (d, *J* = 7.5 Hz, 1H), 6.70 (s, 1H), 6.52 (d, *J* = 7.4 Hz, 1H), 4.01–3.87 (m, 1H), 3.54–3.45 (m, 1H), 3.33 (d, *J* = 15.5 Hz, 1H), 3.19 (dd, *J* = 16.9, 8.4 Hz, 1H), 2.40 (d, *J* = 15.4 Hz, 1H), 2.31 (s, 3H), 1.95–1.83 (m, 1H), 1.83–1.77 (m, 1H), 1.63 (dt, *J* = 12.4, 6.3 Hz, 1H), 0.69–0.58 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 183.6, 155.0, 145.1, 138.6, 130.7, 128.1, 125.3, 123.7, 121.7, 119.9, 118.5, 116.9, 112.8, 61.2, 56.0, 47.4, 35.3, 26.7, 23.3, 16.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{20}BrN_2$ 367.0804; found 367.0811.

7'-bromo-2-methyl-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (3j).

White solid; 35.5 mg, 97% yield, dr 4:1; mp 130–132 °C; column chromatography eluent,

petroleum ether/EtOAc = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.7 Hz, 1H), 7.32–7.21 (m, 2H), 7.06 (s, 1H), 6.94 (t, *J* = 7.5 Hz, 1H), 6.51 (d, *J* = 7.4 Hz, 1H), 6.44 (d, *J* = 8.6 Hz, 1H), 3.97–3.84 (m, 1H), 3.53–3.45 (m, 1H), 3.37 (d, *J* = 15.5 Hz, 1H), 3.18 (dd, *J* = 16.5, 8.9 Hz, 1H), 2.38 (d, *J* = 15.6 Hz, 1H), 2.31 (s, 3H), 1.91–1.83 (m, 1H), 1.82–1.74 (m, 1H), 1.66–1.59 (m, 1H), 0.68–0.58 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 183.6, 155.0, 143.0, 138.6, 132.0, 130.8, 128.1, 125.3, 123.8, 120.0, 119.9, 111.7, 107.4, 61.3, 56.0, 47.5, 35.5, 26.8, 23.3, 16.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{20}BrN_2$ 367.0804; found 367.0807.

6'-bromo-2-methyl-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (3k). White solid; 34.4 mg, 94% yield, dr 3.8:1; mp 148–150 °C; column chromatography eluent, petroleum ether/EtOAc = 15:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.5 Hz, 1H), 7.28 (t, *J* = 7.6 Hz, 1H), 7.06 (t, *J* = 8.1 Hz, 1H), 6.95 (t, *J* = 7.5 Hz, 1H), 6.90 (d, *J* = 7.9 Hz, 1H), 6.61 (d, *J* = 7.4 Hz, 1H), 6.53 (d, *J* = 8.1 Hz, 1H), 3.86 (dd, *J* = 9.1, 6.3 Hz, 1H), 3.48 (t, *J* = 7.9 Hz, 1H), 3.28–3.22 (m, 1H), 3.16 (d, *J* = 16.3 Hz, 1H), 2.76 (d, *J* = 16.3 Hz, 1H), 2.34 (s, 3H), 2.02–1.73 (m, 2H), 1.69–1.60 (m, 1H), 0.70–0.55 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 183.4, 154.9, 145.3, 139.0, 128.8, 128.0, 126.0, 125.3, 123.6, 119.8 (2C), 117.6, 109.4, 60.8, 56.8, 47.5, 36.0, 26.6, 23.3, 16.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{20}BrN_2$ 367.0804; found 367.0803.

2-methyl-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline]-8'-carbonitrile (3l). White solid; 28.2 mg, 90% yield, dr 4.3:1; mp 309–311 °C; column chromatography eluent, petroleum ether/EtOAc = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.7 Hz, 1H), 7.29 (td, *J* = 7.6, 1.0 Hz, 1H), 7.02 (d, *J* = 7.6 Hz, 1H), 6.99–6.94 (m, 1H), 6.92 (dd, *J* = 7.2, 1.3 Hz, 1H), 6.78 (d, *J* = 1.1 Hz, 1H), 6.44 (d, *J* = 7.4 Hz, 1H), 4.02–3.94 (m, 1H), 3.57–3.50 (m, 1H), 3.42 (d, *J* =

15.8 Hz, 1H), 3.21 (dd, *J* = 16.6, 9.1 Hz, 1H), 2.49 (d, *J* = 15.9 Hz, 1H), 2.33 (s, 3H), 1.98–1.83 (m, 2H), 1.66 (ddd, *J* = 12.5, 7.2, 1.6 Hz, 1H), 0.73–0.62 (m, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 183.1, 155.0, 144.2, 138.3, 130.0, 128.3, 125.5, 123.4, 123.3, 120.1, 119.8, 119.4, 112.6, 111.6, 61.3, 55.5, 47.5, 35.8, 26.8, 23.3, 16.2; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{21}H_{19}N_3Na$ 336.1471; found 336.1474.

1-(4-(2-methyl-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-8'-yl)phenyl)ethan-1-one (3m). White solid; 36.1 mg, 89% yield, dr 5:1; mp 258–261 °C; column chromatography eluent, petroleum ether/EtOAc = 10:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (t, *J* = 7.0 Hz, 2H), 7.77 (d, *J* = 8.2 Hz, 2H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.07 (d, *J* = 7.6 Hz, 1H), 6.98–6.90 (m, 2H), 6.82 (s, 1H), 6.61 (d, *J* = 7.4 Hz, 1H), 4.04–3.96 (m, 1H), 3.65–3.58 (m, 1H), 3.47 (d, *J* = 15.5 Hz, 1H), 3.31 (dd, *J* = 16.5, 8.7 Hz, 1H), 2.65 (s, 3H), 2.51 (d, *J* = 15.6 Hz, 1H), 2.34 (s, 3H), 1.94–1.87 (m, 1H), 1.87–1.79 (m, 1H), 1.70–1.64 (m, 1H), 0.72–0.64 (m, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 197.8, 183.9, 155.0, 146.5, 144.4, 139.8, 138.9, 135.7, 130.1, 128.9 (2C), 128.0, 127.2 (2C), 125.2, 123.9, 119.8, 118.4, 114.9, 108.7, 61.4, 56.4, 47.5, 35.5, 26.8, 26.7, 23.3, 16.3; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{28}H_{26}N_2NaO$ 429.1937; found 429.1944.

2-methyl-6a',6b',7',8',9',10',10a',11'-octahydro-5'H-spiro[indole-3,6'-isoindolo[2,1-a]quinoline] (3n). Yellow solid; 30.8 mg, 90% yield, dr 3.8:1; mp 148–150 °C; column chromatography eluent, petroleum ether/EtOAc = 10:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.7 Hz, 1H), 7.28–7.13 (m, 2H), 6.93 (d, *J* = 7.3 Hz, 1H), 6.90 (t, *J* = 7.5 Hz, 1H), 6.66–6.54 (m, 2H), 6.46 (d, *J* = 7.4 Hz, 1H), 4.13 (d, *J* = 9.3 Hz, 1H), 3.44 (d, *J* = 15.3 Hz, 1H), 3.33–3.21 (m, 2H), 2.40–2.30 (m, 4H), 1.95–1.89 (m, 1H), 1.71–1.15 (m, 9H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 184.8, 154.9,

144.5, 139.2, 129.4, 128.1, 127.7, 125.1, 123.7, 119.9, 117.5, 115.5, 109.9, 61.1, 56.1, 53.7, 39.5, 36.9, 36.5, 28.6, 25.7, 24.9, 22.0, 16.9; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{24}H_{27}N_2$ 343.2169; found 343.2170.

2'-methyl-6a,7,8,9,10,11-hexahydro-5H-spiro[azepino[1,2-a]quinoline-6,3'-indole] (3o). Colorless oil; 25.0 mg, 79% yield, dr 4:1; column chromatography eluent, petroleum ether/EtOAc = 15:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.7 Hz, 1H), 7.28 (td, *J* = 7.7, 1.8 Hz, 1H), 7.16 (td, *J* = 7.5, 1.5 Hz, 1H), 7.09–6.91 (m, 3H), 6.75 (d, *J* = 8.5 Hz, 1H), 6.65 (t, *J* = 7.2 Hz, 1H), 3.62 (ddd, *J* = 15.2, 5.7, 3.4 Hz, 1H), 3.48 (dd, *J* = 8.7, 4.9 Hz, 1H), 3.32 (ddd, *J* = 15.0, 9.5, 2.9 Hz, 1H), 3.06 (d, *J* = 16.3 Hz, 1H), 2.79 (d, *J* = 16.3 Hz, 1H), 2.21 (s, 3H), 1.94–1.83 (m, 1H), 1.65–1.32 (m, 7H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 185.7, 154.9, 146.0, 140.6, 129.6, 128.0, 127.8, 124.8, 124.6, 119.8, 118.6, 116.6, 111.9, 61.7, 58.7, 50.7, 33.7, 30.4, 29.1, 27.8, 26.2, 17.6; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{25}N_2$ 317.2012; found 317.2015.

1',2-dimethyl-1',4'-dihydro-2'H-spiro[indole-3,3'-quinoline] (3p). White solid; 12.8 mg, 49% yield; mp 94–96 °C; column chromatography eluent, petroleum ether/EtOAc = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.7 Hz, 1H), 7.31 (td, *J* = 7.6, 1.1 Hz, 1H), 7.22 (td, *J* = 7.8, 0.5 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 7.00–6.94 (m, 2H), 6.75 (d, *J* = 8.2 Hz, 1H), 6.70 (t, *J* = 7.3 Hz, 1H), 3.46 (d, *J* = 11.4 Hz, 1H), 3.13 (d, *J* = 16.0 Hz, 1H), 3.04 (dd, *J* = 11.4, 1.7 Hz, 1H), 2.96 (s, 3H), 2.71 (d, *J* = 16.0 Hz, 1H), 2.26 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 184.6, 154.0, 145.3, 142.2, 129.6, 128.1, 127.9, 125.3, 123.0, 119.9, 118.9, 117.0, 110.8, 55.4, 54.5, 39.0, 33.9, 17.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{19}N_2$ 263.1543; found 263.1544.

5-methoxy-2-methyl-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (3q). Brown oil; 28.6 mg, 90% yield, dr 3.3:1; column chromatography eluent, petroleum

ether/EtOAc = 6:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.5 Hz, 1H), 7.20 (t, *J* = 7.6 Hz, 1H), 6.96 (d, *J* = 7.3 Hz, 1H), 6.77 (dd, *J* = 8.4, 2.5 Hz, 1H), 6.63 (t, *J* = 7.5 Hz, 1H), 6.57 (d, *J* = 8.1 Hz, 1H), 6.11 (d, *J* = 2.4 Hz, 1H), 3.92 (dd, *J* = 9.9, 5.9 Hz, 1H), 3.56–3.48 (m, 4H), 3.40 (d, *J* = 15.5 Hz, 1H), 3.21 (dd, *J* = 16.5, 8.8 Hz, 1H), 2.43 (d, *J* = 15.4 Hz, 1H), 2.28 (s, 3H), 1.98–1.79 (m, 2H), 1.67–1.60 (m, 1H), 0.73–0.63 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 182.0, 157.5, 148.6, 144.0, 140.5, 129.7, 128.2, 119.7, 117.6, 115.9, 112.4, 110.6, 110.1, 61.4, 56.5, 55.3, 47.5, 35.8, 26.8, 23.4, 16.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{23}N_2O$ 319.1805; found 319.1809.

5-fluoro-2-methyl-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (3r). Yellow solid; 28.2 mg, 92% yield, dr 4:1; mp 140–142 °C; column chromatography eluent, petroleum ether/EtOAc = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51–7.39 (m, 1H), 7.23 (t, *J* = 7.7 Hz, 1H), 6.99–6.91 (m, 2H), 6.65 (t, *J* = 7.4 Hz, 1H), 6.59 (d, *J* = 8.1 Hz, 1H), 6.26 (dd, *J* = 8.6, 2.6 Hz, 1H), 3.91 (dd, *J* = 10.5, 5.5 Hz, 1H), 3.55–3.48 (m, 1H), 3.42 (d, *J* = 15.6 Hz, 1H), 3.26 (dd, *J* = 16.5, 8.9 Hz, 1H), 2.44 (d, *J* = 15.5 Hz, 1H), 2.30 (s, 3H), 2.00–1.80 (m, 2H), 1.64 (ddd, *J* = 12.7, 7.5, 1.9 Hz, 1H), 0.69–0.59 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 184.0 (d, *J* = 3.5 Hz), 160.9 (d, *J* = 241.9 Hz), 151.0 (d, *J* = 2.0 Hz), 143.7, 140.9 (d, *J* = 9.3 Hz), 129.6, 128.4, 120.1 (d, *J* = 9.0 Hz), 117.4, 116.2, 114.4 (d, *J* = 23.6 Hz), 111.7 (d, *J* = 25.1 Hz), 110.4, 61.2, 57.1 (d, *J* = 2.1 Hz), 47.3, 35.6, 26.8, 23.2, 16.3; ^{19}F NMR (470 MHz, $CDCl_3$) δ –117.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{20}FN_2$ 307.1605; found 307.1609.

1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (3s). Faint yellow oil; 20.3 mg, 74% yield, dr 1:1; column chromatography eluent, petroleum ether/EtOAc = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.93 (s, 1H), 7.67 (d, *J* = 7.7 Hz, 1H), 7.63 (d, *J* = 7.7 Hz,

1H), 7.38 (td, *J* = 7.6, 1.0 Hz, 1H), 7.31–7.27 (m, 2H), 7.23–7.16 (m, 3H), 7.03 (d, *J* = 7.3 Hz, 1H), 6.98 (t, *J* = 7.4 Hz, 1H), 6.95 (d, *J* = 7.4 Hz, 1H), 6.66–6.61 (m, 2H), 6.61–6.54 (m, 3H), 4.13 (dd, *J* = 9.7, 5.8 Hz, 1H), 3.96 (dd, *J* = 10.0, 5.9 Hz, 1H), 3.58 (d, *J* = 15.5 Hz, 1H), 3.51–3.43 (m, 3H), 3.31 (dd, *J* = 16.5, 8.8 Hz, 1H), 3.21 (dd, *J* = 16.3, 8.9 Hz, 1H), 2.59 (d, *J* = 16.2 Hz, 1H), 2.41 (d, *J* = 15.5 Hz, 1H), 1.92–1.74 (m, 4H), 1.73–1.67 (m, 1H), 1.50 (ddd, *J* = 12.7, 7.5, 2.0 Hz, 1H), 1.00–0.91 (m, 1H), 0.70–0.61 (m, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 176.9, 175.4, 156.1, 155.6, 144.1, 143.9, 141.0, 138.6, 129.6, 128.7, 128.3, 128.2, 128.1, 128.0, 126.6, 126.3, 124.0, 121.6, 121.4, 121.1, 119.8, 117.4, 116.0, 115.9, 111.0, 110.2, 62.8, 60.0, 57.0, 56.9, 47.4, 47.3, 35.8, 34.0, 27.6, 27.0, 23.4, 23.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{19}N_2$ 275.1543; found 275.1541.

5-methoxy-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (3t). White solid; 20.4 mg, 67% yield, dr 1.1:1; mp 132–134 °C; column chromatography eluent, petroleum ether/EtOAc = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.80 (s, 1H), 7.56 (d, *J* = 8.5 Hz, 1H), 7.52 (d, *J* = 8.5 Hz, 1H), 7.22–7.16 (m, 2H), 7.03 (d, *J* = 7.4 Hz, 1H), 6.95 (d, *J* = 7.3 Hz, 1H), 6.89 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.80 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.74 (d, *J* = 2.5 Hz, 1H), 6.66–6.61 (m, 2H), 6.59–6.54 (m, 2H), 6.12 (d, *J* = 2.5 Hz, 1H), 4.13 (dd, *J* = 9.8, 5.8 Hz, 1H), 3.91 (dd, *J* = 10.0, 5.9 Hz, 1H), 3.85 (s, 3H), 3.59–3.54 (m, 4H), 3.52–3.45 (m, 2H), 3.40 (d, *J* = 16.1 Hz, 1H), 3.30 (dd, *J* = 16.5, 8.8 Hz, 1H), 3.20 (dd, *J* = 16.4, 9.0 Hz, 1H), 2.61 (d, *J* = 16.1 Hz, 1H), 2.42 (d, *J* = 15.5 Hz, 1H), 1.96–1.77 (m, 4H), 1.73 (ddd, *J* = 12.6, 7.2, 1.6 Hz, 1H), 1.54 (ddd, *J* = 12.7, 7.5, 2.0 Hz, 1H), 1.03–0.94 (m, 1H), 0.75–0.67 (m, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 174.7, 173.2, 159.0, 158.3, 149.7, 149.3, 144.0, 143.8, 142.7, 140.2, 129.7, 128.7, 128.2, 127.9, 121.6, 121.2, 119.7, 117.1, 115.9, 115.8, 112.5, 112.5, 110.9, 110.6, 110.1, 108.3, 62.8, 60.2,

56.9, 56.8, 55.7, 55.3, 47.4 (2C), 36.0, 34.1, 27.6, 27.0, 23.4, 23.2; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{20}H_{21}N_2O$ 305.1648; found 305.1651.

5-methyl-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (3u). Red solid; 21.6 mg, 75% yield, dr 1.5:1; mp 138–140 °C; column chromatography eluent, petroleum ether/EtOAc = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.20–7.15 (m, 2H), 7.03 (d, *J* = 7.3 Hz, 1H), 6.99 (s, 1H), 6.64 (t, *J* = 7.3 Hz, 1H), 6.58 (d, *J* = 8.1 Hz, 1H), 3.94 (dd, *J* = 10.0, 5.9 Hz, 1H), 3.50–3.45 (m, 1H), 3.43 (d, *J* = 16.1 Hz, 1H), 3.31 (dd, *J* = 16.4, 8.9 Hz, 1H), 2.59 (d, *J* = 16.2 Hz, 1H), 2.42 (s, 3H), 1.93–1.77 (m, 2H), 1.53 (ddd, *J* = 12.6, 7.5, 2.1 Hz, 1H), 1.02–0.93 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ174.4, 153.5, 143.8, 141.1, 136.5, 128.8, 128.7, 127.9, 122.3, 120.8, 119.8, 115.7, 110.9, 62.7, 56.7, 47.4, 35.9, 27.6, 23.2, 21.5; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{20}H_{21}N_2$ 289.1699; found 289.1696.

7-methyl-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (3v). Colorless oil; 18.7 mg, 65% yield, dr 1:1; column chromatography eluent, petroleum ether/EtOAc = 10:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.90 (s, 1H), 7.21–7.15 (m, 4H), 7.09 (d, *J* = 7.6 Hz, 1H), 7.03–6.98 (m, 2H), 6.93 (d, *J* = 7.3 Hz, 1H), 6.88 (t, *J* = 7.5 Hz, 1H), 6.66–6.60 (m, 2H), 6.59–6.54 (m, 2H), 6.38 (d, *J* = 7.4 Hz, 1H), 4.12 (dd, *J* = 9.7, 5.8 Hz, 1H), 3.92 (dd, *J* = 9.9, 5.9 Hz, 1H), 3.56 (d, *J* = 15.5 Hz, 1H), 3.47 (ddd, *J* = 17.5, 8.7, 2.6 Hz, 2H), 3.41 (d, *J* = 16.2 Hz, 1H), 3.30 (dd, *J* = 16.5, 8.7 Hz, 1H), 3.20 (dd, *J* = 16.4, 8.9 Hz, 1H), 2.66–2.53 (m, 7H), 2.39 (d, *J* = 15.6 Hz, 1H), 1.93–1.74 (m, 4H), 1.73–1.67 (m, 1H), 1.50 (ddd, *J* = 12.7, 7.6, 2.1 Hz, 1H), 1.00–0.91 (m, 1H), 0.75–0.61 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 175.7, 174.1, 154.4, 154.0, 144.0, 143.8, 140.8, 138.4, 130.9, 130.5, 129.6, 129.5, 129.4, 128.7, 128.0, 127.9, 126.5, 126.2, 121.3, 119.8, 118.9, 117.4, 115.8, 115.7, 110.9, 110.1, 62.7, 60.0, 57.0, 56.8, 47.3, 47.2,

35.9, 34.0, 27.6, 27.0, 23.4, 23.2, 16.8 (2C); HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{21}N_2$ 289.1699; found 289.1702.

5-fluoro-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (3w). White solid; 23.9 mg, 82% yield, dr 1.2:1; mp 156–158 °C; column chromatography eluent, petroleum ether/EtOAc = 20:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.57 (dd, *J* = 8.5, 4.7 Hz, 1H), 7.24–7.17 (m, 1H), 7.01–6.95 (m, 2H), 6.65 (t, *J* = 7.4 Hz, 1H), 6.59 (d, *J* = 8.1 Hz, 1H), 6.29 (dd, *J* = 8.4, 2.6 Hz, 1H), 4.12 (dd, *J* = 9.8, 5.8 Hz, 1H), 3.59 (d, *J* = 15.6 Hz, 1H), 3.49 (dd, *J* = 12.1, 5.4 Hz, 1H), 3.25 (dd, *J* = 16.4, 8.9 Hz, 1H), 2.43 (d, *J* = 15.6 Hz, 1H), 1.95–1.79 (m, 2H), 1.76–1.70 (m, 1H), 0.72–0.63 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 176.6 (*J* = 3.8 Hz), 161.5 (*J* = 243.5 Hz), 152.0 (*J* = 2.3 Hz), 143.7, 140.6 (*J* = 9.4 Hz), 129.6, 128.4, 121.6 (*J* = 9.0 Hz), 116.8, 116.2, 114.7 (*J* = 23.9 Hz), 111.7 (*J* = 25.0 Hz), 110.4, 59.9, 57.4 (*J* = 2.3 Hz), 47.1, 33.8, 27.0, 23.3; ^{19}F NMR (470 MHz, $CDCl_3$) δ –115.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{18}FN_2$ 293.1449; found 293.1449.

5-chloro-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (3x). White solid; 21.8 mg, 71% yield, dr 1.1:1; mp 149–152 °C; column chromatography eluent, petroleum ether/EtOAc = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (s, 1H,), 7.92 (s, 1H), 7.58 (d, *J* = 8.2 Hz, 1H), 7.55 (d, *J* = 8.2 Hz, 1H), 7.37 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.28 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.23 (t, *J* = 8.0 Hz, 1H), 7.20 (t, *J* = 8.0 Hz, 1H), 7.17 (d, *J* = 2.0 Hz, 1H), 7.04 (d, *J* = 7.4 Hz, 1H), 6.97 (d, *J* = 7.4 Hz, 1H), 6.69–6.64 (m, 2H), 6.60 (d, *J* = 4.6 Hz, 1H), 6.59 (d, *J* = 4.6 Hz, 1H), 6.54 (d, *J* = 2.1 Hz, 1H), 4.11 (dd, *J* = 9.8, 5.8 Hz, 1H), 3.94 (dd, *J* = 10.0, 5.9 Hz, 1H), 3.59 (d, *J* = 15.6 Hz, 1H), 3.51–3.45 (m, 2H), 3.43 (d, *J* = 16.1 Hz, 1H), 3.32 (dd, *J* = 15.5, 7.9 Hz, 1H), 3.27 (dd, *J* = 15.5, 7.9 Hz, 1H), 2.62 (d, *J* = 16.1 Hz, 1H), 2.43 (d, *J* = 15.6 Hz, 1H), 1.98–1.78 (m, 4H),

1.76–1.72 (m, 1H), 1.56 (ddd, *J* = 12.7, 7.6, 2.2 Hz, 1H), 1.01–0.93 (m, 1H), 0.72–0.63 (m, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 177.1, 175.8, 154.5, 154.1, 143.7, 143.6, 142.8, 140.4, 132.5, 132.2, 129.5, 128.7, 128.4, 128.4, 128.3, 128.1, 124.3, 122.2, 122.1, 121.8, 119.3, 116.8, 116.3, 116.0, 111.0, 110.5, 62.6, 59.8, 57.5, 57.5, 47.3, 47.0, 35.7, 33.7, 27.6, 26.9, 23.2, 23.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{18}ClN_2$ 309.1153; found 309.1153.

6-chloro-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (3y). Colorless oil; 20.3 mg, 66% yield; dr 1.2:1; column chromatography eluent, petroleum ether/EtOAc = 10:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.62 (d, *J* = 1.6 Hz, 1H), 7.23–7.17 (m, 1H), 6.97 (dd, *J* = 8.1, 1.9 Hz, 1H), 6.95 (d, *J* = 7.5 Hz, 1H), 6.64 (t, *J* = 7.3 Hz, 1H), 6.58 (d, *J* = 8.1 Hz, 1H), 6.47 (d, *J* = 8.0 Hz, 1H), 4.11 (dd, *J* = 9.7, 5.9 Hz, 1H), 3.57 (d, *J* = 15.5 Hz, 1H), 3.51–3.45 (m, 1H), 3.20 (dd, *J* = 16.4, 8.8 Hz, 1H), 2.39 (d, *J* = 15.5 Hz, 1H), 1.94–1.77 (m, 2H), 1.74–1.68 (m, 1H), 0.70–0.60 (m, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 178.4, 157.1, 143.8, 136.9, 133.7, 129.5, 128.3, 126.2, 124.5, 121.5, 117.0, 116.1, 110.3, 59.9, 56.9, 47.1, 33.9, 26.9, 23.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{18}ClN_2$ 309.1153; found 309.1157.

4-bromo-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (3z). White solid; 23.9 mg, 68% yield, dr >20:1; mp 182–184 °C; column chromatography eluent, petroleum ether/EtOAc = 20:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.60 (dd, *J* = 7.6, 0.7 Hz, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.25 (t, *J* = 7.9 Hz, 1H), 7.19 (t, *J* = 7.7 Hz, 1H), 7.07 (d, *J* = 7.4 Hz, 1H), 6.67 (td, *J* = 7.4, 0.8 Hz, 1H), 6.60 (d, *J* = 8.1 Hz, 1H), 4.59 (dd, *J* = 10.0, 6.0 Hz, 1H), 4.19 (d, *J* = 16.2 Hz, 1H), 3.52–3.43 (m, 1H), 3.35 (dd, *J* = 16.9, 8.1 Hz, 1H), 2.54 (d, *J* = 16.2 Hz, 1H), 1.98–1.90 (m, 2H), 1.70–1.65 (m, 1H), 1.03–0.93 (m, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 176.7, 157.8, 143.7, 138.3, 130.5, 129.9, 128.8, 127.9, 120.6, 119.1, 117.5, 116.0, 111.1, 60.2,

58.6, 47.1, 31.6, 27.4, 23.1; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{18}BrN_2$ 353.0648; found 353.0647.

5-bromo-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (3za). White solid; 26.4 mg, 75% yield, dr 1.4:1; mp 148–150 °C; column chromatography eluent, petroleum ether/EtOAc = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ7.91 (s, 1H), 7.53–7.48 (m, 1H), 7.32 (d, *J* = 0.8 Hz, 1H), 7.19 (t, *J* = 7.8 Hz, 1H), 7.03 (d, *J* = 7.4 Hz, 1H), 6.74–6.63 (m, 2H), 6.61–6.57 (m, 1H), 3.93 (dd, *J* = 9.9, 5.9 Hz, 1H), 3.50–3.45 (m, 1H), 3.42 (d, *J* = 16.1 Hz, 1H), 3.31 (dd, *J* = 15.6, 7.9 Hz, 1H), 2.61 (d, *J* = 16.1 Hz, 1H), 1.94–1.81 (m, 2H), 1.60–1.53 (m, 1H), 1.00–0.92 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 175.7, 154.6, 143.6, 143.2, 131.4, 128.7, 128.1, 125.0, 122.7, 120.5, 119.3, 116.0, 111.0, 62.6, 57.5, 47.3, 35.7, 27.6, 23.2; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{18}BrN_2$ 353.0648; found 353.0648.

2-(1,2,3,3a,4,5-hexahydropyrrolo[1,2-a]quinolin-4-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (4a). Yellow solid; 29.4 mg, 66% yield, dr 2:1; mp 188–191 °C; column chromatography eluent, petroleum ether/EtOAc = 20:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.5 Hz, 1H), 7.28 (t, *J* = 7.6 Hz, 1H), 7.22 (t, *J* = 7.7 Hz, 1H), 7.14 (t, *J* = 7.5 Hz, 1H), 7.05 (d, *J* = 7.2 Hz, 1H), 7.01–6.91 (m, 2H), 6.66–6.56 (m, 3H), 6.55–6.44 (m, 2H), 4.02 (dd, *J* = 9.1, 5.7 Hz, 1H), 3.96 (td, *J* = 10.2, 4.8 Hz, 1H), 3.59–3.44 (m, 3H), 3.34–3.20 (m, 3H), 2.95 (dd, *J* = 15.6, 3.7 Hz, 1H), 2.60–2.49 (m, 1H), 2.40 (d, *J* = 15.2 Hz, 1H), 2.17–2.07 (m, 2H), 2.04–1.94 (m, 1H), 1.91–1.71 (m, 3H), 1.51–1.35 (m, 1H), 0.79–0.63 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 189.1, 155.1, 143.9, 143.8, 138.6, 129.5, 128.4, 128.1, 127.9, 127.7, 125.4, 123.9, 120.5, 120.1, 117.4, 115.8, 114.8, 110.2, 110.1, 62.4, 60.3, 56.7, 47.6, 47.1, 37.8, 36.1, 34.6, 32.0, 27.9, 23.8, 23.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{31}H_{32}N_3$ 446.2591; found 446.2595.

6'-fluoro-2-(6-fluoro-1,2,3,3a,4,5-hexahydropyrrolo[1,2-a]quinolin-4-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (4b). White solid; 28.4 mg, 59% yield, dr 3:1; mp 264–264 °C; column chromatography eluent, petroleum ether/EtOAc = 20:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.5 Hz, 1H), 7.30 (t, *J* = 7.5 Hz, 1H), 7.18–7.10 (m, 1H), 7.10–7.02 (m, 1H), 6.98 (t, *J* = 7.5 Hz, 1H), 6.56 (d, *J* = 7.5 Hz, 1H), 6.46–6.31 (m, 3H), 6.27 (t, *J* = 8.0 Hz, 1H), 4.02–3.85 (m, 2H), 3.53–3.45 (m, 2H), 3.40–3.12 (m, 4H), 2.93 (dd, *J* = 16.1, 12.1 Hz, 1H), 2.66 (d, *J* = 15.8 Hz, 1H), 2.54–2.42 (m, 1H), 2.19 (dt, *J* = 11.4, 5.6 Hz, 1H), 2.15–2.08 (m, 1H), 2.05–1.71 (m, 4H), 1.55–1.44 (m, 1H), 0.82–0.64 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 188.5, 161.8 (d, *J* = 240.1 Hz), 161.8 (d, *J* = 239.3 Hz), 155.0, 145.3 (d, *J* = 7.9 Hz), 145.2 (d, *J* = 7.8 Hz), 138.5, 128.5 (d, *J* = 10.6 Hz), 128.2, 128.0 (d, *J* = 10.8 Hz), 125.7, 123.6, 120.2, 107.5 (d, *J* = 20.3 Hz), 106.0 (d, *J* = 2.0 Hz), 105.8 (d, *J* = 2.0 Hz), 104.6 (d, *J* = 20.0 Hz), 102.6 (d, *J* = 22.5 Hz), 101.6 (d, *J* = 22.5 Hz), 61.8, 59.8, 56.1, 47.9, 47.4, 37.2, 31.9, 28.3 (d, *J* = 4.3 Hz), 27.8, 27.1 (d, *J* = 4.5 Hz), 23.7, 23.3; ^{19}F NMR (470 MHz, $CDCl_3$) δ –117.7, –118.0; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{31}H_{30}F_2N_3$ 482.2402; found 482.2404.

7'-bromo-2-(7-bromo-1,2,3,3a,4,5-hexahydropyrrolo[1,2-a]quinolin-4-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (4c). White solid; 37.8 mg, 63% yield, dr 2:1; mp 224–226 °C; column chromatography eluent, petroleum ether/EtOAc = 20:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.6 Hz, 1H), 7.33–7.25 (m, 2H), 7.18 (d, *J* = 8.5 Hz, 1H), 7.11 (d, *J* = 10.7 Hz, 1H), 7.06 (s, 1H), 6.97 (t, *J* = 7.5 Hz, 1H), 6.48 (t, *J* = 7.6 Hz, 1H), 6.42 (d, *J* = 8.6 Hz, 1H), 6.32 (d, *J* = 8.6 Hz, 1H), 3.98–3.84 (m, 2H), 3.51–3.36 (m, 3H), 3.27–3.14 (m, 3H), 2.86 (dd, *J* = 15.7, 2.9 Hz, 1H), 2.48–2.38 (m, 1H), 2.33 (d, *J* = 15.4 Hz, 1H), 2.14–1.76 (m, 6H), 1.46–1.36 (m, 1H), 0.78–0.69 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 188.0, 154.9, 142.8, 142.8,

138.2, 131.8, 130.8, 130.8, 130.2, 128.2, 125.7, 123.7, 122.4, 120.3, 119.3, 111.7, 111.5, 107.4, 106.4, 62.4, 60.2, 56.3, 47.7, 47.2, 37.4, 35.7, 34.2, 31.9, 27.8, 23.7, 23.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{31}H_{30}Br_2N_3$ 602.0801; found 602.0793.

2-(1,2,3,3a,4,5-hexahydropyrrolo[1,2-a]quinolin-4-yl)-5-methoxy-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (4d). White solid; 27.1 mg, 57% yield, dr 2:1; mp 226–228 °C; column chromatography eluent, petroleum ether/EtOAc = 20:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.4 Hz, 1H), 7.19 (t, *J* = 7.7 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.04 (d, *J* = 7.4 Hz, 1H), 6.95 (d, *J* = 7.3 Hz, 1H), 6.79 (dt, *J* = 8.4, 2.4 Hz, 1H), 6.64–6.54 (m, 3H), 6.48 (t, *J* = 7.7 Hz, 1H), 6.06 (d, *J* = 2.3 Hz, 1H), 4.00 (dd, *J* = 9.3, 5.6 Hz, 1H), 3.93 (td, *J* = 10.2, 4.7 Hz, 1H), 3.56–3.43 (m, 6H), 3.33–3.19 (m, 3H), 2.93 (dd, *J* = 15.7, 3.6 Hz, 1H), 2.55–2.46 (m, 1H), 2.39 (d, *J* = 15.2 Hz, 1H), 2.17–1.78 (m, 6H), 1.50–1.41 (m, 1H), 0.83–0.76 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 186.8, 157.7, 148.9, 143.9, 143.8, 140.1, 129.6, 128.4, 128.2, 127.7, 120.6, 120.2, 117.1, 115.8, 114.8, 112.5, 110.5, 110.0 (2C), 62.4, 60.4, 56.7, 55.3, 47.7, 47.1, 37.7, 36.1, 34.8, 32.0, 27.9, 23.8, 23.4; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{32}H_{34}N_3O$ 476.2696; found 476.2691.

5-fluoro-2-(1,2,3,3a,4,5-hexahydropyrrolo[1,2-a]quinolin-4-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline] (4e). White solid; 25.0 mg, 54% yield, dr 2:1; mp 254–256 °C; column chromatography eluent, petroleum ether/EtOAc = 20:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59–7.41 (m, 1H), 7.21 (t, *J* = 7.7 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.04 (d, *J* = 7.2 Hz, 1H), 7.00–6.92 (m, 2H), 6.64 (t, *J* = 7.3 Hz, 1H), 6.61–6.54 (m, 2H), 6.48 (t, *J* = 7.7 Hz, 1H), 6.22 (dd, *J* = 8.6, 2.4 Hz, 1H), 3.98 (dd, *J* = 9.2, 5.7 Hz, 1H), 3.92 (td, *J* = 10.2, 4.8 Hz, 1H), 3.57–3.43 (m, 3H), 3.33–3.18 (m, 3H), 2.93 (dd, *J* = 15.6, 3.7 Hz, 1H), 2.56–2.47 (m, 1H), 2.38 (d, *J* = 15.3

Hz, 1H), 2.16–2.07 (m, 2H), 2.04–1.74 (m, 4H), 1.50–1.41 (m, 1H), 0.75 (dt, *J* = 12.1, 9.1 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 189.0 (d, *J* = 3.5 Hz), 161.0 (d, *J* = 242.4 Hz), 151.1 (d, *J* = 2.0 Hz), 143.8, 143.5, 140.5 (d, *J* = 9.3 Hz), 129.5, 128.4, 128.4, 127.8, 120.5 (d, *J* = 8.9 Hz), 120.4, 116.8, 116.1, 114.9, 114.5 (d, *J* = 23.8 Hz), 111.7 (d, *J* = 25.0 Hz), 110.3, 110.1, 62.4, 60.1, 57.3 (d, *J* = 2.1 Hz), 47.4, 47.1, 37.8, 36.1, 34.5, 32.0, 27.9, 23.8, 23.3; ^{19}F NMR (470 MHz, $CDCl_3$) δ –116.5; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{31}H_{31}FN_3$ 464.2497; found 464.2501.

11-methoxy-1,2,3,9,9a,14b-hexahydrobenzo[6,7]pyrrolo[1',2':1,2]azepino[3,4-b]indole (5). White solid; 18.3 mg, 60% yield; mp 194–196 °C; column chromatography eluent, petroleum ether/EtOAc = 10:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (s, 1H), 7.26 (d, *J* = 7.4 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.18–7.07 (m, 3H), 6.97 (t, *J* = 7.3 Hz, 1H), 6.77 (d, *J* = 8.7 Hz, 1H), 4.27 (d, *J* = 15.0 Hz, 1H), 3.93 (t, *J* = 8.2 Hz, 1H), 3.89 (s, 3H), 3.75 (d, *J* = 15.0 Hz, 1H), 3.39 (dd, *J* = 17.4, 8.6 Hz, 1H), 3.30 (t, *J* = 7.2 Hz, 1H), 2.48–2.35 (m, 1H), 2.16–1.93 (m, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 154.0, 148.0, 137.3, 136.8, 130.6, 128.6, 127.7, 126.9, 122.9, 118.3, 111.1, 111.0, 108.6, 100.3, 61.7, 56.0, 50.9, 32.4, 29.0, 21.8; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{21}N_2O$ 305.1648; found 305.1647.

2-methyl-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinoline]-1',1',3a',5'-d4 ([D]-3a). White solid; 25.4 mg, 87% yield, dr 3.3:1; mp 237–239 °C; column chromatography eluent, petroleum ether/EtOAc = 5:1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.6 Hz, 1H), 7.30–7.20 (m, 2H), 6.97 (d, *J* = 7.4 Hz, 1H), 6.92 (t, *J* = 7.5 Hz, 1H), 6.64 (t, *J* = 7.5 Hz, 1H), 6.58 (d, *J* = 8.1 Hz, 1H), 6.53 (d, *J* = 7.0 Hz, 1H), 3.40 (s, 0.5H), 2.41 (s, 0.5H), 2.31 (s, 3H), 1.85 (td, *J* = 11.9, 7.2 Hz, 1H), 1.76 (ddd, *J* = 12.4, 7.8, 1.6 Hz, 1H), 1.61 (ddd, *J* = 12.2, 7.2, 1.8 Hz, 1H),

0.62 (td, *J* = 11.8, 7.9 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 184.2, 155.0, 144.1 (d, *J* = 2.1 Hz), 139.0, 129.6 (d, *J* = 8.5 Hz), 128.1 (d, *J* = 1.6 Hz), 127.8, 125.1, 123.9, 119.7, 117.8 (d, *J* = 2.6 Hz), 115.8, 110.2, 60.8 (t, *J* = 21.1 Hz), 56.3 (d, *J* = 2.1 Hz), 46.7 (m), 35.3 (t, *J* = 19.9 Hz), 26.6, 23.1, 16.3; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{17}D_4N_2$ 293.1950; found 293.1956.

Supporting Information

NMR spectra of products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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