Proline triflate catalysed Diels–Alder reaction in the synthesis of tetrahydroquinoline derivatives

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Proline triflate was found to catalyse efficiently the one-pot synthesis of 2H-pyranotetrahydroquinolines from aryl imines, and 3,4-dihydro-2*H*-pyran with high stereoselectivity. The aryl imines were formed *in situ* from aromatic amines and arylaldehydes.

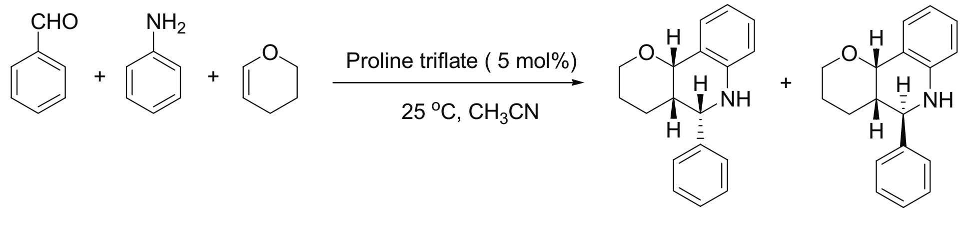
Keywords: tetrahydroquinoline, aza-D-A reactions, proline triflate

Derivatives of tetrahydroquinolines have attracted considerable interest because of their pharmaceutical and biochemical properties,[1] including anti-allergenic,[2] anti-inflammatory[3] and estrogenic activities.[4] The aza-Diels–Alder reactions have been used for the synthesis of heterocycles and natural products.[5] An easy route to tetrahydroquinoline derivatives is *via* the aza-Diels–Alder reaction between aryl imines as heterodienes and various dienophiles in the presence of acid catcalysts.[6-8] Unfortunately, some of the imines are hygroscopic, thermally unstable, and difficult to isolate and purify by column chromatography or distillation.[9] Recently one-pot procedures have been developed for this reaction using lanthanide triflates[10] as catalysts. Different Lewis acids such as $BF_3{\cdot}OEt_2$,[11] $GdCl_3$,[12] $ZrCl_4$[13] have also been used in this reaction.[14-15] However, excess traditional Lewis acid catalysts are needed and some procedures suffer from long reaction times, corrosion and safety problems. Hence, there is still room for improvement to reduce the reaction time and improve yields. Consequently, development of an efficient and versatile method for the preparation of tetrahydroquinolines is an important area of active research.

Recently, our group has reported that metal triflates are excellent catalysts with a wide application in organic synthesis.[16-18] As a part of our ongoing interest in green chemistry and triflate catalysed organic reactions, we report here that proline triflate, obtained from L-proline and trifluoromethanesulfonic acid, is totally a new catalyst. It is cheap to produce, easy to handle and recyclable.

Here we describe the synthesis of tetrahydroquinolines in a one-pot process using a catalytic amount of proline triflate under mild conditions. Generally, the synthetic procedure involves impregnating a mixture of 3,4-dihydro-2*H*-pyran and proline triflate with an acetonitrile solution of benzaldehyde and aniline, to give the corresponding tetrahydroquinolines **3a** and **4a** in 85% yield (Scheme 1).

In order to develop suitable conditions for the above transformation, we investigated the reaction of 3,4-dihydro-2*H*-pyran, benzaldehyde and aniline in various solvents such as tetrahydrofuran, toluene, ether, dichloromethane and acetonitrile. The reaction was very slow in several solvents or under solvent-free conditions. Compared with other catalysts, proline triflate showed the best catalytic effect at 25 °C in CH_3CN (Table 1, entry 1). Significantly, in the absence of catalyst, the reactions did not proceed even after long reaction times (24 h, Table 1, entry 10).



1a **2a** **3a** ***cis-*** **4a** ***trans-***

Scheme 1

Table 1 Effect of solvent on the aza-Diels–Alder reaction of benzaldehyde imine[a]

Entry	Catalyst	Loading/mol%	Solvent	Time/h	Yield[b]/%	**3a/4a** ratio
1	Proline triflate	5	CH_3CN	5	85	25:75
2	Proline triflate	5	toluene	5	10	–
3	Proline triflate	5	Et_2O	5	35	48:52
4	Proline triflate	5	CH_2Cl_2	5	41	51:49
5	Proline triflate	5	THF	5	81	28:72
6	Proline triflate	5	–	5	57	63:37
7	CF_3SO_3H	5	CH_3CN	5	70	31:69
8	L-proline	10	CH_3CN	10	–	–
9	*p*-CH_3PhSO_3H	5	CH_3CN	5	62	33:67
10	None	0	CH_3CN	24	–	–

[a]Reaction conditions: 1 mmol benzaldehyde, benzaldehyde/aniline/dihydropyran = 1 : 1.1 : 1.4, 5-Å molecular sieves, 25 °C.
[b]Yield refers to pure product after column chromatography.

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To investigate the stereoselectivity of the model reaction, we modified several conditions (Table 2). As a result, we found that the *cis*- and *trans*- isomers had a different activation energy. The *cis*- product was obtained at higher substrate concentration and lower temperature, and the *trans*- required a lower substrate concentration and higher temperature. On the other hand, it was found that when the reaction temperature was raised, the amount of *trans*- isomer increased slowly. However, when the amount of CH_3CN was increased from 0 to 3 mL in the model reaction, the proportion of *trans*- isomer increased. Hence, to them the *trans*- isomer, the substrate concentration had a stronger influence than temperature. Most recently, Z.Q. Zhou[19] also reported a similar result. Since the condition **C** gave the *trans*- isomer as the major product under mild conditions, we performed the reaction at room temperature and with a lower substrate concentration.

To explore the scope and limitation of this reaction, we have carried out the reaction of 3,4-dihydro-2*H*-pyran with a range of aromatic aldehydes (1**a–n**) and aromatic amines (**2o–v**) under similar conditions (using CH_3CN and proline triflate). Most of the reactions proceeded smoothly under the essentially mild basic conditions to afford the corresponding tetrahydroquinolines (**3** and **4**) in 71–85% yields (Scheme 2, Table 3).

From Table 3, it can be seen that the process tolerates both electron-withdrawing substituents not only on the benzaldehyde but also aniline. Most cases, the product was obtained as a mixture of **3** *cis*- and **4** *trans*- isomers favouring the *trans*- diastereomer. The two diastereoisomers from thiophene-2-carbaldehyde, aniline, and dihydropyran were obtained in a reasonable yield. It was easy to separate the diastereomers by column chromatography on silica gel and also to characterise them by NMR spectroscopy.

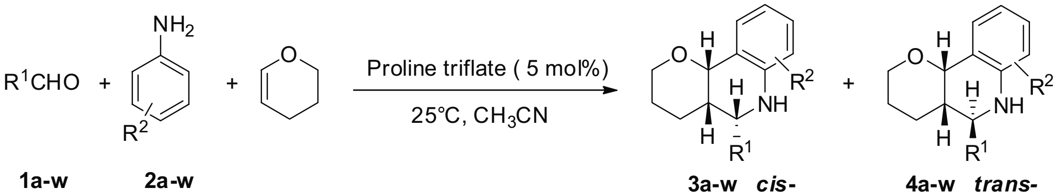
Table 2 One-pot synthesis of pyrano[3,2-*c*]quinolines from aldehydes catalysed by proline triflate[a] under different conditions

Temp. /°C(time/h)	**3a/4a** yield/%[b]Condition A[c]	**3a/4a** yield/%[b]Condition B	**3a/4a** yield/%[b]Condition C
0 (24)	65:35(32)	49:51(53)	43:57(61)
25 (5)	63:37(57)	30:70(72)	25:75(85)
50 (3)	55:45(60)	20:80(78)	12:88(86)

[a] Reaction conditions: 1 mmol benzaldehyde, benzaldehyde/aniline/dihydropyran = 1/1.1/1.4, 5 mol-% proline triflate relative to aldehyde, 5-Å molecular sieves, 25 °C for 5 h.

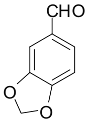
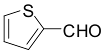
[b] Yield refers to pure product after column chromatography.

[c] Conditions A: 1 mmol PhCHO, solvent-free; condition B: 1 mmol PhCHO, 1 mL CH_3CN; condition C: 1 mmol PhCHO, 3 mL CH_3CN.



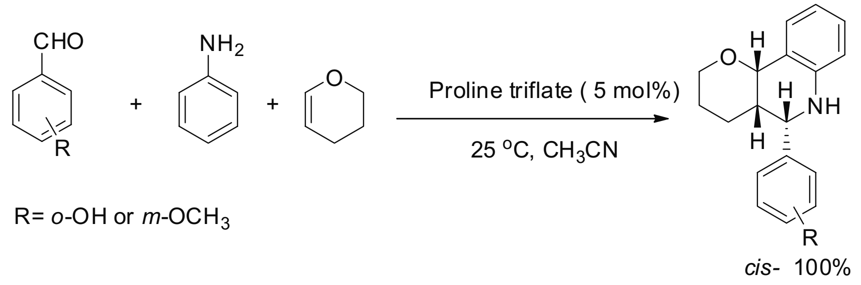
Scheme 2

Table 3 One-pot synthesis of pyrano[3,2-*c*]quinolines from aldehydes catalysed by proline triflate[a,b]

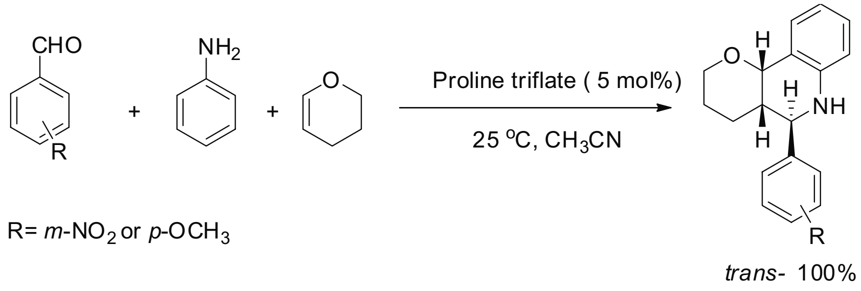
Entry	R^1	R^2	Time/h	Yield/%	**3**/**4** ratio
a	C_6H_5	H	5	85	25:75
b	*p*-Cl-C_6H_4	H	4	83	30:70
c	*p*-Br-C_6H_4	H	4	82	27:73
d	*m*-F-C_6H_4	H	5	76	31:69
e	*m*-Br-C_6H_4	H	4	80	33:67
f	*m*-Cl-C_6H_4	H	4	82	31:69
g	*2,4*-$(OCH_3)_2C_6H_3$	H	5	81	32:68
h		H	5	80	31:69
i	*o*-OCH_3-C_6H_4	H	5	76	33:67
j		H	5	77	26:74
k	*o*-OH-C_6H_4	H	5	81	100:0
l	*m*-OCH_3-C_6H_4	H	5	75	100:0
m	*m*-NO_2-C_6H_4	H	8	78	0:100
n	*p*-OCH_3-C_6H_4	H	7	80	0:100
o	C_6H_5	*p*-Cl	4	84	27:73
p	C_6H_5	*p*-OCH_3	4	82	28:72
q	C_6H_5	*p*-Me	5	80	32:68
r	C_6H_5	*m*-Cl	4	79	30:70
s	C_6H_5	*2*-Me,*3*-Cl	5	78	31:69
t	C_6H_5	*2,5*-$(Me)_2$	6	80	34:66
u	C_6H_5	*3,4*-2F	8	71	31:69
v	C_6H_5	*p*-NO_2	12	–	–
w	*p*-OH-C_6H_4	H	12	–	–

[a] Reaction conditions: 1 mmol benzaldehyde, benzaldehyde/aniline/dihydropyran = 1:1.1:1.4, 5 mol% proline triflate relative to aldehyde, 5-Å molecular sieves. 25 °C.

[b] The reaction was monitored by TLC.



Scheme 3



Scheme 4

Interestingly, when the substrates were 2-hydroxybenzaldehyde and 3-methoxybenzaldehyde, 100% yield of *cis-* isomer were given. In contrast, 3-nitrobenzaldehyde and 4-methoxybenzaldehyde gave the corresponding *trans*-isomers totally (Scheme 4). The reason for this phenomenon is the subject of further study.

Disappointingly, 4-hydroxybenzaldehyde did not react even when the temperature was raised to 80 °C and the reaction time (Table 3, entry **w**) was prolonged. Similarly, 4-nitroaniline did not react under similar conditions (Table 3, entry **v**). The reason that 4-nitroaniline did not react may be attributed to the strong electron-withdrawing effect of the nitro group.

To our disappointment, this reaction was not successful when aliphatic aldehydes were used as a starting material under the same conditions,. When aliphatic aldehydes were used as substrates, the products were complex and inseparable.

In conclusion, we have provided a new catalyst that can act in eco-friendly manner for the aza-Diels–Alder reaction. It is non-volatile, readily available, recyclable and easy to handle. This method not only affords the products in good yields but also avoids the problems associated with complicated workup and enviromental pollution.

Experimental

Melting points were recorded on a Buchi R-535 apparatus and are uncorrected. IR spectra were recorded using KBr pellets on a Nicolet Aviatar-370 instrument. The NMR spectra were measured with a Bruker Advance III 500 or Varian Mercury Plus-400 instrument using $CDCl_3$ as the solvent with TMS as internal standard. Mass spectra were measured with Thermo Finnigan LCQ-Advantage.

General procedure

Proline (20 mmol) was dissolved in water (10 mL) cooled in ice–salt bath. Then trifluoromethanesulfonic acid in aqueous solution (20 mmol mL) was added dropwise. The mixture was stirred for 2 h at 0 °C. The residue was extracted with petroleum ether three times. The combined organic layer was evaporated under reduced pressure to afford the pure proline triflate.

Molecular sieves were added a mixture of benzaldehyde (1.0 mmol), aniline (1.0 mmol) in acetonitrile (3 mL) at 25 °C. The mixture was stirred for 10 min at 25 °C. To this mixture, dihydropyran (1.4 mmol) and proline triflate (0.05 mmol) was added and the reaction stirred for the appropriate time (Table 1). The progress of the reaction was monitored by TLC. After the reaction was complete, water was added, and the product was extracted with EtOAc. The organic layer was dried with anhydrous Na_2SO_4 and concentrated under vacuum. The crude product was purified by column chromatography on silica gel (2% ethyl acetate in petroleum ether) to give pure tetrahydropyranoquinolines **3** and **4** (85%).

Spectral data of tetrahydropyranoquinolines:
(4aS,5S,10bS)-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c] quinoline (**3a**): Solid, m.p. 129–130 °C (Lit.[9] m.p. 129–130 °C). ^1H NMR δ: 7.42–7.28 (m, 6H), 7.08 (t, 1H, J = 8.0 Hz), 6.78 (t, 1H, J = 7.2 Hz), 6.57 (d, 1H, J = 8.0 Hz), 5.31 (d, 1H, J = 5.6 Hz), 4.65 (s, 1H), 3.88 (brs, 1H, NH), 3.58–3.55 (m, 1H), 3.42 (t, 1H, J = 11.6 Hz), 2.14 (s, 1H), 1.55–1.42 (m, 4H). m/z(ESI): 265 (M^+).

(4aS,5R,10bS)-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (**4a**): Pale yellow oil. ^1H NMR δ: 7.36–7.24 (m, 5H), 7.17 (d, 1H, J = 8.0 Hz), 7.01 (t, 1H, J = 8.0 Hz), 6.64 (t, 1H, J = 8.0 Hz), 6.40 (d, 1H, J = 8.0 Hz), 4.60 (d, 1H, J = 10.4 Hz), 4.31 (d, 1H, J = 2.4 Hz), 4.03 (d, 2H, J = 8.8 Hz), 3.67–3.62 (m, 1H), 2.01–1.96 (m, 1H), 1.82–1.72 (m, 1H), 1.61–1.52 (m, 1H), 1.43–1.40 (m, 1H), 1.27–1.22 (m, 1H). m/z(ESI): 265 (M^+).

(4aS,5S,10bS)-5-(4-chlorophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (**3b**): Solid, m.p. 168–169 °C (Lit.[9] m.p. 169–170 °C). ^1H NMR δ: 7.41–7.33 (m, 5H), 7.08 (t, 1H, J = 8.0 Hz), 6.79 (t, 1H, J = 8.0 Hz), 6.59 (d, 1H, J = 8.0 Hz), 5.28 (d, 1H, J = 5.2 Hz), 4.62 (s, 1H), 3.86 (brs, 1H, NH), 3.57 (d, 1H, J = 11.2 Hz), 3.43–3.38 (m, 1H), 2.09 (s, 1H), 1.53–1.24 (m, 4H). ^{13}C NMR δ: 144.8, 139.6, 133.0, 128.4, 128.1, 127.5, 119.8, 118.5, 114.5, 72.5, 60.5, 58.7, 38.8, 25.3, 17.8. m/z(ESI): 299 (M^+).

(4aS,5R,10bS)-5-(4-chlorophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (**4b**): Solid, m.p. 124–126 °C (Lit.[9] m.p. 122–123 °C). ^1H NMR δ: 7.33 (s, 4H), 7.21 (d, 1H, J = 7.6 Hz), 7.08 (t, 1H, J = 7.2 Hz), 6.70 (t, 1H, J = 7.2 Hz), 6.51 (d, 1H, J = 7.6 Hz), 4.65 (t, 1H, J = 5.6 Hz), 4.36 (s, 1H), 4.09–4.06 (m, 2H), 3.71 (t, 1H, J = 11.6 Hz), 2.03–1.98 (m, 1H), 1.81–1.61 (m, 2H), 1.45–1.32 (m, 2H). ^{13}C NMR δ: 144.5, 140.8, 133.4, 130.8, 129.3, 129.1, 128.7, 120.7, 117.7, 114.2, 74.3, 68.5, 54.2, 38.9, 24.0, 21.9. m/z(ESI): 299 (M^+).

(4aS,5S,10bS)-5-(4-bromophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (**3c**)**:** Pale red oil (Lit.[20] m.p. 124–126 °C). ^1H NMR δ: 7.50 (d, 2H, J = 8.4 Hz), 7.42 (d, 1H, J = 7.6 Hz), 7.30 (d, 2H, J = 8.4 Hz), 7.12–7.08 (m, 1H), 6.83–6.79 (m, 1H), 6.61 (d, 1H, J = 7.6 Hz), 5.31 (d, 1H, J = 5.6 Hz), 4.65 (d, 1H, J = 2.0 Hz), 3.83 (brs, 1H, NH), 3.61–3.57 (m, 1H), 3.45–3.36 (m, 1H), 2.12–2.11 (m, 1H), 1.55–1.25 (m, 4H). ^{13}C NMR δ: 144.9, 140.2, 131.5, 128.5, 127.6, 127.0, 121.2, 119.9, 118.6, 114.5, 72.6, 60.6, 58.9, 38.9, 25.3, 18.0. m/z(ESI): 343 (M^+).

(4aS,5R,10bS)-5-(4-bromophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline (**4c**): Solid, m.p. 131–133 °C (Lit.[20] m.p. 127–129 °C). ^1H NMR δ: 7.51–7.48 (m, 2H), 7.31 (d, 2H, J = 8.4 Hz), 7.25–7.21 (m, 1H), 7.12–7.07 (m, 1H), 7.20 (t, 1H, J = 7.6 Hz),

6.53 (d, 1H, J = 8.0 Hz), 4.69 (d, 1H, J = 10.8 Hz), 4.38 (d, 1H, J = 2.8 Hz), 4.11–4.07 (m, 2H), 3.72 (td, 1H, J_1 = 2.4, J_2 = 11.2 Hz), 2.06–2.02 (m, 1H), 1.83–1.76 (m, 1H), 1.71–1.63 (m, 1H), 1.47–1.43 (m, 1H), 1.36–1.33 (m, 1H). ^{13}C NMR δ: 144.4, 141.4, 131.8, 130.9, 129.5, 129.4, 121.6, 120.7, 117.8, 114.3, 74.3, 68.6, 54.4, 38.9, 24.1, 22.0. m/z(ESI): 343 (M$^+$).

(4aS,5S,10bS)-5-(3-fluorophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(3d)**: Solid, m.p. 153–154 °C. IR (cm^{-1}): 3302 (NH). ^{1}H NMR δ: 7.44–7.31 (m, 2H), 7.19–7.09 (m, 3H), 7.02–6.97 (m, 1H), 6.81 (t, 1H, J = 7.6 Hz), 6.62 (d, 1H, J = 8.0 Hz), 5.32 (d, 1H, J = 5.6 Hz), 4.69 (d, 1H, J = 2.0 Hz), 3.85 (brs, 1H, NH), 3.61–3.40 (m, 2H), 2.17–2.16 (m, 1H), 1.56–1.44 (m, 3H), 1.29–1.28 (m, 1H). ^{13}C NMR δ: 164.1, 161.7, 144.8, 144.0, 143.9, 129.9, 129.8, 128.1, 127.6, 122.4, 120.2, 119.9, 118.6, 114.6, 114.4, 114.2, 113.9, 113.6, 72.6, 60.1, 58.9, 38.9, 25.3, 18.0. m/z(ESI): 283 (M$^+$). HRMS-ESI: Calcd for $C_{18}H_{18}FNO$: 283.1372. Found: 283.1389.

(4aS,5R,10bS)-5-(3-fluorophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(4d)**: Pale yellow oil. IR (cm^{-1}): 3364 (NH). ^{1}H NMR δ: 7.36–7.30 (m, 1H), 7.26–7.08 (m, 4H), 7.04–6.99 (m, 1H), 6.72 (td, 1H, J_1 = 1.2, J_2 = 7.6 Hz), 6.55 (d, 1H, J = 8.0 Hz), 4.72 (d, 1H, J = 10.8 Hz), 4.39 (d, 1H, J = 2.8 Hz), 4.12–4.08 (m, 1H), 3.76–3.68 (m, 2H), 2.09–2.03 (m, 1H), 1.86–1.78 (m, 1H), 1.72–1.63 (m, 1H), 1.49–1.46 (m, 1H), 1.39–1.33 (m, 1H). ^{13}C NMR δ: 164.3, 161.9, 145.1 × 2, 144.4, 130.8, 130.1, 130.0, 129.4, 123.5, 120.6, 120.1, 117.7, 114.9, 114.6, 114.4, 114.2, 74.3, 68.5, 54.5, 39.0, 24.1, 22.0. m/z(ESI): 283 (M$^+$). HRMS-ESI: Calcd for $C_{18}H_{18}FNO$: 283.1372. Found: 283.1378.

(4aS,5S,10bS)-5-(3-bromophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(3e)**: Pale red oil. IR (cm^{-1}): 3372 (NH). ^{1}H NMR δ: 7.59 (s, 1H), 7.45–7.41 (m, 2H), 7.33 (d, 1H, J = 7.6 Hz), 7.27–7.23 (m, 1H), 7.10 (t, 1H, J = 7.6 Hz), 6.81 (t, 1H, J = 7.6 Hz), 6.62 (d, 1H, J = 8.0 Hz), 5.31 (d, 1H, J = 5.6 Hz), 4.65 (d, 1H, J = 2.8 Hz), 3.83 (brs, 1H, NH), 3.61–3.57 (m, 1H), 3.46–3.39 (m, 1H), 2.19–2.13 (m, 1H), 1.59–1.44 (m, 3H), 1.29–1.27 (m, 1H). ^{13}C NMR δ: 144.4, 143.2, 130.3, 129.6, 129.5, 127.8, 127.3, 125.2, 122.3, 119.6, 118.3, 114.3, 72.2, 60.3, 58.5, 38.5, 25.0, 17.6. m/z(ESI): 343 (M$^+$). HRMS-ESI: Calcd for $C_{18}H_{18}BrNO$: 343.0572. Found: 343.0580.

(4aS,5R,10bS)-5-(3-bromophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(4e)**: Solid, m.p. 143–145 °C. IR (cm^{-1}): 3363 (NH). ^{1}H NMR δ: 7.59 (s, 1H), 7.47–7.44 (m, 1H), 7.34 (d, 1H, J = 7.2 Hz), 7.26–7.21 (m, 2H), 7.10 (t, 1H, J = 7.6 Hz), 6.72 (t, 1H, J = 7.6 Hz), 6.54 (d, 1H, J = 8.0 Hz), 4.68 (d, 1H, J = 10.8 Hz), 4.38 (d, 2H, J = 2.8 Hz), 4.12–4.08 (m, 2H), 3.76–3.69 (m, 1H), 2.08–2.04 (m, 1H), 1.88–1.76 (m, 1H), 1.72–1.35 (m, 3H). ^{13}C NMR δ: 144.8, 144.4, 131.0, 130.9, 130.8, 130.2, 129.4, 126.6, 122.8, 120.6, 117.8, 114.2, 74.3, 68.6, 54.5, 38.9, 24.1, 22.0. m/z(ESI): 343 (M$^+$). HRMS-ESI: Calcd for $C_{18}H_{18}BrNO$: 343.0572. Found: 343.0575.

(4aS,5S,10bS)-5-(3-chlorophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(3f)**:[21] Pale yellow oil. ^{1}H NMR δ: 7.42 (d, 2H, J = 8.0 Hz), 7.31–7.26 (m, 3H), 7.12–7.08 (m, 1H), 6.81 (t, 1H, J = 7.6 Hz), 6.62 (d, 1H, J = 8.0 Hz), 5.31 (d, 1H, J = 5.6 Hz), 4.66 (d, 1H, J = 2.4 Hz), 3.61–3.57 (m, 1H), 3.46–3.39 (m, 1H), 2.17–2.15 (m, 1H), 1.56–1.44 (m, 4H). m/z(ESI): 299 (M$^+$).

(4aS,5R,10bS)-5-(3-chlorophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(4f)**:[21] Solid, m.p. 91–93 °C. ^{1}H NMR δ: 7.43–7.36 (m, 3H), 7.05–6.97 (m, 2H), 6.59 (d, 1H, J = 7.6 Hz), 6.52 (t, 1H, J = 7.6 Hz), 6.18 (s, 1H), 4.55 (d, 1H, J = 10.4 Hz), 4.28 (d, 1H, J = 3.2 Hz), 3.89–3.87 (m, 1H), 3.59 (dt, 1H, J_1 = 2.0, J_2 = 10.8 Hz), 1.95–1.92 (m, 1H), 1.78–1.60 (m, 2H), 1.30–1.24 (m, 2H). ^{13}C NMR δ: 144.5, 144.4, 134.6, 130.9, 129.9, 128.1, 127.9, 126.1, 120.6, 117.8, 114.2, 74.3, 68.6, 54.5, 38.9, 24.1, 22.0. m/z(ESI): 299 (M$^+$).

(4aS,5S,10bS)-5-(2,4-dimethoxyphenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(3g)**:[22] Solid, m.p. 162–163 °C. ^{1}H NMR δ: 7.44–7.41 (m, 2H), 7.07 (t, 1H, J = 7.2 Hz), 6.77 (t, 1H, J = 7.6 Hz), 6.59 (d, 1H, J = 8.0 Hz), 6.51–6.49 (m, 2H), 5.30 (d, 1H, J = 5.6 Hz), 4.95 (d, 1H, J = 2.0 Hz), 3.82 (d, 6H, J = 3.6 Hz), 3.64–3.57 (m, 2H), 3.42 (t, 1H, J = 11.6 Hz), 2.28–2.26 (m, 1H), 1.60–1.41 (m, 3H), 1.28–1.23 (m, 1H). ^{13}C NMR δ: 160.0, 157.4, 145.8, 127.8, 127.7, 127.6, 121.5, 120.2, 118.0, 114.0, 103.5, 98.5, 72.7, 60.7, 55.4, 55.3, 52.2, 35.5, 25.6, 18.4. m/z (ESI): 325 (M$^+$).

(4aS,5R,10bS)-5-(2,4-dimethoxyphenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(4g)**:[22] Solid, m.p. 144–146 °C. ^{1}H NMR δ: 7.34 (d, 1H, J = 8.4 Hz), 7.24 (t, 1H, J = 7.2 Hz), 7.06 (t, 1H, J = 7.6 Hz), 6.68 (t, 1H, J = 7.2 Hz), 6.52–6.47 (m, 3H), 5.12 (d, 1H, J = 10.0 Hz), 4.40 (d, 1H, J = 2.8 Hz), 4.04–3.99 (m, 1H), 3.81 (s, 6H), 3.68 (td, 1H, J_1 = 2.8, J_2 = 11.2 Hz), 2.10 (s, 1H), 1.92–1.89 (m, 1H), 1.68–1.62 (m, 1H), 1.53–1.49 (m, 1H), 1.34–1.31 (m, 1H). ^{13}C NMR δ: 160.1, 158.6, 145.1, 130.6, 129.0, 128.2, 123.2, 120.5, 117.1, 114.0, 104.7, 98.2, 74.3, 68.0, 55.3, 47.2, 38.3, 24.5, 22.5. m/z(ESI): 325 (M$^+$).

(4aS,5S,10bS)-5-(benzo[d][1,3]dioxol-5-yl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(3h)**: Solid, m.p. 162–163 °C (Lit.[23] m.p. 158–160 °C). ^{1}H NMR δ: 7.41 (d, 1H, J = 7.6 Hz), 7.08 (t, 1H, J = 7.6 Hz), 6.92–6.86 (m, 2H), 6.82–6.77 (m, 2H), 6.58 (d, 1H, J = 8.0 Hz), 5.96 (s, 2H), 5.30 (d, 1H, J = 5.6 Hz), 4.59 (d, 1H, J = 2.0 Hz), 3.81 (brs, 1H, NH), 3.61–3.57 (m, 1H), 3.42 (t, 1H, J = 11.6 Hz), 2.11–2.09 (m, 1H), 1.57–1.36 (m, 4H). ^{13}C NMR δ: 147.6, 146.8, 145.1, 135.1, 128.1, 127.6, 120.0, 119.8, 118.3, 114.4, 108.1, 107.4, 101.0, 72.7, 60.6, 59.1, 39.1, 25.4, 18.1. m/z(ESI): 309 (M$^+$).

(4aS,5R,10bS)-5-(benzo[d][1,3]dioxol-5-yl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(4h)**: Solid, m.p. 143–145 °C (Lit.[23] m.p. 150–152 °C). ^{1}H NMR δ: 7.21 (d, 1H, J = 7.6 Hz), 7.10–7.06 (m, 1H), 6.92–6.85 (m, 2H), 6.79 (d, 1H, J = 8.0 Hz), 6.70 (t, 1H, J = 7.6 Hz), 6.51 (d, 1H, J = 8.4 Hz), 5.96 (s, 2H), 4.63 (d, 1H, J = 10.8 Hz), 4.37 (d, 1H, J = 2.4 Hz), 4.11–4.04 (m, 2H), 3.72 (td, 1H, J_1 = 2.4, J_2 = 11.6 Hz), 2.03–1.09 (m, 1H), 1.84–1.76 (m, 1H), 1.70–1.61 (m, 1H), 1.54–1.50 (m, 1H), 1.35–1.32 (m, 1H). ^{13}C NMR δ: 148.0, 147.2, 144.7, 136.2, 130.9, 129.3, 121.3, 120.7, 117.5, 114.2, 108.1, 107.7, 101.0, 74.6, 68.7, 54.5, 39.0, 24.1, 22.0. m/z(ESI): 309 (M$^+$).

(4aS,5S,10bS)-5-(2-methoxyphenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(3i)**: Solid, m.p. 133–134 °C. IR (cm^{-1}): 3323 (NH). ^{1}H NMR δ: 7.55 (d, 1H, J = 7.6 Hz), 7.43 (d, 1H, J = 7.6 Hz), 7.30–7.25 (m, 1H), 7.08 (t, 1H, J = 7.6 Hz), 6.98 (t, 1H, J = 7.2 Hz), 6.90 (d, 1H, J = 8.0 Hz), 6.78 (t, 1H, J = 7.2 Hz), 6.60 (d, 1H, J = 8.0 Hz), 5.32 (d, 1H, J = 5.6 Hz), 5.03 (s, 1H), 3.84 (s, 3H), 3.68 (brs, 1H, NH), 3.60–3.57 (m, 1H), 3.42 (t, 1H, J = 11.2 Hz), 2.33–2.31 (m, 1H), 1.56–1.25 (m, 4H). ^{13}C NMR δ: 156.4, 145.7, 128.1, 127.9, 127.1, 120.3, 120.2, 120.1, 118.0, 114.5, 110.3, 72.7, 60.6, 55.3, 52.6, 35.2, 25.6, 18.5. m/z(ESI): 295 (M$^+$). HRMS-ESI: Calcd for $C_{19}H_{21}NO_2$: 295.1572. Found: 295.1583.

(4aS,5R,10bS)-5-(2-methoxyphenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(4i)**: Solid, m.p. 136–138 °C. IR (cm^{-1}): 3389 (NH). ^{1}H NMR δ: 7.43 (dd, 1H, J_1 = 1.6, J_2 = 7.6 Hz), 7.27–7.21 (m, 2H), 7.08–7.04 (m, 1H), 6.97–6.88 (m, 2H), 6.69–6.66 (m, 1H), 6.50 (d, 1H, J = 8.0 Hz), 5.18 (d, 1H, J = 10.0 Hz), 4.41 (d, 1H, J = 2.8 Hz), 4.01–3.99 (m, 1H), 3.83 (s, 3H), 3.70–3.63 (m, 2H), 2.13–2.12 (m, 1H), 1.94–1.90 (m, 1H), 1.66–1.61 (m, 1H), 1.51–1.46 (m, 1H), 1.37–1.32 (m, 1H). ^{13}C NMR δ: 157.4, 145.0, 130.9, 130.4, 129.0, 128.3, 128.1, 120.8, 120.3, 117.0, 113.9, 110.4, 74.0, 67.6, 55.3, 38.2, 24.4, 22.6, 18.3. m/z(ESI): 295 (M$^+$). HRMS-ESI: Calcd for $C_{19}H_{21}NO_2$: 295.1572. Found: 295.1581.

(4aS,5S,10bS)-5-(thiophen-2-yl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(3j)**: Solid, m.p. 162–164 °C (Lit.[24] m.p. 155–156 °C). ^{1}H NMR δ: 7.42 (d, 1H, J = 7.2 Hz), 7.25–7.23 (m, 1H), 7.11–7.02 (m, 3H), 6.81 (t, 1H, J = 7.2 Hz), 6.60 (d, 1H, J = 8.0 Hz), 5.28 (d, 1H, J = 5.6 Hz), 4.96 (d, 1H, J = 2.4 Hz), 4.01 (brs, 1H, NH), 3.61–3.58 (m, 1H), 3.45–3.39 (m, 1H), 2.24–2.19 (m, 1H), 1.63–1.47 (m, 4H). ^{13}C NMR δ: 144.7, 144.6, 128.1, 127.6, 126.7, 123.9, 123.8, 120.2, 118.8, 114.6, 72.2, 60.6, 55.6, 39.6, 25.3, 18.4. m/z(ESI): 271 (M$^+$).

(4aS,5R,10bS)-5-(thiophen-2-yl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(4j)**: Solid, m.p. 137–138 °C (Lit.[24] m.p. 135–137 °C). ^{1}H NMR δ: 7.29–7.20 (m, 2H), 7.11–7.06 (m, 2H), 6.99 (t, 1H, J = 4.4 Hz), 6.72 (t, 1H, J = 7.6 Hz), 6.54 (d, 1H, J = 7.6 Hz), 5.05 (d, 1H, J = 10.4 Hz), 4.39 (s, 1H), 4.24 (brs, 1H, NH), 4.09 (d, 1H, J = 11.2 Hz), 3.75–3.69 (m, 1H), 2.06–2.03 (m, 1H), 1.86–1.60 (m, 3H), 1.37–1.35 (m, 1H). ^{13}C NMR δ: 146.2, 144.1, 130.8, 129.3, 126.4, 125.4, 125.0, 120.8, 117.9, 114.3, 74.4, 68.6, 50.7, 40.2, 24.1, 21.9. m/z(ESI): 271 (M$^+$).

2-((4aS,5S,10bS)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-5-yl)phenol **(3k)**: Solid, m.p. 120–121 °C. IR (cm^{-1}): 3342 (NH). ^{1}H NMR δ: 7.42 (d, 1H, J = 7.6 Hz), 7.25–7.19 (m, 3H), 6.94–6.90 (m, 2H), 6.79–6.71 (m, 3H), 5.57 (d, 1H, J = 2.0 Hz), 5.01 (d, 1H, J = 5.2 Hz), 4.02 (td, 1H, J_1 = 2.8, J_2 = 11.6 Hz), 3.81–3.74 (m, 2H), 2.54–2.48 (m, 1H), 1.72–1.60 (m, 3H), 1.38–1.32 (m, 1H). ^{13}C NMR δ: 153.1, 146.9, 129.6, 129.0, 126.7, 121.9, 121.1, 118.1, 116.4, 113.2, 96.4, 60.9, 51.0, 34.8, 24.2, 17.1. m/z(ESI): 281 (M$^+$). HRMS-ESI: Calcd for $C_{18}H_{19}NO_2$: 281.1416. Found: 281.1423.

(4aS,5S,10bS)-5-(3-methoxyphenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(3l)**: Solid, m.p. 119–120 °C. IR (cm^{-1}): 3300 (NH). ^{1}H NMR δ: 7.42 (d, 1H, J = 7.6 Hz), 7.28 (q, 1H, J = 8.0 Hz), 7.09 (t, 1H, J = 7.6 Hz), 7.00–6.98 (m, 2H), 6.86–6.77 (m, 2H), 6.60 (d, 1H, J = 8.0 Hz), 5.32 (d, 1H, J = 5.2 Hz), 4.66 (d, 1H, J = 2.0 Hz), 3.86–3.83 (m, 4H), 3.58 (dd, 1H, J_1 = 3.6, J_2 = 11.2 Hz), 3.45–3.40 (m, 1H), 2.17 (s, 1H), 1.56–1.25 (m, 4H). ^{13}C NMR δ: 159.7, 145.1, 142.9, 129.4, 128.1, 127.6, 120.2, 119.9, 119.1, 118.3, 114.4, 112.6, 72.7, 60.6, 59.3, 55.3, 38.9, 25.4, 18.1. m/z(ESI): 295 (M$^+$). HRMS-ESI: Calcd for $C_{19}H_{21}NO_2$: 295.1572. Found: 295.1574.

(4aS,5R,10bS)-5-(3-nitrophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(4m)**: Solid, m.p. 175–176 °C (Lit.[23] m.p. 160–162 °C). ^{1}H NMR δ: 8.29 (s, 1H), 8.17 (d, 1H, J = 8.0 Hz), 7.75 (d, 1H, J = 7.6 Hz), 7.54 (t, 1H, J = 8.0 Hz), 7.22 (d, 1H, J = 7.6 Hz), 7.11 (t, 1H, J = 7.6 Hz), 6.74 (d, 1H, J = 7.2 Hz), 6.56 (d, 1H, J = 8.0 Hz), 4.80 (d, 1H, J = 10.8 Hz), 4.38 (d, 1H, J = 2.4 Hz), 4.15–4.09 (m, 2H), 3.73 (t, 1H, J = 10.8 Hz), 2.10–2.07 (m, 1H), 1.87–1.66 (m, 2H), 1.40–1.38 (m, 2H). ^{13}C NMR δ: 148.5, 144.7, 144.1, 133.9, 130.8, 129.5, 129.4, 122.9, 122.6, 120.6, 118.0, 114.3, 74.0, 68.4, 54.4, 38.9, 24.0, 22.0. m/z(ESI): 310 (M$^+$).

(4aS,5R,10bS)-5-(4-methoxyphenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(4n)**: Solid, m.p. 136–138 °C (Lit.[23] m.p. 148–150 °C). ^{1}H NMR δ: 7.33 (d, 2H, J = 8.4 Hz), 7.22 (d, 1H, J = 7.6 Hz), 7.08 (t, 1H, J = 7.2 Hz), 6.91 (d, 1H, J = 8.8 Hz), 6.70 (t, 1H, J = 7.6 Hz), 6.51 (d, 1H, J = 8.0 Hz), 4.68 (d, 1H, J = 10.8 Hz), 4.39 (d, 1H, J = 2.4 Hz), 4.11–4.08 (m, 2H), 3.82 (s, 3H), 3.72 (td, 1H, J_1 = 2.4, J_2 = 12.0 Hz), 2.06–2.04 (m, 1H), 1.84–1.81 (m, 1H), 1.68–1.61 (m, 1H), 1.51–1.47 (m, 1H), 1.34–1.30 (m, 1H). ^{13}C NMR δ: 159.3, 144.8, 134.2, 130.9, 129.3, 128.8, 120.7, 117.4, 114.1, 114.0, 74.7, 68.7, 55.3, 54.1, 38.9, 24.1, 22.0. m/z(ESI): 295 (M$^+$).

(4aS,5S,10bS)-9-chloro-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(3o)**: Solid, m.p. 169–170 °C (Lit.[9] m.p. 170–171 °C). ^{1}H NMR δ: 7.39–7.26 (m, 6H), 7.05–7.02 (m, 1H), 6.53 (d, 1H, J = 8.4 Hz), 5.27 (d, 1H, J = 5.2 Hz), 4.66 (s, 1H), 3.89 (brs, 1H, NH), 3.62–3.60 (m, 1H), 3.41 (t, 1H, J = 7.2 Hz), 2.15 (s, 1H), 1.56–1.33 (m, 4H). ^{13}C NMR δ: 143.7, 140.7, 128.4, 128.0, 127.7, 127.3, 126.8, 123.1, 121.6, 115.6, 72.4, 60.8, 59.3, 38.6, 25.3, 18.0. m/z (ESI): 299 (M$^+$).

(4aS,5R,10bS)-9-chloro-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(4o)**: Solid, m.p. 124–125 °C (Lit.[9] m.p. 124–126 °C). ^{1}H NMR δ: 7.40–7.25 (m, 5H), 7.21 (d, 1H, J = 2.4 Hz), 7.03 (dd, 1H, J_1 = 2.4, J_2 = 8.4 Hz), 6.45 (d, 1H, J = 8.8 Hz), 4.67 (d, 1H, J = 10.4 Hz), 4.34 (d, 1H, J = 2.8 Hz), 4.07 (dd, 1H, J_1 = 2.4, J_2 = 10.8 Hz), 3.07 (td, 1H, J_1 = 2.4, J_2 = 10.8 Hz), 2.07–2.04 (m, 1H), 1.85–1.78 (m, 1H), 1.70–1.61 (m, 1H), 1.48–1.45 (m, 1H), 1.37–1.33 (m, 1H). ^{13}C NMR δ: 143.3, 142.0, 130.4, 129.2, 128.7, 128.0, 127.7, 121.9, 121.8, 115.3, 73.9, 68.5, 54.9, 38.6, 24.0, 22.0. m/z(ESI): 299 (M$^+$).

(4aS,5S,10bS)-9-methoxy-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(3p)**: Solid, m.p. 143–145 °C (Lit.[9] m.p. 145–146 °C). ^{1}H NMR δ: 7.43–7.35 (m, 4H), 7.32–7.28 (m, 1H), 7.04–7.03 (m, 1H), 6.72 (dd, 1H, J_1 = 3.2, J_2 = 8.8 Hz), 6.57 (d, 1H, J = 8.8 Hz), 5.31 (d, 1H, J = 5.6 Hz), 4.62 (d, 1H, J = 2.0 Hz), 3.78 (s, 3H), 3.66–3.58 (m, 2H), 3.46–3.40 (m, 1H), 2.17–2.14 (m, 1H), 1.58–1.42 (m, 3H), 1.33–1.25 (m, 1H). ^{13}C NMR δ: 152.9, 144.3, 139.1, 128.3, 127.4, 126.8, 121.1, 115.7, 115.0, 111.9, 72.9, 60.8, 59.6, 55.8, 39.1, 25.3, 17.9. m/z(ESI): 295 (M$^+$).

(4aS,5R,10bS)-9-methoxy-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(4p)**: Pale red oil (Lit.[9] Solid, m.p. 99–100 °C). ^{1}H NMR δ: 7.43–7.30 (m, 5H), 6.82 (d, 1H, J = 2.8 Hz), 6.75 (dd, 1H, J_1 = 2.8, J_2 = 8.8 Hz), 6.50 (d, 1H, J = 8.8 Hz), 4.67 (d, 1H, J = 10.4 Hz), 4.38 (d, 1H, J = 2.8 Hz), 4.10 (d, 1H, J = 11.2 Hz), 3.76–3.69 (m, 4H), 2.11–2.09 (m, 1H), 1.84–1.81 (m, 1H), 1.68–1.60 (m, 1H), 1.49–1.46 (m, 1H), 1.35–1.32 (m, 1H). ^{13}C NMR δ: 152.0, 142.3, 138.9, 128.5, 127.8, 121.3, 116.8, 115.5, 114.8, 74.5, 68.5, 55.9, 55.2, 38.9, 24.1, 22.0. m/z(ESI): 295 (M$^+$).

(4aS,5S,10bS)-9-methyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(3q)**: Solid, m.p. 129–130 °C (Lit.[9] m.p. 129–130 °C). ^{1}H NMR δ: 7.42–7.24 (m, 6H), 6.91 (d, 1H, J = 8.4 Hz), 6.52 (d, 1H, J = 7.6 Hz), 5.30 (d, 1H, J = 5.6 Hz), 4.63 (s, 1H), 3.76 (brs, 1H, NH), 3.58 (d, 1H, J = 11.2 Hz), 3.47–3.36 (m, 1H), 2.27 (s, 3H), 2.16 (s, 1H), 1.57–1.29 (m, 4H). ^{13}C NMR δ: 142.8, 141.3, 128.7, 128.3, 127.7, 127.4 × 2,, 126.8, 119.8, 114.5, 72.8, 60.6, 59.4, 39.0, 25.4, 20.6, 17.9. m/z(ESI): 279 (M$^+$).

(4aS,5R,10bS)-9-methyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(4q)**: Pale red oil.^{1}H NMR δ: 7.35–7.22 (m, 5H), 7.07–6.99 (m, 1H), 6.83 (d, 1H, J = 8.0 Hz), 6.32 (d, 1H, J = 8.0 Hz), 4.55 (d, 1H, J = 10.4 Hz), 4.26 (s, 1H), 4.04–4.01 (m, 1H), 3.86 (brs, 1H, NH), 3.62 (t, 1H, J = 11.2 Hz), 2.19 (s, 3H), 1.98–1.95 (m, 1H), 1.80–1.71 (m, 1H), 1.58–1.49 (m, 1H), 1.41–1.37 (m, 1H), 1.26–1.22 (m, 1H). ^{13}C NMR δ: 142.2, 130.7, 129.7, 129.3, 128.2, 127.5, 127.4, 126.0, 120.3, 114.0, 74.1, 68.1, 54.5, 38.7, 23.8, 21.7, 20.1. m/z(ESI): 279 (M$^+$).

(4aS,5S,10bS)-8-chloro-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(3r)**:[25] Solid, m.p. 165–167 °C. ^{1}H NMR δ: 7.39–7.25 (m, 6H), 6.74 (dd, 1H, J_1 = 2.0, J_2 = 8.4 Hz), 6.59 (d, 1H, J = 2.0 Hz), 5.25 (d, 1H, J = 5.6 Hz), 4.68 (d, 1H, J = 2.4 Hz), 3.93 (brs, 1H, NH), 3.60–3.57 (m, 1H), 3.41–3.36 (m, 1H), 2.17–2.12 (m, 1H), 1.60–1.42 (m, 3H), 1.31–1.29 (m, 1H). ^{13}C NMR δ: 146.1, 140.5, 133.5, 128.9, 128.4, 127.7, 126.7, 118.2, 113.8, 72.3, 60.6, 59.3, 38.6, 25.3, 18.0. m/z(ESI): 299 (M$^+$).

(4aS,5R,10bS)-8-chloro-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(4r)**:[25] Solid, m.p. 104–106 °C. ^{1}H NMR δ: 7.39–7.31 (m, 5H), 7.13 (d, 1H, J = 8.0 Hz), 6.65 (dd, 1H, J_1 = 2.0, J_2 = 8.0 Hz), 6.51 (d, 1H, J = 2.0 Hz), 4.68 (d, 1H, J = 10.8 Hz), 4.35 (d, 1H, J = 2.8 Hz), 4.07 (dt, 1H, J_1 = 2.8, J_2 = 11.6 Hz), 3.70 (td, 1H, J_1 = 2.8, J_2 = 11.6 Hz), 2.08–2.02 (m, 1H), 1.88–1.79 (m, 1H), 1.69–1.60 (m, 1H), 1.49–1.45 (m, 1H), 1.37–1.33 (m, 1H). ^{13}C NMR δ: 145.6, 141.8, 134.7, 132.0, 128.7, 128.0, 127.7, 119.1, 117.4, 113.6, 73.8, 68.4, 54.7, 38.7, 24.0, 22.0. m/z(ESI): 299 (M$^+$).

(4aS,5S,10bS)-8-chloro-7-methyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(3s)**: Solid, m.p. 137–139 °C. IR (cm^{-1}): 3362 (NH). ^{1}H NMR δ: 7.46–7.33 (m, 5H), 7.24 (d, 1H, J = 8.8 Hz), 6.84 (d, 1H, J = 8.4 Hz), 5.30 (d, 1H, J = 5.2 Hz), 4.70 (s, 1H), 3.82 (brs, 1H, NH), 3.59–3.56 (m, 1H), 3.38 (t, 1H, J = 11.2 Hz), 2.22–2.16 (m, 4H), 1.55–1.30 (m, 4H). ^{13}C NMR δ: 144.3, 140.9, 133.4, 128.5, 127.7, 126.8, 125.8, 119.0, 118.7, 118.0, 72.6, 60.6, 59.3, 38.3, 25.3, 18.0, 13.6. m/z(ESI): 313 (M$^+$). HRMS-ESI: Calcd for $C_{19}H_{20}ClNO$: 313.1312. Found: 313.1318.

(4aS,5R,10bS)-8-chloro-7-methyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(4s)**: Solid, m.p. 142–143 °C. IR (cm^{-1}): 3401 (NH). ^{1}H NMR δ: 7.45–7.35 (m, 5H), 7.04 (d, 1H, J = 8.0 Hz), 6.75 (d, 1H, J = 8.4 Hz), 4.74 (d, 1H, J = 11.2 Hz), 4.37 (d, 1H, J = 2.8 Hz), 4.11–4.07 (m, 1H) 3.71 (td, 1H, J_1 = 2.4, J_2 = 11.6 Hz), 2.12 (s, 3H), 2.07–2.03 (m, 1H), 1.90–1.81 (m, 1H), 1.70–1.61 (m, 1H), 1.48–1.45 (m, 1H), 1.37–1.33 (m, 1H). ^{13}C NMR δ: 143.8, 142.2, 134.6, 129.0, 128.8, 128.1 × 2, 127.8, 118.7, 117.8, 77.3, 77.0, 76.7, 74.4, 68.6, 54.9, 38.4, 24.0, 21.9, 13.4. m/z(ESI): 313 (M$^+$). HRMS-ESI: Calcd for $C_{19}H_{20}ClNO$: 313.1312. Found: 313.1320.

(4aS,5S,10bS)-7,10-dimethyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(3t)**:[6] Solid, m.p. 112–113 °C. ^{1}H NMR δ: 7.45 (d, 2H, J = 7.6 Hz), 7.39–7.35 (m, 2H), 7.32–7.28 (m, 1H), 6.92 (d, 1H, J = 7.6 Hz), 6.53 (d, 1H, J = 7.6 Hz), 5.32 (d, 1H, J = 5.6 Hz), 4.60 (d, 1H, J = 2.8 Hz), 3.74 (brs, 1H, NH), 3.55–3.52 (m, 1H), 3.27 (td, 1H, J_1 = 2.4, J_2 = 10.8 Hz), 2.37 (s, 3H), 2.12 (s, 3H), 1.84–1.74 (m, 1H), 1.47–1.28 (m, 4H). ^{13}C NMR δ: 144.1, 142.0, 137.3, 129.1, 128.3, 127.4, 127.1, 120.3, 119.1, 118.3, 73.3, 61.6, 59.1, 38.6, 24.3, 21.3, 19.3, 17.4. m/z(ESI): 293 (M$^+$).

(4aS,5R,10bS)-7,10-dimethyl-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(4t)**:[6] Solid, m.p. 109–111 °C. ^{1}H NMR δ: 7.50–7.48 (m, 2H), 7.42–7.35 (m, 3H), 6.90 (d, 1H, J = 7.6 Hz), 6.51 (d, 1H, J = 7.6 Hz), 4.75 (d, 1H, J = 11.6 Hz), 4.50 (d, 1H, J = 2.4 Hz), 4.14–4.10 (m, 1H), 3.73–3.66 (m, 1H), 2.35 (s, 3H), 2.05–2.02 (m, 4H), 1.92–1.87 (m, 1H), 1.70–1.63 (m, 1H), 1.50–1.45 (m, 1H), 1.35–1.31 (m, 1H). ^{13}C NMR δ: 142.7, 142.6, 136.4, 129.9, 128.6, 128.0, 120.1, 119.0, 118.8, 118.5, 72.3, 68.8, 54.3, 39.2, 24.2, 21.9, 18.1, 17.1. m/z(ESI): 293 (M$^+$).

(5S)-8,9-difluoro-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(3u)**: Solid, m.p. 151–152 °C. IR (cm^{-1}): 3371 (NH). ^{1}H NMR δ: 7.39–7.31 (m, 5H), 7.24–7.19 (m, 1H), 6.41–6.36 (m, 1H), 5.23 (d, 1H, J = 5.2 Hz), 4.65 (s, 1H), 3.82 (brs, 1H, NH), 3.60 (dd, 1H, J_1 = 2.0, J_2 = 11.2 Hz), 3.40–3.34 (m, 1H), 2.17–2.14 (m, 1H), 1.54–1.44 (m, 3H), 1.33–1.32 (m, 1H). ^{13}C NMR δ: 151.3, 151.1, 148.9, 148.7, 145.2, 145.0, 142.8, 142.7, 141.7, 141.6, 140.5, 128.5, 127.7, 126.7, 120.2, 115.9, 115.8, 102.8, 102.6, 72.1, 60.7, 59.5, 38.5, 25.2, 17.9. m/z(ESI): 301 (M$^+$). HRMS-ESI: Calcd for $C_{18}H_{17}F_2NO$: 301.1356. Found: 301.1365.

(5R)-8,9-difluoro-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinoline **(4u)**: Solid, m.p. 156–157 °C. IR (cm^{-1}): 3344 (NH). ^{1}H NMR δ: 7.40–7.33 (m, 5H), 7.04 (dd, 1H, J_1 = 8.8, J_2 = 10.4 Hz), 6.31 (dd, 1H, J_1 = 6.8, J_2 = 12.0 Hz), 4.65 (d, 1H, J = 10.4 Hz), 4.31 (d, 1H, J = 2.4 Hz), 4.09–4.05 (m, 1H), 3.69 (td, 1H, J_1 = 2.4, J_2 = 11.6 Hz), 2.07–2.04 (m, 1H), 1.84–1.77 (m, 1H), 1.69–1.60 (m, 1H), 1.45–1.36 (m, 1H), 1.36–1.33 (m, 1H). ^{13}C NMR δ: 21.9, 23.9, 38.6, 54.8, 68.5, 73.6, 102.4, 118.7, 118.8, 127.7, 128.1, 128.8, 141.5, 149.8, 141.5, 128.8, 128.1, 127.7, 118.8, 118.7, 102.4, 73.6, 68.5, 54.8, 38.6, 23.9, 21.9. m/z(ESI): 301 (M$^+$). HRMS-ESI: Calcd for $C_{18}H_{17}F_2NO$: 301.1356. Found: 301.1354.

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