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Asymmetric Synthesis of Cyclopentene-Fused Tetrahydroquinolines via N-Heterocyclic Carbene Catalyzed Domino Reactions

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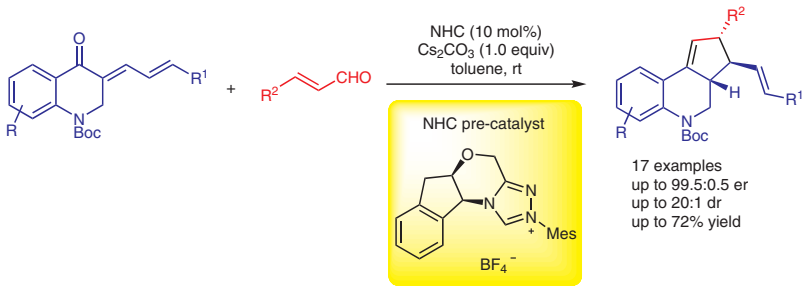

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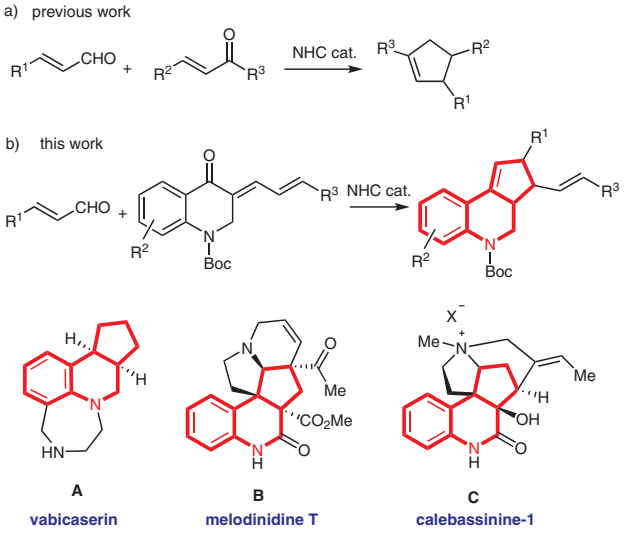
Abstract A new strategy for the N-heterocyclic carbene catalyzed asymmetric synthesis of cyclopentene-fused tetrahydroquinoline derivatives has been developed. The one-pot organocatalytic domino protocol allows a direct entry to the characteristic cyclopenta[*c*]tetrahydroquinoline core of many alkaloids and some potential drugs employing readily available quinolinone and enal substrates in good domino yields and stereoselectivities.

Key words asymmetric synthesis, domino reaction, N-heterocyclic carbene, organocatalysis, cyclopenta[*c*]quinoline

Over the last decades, N-heterocyclic carbenes (NHCs) have emerged as a powerful tool in catalytic asymmetric organic synthesis.[1] Beside the classical benzoin and Stetter reactions, the NHC-organocatalysis repertoire has recently been dramatically extended by novel activation modes and a variety of cycloaddition/annulation reactions are now at our disposal. In 2004, Glorius and Burstein and Bode et al. independently reported their pioneering NHC-catalyzed [3+2]-cycloaddition reaction of enals and aldehydes.[2] Since then a series of NHC-catalyzed [3+n]-cycloaddition reactions of enals have been developed for the synthesis of a variety of carbocycles and heterocycles.[3] However, compared to the well-established NHC-catalyzed cycloaddition reactions via homoenolate equivalents for the synthesis of heterocycles, the corresponding cycloadditions for the synthesis carbocycles have remained limited. In 2006, Nair et al. reported an efficient protocol for the synthesis of trisubstituted cyclopentenes through an NHC-catalyzed a^3-d^3 Umpolung/Michael/aldol/ lactonization/decarboxylation domino sequence (Scheme 1, a).[4] Later, the asymmetric version of this transformation was successfully realized by Bode and co-workers.[5] In 2009, Scheidt and co-workers further developed this protocol by the combination of Lewis acid and NHC catalysis and obtained better enantioselectivities and a wider reaction scope.[6] Further elegant NHC-catalyzed asymmetric syntheses of cyclopentene derivatives have recently been reported by Studer et al.,[7] Biju et al.,[8] and Ye et al.[9] Very recently Glorius et al. and our group successfully realized [3+2] cycloadditions of enals and C–C double bonds for the asymmetric synthesis of cyclopentanes.[10] Despite this progress, the application of organocatalytic methods for the stereoselective construction of more complex cyclopentene or cyclopentane derivatives is still highly desirable.[11] Inspired by vabicaserin (**A**), a potent 5-hydroxytryptamine 2C receptor agonist, which is under development for its antipsychotic properties,[12a–c] melodinine T (**B**),[12d] and calebassinine-1 (**C**),[12e] all containing a characteristic cyclopenta[*c*]tetrahydroquinoline central core, we now report an NHC-catalyzed domino reaction for the asymmetric synthesis of cyclopenta[*c*]quinoline derivatives (Scheme 1, b).

Initially, we investigated the reaction with tetrahydroquinolinone **1a** and cinnamaldehyde (**2a**) as the substrates. Using Cs_2CO_3 as the base and CH_2Cl_2 as the solvent, different NHC precatalysts were screened at room temperature (Table 1, entries 1–5). It turned out that the desired product **4a** was obtained in 52% yield with 82:18 er and 20:1 dr in the presence of precatalyst **3e** (entry 5). Solvent effects were next investigated (entries 6–9); toluene gave the best result, with product **4a** obtained in 50% yield with 89.5:10.5 er and 12:1 dr (entry 9).

With the optimized reaction conditions in hand, we then investigated the substrate scope (Scheme 2). Enals with electron-donating or electron-withdrawing substituents all worked well, leading to the desired tricyclic heterocycles **4a–f** in good domino yields with moderate to excellent stereoselectivities. Notably, the reaction of 2-methoxycinnamaldehyde led to product **4c** in 50% yield with 8:1 dr

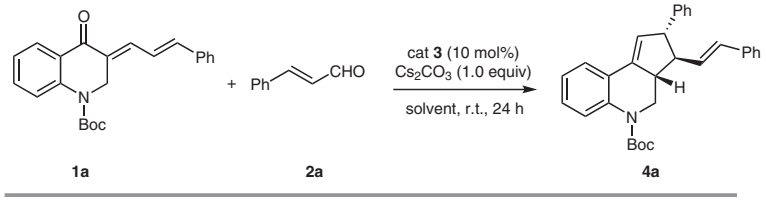


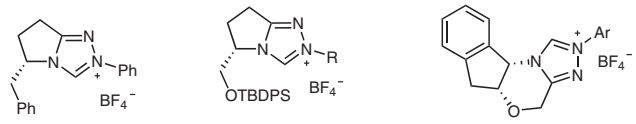
Scheme 1 NHC-catalyzed cyclopentene synthesis and typical molecules containing the cyclopenta[*c*]tetrahydroquinoline core

and 99.5:0.5 er. In addition, hexa-2,4-dienal (**2g**) was also tolerated. When the nitrogen protecting group was changed from Boc to the benzyloxycarbonyl (Cbz) group, the domino reactions also worked well and gave the desired cyclopentene-fused tetrahydroquinoline products **4h** and **4i** in good yields with good to high stereoselectivities. The reaction scope of the tetrahydroquinolinone substrates **1** was then investigated. Heteroaryl- and aryl-substituted quinolinones could be successfully used in this domino reaction (**4j**,**k**). Further variation of the substituent on the tetrahydroquinolinone phenyl ring of the substrates **1** revealed that both electron-withdrawing (4-F) and electron-donating groups (4-Me, 5-MeO) were well tolerated (**4l–n**). An important extension of the new domino protocol is the fact that the corresponding chromane (X = O), naphthalene, and indane (X = C) derivatives also can be synthesized; products **4o–q** were obtained in moderate to good stereoselectivities, albeit in lower yields.

The absolute configuration of **4i** was established by X-ray crystal structure analysis[13] and the other product configurations were assigned by analogy (Figure 1).

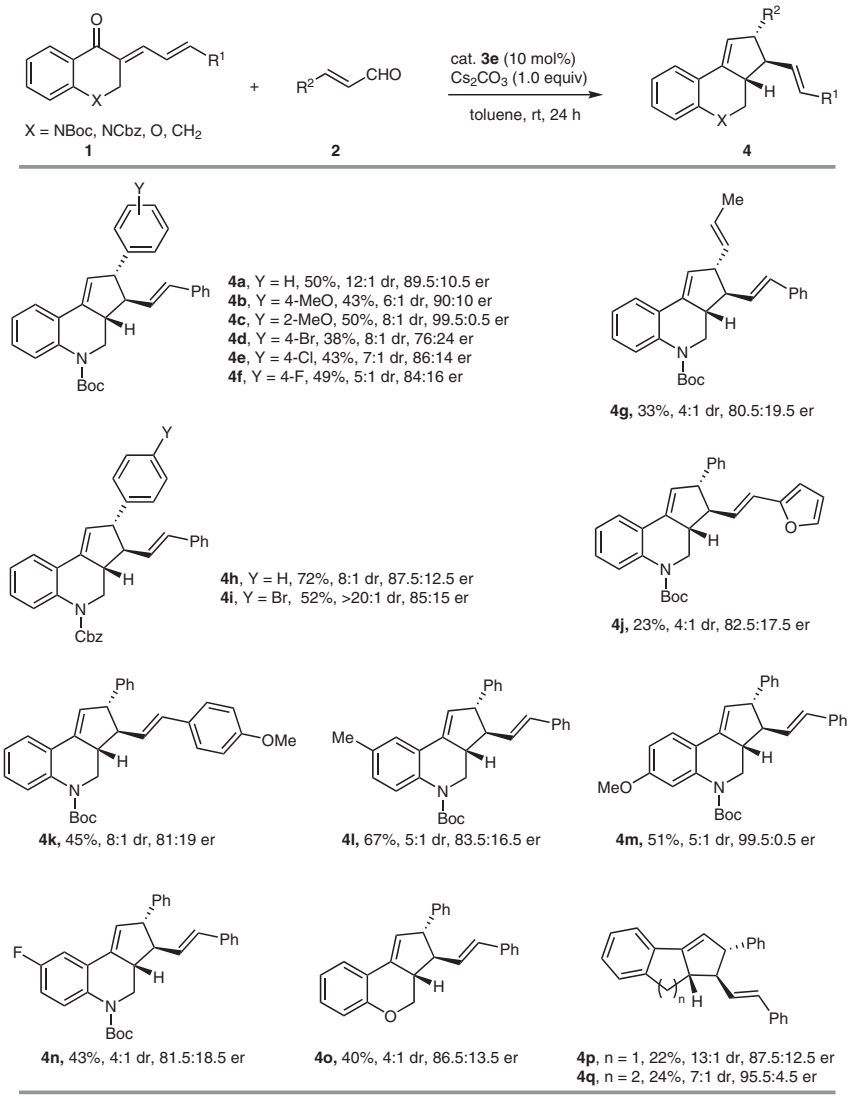
Table 1 Screening of the Optimal Reaction Conditions[a]





Entry	Cat.	Solvent	Yield (%)[b]	er[c]	dr[d]
1	**3a**	CH_2Cl_2	12	53.5:46.5	nd
2	**3b**	CH_2Cl_2	6	54:46	nd
3	**3c**	CH_2Cl_2	9	57:43	nd
4	**3d**	CH_2Cl_2	7	74.5:25.5	nd
5	**3e**	CH_2Cl_2	52	82:18	20:1
6	**3e**	Et_2O	33	85:15	8:1
7	**3e**	MeCN	55	74.5:25.5	8:1
8	**3e**	dioxane	40	88.5:11.5	12:1
9	**3e**	toluene	50	89.5:10.5	12:1

[a] Reaction conditions: **1a** (0.2 mmol, 1.0 equiv), **2a** (0.6 mmol, 3.0 equiv), catalyst (0.02 mmol, 10 mol%), base (0.2 mmol, 1.0 equiv), solvent (1 mL), r.t., 24 h.
[b] Yield of **4a** after column chromatography.
[c] The ee value was determined by HPLC on a chiral stationary phase.
[d] The dr was determined by ^{1}H NMR; nd = not determined.



Scheme 2 Reaction scope (yields of isolated compounds **4** after column chromatography; dr determined by ^{1}H NMR; ee determined by HPLC on a chiral stationary phase)

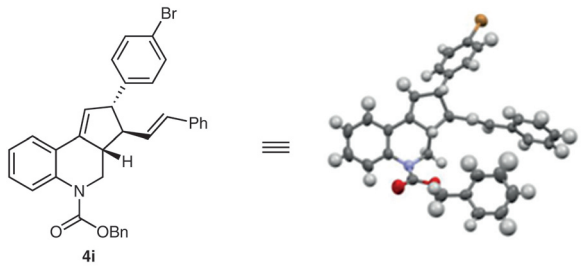
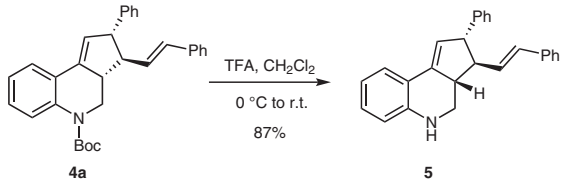


Figure 1 X-ray crystal structure of **4i**

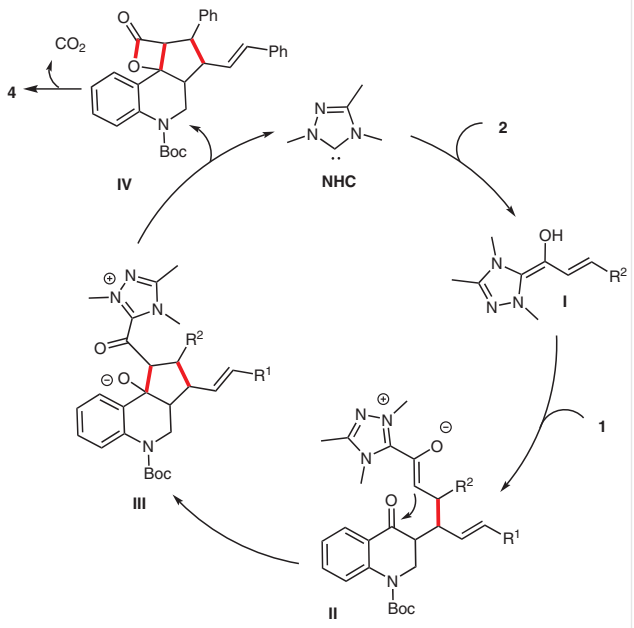
To allow further reactions at the quinoline nitrogen, it was shown that the Boc protecting group can be removed by treatment with TFA in CH_2Cl_2, resulting in the N-unprotected product **5** in 87% yield (Scheme 3).



Scheme 3

A proposal for the reaction mechanism of this domino process is given in Scheme 4. The catalytic cycle is initiated by the formation of the Breslow intermediate **I** via addition of the NHC to enal **2**. The subsequent Michael addition of the Breslow intermediate **I** to the diene-substituted tetrahydroquinolinone **1** leads to adduct **II** after a proton shift. An intramolecular aldol reaction delivers **III**, which forms

the β-lactone **IV** and returns the NHC catalyst for further cycles. The final decarboxylation then generates the cyclopenta[*c*]quinoline product **4** (Scheme 4).



Scheme 4 Proposed catalytic cycle for the NHC-catalyzed asymmetric synthesis of cyclopenta[*c*]tetrahydroquinoline derivatives

In conclusion, a new strategy for the asymmetric synthesis of cyclopenta[*c*]quinoline derivatives has been developed via an NHC-catalyzed domino process between a diene moiety bearing tetrahydroquinolinones and enals. The organocatalytic one-pot protocol delivers the desired cyclopentene-fused tetrahydroquinolines in moderate to good yields and good stereoselectivities under mild conditions.

Unless otherwise noted, all commercially available compounds were used without further purification. Anhydrous toluene was purified by distillation over Na. The products were purified by column chromatography on Merck silica gel 60, particle size 0.040–0.063 mm (230–240 mesh, flash). For TLC analysis, Merck precoated TLC plates (silica gel 60 GF254 0.25 mm) were used. Visualization of the developed TLC plates was performed with ultraviolet irradiation (254 nm). Optical rotation values were measured on a PerkinElmer 241 polarimeter and reported as follows: $[\alpha]_D^T$ [*c* (g/100 mL), solvent]. High-resolution mass spectra were acquired on a ThermoFisher Scientific LTQ-Orbitrap XL. IR spectra were recorded on a PerkinElmer Spectrum 100 FT-IR spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded at r.t. on Inova 400 or Agilent VNMRS 600 spectrometers. Chemical shifts (δ) are given in ppm relative to the solvent residual peak ($CDCl_3$, δ = 7.26) as external standard. Analytical HPLC was performed on a Hewlett-Packard 1100 Series instrument using chiral stationary phases (Daicel IA, IB, IC, IG, AD, OD, (*s*,*s*)-Whelk O1). Standard abbreviations are used to denote spin multiplicities. The melting points were obtained with an LLG MPM-H2 apparatus. The carbene catalysts **3a–e**[14] and quinolinones **1**[15] were prepared according to literature procedures. The racemic samples of the cyclopenta[*c*]quinoline derivatives **4** were prepared by using the racemic precatalyst with Cs_2CO_3.

Cyclopenta[*c*]quinoline Derivatives 4; General Procedure

To an argon-filled and dried Schlenk vial were added dienone **1** (0.5 mmol, 1.0 equiv) and precatalyst **3e** (21 mg, 0.05 mmol, 10 mol%) in toluene (2.0 mL), followed by the addition of enal **2** (1.5 mmol, 3.0 equiv) and Cs_2CO_3 (163 mg, 0.5 mmol, 1.0 equiv). The mixture was stirred at r.t. (36 h) until completion of the reaction (monitored by TLC). After purification by column chromatography (silica gel) the desired product was obtained as a pale yellow oil or foamy solid.

tert-Butyl (2*R*,3*R*,3a*S*)-2-Phenyl-3-[(*E*)-styryl]-2,3,3a,4-tetrahydro-5*H*-cyclopenta[*c*]quinoline-5-carboxylate (4a)

Compound **4a** was isolated after flash chromatography (silica gel, silica gel, *n*-pentane/EtOAc, 20:1); yield: 112 mg (50%); pale yellow foamy solid; $[\alpha]_D^{27}$ +119 (*c* 0.5, CH_2Cl_2).

HPLC: Chiralpak OD, *n*-heptane/*i*PrOH (97:3), 0.5 mL/min, t_R (major) = 14.72 min, t_R (minor) = 13.18 min; *T* = 30 °C; 89.5:10.5 er.

IR (ATR): 3388, 2947, 2329, 2076, 1697, 1465, 1353, 1154, 859, 737 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ (major) = 7.69–7.64 (m, 2 H, Ph*H*), 7.36–7.34 (m, 2 H, Ph*H*) 7.33–7.30 (m, 4 H, Ph*H*), 7.26–7.22 (m, 5 H, Ph*H*), 7.11–7.08 (m, 1 H, Ph*H*), 6.42 (dd, *J* = 15.8, 8.1 Hz, 1 H, C*H*=CHPh), 6.28 (d, *J* = 15.8 Hz, 1 H, CH=C*H*Ph), 6.23–6.23 (m, 1 H, C=CH), 4.75 (dd, *J* = 12.4, 4.7 Hz, 1 H, NCH*H*), 3.95–3.92 (m, 1 H, NC*H*H), 3.11–3.05 (m, 1 H, PhCH), 2.92–2.88 (m, 1 H, C*H*CH=CHPh), 2.63–2.58 (m, 1 H, CH_2CH), 1.53 (s, 9 H, Boc).

^{13}C NMR (151 MHz, $CDCl_3$): δ (major) = 153.4, 143.4, 139.4, 137.4, 137.2, 131.7, 129.8, 128.5 (2 C), 128.4 (2 C), 127.9 (2 C), 127.5, 127.2, 126.6, 126.2 (2 C), 125.3, 125.2, 124.5, 124.0, 123.9, 81.2, 59.6, 57.1, 49.0, 48.3, 28.4 (3 C).

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{31}NO_2Na$: 472.2247; found: 472.2241.

tert-Butyl (2*R*,3*R*,3a*S*)-2-(4-Methoxyphenyl)-3-[(*E*)-styryl]-2,3,3a,4-tetrahydro-5*H*-cyclopenta[*c*]quinoline-5-carboxylate (4b)

Compound **4b** was isolated after flash chromatography (silica gel, *n*-pentane/EtOAc, 20:1); yield: 103 mg (43%); pale yellow foamy solid; $[\alpha]_D^{27}$ +169 (*c* 0.5, CH_2Cl_2).

HPLC: Chiralpak IA, *n*-heptane/*i*PrOH (97:3), 0.5 mL/min, t_R (major) = 13.66 min, t_R (minor) = 19.11 min; *T* = 30 °C; 90:10 er.

IR (ATR): 2972, 2928, 2331, 2132, 2012, 1927, 1696, 1597, 1478, 1361, 1238, 1154, 1035, 965, 861, 749, 694 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ (major) = 7.68–7.66 (m, 2 H, Ph*H*), 7.38–7.37 (m, 2 H, Ph*H*), 7.34–7.31 (m, 2 H, Ph*H*), 7.25–7.23 (m, 2 H, Ph*H*), 7.18–7.17 (m, 2 H, Ph*H*), 7.12–7.09 (m, 1 H, Ph*H*), 6.89–6.87 (m, 2 H, Ph*H*), 6.43 (dd, *J* = 16.0, 8.3 Hz, 1 H, C*H*=CHPh), 6.30 (d, *J* = 16.0 Hz, 1 H, CH=C*H*Ph), 6.22–6.21 (m, 1 H, C=CH), 4.74 (dd, *J* = 12.4, 4.7 Hz, 1 H, NCH*H*), 3.91–3.90 (m, 1 H, NC*H*H), 3.81 (s, 3 H, OCH_3), 3.10–3.05 (m, 1 H, PhCH), 2.93–2.89 (m, 1 H, C*H*CH=CHPh), 2.60–2.55 (m, 1 H, CH_2CH), 1.55 (s, 9 H, Boc).

^{13}C NMR (151 MHz, $CDCl_3$): δ (major) = 158.3, 153.4, 139.2, 137.4, 137.3, 135.6, 131.6, 129.9, 128.8 (2 C), 128.5 (2 C), 127.5, 127.2, 126.2 (2 C), 125.7, 125.3, 124.5, 124.0 (2 C), 113.8 (2 C), 81.2, 59.7, 56.3, 55.3, 48.9, 48.3, 28.4 (3 C).

HRMS (ESI$^+$): m/z [M + Na]$^+$ calcd for $C_{32}H_{33}NO_3Na$: 502.2353; found: 502.2350.

tert-Butyl (2*R*,3*R*,3a*S*)-2-(2-Methoxyphenyl)-3-[(*E*)-styryl]-2,3,3a,4-tetrahydro-5*H*-cyclopenta[*c*]quinoline-5-carboxylate (4c)

Compound **4c** was isolated after flash chromatography (silica gel, *n*-pentane/EtOAc, 20:1); yield: 120 mg (50%); pale yellow foamy solid; $[\alpha]_D^{27}$ +154 (*c* 0.5, CH_2Cl_2).

HPLC: Chiralpak IA, *n*-heptane/*i*PrOH (97:3), 0.5 mL/min, t_R (major) = 11.40 min, t_R (minor) = 12.42 min; *T* = 30 °C; 99.5:0.5 er.

IR (ATR): 3374, 2932, 2316, 1698, 1471, 1350, 1149, 857, 739 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ (major) = 7.66–7.64 (m, 2 H, Ph*H*), 7.35–7.34 (m, 2 H, Ph*H*), 7.31–7.28 (m, 2 H, Ph*H*), 7.25–7.23 (m, 1 H, Ph*H*), 7.22–7.19 (m, 3 H, Ph*H*), 7.09–7.07 (m, 1 H, Ph*H*), 6.97–6.94 (m, 1 H, Ph*H*), 6.87–6.85 (m, 1 H, Ph*H*), 6.47 (dd, *J* = 15.8, 8.1 Hz, 1 H, C*H*=CHPh), 6.30 (d, *J* = 15.8 Hz, 1 H, CH=C*H*Ph), 6.19–6.18 (m, 1 H, C=CH), 4.74 (dd, *J* = 12.3, 4.7 Hz, 1 H, NCH*H*), 4.51–4.50 (m, 1 H, NC*H*H), 3.76 (s, 3 H, OCH_3), 3.08–3.03 (m, 1 H, PhCH), 2.92–2.88 (m, 1 H, C*H*CH=CHPh), 2.67–2.62 (m, 1 H, CH_2CH), 1.53 (s, 9 H, Boc).

^{13}C NMR (151 MHz, $CDCl_3$): δ (major) = 157.2, 153.5, 138.6, 137.6, 137.2, 131.8, 130.9, 130.3, 128.4 (2 C), 128.1, 127.5, 127.2, 126.9, 126.2, 126.1 (2 C), 125.2, 124.4, 124.2, 123.9, 120.8, 110.6, 81.1, 58.9, 55.5, 49.0, 48.9, 48.2, 28.4 (3 C).

HRMS (ESI$^+$): m/z [M + Na]$^+$ calcd for $C_{32}H_{33}NO_3Na$: 502.2353; found: 502.2345.

tert-Butyl (2*R*,3*R*,3a*S*)-2-(4-Bromophenyl)-3-[(*E*)-styryl]-2,3,3a,4-tetrahydro-5*H*-cyclopenta[*c*]quinoline-5-carboxylate (4d)

Compound **4d** was isolated after flash chromatography (silica gel, *n*-pentane/EtOAc, 20:1); yield: 100 mg (38%); pale yellow foamy solid; $[\alpha]_D^{27}$ +148 (*c* 0.5, CH_2Cl_2).

HPLC: Chiralpak IB, *n*-heptane/EtOH (9:1), 0.3 mL/min, t_R (major) = 13.19 min, t_R (minor) = 14.08 min; *T* = 30 °C; 76:24 er.

IR (ATR): 3734, 2935, 2644, 2324, 2210, 2051, 1695, 1472, 1356, 1153, 974, 840, 747 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ (major) = 7.66–7.65 (m, 2 H, Ph*H*), 7.44–7.42 (m, 2 H, Ph*H*), 7.36–7.34 (m, 2 H, Ph*H*), 7.33–7.29 (m, 2 H, Ph*H*), 7.25–7.22 (m, 2 H, Ph*H*), 7.14–7.08 (m, 3 H, Ph*H*), 6.38 (dd, *J* = 15.8, 8.2 Hz, 1 H, C*H*=CHPh), 6.26 (d, *J* = 15.8 Hz, 1 H, CH=C*H*Ph), 6.17–6.17 (m, 1 H, C=CH), 4.72 (dd, *J* = 12.4, 4.7 Hz, 1 H, NCH*H*), 3.90–3.87 (m, 1 H, NC*H*H), 3.09–3.04 (m, 1 H, PhCH), 2.90–2.86 (m, 1 H, C*H*CH=CHPh), 2.55–2.50 (m, 1 H, CH_2CH), 1.52 (s, 9 H, Boc).

^{13}C NMR (151 MHz, $CDCl_3$): δ (major) = 153.4, 142.4, 140.0, 137.5, 137.0, 132.1, 131.5 (2 C), 129.6 (2 C), 129.3, 128.5 (2 C), 127.7, 127.4, 126.2 (2 C), 125.2, 124.5, 124.5, 124.0, 123.7, 120.4, 81.3, 59.8, 56.5, 49.0, 48.2, 28.4 (3 C).

HRMS (ESI$^+$): m/z [M + Na]$^+$ calcd for $C_{31}H_{30}NO_2BrNa$: 550.1352; found: 550.1348.

tert-Butyl (2*R*,3*R*,3a*S*)-2-(4-Chlorophenyl)-3-[(*E*)-styryl]-2,3,3a,4-tetrahydro-5*H*-cyclopenta[*c*]quinoline-5-carboxylate (4e)

Compound **4e** was isolated after flash chromatography (silica gel, *n*-pentane/EtOAc, 20:1); yield: 104 mg (43%); pale yellow oil; $[\alpha]_D^{27}$ +172 (*c* 0.5, CH_2Cl_2).

HPLC: Chiralpak IB, *n*-heptane/*i*PrOH (97:3), 0.5 mL/min, t_R (major) = 9.90 min, t_R (minor) = 11.74 min; *T* = 30 °C; 86:14 er.

IR (ATR): 3395, 3028, 2974, 2925, 2876, 2358, 2218, 2169, 2060, 2006, 1929, 1809, 1696, 1602, 1481, 1360, 1234, 1153, 1047, 1015, 966, 828, 747, 693 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ (major) = 7.68–7.66 (m, 2 H, Ph*H*), 7.37–7.34 (m, 2 H, Ph*H*), 7.34–7.31 (m, 2 H, Ph*H*), 7.30–7.28 (m, 2 H, Ph*H*), 7.27–7.23 (m, 2 H, Ph*H*), 7.18–7.17 (m, 2 H, Ph*H*), 7.21–7.09 (m, 1 H, Ph*H*), 6.40 (dd, *J* = 15.8, 8.3 Hz, 1 H, C*H*=CHPh), 6.27 (d, *J* = 15.8 Hz, 1 H, CH=C*H*Ph), 6.19–6.18 (m, 1 H, C=CH), 4.74 (dd, *J* = 12.4, 4.7 Hz, 1 H, NCH*H*), 3.92–3.90 (m, 1 H, NC*H*H), 3.11–3.05 (m, 1 H, PhCH), 2.92–2.88 (m, 1 H, C*H*CH=CHPh), 2.56–2.52 (m, 1 H, CH_2CH), 1.54 (s, 9 H, Boc).

^{13}C NMR (151 MHz, $CDCl_3$): δ (major) = 153.4, 141.9, 139.9, 137.5, 137.0, 132.3, 132.1, 129.3, 129.2 (2 C), 128.6 (2 C), 128.5 (2 C), 127.7, 127.4, 126.2 (2 C), 125.3, 124.6, 124.5, 124.0, 123.7, 81.3, 59.9, 56.5, 49.0, 48.2, 28.4 (3 C).

HRMS (ESI$^+$): m/z [M + Na]$^+$ calcd for $C_{31}H_{30}NO_2ClNa$: 506.1857; found: 506.1862.

tert-Butyl (2*R*,3*R*,3a*S*)-2-(4-Fluorophenyl)-3-[(*E*)-styryl]-2,3,3a,4-tetrahydro-5*H*-cyclopenta[*c*]quinoline-5-carboxylate (4f)

Compound **4f** was isolated after flash chromatography (silica gel, *n*-pentane/EtOAc, 20:1); yield: 114 mg (49%); pale yellow oil; $[\alpha]_D^{27}$ +125 (*c* 0.5, CH_2Cl_2).

HPLC: (*s*,*s*)-Whelk O1, *n*-heptane/*i*PrOH (7:3), 0.5 mL/min, t_R (major) = 12.19 min, t_R (minor) = 10.16 min; *T* = 30 °C; 84:16 er.

IR (ATR): 2968, 2294, 1691, 1480, 1347, 1172, 860, 734 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (major) = 7.68–7.64 (m, 2 H, Ph*H*), 7.37–7.29 (m, 4 H, Ph*H*), 7.26–7.17 (m, 4 H, Ph*H*), 7.11–7.07 (m, 1 H, Ph*H*), 7.02–6.98 (m, 2 H, Ph*H*), 6.40 (dd, *J* = 15.8, 8.1 Hz, 1 H, C*H*=CHPh), 6.26 (d, *J* = 15.8 Hz, 1 H, CH=C*H*Ph), 6.19–6.18 (m, 1 H, C=CH), 4.73 (dd, *J* = 12.2, 4.4 Hz, 1 H, NCH*H*), 3.92–3.89 (m, 1 H, NC*H*H), 3.10–3.03 (m, 1 H, PhCH), 2.93–2.86 (m, 1 H, C*H*CH=CHPh), 2.57–2.50 (m, 1 H, CH_2CH), 1.53 (s, 9 H, Boc).

^{13}C NMR (101 MHz, $CDCl_3$): δ (major) = 162.9, 160.5, 153.4, 139.7, 137.5, 137.1, 132.0, 129.5, 129.3, 129.2, 128.5 (2 C), 127.6, 127.3, 126.2 (2 C), 125.3, 124.9, 124.5, 124.0, 123.8, 115.3, 115.1, 81.3, 59.9, 56.3, 49.0, 48.3, 28.4 (3 C).

HRMS (ESI$^+$): m/z [M + Na]$^+$ calcd for $C_{31}H_{30}NO_2FNa$: 490.2153; found: 490.2144.

tert-Butyl (2*R*,3*R*,3a*S*)-2-[(*E*)-Prop-1-en-1-yl]-3-[(*E*)-styryl]-2,3,3a,4-tetrahydro-5*H*-cyclopenta[*c*]quinoline-5-carboxylate (4g)

Compound **4g** was isolated after flash chromatography (silica gel, *n*-pentane/EtOAc, 20:1); yield: 68 mg (33%); pale yellow oil; $[\alpha]_D^{27}$ +112 (*c* 0.5, CH_2Cl_2).

HPLC: Chiralpak IA, *n*-heptane/*i*PrOH (97:3), 0.5 mL/min, t_R (major) = 8.03 min, t_R (minor) = 8.58 min; *T* = 30 °C; 80.5:19.5 er.

IR (ATR): 3386, 2938, 2290, 2087, 1697, 1461, 1355, 1156, 963, 865, 737 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (major) = 7.60–7.57 (m, 2 H, Ph*H*), 7.40–7.35 (m, 2 H, Ph*H*), 7.33–7.29 (m, 2 H, Ph*H*), 7.25–7.21 (m, 1 H, Ph*H*), 7.20–7.15 (m, 1 H, Ph*H*), 7.06–7.02 (m, 1 H, Ph*H*), 6.47 (d, *J* = 15.9 Hz, 1 H, CH=C*H*Ph), 6.34 (dd, *J* = 15.9, 7.8 Hz, 1 H, C*H*=CHPh), 6.06–6.05 (m, 1 H, C=CH), 5.58–5.51 (m, 1 H, CH_3CH=C*H*), 5.45–5.38 (m, 1 H, CH_3CH=CH), 4.68 (dd, *J* = 12.2, 4.4 Hz, 1 H, NCH*H*), 3.34–3.30 (m, 1 H, NC*H*H), 2.96–2.89 (m, 1 H, PhCH), 2.82–2.76 (m, 1 H, C*H*CH=CHPh), 2.40–2.33 (m, 1 H, CH_2CH), 1.69–1.66 (m, 3 H, CH_3), 1.49 (s, 9 H, Boc).

^{13}C NMR (101 MHz, $CDCl_3$): δ (major) = 153.4, 138.3, 137.4, 137.3, 132.3, 131.2, 130.5, 128.5 (2 C), 127.3, 127.1, 126.3, 126.2 (2 C), 125.4, 125.1, 124.3, 124.1, 123.9, 81.1, 56.2, 54.0, 48.7, 48.3, 28.3 (3 C), 18.0.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{28}H_{31}NO_2Na$: 436.2247; found: 436.2238.

Benzyl (2*R*,3*R*,3a*S*)-2-Phenyl-3-[(*E*)-styryl]-2,3,3a,4-tetrahydro-5*H*-cyclopenta[*c*]quinoline-5-carboxylate (4h)

Compound **4h** was isolated after flash chromatography (silica gel, *n*-pentane/EtOAc, 20:1); yield: 174 mg (72%); pale yellow foamy solid; $[\alpha]_D^{27}$ +140 (*c* 0.5, CH_2Cl_2).

HPLC: Chiralpak AD, *n*-heptane/*i*PrOH (92:8), 0.7 mL/min, t_R (major) = 15.32 min, t_R (minor) = 17.84 min; *T* = 30 °C; 87.5:12.5 er.

IR (ATR): 3339, 3031, 2933, 2739, 2322, 2088, 1954, 1762, 1678, 1488, 1454, 1393, 1345, 1301, 1210, 1126, 1062, 972, 846, 748, 695 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (major) = 7.76–7.74 (m, 1 H, PhH), 7.70–7.68 (m, 1 H, PhH), 7.60–7.45 (m, 1 H, PhH), 7.41–7.38 (m, 2 H, PhH), 7.36–7.30 (m, 8 H, PhH), 7.28–7.24 (m, 5 H, PhH), 7.16–7.12 (m, 1 H, PhH), 6.43 (dd, *J* = 15.9, 8.0 Hz, 1 H, CH=CHPh), 6.29 (d, *J* = 15.9 Hz, 1 H, CH=CHPh), 6.26–6.25 (m, 1 H, C=CH), 5.35 (d, *J* = 12.4 Hz, 1 H, PhCHH), 5.21 (d, *J* = 12.4 Hz, 1 H, PhCHH), 4.84 (dd, *J* = 12.0, 4.3 Hz, 1 H, NCHH), 3.98–3.94 (m, 1 H, NCHH), 3.15–3.08 (m, 1 H, PhCH), 3.04–2.98 (m, 1 H, CHCH=CHPh), 2.66–2.60 (m, 1 H, CH_2CH).

^{13}C NMR (101 MHz, $CDCl_3$): δ (major) = 154.3, 143.3, 139.1, 137.1, 136.9, 136.3, 131.8, 129.7, 128.6 (2 C), 128.5 (4 C), 128.1, 127.9 (4 C), 127.8, 127.3, 126.7, 126.3 (2 C), 125.6, 125.0, 124.6, 124.4, 124.1, 67.7, 59.5, 57.1, 49.1, 48.6.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{34}H_{29}NO_2Na$: 506.2091; found: 506.2087.

Benzyl (2*R*,3*R*,3a*S*)-2-(4-Bromophenyl)-3-[(*E*)-styryl]-2,3,3a,4-tetrahydro-5*H*-cyclopenta[*c*]quinoline-5-carboxylate (4i)

Compound **4i** was isolated after flash chromatography (silica gel, *n*-pentane/EtOAc, 20:1); yield: 146 mg (52%); pale yellow solid; mp 71–73 °C ; $[\alpha]_D^{27}$ +105 (*c* 0.5, CH_2Cl_2).

HPLC: Chiralpak AD, n-heptane/iPrOH (92:8), 0.7 mL/min, t_R (major) = 22.62 min, t_R (minor) = 32.45 min; *T* = 30 °C; 85:15 er.

IR (ATR): 3020, 2924, 2878, 2328, 2162, 2078, 1999, 1887, 1768, 1703, 1600, 1484, 1455, 1389, 1348, 1296, 1259, 1195, 1135, 1052, 1007, 966, 905, 861, 823, 748, 693 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ (major) = 7.75–7.73 (m, 1 H, PhH), 7.69–7.67 (m, 1 H, PhH), 7.45–7.44 (m, 2 H, PhH), 7.39–7.38 (m, 2 H, PhH), 7.36–7.33 (m, 4 H, PhH), 7.33–7.31 (m, 3 H, PhH), 7.28–7.25 (m, 2 H, PhH), 7.15–7.11 (m, 3 H, PhH), 6.39 (dd, *J* = 15.8, 8.3 Hz, 1 H, CH=CHPh), 6.27 (d, *J* = 15.8 Hz, 1 H, CH=CHPh), 6.20–6.19 (m, 1 H, C=CH), 5.33 (d, *J* = 12.4 Hz, 1 H, PhCHH), 5.21 (d, *J* = 12.4 Hz, 1 H, PhCHH), 4.82 (dd, *J* = 12.3, 4.6 Hz, 1 H, NCHH), 3.92–3.89 (m, 1 H, NCHH), 3.12–3.08 (m, 1 H, PhCH), 3.01–2.97 (m, 1 H, CHCH=CHPh), 2.57–2.52 (m, 1 H, CH_2CH).

^{13}C NMR (151 MHz, $CDCl_3$): δ (major) = 154.2, 142.4, 139.6, 137.0, 136.9, 136.2, 132.2, 131.6 (2 C), 129.6 (2 C), 129.2, 128.6 (4 C), 128.1, 128.0, 127.9 (2 C), 127.5, 126.3 (2 C), 125.0, 124.8, 124.6, 124.5, 123.8, 120.5, 67.8, 59.7, 56.5, 49.1, 48.5.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{34}H_{28}NO_2BrNa$: 584.1196; found: 584.1193.

***tert*-Butyl (2*R*,3*R*,3a*S*)-3-[(*E*)-2-(Furan-2-yl)vinyl]-2-phenyl-2,3,3a,4-tetrahydro-5*H*-cyclopenta[*c*]quinoline-5-carboxylate (4j)**

Compound **4j** was isolated after flash chromatography (silica gel, *n*-pentane/EtOAc, 20:1); yield: 50 mg (23%); pale yellow oil; $[\alpha]_D^{27}$ +140 (*c* 0.5, CH_2Cl_2).

HPLC: Chiralpak IA, *n*-heptane/EtOH (97:3), 0.5 mL/min, t_R (major) = 9.71 min, t_R (minor) = 10.63 min; *T* = 30 °C; 82.5:17.5 er.

IR (ATR): 2971, 2926, 2873, 2293, 2089, 1834, 1696, 1604, 1468, 1360, 1235, 1152, 1046, 961, 861, 747, 700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (major) = 7.65–7.62 (m, 2 H, PhH), 7.32–7.29 (m, 3 H, PhH), 7.24–7.19 (m, 4 H, PhH), 7.09–7.05 (m, 1 H, furanH), 6.38–6.30 (m, 2 H, furanH and CH=CHfuran), 6.21–6.17 (m, 1 H, furanH), 6.12–6.07 (m, 2 H, CH=CHfuran and C=CH), 4.70 (dd, *J* = 12.3, 4.6 Hz, 1 H, NCHH), 3.92–3.89 (m, 1 H, NCHH), 3.09–3.00 (m, 1 H, PhCH), 2.89–2.83 (m, 1 H, CHCH=CHPh), 2.57–2.50 (m, 1 H, CH_2CH), 1.52 (s, 9 H, Boc).

^{13}C NMR (101 MHz, $CDCl_3$): δ (major) = 153.4, 152.6, 143.4, 141.5, 139.3, 137.4, 128.5, 128.4 (2 C), 127.8 (2 C), 127.5, 126.6, 125.3, 125.2, 124.5, 123.9 (2 C), 120.1, 111.1, 107.0, 81.2, 59.3, 57.0, 49.0, 48.2, 28.3 (3 C).

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{29}H_{29}NO_3Na$: 462.2040; found: 462.2043.

***tert*-Butyl (2*R*,3*R*,3a*S*)-3-[(*E*)-4-Methoxystyryl]-2-phenyl-2,3,3a,4-tetrahydro-5*H*-cyclopenta[*c*]quinoline-5-carboxylate (4k)**

Compound **4k** was isolated after flash chromatography (silica gel, *n*-pentane/EtOAc, 20:1); yield: 108 mg (45%); pale yellow oil; $[\alpha]_D^{27}$ +142 (*c* 0.5, CH_2Cl_2).

HPLC: Chiralpak IG, *n*-heptane/*i*PrOH (9:1), 0.5 mL/min, t_R (major) = 6.88 min, t_R (minor) = 7.76 min; *T* = 30 °C; 81:19 er.

IR (ATR): 3029, 2974, 2928, 2645, 2179, 2112, 1999, 1885, 1829, 1769, 1695, 1605, 1510, 1480, 1456, 1362, 1301, 1243, 1157, 1032, 967, 857, 822, 754, 699 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ (major) = 7.68–7.66 (m, 2 H, PhH), 7.34–7.29 (m, 4 H, PhH), 7.26–7.23 (m, 4 H, PhH), 7.11–7.09 (m, 1 H, PhH), 6.87–6.85 (m, 2 H, PhH), 6.29 (dd, *J* = 15.8, 7.6 Hz, 1 H, CH=CHPh), 6.24–6.22 (m, 2 H, CH=CHPh and C=CH), 4.75 (dd, *J* = 12.3, 4.7 Hz, 1 H, NCHH), 3.94–3.91 (m, 1 H, NCHH), 3.82 (s, 3 H, OCH_3), 3.10–3.05 (m, 1 H, PhCH), 2.92–2.88 (m, 1 H, CHCH=CHPh), 2.61–2.57 (m, 1 H, CH_2CH), 1.54 (s, 9 H, Boc).

^{13}C NMR (151 MHz, $CDCl_3$): δ (major) = 158.9, 153.5, 143.5, 139.4, 137.4, 131.0, 130.1, 128.4 (2 C), 127.9 (2 C), 127.6, 127.5, 127.3 (2 C), 126.6, 125.4, 125.2, 124.5, 124.0, 123.9, 113.9 (2 C), 81.2, 59.6, 57.1, 55.3, 49.0, 48.3, 28.4 (3 C).

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{32}H_{33}NO_3Na$: 502.2353; found: 502.2351.

***tert*-Butyl (2*R*,3*R*,3a*S*)-8-Methyl-2-phenyl-3-[(*E*)-styryl]-2,3,3a,4-tetrahydro-5*H*-cyclopenta[*c*]quinoline-5-carboxylate (4l)**

Compound **4l** was isolated after flash chromatography (silica gel, *n*-pentane/EtOAc, 20:1); yield: 155 mg (67%); pale yellow foamy solid; $[\alpha]_D^{27}$ +103 (*c* 0.5, CH_2Cl_2).

HPLC: Chiralpak IA, *n*-heptane/*i*PrOH (97:3), 0.5 mL/min, t_R (major) = 8.73 min, t_R (minor) = 9.23 min; *T* = 30 °C; 83.5:16.5 er.

IR (ATR): 2929, 2316, 1696, 1473, 1356, 1156, 988, 843, 730 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (major) = 7.55–7.53 (m, 1 H, PhH), 7.47 (s, 1 H, PhH), 7.35–7.28 (m, 6 H, PhH), 7.25–7.19 (m, 4 H, PhH), 7.06–7.04 (m, 1 H, PhH), 6.42 (dd, *J* = 15.8, 8.0 Hz, 1 H, CH=CHPh), 6.27 (d,

J = 15.8 Hz, 1 H, CH=C*H*Ph), 6.22–6.20 (m, 1 H, C=CH), 4.72 (dd, *J* = 12.2, 4.6 Hz, 1 H, NCH*H*), 3.95–3.91 (m, 1 H, NC*H*H), 3.10–3.03 (m, 1 H, PhCH), 2.90–2.84 (m, 1 H, C*H*CH=CHPh), 2.62–2.55 (m, 1 H, CH_2CH), 2.34 (s, 3 H, CH_3), 1.53 (s, 9 H, Boc).

^{13}C NMR (101 MHz, $CDCl_3$): δ (major) = 153.5, 143.5, 139.5, 137.2, 135.0, 133.4, 131.6, 129.8, 128.5, 128.4 (4 C), 127.9 (2 C), 127.2, 126.6, 126.2 (2 C), 125.1, 125.0, 124.6, 123.7, 81.0, 59.6, 57.1, 49.0, 48.4, 28.4 (3 C), 20.8.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{32}H_{33}NO_2Na$: 486.2404; found: 486.2400.

tert-Butyl (2*R*,3*R*,3a*S*)-7-Methoxy-2-phenyl-3-[(*E*)-styryl]-2,3,3a,4-tetrahydro-5*H*-cyclopenta[*c*]quinoline-5-carboxylate (4m)

Compound **4m** was isolated after flash chromatography (silica gel, *n*-pentane/EtOAc, 20:1); yield: 122 mg (51%); pale yellow foamy solid; $[\alpha]_D^{27}$ +178 (*c* 0.5, CH_2Cl_2).

HPLC: Chiralpak IA, *n*-heptane/*i*PrOH (97:3), 0.5 mL/min, t_R (major) = 11.95 min, t_R (minor) = 15.19 min; *T* = 30 °C; 99.5:0.5 er.

IR (ATR): 2930, 2333, 2084, 1697, 1608, 1469, 1356, 1156, 1054, 843, 736 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (major) = 7.57–7.55 (m, 1 H, Ph*H*), 7.35–7.27 (m, 6 H, Ph*H*), 7.26–7.18 (m, 5 H, Ph*H*), 6.70–6.68 (m, 1 H, Ph*H*), 6.40 (dd, *J* = 15.9, 8.0 Hz, 1 H, C*H*=CHPh), 6.26 (d, *J* = 15.9 Hz, 1 H, CH=C*H*Ph), 6.04–6.03 (m, 1 H, C=CH), 4.72 (dd, *J* = 12.2, 4.5 Hz, 1 H, NCH*H*), 3.92–3.88 (m, 1 H, NC*H*H), 3.82 (s, 3 H, OCH_3), 3.07–2.99 (m, 1 H, PhCH), 2.89–2.83 (m, 1 H, C*H*CH=CHPh), 2.59–2.52 (m, 1 H, CH_2CH), 1.53 (s, 9 H, Boc).

^{13}C NMR (101 MHz, $CDCl_3$): δ (major) = 159.0, 153.3, 143.7, 139.1, 138.6, 137.3, 131.6, 130.0, 128.4 (4 C), 127.8 (2 C), 127.2, 126.5, 126.2 (2 C), 125.5, 122.7, 117.1, 111.5, 109.5, 81.3, 59.4, 57.0, 55.4, 48.9, 48.5, 28.4 (3 C).

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{32}H_{33}NO_3Na$: 502.2353; found: 502.2348.

tert-Butyl (2*R*,3*R*,3a*S*)-8-Fluoro-2-phenyl-3-[(*E*)-styryl]-2,3,3a,4-tetrahydro-5*H*-cyclopenta[*c*]quinoline-5-carboxylate (4n)

Compound **4n** was isolated after flash chromatography (silica gel, *n*-pentane/EtOAc, 20:1); yield: 100 mg (43%); pale yellow foamy solid; $[\alpha]_D^{27}$ +137 (*c* 0.5, CH_2Cl_2).

HPLC: Chiralpak IG, *n*-heptane/*i*PrOH (9:1), 0.5 mL/min, t_R (major) = 5.16 min, t_R (minor) = 5.88 min; *T* = 30 °C; 81.5:18.5 er.

IR (ATR): 3850, 3432, 2928, 2551, 2451, 2186, 2067, 1978, 1958, 1698, 1480, 1359, 1154, 1035, 966, 854, 741 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (major) = 7.62–7.58 (m, 1 H, Ph*H*), 7.34–7.27 (m, 7 H, Ph*H*), 7.26–9.19 (m, 4 H, Ph*H*), 6.95–6.90 (m, 1 H, Ph*H*), 6.39 (dd, *J* = 15.9, 7.9 Hz, 1 H, C*H*=CHPh), 6.26 (d, *J* = 15.9 Hz, 1 H, CH=C*H*Ph), 6.21–6.20 (m, 1 H, C=CH), 4.69 (dd, *J* = 12.3, 4.6 Hz, 1 H, NCH*H*), 3.94–3.90 (m, 1 H, NC*H*H), 3.08–3.00 (m, 1 H, PhCH), 2.88–2.82 (m, 1 H, C*H*CH=CHPh), 2.63–2.56 (m, 1 H, CH_2CH), 1.51 (s, 9 H, Boc).

^{13}C NMR (101 MHz, $CDCl_3$): δ(major) = 160.4, 158.0, 153.4, 143.0, 138.9, 137.1, 133.5 (2 C), 131.8, 129.5, 128.5 (2 C), 127.8, 127.3, 127.0 (2 C), 126.8, 126.7, 126.2, 114.8, 114.6, 110.2, 110.0, 81.3, 59.5, 57.0, 48.7, 48.2, 28.3 (3 C).

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{30}NO_2FNa$: 490.2153; found: 490.2152.

(2*R*,3*R*,3a*S*)-2-Phenyl-3-[(*E*)-styryl]-2,3,3a,4-tetrahydrocyclopenta[*c*]chromene (4o)

Compound **4o** was isolated after flash chromatography (silica gel, *n*-pentane/EtOAc, 20:1); yield: 70 mg (40%); pale yellow oil; $[\alpha]_D^{27}$ +67 (*c* 0.5, CH_2Cl_2).

HPLC: Chiralpak IB, *n*-heptane/*i*PrOH (97:3), 0.5 mL/min, t_R (major) = 16.93 min, t_R (minor) = 13.54 min; *T* = 30 °C; 86.5:13.5 er.

IR (ATR): 3439, 3028, 2924, 2873, 2318, 2079, 1946, 1877, 1805, 1722, 1603, 1575, 1478, 1453, 1377, 1310, 1223, 1153, 1115, 1073, 1034, 999, 968, 911, 862, 833, 749, 695, 542 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ (major) = 7.61–7.60 (m, 1 H, Ph*H*), 7.40–7.34 (m, 6 H, Ph*H*), 7.30–7.27 (m, 4 H, Ph*H*), 7.25–7.23 (m, 1 H, Ph*H*), 7.00–6.98 (m, 2 H, Ph*H*), 6.45 (dd, *J* = 15.8, 8.4 Hz, 1 H, C*H*=CHPh), 6.27 (d, *J* = 15.8 Hz, 1 H, CH=C*H*Ph), 6.17–6.13 (m, 1 H, C=CH), 4.60 (dd, *J* = 10.0, 4.8 Hz, 1 H, OCH*H*), 4.01–3.99 (m, 1 H, OC*H*H), 3.88–3.82 (m, 1 H, PhCH), 3.26–3.20 (m, 1 H, C*H*CH=CHPh), 2.64–2.60 (m, 1 H, CH_2CH).

^{13}C NMR (151 MHz, $CDCl_3$): δ (major) =154.4, 143.6, 137.1, 136.8, 131.6, 130.0, 129.5, 128.6 (2 C), 128.5 (2 C), 127.9 (2 C), 127.4, 127.3, 126.7, 126.2 (2 C), 125.3, 123.2, 121.0, 117.5, 71.2, 58.4, 57.6, 47.3.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{22}ONa$: 373.1563; found: 373.1557.

(2*R*,3*S*,3a*S*)-2-Phenyl-3-[(*E*)-styryl]-3,3a,4,5-tetrahydro-2*H*-cyclopenta[*a*]naphthalene (4p)

Compound **4p** was isolated after flash chromatography (silica gel, *n*-pentane/EtOAc, 20:1); yield: 38 mg (22%); pale yellow oil; $[\alpha]_D^{27}$ +192 (*c* 0.5, CH_2Cl_2).

HPLC: Chiralpak IA, *n*-heptane/EtOH (97:3), 0.5 mL/min, t_R (major) = 8.42 min, t_R (minor) = 8.80 min; *T* = 30 °C; 87.5:12.5 er.

IR (ATR): 3456, 3020, 2931, 1740, 1602, 1451, 1367, 1215, 962, 729 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ (major) = 7.70–6.68 (m, 1 H, Ph*H*), 7.39–3.38 (m, 2 H, Ph*H*), 7.34–7.31 (m, 4 H, PhH), 7.29–7.28 (m, 2 H, PhH), 7.26–7.23 (m, 2 H, Ph*H*), 7.22–7.20 (m, 3 H, Ph*H*), 6.45 (dd, *J* = 15.8, 8.6 Hz, 1 H, C*H*=CHPh), 6.27 (d, *J* = 15.8 Hz, 1 H, CH=C*H*Ph), 6.20–6.19 (m, 1 H, C=CH), 3.98–3.96 (m, 1 H, PhCH), 2.99–2.88 (m, 3 H, ArCH*H*, ArC*H*H and PhCH=CHC*H*), 2.63–2.58 (m, 1 H, CH_2CH_2CH), 2.23–2.19 (m, 1 H, $ArCH_2CHH$), 1.62–1.56 (m, 1 H, $ArCH_2CHH$).

^{13}C NMR (151 MHz, $CDCl_3$): δ (major) = 144.4, 142.4, 137.5, 137.2, 131.3, 131.2, 129.2, 128.5 (2 C), 128.3 (2 C), 127.8 (2 C), 127.6, 127.1, 126.4, 126.1 (4 C), 124.6, 123.8, 62.1, 57.4, 50.5, 30.6, 28.6.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{27}H_{24}Na$: 371.1770; found: 371.1771.

(1*S*,2*R*,8a*S*)-2-Phenyl-1-[(*E*)-styryl]-1,2,8,8a-tetrahydrocyclopenta[*a*]indene (4q)

Compound **4q** was isolated after flash chromatography (silica gel, *n*-pentane/EtOAc, 20:1); yield: 40 mg (24%); pale yellow oil; $[\alpha]_D^{27}$ +62 (*c* 0.5, CH_2Cl_2).

HPLC: Chiralpak IB, *n*-heptane/*i*PrOH (99:1), 0.5 mL/min, t_R (major) = 15.62 min, t_R (minor) = 12.29 min; *T* = 30 °C; 95.5:4.5 er.

IR (ATR): 3456, 3018, 2331, 1740, 1602, 1367, 1214, 963, 729 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ (major) = 7.55–7.53 (m, 1 H, Ph*H*), 7.43–7.37 (m, 3 H, Ph*H*), 7.36–7.32 (m, 6 H, Ph*H*), 7.31–7.24 (m, 4 H, Ph*H*), 6.49 (dd, *J* = 15.9, 7.7 Hz, 1 H, C*H*=CHPh), 6.32 (d, *J* = 15.9 Hz, 1 H, CH=

C*H*Ph), 5.89–5.88 (m, 1 H, C=CH), 4.24–4.22 (m, 1 H, PhCH), 3.63–3.57 (m, 1 H, C*H*CH=CHPh), 3.16 (dd, *J* = 15.8, 8.4 Hz, 1 H, CH*H*), 2.86–2.81 (m, 1 H, ArCH$_2$C*H*), 2.76 (dd, *J* = 15.8, 8.4 Hz, 1 H, C*H*H).

^{13}C NMR (151 MHz, CDCl$_3$): δ (major) = 152.8, 149.7, 143.6, 137.5, 136.3, 130.8, 130.7, 128.5 (2 C), 128.4 (2 C), 128.3, 128.0 (2 C), 127.1, 126.9, 126.5, 126.2 (2 C), 126.0, 122.1, 120.1, 63.4, 63.0, 56.7, 35.7.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{22}Na$: 357.1614; found: 357.1615.

(*E*)-2-Phenyl-3-styryl-3,3a,4,5-tetrahydro-2*H*-cyclopenta[*c*]quinoline (5)

To a solution of the Boc-protected quinoline **4a** (0.1 mmol) in anhyd CH_2Cl_2 (1 mL) at 0 °C was added trifluoroacetic acid (0.11 mL) over 1 min. The reaction mixture was stirred for 1 h during which time the mixture warmed to r.t. The mixture was concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (10 mL) and washed with sat. aq $NaHCO_3$ solution (10 mL). The aqueous phase was extracted with CH_2Cl_2 (10 mL) and the organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. After purification by column chromatography (silica gel, *n*-pentane/EtOAc, 20:1), the desired product **5** was obtained as a colorless solid; mp 68–70 °C; yield: 31 mg (87%); $[\alpha]_D^{27}$ +105 (*c* 0.5, CH_2Cl_2).

IR (ATR): 3398, 3345, 3013, 2927, 2855, 2324, 2165, 2109, 1993, 1940, 1866, 1740, 1622, 1587, 1494, 1459, 1365, 1301, 1238, 1168, 1141, 1103, 1052, 1023, 967, 932, 862, 839, 807, 747, 689 cm^{-1}.

^{1}H NMR (600 MHz, CDCl$_3$): δ (major) = 7.53–7.51 (m, 1 H, PhH), 7.37–7.35 (m, 2 H, PhH), 7.34–7.31 (m, 4 H, PhH), 7.27–7.22 (m, 4 H, PhH), 7.10–7.07 (m, 1 H, PhH), 6.74–6.72 (m, 1 H, PhH), 6.63–6.61 (m, 1 H, PhH), 6.44 (dd, *J* = 15.8, 8.6 Hz, 1 H, C*H*=CHPh), 6.23 (d, *J* = 15.8 Hz, 1 H, CH=C*H*Ph), 6.04–6.03 (m, 1 H, C=CH), 4.08 (br, 1 H, NH), 3.98–3.96 (m, 1 H, PhCH), 3.57 (dd, *J* = 9.9, 4.6 Hz, 1 H, NCH*H*), 3.13–3.08 (m, 1 H, NC*H*H), 3.07–3.03 (m, 1 H, C*H*CH=CHPh), 2.60–2.56 (m, 1 H, CH$_2$C*H*).

^{13}C NMR (151 MHz, CDCl$_3$): δ (major) = 144.5, 144.3, 139.2, 137.3, 131.2, 130.8, 128.9, 128.5 (2 C), 128.4 (2 C), 127.8 (2 C), 127.2, 126.4, 126.1 (2 C), 125.4, 121.6, 117.9, 115.1, 60.0, 57.5, 48.4, 47.3, 28.4.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{23}NNa$: 372.1723; found: 372.1719.

Dihydroquinolinone 1a; Typical Procedure

Steps 1 and 2: To a suspension of aniline (1.8 mL, 20 mmol) and K_2CO_3 (3.3 g, 24 mmol) in CH_2Cl_2 (20 mL) at 0 °C was added dropwise 3-bromopropanoyl chloride (2.5 mL, 24 mmol). The mixture was stirred at 0 °C for 5 min and allowed to warm to r.t. for another 3 h. The reaction was quenched with H_2O and extracted with EtOAc (3 × 15 mL). The combined organic layers were evaporated, and the residue was recrystallized from a hot solution of petroleum ether/EtOAc (1:1) to afford 3.42 g (15 mmol, 75%) of crude 3-bromo-*N*-phenylpropanamide as colorless crystals. This solid was then dissolved in DMF (20 mL) and cooled to 0 °C. To this solution was added sodium *tert*-butoxide (1.57 g, 16.5 mmol) in one portion, and the mixture was gradually allowed to warm to r.t. The reaction was quenched with H_2O after 3 h and extracted with EtOAc (30 mL). The combined organic layers were evaporated, and the residue was recrystallized from a hot solution of petroleum ether/EtOAc (1:1) to afford 1-phenylazetidin-2-one as a red solid; yield: 1.32 g (60%). Step 3: To a solution of 1-phenylazetidin-2-one (1.32 g, 9 mmol) in DCE (30 mL) at 0 °C was added trifluoromethanesulfonic acid (1.06 mL, 12 mmol). The solution was stirred at r.t. for 60 min, quenched with sat. aq $NaHCO_3$, extracted with EtOAc, dried over anhyd Na_2SO_4, and concentrated in vacuo to yield a clear oil; yield: 1.08 g (82%). Step 4: The 4-azachromanone (1.08 g, 7.4 mmol) was dissolved in CH_2Cl_2 (20 mL) and then triethylamine (1.03 mL, 7.4 mmol) and DMAP (0.9 g, 7.4 mmol) were added. To the solution di-*tert*-butyl dicarbonate (3.3 g, 14.8 mmol) was added portionwise. The reaction was stirred at r.t. for 2 h, then concentrated on a rotary evaporator to an oil. The oil was chromatographed (silica gel, EtOAc/*n*-hexane, 1:9) to give a clear colorless oil; yield: 1.35 g (74%). Step 5: A mixture of *tert*-butyl 4-oxo-3,4-dihydroquinoline-1(2*H*)-carboxylate (1.35 g, 5.5 mmol), cinnamaldehyde (0.87 mL, 6.6 mmol), 10% KOH (12 mL), and EtOH (35 mL) was stirred at r.t. for 3 h, then poured into crushed ice. The precipitate was separated by filtration, washed free of base, and recrystallized from MeOH; this gave product **1a**; yield: 1.01 g (51%); yellow solid; mp 150–152 °C.

tert-Butyl (*E*)-4-Oxo-3-[(*E*)-3-phenylallylidene]-3,4-dihydroquinoline-1(2*H*)-carboxylate (1a)

Yellow solid; mp 150–152 °C; yield: 1.01 g (14%).

IR (ATR): 3077, 2986, 2644, 2328, 2112, 2044, 1881, 1694, 1582, 1467, 1361, 1315, 1231, 1148, 1017, 952, 853, 745, 683 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ = 8.05–8.02 (m, 1 H, Ph*H*), 7.64–7.62 (m, 1 H, Ph*H*), 7.55–7.48 (m, 4 H, C*H*CH=CHPh and Ph*H*), 7.41–7.34 (m, 3 H, Ph*H*), 7.23–7.18 (m, 1 H, Ph*H*), 7.15–7.08 (m, 2 H, CHC*H*=C*H*Ph), 4.92 (d, *J* = 1.5 Hz, 2 H, NCH$_2$), 1.54 (s, 9 H, Boc).

^{13}C NMR (101 MHz, CDCl$_3$): δ = 184.2, 152.6, 143.2, 143.1, 136.1, 135.9, 133.2, 130.8, 129.4, 128.9 (2 C), 127.9, 127.4 (2 C), 127.3, 124.5, 124.3, 122.3, 82.1, 45.0, 28.3 (3 C).

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{23}NO_3Na$: 384.1570; found: 384.1570.

Benzyl (*E*)-4-Oxo-3-[(*E*)-3-phenylallylidene]-3,4-dihydroquinoline-1(2*H*)-carboxylate (1b)

Yellow solid; mp 155–157 °C; yield: 1.26 g (16%).

IR (ATR): 3407, 3035, 2645, 2330, 2088, 1953, 1825, 1708, 1665, 1587, 1467, 1399, 1328, 1227, 1148, 1031, 964, 849, 741, 687 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ = 8.07–8.05 (m, 1 H, Ph*H*), 7.71–7.69 (m, 1 H, Ph*H*), 7.54–7.47 (m, 4 H, C*H*CH=CHPh and Ph*H*), 7.41–7.32 (m, 8 H, Ph*H*), 7.27–7.23 (m, 1 H, Ph*H*), 7.10–7.08 (m, 2 H, CHC*H*=C*H*Ph), 5.27 (s, 2 H, COC*H*$_2$Ph), 4.98 (d, *J* = 1.5 Hz, 2 H, NCH$_2$).

^{13}C NMR (101 MHz, CDCl$_3$): 183.9, 153.6, 143.4, 142.6, 136.3, 136.0, 135.7, 133.5, 130.2, 129.5, 128.8 (2 C), 128.6 (2 C), 128.4, 128.1 (2 C), 128.0, 127.5 (2 C), 127.3, 125.0, 124.0, 122.2, 68.3, 45.4.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{21}NO_3Na$: 418.1414; found: 418.1418.

tert-Butyl (*E*)-3-[(*E*)-3-(Furan-2-yl)allylidene]-4-oxo-3,4-dihydroquinoline-1(2*H*)-carboxylate (1c)

Yellow solid; mp 158–160 °C; yield: 0.84 g (12%).

IR (ATR): 3816, 3458, 2979, 2642, 2327, 2217, 2103, 1992, 1911, 1738, 1692, 1576, 1467, 1363, 1225, 1148, 1059, 1014, 956, 860, 746 cm^{-1}.

^{1}H NMR (600 MHz, CDCl$_3$): δ = 8.03–8.01 (m, 1 H, PhH), 7.64–7.62 (m, 1 H, Ph*H*), 7.50–7.46 (m, 2 H, PhH), 7.42 (d, *J* = 12.2 Hz, 1 H, C*H*CH=CHPh), 7.21–7.18 (m, 1 H, furan*H*), 7.03 (dd, *J* = 15.1, 12.2 Hz, 1 H, CHC*H*=CHPh), 6.84 (d, *J* = 15.1 Hz, 1 H, CHCH=C*H*Ph), 6.52–6.46 (m, 2 H, furan*H*), 4.88 (d, *J* = 1.6 Hz, 2 H, NCH$_2$), 1.53 (s, 9 H, Boc).

^{13}C NMR (151 MHz, CDCl$_3$): δ = 184.1, 152.7, 152.4, 144.1, 143.3, 135.5, 133.2, 130.8, 129.1, 127.9, 127.4, 124.5, 124.3, 120.8, 112.8, 112.4, 82.1, 45.0, 28.3 (3 C).

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{21}NO_4Na$: 374.1363; found: 374.1363.

***tert*-Butyl (*E*)-3-[(*E*)-3-(4-Methoxyphenyl)allylidene]-4-oxo-3,4-dihydroquinoline-1(2*H*)-carboxylate (1d)**

Yellow solid; mp 155–157 °C; yield: 1.28 g (16%).

IR (ATR): 2980, 2928, 2845, 2331, 2182, 2105, 1995, 1890, 1696, 1662, 1570, 1462, 1356, 1315, 1239, 1157, 1014, 954, 822, 749 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 8.04–8.02 (m, 1 H, Ph*H*), 7.63–7.71 (m, 1 H, Ph*H*), 7.51–7.47 (m, 4 H, C*H*CH=CHPh and Ph*H*), 7.21–7.19 (m, 1 H, Ph*H*), 7.05 (d, *J* = 15.2 Hz, 1 H, CHCH=C*H*Ph), 7.00 (dd, *J* = 15.2, 11.0 Hz, 1 H, CHC*H*=CHPh), 6.91–6.90 (m, 2 H, Ph*H*), 4.89 (d, *J* = 1.5 Hz, 2 H, NCH_2), 3.84 (s, 3 H, OCH_3), 1.53 (s, 9 H, Boc).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 184.2, 160.8, 152.7, 143.2, 143.0, 136.6, 133.1, 129.6, 129.0 (3 C), 127.9, 127.5, 124.5, 124.3, 120.3, 114.4 (2 C), 82.0, 55.4, 44.9, 28.3 (3 C).

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{25}NO_4Na$: 414.1676; found: 414.1682.

***tert*-Butyl (*E*)-6-Methyl-4-oxo-3-[(*E*)-3-phenylallylidene]-3,4-dihydroquinoline-1(2*H*)-carboxylate (1e)**

Yellow solid; mp 159–161 °C; yield: 0.68 g (9%).

IR (ATR): 2975, 2924, 2326, 2105, 1991, 1905, 1697, 1597, 1490, 1360, 1299, 1234, 1146, 1026, 969, 823, 752, 689 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 7.83–7.83 (m, 1 H, Ph*H*), 7.54–7.48 (m, 4 H, Ph*H* and C*H*CH=CHPh), 7.39–7.37 (m, 2 H, Ph*H*), 7.35–7.30 (m, 2 H, Ph*H*), 7.14 (dd, *J* = 15.3, 11.1 Hz, 1 H, CHC*H*=CHPh), 7.09 (d, *J* = 15.3 Hz, 1 H, CHCH=C*H*Ph), 4.89 (d, *J* = 1.6 Hz, 2 H, NCH_2), 2.37 (s, 3 H, CH_3), 1.53 (s, 9 H, Boc).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 184.4, 152.8, 143.0, 140.9, 136.1, 135.9, 134.3, 134.2, 131.0, 129.4, 128.9 (2 C), 127.8, 127.4 (2 C), 127.1, 124.2, 122.4, 81.9, 44.9, 28.3 (3 C), 20.7.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{25}NO_3Na$: 398.1727; found: 398.1726.

***tert*-Butyl (*E*)-7-Methoxy-4-oxo-3-[(*E*)-3-phenylallylidene]-3,4-dihydroquinoline-1(2*H*)-carboxylate (1f)**

Yellow solid; mp 162–165 °C; yield: 0.86 g (11%).

IR (ATR): 2975, 2324, 2107, 1996, 1916, 1701, 1659, 1593, 1452, 1359, 1238, 1143, 1024, 957, 857, 745, 685 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.99–7.97 (m, 1 H, PhH), 7.52–7.47 (m, 3 H, C*H*CH=CHPh and Ph*H*), 7.38–7.31 (m, 3 H, Ph*H*), 7.17–7.16 (m, 1 H, Ph*H*), 7.12–7.03 (m, 2 H, CHC*H*=C*H*Ph), 6.75–6.73 (m, 1 H, Ph*H*), 4.88 (d, *J* = 1.5 Hz, 2 H, NCH_2), 3.86 (s, 3 H, CH_3O), 1.53 (s, 9 H, Boc).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 183.2, 163.7, 152.5, 145.1, 142.5, 136.2, 135.3, 130.7, 129.9, 129.3, 128.8 (2 C), 127.3 (2 C), 122.4, 120.9, 111.7, 108.4, 82.2, 55.5, 45.2, 28.3 (3 C).

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{25}NO_4Na$: 414.1676; found: 414.1680.

***tert*-Butyl (*E*)-6-Fluoro-4-oxo-3-[(*E*)-3-phenylallylidene]-3,4-dihydroquinoline-1(2*H*)-carboxylate (1g)**

Yellow solid; mp 175–177 °C; yield: 0.45 g (6%).

IR (ATR): 2972, 2925, 2317, 2109, 1913, 1700, 1666, 1593, 1484, 1441, 1361, 1304, 1241, 1146, 1025, 975, 884, 838, 758, 715 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 7.69–7.67 (m, 1 H, Ph*H*), 7.63–7.61 (m, 1 H, Ph*H*), 7.55–7.50 (m, 3 H, Ph*H* and C*H*CH=CHPh), 7.40–7.33 (m, 3 H, Ph*H*), 7.22–7.19 (m, 1 H, Ph*H*), 7.16–7.09 (m, 2 H, CHC*H*=C*H*Ph), 4.89 (d, *J* = 1.6 Hz, 2 H, NCH_2), 1.53 (s, 9 H, Boc).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 183.3, 160.2, 158.6, 152.6, 143.7, 139.4, 136.7, 136.0, 130.2, 129.6, 128.9 (2 C), 127.5 (2 C), 126.4, 122.2, 120.6 and 120.4 (1 C), 113.5 and 113.4 (1 C), 82.3, 45.0, 28.3 (3 C).

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{22}NO_3FNa$: 402.1476; found: 402.1478.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0036-1591995.

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