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Facile construction of diverse polyheterocyclic scaffolds *via* gold-catalysed dearomative spirocyclization/1,6-addition cascade†

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A gold-catalysed post-Ugi chemo- and diastereoselective cascade dearomative spirocyclization/1,6-addition sequence is disclosed for the synthesis of diverse fused polyheterocyclic scaffolds bearing indole, pyrrole, benzothiophene, furan or electron-rich arene moieties from easily available building blocks. The effectiveness and efficiency of this diversity-oriented approach has been proved in the rapid construction of 28 fused polyheterocyclic scaffolds with a good building-block variability and structural complexity in two operational steps.

Introduction

The development of efficient strategies for the synthesis of small molecules with architectural complexity and functional diversity for drug discovery processes¹ has always attracted the synthetic community. Polyheterocyclic scaffolds, frequently encountered in various biologically active natural products and pharmaceuticals, are of the utmost interest for library generation (Fig. 1).² Towards this end, post-transformations of multicomponent reaction adducts, facilitated by transition-metal catalysis, referring as the build/couple/pair strategy, afford exciting opportunities for the diversity-oriented synthesis of heterocycles in an efficient manner.³

ortho-Dearomatization of phenols, enabled by various oxidation reagents or transition-metal catalysts,⁴ could efficiently generate reactive masked *ortho*-benzoquinones (MOBs),⁵ which have extensively been employed in inter- or intramolecular [4 + 2] cycloadditions with various dienophiles, delivering bridged polycyclic frameworks like diterpenoid alkaloids

(Scheme 1a).⁶ However, to the best of our knowledge, there are only rare cases where nucleophile, including electron-rich (hetero)arenes (ERH), are used to capture the newly formed cyclohexa-2,4-dienone through 1,6-conjugate addition.⁷ This should allow to further increase structural diversity and complexity.⁸ Recently, gold catalysis has revealed its high efficiency and functional group tolerance for the construction of complex three-dimensional heterocyclic scaffolds through sequential dearomative *ipso*-spirocyclization of phenols⁹ and Michael addition with various nucleophiles.¹⁰

Inspired by these results, we envisaged that a gold-catalysed post-Ugi cascade *ortho*-dearomatization/spirocarbocyclization/1,6-conjugate addition sequence could lead to a diversity-oriented approach for the streamlined synthesis of complex fused polyheterocyclic scaffolds embedding indole, pyrrole, benzothiophene, furan or electron-rich arene moieties (Scheme 1b).

Results and discussion

The acyclic precursor **1a**, assembled *via* Ugi four-component reaction (U-4CR)¹¹ of indole-2-carboxaldehyde, 2-aminophenol,

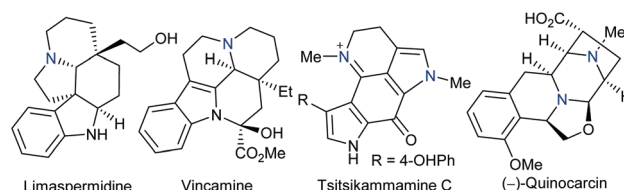


Fig. 1 Representative bioactive fused polyheterocycles.

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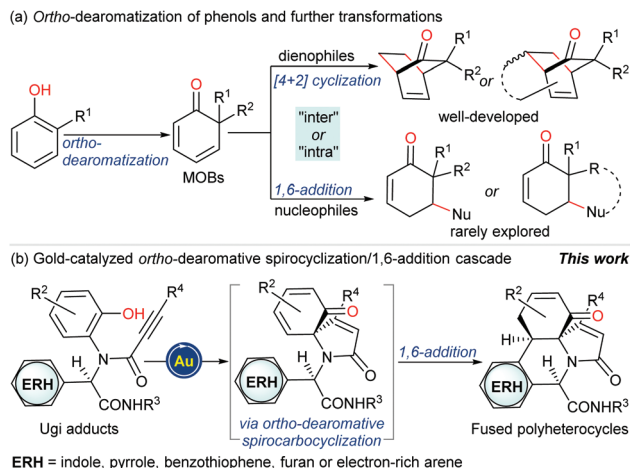
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Scheme 1 Dearomative cascade strategies towards complex scaffolds.

tert-butyl isocyanide, and 2-butyric acid, was chosen as a model substrate to examine the feasibility of the cascade reaction. The reaction was firstly performed with IPrAuCl/AgOTf (10 mol%) in chloroform at room temperature for 24 h yielding the desired indole-fused polyheterocycle **2a** in 38% yield (Table 1, entry 1). Pleasingly, further increasing the reaction temperature to 70 °C afforded the desired polyheterocycle **2a** in 55% yield within 2 h (Table 1, entry 2). Subsequent examination of other gold catalysts with AgOTf (Table 1,

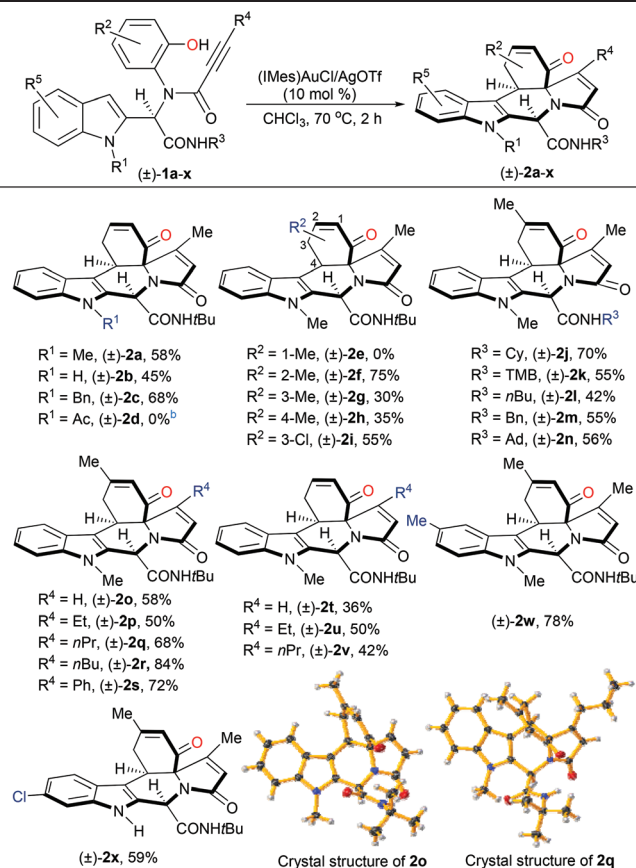
Table 1 Optimization studies^a

Entry	Catalysts	Solvent	T/h	Temp./ °C	Yield of (±)-2a ^b /%
1	IPrAuCl/AgOTf	CDCl ₃	24	r.t.	38 ^c
2	IPrAuCl/AgOTf	CDCl ₃	2	70	55
3	XPhosAuCl/AgOTf	CDCl ₃	2	70	36
4	JohnPhosAuCl/AgOTf	CDCl ₃	2	70	37
5	CyJohnPhosAuCl/AgOTf	CDCl ₃	2	70	Trace
6	MorDalPhosAuCl/AgOTf	CDCl ₃	2	70	42
7	(Ph ₃ P)AuCl/AgOTf	CDCl ₃	2	70	54
8	(IMes)AuCl/AgOTf	CDCl ₃	2	70	65(58 ^c)
9	(IMes)AuCl/AgOAc	CDCl ₃	2	70	26
10	(IMes)AuCl/AgBF ₄	CDCl ₃	2	70	38
11	(IMes)AuCl/AgSbF ₆	CDCl ₃	2	70	Trace
12	(IMes)AuCl/AgOTf	MeCN	2	70	30
13	(IMes)AuCl/AgOTf	MeOH	2	70	11
14	(IMes)AuCl/AgOTf	Toluene	2	70	Trace
15	AgOTf	CDCl ₃	2	70	Trace
16	—	CDCl ₃	2	70	n.d.

^a Unless otherwise stated, all reactions were performed with **1a** (0.05 mmol) and a catalyst loading of 10 mol% in a screw-cap vial with solvent (1 mL). ^b Yields based on ¹H NMR analysis using 2,4,6-trimethoxybenzaldehyde as internal standard. ^c Isolated yield. IMes = 1,3-bis(2,4,6-trimethylphenyl)imidazole-2-ylidene.

entries 3–8), showed that the application of [(IMes)AuOTf] afforded **2a** in an optimised yield of 58% (Table 1, entry 8). Unfortunately, no amelioration was observed during the further screening of different combinations of IMesAuCl with other silver salts (Table 1, entries 9–11), or employing other solvents (Table 1, entries 12–14). No desired product was obtained using only AgOTf or in the absence of cationic gold catalyst (Table 1, entries 15 and 16).

Next, we evaluated the scope and limitations of this process under optimal conditions (Table 1, entry 8) and the results are summarized in Table 2. Substrates with a hydrogen or benzyl group at the indole nitrogen atom gave **2b** and **2c** in moderate to good yields, while the acetyl-protected substrate (**2d**) was unsuited for this cascade process. Apart from a methyl group on the α -position of the newly formed cyclohexenone (**2e**), the R²-substituent (Me, Cl) on other positions was well-tolerated, yielding the fused polyheterocycles **2f–i** in 30–75% yield. Various R³-substituents on the secondary amide moiety, were found to be compatible, generating **2j–n** in yields of 42–70%. Similarly, substrates bearing hydrogen (**2o**, **2t**), an alkyl (**2p–r**, **2u**, **2v**) or an aromatic (**2s**) R⁴-group on the propiolamide

Table 2 Construction of indole-embedded triheterocycle library^a

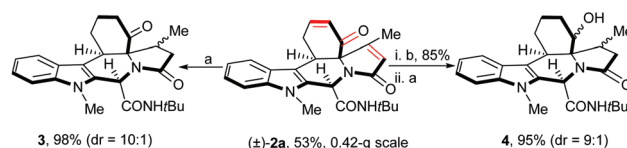
^a All reactions were conducted with **1a–x** (0.20 mmol) and 10 mol% of (IMes)AuCl/AgOTf in a screw-cap vial with CHCl₃ (2 mL) for 2 h; all yields are isolated yields. ^b The precursor decomposes at 70 °C. TMB = 1,1,3,3-tetramethylbutyl; Ad = 1-adamantyl.

fragment, also afforded the desired products in moderate to good yields. Substrates with a chloro- or a methyl-group on the phenyl ring of the indole core, were also well transformed into polyheterocycles **2w** and **2x** in yields of 59% and 78%, respectively. Moreover, the X-ray crystallographic analysis of compounds **2o** and **2q** were conducted for the absolute definition of their structures.¹²

Additionally, various Ugi adducts derived from other (hetero)aromatic aldehydes were evaluated under the optimal conditions (Table 3). We were delighted to observe that the substrates bearing pyrrole (**2ba** and **2bb**), benzo[*b*]thiophene (**2bc**) or furan (**2bd**) worked well, providing the corresponding polyheterocyclic skeletons in yields of 52–75%. Pleasingly, while installing strong electron donating groups like pyrrolidine or trimethoxy on the phenyl ring of the Ugi adduct, this cascade sequence also preceded smoothly, delivering the benzene-annulated tricycles **2be** and **2bf** in 54% and 65% yields, respectively.

The preparative-scale synthesis of indole-fused polyheterocycle **2a** was performed with 6 mol% gold catalyst in 53% yields. Then its further selective hydrogenation was investigated (Scheme 2). Hydrogenation of the double bonds in both the cyclohexenone and the α,β -unsaturated γ -lactam moiety of **2a**, occurred under Pd/C catalysis at 20 atm, affording the polyheterocycle **3** in 98% yield. On the other hand, the carbonyl group of the cyclohexenone could be chemoselectively reduced by NaBH₄. Upon further treating the product with Pd/C catalyst at 20 atm of H₂, product **4** was obtained in 95% yield.

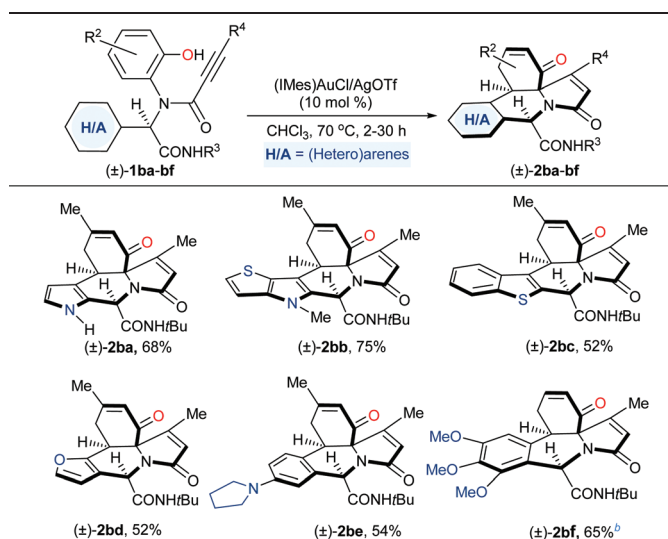
To get insight in the role of the gold catalyst in the 1,6-addition, the spirocarbocyclic C2-linked indole **2y'** was first obtained in 58% yield through treating the Ugi adduct **1y** derived from the *N*-Boc-protected indole-2-carbaldehyde with



Scheme 2 Hydrogenation of heterocycle **2a**. Reaction conditions: ^a Pd/C, H₂ (20 atm), MeOH, r.t., 16 h; ^b NaBH₄, MeOH, r.t., 0.5 h.

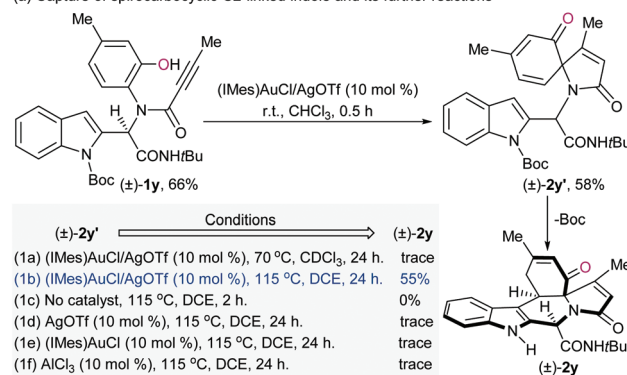
(IMes)AuCl/AgOTf (10 mol%) at room temperature for 0.5 h (Scheme 3a). Then, the intermediate **2y'** was subjected to standard conditions and only traces of the fused heterocycle **2y** were formed. Increasing the reaction temperature to 115 °C furnished the fused framework **2y** with concomitant loss of the boc-group, in 55% yield. The reactions were also performed in the absence of catalyst or with the separate application of (IMes)AuCl, AgOTf or AlCl₃, and almost no desired product was detected. Thus it was ascertained that this intramolecular 1,6-addition of cyclohexa-2,4-dienone with the C3 of the indole is catalysed by the cationic gold species.¹³ Moreover, a deuterium-labeling experiment on the cascade *ortho*-dearomatization/spirocarbocyclization/1,6-addition sequence of Ugi adduct **1s** was conducted under the standard conditions with 6 equiv. of deuterated methanol in chloroform. Based on the NMR spectra of fused polyheterocycle **2s-D**, only 22% of the deuterium locating on the endocyclic double bond of the pyrrole ring was observed (Scheme 3b). This result indicated that the cationic gold species activates the C–C triple bonds in the dearomative spirocyclization step and facilitates the 1,6-addition by its oxophilic activation on the oxygen of newly formed cyclohexa-2,4-dienone, instead of the alkynophilic activation on the C–C double bonds.

Table 3 Synthesis of diverse (hetero)arene-fused triheterocycles^a

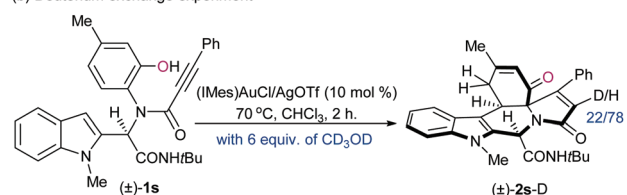


^a All reactions were carried out with **1ba–bf** (0.20 mmol) and 10 mol% of (IMes)AuCl/AgOTf in a screw-cap vial with CHCl₃ (2 mL) for 2 h; all yields are isolated yields. ^b 30 h.

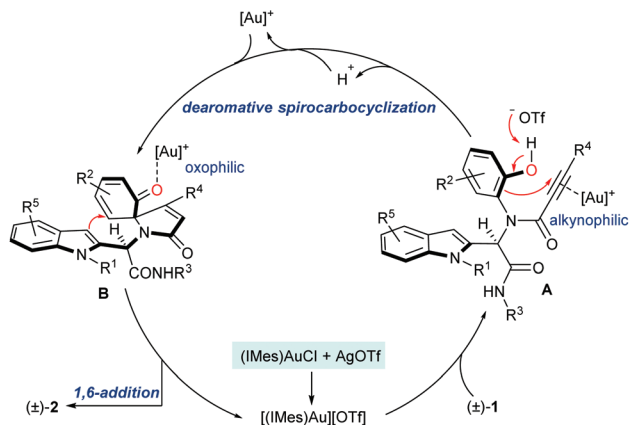
(a) Capture of spirocarbocyclic C2-linked indole and its further reactions



(b) Deuterium exchange experiment



Scheme 3 Control experiments.



Scheme 4 Proposed mechanism of the gold-catalysed *ortho*-dearomatization cascade.

A proposed mechanism of this gold-catalysed *ortho*-dearomatization cascade is depicted in Scheme 4.¹⁴ Nucleophilic attack of the C2 of the phenol moiety to the cationic gold(i)-activated C-C triple bond, facilitated by the concomitant deprotonation by the OTf counter-anion occurs in a 5-*endo*-dig fashion, delivering the spirocyclic intermediate **B** containing the 2,4-cyclohexadienone core.⁹ Then, the gold catalyst acts as an oxophilic Lewis acid¹⁵ to facilitate the subsequent intramolecular 1,6-conjugated addition of the newly formed cyclohexadienone with the C3 of the indole (or other electron-rich (hetero)arenes) affording the indole- (or other (hetero)arene)-fused triheterocycle **2**.

Conclusions

In summary, we have elaborated a diversity-oriented protocol for the construction of diverse polyheterocyclic scaffolds through the combination of an Ugi-4CR and subsequent gold-catalysed chemo- and diastereoselective cascade *ortho*-dearomatization/spirocarboxylation/1,6-conjugated addition sequence. A total of 28 fused polyheterocyclic scaffolds bearing indole, pyrrole, benzothiophene, furan or electron-rich arene cores with a high structural variability and complexity were synthesized from easily available building blocks.

Experimental section

Synthesis of Ugi adducts 1a-x and 1ba-bf

A screw-cap vial equipped with a magnetic stir bar was charged with aldehyde (0.8 mmol, 1.0 equiv.), amine (0.88 mmol, 1.1 equiv.), alkynoic acid (0.88 mmol, 1.1 equiv.), isonitrile (0.88 mmol, 1.1 equiv.), Na₂SO₄ (0.2 g) and methanol (3 mL). The reaction mixture was stirred at room temperature for 24–48 h. The reaction solution was diluted with water (25 mL) and extracted with EtOAc (50 mL). The organic layer was washed with brine (25 mL), dried over MgSO₄ and then concentrated under reduced pressure. The obtained residue

was purified by column chromatography on silica gel with EtOAc/heptane (v/v, 1/2) to provide the desired Ugi products **1a-x** and **1ba-bf** as solid.

General procedure to polyheterocycles 2a-x and 2ba-bf

The Ugi products **1a-x** and **1ba-bf** (0.20 mmol) were added into a screw-cap vial charged with *in situ* generated cationic gold catalyst (IMes)AuOTf (10 mol%) and chloroform (2 mL). After stirring at 70 °C for 2 h, the reaction mixture was diluted with dichloromethane and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with EtOAc/heptane (v/v, 1/2) to deliver the fused polyheterocyclic scaffolds **2a-x** and **2ba-bf**.

N-(tert-Butyl)-5,10-dimethyl-4,7-dioxo-3,4,7,9,10,14c-hexahydroindolo[2,3-c]pyrrolo[2,1-j]quinoline-9-carboxamide (2a). Pale yellow solid, yield 58%, mp: 205–207 °C. ¹H NMR (400 MHz, CDCl₃) δ = 7.55 (d, *J* = 7.9 Hz, 1H), 7.30 (d, *J* = 8.2 Hz, 1H), 7.24–7.18 (m, 1H), 7.12–7.06 (m, 1H), 7.02 (s, 1H), 6.84 (ddd, *J* = 10.0, 6.9, 3.1 Hz, 1H), 6.06–5.90 (m, 2H), 5.64 (d, *J* = 1.7 Hz, 1H), 4.00 (dd, *J* = 6.9, 1.7 Hz, 1H), 3.58 (s, 3H), 3.12 (dt, *J* = 21.5, 2.9 Hz, 1H), 2.97 (dd, *J* = 21.5, 5.7 Hz, 1H), 2.06 (d, *J* = 1.7 Hz, 3H), 1.40 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ = 201.2, 171.5, 165.8, 160.0, 138.3, 129.6, 128.1, 124.8, 124.5, 123.0, 122.0, 120.2, 119.2, 109.4, 108.7, 73.2, 51.6, 51.5, 39.3, 38.3, 30.3, 28.6, 15.8. HRMS (ESI) calculated for C₂₅H₂₈N₃O₃ [M + H]⁺: 418.2131, found 418.2135.

N-(tert-Butyl)-5-methyl-4,7-dioxo-3,4,7,9,10,14c-hexahydroindolo[2,3-c]pyrrolo[2,1-j]quinoline-9-carboxamide (2b). Pale yellow solid, yield 45%, mp: 152–153 °C. ¹H NMR (400 MHz, CDCl₃) δ = 9.40 (s, 1H), 7.60 (s, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.88 (ddd, *J* = 9.9, 6.8, 2.4 Hz, 1H), 6.11–5.88 (m, 2H), 5.55 (d, *J* = 2.2 Hz, 1H), 3.95 (dd, *J* = 6.8, 2.4 Hz, 1H), 3.08 (dd, *J* = 23.4, 4.8 Hz, 1H), 2.99 (dt, *J* = 23.4, 2.8 Hz, 1H), 2.19 (d, *J* = 1.6 Hz, 3H), 1.39 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ = 205.1, 172.1, 167.2, 159.6, 136.8, 128.2, 128.1, 125.1, 124.5, 123.6, 122.3, 120.2, 119.6, 111.7, 107.2, 76.0, 52.9, 51.6, 40.1, 39.4, 28.4, 16.7. HRMS (ESI) calculated for C₂₄H₂₆N₃O₃ [M + H]⁺: 404.1974, found 404.1964.

10-Benzyl-N-(tert-butyl)-5-methyl-4,7-dioxo-3,4,7,9,10,14c-hexahydroindolo[2,3-c]pyrrolo[2,1-j]quinoline-9-carboxamide (2c). Pale yellow solid, yield 68%, mp: 182–183 °C. ¹H NMR (300 MHz, CDCl₃) δ = 7.60 (d, *J* = 7.5 Hz, 1H), 7.28–7.21 (m, 4H), 7.17 (ddd, *J* = 8.1, 6.9, 1.3 Hz, 1H), 7.10 (ddd, *J* = 8.1, 6.8, 1.3 Hz, 1H), 7.04–6.97 (m, 2H), 6.93 (s, 1H), 6.87 (ddd, *J* = 10.0, 6.9, 3.1 Hz, 1H), 6.05–5.99 (m, 1H), 5.97 (q, *J* = 1.6 Hz, 1H), 5.41 (d, *J* = 17.0 Hz, 1H), 5.36 (d, *J* = 1.7 Hz, 1H), 5.09 (d, *J* = 17.0 Hz, 1H), 4.05 (dd, *J* = 6.8, 1.7 Hz, 1H), 3.17 (dt, *J* = 21.4, 2.9 Hz, 1H), 2.98 (dd, *J* = 21.4, 5.7 Hz, 1H), 2.06 (d, *J* = 1.6 Hz, 3H), 1.39 (s, 9H). ¹³C NMR (151 MHz, CDCl₃) δ = 201.2, 171.3, 165.9, 159.9, 138.3, 137.0, 129.5, 128.9, 128.1, 127.7, 126.5, 125.0, 124.7, 123.0, 122.3, 120.3, 119.5, 110.1, 109.7, 73.0, 51.9, 51.6, 47.6, 39.4, 38.1, 28.6, 15.8. HRMS (ESI) calculated for C₃₁H₃₂N₃O₃ [M + H]⁺: 494.2444, found 494.2430.

N-(tert-Butyl)-2,5,10-trimethyl-4,7-dioxo-1,4,7,9,10,14c-hexahydroindolo[2,3-c]pyrrolo[2,1-j]quinoline-9-carboxamide (2f).

Pale yellow solid, yield 75%, mp: 196–198 °C. ^1H NMR (400 MHz, CDCl_3) δ = 7.65 (d, J = 8.0 Hz, 1H), 7.30 (d, J = 8.1 Hz, 1H), 7.20 (t, J = 7.6 Hz, 1H), 7.08 (t, J = 7.6 Hz, 1H), 7.05 (s, 1H), 6.01 (q, J = 1.6 Hz, 1H), 5.99 (s, 1H), 5.62–5.58 (m, 1H), 3.92 (d, J = 5.7 Hz, 1H), 3.67 (d, J = 18.9 Hz, 1H), 3.57 (s, 3H), 3.22 (dd, J = 18.9, 5.7 Hz, 1H), 2.18 (d, J = 1.6 Hz, 3H), 1.94 (s, 3H), 1.41 (s, 9H). ^{13}C NMR (101 MHz, CDCl_3) δ = 189.2, 171.5, 165.6, 160.2, 159.8, 138.5, 131.7, 125.7, 124.8, 123.4, 121.6, 119.3, 119.1, 109.7, 108.3, 72.7, 51.6, 51.5, 36.5, 32.7, 30.3, 28.6, 24.9, 14.9. HRMS (ESI) calculated for $\text{C}_{26}\text{H}_{30}\text{N}_3\text{O}_3$ $[\text{M} + \text{H}]^+$: 432.2287, found 432.2279.

***N*-(*tert*-Butyl)-1,5,10-trimethyl-4,7-dioxo-3,4,7,9,10,14c-hexahydroindolo[2,3-*c*]pyrrolo[2,1-*f*]quinoline-9-carboxamide (2g).** Pale yellow solid, yield 30%, mp: 181–183 °C. ^1H NMR (400 MHz, CDCl_3) δ = 7.55 (d, J = 8.1 Hz, 1H), 7.31 (d, J = 8.3 Hz, 1H), 7.24–7.18 (m, 1H), 7.12–7.00 (m, 2H), 6.04 (q, J = 1.6 Hz, 1H), 5.86–5.76 (m, 1H), 5.62 (d, J = 1.7 Hz, 1H), 3.68 (t, J = 1.6 Hz, 1H), 3.57 (s, 3H), 3.03 (dt, J = 19.9, 2.9 Hz, 1H), 2.83 (dd, J = 19.9, 6.7 Hz, 1H), 2.43 (dd, J = 2.9, 1.5 Hz, 3H), 2.02 (d, J = 1.6 Hz, 3H), 1.38 (s, 9H). ^{13}C NMR (151 MHz, CDCl_3) δ = 202.0, 171.4, 165.6, 160.4, 138.4, 136.3, 130.3, 124.3, 123.8, 121.9, 120.6, 119.4, 119.4, 119.4, 109.5, 107.3, 72.5, 51.7, 51.5, 43.2, 39.6, 31.9, 30.9, 30.4, 28.7, 28.5, 25.7, 22.7, 15.4, 14.1. HRMS (ESI) calculated for $\text{C}_{26}\text{H}_{30}\text{N}_3\text{O}_3$ $[\text{M} + \text{H}]^+$: 432.2287, found 432.2279.

***N*-(*tert*-Butyl)-5,10,14c-trimethyl-4,7-dioxo-3,4,7,9,10,14c-hexahydroindolo[2,3-*c*]pyrrolo[2,1-*f*]quinoline-9-carboxamide (2h).** Pale yellow solid, yield 35%, mp: 205–206 °C. ^1H NMR (400 MHz, CDCl_3) δ = 7.58 (d, J = 8.0 Hz, 1H), 7.30 (d, J = 8.3 Hz, 1H), 7.23 (s, 1H), 7.20 (d, J = 8.0 Hz, 1H), 7.08 (t, J = 7.5 Hz, 1H), 6.62 (dd, J = 10.0, 3.1 Hz, 1H), 6.07 (q, J = 1.6 Hz, 1H), 5.97 (ddd, J = 10.0, 5.7, 2.6 Hz, 1H), 5.66 (s, 1H), 3.56 (s, 3H), 3.05 (dt, J = 21.5, 2.9 Hz, 1H), 2.95 (dd, J = 21.5, 5.7 Hz, 1H), 2.03 (d, J = 1.6 Hz, 3H), 1.41 (s, 9H), 1.22 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ = 201.3, 172.1, 165.5, 158.4, 138.4, 134.4, 128.5, 124.9, 123.6, 123.2, 121.9, 120.1, 119.2, 115.4, 109.5, 77.7, 51.8, 51.5, 40.5, 39.0, 30.9, 30.4, 28.6, 24.3, 16.4. HRMS (ESI) calculated for $\text{C}_{26}\text{H}_{30}\text{N}_3\text{O}_3$ $[\text{M} + \text{H}]^+$: 432.2287, found 432.2277.

***N*-(*tert*-Butyl)-2-chloro-5,10-dimethyl-4,7-dioxo-3,4,7,9,10,14c-hexahydroindolo[2,3-*c*]pyrrolo[2,1-*f*]quinoline-9-carboxamide (2i).** Pale yellow solid, yield 55%, mp: 177–179 °C. ^1H NMR (600 MHz, CDCl_3) δ = 7.53 (d, J = 8.0 Hz, 1H), 7.31 (d, J = 8.2 Hz, 1H), 7.24 (t, J = 7.7 Hz, 1H), 7.13 (t, J = 7.5 Hz, 1H), 7.03 (s, 1H), 6.93 (dd, J = 7.5, 2.9 Hz, 1H), 6.03 (q, J = 1.6 Hz, 1H), 5.62 (s, 1H), 4.01 (d, J = 7.5 Hz, 1H), 3.57 (s, 3H), 3.47 (dd, J = 22.0, 2.9 Hz, 1H), 3.16 (d, J = 22.0 Hz, 1H), 2.10 (d, J = 1.6 Hz, 3H), 1.41 (s, 9H). ^{13}C NMR (151 MHz, CDCl_3) δ = 198.1, 171.3, 165.5, 158.9, 138.3, 129.6, 129.5, 128.5, 124.5, 124.5, 123.5, 122.2, 119.9, 119.7, 109.5, 108.0, 72.9, 51.6, 45.9, 38.1, 30.4, 28.6, 28.5, 15.4. HRMS (ESI) calculated for $\text{C}_{25}\text{H}_{27}\text{ClN}_3\text{O}_3$ $[\text{M} + \text{H}]^+$: 452.1741, found 452.1732.

***N*-Cyclohexyl-2,5,10-trimethyl-4,7-dioxo-1,4,7,9,10,14c-hexahydroindolo[2,3-*c*]pyrrolo[2,1-*f*]quinoline-9-carboxamide (2j).** Pale yellow solid, yield 70%, mp: 142–143 °C. ^1H NMR (600 MHz, CDCl_3) δ = 7.66 (d, J = 8.0 Hz, 1H), 7.32 (d, J =

8.2 Hz, 1H), 7.22 (t, J = 7.7 Hz, 1H), 7.13 (d, J = 8.3 Hz, 1H), 7.10 (t, J = 7.6 Hz, 1H), 6.02–6.01 (m, 1H), 6.00 (t, J = 1.3 Hz, 1H), 5.67 (s, 1H), 3.93 (d, J = 5.9 Hz, 1H), 3.85–3.74 (m, 1H), 3.68 (d, J = 19.1 Hz, 1H), 3.58 (s, 3H), 3.24 (dd, J = 19.1, 5.9 Hz, 1H), 2.18 (s, 3H), 2.13–2.06 (m, 1H), 1.95 (s, 3H), 1.94–1.92 (m, 1H), 1.78–1.67 (m, 2H), 1.63–1.52 (m, 1H), 1.46–1.18 (m, 5H). ^{13}C NMR (151 MHz, CDCl_3) δ = 189.3, 171.6, 165.9, 160.3, 159.8, 138.5, 131.5, 125.6, 124.8, 123.3, 121.7, 119.3, 119.2, 109.8, 108.4, 72.9, 51.0, 48.3, 36.6, 33.1, 32.7, 32.5, 30.4, 25.7, 25.0, 24.8, 24.6, 14.9. HRMS (ESI) calculated for $\text{C}_{28}\text{H}_{32}\text{N}_3\text{O}_3$ $[\text{M} + \text{H}]^+$: 458.2444, found 458.2445.

2,5,10-Trimethyl-4,7-dioxo-*N*-(2,4,4-trimethylpentan-2-yl)-1,4,7,9,10,14c-hexahydroindolo[2,3-*c*]pyrrolo[2,1-*f*]quinoline-9-carboxamide (2k). Yellow solid, yield 55%, mp: 158–159 °C. ^1H NMR (600 MHz, CDCl_3) δ = 7.65 (d, J = 8.0 Hz, 1H), 7.30 (d, J = 8.3 Hz, 1H), 7.20 (t, J = 7.5 Hz, 1H), 7.08 (t, J = 7.5 Hz, 1H), 6.99 (s, 1H), 6.02–6.00 (m, 1H), 5.99 (s, 1H), 5.59 (s, 1H), 3.96–3.81 (m, 1H), 3.66 (d, J = 18.8 Hz, 1H), 3.56 (s, 3H), 3.21 (dd, J = 18.8, 5.0 Hz, 1H), 2.17 (s, 3H), 1.93 (s, 3H), 1.90 (d, J = 14.9 Hz, 1H), 1.58 (d, J = 14.9 Hz, 1H), 1.52 (s, 3H), 1.46 (s, 3H), 1.09 (s, 9H). ^{13}C NMR (151 MHz, CDCl_3) δ = 189.2, 171.4, 165.3, 160.2, 159.9, 138.5, 131.8, 125.7, 124.7, 123.2, 121.6, 119.2, 119.1, 109.7, 108.3, 72.7, 55.7, 53.0, 51.8, 36.5, 32.7, 31.6, 31.6, 30.4, 28.5, 28.2, 24.9, 15.0. HRMS (ESI) calculated for $\text{C}_{30}\text{H}_{38}\text{N}_3\text{O}_3$ $[\text{M} + \text{H}]^+$: 488.2913, found 488.2904.

***N*-Butyl-2,5,10-trimethyl-4,7-dioxo-1,4,7,9,10,14c-hexahydroindolo[2,3-*c*]pyrrolo[2,1-*f*]quinoline-9-carboxamide (2l).** Pale yellow solid, yield 42%, mp: 182–183 °C. ^1H NMR (600 MHz, CDCl_3) δ = 7.69 (d, J = 8.0 Hz, 1H), 7.35 (d, J = 8.3 Hz, 1H), 7.24 (t, J = 7.5 Hz, 1H), 7.16 (t, J = 5.2 Hz, 1H), 7.12 (t, J = 7.5 Hz, 1H), 6.04 (q, J = 1.5 Hz, 1H), 6.02 (s, 1H), 5.71 (s, 1H), 3.96 (d, J = 6.0 Hz, 1H), 3.71 (d, J = 19.1 Hz, 1H), 3.61 (s, 3H), 3.39–3.30 (m, 2H), 3.27 (dd, J = 19.1, 6.0 Hz, 1H), 2.21 (d, J = 1.5 Hz, 3H), 1.98 (s, 3H), 1.67–1.57 (m, 2H), 1.51–1.35 (m, 2H), 0.98 (t, J = 7.4 Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ = 189.3, 171.6, 167.0, 160.4, 159.8, 138.6, 131.4, 125.6, 124.8, 123.3, 121.7, 119.4, 119.1, 109.8, 108.5, 72.9, 50.8, 39.6, 36.6, 32.8, 31.4, 30.4, 25.0, 20.2, 14.9, 13.8. HRMS (ESI) calculated for $\text{C}_{26}\text{H}_{30}\text{N}_3\text{O}_3$ $[\text{M} + \text{H}]^+$: 432.2287, found 432.2286.

***N*-Benzyl-2,5,10-trimethyl-4,7-dioxo-1,4,7,9,10,14c-hexahydroindolo[2,3-*c*]pyrrolo[2,1-*f*]quinoline-9-carboxamide (2m).** Pale yellow solid, yield 55%, mp: 187–189 °C. ^1H NMR (400 MHz, CDCl_3) δ = 7.67 (d, J = 8.0 Hz, 1H), 7.49 (t, J = 5.7 Hz, 1H), 7.41 (d, J = 7.0 Hz, 2H), 7.38–7.29 (m, 3H), 7.29–7.26 (m, 1H), 7.24–7.18 (m, 1H), 7.16–7.05 (m, 1H), 6.01 (s, 2H), 5.74 (q, J = 1.5 Hz, 1H), 4.68 (dd, J = 14.9, 6.4 Hz, 1H), 4.40 (dd, J = 14.9, 4.7 Hz, 1H), 3.94 (d, J = 6.0 Hz, 1H), 3.70 (d, J = 19.0 Hz, 1H), 3.58 (s, 3H), 3.25 (dd, J = 19.0, 5.1 Hz, 1H), 2.20 (d, J = 1.5 Hz, 3H), 1.97 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ = 189.4, 171.5, 167.1, 160.6, 159.8, 138.6, 138.3, 131.2, 128.6, 128.6, 127.8, 127.7, 127.3, 125.6, 124.8, 123.3, 121.8, 119.4, 119.2, 109.8, 108.6, 73.0, 50.7, 43.9, 36.7, 32.8, 30.4, 25.0, 15.0. HRMS (ESI) calculated for $\text{C}_{29}\text{H}_{28}\text{N}_3\text{O}_3$ $[\text{M} + \text{H}]^+$: 466.2131, found 466.2126.

***N*-((3*s*,5*s*,7*s*)-Adamantan-1-yl)-2,5,10-trimethyl-4,7-dioxo-1,4,7,9,10,14c-hexahydroindolo[2,3-*c*]pyrrolo[2,1-*f*]quinoline-9-carboxamide (2n).** Yellow solid, yield 56%, mp: 159–160 °C.

^1H NMR (400 MHz, CDCl_3) δ = 7.65 (d, J = 8.0 Hz, 1H), 7.30 (d, J = 8.2 Hz, 1H), 7.20 (t, J = 7.5 Hz, 1H), 7.08 (t, J = 7.5 Hz, 1H), 6.93 (s, 1H), 6.07–5.90 (m, 2H), 5.61 (s, 1H), 3.91 (d, J = 5.6 Hz, 1H), 3.67 (d, J = 19.0 Hz, 1H), 3.57 (s, 3H), 3.22 (dd, J = 19.0, 5.0 Hz, 1H), 2.17 (s, 3H), 2.15–1.99 (m, 8H), 1.94 (s, 3H), 1.79–1.54 (m, 7H). ^{13}C NMR (151 MHz, CDCl_3) δ = 189.3, 171.4, 165.3, 160.3, 159.7, 138.5, 131.8, 125.7, 124.8, 123.5, 121.6, 119.3, 119.1, 109.7, 108.3, 72.7, 52.1, 51.7, 41.3, 36.5, 36.4, 32.7, 30.3, 29.5, 24.9, 14.9. HRMS (ESI) calculated for $\text{C}_{32}\text{H}_{36}\text{N}_3\text{O}_3$ $[\text{M} + \text{H}]^+$: 510.2757, found 510.2750.

***N*-(*tert*-Butyl)-2,10-dimethyl-4,7-dioxo-1,4,7,9,10,14c-hexahydroindolo[2,3-*c*]pyrrolo[2,1-*f*]quinoline-9-carboxamide (2o).** Pale yellow solid, yield 58%, mp: 236–237 °C. ^1H NMR (400 MHz, CDCl_3) δ = 7.64 (d, J = 8.1 Hz, 1H), 7.31–7.27 (m, 2H), 7.25 (s, 1H), 7.23–7.17 (m, 1H), 7.11–7.02 (m, 1H), 6.38 (d, J = 6.0 Hz, 1H), 6.00–5.83 (m, 1H), 5.61 (d, J = 1.6 Hz, 1H), 3.75 (d, J = 5.3 Hz, 1H), 3.65 (dd, J = 18.5, 2.1 Hz, 1H), 3.59 (s, 3H), 3.20–3.03 (m, 1H), 2.00 (t, J = 1.2 Hz, 3H), 1.43 (s, 9H). ^{13}C NMR (151 MHz, CDCl_3) δ = 188.1, 171.5, 165.3, 159.6, 145.1, 138.6, 131.7, 128.1, 126.0, 124.9, 121.7, 119.4, 119.2, 109.8, 107.3, 73.4, 52.4, 51.5, 38.0, 32.4, 30.6, 28.6, 24.7. HRMS (ESI) calculated for $\text{C}_{25}\text{H}_{28}\text{N}_3\text{O}_3$ $[\text{M} + \text{H}]^+$: 418.2131, found 418.2124.

***N*-(*tert*-Butyl)-5-ethyl-2,10-dimethyl-4,7-dioxo-1,4,7,9,10,14c-hexahydroindolo[2,3-*c*]pyrrolo[2,1-*f*]quinoline-9-carboxamide (2p).** Pale yellow solid, yield 50%, mp: 206–208 °C. ^1H NMR (400 MHz, CDCl_3) δ = 7.65 (d, J = 8.0 Hz, 1H), 7.30 (d, J = 8.2 Hz, 1H), 7.20 (t, J = 7.6 Hz, 1H), 7.08 (t, J = 7.6 Hz, 1H), 7.04 (s, 1H), 6.02 (t, J = 1.9 Hz, 1H), 5.97 (s, 1H), 5.62 (d, J = 1.6 Hz, 1H), 3.93 (d, J = 5.9 Hz, 1H), 3.66 (d, J = 18.9 Hz, 1H), 3.57 (s, 3H), 3.22 (dd, J = 18.9, 5.2 Hz, 1H), 2.69–2.55 (m, 1H), 2.39–2.24 (m, 1H), 1.92 (s, 3H), 1.41 (s, 9H), 1.23 (t, J = 7.2 Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ = 189.3, 171.6, 166.3, 165.6, 160.2, 138.5, 131.7, 125.5, 124.8, 121.6, 120.8, 119.2, 119.1, 109.7, 108.4, 72.5, 51.5, 51.4, 36.3, 32.8, 30.2, 28.6, 25.0, 21.7, 11.4. HRMS (ESI) calculated for $\text{C}_{27}\text{H}_{32}\text{N}_3\text{O}_3$ $[\text{M} + \text{H}]^+$: 446.2444, found 446.2431.

***N*-(*tert*-Butyl)-2,10-dimethyl-4,7-dioxo-5-propyl-1,4,7,9,10,14c-hexahydroindolo[2,3-*c*]pyrrolo[2,1-*f*]quinoline-9-carboxamide (2q).** Pale yellow solid, yield 68%, mp: 152–153 °C. ^1H NMR (600 MHz, CDCl_3) δ = 7.67 (d, J = 8.0 Hz, 1H), 7.33 (d, J = 8.2 Hz, 1H), 7.22 (t, J = 7.6 Hz, 1H), 7.11 (t, J = 7.5 Hz, 1H), 7.05 (s, 1H), 6.04 (t, J = 1.28 Hz, 1H), 6.00 (s, 1H), 5.65 (d, J = 1.5 Hz, 1H), 3.96 (d, J = 5.9 Hz, 1H), 3.69 (d, J = 18.8 Hz, 1H), 3.60 (s, 3H), 3.25 (dd, J = 18.8, 5.5 Hz, 1H), 2.67–2.48 (m, 1H), 2.35–2.15 (m, 1H), 1.96 (s, 3H), 1.80–1.57 (m, 2H), 1.44 (s, 9H), 1.03 (t, J = 7.3 Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ = 189.2, 171.7, 165.6, 164.8, 160.2, 138.5, 131.7, 125.7, 124.8, 121.6, 121.2, 119.2, 119.1, 109.7, 108.5, 72.6, 51.5, 51.5, 36.4, 32.9, 30.5, 30.2, 28.6, 25.0, 20.5, 13.8. HRMS (ESI) calculated for $\text{C}_{28}\text{H}_{34}\text{N}_3\text{O}_3$ $[\text{M} + \text{H}]^+$: 460.2600, found 460.2597.

***N*-(*tert*-Butyl)-5-butyl-2,10-dimethyl-4,7-dioxo-1,4,7,9,10,14c-hexahydroindolo[2,3-*c*]pyrrolo[2,1-*f*]quinoline-9-carboxamide (2r).** Pale yellow solid, yield 84%, mp: 125–126 °C. ^1H NMR (400 MHz, CDCl_3) δ = 7.65 (d, J = 8.0 Hz, 1H), 7.30 (d, J = 8.2 Hz, 1H), 7.20 (t, J = 7.6 Hz, 1H), 7.08 (t, J = 7.6 Hz, 1H), 7.02

(s, 1H), 6.01 (t, J = 1.9 Hz, 1H), 5.98 (s, 1H), 5.62 (d, J = 1.5 Hz, 1H), 3.93 (d, J = 6.1 Hz, 1H), 3.66 (d, J = 18.8 Hz, 1H), 3.57 (s, 3H), 3.22 (dd, J = 18.8, 5.1 Hz, 1H), 2.62–2.45 (m, 1H), 2.32–2.18 (m, 1H), 1.93 (s, 3H), 1.73–1.50 (m, 2H), 1.41 (s, 9H), 1.39–1.35 (m, 2H), 0.94 (t, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ = 189.2, 171.7, 165.7, 165.0, 160.2, 138.5, 131.7, 125.7, 124.8, 121.6, 121.2, 119.2, 119.1, 109.7, 108.5, 72.6, 51.5, 51.5, 36.4, 32.9, 30.2, 29.3, 28.6, 28.1, 25.0, 22.4, 13.9. HRMS (ESI) calculated for $\text{C}_{29}\text{H}_{36}\text{N}_3\text{O}_3$ $[\text{M} + \text{H}]^+$: 474.2757, found 474.2751.

***N*-(*tert*-Butyl)-2,10-dimethyl-4,7-dioxo-5-phenyl-1,4,7,9,10,14c-hexahydroindolo[2,3-*c*]pyrrolo [2,1-*f*]quinoline-9-carboxamide (2s).** Pale yellow solid, yield 72%, mp: 246–247 °C. ^1H NMR (400 MHz, CDCl_3) δ = 7.52 (d, J = 8.1 Hz, 1H), 7.48–7.41 (m, 1H), 7.38 (t, J = 7.5 Hz, 2H), 7.30 (d, J = 8.3 Hz, 1H), 7.26 (d, J = 7.3 Hz, 2H), 7.18 (t, J = 7.6 Hz, 1H), 7.02 (t, J = 7.6 Hz, 1H), 6.98 (s, 1H), 6.23 (s, 1H), 6.10 (s, 1H), 5.71 (s, 1H), 3.92 (d, J = 4.7 Hz, 1H), 3.60 (s, 3H), 3.23 (dd, J = 18.3, 2.0 Hz, 1H), 2.32–2.24 (m, 1H), 1.73 (s, 3H), 1.45 (s, 9H). ^{13}C NMR (151 MHz, CDCl_3) δ = 189.2, 170.9, 165.5, 162.5, 161.4, 138.6, 133.8, 131.6, 129.7, 128.6, 127.0, 126.9, 124.7, 124.4, 121.7, 119.3, 119.2, 109.7, 108.3, 72.6, 51.7, 51.6, 37.1, 32.1, 30.3, 28.6, 24.9. HRMS (ESI) calculated for $\text{C}_{31}\text{H}_{32}\text{N}_3\text{O}_3$ $[\text{M} + \text{H}]^+$: 494.2444, found 494.2440.

***N*-(*tert*-Butyl)-10-methyl-4,7-dioxo-1,4,7,9,10,14c-hexahydroindolo[2,3-*c*]pyrrolo[2,1-*f*]quinoline-9-carboxamide (2t).** Pale yellow solid, yield 36%, mp: 194–195 °C. ^1H NMR (300 MHz, CDCl_3) δ = 7.56 (d, J = 8.0 Hz, 1H), 7.31 (d, J = 5.9 Hz, 1H), 7.29 (s, 1H), 7.24–7.17 (m, 2H), 7.12–7.03 (m, 1H), 6.80–6.68 (m, 1H), 6.34 (d, J = 6.0 Hz, 1H), 6.10–5.97 (m, 1H), 5.66 (d, J = 1.8 Hz, 1H), 3.95 (dd, J = 6.6, 1.7 Hz, 1H), 3.61 (s, 3H), 3.11–2.94 (m, 2H), 1.44 (s, 9H). ^{13}C NMR (75 MHz, CDCl_3) δ = 199.3, 171.5, 165.6, 138.4, 129.0, 127.6, 126.8, 124.6, 122.0, 119.3, 109.5, 108.4, 75.2, 52.4, 52.4, 51.5, 40.3, 39.1, 28.6. HRMS (ESI) calculated for $\text{C}_{24}\text{H}_{26}\text{N}_3\text{O}_3$ $[\text{M} + \text{H}]^+$: 404.1974, found 404.1978.

***N*-(*tert*-Butyl)-5-ethyl-10-methyl-4,7-dioxo-1,4,7,9,10,14c-hexahydroindolo[2,3-*c*]pyrrolo[2,1-*f*]quinoline-9-carboxamide (2u).** Pale yellow solid, yield 50%, mp: 177–179 °C. ^1H NMR (400 MHz, CDCl_3) δ = 7.54 (d, J = 7.9 Hz, 1H), 7.30 (d, J = 8.3 Hz, 1H), 7.26–7.13 (m, 1H), 7.13–7.04 (m, 1H), 7.03 (s, 1H), 6.87–6.79 (m, 1H), 6.01 (t, J = 2.0 Hz, 1H), 5.99–5.93 (m, 1H), 5.64 (d, J = 1.6 Hz, 1H), 4.02–3.93 (m, 1H), 3.57 (s, 3H), 3.11 (dt, J = 21.4, 2.9 Hz, 1H), 2.96 (dd, J = 21.5, 5.7 Hz, 1H), 2.68–2.37 (m, 1H), 2.19–2.04 (m, 1H), 1.40 (s, 9H), 1.18 (t, J = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ = 201.5, 171.6, 166.3, 165.8, 138.3, 129.6, 128.2, 124.8, 124.5, 121.9, 120.4, 120.2, 119.2, 109.4, 108.7, 72.8, 51.5, 39.3, 38.2, 30.3, 28.6, 22.8, 11.2. HRMS (ESI) calculated for $\text{C}_{26}\text{H}_{30}\text{N}_3\text{O}_3$ $[\text{M} + \text{H}]^+$: 432.2287, found 432.2277.

***N*-(*tert*-Butyl)-10-methyl-4,7-dioxo-5-propyl-3,4,7,9,10,14c-hexahydroindolo[2,3-*c*]pyrrolo[2,1-*f*]quinoline-9-carboxamide (2v).** Pale yellow solid, yield 42%, mp: 141–143 °C. ^1H NMR (400 MHz, CDCl_3) δ = 7.55 (dt, J = 8.0, 0.9 Hz, 1H), 7.30 (dt, J = 8.2, 0.9 Hz, 1H), 7.24–7.16 (m, 1H), 7.12–7.06 (m, 1H), 7.02 (s, 1H), 6.85 (ddd, J = 10.0, 6.9, 3.1 Hz, 1H), 6.00 (t, J = 1.8 Hz, 1H), 5.99–5.95 (m, 1H), 5.64 (d, J = 1.7 Hz, 1H), 4.01 (dd,

$J = 6.9, 1.6$ Hz, 1H), 3.58 (s, 3H), 3.11 (dt, $J = 21.4, 2.9$ Hz, 1H), 2.97 (dd, $J = 21.4, 5.8$ Hz, 1H), 2.50–2.34 (m, 1H), 2.19–1.96 (m, 1H), 1.64–1.50 (m, 2H), 1.40 (s, 9H), 0.99 (t, $J = 7.3$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) $\delta = 201.4, 171.7, 165.8, 164.8, 138.3, 129.6, 128.2, 124.8, 124.5, 122.7, 121.9, 121.0, 120.2, 119.2, 109.4, 109.3, 108.7, 72.8, 51.6, 51.5, 39.3, 38.1, 31.4, 30.3, 28.5, 28.4, 20.2, 13.8$. HRMS (ESI) calculated for $\text{C}_{27}\text{H}_{32}\text{N}_3\text{O}_3$ $[\text{M} + \text{H}]^+$: 446.2444, found 446.2449.

***N*-(*tert*-Butyl)-2,5,10,13-tetramethyl-4,7-dioxo-1,4,7,9,10,14c-hexahydroindolo[2,3-*c*]pyrrolo [2,1-*f*]quinoline-9-carboxamide (2w).** Pale yellow solid, yield 78%, mp: 219–220 °C. ^1H NMR (600 MHz, CDCl_3) $\delta = 7.42$ (s, 1H), 7.18 (d, $J = 8.4$ Hz, 1H), 7.07–6.98 (m, 2H), 6.01 (d, $J = 1.6$ Hz, 1H), 5.99 (s, 1H), 5.59 (d, $J = 1.6$ Hz, 1H), 3.93–3.88 (m, 1H), 3.71–3.61 (m, 1H), 3.54 (s, 3H), 3.21 (dd, $J = 18.9, 4.8$ Hz, 1H), 2.45 (s, 3H), 2.17 (s, 3H), 1.95 (s, 3H), 1.41 (s, 9H). ^{13}C NMR (151 MHz, CDCl_3) $\delta = 189.2, 171.5, 165.7, 160.3, 159.8, 137.0, 131.6, 128.3, 125.6, 125.0, 123.4, 123.2, 118.9, 109.4, 107.8, 72.7, 51.6, 51.4, 36.4, 32.7, 31.9, 30.3, 29.0, 28.6, 25.0, 22.7, 21.7, 14.9, 14.1$. HRMS (ESI) calculated for $\text{C}_{27}\text{H}_{32}\text{N}_3\text{O}_3$ $[\text{M} + \text{H}]^+$: 446.2444, found 446.2432.

***N*-(*tert*-Butyl)-12-chloro-2,5-dimethyl-4,7-dioxo-1,4,7,9,10,14c-hexahydroindolo[2,3-*c*]pyrrolo[2,1-*f*]quinoline-9-carboxamide (2x).** Pale yellow solid, yield 59%, mp: 204–205 °C. ^1H NMR (600 MHz, CDCl_3) $\delta = 9.40$ (s, 1H), 7.54 (s, 1H), 7.45 (d, $J = 8.6$ Hz, 1H), 7.31 (d, $J = 1.8$ Hz, 1H), 7.03 (dd, $J = 8.5, 1.8$ Hz, 1H), 6.49 (d, $J = 7.0$ Hz, 1H), 6.01 (q, $J = 1.6$ Hz, 1H), 5.51 (d, $J = 2.3$ Hz, 1H), 3.84 (d, $J = 5.8$ Hz, 1H), 2.96 (d, $J = 22.9$ Hz, 1H), 2.88 (d, $J = 22.9$ Hz, 1H), 2.13 (d, $J = 1.6$ Hz, 3H), 1.89 (s, 3H), 1.39 (s, 9H). ^{13}C NMR (151 MHz, CDCl_3) $\delta = 204.8, 172.1, 167.1, 159.4, 137.2, 133.2, 128.8, 128.2, 123.9, 123.6, 121.6, 120.8, 120.4, 111.6, 108.2, 75.6, 52.8, 51.6, 43.8, 39.6, 28.4, 22.4, 16.3$. HRMS (ESI) calculated for $\text{C}_{25}\text{H}_{27}\text{ClN}_3\text{O}_3$ $[\text{M} + \text{H}]^+$: 452.1741, found 452.1738.

***tert*-Butyl 2-(2-(*tert*-butylamino)-1-(4,8-dimethyl-2,10-dioxo-1-azaspiro[4.5]deca-3,6,8-trien-1-yl)-2-oxoethyl)-1*H*-indole-1-carboxylate (2y).** Yellow solid, yield 58%, mp: 161–162 °C. ^1H NMR (400 MHz, CDCl_3) $\delta = 8.06$ (d, $J = 8.4$ Hz, 1H), 7.98 (s, 1H), 7.36 (d, $J = 7.7$ Hz, 1H), 7.32–7.27 (m, 1H), 7.18 (t, $J = 7.5$ Hz, 1H), 6.32 (s, 1H), 6.27 (s, 1H), 6.07 (q, $J = 1.6$ Hz, 1H), 5.87 (s, 1H), 5.71 (d, $J = 9.5$ Hz, 1H), 5.46 (dd, $J = 9.5, 1.4$ Hz, 1H), 1.66 (s, 9H), 1.65 (s, 3H), 1.48 (s, 9H), 1.37 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) $\delta = 196.4, 171.5, 167.6, 157.0, 156.8, 149.7, 137.9, 135.9, 134.9, 128.1, 126.2, 125.3, 124.7, 124.2, 123.1, 121.0, 116.2, 113.3, 85.2, 56.7, 51.4, 34.1, 28.6, 28.4, 28.4, 28.3, 22.4, 22.3, 14.1, 12.1$. HRMS (ESI) calculated for $\text{C}_{30}\text{H}_{36}\text{N}_3\text{O}_5$ $[\text{M} + \text{H}]^+$: 518.2655, found 518.2659.

***tert*-Butyl 9-(*tert*-butylcarbamoyl)-2,5-dimethyl-4,7-dioxo-1,7,9,14c-tetrahydroindolo[2,3-*c*]pyrrolo[2,1-*f*]quinoline-10(4*H*)-carboxylate (2y).** Yellow solid, yield 55%, mp: 175–177 °C. ^1H NMR (300 MHz, CDCl_3) $\delta = 9.44$ (s, 1H), 7.75 (s, 1H), 7.65 (d, $J = 8.0$ Hz, 1H), 7.37 (d, $J = 8.0$ Hz, 1H), 7.17 (ddd, $J = 8.1, 7.1, 1.2$ Hz, 1H), 7.08 (ddd, $J = 8.1, 7.1, 1.2$ Hz, 1H), 6.07 (q, $J = 1.5$ Hz, 1H), 5.97 (q, $J = 2.5, 1.4$ Hz, 1H), 5.53 (d, $J = 2.2$ Hz, 1H), 3.87–3.67 (m, 2H), 3.37–3.19 (m, 1H), 2.24 (d, $J = 1.5$ Hz, 3H), 2.10 (t, $J = 1.2$ Hz, 3H), 1.39 (s, 9H). ^{13}C NMR (151 MHz, CDCl_3) $\delta = 193.0, 171.8, 167.2, 161.8, 159.2, 137.0, 130.3, 126.5,$

125.3, 124.6, 122.0, 119.8, 119.2, 112.1, 106.1, 74.8, 52.9, 51.5, 39.1, 32.7, 31.9, 29.7, 28.4, 24.6, 22.7, 15.4, 14.1. HRMS (ESI) calculated for $\text{C}_{25}\text{H}_{28}\text{N}_3\text{O}_3$ $[\text{M} + \text{H}]^+$: 418.2131, found 418.2135.

***N*-(*tert*-Butyl)-2,5-dimethyl-4,7-dioxo-1,4,7,9,10,12b-hexahydro-dipyrrolo[2,3-*c*:2',1'-*f*]quinoline-9-carboxamide (2ba).** Pale yellow solid, yield 68%, mp: 172–173 °C. ^1H NMR (400 MHz, CDCl_3) $\delta = 9.13$ (s, 1H), 7.53 (s, 1H), 6.70 (td, $J = 2.7, 0.9$ Hz, 1H), 6.26–6.14 (m, 1H), 6.00–5.85 (m, 2H), 5.41–5.36 (m, 1H), 3.58 (d, $J = 6.2$ Hz, 1H), 2.98 (d, $J = 23.0$ Hz, 1H), 2.87 (d, $J = 22.9$ Hz, 1H), 2.10 (d, $J = 1.6$ Hz, 3H), 1.85 (s, 3H), 1.38 (s, 9H). ^{13}C NMR (151 MHz, CDCl_3) $\delta = 204.9, 172.3, 167.9, 159.2, 132.0, 123.5, 122.4, 120.5, 119.0, 116.0, 105.3, 76.2, 53.0, 51.3, 43.8, 39.4, 28.4, 22.4, 15.9$. HRMS (ESI) calculated for $\text{C}_{21}\text{H}_{26}\text{N}_3\text{O}_3$ $[\text{M} + \text{H}]^+$: 368.1974, found 368.1987.

***N*-(*tert*-Butyl)-2,5-dimethyl-4,7-dioxo-1,4,7,9,10,13c-hexahydro-pyrrolo[2,1-*f*]thieno[2',3':4,5] pyrrolo[2,3-*c*]quinoline-9-carboxamide (2bb).** Pale yellow solid, yield 75%, mp: 168–169 °C. ^1H NMR (400 MHz, CDCl_3) $\delta = 7.14$ (s, 1H), 7.04 (d, $J = 5.2$ Hz, 1H), 6.90 (d, $J = 5.2$ Hz, 1H), 6.01 (q, $J = 1.5$ Hz, 1H), 5.97 (s, 1H), 5.59 (d, $J = 1.5$ Hz, 1H), 3.66–3.61 (m, 1H), 3.58 (s, 3H), 3.19 (d, $J = 3.5$ Hz, 2H), 2.15 (d, $J = 1.5$ Hz, 3H), 2.02 (s, 3H), 1.40 (s, 9H). ^{13}C NMR (151 MHz, CDCl_3) $\delta = 189.0, 171.6, 165.8, 159.8, 159.3, 142.0, 128.5, 126.0, 123.7, 123.0, 118.1, 110.6, 110.4, 72.8, 51.9, 51.4, 36.2, 33.3, 32.8, 28.6, 24.6, 14.8$. HRMS (ESI) calculated for $\text{C}_{24}\text{H}_{28}\text{N}_3\text{O}_3\text{S}$ $[\text{M} + \text{H}]^+$: 438.1851, found 438.1841.

***N*-(*tert*-Butyl)-2,5-dimethyl-4,7-dioxo-4,7,9,14c-tetrahydro-1*H*-benzo[4,5]thieno[2,3-*c*]pyrrolo [2,1-*f*]quinoline-9-carboxamide (2bc).** Pale yellow solid, yield 52%, mp: 186–188 °C. ^1H NMR (400 MHz, CDCl_3) $\delta = 7.82$ (t, $J = 2.1$ Hz, 1H), 7.80 (t, $J = 2.1$ Hz, 1H), 7.36–7.28 (m, 3H), 6.07 (q, $J = 1.5$ Hz, 1H), 6.03 (s, 1H), 5.64 (d, $J = 2.3$ Hz, 1H), 3.92 (d, $J = 6.3$ Hz, 1H), 3.82 (d, $J = 19.3$ Hz, 1H), 3.29 (dd, $J = 19.3, 6.0$ Hz, 1H), 2.22 (d, $J = 1.5$ Hz, 3H), 1.98 (s, 3H), 1.40 (s, 9H). ^{13}C NMR (151 MHz, CDCl_3) $\delta = 191.9, 171.4, 166.3, 161.8, 159.8, 141.9, 136.6, 135.1, 126.8, 126.2, 124.1, 124.1, 123.9, 123.2, 121.9, 72.8, 55.3, 51.5, 39.6, 32.7, 29.7, 28.4, 24.8, 15.2$. HRMS (ESI) calculated for $\text{C}_{25}\text{H}_{27}\text{N}_2\text{O}_3\text{S}$ $[\text{M} + \text{H}]^+$: 435.1742, found 435.1735.

***N*-(*tert*-Butyl)-2,5-dimethyl-4,7-dioxo-4,7,9,12b-tetrahydro-1*H*-furo[3,2-*c*]pyrrolo[2,1-*f*]quinoline-9-carboxamide (2bd).** Pale yellow solid, yield 52%, mp: 199–200 °C. ^1H NMR (400 MHz, CDCl_3) $\delta = 7.38$ (s, 1H), 7.30–7.27 (m, 1H), 6.67 (d, $J = 1.9$ Hz, 1H), 6.02 (q, $J = 1.7$ Hz, 1H), 6.00 (s, 1H), 5.32 (d, $J = 2.6$ Hz, 1H), 3.55–3.46 (m, 1H), 3.31 (d, $J = 19.4$ Hz, 1H), 3.05 (dd, $J = 19.4, 5.2$ Hz, 1H), 2.14 (d, $J = 1.7$ Hz, 3H), 2.08 (s, 3H), 1.37 (s, 9H). ^{13}C NMR (101 MHz, CDCl_3) $\delta = 191.6, 171.8, 167.0, 161.1, 158.3, 145.4, 142.5, 126.1, 124.5, 116.6, 110.7, 73.5, 53.2, 51.1, 37.5, 30.2, 28.5, 24.6, 14.7$. HRMS (ESI) calculated for $\text{C}_{21}\text{H}_{25}\text{N}_2\text{O}_4$ $[\text{M} + \text{H}]^+$: 369.1814, found 369.1808.

***N*-(*tert*-Butyl)-2,5-dimethyl-4,7-dioxo-11-(pyrrolidin-1-yl)-4,7,9,13b-tetrahydro-1*H*-pyrrolo[2,1-*e*]phenanthridine-9-carboxamide (2be).** Pale yellow solid, yield 54%, mp: 231–233 °C. ^1H NMR (400 MHz, CDCl_3) $\delta = 7.68$ (s, 1H), 7.09 (d, $J = 8.6$ Hz, 1H), 6.84 (s, 1H), 6.46 (d, $J = 6.7$ Hz, 1H), 6.30 (d, $J = 7.1$ Hz, 1H), 6.01 (q, $J = 1.5$ Hz, 1H), 5.20 (s, 1H), 3.53 (d, $J = 7.0$ Hz, 1H), 3.33–3.15 (m, 4H), 2.91 (ddd, $J = 22.6, 2.5, 1.3$ Hz, 1H),

2.81 (d, $J = 22.6$ Hz, 1H), 2.10 (d, $J = 1.5$ Hz, 3H), 2.01–1.93 (m, 4H), 1.91 (s, 3H), 1.40 (s, 9H). ^{13}C NMR (151 MHz, CDCl_3) $\delta = 205.24, 172.0, 168.7, 158.6, 133.7, 131.0, 127.9, 125.2, 123.5, 75.5, 58.7, 50.8, 47.6, 44.1, 41.9, 28.4, 25.4, 22.5, 16.7$. HRMS (ESI) calculated for $\text{C}_{27}\text{H}_{34}\text{N}_3\text{O}_3$ $[\text{M} + \text{H}]^+$: 448.2600, found 448.2603.

***N*-(*tert*-Butyl)-11,12,13-trimethoxy-5-methyl-4,7-dioxo-4,7,9,13b-tetrahydro-1*H*-pyrrolo[2,1-*e*]phenanthridine-9-carboxamide (2bf).** Pale yellow solid, yield 65%, mp: 235–237 °C. ^1H NMR (300 MHz, CDCl_3) $\delta = 7.18$ (ddd, $J = 10.2, 6.4, 2.6$ Hz, 1H), 6.65 (s, 1H), 6.37 (ddd, $J = 10.2, 2.6, 0.8$ Hz, 1H), 6.25 (s, 1H), 5.91 (q, $J = 1.5$ Hz, 1H), 5.68 (s, 1H), 4.15–4.04 (m, 1H), 3.86 (s, 3H), 3.86 (s, 3H), 3.83 (s, 3H), 2.72–2.54 (m, 1H), 2.38 (ddt, $J = 18.6, 10.5, 2.6$ Hz, 1H), 2.01 (d, $J = 1.5$ Hz, 3H), 1.25 (s, 9H). ^{13}C NMR (151 MHz, CDCl_3) $\delta = 194.3, 176.8, 168.3, 163.6, 152.5, 151.2, 150.6, 141.3, 129.5, 129.4, 123.7, 119.4, 108.8, 74.8, 61.4, 60.7, 58.2, 55.9, 51.7, 32.2, 31.9, 31.1, 29.0, 28.1, 22.7, 14.1, 14.0$. HRMS (ESI) calculated for $\text{C}_{25}\text{H}_{31}\text{N}_2\text{O}_6$ $[\text{M} + \text{H}]^+$: 455.2182, found 455.2189.

Conflicts of interest

There are no conflicts to declare.

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