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Diastereoselective synthesis of functionalised carbazoles *via* a sequential Diels–Alder/ene reaction strategy†

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An operationally simple one-pot, three-component, diastereoselective synthesis of saturated carbazoles and related pyridazino[3,4-*b*]indoles, based on two sequential intermolecular pericyclic reactions, is described. The reaction sequence involves an intermolecular Diels–Alder (D–A) reaction of a 3-vinyl-1*H*-indole, containing an electron withdrawing N-protecting group, with a suitable dienophile. Due to the electron withdrawing nature of the N-protecting group the resultant D–A cycloadducts are sufficiently stabilised to allow for a subsequent *in situ* diastereospecific intermolecular ene reaction to take place with an added enophile, generating functionalised carbazoles with relative stereocontrol of up to four stereocentres.

Introduction

Carbazole scaffolds are common in many bioactive compounds (*e.g.* staurosporine)[1,2] with the indolocarbazole scaffold in particular being found in a number of molecules with potential therapeutic application, several of which have entered clinical trials for the treatment of cancer (midostaurin (PKC412), lestaurtinib (CEP-701), CEP-751, CEP-1347, edotecarin and becatecarin).[3,4] Therefore there is a growing interest in the development of new synthetic routes to functionalised carbozoles.[5–9] Herein we describe our progress in the development of a diastereoselective one-pot, three-component approach for the synthesis of functionalised, partially saturated carbazoles and pyridazino[3,4-*b*]indoles.

Results and discussion

The vinyl-indole synthesis of carbazoles, originally developed by Nolan, Pindur, Porter and others, involves the D–A cycloaddition of a 2- or 3-vinyl-1*H*-indole (typically either unprotected or containing an electron donating N-protecting group) with a dienophile.[10–22] The resulting D–A cycloadducts are often unstable and are therefore typically oxidised or undergo an *in situ* 1,3-H shift to rearomatise the indole. We postulated that if the intermediate D–A cycloadduct could instead be intercepted *via* an alternative intermolecular reaction this would provide a new multi-component route to functionalised carbazoles. Following on from our recent work on the D–A reactions of vinyl-imidazoles,[23,24] we decided to investigate if the D–A cycloadducts of 3-vinyl-1*H*-indoles could be reacted *in situ* with enophiles to give a new stereoselective three-component, intermolecular D–A/intermolecular ene approach to the carbazole or pyridazino[3,4-*b*]indole scaffold (Fig. 1).[25–29]

We decided to focus our investigation on the D–A reactions of 3-vinyl-1*H*-indoles containing an electron withdrawing

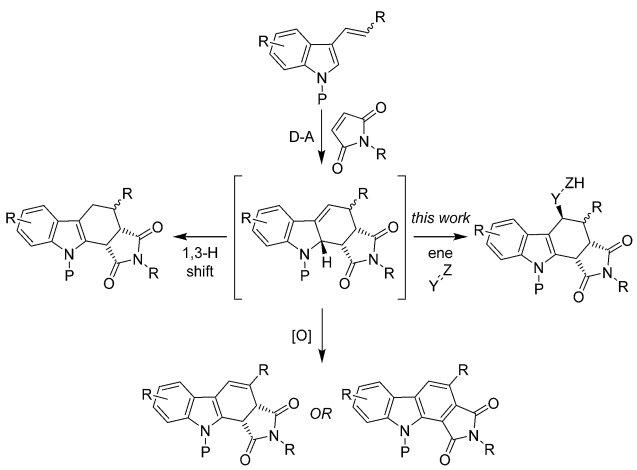

Fig. 1 Typical products of the D–A reaction between 3-vinyl-1*H*-indoles and maleimides verses our proposed trapping of the D–A cycloadduct *via* an intermolecular ene reaction.

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† Electronic supplementary information (ESI) available: ^{1}H and ^{13}C spectra for all new compounds, crystal data and structure refinement tables for compounds **2a**, **2b**, **2d**, **3l**, **3r**, **3u** and **3v**. The crystallographic coordinates of **2a**, **2b**, **2d**, **3l**, **3r**, **3u** and **3v** have been deposited with the Cambridge Crystallographic Data Centre, deposition nos. CCDC 952356, 1040305, 1040306, 952229, 1040307, 1040308 and 952357. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c5ra00499c

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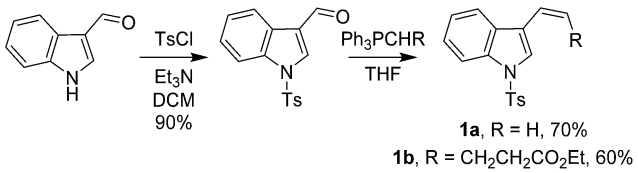


Scheme 1 Synthesis of *N*-tosyl-3-alkenyl-1*H*-indoles **1(a and b)**.

N-protecting group as we postulated that this would stabilise the desired D–A cycloadducts sufficiently to allow either isolation or further *in situ* chemistry.[19,20] Despite the extensive body of work that has been published on the vinyl-indole synthesis of carbazoles,[11–18] the incorporation of electron withdrawing N-protecting groups has been less well studied with the phenylsulfonyl group being the most common.[25,30–33] We therefore decide to focus our initial investigation on tosyl protected systems and embarked on the synthesis of two *N*-tosyl protected 3-alkenyl-indoles through reaction of 1*H*-indole-3-carbaldehyde with tosyl chloride, followed by a Wittig reaction with methylenetriphenyl-λ^5-phosphane or ethyl 4-(triphenyl-λ^5-phosphanylidene)butanoate to give **1a** and **1b** respectively (Scheme 1).

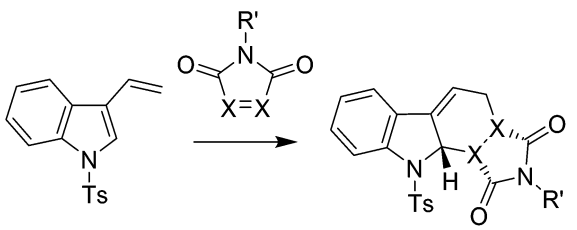
When we reacted 1-tosyl-3-vinyl-1*H*-indole **1a** with 1-methyl-1*H*-pyrrole-2,5-dione in DCM at reflux for 48 hours, we were pleased to isolate, in a 74% yield, the *N*-tosyl protected *endo*-cycloadduct **2a**, which showed little propensity towards spontaneous rearomatisation or oxidation. Whilst 4-phenyl-1,2,4-triazole-3,5-dione (PTAD) reacted rapidly with **1a** at −78 °C in DCM to give the stable D–A cycloadduct **2b** in 88% yield (Table 1).

Attempts to react the more sterically demanding ethyl (*Z*)-5-(1-tosyl-1*H*-indol-3-yl)pent-4-enoate **1b** with 1*H*-pyrrole-2,5-diones under thermal conditions proved unsuccessful with no D–A reaction being observed after prolonged heating in toluene, DCM or iso-propanol. The addition of 20 mol% of 1,3-bis(3,5-bis(trifluoromethyl)phenyl)thiourea[34] also showed no improvement in the D–A reaction, whilst the addition of one equivalent of $TiCl_4$ at −78 °C for 10 minutes resulted in an efficient D–A reaction but was accompanied by the unwanted rearomatisation of the indole. Addition of one equivalent of $AlCl_3$ or Me_2AlCl in DCM at r.t., followed by heating to reflux gave low yields of the desired product **2c** along with recovered starting material. Further optimisation resulted in a final protocol whereby 2 equivalents of Me_2AlCl were added to a DCM solution of **1b** and the requisite 1*H*-pyrrole-2,5-dione at −78 °C, followed by warming to reflux in DCM for 48 hours to give *N*-tosyl protected D–A cycloadducts **2(c–e)** in good yields (Table 2). The structures of **2(a)**, **2(b)** and **2(d)** were confirmed by single crystal X-ray analysis and are consistent with an *endo*-selective D–A reaction (see ESI†).

Next we examined the reactivity of *N*-tosyl protected *endo*-cycloadducts **2(a–e)** towards enophiles. Reaction of **2a** with nitrosobenzene proceeded well at r.t. in 18 hours to give the ene adduct **3a** in 68% isolated yield. We therefore reacted D–A adducts **2(a–e)** with nitrosobenzene and 1-methyl-2-nitrosobenzene at r.t. in DCM, giving high yields of the corresponding ene adducts **3(a, b and e–h)**. The ene reactions of **2(a–c)** also proceeded smoothly with PTAD at 0 °C to give **3(c, i and j)**. The reaction of **2a** with 2,3,4,5,6-pentafluorobenzaldehyde under thermal conditions was unsuccessful. However addition of one equivalent of Me_2AlCl at −78 °C to a mixture of **2a** and 2,3,4,5,6-pentafluorobenzaldehyde resulted in formation of the ene cycloadduct **3d** as a 6 : 1 mixture of diastereomers, epimeric at the *exo*-cyclic hydroxyl position[35] (Table 3).

Since both the D–A and ene reactions are performed in DCM we then decided to examine the potential for reaction telescoping by attempting a D–A/ene reaction sequence under "domino" conditions.[36] 1-Tosyl-3-vinyl-1*H*-indole **1a**, 1-methyl-

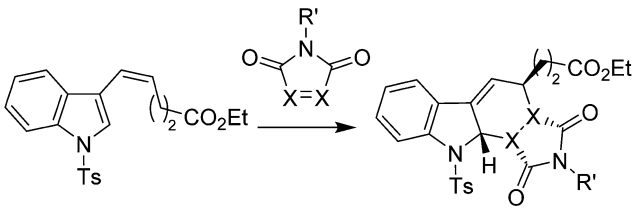
Table 1 D–A reactions of *N*-tosyl protected 1-tosyl-3-vinyl-1*H*-indole **1a**



	Starting material	Dienophile	Reaction Conditions	R′	X	Yield[a]	Product
1	**1a**		40 °C, 48 h	Me	CH	76%	**2a**[b]
2	**1a**		−78 °C, 3.5 h	Ph	N	88%	**2b**[b]

[a] Isolated yields. [b] Structure confirmed by single crystal X-ray analysis.

Table 2 D–A reactions of ethyl (*Z*)-5-(1-tosyl-1*H*-indol-3-yl)pent-4-enoate **1b**



	Starting material	Dienophile	Reaction conditions	R′	X	Yield[a]	Product
1	**1b**		2 eq. Me_2AlCl, −78 °C 30 min, then 40 °C 48 h	Me	CH	85%	**2c**
2	**1b**		2 eq. Me_2AlCl, −78 °C 30 min, then 40 °C 48 h	H	CH	64%	**2d**[b]
3	**1b**		2 eq. Me_2AlCl, −78 °C 30 min, then 40 °C 48 h	Ph	CH	71%	**2e**

[a] Isolated yields. [b] Structure confirmed by single crystal X-ray analysis.

1*H*-pyrrole-2,5-dione and nitrosobenzene were stirred together for 5 days at r.t. in DCM, until **1a** had been consumed by TLC. Examination of the crude reaction mixture showed the formation of a number of by-products (including a rearomatised isomer of D–A cycloadduct **2a**) but the desired domino D–A/ene product **3a** could be isolated as a single diastereomer in a 40% yield.

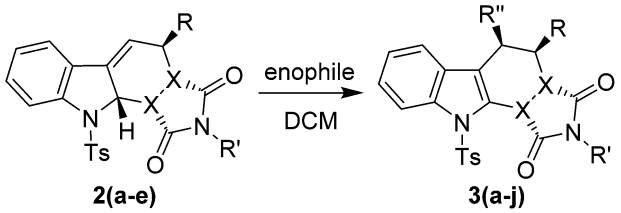
To improve both the yield and reaction flexibility whilst maintaining operational simplicity we next examined a one-pot, sequential addition approach. 1-Tosyl-3-vinyl-1*H*-indole **1a** and 5-methoxy-1-tosyl-3-vinyl-1*H*-indole **1c** (synthesised as previously *via* tosyl protection of 5-methoxy-1*H*-indole-3-carbaldehyde followed by a Wittig reaction with methylenetriphenyl-λ^5-phosphane) were reacted with 1-methyl-1*H*-pyrrole-2,5-dione or 1*H*-pyrrole-2,5-dione in refluxing DCM for 48 hours to give the corresponding D–A cycloadducts. Nitrosobenzene, 1-methyl-2-nitrosobenzene, 2,3,4,5,6-pentafluorobenzaldehyde with one equivalent of Me_2AlCl, or PTAD, were then added directly to the reaction vessels containing the D–A cycloadducts and the ene reactions conducted were under the previously optimised conditions, depending on the enophile. This one-pot three-component approach gave the corresponding D–A/ene products **3(a–d and k–q)** in excellent (70–89%) yields with no purification or work-up of the intermediate D–A cycloadducts required (Table 4).

We therefore continued with this approach, reacting **1a** and **1c** with PTAD as the dienophile followed by *in situ* addition of enophiles (nitrosobenzene, 1-methyl-2-nitrosobenzene, or PTAD) again giving the D–A/ene products **3(e, f, r and s)** cleanly and in good yields (Table 4).

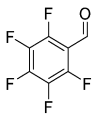
We then decided to examine the range of electron withdrawing N-protecting groups tolerated in our one-pot D–A/ene reaction sequence with a view towards flexibility in the deprotection of the products. Boc protection of 1*H*-indole-3-carbaldehyde proceeded in high yield (triethylamine, Boc anhydride, DCM, 18 h, r.t.), however attempts to synthesise *tert*-butyl 3-vinyl-1*H*-indole-1-carboxylate, by reaction of *tert*-butyl 3-formyl-1*H*-indole-1-carboxylate with methylenetriphenyl-λ^5-phosphane, gave only a 13% yield of the desired product with the major products arising from loss of the Boc group. We therefore focused our efforts on use of the DMAS (dimethylaminosulfonyl) and Cbz protecting groups, and synthesised *N*,*N*-dimethyl-3-vinyl-1*H*-indole-1-sulfonamide **1d** (DMAS), benzyl-3-vinyl-1*H*-indole-1-carboxylate **1e** and benzyl-5-methoxy-3-vinyl-1H-indole-1-carboxylate **1f** (Cbz) *via* appropriate protection of 1*H*-indole-3-carbaldehyde followed by reaction with methylenetriphenyl-λ^5-phosphane as previously.

N,*N*-Dimethyl-3-vinyl-1*H*-indole-1-sulfonamide **1d** was reacted in DCM with 1*H*-pyrrole-2,5-dione, 1-methyl-1*H*-pyrrole-2,5-dione, 1-phenyl-1*H*-pyrrole-2,5-dione and PTAD. After 48 hours at 40 °C for the maleimides, or 1 hour at −78 °C for PTAD, the D–A reactions were complete and *in situ* ene reactions with nitrosobenzene, 1-methyl-2-nitrosobenzene, 1,3-dibromo-2-nitrosobenzene[23] or 2,3,4,5,6-pentafluorobenzaldehyde (catalysed by one equivalent of Me_2AlCl) were carried out to give 69–77% isolated yields of the desired three-component D–A/ene products **3(t–x)** (Table 4). Cbz protected 3-vinyl-1*H*-indoles **1(e and f)** also underwent D–A reactions with 1*H*-pyrrole-2,5-dione, 1-methyl-1*H*-pyrrole-2,5-dione or PTAD followed by *in situ* ene reactions with nitrosobenzene, 1-methyl-2-nitrosobenzene or PTAD to give 54–82% yields of **3(y–ll)** (Table 4). The Cbz protected products **3(y–ll)** were isolable by silica gel chromatography but proved less stable than their DMAS or Tos protected counterparts. NMR investigations of these compounds showed evidence of decomposition in solution at r.t., however they could be stored as solids under an

Table 3 Ene reactions of *N*-tosyl protected cycloadducts **2(a–e)**



2(a-e) **3(a-j)**

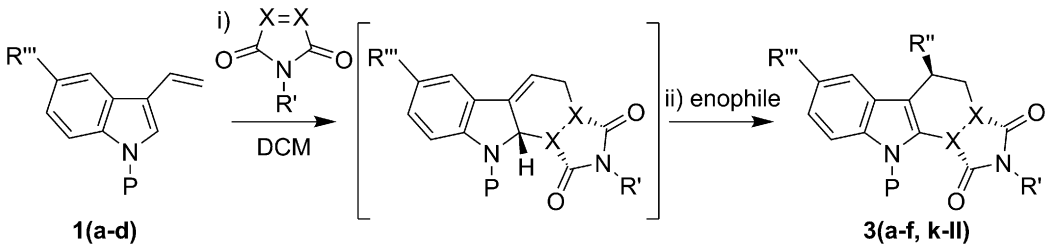
	Starting material	R	R′	X	Enophile	Reaction conditions	R″	Yield[a]	Product
1	**2a**	H	Me	CH		r.t., 18 h	N(Ph)OH	68%	**3a**
2	**2a**	H	Me	CH		r.t., 18 h	N(*o*-Tol)OH	72%	**3b**
3	**2a**	H	Me	CH		0 °C, 2.5 h		73%	**3c**
4	**2a**	H	Me	CH		1 eq. Me_2AlCl, −78 °C, 15 min r.t., 18 h	$CH(C_6F_5)OH$	82%	**3d**[b]
5	**2b**	H	Ph	N		r.t., 18 h	N(Ph)OH	74%	**3e**
6	**2b**	H	Ph	N		r.t., 18 h	N(*o*-Tol)OH	72%	**3f**
7	**2c**	$(CH_2)_2CO_2Et$	Me	CH		r.t., 24 h	N(*o*-Tol)OH	59%	**3g**
8	**2e**	$(CH_2)_2CO_2Et$	Ph	CH		r.t., 24 h	N(*o*-Tol)OH	58%	**3h**
9	**2c**	$(CH_2)_2CO_2Et$	Me	CH		0 °C, 6 h		56%	**3i**
10	**2d**	$(CH_2)_2CO_2Et$	H	CH		0 °C, 6 h		56%	**3j**

[a] Isolated yields. [b] Isolated as a 6 : 1 mixture of diastereomers.

atmosphere of nitrogen at −20 °C for months at a time. Interestingly the ene reactions of 2,3,4,5,6-pentafluorobenzaldehyde with D–A cycloadducts **3(d, m, p and v)** gave a mixture of diastereomers at the *exo*-cyclic hydroxyl group, with ratios from 5 : 1 to >25 : 1. The relative stereochemistry of **3v** was confirmed through the solution of a single crystal X-ray structure (see ESI†) and is consistent with an *endo*-selective ene reaction, providing some support for an ene mechanism in this reaction rather than a nucleophilic attack of the D–A cycloadducts to the carbonyl carbon of the aldehyde in the manner of an vinylogous enamine.[37]

Finally we investigated the deprotection of our D–A/ene reaction products. Tosyl and DMAS protected compounds **3(a–x)** proved intransient to a range of basic (NaOH, KOH or KOEt in EtOH, MeOH or H_2O with Bu_4NBr) and reducing (Mg, Mg/Hg or Na/Hg) deprotection conditions. We therefore focused on the deprotection of Cbz protected compounds **3(y–ll)**. Initial attempts at Cbz removal with H_2 and Pd/C proved unsuccessful. Atmospheric pressure hydrogenation with Adam's catalyst in either MeOH and EtOH resulted in the removal of the Cbz group from **3z**, however unexpected

Table 4 One-pot D–A/ene reactions of N-protected 3-vinyl-1*H*-indoles



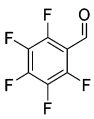
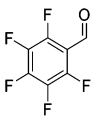
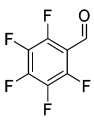
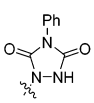
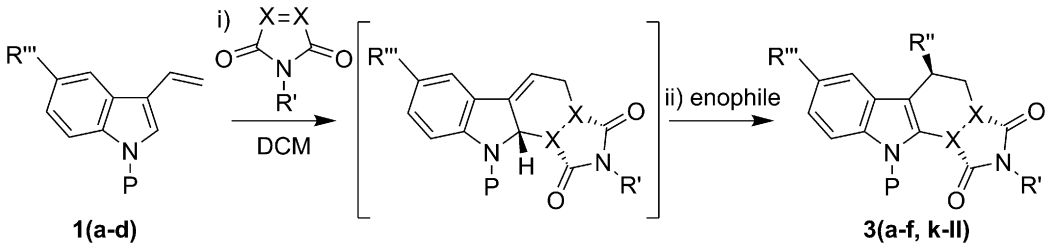
	Starting Material	P	R‴	R′	X	Enophile	R″	Reaction conditions	Product	Yield[a]
1	**1a**	Tos	H	Me	CH		–N(Ph)OH	(i) 40 °C, 48 h, (ii) r.t., 18 h	**3a**	71%
2	**1a**	Tos	H	Me	CH		–N(*o*-Tol)OH	(i) 40 °C, 48 h, (ii) r.t., 18 h	**3b**	71%
3	**1a**	Tos	H	Me	CH			(i) 40 °C, 48 h, (ii) 0 °C, 4 h	**3c**	76%
4	**1a**	Tos	H	Me	CH		–CH(C_6F_5)OH	(i) 40 °C, 48 h, (ii) Me_2AlCl, −78 °C to r.t., 18 h	**3d**	72%[b]
5	**1a**	Tos	H	Ph	N		–N(Ph)OH	(i) −78 °C, 4 h, (ii) r.t., 24 h	**3e**	66%
6	**1a**	Tos	H	Ph	N		–N(*o*-Tol)OH	(i) −78 °C, 4 h, (ii) r.t., 24 h	**3f**	66%
7	**1a**	Tos	H	H	CH		–N(Ph)OH	(i) 40 °C, 48 h, (ii) r.t., 4 h	**3k**	89%
8	**1a**	Tos	H	H	CH		–N(*o*-Tol)OH	(i) 40 °C, 48 h, (ii) r.t., 4 h	**3l**	82%[c]
9	**1a**	Tos	H	H	CH		–CH(C_6F_5)OH	(i) 40 °C, 48 h, (ii) Me_2AlCl, 0 °C to r.t., 18 h	**3m**	71%[d]
10	**1a**	Tos	H	H	CH			(i) 40 °C, 48 h, (ii) 0 °C, 4 h	**3n**	75%
11	**1c**	Tos	OMe	H	CH		–N(*o*-Tol)OH	(i) 40 °C, 48 h, (ii) r.t., 24 h	**3o**	76%
12	**1c**	Tos	OMe	Me	CH		–CH(C_6F_5)OH	(i) 40 °C, 48 h, (ii) Me_2AlCl, −78 °C, 15 min then r.t., 18 h	**3p**	70%[e]
13	**1c**	Tos	OMe	H	CH			(i) 40 °C, 48 h, (ii) 0 °C, 4 h	**3q**	72%

Table 4 (*Contd.*)



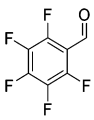
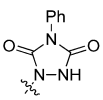
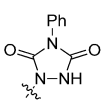
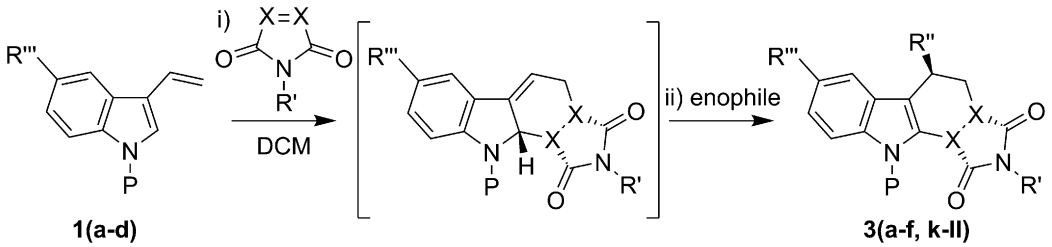
	Starting Material	P	R‴	R′	X	Enophile	R″	Reaction conditions	Product	Yield[a]
14	**1a**	Tos	H	Ph	N			(i) −78 °C, 4 h, (ii) 0 °C, 4 h	**3r**	65%[c]
15	**1c**	Tos	OMe	Ph	N		–N(*o*-Tol)OH	(i) −78 °C then r.t. 23 h, (ii) r.t., 23 h	**3s**	72%
16	**1d**	DMAS	H	Me	CH		–N(*o*-Tol)OH	(i) 40 °C, 48 h, (ii) r.t., 3 h	**3t**	74%
17	**1d**	DMAS	H	Ph	CH		–N(2,4-$(Br)_2C_6H_4$)-OH	(i) 40 °C, 48 h, (ii) r.t., 18 h	**3u**	69%[c]
18	**1d**	DMAS	H	Me	CH		–CH(C_6F_5)OH	(i) 40 °C, 48 h, (ii) Me_2AlCl, −78 °C, 1 h	**3v**	77%[c,f]
19	**1d**	DMAS	H	Ph	N		–N(*o*-Tol)OH	(i) −78 °C, 1 h, (ii) r.t., 4 h	**3w**	76%
20	**1d**	DMAS	H	H	CH		–N(*o*-Tol)OH	(i) 40 °C, 48 h, (ii) r.t., 3 h	**3x**	77%
21	**1e**	Cbz	H	Me	CH		–N(Ph)OH	(i) 40 °C, 24 h, (ii) r.t., 18 h	**3y**	74%
22	**1e**	Cbz	H	Me	CH		–N(*o*-Tol)OH	(i) 40 °C, 24 h, (ii) r.t., 18 h	**3z**	78%
23	**1e**	Cbz	H	Me	CH			(i) 40 °C, 24 h, (ii) 0 °C, 1 h then r.t., 18 h	**3aa**	54%
24	**1e**	Cbz	H	H	CH		–N(Ph)OH	(i) 40 °C, 24 h, (ii) r.t., 18 h	**3bb**	70%
25	**1e**	Cbz	H	H	CH		–N(*o*-Tol)OH	(i) 40 °C, 24 h, (ii) r.t., 4 h	**3cc**	83%
26	**1e**	Cbz	H	H	CH			(i) 40 °C, 24 h, (ii) 0 °C, 1 h	**3dd**	58%

Table 4 (*Contd.*)



	Starting Material	P	R‴	R′	X	Enophile	R″	Reaction conditions	Product	Yield[a]
27	**1e**	Cbz	H	Ph	N		–N(Ph)OH	(i) −78 °C, 5 h, (ii) r.t., 3 h	**3ee**	72%
28	**1e**	Cbz	H	Ph	N		–N(*o*-Tol)OH	(i) −78 °C, 5 h, (ii) r.t., 18 h	**3ff**	68%
29	**1f**	Cbz	OMe	Me	CH		–N(Ph)OH	(i) 40 °C, 18 h, (ii) r.t., 1.5 h	**3gg**	73%
30	**1f**	Cbz	OMe	Me	CH		–N(*o*-Tol)OH	(i) 40 °C, 18 h, (ii) r.t., 3 h	**3hh**	74%
31	**1f**	Cbz	OMe	H	CH		–N(Ph)OH	(i) 40 °C, 18 h, (ii) r.t., 2.5 h	**3ii**	79%
32	**1f**	Cbz	OMe	H	CH		–N(*o*-Tol)OH	(i) 40 °C, 18 h, (ii) r.t., 3.5 h	**3jj**	76%
33	**1f**	Cbz	OMe	Ph	N		–N(Ph)OH	(i) −78 °C, 1.5 h, (ii) r.t., 20 h	**3kk**	78%
34	**1f**	Cbz	OMe	Ph	N		–N(*o*-Tol)OH	(i) −78 °C, 1.5 h, (ii) r.t., 24 h	**3ll**	82%

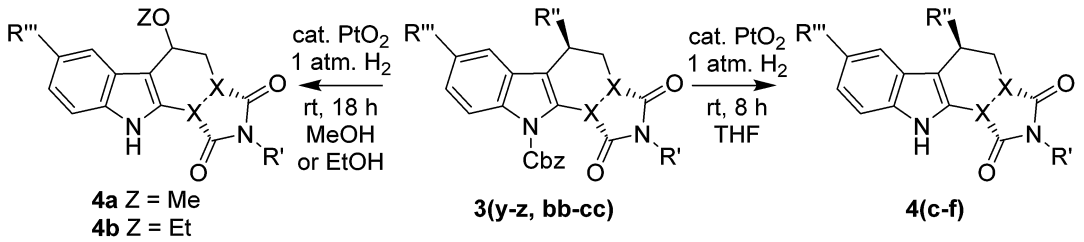
[a] Isolated yields. [b] 5 : 1 *endo* : *exo*. [c] Structure confirmed by single crystal X-ray analysis. [d] 25 : 1 *endo* : *exo*. [e] 10 : 1 *endo* : *exo*. [f] Only one diastereomer observed.

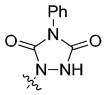
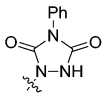
nucleophilic substitutions of the hydroxy(aryl)amino group by MeOH or EtOH also occurred to give **4a** and **4b** respectively. This gave the first indication that the removal of the electronically stabilising N-protecting group perhaps unsurprisingly lowers the activation energy barrier towards substitution chemistry at the indolylic position.[38–40] Replacement of the alcoholic solvent with THF resulted in a cleaner deprotection of Cbz protected indoles **3(y–ll)** to give **4(c–p)** in 38–91% yields. However the products **4(c–p)** showed some evidence of decomposition in $CDCl_3$ after a few hours at r.t., with the appearance of new peaks in the ^{1}H NMR spectra. Therefore NMR analysis of **4(c–p)** was carried out in either d_2-DCM or d_6-DMSO (depending on solubility) in which decomposition was slowed, although the appearance of minor peaks in the ^{1}H NMR could still be observed over time. The deprotection of indoles **3(y–ll)** with H_2 and Adam's catalyst in THF has allowed us to successfully demonstrate a one-pot, three-component approach to our target library of deprotected partially saturated carbazoles and pyridazino[3,4-*b*]indoles, which will be the focus of future investigations (Table 5).

Conclusions

In conclusion, we have developed a practically simple three-component approach to Tos, DMAS and Cbz protected partially saturated carbazoles and pyridazino[3,4-*b*]-indoles, based on a one-pot D–A/ene reaction, including the examination of a deprotection strategy of the Cbz

Table 5 Deprotection of 3(y, z, bb and cc)



	Starting material	R′	X	R″	R″	Solvent	Product	Yield[a]
1	**3z**	Me	CH	–N(*o*-Tol)OH	H	MeOH	**4a**	60%
2	**3z**	Me	CH	–N(*o*-Tol)OH	H	EtOH	**4b**	24%
3	**3y**	Me	CH	–N(Ph)OH	H	THF	**4c**	75%
4	**3z**	Me	CH	–N(*o*-Tol)OH	H	THF	**4d**	87%
5	**3aa**	Me	CH		H	THF	**4e**	91%
6	**3bb**	H	CH	–N(Ph)OH	H	THF	**4f**	41%
7	**3cc**	H	CH	–N(*o*-Tol)OH	H	THF	**4g**	70%
8	**3dd**	H	CH		H	THF	**4h**	64%
9	**3ee**	Ph	N	–N(Ph)OH	H	THF	**4i**	65%
10	**3ff**	Ph	N	–N(*o*-Tol)OH	H	THF	**4j**	44%
11	**3gg**	Me	CH	–N(Ph)OH	OMe	THF	**4k**	70%
12	**3hh**	Me	CH	–N(*o*-Tol)OH	OMe	THF	**4l**	70%
13	**3ii**	H	CH	–N(Ph)OH	OMe	THF	**4m**	60%
14	**3jj**	H	CH	–N(*o*-Tol)OH	OMe	THF	**4n**	85%
15	**3kk**	Ph	N	–N(Ph)OH	OMe	THF	**4o**	38%
16	**3ll**	Ph	N	–N(*o*-Tol)OH	OMe	THF	**4p**	61%

[a] Isolated yields.

group. Current work is looking into controlling the reactivity and biological activity of the final products as well as investigating enantioselective D–A/ene approaches for molecules of this type.

Experimental

3-Vinyl-1*H*-indole

In a Schlenk flask, methyltriphenylphosphonium iodide (2.14 g, 5.3 mmol) was dissolved in dry THF (13 mL). The solution was cooled to −78 °C and ^{n}butyllithium (2.9 mL, 4.6 mmol) was added over 10 minutes. The yellow solution was warmed to 0 °C and was left to stir for 1 hour before being cooled to −78 °C. In a separate Schlenk flask, 1*H*-indole-3-carboxylate (0.67 g, 4.6 mmol) was dissolved in THF (7 mL) and to the solution sodium bis(trimethylsilyl)amide (2.3 mL, 4.6 mmol) was added. This solution was transferred into the first Schlenk flask and the red solution was allowed to stir at room temperature for 1 hour. The reaction was poured into water (30 mL) and extracted with ethyl acetate (2 × 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed under pressure to leave the crude product as yellow oil. The product was purified using column chromatography (petrol (40/60)–diethyl ether 7 : 3, column diameter = 4 cm, silica = 20 cm) to give 3-vinyl-1*H*-indole (0.636 g, 4.4 mmol, 95%) as a yellow powder.

Mp: 78.4–80.7 °C; R_f: 0.76 (Pet(40/60)–EA, 1 : 1); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 8.02 (1H, br s), 7.85–7.80 (1H, m), 7.32–7.28 (1H, m), 7.18 (1H, s), 7.18–7.09 (2H, m), 6.83 (1H, ddd, J = 17.7, 11.2, 0.5 Hz), 5.65 (1H, dd, J = 17.7, 1.5 Hz), 5.11 (1H, dd, J = 11.2, 1.5 Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ 136.8, 129.5, 125.7, 123.6, 122.6, 120.4, 120.2, 115.9, 111.4, 110.9; IR (neat): ν_{max}/cm^{-1} 3660, 2981.

1a – 1-tosyl-3-vinyl-1*H*-indole

Into a Schlenk flask, was placed 1*H*-indole-3-carbaldehyde (5.0 g, 34.5 mmol) and DCM (100 mL). The resulting stirred solution was cooled to 0 °C before triethylamine (12 mL, 86.2 mmol) was added dropwise *via* syringe. To the stirred solution, *p*-toluenesulfonyl chloride (7.23 g, 37.9 mmol) in DCM was added dropwise over a period of 20 minutes. The solution was stirred at 0 °C for a further one hour before warming to room temperature over 18 hours. The solution was washed into a separating funnel with DCM (20 mL) and washed with water (2 × 100 mL) and brine (100 mL). The organic extracts were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure to give the crude product as a pale orange oil.

The product was purified by recrystallisation from hot ethyl acetate (150 mL) to give 1-tosyl-1*H*-indole-3-carbaldehyde (8.38 g, 28 mmol, 82%) as orange crystals.

Mp: 145.3–148.8 °C; R_f: 0.83 (Pet(40/60)–EA 1 : 4); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 10.11 (1H, s), 8.29–8.26 (1H, m), 8.19–8.16 (1H, m), 8.16 (1H, s), 7.89–7.85 (1H, m), 7.78 (2H, d, J = 8.4 Hz), 7.36–7.25 (2H, m), 7.22 (2H, d, J = 8.4 Hz), 2.29 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$): δ 185.3, 146.1, 136.2, 135.4, 134.1, 130.3, 130.2, 127.2, 127.1, 126.2, 124.9, 122.5, 122.2, 113.1, 21.5; IR (neat): ν_{max}/cm^{-1} 3140, 1663; anal. calcd for $C_{16}H_{13}NO_3S$: C, 64.20; H, 4.38; N, 4.68. Found: C, 63.97; H, 4.52; N, 4.72.

A Schlenk flask was charged with methyltriphenylphosphonium iodide (1.29 g, 3.2 mmol) dissolved in dry THF (25 mL) under a nitrogen atmosphere. The solution was cooled to −78 °C and ^{n}butyllithium (1.81 mL, 2.97 mmol) was added dropwise *via* syringe over 10 minutes. The solution was warmed to 0 °C and left to stir for 2 hours. In a separate Schlenk flask, 1-tosylindoline-3-carbaldehyde (0.8 g, 2.7 mmol) was dissolved in THF (5 mL). The indole solution was transferred *via* cannula to the Schlenk flask containing the solution of methyltriphenylphosphonium iodide and the solution was stirred for 18 hours. The reaction poured into water (50 mL) and extracted with ether (3 × 40 mL). The organic layers were washed with brine (20 mL), dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure to leave the crude product as an orange oil. The crude product was purified by column chromatography (petrol (40/60)–ethyl acetate; 10 : 1, 2 cm diameter column) to give 1-tosyl-3-vinyl-1*H*-indole (0.56 g, 3.9 mmol, 70%) as a pale yellow powder.

Mp: 90.3–94.6 °C; R_f: 0.86 (Pet(40/60)–EA, 1 : 1); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.93–7.90 (1H, m), 7.69 (2H, d, J = 8.4 Hz), 7.70–7.65 (1H, m), 7.53 (1H, s), 7.29–7.19 (2H, m), 7.29–7.17 (2H, m), 7.15 (2H, d, J = 8.4 Hz), 6.70 (1H, app ddd, J = 17.9, 11.3, 0.7 Hz), 5.72 (dd, 1H, J = 17.9, 1.2 Hz), 5.28 (1H, dd, J = 11.3, 1.2 Hz), 2.26 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 145.1, 135.6, 135.2, 130.0, 129.1, 127.6, 126.9, 125.0, 124.2, 123.6, 121.0, 120.5, 115.4, 113.8, 21.7; IR (neat): ν_{max}/cm^{-1} 3119, 3072; anal. calcd for $C_{17}H_{15}NO_2S$: C, 68.66; H, 5.08; N, 4.71. Found: C, 68.70; H, 5.21; N, 4.61.

1b – ethyl (*Z*)-5-(1-tosyl-1*H*-indol-3-yl)pent-4-enoate

In a Schlenk flask, (4-ethoxy-4-oxobutyl) triphenylphosphonium bromide (3.32 g, 7.26 mmol) was dissolved in dry THF (20 mL). The solution was cooled to −78 °C and sodium bis (trimethylsilyl) amide (1.00 M in THF, 8.58 mL, 8.58 mmol) was added dropwise over 10 min. The mixture was warmed to 0 °C and left to stir. After 2 hours, 1-(toluene-4-sulfonyl)-1*H*-indol-3-carboxaldehyde (2.00 g, 6.60 mmol) was dissolved in dry THF (10 mL) in a separate round bottomed flask, and transferred *via* cannula into the reaction solution. The reaction mixture was stirred at room temperature and for 48 hours, quenched with saturated $NH_4Cl_{(aq.)}$ (30 mL), extracted with EtOAc (2 × 200 mL), and the combined organic layers washed with brine, dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure to give a crude product as orange oil. The product was purified by column chromatography (petrol (40/60)–ethyl acetate 10 : 1) to give two fractions the first containing ethyl (*Z*)-5-(1-tosyl-1*H*-indol-3-yl)pent-4-enoate (1.568 g, 3.94 mmol, 60%) as a colourless oil, and a second fraction containing a 20 : 1 mixture of (*Z*) and (*E*) ethyl-5-(1-tosyl-1*H*-indol-3-yl)pent-4-enoate (0.294 g, 0.739 mmol, 11%) also as a colourless oil.

R_f: 0.70 (Pet(40/60)–EA 7 : 3); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.97 (1H, d, J = 7.9 Hz, 1H), 7.77 (2H, d, J = 7.8 Hz), 7.57 (1H, s), 7.49 (1H, d, J = 7.9 Hz), 7.32 (1H, t, J = 7.9 Hz), 7.25 (1H, t, J = 7.9 Hz), 7.20 (2H, d, J = 7.8 Hz), 6.44 (1H, d, J = 11.2 Hz), 5.78 (1H, dt, J = 11.2, 7.5 Hz), 4.14 (2H, q, J = 6.5 Hz), 2.67–2.62 (2H, m), 2.48 (2H, t, J = 6.9 Hz), 2.30 (3H, s), 1.24 (3H, t, J = 6.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 172.8, 145.1, 135.1, 134.6, 132.1, 130.8, 129.9, 126.8, 124.9, 123.6, 123.4, 119.5, 118.96, 113.6, 60.5, 34.1, 25.2, 21.6, 14.3; IR (neat): ν_{max}/cm^{-1}: 1727, 1597. MS (pNSI): 415.2 (100%, $[M + NH_4]^+$), 398.1 (20%, $[M + H]^+$), 420.1 (10%, $[M + Na]^+$); HRMS (pNSI): calcd $C_{22}H_{24}NO_4S$ $[M + H]^+$: 398.14120; observed: 398.14120.

1c – 5-methoxy-1-tosyl-3-vinyl-1*H*-indole

To a stirred round bottomed flask was added 5-methoxy-1*H*-indole-3-carbaldehyde (0.70 g, 4.00 mmol) and DCM (20 mL) and the solution was cooled to 0 °C. To the stirred solution was added triethylamine (1.40 mL, 10.0 mmol) and the resulting solution was stirred at 0 °C for 1 hour. To the stirred solution was added *p*-toluenesulfonyl chloride (0.84 g, 4.40 mmol) in DCM (10 mL) and the solution was stirred at room temperature for 18 hours. The reaction was poured into water (50 mL) and extracted with DCM (3 × 20 mL). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure to leave the crude product as a pale orange solid. The product was purified using column chromatography (petrol (40/60)–ether–DCM 2 : 1 : 1, column diameter = 2 cm, silica = 15 cm) to give 5-methoxy-1-tosyl-1*H*-indole-3-carbaldehyde (1.14 g, 3.48 mmol, 87%) as a pale brown powder.

Mp: 126.1–128.4 °C; R_f: 0.71 (Pet(40/60)–Et_2O–DCM 2 : 1 : 1); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 10.07 (1H, s), 8.19 (1H, s), 7.86–7.83 (1H, m), 7.84 (2H, d, J = 8.5 Hz), 7.72 (1H, d, J = 2.6 Hz), 7.29 (2H, d, J = 8.5 Hz), 7.02 (1H, dd, J = 9.1, 2.6 Hz), 3.86 (3H, s), 2.38 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 185.6, 157.8, 146.2, 136.8, 134.4, 130.4, 129.8, 127.4, 127.2, 122.3, 116.2, 114.2, 104.1, 55.8, 21.8; IR (neat): ν_{max}/cm^{-1} 3128, 2832, 1671; anal. calcd for $C_{17}H_{15}NO_4S$: C, 61.99; H, 4.59; N, 4.25. Found: C, 61.77; H, 4.70; N, 4.29.

In a Schlenk flask, methyltriphenylphosphonium iodide (1.35 g, 3.34 mmol) was dissolved in dry THF (30 mL). The solution was cooled to −78 °C and ^{n}BuLi (1.2 mL, 3.03 mmol) was added over 5 minutes. The yellow solution was warmed to 0 °C and was allowed to stir for 1 hour before being cooled to −78 °C. To the stirred solution, 5-methoxy-1-tosyl-1*H*-indole-3-carbaldehyde (1.00 g, 3.03 mmol) in DCM (10 mL) was added and the solution was stirred at room temperature for 3 hours. The reaction was poured into water (40 mL) and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed under pressure to leave the crude product an orange oil. The product was purified using column chromatography (petrol (40/60)–

ethyl acetate 2 : 1, column diameter = 2 cm, silica = 16 cm) to give 5-methoxy-1-tosyl-3-vinyl-1*H*-indole (0.79 g, 2.42 mmol, 80%) as a brown powder.

Mp: 101.4–103.9 °C; R_f: 0.66 (Pet(40/60)–EA 2 : 1); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.87 (1H, d, J = 9.0 Hz), 7.73 (2H, d, J = 8.4 Hz), 7.55 (1H, s), 7.19 (2H, d, J = 8.3 Hz), 7.14 (1H, d, J = 2.5 Hz), 6.93 (1H, dd, J = 9.0, 2.5 Hz), 6.72 (1H, dd, J = 17.9, 11.3 Hz), 5.73 (1H, dd, J = 17.9, 1.1 Hz), 5.32 (1H, dd, J = 11.3, 1.1 Hz), 3.82 (3H, s), 2.31 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 156.7, 145.0, 135.1, 130.3, 130.1, 130.0, 127.6, 126.9, 124.9, 121.1, 115.2, 114.7, 113.7, 103.2, 55.8, 21.7; IR (neat): ν_{max}/cm^{-1} 3128, 2832, 1671; MS (pNSI): 328.1 (100%, $(M + H)^+$), 350.1 (15%, $(M + Na)^+$), 672.2 $(2M + NH_4)^+$; HRMS (pNSI): calcd for $C_{18}H_{18}NO_3S$ $[M + H]^+$: 328.1002; observed: 328.1007.

1d – *N*,*N*-dimethyl-3-vinyl-1*H*-indole-1-sulfonamide

To a stirred round bottomed flask was added 1*H*-indole-3-carbaldehyde (3.0 g, 20.7 mmol) and THF (70 mL) and the solution was cooled to 0 °C. To the stirred solution was added sodium hydride (1.7 g, 41.4 mmol) in THF (30 mL) and the resulting solution was stirred at 0 °C for 1 hour. To the stirred solution was added dimethylsulfamoyl chloride (2.4 mL, 20.7 mmol) and the solution was stirred at room temperature for 18 hours. The reaction was poured into water (100 mL) and extracted with DCM (3 × 60 mL). The combined organic extracts were dried over MgSO4, filtered and the solvent was removed under reduced pressure to leave the crude product as a pale red pink solid. The product was purified by recrystallization from ethyl acetate to give 3-formyl-*N*,*N*-dimethyl-1*H*-indole-1-sulfonamide (97%, 5.07 g, 20.1 mmol) as a pink powder.

Mp: 149.0–150.9 °C; R_f: 0.63 (Pet(40/60)–EA, 1 : 1); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 10.08 (1H, s), 8.31 (1H, app dd, J = 7.2, 1.4 Hz), 8.09 (1H, s), 7.94–7.88 (1H, m), 7.40 (2H, app ddd, J = 5.9, 3.3, 1.6 Hz), 2.91 (6H, s); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 185.5, 137.3, 136.0, 126.1, 125.9, 124.9, 122.6, 120.8, 113.6, 38.6; IR (neat): ν_{max}/cm^{-1} 3124, 2945, 1662; anal. calcd for $C_{11}H_{12}N_2O_3S$: C, 52.37; H, 4.79; N, 11.10. Found: C, 52.23; H, 4.91; N, 10.92.

In a Schlenk flask, methyltriphenylphosphonium iodide (7.00 g, 17.4 mmol) was dissolved in dry THF (75 mL). The solution was cooled to −78 °C and ^{n}BuLi (6.4 mL, 15.9 mmol) was added over 10 minutes. The yellow solution was warmed to 0 °C and was left to stir for 1 hour before being cooled to −78 °C. To the stirred solution, 3-formyl-*N*,*N*-dimethyl-1*H*-indole-1-sulfonamide (4.00 g, 15.9 mmol) was added and the solution was stirred at room temperature for 3 hours. The reaction was poured into water (70 mL) and extracted with ethyl acetate (3 × 50 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed under pressure to leave the crude product as yellow oil. The product was purified using column chromatography (petrol (40/60)–diethyl ether 4 : 1, column diameter = 3 cm, silica = 14 cm) to give *N*,*N*-dimethyl-3-vinyl-1*H*-indole-1-sulfonamide (3.11 g, 12.4 mmol, 78%) as a pale orange powder.

Mp: 68.7–67.8 °C; R_f: 0.63 (Pet(40/60)–EA 2 : 1); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.98 (1H, dd, J = 8.0, 1.4 Hz), 7.85 (1H, dd, J = 7.7, 1.5 Hz), 7.35 (2H, app ddd, J = 7.0, 5.3, 1.6 Hz), 6.83 (1H, dd, J = 17.8, 11.2 Hz), 5.84 (1H, dd, J = 17.8, 1.2 Hz), 5.38 (1H, dd, J = 11.3, 1.2 Hz), 2.86 (6H, s); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 136.1, 128.2, 127.8, 125.2, 124.7, 123.1, 120.4, 118.8, 114.9, 114.0, 38.6; IR (neat): ν_{max}/cm^{-1} 3123, 2945; anal. calcd for $C_{12}H_{14}N_2O_2S$: C, 57.58; H, 5.64; N, 11.19. Found: C, 57.68; H, 5.75; N, 11.05.

1e – benzyl-3-vinyl-1*H*-indole-1-carboxylate

To a solution of 1*H*-indole-3-carbaldehyde (1.0 g, 6.9 mmol) in DCM (20 mL) at 0 °C was added triethylamine (1.8 mL, 17.3 mmol) dropwise. The solution was stirred at room temperature for 1 hour before benzyl chloroformate (1.4 mL, 8.3 mmol) was added. The solution was stirred for 18 hours after which it was poured into water and extracted with DCM (3 × 20 mL). The organic fractions were combined, dried with $MgSO_4$, filtered and the solvent was removed under reduced pressure to give the crude product as an orange powder. The crude product was purified by column chromatography (column diameter = 2.5 cm, eluent = petrol (40/60)–ethyl acetate 2 : 1) to give benzyl-3-formyl-1*H*-indole-1-carboxylate (1.74 g, 6.35 mmol, 92%) as a pale orange powder.

Mp: 91–92 °C; R_f: 0.68 (Pet–EA, 2 : 1); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 10.06 (1H, s), 8.30–8.25 (1H, m), 8.23 (1H, s), 8.17 (1H, d, J = 8.0 Hz), 7.50 (2H, app dd, J = 7.7, 1.8 Hz), 7.42 (3H, app ddd, J = 6.6, 5.1, 1.5 Hz), 7.38 (1H, app t, J = 1.6 Hz), 7.37–7.34 (1H, m), 5.49 (2H, s); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 185.8, 150.2, 136.1, 136.1, 134.3, 129.3, 129.0, 128.9, 126.5, 126.1, 125.0, 122.3, 122.3, 115.2, 69.9; IR (neat): ν_{max}/cm^{-1} 3127, 3008, 1733; MS (pNSI): 280.1 (100%, $(M + H)^+$), 302.1 (96%, $(M + Na)^+$), 581.2 (25%, $(2M + Na)^+$); HRMS (pNSI): calcd for $C_{17}H_{14}NO_3$ $[M + H]^+$: 280.0968; observed: 280.0970.

To a stirred Schlenk flask, methylenetriphenylphosphorane (2.38 g, 5.90 mmol) was dissolved in dry THF (30 mL). The solution was cooled to −78 °C and ^{n}BuLi (2.15 mL, 5.35 mmol) was added over 10 minutes. The yellow solution was warmed to 0 °C and was left to stir for 1 hour before being cooled to −78 °C. To the stirred solution, benzyl 3-formyl-1*H*-indole-1-carboxylate (1.50 g, 5.35 mmol) was added and the solution was stirred at room temperature for 3 hours. The reaction was poured into water (50 mL) and extracted with ethyl acetate (3 × 40 mL). The combined organic layers were dried with $MgSO_4$, filtered and the solvent removed under pressure to leave the crude product as yellow oil. The product was purified using column chromatography (petrol (40/60)–ethyl acetate 2 : 1, column diameter = 2 cm, silica = 15 cm) to give benzyl-3-vinyl-1*H*-indole-1-carboxylate (1.14 g, 4.07 mmol, 76%) as a yellow powder.

Mp: 43–45 °C; R_f: 0.73 (Pet(40/60)–EA, 2 : 1); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 8.33 (1H, d, J = 7.1 Hz), 7.91–7.86 (1H, m), 7.74 (1H, s), 7.58–7.55 (2H, m), 7.52–7.44 (4H, m), 7.43–7.36 (1H, m), 6.87 (1H, dd, J = 17.8, 11.3 Hz), 5.96–5.87 (1H, d, J = 17.8 Hz), 5.51 (2H, s), 5.44 (1H, d, J = 11.3 Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 150.8, 135.1, 128.9, 128.9, 128.8, 128.6, 128.4, 128.0, 125.1, 123.6, 123.4, 120.2, 120.2, 115.5, 115.0, 68.9; IR (neat): ν_{max}/cm^{-1} 3153, 2962, 1729; MS (pAPCI): 181.1 (50%), 260.1 (100%), 278.1 (25%, $(M + H)^+$);

HRMS (pAPCI): calcd for $C_{18}H_{16}NO_2$ $[M + H]^+$: 278.1176; observed: 278.1173.

1f – benzyl-5-methoxy-3-vinyl-1*H*-indole-1-carboxylate

To a stirred Schlenk flask, methylenetriphenylphosphorane (3.54 g, 8.70 mmol) was dissolved in dry THF (34 mL). The solution was cooled to −78 °C and ^{n}BuLi (3.1 mL, 7.87 mmol) was added over 10 minutes. The yellow solution was warmed to 0 °C and was left to stir for 1 hour before being cooled to −78 °C. In a separate Schlenk flask, 5-methoxy-1*H*-indole-3-carbaldehyde (1.38 g, 7.87 mmol) was dissolved in THF (10 mL) and to the solution sodium bis(trimethylsilyl)amide (7.87 mL, 7.87 mmol) was added. This solution was transferred into the first Schlenk flask and the red solution was allowed to stir at room temperature for 1 hour. The reaction was poured into water (50 mL) and extracted with ethyl acetate (2 × 30 mL). The combined organic layers were dried with $MgSO_4$, filtered and the solvent removed under pressure to leave the crude product as yellow oil. The product was purified using column chromatography (petrol (40/60)–diethyl ether 2 : 1, column diameter = 2.5 cm, silica = 16 cm) to give 5-methoxy-3-vinyl-1*H*-indole (1.38 g, 7.6 mmol, 97%) as a yellow powder.

Mp: 190–193 °C; R_f: 0.49 (Pet–Et_2O, 2 : 1); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 8.28 (1H, s), 7.66 (1H, d, J = 2.4 Hz), 7.29 (1H, d, J = 8.8 Hz), 7.24 (1H, d, J = 2.7 Hz), 7.20–7.10 (2H, m), 7.18 (1H, d, J = 2.5 Hz), 7.15 (2H, dd, J = 4.5, 2.1 Hz), 7.10 (1H, s), 5.95 (1H, dd, J = 17.8, 1.5 Hz), 5.46 (1H, dd, J = 11.2, 1.5 Hz), 4.07 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 154.4, 132.5, 130.8, 126.4, 126.1, 114.2, 113.0, 112.0, 109.1, 102.0, 55.9; IR (neat): ν_{max}/cm^{-1} 3410, 2925, 2836; MS (pNSI): 174.1 (100%, $(M + H)^+$), 520.3 (100%, $(3M + H)^+$); HRMS (pNSI): calcd for $C_{11}H_{12}NO$ $[M + H]^+$: 174.0913; observed: 174.0912.

To a stirred Schlenk flask, 5-methoxy-3-vinyl-1*H*-indole (1.15 g, 6.61 mmol) was dissolved in THF (30 mL) and the solution was cooled to 0 °C. To the stirred solution, sodium bis(trimethylsilyl)amide (7.27 mL, 7.27 mmol) was added and the solution was stirred for 30 minutes before benzyl chloroformate (0.90 mL, 6.61 mmol) was added. The solution was stirred for 30 minutes at room temperature before being added to water (50 mL) and extracted with ethyl acetate (3 × 30 mL). The combined organic washings were dried with $MgSO_4$, filtered and the solvent was removed under reduced pressure to give the crude product as an orange oil. The product was purified using column chromatography (petrol (40/60)–ethyl acetate 5 : 1, column diameter = 2.0 cm, silica = 15 cm) to give benzyl-5-methoxy-3-vinyl-1*H*-indole-1-carboxylate (1.78 g, 4.7 mmol, 71%) as a pale yellow oil.

R_f: 0.82 (Pet(40/60)–EA, 5 : 1); ^{1}H NMR (400 MHz), δ_H 8.09 (1H, s), 7.66 (1H, s), 7.50 (2H, d, J = 7.2 Hz), 7.45–4.37 (1H, m), 7.25 (1H, d, J = 2.5 Hz), 6.96 (1H, dd, J = 9.0, 2.2 Hz), 6.79 (1H, dd, J = 17.8, 11.4 Hz), 5.80 (1H, d, J = 17.8 Hz), 5.42 (2H, s), 5.34 (1H, d, J = 11.4 Hz), 3.85 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 156.4, 135.2, 129.7, 128.9, 128.9, 128.7, 128.6, 128.0, 124.1, 124.1, 120.0, 116.1, 114.8, 113.3, 103.3, 68.8, 55.8; IR (neat): ν_{max}/cm^{-1} 2955, 2834, 1726; MS (pAPCI): 181.1 (32%), 260.1 (100%), 308.1 (28%, $(M + H)^+$); HRMS (pAPCI): calcd for $C_{19}H_{18}NO_3$ $[M + H]^+$: 308.1281; observed: 308.1277.

2a – (3a*S**,10b*S**)-2-methyl-10-tosyl-4,10,10a,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione

Into a round bottomed flask, 1-tosyl-3-vinyl-1*H*-indole (2.0 g, 6.7 mmol) and DCM (10 mL) was added. To the stirred solution, *N*-methylmalemide (0.75 g, 6.7 mmol) was added and the solution was stirred at 40 °C for 48 hours. The solvent was removed under reduced pressure to leave the crude product as orange oil. The product was purified by column chromatography (petrol (40/60)–ethyl acetate, 4 : 1, column diameter = 4 cm, silica = 15 cm) to give (3a*S**,10b*S**)-2-methyl-10-tosyl-4,10,10a,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione (2.01 g, 5.0 mmol, 76%) as a white powder.

Mp: 204.2–208.0 °C; R_f: 0.09 (Pet(40/60)–EA, 1 : 1); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.72 (2H, d, J = 8.0 Hz), 7.61 (1H, d, J = 8.5 Hz), 7.21–7.19 (2H, d, J = 8.0), 7.21–7.16 (1H, m), 6.92 (1H, app t, J = 7.5 Hz), 6.01–5.96 (1H, m), 4.47 (1H, dd, J = 7.0, 3.3 Hz), 3.99 (1H, app t, J = 8.1 Hz), 3.12 (1H, app t, J = 8.1 Hz), 2.99–2.92 (1H, m), 2.76 (3H, s), 2.30 (3H, s), 2.11 (1H, ddd, J = 18.0, 6.4, 2.4 Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 178.9, 174.2, 144.7, 144.6, 137.4, 134.3, 130.4, 129.9, 127.5, 126.4, 123.9, 121.0, 115.4, 112.9, 61.6, 43.3, 37.2, 25.3, 25.1, 21.7; IR (neat): ν_{max}/cm^{-1} 2981, 2889, 1694; MS (pNSI): 409.2 (61%, $(M + H)^+$), 426.1 (100%, $(M + (NH_4))^+$), 834.3 (52%, $(2M + (NH_4))^+$); HRMS (pNSI): calcd $C_{22}H_{21}N_2O_4S$ $[M + H]^+$: 409.1217; observed: 409.1218.

2b – 2-phenyl-11-tosyl-11,11a-dihydro-1*H*,5*H*-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-1,3(2*H*)-dione

To a stirred round bottomed flask was added 1-tosyl-3-vinyl-1*H*-indole (100 mg, 0.34 mmol) and DCM (7 mL) and the solution was cooled to −78 °C. To the stirred solution was added 4-phenyl-3*H*-1,2,4-triazole-3,5(4*H*)-dione (60 mg, 0.34 mmol) and the resulting solution was stirred at −78 °C for 3.5 hours before the solvent was removed under reduced pressure to leave the crude product as a pale red solid. The product was purified by column chromatography (petrol (40/60)–ether–DCM 2 : 1 : 1, column diameter = 1 cm, silica = 20 cm) to give 2-phenyl-11-tosyl-11,11a-dihydro-1*H*,5*H*-[1,2,4]triazolo[1′,2′:1,2]pyridazino-[3,4-*b*]indole-1,3(2*H*)-dione (88%, 140 mg, 0.30 mmol) as a pale red powder.

Mp: 160.1–162.8 °C; R_f: 0.14 (Pet(40/60)–Et_2O–DCM 2 : 1 : 1); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.86 (2H, d, J = 8.4 Hz), 7.63–7.55 (2H, m), 7.51–7.46 (2H, m), 7.46–7.42 (1H, m), 7.42–7.39 (1H, m), 7.38–7.34 (2H, m), 7.26–7.22 (2H, m), 7.09 (1H, app td, J = 7.5, 1.0 Hz), 6.26 (1H, td, J = 2.6, 1.8 Hz), 6.18 (1H, app dt, J = 5.3, 2.7 Hz), 4.56–4.46 (1H, app td, J = 17.6, 2.8 Hz), 4.39 (1H, ddd, J = 17.6, 5.2, 1.9 Hz), 2.37 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 152.7, 150.8, 144.7, 143.7, 135.6, 134.8, 131.5, 130.4, 129.6, 128.9, 128.5, 128.1, 126.8, 125.7, 125.2, 120.9, 117.4, 113.8, 74.8, 44.6, 21.4; IR (neat): ν_{max}/cm^{-1} 3070, 2926, 1719; MS (pNSI): 473.1 (100%, $(M + H)^+$),

522.2 (30%); HRMS (pNSI): calcd for $C_{25}H_{21}N_4O_4S$ $[M + H]^+$: 473.1278; observed: 473.1277.

2c – ethyl-3-((3a*S**,4*R**,10b*S**)-2-methyl-1,3-dioxo-10-tosyl-1,2,3,3a,4,10,10a,10b-octahydropyrrolo[3,4-*a*]carbazol-4-yl) propanoate

Dimethylaluminum chloride (1.0 M in hexane, 9.38 ml, 9.38 mmol) was added dropwise to a solution of *N*-methyl-maleimide (0.521 g, 4.69 mmol) in dry DCM (15 mL) at −78 °C. The mixture left to stir for 30 min. A solution of ethyl-(*Z*)-5-(1-tosyl-1*H*-indol-3-yl) pent-4-enoate (4.69 mmol, 1.863 g) in dry DCM (15 mL) was added dropwise at −78 °C. The reaction mixture was then warmed to reflux for 48 hours and quenched with saturated $NaHCO_{3(aq.)}$ (20 mL) and extracted with DCM (2 × 100 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure to give the crude yellow solid. The product was purified by column chromatography (petrol (40/60)–ethyl acetate 2 : 1) to yield ethyl 3-((3a*S**,4*R**,10b*S**)-2-methyl-1,3-dioxo-10-tosyl-1,2,3,3a,4,10,10a,10b-octahydropyrrolo[3,4-*a*]-carbazol-4-yl)propanoate in (2.038 g, 4.01 mmol, 85%) a bright yellow solid.

Mp: 187–188 °C; R_f: 0.3 (Pet(40/60)–EA 2 : 1); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.79 (2H, d, J = 7.3 Hz), 7.62 (1H, d, J = 7.0 Hz), 7.25–7.21 (4H, m), 6.95 (1H, t, J = 7.0 Hz), 6.09 (1H, dd, J = 3.7, 6.7 Hz), 4.85 (1H, dd, J = 3.7, 6.9 Hz), 4.15 (1H, t, J = 6.9 Hz), 4.07 (2H, m), 3.15–3.12 (1H, m), 3.05–3.02 (1H, m), 2.83 (3H, s), 2.43–2.36 (2H, m), 2.35 (3H, s), 1.91–1.75 (2H, m), 1.19 (3H, t, J = 7.3 Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 178.6, 174.0, 172.79, 144.6, 144.0, 136.6, 134.0, 130.5, 130.0, 127.5, 126.6, 123.9, 121.0, 116.3, 115.4, 60.6, 59.9, 44.22, 42.98, 37.2, 33.1, 28.3, 25.3, 21.70, 14.3; IR (neat): ν_{max}/cm^{-1}: 1776, 1698; HRMS (pNSI): calcd $C_{27}H_{29}N_2O_6S$ $[M + H]^+$: 509.1741; observed: 509.1731.

2d – ethyl-3-((3a*S**,4*R**,10b*S**)-1,3-dioxo-10-tosyl-1,2,3,3a,4,10,10a,10b-octahydropyrrolo[3,4-*a*]carbazol-4-yl) propanoate

Dimethyl aluminum chloride (1.0 M in hexane, 2.86 mL, 2.86 mmol) was added dropwise to a solution of *N*-maleimide (0.14 g, 1.43 mmol) in dry DCM (5 mL) at −78 °C. The mixture left to stir for 30 min. A solution of ethyl-(*Z*)-5-(1-tosyl-1*H*-indol-3-yl)-pent-4-enoate (0.57 g, 1.43 mmol) in dry DCM (10 mL) was added. The reaction mixture was slowly heated to reflux for 48 h, quenched with saturated $NaHCO_{3(aq.)}$ (5 mL). The organic layer was extracted with DCM (1 × 100 mL), washed with brine, dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure to give the crude yellow solid product which was purified by column chromatography (petrol (40/60)–ethyl acetate 2 : 1 gradient to 1 : 1 petrol–ethyl acetate) to yield ethyl 3-((3a*S**,4*R**,10b*S**)-1,3-dioxo-10-tosyl-1,2,3,3a,4,10,10a,10b-octa-hydropyrrolo[3,4-*a*]carbazol-4-yl)propanoate in (0.452 g, 0.91 mmol, 64%) as a white solid.

Mp: 218–220 °C; R_f: 0.14 (Pet(40/60)–EA 1 : 1); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.78 (2H, d, J = 6.9 Hz), 7.64 (1H, d, J = 6.8 Hz), 7.27–7.22 (4H, m), 6.98 (1H, t, J = 7.8 Hz), 6.16 (1H, dd, J = 3.6, 7.1 Hz), 4.84 (1H, dd, J = 3.6, 7.3 Hz), 4.18 (1H, t, J = 7.3 Hz), 4.12–4.05 (2H, m), 3.16–1.12 (1H, m), 3.10 (1H, t, J = 7.3 Hz), 2.40 (2H, t, J = 7.3 Hz), 2.35 (3H, s), 1.89–1.76 (2H, m), 1.20 (3H, t, J = 7.5 Hz). ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 178.3, 173.6, 172.7, 144.5, 144.1, 136.6, 133.8, 130.5, 129.8, 127.5, 126.6, 123.8, 120.0, 116.4, 115.5, 60.8, 59.6, 45.2, 44.0, 36.9, 33.0, 27.8, 21.5, 14.1; IR (neat): ν_{max}/cm^{-1}: 3657, 2981, 1776, 1703; MS (pNSI): 512.18 (100%, $[M + NH_4]^+$), 495.15 (55%, $[M + H]^+$), 340.14 (31%, [M − Ts]); HRMS (pNSI): calcd $C_{26}H_{27}N_2O_6S$ $[M + H]^+$: 495.1584; observed: 495.1585.

2e – ethyl 3-((3a*S**,4*R**,10b*S**)-1,3-dioxo-2-phenyl-10-tosyl-1,2,3,3a,4,10,10a,10b-octahydropyrrolo[3,4-*a*]carbazol-4-yl) propanoate

Dimethyl aluminum chloride (1.0 M in THF, 2.39 mL, 2.39 mmol) was added dropwise to a solution of *N*-phenylmaleimide (0.207 g, 1.19 mmol) in dry DCM (5 mL) at −78 °C. The mixture left to stir for 30 min. A solution of ethyl (*Z*)-5-(1-tosyl-1*H*-indol-3-yl) pent-4-enoate (0.475 g, 1.19 mmol) in dry DCM (10 mL) was added. The reaction mixture was heated to reflux for 48 h, quenched with saturated $NaHCO_{3(aq.)}$ (10 mL) and extracted with DCM (100 mL). The organic layer was washed with brine, dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure to give the crude yellow solid product which was purified by column chromatography (petrol (40/60)–ethyl acetate 2 : 1) to yield ethyl 3-((3a*S**,4*R**,10b*S**)-1,3-dioxo-2-phenyl-10-tosyl-1,2,3,3a,4,10,10a,10b-octahydropyrrolo[3,4-*a*]carbazol-4-yl)propanoate in (0.5095 g, 0.84 mmol, 71%) as a white solid.

Mp: 201–203 °C; R_f: 0.2 (Pet(40/60)–EA 2 : 1); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.81 (2H, d, J = 7.3 Hz), 7.60 (1H, d, J = 7.3 Hz), 7.34–7.21 (7H, m), 7.06 (2H, d, J = 7.3 Hz), 6.97 (1H, t, J = 7.3 Hz), 6.20 (1H, dd, J = 3.4, 7.1 Hz), 4.59 (1H, dd, J = 3.4, 7.1 Hz), 4.18 (1H, t, J = 7.3 Hz), 4.13–4.05 (2H, m), 3.26–3.20 (2H, m), 2.45–2.40 (2H, m), 2.35 (3H, s), 1.89–1.85 (2H, m), 1.20 (3H, t, J = 6.9 Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 177.5, 172.9, 172.7, 144.6, 144.3, 137.0, 134.1, 131.7, 130.7, 130.0, 129.0, 128.5, 127.6, 126.7, 126.3, 124.0, 120.9, 116.2, 115.5, 60.8, 60.0, 44.3, 43.1, 37.7, 33.2, 28.3, 21.6, 14.2; IR (neat): ν_{max}/cm^{-1}: 1776, 1703; MS (pNSI): 588.21 (100%, $[M + NH_4]^+$), 1158.39 (33%, $[2M + NH_4]^+$); HRMS (pNSI): calcd $C_{32}H_{31}N_2O_6S$ $[M + H]^+$: 571.18; observed: 571.1891.

3a – (3a*S**,5*S**,10b*S**)-5-(hydroxy(phenyl)amino)-2-methyl-10-tosyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione

To a stirred round bottomed flask was added 1-tosyl-3-vinyl-1*H*-indole (100 mg, 0.34 mmol), DCM (5 mL) and 1-methyl-1*H*-pyrrole-2,5-dione (38 mg, 0.34 mmol). The resulting solution was heated at reflux for 48 hours. The reaction was allowed to cool to room temperature, nitrosobenzene (40 mg, 0.34 mmol) was added, and the solution was stirred at room temperature for 18 hours. The solvent was removed under reduced pressure to leave the crude product as a pale yellow solid which was purified by column chromatography (petrol (40/60)–ethyl acetate 4 : 1, column diameter = 1 cm, silica = 16 cm) to give (3a*S**,5*S**,10b*S**)-5-(hydroxy(phenyl)amino)-2-methyl-10-tosyl-

4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione as a yellow powder (71%, 128 mg, 0.24 mmol).

Mp: 196.8–199.5 °C; R_f: 0.64 (Pet(40/60)–EA, 1 : 1); ^{1}H NMR (500 MHz, CD_2Cl_2): δ_H 7.94 (1H, d, J = 8.4 Hz), 7.69 (2H, d, J = 8.2 Hz), 7.60 (1H, d, J = 7.9 Hz), 7.32–7.25 (3H, m), 7.23 (2H, d, J = 8.2 Hz), 7.18–7.13 (3H, m), 7.02 (1H, t, J = 7.3 Hz), 5.06 (1H, d, J = 8.0 Hz), 4.75 (1H, app. t, J = 5.9 Hz), 4.72 (1H, s), 3.64 (1H, app q, J = 7.2 Hz), 2.95 (3H, s), 2.43 (1H, app dt, J = 13.6, 6.4 Hz), 2.35 (3H, s), 2.06 (1H, ddd, J = 13.6, 7.2, 4.9); ^{13}C NMR (101 MHz, CD_2Cl_2): δ_C 178.1, 173.6, 150.7, 145.3, 137.5, 134.9, 131.4, 129.7, 128.9, 128.9, 126.8, 125.2, 124.2, 122.6, 121.7, 120.2, 117.2, 115.4, 58.0, 40.5, 39.5, 25.0, 23.3, 21.4; IR (neat): ν_{max}/cm^{-1} 3661, 2990, 2886, 1690; MS (pNSI): 407.1 (66%, $(M - (C_6H_5NOH))^+$), 516.2 (49%, $(M + H)^+$), 533.2 (100%, $(M + NH_4)^+$), 1031.3 (57%, $(2M + H)^+$), 1053.3 (13%, $(2M + Na)^+$); HRMS (pNSI): calcd for $C_{28}H_{26}N_3O_5S$ $[M + H]^+$: 516.1588; observed: 516.1584.

Note: ^{1}H NMR run at 35 °C, broad signals observed at room temperature.

3b – (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-2-methyl-10-tosyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione

To a stirred round bottomed flask was added 1-tosyl-3-vinyl-1*H*-indole (100 mg, 0.34 mmol), DCM (5 mL) and 1-methyl-1*H*-pyrrole-2,5-dione (38 mg, 0.34 mmol). The resulting solution was heated at reflux for 48 hours. The reaction was allowed to cool to room temperature, 1-methyl-2-nitrosobenzene (42 mg, 0.17 mmol) was added and the solution was stirred at room temperature for 18 hours. The solvent was removed under reduced pressure to leave the crude product as a pale yellow solid. The product was purified by column chromatography (petrol (40/60)–ethyl acetate 4 : 1, column diameter = 1 cm, silica = 14 cm) to give (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-2-methyl-10-tosyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]-carbazole-1,3(2*H*,3a*H*)-dione (71%, 128 mg, 0.24 mmol) as a yellow powder.

Mp: 193.0–196.7 °C; R_f: 0.59 (Pet(40/60)–EA 1 : 1); ^{1}H NMR (400 MHz, CD_2Cl_2): δ_H 7.89 (1H, d, J = 8.3 Hz), 7.65 (2H, d, J = 8.4 Hz), 7.40 (1H, d, J = 7.9 Hz), 7.28 (1H, d, J = 7.7 Hz), 7.21–7.18 (3H, m), 7.13–6.99 (4H, m), 5.04 (1H, d, J = 8.1 Hz), 4.87 (1H, s), 4.27 (1H, app t, J = 5.4 Hz), 3.73 (1H, app td, J = 8.0, 6.1 Hz), 2.91 (3H, s), 2.58 (1H, app dt, J = 12.9, 6.2 Hz), 2.32 (3H, s), 2.25 (3H, s), 1.95 (1H, ddd, J = 12.9, 7.8, 4.5 Hz); ^{13}C NMR (101 MHz, CD_2Cl_2): δ_C 178.2, 173.6, 149.3, 145.3, 137.3, 134.9, 131.6, 130.9, 129.7, 129.7, 129.2, 126.8, 126.2, 125.0, 124.9, 124.1, 121.4, 120.5, 115.3, 57.3, 40.6, 39.4, 25.0, 24.6, 21.4, 18.3; IR (neat): ν_{max}/cm^{-1} 3662, 2990, 2886, 1701; MS (pNSI): 407.1 (98%, $(M - ((o\text{-}CH_3) - C_6H_4NOH))^+$), 530.2 (52%, $(M + H)^+$), 547.2 (65%, $(M + NH_4)^+$), 1059.3 (100%, $(2M + H)^+$); HRMS (pNSI): calcd for $C_{29}H_{28}N_3O_5S$ $[M + H]^+$: 530.1744; observed: 530.1743.

3c – (3a*S**,5*S**,10b*S**)-5-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-2-methyl-10-tosyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione

To a stirred round bottomed flask was added 1-tosyl-3-vinyl-1*H*-indole (100 mg, 0.34 mmol), DCM (5 mL) and 1-methyl-1*H*-pyrrole-2,5-dione (38 mg, 0.34 mmol) and the resulting solution was heated at reflux for 48 hours. The reaction was cooled to 0 °C before PTAD (60 mg, 0.34 mmol) was added. The reaction was stirred at 0 °C for 4 hours. The solvent was removed under reduced pressure to leave the crude product as a pale red powder. The product was purified by column chromatography (petrol (40/60)–ethyl acetate 4 : 1, column diameter = 1 cm, silica = 14 cm) to give (3a*S**,5*S**,10b*S**)-5-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-2-methyl-10-tosyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione (76%, 150 mg, 0.26 mmol) as a white powder.

Mp: 183.4–187.7 °C; R_f: 0.05 (Pet(40/60)–EA 1 : 1); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.84 (2H, d, J = 8.4 Hz), 7.67 (1H, d, J = 8.2 Hz), 7.52 (1H, d, J = 7.6 Hz), 7.46–7.31 (5H, m), 7.29–7.19 (2H, m), 7.17 (2H, d, J = 8.3 Hz), 5.55 (1H, app t, J = 4.7 Hz), 5.08 (1H, d, J = 7.7 Hz), 3.66 (1H, ddd, J = 10.5, 7.7, 5.8 Hz), 2.96 (3H, s), 2.49 (1H, app dt, J = 14.8, 5.3 Hz), 2.28 (3H, s), 2.14 (1H, ddd, J = 14.8, 10.5, 5.5 Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 177.4, 173.4, 153.6, 152.8, 145.5, 137.0, 135.3, 132.3, 130.8, 130.0, 129.3, 128.5, 127.5, 126.9, 125.7, 125.6, 124.3, 119.4, 115.4, 114.9, 47.8, 40.3, 39.0, 28.4, 25.4, 21.7; IR (neat): ν_{max}/cm^{-1} 3665, 2984, 2884, 1699; MS (pNSI): 601.2 (100%, $(M + NH_4)^+$), 1184.3 (13%, $(2M + NH_4)^+$); HRMS (pNSI): calcd for $C_{30}H_{29}N_6O_6S$ $[M + NH_4]^+$: 601.1864; observed: 601.1861.

3d – (3a*S**,5*S**,10b*S**)-5-((*S**)-hydroxy(perfluorophenyl)methyl)-2-methyl-10-tosyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione

To a stirred round bottomed flask was added 1-tosyl-3-vinyl-1*H*-indole (100 mg, 0.34 mmol) DCM (5 mL) and 1-methyl-1*H*-pyrrole-2,5-dione (38 mg, 0.34 mmol) and the resulting solution was heated at reflux for 48 hours. The reaction was cooled to −78 °C and 2,3,4,5,6-pentafluorobenzaldehyde (0.04 mL, 0.34 mmol) was added followed by DMAC (1 M in hexane, 0.34 mL, 0.34 mmol). The reaction was stirred at −78 °C for 15 minutes before being allowed to warm to room temperature. The reaction was stirred at room temperature for 18 hours. The reaction was poured into saturated sodium bicarbonate solution (10 mL) and extracted with DCM (2 × 10 mL). The combined organic layers were dried with $MgSO_4$, filtered and the solvent was removed under reduced pressure to give the crude product as a pale brown solid. The product was purified by column chromatography (petrol (40/60)–ethyl acetate 3 : 1, column diameter = 2 cm, silica = 15 cm) to give a separable 5 : 1 mixture of (3a*S**,5*S**,10b*S**)-5-((*S**)-hydroxy(perfluorophenyl)methyl)-2-methyl-10-tosyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]-carbazole-1,3(2*H*,3a*H*)-dione and (3a*S**,5*S**,10b*S**)-5-((*R**)-hydroxy(perfluorophenyl)methyl)-2-methyl-10-tosyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione (72%, 149 mg, 0.25 mmol).

Major diastereomer: Mp: 120.4–121.7 °C; R_f: 0.24 (Pet(40/60)–EA 3 : 1); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H δ 7.85 (3H, app d, J = 8.4 Hz), 7.31–7.22 (4H, m), 7.22–7.14 (1H, m), 5.13 (1H, d, J = 8.1 Hz), 4.99 (1H, d, J = 7.5 Hz), 3.71–3.52 (2H, m), 3.01 (3H, s), 2.38 (3H, s), 2.20–2.10 (1H, m), 1.67 (1H, app td, J = 13.8, 5.3 Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 177.7, 173.3, 145.3, 137.4, 135.4, 129.8,

129.7, 129.6, 127.2, 125.3, 123.9, 120.1, 119.9, 115.2, 70.2, 41.5, 39.1, 36.9, 28.7, 25.2, 21.7; IR (neat): ν_{max}/cm^{-1} 3371, 2981, 2889, 1690; MS (pNSI): 605.1 (40%, $(M + H)^+$), 622.1 (88%, $(M + NH_4)^+$), 627.1 (100%, $(M + Na)^+$), 643.1 (17%), 709.1 (15%); HRMS (pNSI): calcd for $C_{29}H_{21}F_5N_2NaO_5S$ $[M + Na]^+$: 627.0984; observed: 627.0968. *Note: ^{13}C NMR missing peaks due to C–F coupling.*

3e – 6-(hydroxy(phenyl)amino)-2-phenyl-11-tosyl-5,6-dihydro-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-1,3(2*H*,11*H*)-dione

To a stirred round bottomed flask was added 1-tosyl-3-vinyl-1*H*-indole (100 mg, 0.34 mmol) and DCM (5 mL) and the solution was cooled to −78 °C. To this solution PTAD (70 mg, 0.34 mmol) was added and the reaction was stirred at −78 °C for 3.5 hours. The reaction was warmed to room temperature, nitrosobenzene (44 mg, 0.34 mmol) was added and the reaction was stirred for 18 hours. The solvent was removed under reduced pressure to leave the crude product as a pale yellow oil. The product was purified by column chromatography (column diameter = 1 cm, silica = 16 cm, eluent = petrol (40/60)–ether–DCM 2 : 1 : 1) to give 6-(hydroxy(phenyl)amino)-2-phenyl-11-tosyl-5,6-dihydro-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-1,3(2*H*,11*H*)-dione (72%, 54 mg, 0.09 mmol) as a white powder.

Mp: 176.1–180.0 °C; R_f: 0.48 (Pet(40/60)–Et_2O 2 : 1); ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.03 (1H, d, $J = 8.3$ Hz), 7.62 (2H, d, $J = 8.1$ Hz), 7.56 (2H, d, $J = 7.6$ Hz), 7.46 (2H, app t, $J = 7.7$ Hz), 7.42–7.36 (1H, m), 7.23–7.07 (7H, m), 7.05–6.99 (2H, m), 6.59 (1H, d, $J = 7.4$ Hz), 5.81 (1H, br s), 5.18 (1H, d, $J = 13.5$ Hz), 4.59 (1H, s), 3.23 (1H, d, $J = 13.5$ Hz), 2.30 (3H, s); ^{13}C NMR (101 MHz, DMSO-d_6): δ_C 152.7, 152.2, 150.5, 146.0, 134.9, 132.9, 132.5, 131.8, 130.4, 129.8, 129.3, 129.2, 128.5, 127.3, 127.3, 125.5, 125.4, 122.5, 119.8, 117.6, 116.6, 108.6, 55.9, 44.6, 21.6; IR (neat): ν_{max}/cm^{-1} 2981, 2884, 1714; MS (pAPCI): 138.1 (100%), 157.0 (95%), 213.1 (50%), 248.1 (86%), 279.1 (62%), 317.1 (33%), 333.1 (29%), 471.1 (31%), 564.2 (11%), 580.2 (10%, $(M + H)^+$); HRMS (pAPCI): calcd for $C_{31}H_{26}N_5O_5S$ $[M + H]^+$: 580.1649; observed: 580.1640.

3f – 6-(hydroxy(*o*-tolyl)amino)-2-phenyl-11-tosyl-5,6-dihydro-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-1,3(2*H*,11*H*)-dione

To a stirred round bottomed flask was added 1-tosyl-3-vinyl-1*H*-indole (100 mg, 0.34 mmol) and DCM (5 mL) and the solution cooled to −78 °C. To this solution PTAD (70 mg, 0.34 mmol) was added and the reaction was stirred at −78 °C for 3.5 hours. The reaction was warmed to room temperature and 1-methyl-2-nitrosobenzene (42 mg, 0.34 mmol) was added and the reaction was stirred for 18 hours. The solvent was removed under reduced pressure to leave the crude product as a pale yellow oil. The product was purified by column chromatography (column diameter = 1 cm, silica = 14 cm, eluent = petrol (40/60)–ether–DCM 2 : 1 : 1) to give 6-(hydroxy(*o*-tolyl)amino)-2-phenyl-11-tosyl-5,6-dihydro-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-1,3(2*H*,11*H*)-dione as a white powder (78%, 60 mg, 0.10 mmol).

Mp: 149.7–153.1 °C; R_f: 0.32 (Pet(40/60)–Et_2O–DCM 2 : 1 : 1); ^1H NMR (300 MHz, $CDCl_3$): δ_H 7.99 (1H, d, $J = 8.3$ Hz), 7.61–7.58 (5H, m), 7.43–7.40 (1H, m), 7.47 (2H, app t, $J = 7.7$ Hz), 7.40–7.37 (1H, m), 7.18 (2H, app t, $J = 7.8$ Hz), 7.11 (2H, d, $J = 8.2$ Hz), 6.97 (2H, app q, $J = 7.2$ Hz), 6.85 (1H, d, $J = 7.5$ Hz), 6.50 (1H, d, $J = 7.8$ Hz), 5.93 (1H, s), 5.24 (1H, d, $J = 13.5$ Hz), 4.44 (1H, s), 3.11 (1H, d, $J = 13.5$ Hz), 2.29 (3H, s), 1.91 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 153.3, 150.3, 148.7, 145.4, 135.1, 133.7, 132.0, 131.7, 131.3, 130.6, 129.6, 129.3, 128.7, 127.9, 127.2, 127.0, 126.8, 125.9, 124.9, 124.8, 122.6, 118.0, 116.8, 107.0, 59.1, 44.5, 21.7, 17.8; IR (neat): ν_{max}/cm^{-1} 3068, 2981, 1713; MS (pAPCI): 138.1 (100%), 157.0 (82%), 262.1 (55%), 279.1 (76%), 317.1 (50%), 391.3 (37%), 471.1 (21%), 594.2 (10%, $(M + H)^+$); HRMS (pAPCI): calcd for $C_{32}H_{28}N_5O_5S$ $[M + H]^+$: 594.1806; observed: 594.1801.

3g – ethyl 3-((3a*S**,4*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-2-methyl-1,3-dioxo-10-tosyl-1,2,3,3a,4,5,10,10b-octahydropyrrolo[3,4-*a*]carbazol-4-yl)propanoate

A solution of 2-nitrosotoluene (0.035 g, 0.29 mmol) and ethyl 3-((3a*S**,4*R**,10b*S**)-2-methyl-1,3-dioxo-10-tosyl-1,2,3,3a,4,10,10a,10b-octahydropyrrolo[3,4-*a*]carbazol-4-yl)propanoate (0.150 g, 0.29 mmol) in dry DCM (10 mL) was stirred at room temperature for 24 hours. The solvent was removed under reduced pressure to give the crude green solid product which was purified by column chromatography (petrol (40/60)–ethyl acetate 2 : 1) to give ethyl 3-((3a*S**,4*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-2-methyl-1,3-dioxo-10-tosyl-1,2,3,3a,4,5,10,10b-octahydropyrrolo[3,4-*a*]carbazol-4-yl)propanoate (0.109 g, 0.17 mmol, 59%) as a bright yellow solid.

Mp: 190–192 °C; R_f: 0.26 (Pet(40/60)–EA 2 : 1); ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.95 (1H, d, $J = 7.2$ Hz), 7.61 (2H, d, $J = 7.2$ Hz), 7.18 (2H, d, $J = 7.2$ Hz), 7.10 (1H, d, $J = 7.2$ Hz), 7.05 (1H, t, $J = 7.2$ Hz), 6.81 (1H, t, $J = 7.2$ Hz), 6.65 (1H, t, $J = 7.5$ Hz), 6.19 (1H, t, $J = 7.5$ Hz), 5.88 (1H, d, $J = 7.2$ Hz), 5.46 (1H, d, $J = 7.2$ Hz), 4.99 (1H, br s), 4.95 (1H, d, $J = 7.2$ Hz), 4.30 (1H, d, $J = 4.6$ Hz), 4.11 (2H, q, $J = 7.0$ Hz), 3.80–3.75 (1H, m), 3.01 (3H, s), 2.70–2.54 (4H, m), 2.41 (3H, s), 2.33 (3H, s), 1.92–1.85 (1H, m), 1.24 (3H, t, $J = 7.0$ Hz). ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 178.2, 173.3, 149.9, 144.6, 139.9, 137.1, 134.1, 131.9, 130.6, 130.3, 129.4, 128.7, 127.0, 125.7, 124.8, 124.4, 123.6, 122.1, 118.9, 118.0, 115.7, 60.6, 57.8, 45.1, 42.4, 40.0, 32.5, 25.2, 23.3, 21.6, 18.5, 14.3; IR (neat): ν_{max}/cm^{-1}: 3655, 2980, 1702; MS (pNSI): 507.15 (100%, [M − (Tol-N-OH)]), 652.20 (55%, $[M + Na]^+$); HRMS (pNSI): calcd $C_{34}H_{35}N_3O_7S$ $[M + Na]^+$: 652.2088; observed: 652.2082.

3h – ethyl 3-((3a*S**,4*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-1,3-dioxo-2-phenyl-10-tosyl-1,2,3,3a,4,5,10,10b-octahydropyrrolo[3,4-*a*]carbazol-4-yl)propanoate

A solution of 2-nitrosotoluene (0.016 g, 0.13 mmol) and ethyl 3-((3a*S**,4*R**,10b*S**)-1,3-dioxo-2-phenyl-10-tosyl-1,2,3,3a,4,10,10a,10b-octahydropyrrolo[3,4-*a*]carbazol-4-yl)propanoate (0.08 g, 0.13 mmol) in dry DCM (10 mL) was stirred at room temperature for 24 hours. The solvent was removed under reduced pressure to give the crude yellow product which was purified by column chromatography (petrol (40/60)–ethyl acetate 2 : 1) to give ethyl 3-((3a*S**,4*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-1,3-dioxo-2-

phenyl-10-tosyl-1,2,3,3a,4,5,10,10b-octahydropyrrolo[3,4-*a*]-carbazol-4-yl)propanoate in (0.415 g, 0.059 mmol, 58%) as a bright yellow solid.

Mp: 182–184 °C; R_f: 0.34 (Pet(40/60)–EA 2 : 1); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.94 (1H, d, J = 6.7 Hz), 7.64 (2H, d, J = 6.7 Hz), 7.45–7.37 (5H, m), 7.20–7.00 (4H, m), 6.84 (1H, t, J = 6.9 Hz), 6.66 (1H, t, J = 6.9 Hz), 6.24 (1H, t, J = 6.2 Hz), 5.95 (1H, d, J = 6.9 Hz), 5.66 (1H, d, J = 6.4 Hz), 5.20 (1H, d, J = 7.4 Hz), 4.99 (1H, br s), 4.39 (1H, d, J = 4.0 Hz), 4.08 (2H, q, J = 7.2 Hz), 4.03–3.98 (1H, m), 2.72–2.61 (4H, m), 2.42 (3H, s), 2.33 (3H, s), 2.14–2.08 (1H, m). 1.20 (3H, t, J = 7.2 Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 177.0, 173.3, 172.2, 150.1, 144.6, 137.1, 134.2, 131.0, 131.8, 130.5, 130.3, 129.4, 129.0, 128.6, 128.5, 127.0, 126.5, 125.8, 124.8, 124.5123.5, 122.2, 119.1, 118.1, 115.6, 60.0, 57.7, 45.3, 42.6, 40.0, 32.4, 23.1, 21.6, 18.5, 14.5; IR (neat): ν_{max}/cm^{-1}: 3858, 3826, 1709, 1595; MS (pNSI): 569.17 (100%, [M − N(OH)(*o*-Tol)]), 692.24 (30%, $[M + H]^+$); HRMS (pNSI): calcd $C_{39}H_{36}N_3O_7S$ $[M - H]^+$: 690.2268; observed: 690.2266.

3i – ethyl 3-((3a*S**,4*S**,5*S**,10b*S**)-5-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-2-methyl-1,3-dioxo-10-tosyl-1,2,3,3a,4,5,10,10b-octahydropyrrolo[3,4-*a*]carbazol-4-yl) propanoate

A solution of 4-phenyl-3*H*-1,2,4-triazole-3,5(4*H*)-dione (0.052 g, 0.29 mmol) and ethyl 3-((3a*S**,4*R**,10b*S**)-2-methyl-1,3-dioxo-10-tosyl-1,2,3,3a,4,10,10a,10b-octahydropyrrolo[3,4-*a*]carbazol-4-yl)propanoate (0.150 g, 0.29 mmol) in dry DCM (10 mL) was stirred at 0 °C for 6 hours. The solvent was removed under reduced pressure to give the crude product which was purified by column chromatography (petrol (40/60)–ethyl acetate 1 : 1) to give ethyl 3-((3a*S**,4*S**,5*S**,10b*S**)-5-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-2-methyl-1,3-dioxo-10-tosyl-1,2,3,3a,4,5,10,10b-octahydropyrrolo[3,4-*a*]carbazol-4-yl)propanoate in (56%, 0.110 g, 0.161 mmol) as a white solid.

Mp: 264–265 °C; R_f: 0.30 (Pet(40/60)–EA 1 : 1); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.86 (1H, br s), 7.78 (2H, d, J = 7.0 Hz), 7.71 (1H, d, J = 7.9 Hz), 7.47 (1H, d, J = 7.9 Hz), 7.44–7.40 (1H, m), 7.36–7.30 (3H, m), 7.23–7.17 (2H, m), 7.02 (2H, d, J = 7.0 Hz), 5.66 (1H, d, J = 6.2 Hz), 5.04 (1H, d, J = 6.5 Hz), 4.08 (2H, q, J = 6.2 Hz), 3.44 (1H, dd, J = 6.5, 11.9 Hz), 3.02 (3H, s), 2.68–2.51 (3H, m), 2.15 (3H, s), 2.14–2.09 (1H, m), 1.90–1.82 (1H, m), 1.20 (3H, t, J = 6.2 Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 176.6, 173.4, 173.2, 153.6, 152.6, 145.2, 136.8, 135.5, 132.1, 130.7, 129.7, 129.3, 128.6, 127.2, 126.8, 125.6, 124.2, 119.0, 114.8, 114.4, 60.8, 44.3, 42.0, 39.3, 30.9, 25.4, 23.0, 21.5, 14.2; IR (neat): ν_{max}/cm^{-1}: 3659, 1775, 1691; MS (pNSI): 701.23 (100%, $[M + NH_4]^+$), 1384.44 (17%, $[2M + NH_4]^+$); HRMS (pNSI): calcd $C_{35}H_{34}N_5O_8S$ $[M + H]^+$: 684.2123; observed: 684.2115.

3j – ethyl 3-((3a*S**,4*S**,5*S**,10b*S**)-5-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-1,3-dioxo-10-tosyl-1,2,3,3a,4,5,10,10b-octahydropyrrolo[3,4-*a*]carbazol-4-yl)propanoate

A solution of 4-phenyl-3*H*-1,2,4-triazole-3,5(4*H*)-dione (0.037 g, 0.21 mmol) and ethyl 3-((3a*S**,4*R**,10b*S**)-1,3-dioxo-10-tosyl-1,2,3,3a,4,10,10a,10b-octahydropyrrolo[3,4-*a*]carbazol-4-yl)-propanoate (0.105 g, 0.21 mmol) in dry DCM (10 mL) was stirred at 0 °C for 6 h. The solvent was removed to give the crude white solid product which was purified by trituration from DCM to yield ethyl 3-((3a*S**,4*S**,5*S**,10b*S**)-5-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-1,3-dioxo-10-tosyl-1,2,3,3a,4,5,10,10b-octahydropyrrolo[3,4-*a*]carbazol-4-yl)propanoate in (57%, 0.08 g, 0.119 mmol) as a white solid.

Mp: 269–271 °C; ^{1}H NMR (300 MHz, d_6-DMSO): δ_H 11.44 (1H, br s), 10.68 (1H, br s), 7.87–7.76 (3H, m), 7.51–7.39 (4H, m), 7.29–7.25 (6H, m), 5.69 (1H, d, J = 6.1 Hz), 5.28 (1H, d, J = 6.8 Hz), 4.05 (2H, q, J = 6.8 Hz), 3.45 (1H, dd, J = 6.8, 11.3 Hz), 3.58–3.52 (1H, m), 2.67–2.65 (1H, m), 2.25 (3H, s), 2.49–2.44 (2H, m), 1.80–1.70 (1H, m), 1.18 (3H, t, J = 6.8 Hz); ^{13}C NMR (101 MHz, d_6-DMSO): 178.6, 175.0, 172.99, 154.4, 153.1, 145.5, 136.6, 134.9, 133.1, 131.7, 130.4, 129.4, 128.6, 127.6, 127.1, 126.3, 125.6, 124.5, 119.3, 115.9, 114.9, 60.3, 45.2, 43.0, 38.0, 30.7, 23.6, 21.4, 14.5; IR (neat): ν_{max}/cm^{-1}: 3659, 1775, 1692; MS (pNSI): 687.22 (100%, $[M + NH_4]^+$), 1356.41 (27%, $[2M + NH_4]^+$), 692.17 (12%, $[M + Na]^+$); HRMS (pNSI): calcd $C_{34}H_{35}N_6O_8S$ $[M + H]^+$: 687.2232; observed: 687.2229.

3k – (3a*S**,5*S**,10b*S**)-5-(hydroxy(phenyl)amino)-10-tosyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione

To a stirred round bottomed flask was added 1-tosyl-3-vinyl-1*H*-indole (100 mg, 0.34 mmol), DCM (5 mL) and 1*H*-pyrrole-2,5-dione (33 mg, 0.34 mmol) and the resulting solution was heated at reflux for 48 hours. The reaction was cooled to room temperature and nitrosobenzene (36 mg, 0.34 mmol) was added. The reaction was stirred at room temperature for 4 hours before the solvent was removed under reduced pressure to leave the crude product as a white solid. The product was purified by trituration from DCM to give (3a*S**,5*S**,10b*S**)-5-(hydroxy-(phenyl)amino)-10-tosyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]-carbazole-1,3(2*H*,3a*H*)-dione (89%, 151 mg, 0.30 mmol) as a white powder.

Mp: 203.7–206.9 °C; R_f: 0.15 (Pet(40/60)–EA 2 : 1); ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 11.26 (1H, s), 8.45 (1H, s), 7.88 (1H, d, J = 8.3 Hz). 7.76 (2H, d, J = 8.2 Hz), 7.42 (1H, d, J = 7.8 Hz), 7.33 (2H, d, J = 8.2 Hz), 7.29–7.04 (5H, m), 6.89 (1H, t, J = 7.2 Hz), 5.17 (1H, d, J = 7.8 Hz), 4.88 (1H, app t, J = 4.4 Hz), 3.65 (1H, app td, J = 8.8, 5.9 Hz), 2.32 (3H, s), 2.36–2.27 (1H, m), 1.81 (1H, ddd, J = 14.0, 9.4, 5.0 Hz); ^{13}C NMR (101 MHz, DMSO-d_6): δ_C 179.4, 174.7, 152.0, 144.7, 136.4, 135.0, 131.5, 129.8, 128.9, 128.4, 126.6, 124.4, 123.4, 121.2, 120.7, 120.6, 117.0, 114.4, 56.8, 41.5, 40.6, 25.2, 20.9; IR (neat): ν_{max}/cm^{-1} 3452, 2981, 1715; MS (pNSI): 393.1, (100%, $(M - (C_6H_5NOH)^+)$), 502.1 (14%, $(M + H)^+$), 519.2 (96%, $(M + NH_4)^+$), 524.1 (17%, $(M + Na)^+$), 1003.3 (40%, $(2M + H)^+$), 1025.3 (15%, $(2M + Na)^+$); HRMS (pNSI): calcd for $C_{27}H_{24}N_3O_5S$ $[M + H]^+$: 502.1431; observed: 502.1428.

3l – (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-10-tosyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione

To a stirred round bottomed flask was added 1-tosyl-3-vinyl-1*H*-indole (100 mg, 0.34 mmol), DCM (5 mL) and 1*H*-pyrrole-2,5-dione (33 mg, 0.34 mmol) was added and the resulting

solution was heated at reflux for 48 hours. The reaction was cooled to room temperature and 1-methyl-2-nitrosobenzene (41 mg, 0.34 mmol) was added. The reaction was stirred at room temperature for 4 hours before the solvent was removed under reduced pressure to leave the crude product as a pale yellow solid. The product was purified by column chromatography (petrol (40/60)–ether–DCM 2 : 1 : 1, column diameter = 2 cm, silica = 14 cm) to give (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl) amino)-10-tosyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione (82%, 143 mg, 0.28 mmol) as a yellow powder.

Mp: 171.1–174.0 °C; R_f: 0.13 (Pet(40/60)–EA 2 : 1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (1H, d, J = 8.4 Hz), 7.73 (2H, d, J = 8.2 Hz), 7.77 (1H, s), 7.35 (2H, dd, J = 15.7, 7.9 Hz), 7.20 (3H, app d, J = 8.2 Hz), 7.09 (2H, d, J = 7.5 Hz), 7.07–7.00 (2H, m), 5.17 (1H, d, J = 8.1 Hz), 4.75 (1H, s), 4.39 (1H, app t, J = 5.1 Hz), 3.80 (1H, app q, J = 8.3, 5.7 Hz), 2.64 (1H, app dt, J = 13.1, 5.5 Hz), 2.34 (3H, s), 2.26 (3H, s), 1.96 (1H, ddd, J = 15.9, 7.9, 3.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 178.3, 173.4, 149.3, 144.7, 137.4, 135.8, 131.3, 130.9, 129.8, 129.6, 129.5, 129.0, 127.0, 126.3, 125.1, 124.7, 123.7, 121.5, 120.1, 115.3, 57.3, 42.0, 40.8, 26.0, 21.4, 18.3; IR (neat): ν_{max}/cm^{-1} 3294, 2981, 1713; MS (pAPCI): 293.1 (16%), 332.1 (13%), 342.1 (16%), 393.1 (100%, (M − (*o*-Tol) N(OH))$^+$), 489.1 (54%, (M − H_2O)$^+$), 516.2 (26%, (M + H)$^+$); HRMS (pAPCI): calcd for $C_{28}H_{26}N_3O_5S$ [M + H]$^+$: 516.1588; observed: 516.1576.

3m – (3a*S**,5*S**,10b*S**)-5-((*S**)-hydroxy(perfluorophenyl) methyl)-10-tosyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione

To a stirred round bottomed flask was added 1-tosyl-3-vinyl-1*H*-indole (100 mg, 0.34 mmol), DCM (5 mL) and 1*H*-pyrrole-2,5-dione (33 mg, 0.34 mmol). The resulting solution was heated at reflux for 48 hours. The reaction was cooled to 0 °C and pentafluorobenzaldehyde (67 mg, 0.34 mmol) and DMAC (1 M in hexane, 0.34 mL, 0.34 mmol) were added. The solution was stirred at 0 °C for 1 hour and then warmed to room temperature for 18 hours. The reaction was poured into sodium bicarbonate (15 mL) and extracted with DCM. The combined organic layers were dried with MgSO4, filtered and the solvent was removed under reduced pressure to give the crude product as an off white solid. The product was purified by column chromatography (diameter = 1.5 cm, silica = 15 cm, eluent = petrol (40/60)–EA 2 : 1) to give (3a*S**,5*S**,10b*S**)-5-((*S**)-hydroxy(perfluorophenyl) methyl)-10-tosyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione (71%, 0.1427 g, 0.24 mmol) as an off white solid.

Mp: 181.3–185.1 °C; R_f: 0.22 (Pet(40/60)–EA 2 : 1); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.03 (1H, br s), 7.81 (3H, app d, J = 7.9 Hz), 7.28 (1H, d, J = 8.0 Hz), 7.25–7.22 (3H, m), 7.16 (1H, app t, J = 7.6 Hz), 5.08 (1H, d, J = 8.3 Hz), 5.05 (1H, d, J = 7.4 Hz), 3.61–3.66 (1H, m), 3.49–3.57 (1H, m), 2.34 (3H, s), 2.09 (1H, dd, J = 14.0, 4.5 Hz), 1.74 (1H, app td, J = 13.9, 5.3 Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 177.4, 173.0, 145.3, 137.4, 135.5, 129.8, 129.7, 129.1, 127.1, 125.5, 123.9, 120.2, 120.0, 115.3, 70.2, 42.5, 40.3, 36.8, 28.5, 21.7; IR (neat): ν_{max}/cm^{-1} 3240, 2981, 1717; MS (pAPCI): 157.0 (79%), 221.1 (61%), 393.1 (15%, (M − (C_6F_5COH)$^+$)), 443.1 (51%), 573.1 (8%, (M − H_2O)$^+$), 591.1 (100%, (M + H)$^+$); HRMS (pAPCI): calcd for $C_{28}H_{20}F_5N_2O_5S$ [M + H]$^+$: 591.1008; observed: 591.1001. *Note*: *^{13}C NMR missing peaks due to C–F coupling.*

3n – (3a*S**,5*S**,10b*S**)-5-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-10-tosyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione

To a stirred round bottomed flask was added 1-tosyl-3-vinyl-1*H*-indole (100 mg, 0.34 mmol), DCM (5 mL) and 1*H*-pyrrole-2,5-dione (33 mg, 0.34 mmol). The resulting solution was heated at reflux for 48 hours. The reaction was cooled to 0 °C and PTAD was added. The solution was stirred at 0 °C for 4 hours and the solvent was removed under reduced pressure to give the crude product as pale red. The product was purified by column chromatography (diameter = 1.5 cm, silica = 17 cm, eluent = petrol (40/60)–EA 1 : 1) to give (3a*S**,5*S**,10b*S**)-5-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-10-tosyl-4,5,10,10b-tetrahydropyrrolo-[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione (23%, 0.044 g, 0.08 mmol) as an off white solid.

Mp: 206.4–209.7 °C; R_f: 0.10 (Pet(40/60)–EA 2 : 1); ^{1}H NMR (400 MHz, DMSO-d_6): δ_C 11.37 (1H, s), 10.77 (1H, s), 7.82 (2H, d, J = 8.3 Hz), 7.72 (1H, d, J = 7.9 Hz), 7.48–7.43 (2H, m), 7.42–7.35 (4H, m), 7.28 (2H, d, J = 8.5 Hz), 7.25–7.18 (2H, m), 5.46 (1H, app t, J = 4.9 Hz), 5.19 (1H, d, J = 7.7 Hz), 3.77–3.65 (1H, m), 2.41 (1H, app dt, J = 9.8, 5.1 Hz), 2.26 (3H, s), 2.24–2.16 (1H, m); ^{13}C NMR (101 MHz, $CDCl_3$): δ_H 178.8, 173.6, 153.6, 152.4, 145.4, 136.9, 135.3, 132.2, 130.9, 129.9, 129.2, 128.4, 127.5, 126.9, 125.7, 125.6, 124.2, 119.3, 115.1, 114.8, 47.3, 41.5, 40.2, 28.8, 21.7; IR (neat): ν_{max}/cm^{-1} 3194, 2981, 2980, 1699; MS (pNSI): 587.2 (100% (M + NH_4)$^+$), 592.1 (30% (M + Na)$^+$); HRMS (pNSI): calcd for $C_{29}H_{27}N_6O_6S$ [M + NH_4]$^+$: 587.1707; observed: 587.1706.

3o – (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-7-methoxy-10-tosyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione

To a stirred round bottomed flask was added 6-methoxy-1-tosyl-3-vinyl-1H-indole (111 mg, 0.34 mmol), DCM (5 mL) and 1*H*-pyrrole-2,5-dione (33 mg, 0.34 mmol). The resulting solution was heated at reflux for 48 hours. The reaction was cooled to room temperature and 1-methyl-2-nitrosobenzene (41 mg, 0.34 mmol) was added. The reaction was stirred at room temperature for 24 hours before the solvent was removed under reduced pressure to leave the crude product as a pale yellow solid. The product was purified by column chromatography (petrol (40/60)–ethyl acetate 2 : 1) to give (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-7-methoxy-10-tosyl-4,5,10,10b-tetrahydro pyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione (76%, 141 mg, 0.26 mmol) as a light brown solid.

Mp: 185 °C decomposed; R_f: 0.26 (Pet(40/60)–EA 4 : 3); ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 11.19 (1H, s), 8.34 (1H, s), 7.69 (1H, d, J = 9.1 Hz), 7.61 (2H, d, J = 8.2 Hz), 7.27 (2H, d, J = 8.2 Hz), 7.08–6.97 (2H, m), 6.95–6.85 (2H, m), 6.72 (1H, dd, J = 9.1, 2.4 Hz), 6.40 (1H, s), 5.07 (1H, d, J = 7.9 Hz), 4.20 (1H, app t, J = 4.4 Hz), 3.76 (1H, app q, J = 8.4 Hz), 3.47 (3H, s), 2.53–2.47 (1H,

m), 2.28 (s, 3H), 2.08 (s, 3H), 1.75 (1H, ddd, $J = 13.6, 9.8, 4.4$ Hz); ^{13}C NMR (101 MHz, DMSO-d_6): δ_C 180.5, 175.4, 156.3, 151.7, 145.3, 134.7, 133.1, 131.1, 131.0, 130.8, 130.3, 129.7, 127.1, 126.4, 124.6, 122.1, 121.2, 115.9, 113.8, 103.3, 57.1, 55.3, 42.2, 26.9, 21.5, 21.3, 18.5; IR (neat): $\nu_{(max)}$/cm^{-1} 3388, 3071, 2552, 1727; MS (pNSI): 355.1 (50%), 371.1 (100%), 423.1 (57%), 445.1 (30%), 546.2 (5%, $(M + H)^+$), 568.2 (16%, $(M + Na)^+$), 584.1 (21%); HRMS (pNSI): calcd for $C_{29}H_{28}N_3O_6S_1$ $[M + H]^+$: 546.1693; observed: 546.1690.

3p – (3a*S**,5*S**,10b*S**)-5-((*S**)-hydroxy(perfluorophenyl) methyl)-7-methoxy-2-methyl-10-tosyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione

To a stirred round bottomed flask was added 5-methoxy-1-tosyl-3-vinyl-1*H*-indole (112 mg, 0.34 mmol), DCM (5 mL) and 1-methyl-1*H*-pyrrole-2,5-dione (38 mg, 0.34 mmol). The reaction was heated at reflux for 48 hours. The reaction was cooled to −78 °C and pentafluorobenzaldehyde (0.04 mL, 0.34 mmol) and DMAC (1 M in hexane, 0.34 mL, 0.34 mmol) were added. The solution was stirred at −78 °C for 15 minutes and then at room temperature for 18 hours. The solvent was removed under reduced pressure to give the crude product as an off white solid. The product was purified by column chromatography (column diameter = 2 cm, silica = 15 cm, eluent = petrol (40/60)–EA 3 : 1) to give a 8 : 1 mixture of (3a*S**,5*S**,10b*S**)-5-((*S**)-hydroxy-(perfluorophenyl)methyl)-7-methoxy-2-methyl-10-tosyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione and (3a*S**,5*S**,10b*S**)-5-((*R**)-hydroxy(perfluorophenyl)methyl)-7-methoxy-2-methyl-10-tosyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]-carbazole-1,3(2*H*,3a*H*)-dione (70%, 0.151 mg, 0.24 mmol) as a white powder.

Major diastereomer: Mp: 136.7–139.0 °C; R_f: 0.40 (Pet(40/60)–EA 2 : 1); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.76 (2H, d, $J = 8.3$ Hz), 7.69 (1H, d, $J = 9.1$ Hz), 7.22 (2H, d, $J = 8.3$ Hz), 6.83 (1H, dd, $J = 9.1, 2.5$ Hz), 6.72 (1H, d, $J = 2.5$ Hz), 5.08 (1H, d, $J = 8.3$ Hz), 4.87 (1H, d, $J = 7.4$ Hz), 3.71 (3H, s), 3.58–3.47 (2H, m), 2.94 (3H, s), 2.34 (3H, s), 2.11–2.04 (1H, m), 1.60 (1H, td, $J = 13.9, 5.3$ Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 177.7, 173.2, 156.8, 145.2, 135.2, 132.0, 130.9, 130.3, 129.8, 127.0, 120.6, 116.2, 114.0, 102.6, 70.2, 55.6, 41.5, 39.0, 36.9, 28.6, 25.3, 21.7; IR (neat): ν_{max}/cm^{-1} 2981, 2884, 1709; MS (pAPCI): 157.0 (80%), 221.1 (92%), 281.1 (49%) 475.1 (94%), 635.1 (100%, $(M + H)^+$); HRMS (pAPCI): calcd for $C_{30}H_{24}F_5N_2O_6S$ $[M + H]^+$: 635.1270; observed: 635.1266. *Note*: *^{13}C NMR missing peaks due to C–F coupling.*

3q – (3a*S**,5*S**,10b*S**)-5-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-7-methoxy-10-tosyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*] carbazole-1,3(2*H*,3a*H*)-dione

To a stirred round bottomed flask was added 5-methoxy-1-tosyl-3-vinyl-1*H*-indole (112 mg, 0.34 mmol), DCM (5 mL) and 1*H*-pyrrole-2,5-dione (33 mg, 0.34 mmol). The reaction was heated at reflux for 48 hours. The reaction was cooled to 0 °C and PTAD (60 mg, 0.34 mmol) was added. The reaction was stirred at 0 °C for 4 hours before the solvent was removed under reduced pressure to give the crude product as a pale red solid. The product was purified by column chromatography (column diameter = 2 cm, silica = 16 cm, eluent = petrol (40/60)–EA 1 : 1) to give (3a*S**,5*S**,10b*S**)-5-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-7-methoxy-10-tosyl-4,5,10,10b-tetrahydropyrrolo-[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione (75%, 0.152 mg, 0.25 mmol) as a pale yellow powder.

Mp: 189.9–193.3 °C; R_f: 0.07 (Pet(40/60)–EA 1 : 1); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.31 (1H, br), 7.67 (2H, d, $J = 7.5$ Hz), 7.55 (1H, d, $J = 8.8$ Hz), 7.38–7.23 (5H, m), 7.00 (2H, d, $J = 7.8$ Hz), 6.90 (1H, s), 6.80 (1H, d, $J = 8.9$ Hz), 5.53 (1H, br s), 5.18 (1H, d, $J = 6.7$ Hz), 3.74–3.69 (1H, m), 3.64 (3H, s), 2.48–2.55 (1H, m), 2.17 (3H, s), 2.12–2.02 (2H, m); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 179.0, 173.9, 156.9, 153.7, 152.7, 145.2, 135.1, 132.7, 131.5, 131.0, 129.8, 129.2, 128.4, 128.0, 127.2, 125.6, 115.9, 115.5, 114.3, 101.9, 55.7, 47.6, 41.6, 40.1, 28.8, 21.6; IR (neat): ν_{max}/cm^{-1} 2972, 2885, 1781, 1709; MS (pNSI): 617.2 (69%, $(M + NH_4)^+$), 622.1 (100%, $(M + Na)^+$), 644.1 (48%); HRMS (pNSI): calcd for $C_{30}H_{29}N_6O_7S$ $[M + NH_4]^+$: 617.1813; observed: 617.1817.

3r – 6-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-2-phenyl-11-tosyl-5,6-dihydro-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*] indole-1,3(2*H*,11*H*)-dione

To a stirred round bottomed flask was added 1-tosyl-3-vinyl-1*H*-indole (100 mg, 0.34 mmol) and DCM (5 mL). The resulting solution was cooled to −78 °C and then PTAD (70 mg, 0.34 mmol) was added. The reaction was stirred at −78 °C for 3.5 hours. The reaction was warmed to 0 °C and a further equivalent of PTAD (60 mg, 0.34 mmol) was added. The reaction was stirred 0 °C for 4 hours, resulting in the formation of a white precipitate. The reaction mixture was filtered and 6-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-2-phenyl-11-tosyl-5,6-dihydro-[1,2,4]triazolo[1′,2′:1,2] pyridazino[3,4-*b*]indole-1,3(2*H*,11*H*)-dione (65%, 134 mg, 0.207 mmol) was recovered as a white powder.

Mp: 227.8–230.6 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 10.76 (1H, s, NH), 7.91 (1H, d, $J = 7.8$ Hz), 7.61 (2H, d, $J = 8.3$ Hz), 7.48–7.24 (15H, m), 5.52 (1H, s), 4.76 (1H, d, $J = 13.8$ Hz), 3.86 (1H, d, $J = 13.8$ Hz), 2.24 (3H, s); ^{13}C NMR (101 MHz, DMSO-d_6): δ_C 154.3, 153.5, 150.6, 149.5, 146.0, 135.1, 133.3, 133.0, 131.7, 131.5, 130.4, 129.6, 129.5, 129.4, 128.8, 128.1, 127.6, 127.5, 126.9, 125.9, 125.4, 119.3, 116.8, 104.1, 48.8, 43.3, 21.6; IR (neat): ν_{max}/cm^{-1} 2971, 2883, 1714; MS (pNSI): 263.0 (36%), 345.0 (51%), 371.1 (42%), 665.2 (89%, $(M + NH_4)^+$), 670.1 (100%, $(M + Na)^+$); HRMS (pNSI): calcd for $C_{33}H_{25}N_7NaO_6S$ $[M + Na]^+$: 670.1479; observed: 670.1475.

3s – 6-(hydroxy(phenyl)amino)-2-phenyl-11-tosyl-5,6-dihydro-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-1,3(2*H*,11*H*)-dione

To a stirred round bottomed flask was added 1-tosyl-3-vinyl-1*H*-indole (100 mg, 0.34 mmol) and DCM (5 mL) and the solution was cooled to −78 °C. To this solution PTAD (70 mg, 0.34 mmol) was added and the reaction was stirred at −78 °C for 3.5 hours. The reaction was warmed to room temperature nitrosobenzene (44 mg, 0.34 mmol) was added and the reaction was stirred for 18 hours. The solvent was removed under reduced pressure to leave the crude product as a pale

yellow oil. The product was purified by column chromatography (column diameter = 1 cm, silica = 16 cm, eluent = petrol (40/60)–ether–DCM 2 : 1 : 1) to give 6-(hydroxy(phenyl) amino)-2-phenyl-11-tosyl-5,6-dihydro-[1,2,4]triazolo[1′,2′:1,2] pyridazino[3,4-*b*]indole-1,3(2*H*,11*H*)-dione (72%, 141 mg, 0.24 mmol) as a white powder.

Mp: 176.1–180.0 °C; R_f: 0.48 (Pet(40/60)–Et_2O 2 : 1); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.03 (1H, d, J = 8.3 Hz), 7.62 (2H, d, J = 8.1 Hz), 7.56 (2H, d, J = 7.6 Hz), 7.46 (2H, app t, J = 7.7 Hz), 7.42–7.36 (1H, m), 7.23–7.07 (7H, m), 7.05–6.99 (2H, m), 6.59 (1H, d, J = 7.4 Hz), 5.81 (1H, br s), 5.18 (1H, d, J = 13.5 Hz), 4.59 (1H, s), 3.23 (1H, d, J = 13.5 Hz), 2.30 (3H, s); ^{13}C NMR (101 MHz, DMSO-d_6): δ_C 152.7, 152.2, 150.5, 146.0, 134.9, 132.9, 132.5, 131.8, 130.4, 129.8, 129.3, 129.2, 128.5, 127.3, 127.3, 125.5, 125.4, 122.5, 119.8, 117.6, 116.6, 108.6, 55.9, 44.6, 21.6; IR (neat): ν_{max}/cm^{-1} 2981, 2884, 1714; MS (pAPCI): 138.1 (100%), 157.0 (95%), 213.1 (50%), 248.1 (86%), 279.1 (62%), 317.1 (33%), 333.1 (29%), 471.1 (31%), 564.2 (11%), 580.2 (10%, $(M + H)^+$); HRMS (pAPCI): calcd for $C_{31}H_{26}N_5O_5S$ $[M + H]^+$: 580.1649; observed: 580.1640.

3t – (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-*N*,*N*,2-trimethyl-1,3-dioxo-1,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(2*H*)-sulfonamide

To a stirred bottomed flask was added *N*,*N*-dimethyl-3-vinyl-1*H*-indole-1-sulfonamide (85 mg, 0.34 mmol), DCM (5 mL) and 1-methyl-1*H*-pyrrole-2,5-dione (38 mg, 0.34 mmol). The solution was heated at reflux for 48 hours. The reaction was cooled to room temperature and 1-methyl-2-nitrosobenzene (41 mg, 0.34 mmol) was added. The reaction was stirred for 3 hours at room temperature before the solvent was removed under reduced pressure to give the crude product. The crude product was purified by column chromatography (column diameter = 2 cm, silica = 16 cm, eluent = petrol (40/60)–ethyl acetate 2 : 1) to give (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-*N*,*N*,2-trimethyl-1,3-dioxo-1,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(2*H*)-sulfonamide (74%, 0.122 g, 0.25 mmol) as an off white solid.

Mp: 169.3–171.9 °C; R_f: 0.32 (Pet(40/60)–EA 2 : 1); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.84 (1H, d, J = 8.4 Hz), 7.60 (1H, d, J = 7.9 Hz), 7.50 (1H, d, J = 8.0 Hz), 7.28 (1H, app t, J = 7.8 Hz), 7.21–7.16 (2H, m), 7.13 (1H, d, J = 8.1 Hz), 7.07–7.03 (1H, m), 4.98–4.96 (2H, m), 4.35–4.31 (1H, m), 3.69 (1H, app t, J = 7.7 Hz), 2.93 (9H, s), 2.60 (1H, app dt, J = 13.1, 6.2 Hz), 2.33 (3H, s), 1.97 (1H, ddd, J = 13.1, 7.7, 4.6 Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 178.4, 173.8, 149.2, 137.4, 131.9, 131.1, 129.6, 128.4, 126.6, 125.3, 124.7, 123.7, 121.5, 120.4, 118.8, 115.0, 57.5, 40.5, 39.4, 38.4, 25.2, 24.7, 18.7; IR (neat): ν_{max}/cm^{-1} 3426, 2981, 1712; MS (pAPCI): 221.1 (9%), 251.1 (13%), 360.1 (100%, $(M - (o\text{-Tol})N(OH))^+$), 465.2 (15%, $(M - H_2O)^+$), 483.2 (15%, $(M + H)^+$); HRMS (pAPCI): calcd for $C_{24}H_{27}N_4O_5S_1$ $[M + H]^+$: 483.1697; observed: 483.1685.

3u – (3a*S**,5*S**,10b*S**)-5-((2,6-dibromophenyl) (hydroxy) amino)-*N*,*N*-dimethyl-1,3-dioxo-2-phenyl-1,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(2*H*)-sulfonamide

To a stirred round bottomed flask was added *N*,*N*-dimethyl-3-vinyl-1*H*-indole-1-sulfonamide (85 mg, 0.34 mmol), DCM (5 mL) and 1-phenyl-1*H*-pyrrole-2,5-dione (59 mg, 0.34 mmol) and the resulting solution was heated at reflux for 48 hours. The reaction was cooled to room temperature and 2,6-dibromonitrosobenzene (90 mg, 0.34 mmol) was added. The reaction was stirred at room temperature for 18 hours and the solvent was removed under reduced pressure to give the crude product as a pale yellow solid. The product was purified by column chromatography (petrol (40/60)–ethyl acetate 3 : 1, column diameter = 2 cm, silica = 17 cm) to give (3a*S**,5*S**,10b*S**)-5-((2,6-dibromophenyl) (hydroxy)amino)-*N*,*N*-dimethyl-1,3-dioxo-2-phenyl-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-sulfonamide (69%, 162 mg, 0.23 mmol) as a pale orange powder.

Mp: 241–242 °C; R_f: 0.43 (Pet(40/60)–Et_2O 4 : 1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (2H, d, J = 7.8 Hz), 7.46–7.30 (7H, m), 7.15 (1H, app t, J = 7.4 Hz), 7.02 (1H, app t, J = 7.5 Hz), 6.71 (1H, app td, J = 8.0, 2.1 Hz), 6.05 (1H, s), 5.49–5.47 (1H, m), 5.17–5.12 (1H, m), 4.35–4.27 (1H, m), 3.18–3.11 (1H, m), 2.92 (6H, s), 1.80 (1H, app t, J = 13.1 Hz); ^{13}C NMR (101 MHz, CD_2Cl_2): δ_C 177.9, 172.5, 144.6, 136.1, 134.3, 132.7, 132.1, 132.0, 129.5, 129.1, 128.6, 128.2, 126.6, 124.0, 122.8, 119.2, 115.1, 113.6, 77.6, 54.7, 42.7, 39.0, 38.0, 30.0; IR (neat): ν_{max}/cm^{-1} 3431, 2927, 1780, 1715; MS (pNSI): 422.1 (25%, $(M - N(OH)C_6H_3Br_2)^+$), 689.0 (76% $(M + H)^+$), 711.0 (54%, $(M + Na)^+$), HRMS (pNSI): calcd $C_{28}H_{25}Br_2N_4O_5S$ $[M + H]^+$: 688.9888; observed: 688.9886.

3v – (3a*S**,5*S**,10b*S**)-5-((*S**)-hydroxy(perfluorophenyl) methyl)-*N*,*N*-dimethyl-1,3-dioxo-1,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(2*H*)-sulfonamide

To a stirred round bottomed flask was added *N*,*N*-dimethyl-3-vinyl-1*H*-indole-1-sulfonamide (85 mg, 0.34 mmol), DCM (5 mL) and 1-methyl-1*H*-pyrrole-2,5-dione (38 mg, 0.34 mmol). The reaction was heated at reflux for 48 hours. The reaction was cooled to −78 °C and pentafluorobenzaldehyde (66 mg, 0.34 mmol) and DMAC (1 M in hexane, 0.34 mL, 0.34 mmol) were added and the reaction was stirred for 1 hour. The reaction was poured into a solution of sodium bicarbonate (10 mL) and extracted with DCM (3 × 10 mL). The combined organic extracts were dried with $MgSO_4$, filtered and the solvent was removed under reduced pressure to leave the crude product as a pale pink solid. The product was purified by column chromatography (diameter = 2 cm, silica = 17 cm, eluent = petrol (40/60)–EA 2 : 1) to give (3a*S**,5*S**,10b*S**)-5-((*S**)-hydroxy(perfluorophenyl)methyl)-*N*,*N*-dimethyl-1,3-dioxo-1,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(2*H*)-sulfonamide (77%, 0.145 g, 0.26 mmol) as a pale pink solid.

Mp: 255.8–257.2 °C; R_f: 0.30 (Pet(40/60)–EA 2 : 1); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.77 (1H, d, J = 8.3 Hz), 7.39 (1H, d, J = 7.8 Hz), 7.33–7.28 (1H, m), 7.21 (1H, app t, J = 7.8 Hz), 5.14 (1H, d, J = 8.0 Hz), 4.80 (1H, d, J = 7.3 Hz), 3.67–3.62 (1H, m), 3.48 (1H, ddd, J = 12.8, 7.2, 5.0 Hz), 2.98 (6H, s), 2.93 (3H, s), 2.49 (1H, br s), 2.06 (1H, app dd, J = 14.9, 4.1 Hz), 1.59 (1H, app dt, J = 13.8, 6.9 Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 177.8, 173.4, 137.2, 130.0, 129.3, 125.0, 123.5, 120.0, 118.2, 114.6, 70.3, 41.5, 39.2, 38.2, 36.7, 28.6, 25.2; IR (neat): ν_{max}/cm^{-1} 3415, 2972, 2884, 1713; MS (pNSI): 371.1 (22%), 558.1 (81% $(M + H)^+$), 580.1 (100%, $(M + Na)^+$), HRMS (pNSI): calcd $C_{24}H_{20}F_5N_3O_5S$ $[M + H]^+$: 558.1117; observed: 558.1118.

Note: ^{13}C NMR missing peaks due to C–F coupling.

3w – 6-(hydroxy(*o*-tolyl)amino)-*N*,*N*-dimethyl-1,3-dioxo-2-phenyl-2,3,5,6-tetrahydro-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-11(1*H*)-sulfonamide

To a stirred round bottomed flask was added *N*,*N*-dimethyl-3-vinyl-1*H*-indole-1-sulfonamide (85 mg, 0.34 mmol), DCM (5 mL) and cooled to −78 °C. To this solution PTAD (60 mg, 0.34 mmol) was added and the reaction stirred at −78 °C for 1 hour. 1-Methyl-2-nitrosobenzene (41 mg, 0.34 mmol) was added and the reaction was stirred 4 hours before the solvent was removed under reduced pressure to give the crude product. The crude product was purified by column chromatography (column diameter = 2 cm, silica = 16 cm, eluent = petrol (40/60)–ethyl acetate 2 : 1) to give 6-(hydroxy(*o*-tolyl)amino)-*N*,*N*-dimethyl-1,3-dioxo-2-phenyl-2,3,5,6-tetrahydro-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-11(1*H*)-sulfonamide (76%, 0.141 g) as an off white solid.

Mp: 168.5–172.8 °C; R_f: 0.25 (Pet(40/60)–EA 2 : 1); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.87 (1H, d, J = 8.3 Hz), 7.73 (1H, d, J = 8.1 Hz), 7.60 (2H, d, J = 7.4 Hz), 7.51 (2H, t, J = 7.6 Hz), 7.46–7.38 (1H, m), 7.30–7.18 (2H, m), 7.04 (2H, t, J = 7.5 Hz), 6.90 (1H, d, J = 7.6 Hz), 6.71 (1H, d, J = 7.8 Hz), 5.76 (1H, s), 5.37 (1H, d, J = 14.1 Hz), 4.66 (1H, s), 3.46 (1H, d, J = 14.1 Hz), 2.90 (6H, s), 1.94 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 153.5, 150.5, 148.7, 135.1, 132.1, 131.9, 131.2, 130.6, 129.4, 128.7, 127.1, 126.9, 126.8, 125.9, 124.4, 124.2, 122.7, 118.1, 115.9, 104.7, 59.4, 44.7, 38.7, 17.9; IR (neat): ν_{max}/cm^{-1} 3322, 2971, 1707; MS (pNSI): 339.1 (33%), 424.1 (94%, $(M - MeC_6H_4NOH)^+$), 547.2 (72%, $(M + H)^+$), 569.2 (100%, $(M + Na)^+$); HRMS (pNSI): calcd $C_{27}H_{27}N_6O_5S$ $[M + H]^+$: 547.1758; observed: 547.1761.

3x – (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-*N*,*N*-dimethyl-1,3-dioxo-1,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(2*H*)-sulfonamide

To a round bottomed flask was added *N*,*N*-dimethyl-3-vinyl-1*H*-indole-1-sulfonamide (85 mg, 0.34 mmol), DCM (5 mL) and 1*H*-pyrrole-2,5-dione (33 mg, 0.34 mmol). The reaction was heated at reflux for 48 hours and then cooled to room temperature. 1-Methyl-2-nitrosobenzene (41 mg, 0.34 mmol) was added and the reaction is stirred for 4.5 hours. The solvent was removed to give the crude product as pale yellow solid. The crude product was purified by trituration from DCM to give (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-*N*,*N*-dimethyl-1,3-dioxo-1,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(2*H*)-sulfonamide (77%, 123 mg, 0.26 mmol) as a white solid.

Mp: 199.9–201.0 °C; R_f: 0.64 (Pet(40/60)–EA 3 : 1); ^{1}H NMR (300 MHz, DMSO-d_6): δ_H 11.15 (1H, s), 8.38 (1H, s), 7.88 (1H, d, J = 8.4 Hz), 7.36 (1H, d, J = 7.9 Hz), 7.31–7.20 (2H, m), 7.13 (3H, app dt, J = 14.3, 7.3 Hz), 7.01 (1H, d, J = 7.3 Hz), 4.98 (1H, d, J = 7.8 Hz), 4.38 (1H, app t, J = 4.8 Hz), 3.73 (1H, app q, J = 7.8 Hz), 2.70 (6H, s), 2.45–2.37 (1H, m), 2.36 (3H, s), 1.77–1.65, 1.77 (1H, m); ^{13}C NMR (101 MHz, DMSO-d_6): δ_C 180.4, 175.5, 151.6, 137.2, 133.2, 131.1, 129.3, 129.1, 126.6, 124.4, 124.3, 123.4, 121.8, 121.1, 118.6, 115.3, 56.5, 42.2, 41.1, 38.7, 26.6, 18.9; IR (neat): ν_{max}/cm^{-1} 3426, 2981, 1712; MS (pAPCI): 237.1 (60%), 346.1 (100%, $(M - MeC_6H_4NOH)^+$), 451.1 (25%, $(M - H_2O)^+$), 469.2 (22%, $(M + H)^+$); HRMS (pAPCI): calcd $C_{23}H_{25}N_4O_5S$ $[M + H]^+$: 469.1540; observed: 469.1537.

3y – benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(phenyl)amino)-2-methyl-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate

To a stirred Schlenk flask was added benzyl 3-vinyl-1*H*-indole-1-carboxylate (94 mg, 0.34 mmol), DCM (5 mL) and 1-methyl-1*H*-pyrrole-2,5-dione (33 mg, 0.34 mmol). The resulting solution was heated at reflux for 24 hours. The reaction was allowed to cool to room temperature and to the stirred solution nitrosobenzene (36 mg, 0.34 mmol) was added and the solution was stirred for 18 hours. The solvent was removed under reduced pressure to leave the crude product as a pale yellow solid. The product was purified by column chromatography (petrol (40/60)–ethyl acetate 3 : 1, column diameter = 2 cm, silica = 14 cm) to give benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(phenyl)amino)-2-methyl-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate (74%, 124 mg, 0.25 mmol) as a yellow powder.

Mp: 105.7–109.2 °C; R_f: 0.34 (Pet(40/60)–EA 2 : 1); ^{1}H NMR (400 MHz, CD_2Cl_2): δ_H 8.10 (1H, br d, J = 8.1 Hz), 7.70 (1H, br d, J = 7.3 Hz), 7.49 (2H, br d, J = 6.6 Hz), 7.39 (3H, br app q, J = 6.9, 6.4 Hz), 7.35–7.25 (3H, br m), 7.22–7.13 (3H, br m), 7.01 (1H, br app t, J = 6.7 Hz), 5.55 (1H, d, J = 11.8 Hz), 5.41 (1H, d, J = 11.8 Hz), 4.88 (1H, br d, J = 6.8 Hz), 4.87 (1H, br s), 4.80–4.77 (1H, br m), 3.54–3.41 (1H, br m), 2.85 (3H, s), 2.40–2.25 (1H, br m), 2.08–1.93 (1H, br m); ^{13}C NMR (101 MHz, CD_2Cl_2): δ_C 178.4, 174.6, 151.6, 151.0, 137.0, 135.0, 130.0, 129.0, 128.9, 128.8, 128.8, 127.6, 125.0, 123.3, 122.3, 120.0, 118.3, 117.1, 115.1, 69.5, 57.7, 40.2, 39.2, 24.9, 22.6; IR (neat): ν_{max}/cm^{-1} 3433, 2953, 1699; MS (pNSI): 387.1 (97%, $(M - N(OH)Ph)^+$), 494.2 (100%, $(M - H)^+$), 518.2 (30%, $(M + Na)^+$), 991.4 (15%, $(2M + H)^+$), 1013.3 (10%, $(2M + Na)^+$); HRMS (pNSI): calcd $C_{29}H_{25}N_3O_5Na$ $[M + Na]^+$: 518.1686; observed: 518.1676.

3z – benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-2-methyl-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate

To a stirred Schlenk flask was added benzyl 3-vinyl-1*H*-indole-1-carboxylate (94 mg, 0.34 mmol), DCM (5 mL) and 1-methyl-1*H*-pyrrole-2,5-dione (33 mg, 0.34 mmol). The resulting solution was heated at reflux for 24 hours. The reaction was allowed to cool to room temperature and to the stirred solution 1-methyl-2-nitrosobenzene (41 mg, 0.34 mmol) was added and the solution was stirred for 18 hours. The solvent was removed under reduced pressure to leave the crude product as a pale yellow solid. The product was purified by column chromatography (petrol (40/60)–ethyl acetate 3 : 1, column diameter = 2 cm, silica = 16 cm) to give benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-2-methyl-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylateas (78%, 135 mg, 0.26 mmol) as a yellow powder.

Mp: 128.4–131.5 °C; R_f: 0.45 (Pet(40/60)–EA 3 : 1); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.11 (1H, d, J = 8.3 Hz), 7.59 (1H, d, J = 7.8 Hz), 7.55 (1H, d, J = 8.1 Hz), 7.50–7.48 (2H, m), 7.45–7.38

(3H, m), 7.29–7.23 (1H, m), 7.20 (1H, app t, $J = 7.6$ Hz), 7.14 (1H, d, $J = 7.6$ Hz), 7.10 (1H, d, $J = 7.8$ Hz), 7.05 (1H, d, $J = 7.3$ Hz), 5.56 (1H, d, $J = 11.8$ Hz), 5.46 (1H, d, $J = 11.8$ Hz), 5.02 (1H, s), 4.93 (1H, d, $J = 7.6$ Hz), 4.38 (1H, t, $J = 5.2$ Hz), 3.63 (1H, app q, $J = 6.9$ Hz), 2.91 (3H, s), 2.59 (1H, app dt, $J = 12.3$, 6.0 Hz), 2.29 (3H, s), 1.92 (1H, ddd, $J = 12.5$, 7.5, 4.6 Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 178.5, 174.6, 151.7, 149.2, 136.8, 134.8, 131.1, 129.9, 129.0, 129.0, 128.9, 128.9, 127.7, 126.6, 125.3, 125.0, 123.3, 121.5, 120.1, 118.1, 115.3, 69.6, 57.4, 40.4, 39.1, 25.2, 24.1, 18.6; IR (neat): ν_{max}/cm^{-1} 3450, 2954, 1699; MS (pNSI): 343.1 (40%), 387.1 (82%, (M − (N(OH)(*o*-Tol)))$^+$), 508.2 (100%, (M − (H_2) + H)$^+$), 532.2 (59%, (M + Na)$^+$); HRMS (pNSI): calcd $C_{30}H_{27}N_3O_5Na$ [M + Na]$^+$: 532.1843; observed: 532.1834.

3aa – (3a*S**,5*S**,10b*S**)-5-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-2-methyl-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate

To a stirred Schlenk flask was added benzyl 3-vinyl-1*H*-indole-1-carboxylate (189 mg, 0.68 mmol), 1-methyl-1*H*-pyrrole-2,5-dione (76 mg, 0.68 mmol) and DCM (10 mL). The reaction mixture was heated at reflux for 24 hours. The reaction was cooled to 0 °C and then 4-phenyl-1,2,4-triazolidine-3,5-dione (120 mg, 0.68 mmol) was added. The reaction was stirred at 0 °C for 1 hour then at room temperature for 18 hours. The solvent was removed under reduced pressure to leave the crude product as an orange powder. The product was purified by column chromatography (petrol (40/60)–ethyl acetate 1 : 1, column diameter = 2 cm, silica = 20 cm) to give (3a*S**,5*S**,10b*S**)-5-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-2-methyl-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]-carbazole-10(1*H*)-carboxylate (54%, 207 mg, 0.37 mmol) as an off-white powder and (3a*S**,5*S**,10b*S**)-5-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-2-methyl-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate (27%, 76 mg, 0.19 mmol) as a white powder.

Mp: 202.3–203.9 °C; R_f: 0.15 (Pet(40/60)–EA 1 : 1); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.38 (1H, s), 8.07 (1H, d, $J = 8.4$ Hz), 7.51 (1H, app dt, $J = 7.6$, 0.9 Hz), 7.49–7.37 (4H, m), 7.39–7.33 (6H, m), 7.30 (1H, ddd, $J = 8.6$, 7.3, 1.3 Hz), 7.21 (1H, app td, $J = 7.5$, 1.0 Hz), 5.53 (1H, app t, $J = 5.2$ Hz), 5.44 (1H, d, $J = 11.8$ Hz), 5.38 (1H, d, $J = 11.8$ Hz), 4.89 (1H, d, $J = 8.0$ Hz), 3.50 (1H, ddd, $J = 9.6$, 8.0, 5.5 Hz), 2.87 (3H, s), 2.41 (1H, app dt, $J = 14.2$, 5.5 Hz), 2.14 (1H, ddd, $J = 14.2$, 9.5, 5.5 Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 177.4, 173.6, 153.6, 152.2, 151.3, 136.9, 134.5, 130.9, 130.8, 129.3, 129.1, 128.9, 128.9, 128.4, 126.1, 125.8, 125.3, 123.8, 118.8, 115.7, 113.8, 69.8, 47.5, 40.0, 38.4, 27.5, 25.2; IR (neat): ν_{max} cm^{-1} 3462, 2969, 1699; MS (pNSI): 199.2 (16%), 387.1 (19%, (M − PTAD)$^+$), 564.2 (59%, (M + H)$^+$), 581.2 (100%, (M + NH_4)$^+$), 643.2 (15%), 1144.4 (39%, (2M + NH_4)$^+$); HRMS (pNSI): calcd $C_{31}H_{26}N_5O_6$ [M + H]$^+$: 564.1878; observed: 564.1873.

3bb – benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(phenyl)amino)-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate

To a stirred Schlenk flask was added benzyl 3-vinyl-1*H*-indole-1-carboxylate (189 mg, 0.68 mmol), 1*H*-pyrrole-2,5-dione (66 mg, 0.68 mmol) and DCM (10 mL). The resulting solution was heated at reflux for 24 hours. The reaction was allowed to cool to room temperature and to the stirred solution nitrosobenzene (73 mg, 0.68 mmol) was added and the solution was stirred for 18 hours. The solvent was removed under reduced pressure to leave the crude product as a yellow powder. The product was purified by column chromatography (petrol (40/60)–ethyl acetate 2 : 1, column diameter = 2 cm, silica = 20 cm) to give benzyl(3a*S**,5*S**,10b*S**)-5-(hydroxy(phenyl)amino)-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate (70%, 230 mg, 0.48 mmol) as a yellow powder.

Mp: 177.1–177.8 °C; R_f: 0.38 (Pet(40/60)–EA 2 : 1); ^{1}H NMR (500 MHz, CD_2Cl_2): δ_H 8.20 (1H, s), 8.11 (1H, d, $J = 8.3$ Hz), 7.66 (1H, d, $J = 7.8$ Hz), 7.50 (2H, dd, $J = 7.9$, 1.6 Hz), 7.43–7.36 (3H, m), 7.33 (2H, app t, $J = 7.8$ Hz), 7.28 (1H, app t, $J = 7.8$ Hz), 7.22 (2H, d, $J = 8.0$ Hz), 7.16 (1H, app t, $J = 7.5$ Hz), 7.02 (1H, app t, $J = 7.3$ Hz), 5.55 (1H, d, $J = 11.9$ Hz), 5.40 (1H, d, $J = 11.9$ Hz), 5.19 (1H, s), 4.96 (1H, br d, $J = 8.1$ Hz), 4.82 (1H, app t, $J = 5.7$ Hz), 3.56 (1H, br app q, $J = 7.4$ Hz), 2.35 (1H, br app dd, $J = 13.4$, 6.7 Hz), 2.00–1.92 (1H, br m); ^{13}C NMR (101 MHz, CD_2Cl_2): δ_C 178.5, 174.5, 151.6, 150.7, 136.9, 134.9, 129.7, 129.0, 128.9, 128.9, 128.8, 127.6, 125.1, 123.3, 122.6, 119.8, 118.0, 117.3, 115.2, 69.5, 57.7, 41.4, 40.6, 23.0; IR (neat): ν_{max}/cm^{-1} = 3418, 3329, 2970, 1705; MS (pNSI): 199.2 (87%), 373.1 (68%, (M − (N(OH)Ph))$^+$), 480.2 (100%, (M − (H_2) + H)$^+$); HRMS (pNSI): calcd $C_{28}H_{23}N_3O_5Na$ [M + Na]$^+$: 504.1530; observed: 504.1522.

3cc – benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate

To a stirred Schlenk flask was added benzyl 3-vinyl-1*H*-indole-1-carboxylate (94 mg, 0.34 mmol), DCM (5 mL) and 1*H*-pyrrole-2,5-dione (33 mg, 0.34 mmol). The resulting solution was heated at reflux for 24 hours. The reaction was allowed to cool to room temperature and to the stirred solution 1-methyl-2-nitrosobenzene (41 mg, 0.34 mmol) was added and the solution was stirred for 4 hours. The solvent was removed under reduced pressure to leave the crude product as a pale yellow solid. The product was purified by column chromatography (petrol (40/60)–ethyl acetate 3 : 2, column diameter = 2 cm, silica = 16 cm) to give benzyl-(3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]-carbazole-10(1*H*)-carboxylate (83%, 140 mg, 0.28 mmol) as a yellow powder.

Mp: 181.4–183.9 °C; R_f: 0.48 (Pet(40/60)–EA 3 : 2); ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 11.26 (1H, s), 8.41 (1H, s), 7.93 (1H, d, $J = 8.3$ Hz), 7.51 (2H, d, $J = 7.0$ Hz), 7.45–7.33 (4H, m), 7.18–7.08 (3H, m), 7.03–6.91 (3H, m), 5.56 (1H, d, $J = 12.1$ Hz), 5.32 (1H, d, $J = 12.1$ Hz), 4.96 (1H, d, $J = 8.0$ Hz), 4.34 (1H, app t, $J = 3.7$ Hz), 3.73 (1H, app q, $J = 8.7$ Hz), 2.50–2.44 (1H, m), 2.17 (3H, s), 1.74–1.64 (1H, m); ^{13}C NMR (101 MHz, DMSO-d_6): δ_C 180.6, 176.5, 151.6, 136.2, 135.7, 131.1, 130.8, 130.0, 129.2, 129.1, 129.1, 128.2, 126.6, 124.7, 124.5, 122.9, 122.2, 120.6, 117.5, 114.4, 69.2, 57.1, 41.8, 40.2, 26.7, 18.6; IR (neat): ν_{max}/cm^{-1} 3495, 3325, 2953, 1711; MS (pNSI): 373.1 (51%, (M − (N(OH)(*o*-Tol)))$^+$), 494.2

(16%, (M − (H_2) + H)$^+$), 518.2 (21%, (M + Na)$^+$); HRMS (pNSI): calcd $C_{29}H_{25}N_3O_5Na$ [M + Na]$^+$: 518.1686; observed: 518.1681.

3dd – benzyl (3a*S**,5*S**,10b*S**)-5-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate

To a stirred Schlenk flask was added benzyl 3-vinyl-1*H*-indole-1-carboxylate (189 mg, 0.68 mmol), DCM (10 mL) and 1*H*-pyrrole-2,5-dione (66 mg, 0.68 mmol). The resulting solution was heated at reflux for 24 hours. The reaction was cooled to 0 °C and 4-phenyl-1,2,4-triazolidine-3,5-dione (120 mg, 0.68 mmol) was added. The solution was stirred at 0 °C for 1 hour. The solvent was removed under reduced pressure to leave the crude product as an off white solid. The product was purified by column chromatography (petrol (40/60)–ethyl acetate 1 : 1, column diameter = 2 cm, silica = 13 cm) to give benzyl (3a*S**,5*S**,10b*S**)-5-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate (58%, 216 mg, 0.39 mmol) as a pale pink powder.

Mp: 174.6–177.1 °C; R_f: 0.06 (Pet(40/60)–EA 1 : 1); ^{1}H NMR (400 MHz, CD_2Cl_2): δ_H 8.78 (1H, s), 8.05 (1H, d, J = 8.3 Hz), 7.54 (1H, d, J = 7.7 Hz), 7.44–7.38 (6H, m), 7.38–7.30 (4H, m), 7.30–7.24 (1H, m), 7.20 (1H, app t, J = 7.5 Hz), 5.51 (1H, app t, J = 5.3 Hz), 5.45 (1H, d, J = 11.9 Hz), 5.31 (1H, d, J = 11.9 Hz), 4.98 (1H, d, J = 7.9 Hz), 3.46 (1H, app q, J = 8.1 Hz), 2.36–2.30 (1H, m), 2.18 (1H, ddd, J = 13.9, 8.6, 5.3 Hz); ^{13}C NMR (101 MHz, CD_2Cl_2): δ_C 178.1, 173.8, 153.7, 152.4, 151.4, 136.8, 134.7, 131.1, 130.6, 129.1, 128.9, 128.8, 128.8, 128.4, 126.2, 125.7, 125.6, 123.7, 119.0, 115.5, 114.2, 69.7, 47.7, 41.0, 39.5, 26.8; IR (neat): ν_{max}/cm^{-1} = 3169, 2975, 1699; MS (pNSI): 279.1 (38%), 373.1 (13%, (M − PTAD)$^+$), 550.2 (21%, (M + H)$^+$), 567.2 (100% (M + NH_4)$^+$), 1116.4 (39%, (2M + NH_4)$^+$), 1666.5 (6%, (3M + NH_4)$^+$); HRMS (pNSI): calcd $C_{30}H_{24}N_5O_6$ [M + H]$^+$: 550.1721; observed: 550.1719.

3ee – benzyl (*R**)-6-(hydroxy(phenyl)amino)-1,3-dioxo-2-phenyl-2,3,5,6-tetrahydro-1*H*,11*H*-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-11-carboxylate

To a stirred Schlenk flask was added benzyl 3-vinyl-1*H*-indole-1-carboxylate (189 mg, 0.68 mmol) and DCM (10 mL). The solution was cooled to −78 °C and 4-phenyl-1,2,4-triazolidine-3,5-dione (120 mg, 0.68 mmol) was added. The reaction was stirred at −78 °C for 5 hours. The reaction was warmed to room temperature, nitrosobenzene (73 mg, 0.68 mmol) was added and the reaction was stirred for 3 hours. The solvent was removed under reduced pressure to leave the crude product as a pale yellow oil. The product was purified by column chromatography (petrol (40/60)–ethyl acetate 2 : 1, column diameter = 1 cm, silica = 16 cm) to give benzyl (*R**)-6-(hydroxy(phenyl)amino)-1,3-dioxo-2-phenyl-2,3,5,6-tetrahydro-1*H*,11*H*-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-11-carboxylate (72%, 274 mg, 0.49 mmol) as a white powder.

Mp: 101.2–103.1 °C; R_f: 0.53 (Pet(40/60)–EA 2 : 1); ^{1}H NMR (400 MHz, CD_2Cl_2): δ_H 8.09 (1H, d, J = 8.2 Hz), 7.51–7.38 (8H, m), 7.38–7.24 (5H, m), 7.23–7.07 (4H, m), 6.87 (1H, d, J = 7.9 Hz), 6.36 (1H, s), 5.52 (1H, d, J = 12.1 Hz), 5.39 (1H, d, J = 12.1 Hz), 5.22 (1H, dd, J = 14.0, 1.7 Hz), 4.97–4.89 (1H, m), 3.66 (1H, dd, J = 14.0, 3.4 Hz); ^{13}C NMR (101 MHz, CD_2Cl_2): δ_C 147.2, 147.0, 146.6, 145.6, 131.0, 130.1, 127.3, 126.2, 125.4, 125.2, 124.9, 124.9, 124.9, 124.8, 124.8, 122.4, 122.3, 120.7, 120.5119.7, 115.8, 114.5, 110.5, 97.2, 66.2, 55.1, 39.6; IR (neat): ν_{max}/cm^{-1} = 3337, 3063, 1716; MS (pAPCI): 395.1 (100%), 451.1 (59%, (M − (N(OH)Ph))$^+$), 542.2 (5%, (M − (H_2O) + H)$^+$), 558.2 (1%, (M − H)$^+$), 560.2 (1%, (M + H)$^+$); HRMS (pAPCI): calcd $C_{32}H_{26}N_5O_5$ [M + H]$^+$: 560.1928; observed: 560.1913.

3ff – benzyl (*R**)-6-(hydroxy(*o*-tolyl)amino)-1,3-dioxo-2-phenyl-2,3,5,6-tetrahydro-1*H*,11*H*-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-11-carboxylate

To a stirred Schlenk flask was added benzyl 3-vinyl-1*H*-indole-1-carboxylate (94 mg, 0.34 mmol) and DCM (10 ml). The reaction mixture was cooled to −78 °C and 4-phenyl-1,2,4-triazolidine-3,5-dione (60 mg, 0.34 mmol) was added. The reaction mixture was stirred at −78 °C for 5 hours, 1-methyl-2-nitrosobenzene was added (41 mg, 0.34 mmol) and the reaction stirred at room temperature for 18 hours. The solvent was removed under reduced pressure to leave the crude product as a yellow powder. The product was purified by column chromatography (petrol (40/60)–ethyl acetate 3 : 1, column diameter = 2 cm, silica = 20 cm) to give benzyl (*R**)-6-(hydroxy(*o*-tolyl)amino)-1,3-dioxo-2-phenyl-2,3,5,6-tetrahydro-1*H*,11*H*-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-11-carboxylate (68%, 132 mg, 0.23 mmol) as an off white powder.

Mp: 163.8–165.1 °C; R_f: 0.49 (Pet(40/60)–EA 3 : 1); ^{1}H NMR (400 MHz, CD_2Cl_2): δ_H 8.01 (1H, d, J = 8.3 Hz), 7.65 (1H, dd, J = 8.1, 1.3 Hz), 7.54–7.38 (7H, m), 7.35 (3H, dd, J = 5.0, 2.1 Hz), 7.19 (2H, app dtd, J = 8.5, 7.2, 6.7, 1.4 Hz), 6.99 (2H, app tdd, J = 7.5, 3.4, 1.2 Hz), 6.90 (1H, dd, J = 7.7, 1.4 Hz), 6.75 (1H, d, J = 7.8 Hz), 5.87 (1H, s, OH), 5.48 (1H, d, J = 11.9 Hz), 5.34 (1H, d, J = 11.9 Hz), 5.19 (1H, dd, J = 14.1, 2.3 Hz), 4.63 (1H, app t, J = 2.3 Hz), 3.52 (1H, dd, J = 14.1, 2.3 Hz), 1.94 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 151.9, 150.3, 150.0, 148.8, 134.6, 133.6, 131.6, 131.1, 130.6, 130.0, 129.4, 128.9, 128.9, 128.8, 128.8, 127.0, 126.6, 126.0, 125.7, 124.4, 123.6, 122.7, 117.9, 114.6, 101.7, 70.1, 58.6, 43.5, 17.7; IR (neat): ν_{max}/cm^{-1} = 3291, 2981, 1782, 1737, 1699; MS (pNSI): 199.2 (100%), 407.2 (79%), 451.1 (81%, (M − (N(OH)(*o*-Tol)))$^+$), 572.2 (25%, (M − H)$^+$), 596.2 (65%, (M + Na)$^+$); HRMS (pNSI): calcd $C_{33}H_{27}N_5O_5Na$ [M + Na]$^+$: 596.1904; observed: 596.1898.

3gg – benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(phenyl)amino)-7-methoxy-2-methyl-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate

To a stirred Schlenk flask was added benzyl 5-methoxy-3-vinyl-1*H*-indole-1-carboxylate (209 mg, 0.68 mmol), DCM (10 mL) and 1-methyl-1*H*-pyrrole-2,5-dione (76 mg, 0.68 mmol). The resulting solution was heated at reflux for 18 hours. The reaction was cooled to room temperature and nitrosobenzene (72 mg, 0.68 mmol) was added and the reaction was stirred for 1.5 hours. The solvent was removed under reduced pressure to leave the crude product as a pale orange oil. The product was purified by column chromatography (petrol (40/60)–ethyl acetate 2 : 1,

column diameter = 1 cm, silica = 16 cm) to give benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(phenyl)amino)-7-methoxy-2-methyl-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate (73%, 218 mg, 0.44 mmol) as an orange powder.

Mp: 106.8–110.2 °C; R_f: 0.65 (Pet(40/60)–EA 2 : 1); ^{1}H NMR (400 MHz, CD_2Cl_2): δ_H 7.97 (1H, br d, J = 8.3 Hz), 7.49–7.47 (2H, m), 7.41–7.37 (3H, m), 7.33–7.30 (2H, m), 7.21–7.19 (2H, m), 7.05–7.00 (2H, m), 6.85 (1H, br d, J = 8.4 Hz), 5.53 (1H, d, J = 11.9 Hz), 5.39 (1H, d, J = 11.9 Hz), 5.02 (1H, br s), 4.91–4.87 (1H, m), 4.75 (1H, br s), 3.68 (3H, s), 3.50 (1H, br s), 2.86 (3H, s), 2.36 (1H, br s), 2.01 (1H, br s); ^{13}C NMR (101 MHz, CD_2Cl_2): δ_C 178.3, 174.5, 156.3, 151.5, 151.1, 135.0, 131.5, 130.7, 129.0, 128.9, 128.8, 128.8, 128.4, 122.4, 117.7, 117.2, 115.9, 113.4, 102.4, 69.4, 57.9, 55.6, 40.3, 39.2, 24.9, 23.4; IR (neat): ν_{max}/cm^{-1} = 3408, 2969, 2890, 1699; MS (pNSI): 417.1 (100%, (M − (N(OH)Ph))$^+$), 524.2 (68%, (M − (H_2) + H)$^+$), 548.2 (16%, (M + Na)$^+$), 1073.4 (4%, (2M + Na)$^+$); HRMS (pNSI): calcd $C_{30}H_{27}N_3O_6Na$ [M + Na]$^+$: 548.1792; observed: 548.1785.

3hh – benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-7-methoxy-2-methyl-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate

To a stirred Schlenk flask was added benzyl 5-methoxy-3-vinyl-1*H*-indole-1-carboxylate (209 mg, 0.68 mmol), DCM (10 mL) and 1-methyl-1*H*-pyrrole-2,5-dione (76 mg, 0.68 mmol). The resulting solution was heated at reflux for 18 hours. The reaction was cooled to room temperature and 1-methyl-2-nitrosobenzene (82 mg, 0.68 mmol) was added. The solution was stirred at room temperature for 3 hours. The solvent was removed under reduced pressure to leave the crude product as a pale yellow solid. The product was purified by column chromatography (petrol (40/60)–ethyl acetate 2 : 1, column diameter = 2 cm, silica = 15 cm) to give benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-7-methoxy-2-methyl-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate (74%, 279 mg, 0.50 mmol) as a pale yellow powder.

Mp: 107.6–110.1 °C; R_f: 0.29 (Pet(40/60)–EA 2 : 1); ^{1}H NMR (400 MHz, CD_2Cl_2): δ_H 7.93 (1H, d, J = 9.1 Hz), 7.54 (1H, dd, J = 8.1, 1.3 Hz), 7.49–7.45 (2H, m), 7.43–7.35 (3H, m), 7.19 (1H, ddd, J = 7.6, 6.9, 1.9 Hz), 7.10–7.01 (2H, m), 6.88 (1H, d, J = 2.6 Hz), 6.80 (1H, dd, J = 9.1, 2.6 Hz), 5.52 (1H, d, J = 11.9 Hz), 5.37 (1H, d, J = 11.9 Hz), 5.18 (1H, s), 4.87 (1H, d, J = 8.1 Hz), 4.33–4.29 (1H, m), 3.65 (3H, s), 3.67–3.61 (1H, m), 2.86 (3H, s), 2.61 (1H, app dt, J = 13.4, 5.9 Hz), 2.22 (3H, s), 1.86 (1H, ddd, J = 13.4, 8.5, 4.3 Hz); ^{13}C NMR (101 MHz, CD_2Cl_2): δ_C 178.4, 174.4, 156.1, 151.6, 149.8, 135.0, 134.9, 131.2, 130.8, 130.6, 130.4, 128.8, 128.8, 128.5, 126.4, 125.3, 121.7, 117.5, 115.7, 113.6, 102.0, 69.3, 57.8, 55.4, 40.5, 38.9, 25.0, 24.9, 18.2; IR (neat): ν_{max}/cm^{-1} = 3370, 2965, 2887, 1699; MS (pNSI): 207.1 (39%), 417.1 (34%, (M − (N(OH)(*o*-Tol)))$^+$), 438.2 (100%, (M − (H_2) + H)$^+$), 1075.4 (15%, (2(M − (H_2) + H)$^+$)); HRMS (pNSI): calcd $C_{31}H_{28}N_3O_6$ [M − (H_2) + H]$^+$: 538.1976; observed: 538.1973.

3ii – benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(phenyl)amino)-7-methoxy-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate

To a stirred Schlenk flask was added benzyl 5-methoxy-3-vinyl-1*H*-indole-1-carboxylate (209 mg, 0.68 mmol), DCM (10 mL) and 1*H*-pyrrole-2,5-dione (66 mg, 0.68 mmol). The resulting solution was heated at reflux for 18 hours. The reaction was cooled to room temperature and nitrosobenzene (72 mg, 0.68 mmol) was added and the reaction was stirred for 2.5 hours. The solvent was removed under reduced pressure to leave the crude product as a pale orange oil. The product was purified by column chromatography (petrol (40/60)–ethyl acetate 2 : 1, column diameter = 1 cm, silica = 16 cm) to give benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(phenyl)amino)-7-methoxy-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate (79%, 317 mg, 0.54 mmol) as a pale orange powder.

Mp: 134.2–136.9 °C; R_f: 0.34 (Pet(40/60)–EA 3 : 2); ^{1}H NMR (400 MHz, CD_2Cl_2): δ_H 8.42 (1H, br s), 7.94 (1H, d, J = 9.0 Hz), 7.47–7.44 (2H, m), 7.40–7.34 (3H, m), 7.30–7.27 (2H, m), 7.19–7.17 (2H, m), 7.01–6.98 (1H, m), 6.93 (1H, br s), 6.81 (1H, d, J = 9.0 Hz), 5.49 (1H, d, J = 11.9 Hz), 5.39 (1H, br s), 5.34 (1H, d, J = 11.9 Hz), 4.92 (1H, br d, J = 6.2 Hz), 4.74 (1H, br s), 3.64 (3H, s), 3.57–3.51 (1H, br m), 2.39–2.35 (1H, br m), 1.91–1.89 (1H, br m); ^{13}C NMR (101 MHz, CD_2Cl_2): δ_C 178.6, 174.4, 156.2, 151.5, 151.0, 135.0, 131.4, 130.3, 129.0, 128.9, 128.8, 128.8, 128.4, 122.6, 117.5, 117.4, 116.0, 113.5, 102.3, 69.4, 57.9, 55.6, 41.5, 40.5, 24.0; IR (neat): ν_{max}/cm^{-1} = 3233, 2952, 1708; MS (pNSI): 403.1 (37%, (M − (N(OH)Ph))$^+$), 510.2 (100%, (M − (H_2) + H)$^+$), 532.1 (26%, (M − (H_2) + Na)$^+$); HRMS (pNSI): calcd $C_{29}H_{24}N_3O_6$ [M − (H_2) + H]$^+$: 510.1654; observed: 510.1660.

3jj – benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-7-methoxy-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate

To a stirred Schlenk flask was added benzyl 5-methoxy-3-vinyl-1*H*-indole-1-carboxylate (209 mg, 0.68 mmol), DCM (10 mL) and 1*H*-pyrrole-2,5-dione (66 mg, 0.68 mmol). The resulting solution was heated at reflux for 18 hours. The reaction was cooled to room temperature and 1-methyl-2-nitrosobenzene (82 mg, 0.68 mmol) was added. The solution was stirred at room temperature for 3.5 hours. The solvent was removed under reduced pressure to leave the crude product as a pale yellow solid. The product was purified by column chromatography (petrol (40/60)–ethyl acetate 2 : 1, column diameter = 2 cm, silica = 14 cm) to give benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-7-methoxy-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate (76%, 255 mg, 0.52 mmol) as a pale yellow powder.

Mp: 193.0–195.6 °C; R_f: 0.20 (Pet(40/60)–EA 2 : 1); ^{1}H NMR (400 MHz, CD_2Cl_2): δ_H 7.92 (1H, d, J = 9.7 Hz), 7.81 (1H, s), 7.53 (1H, d, J = 7.8 Hz), 7.46 (2H, dd, J = 7.8, 1.6 Hz), 7.42–7.33 (3H, m), 7.21–7.15 (1H, m), 7.09–7.00 (2H, m), 6.84–6.75 (2H, m), 5.50 (1H, d, J = 11.9 Hz), 5.35 (1H, d, J = 11.9 Hz), 5.16 (1H, s), 4.96 (1H, d, J = 7.6 Hz), 4.37 (1H, app t, J = 4.9 Hz), 3.71 (1H, app td, J = 8.7, 5.6 Hz), 3.64 (3H, s), 2.64 (1H, app dt, J = 13.6, 5.6 Hz), 2.21 (3H, s), 1.88 (1H, ddd, J = 13.6, 9.3, 4.3 Hz); ^{13}C NMR (101 MHz, DMSO-d_6): δ_C 180.6, 176.4, 155.6, 151.8, 151.7, 135.8, 131.6, 130.8, 130.7, 130.2, 129.1, 129.1, 129.0, 126.7, 124.8, 122.3, 117.2, 115.2, 113.5, 102.7, 69.1, 57.3, 55.5, 41.9, 40.3, 27.2, 18.5; IR (neat): ν_{max}/cm^{-1} = 3457, 3367, 2981, 2886, 1712; MS (pNSI): 403.1 (100%, (M − (N(OH)(*o*-Tol)))$^+$), 524.1 (75%, (M − (H_2) + H)$^+$), 548.2 (16%, (M + Na)$^+$),

1073.4 (5%, $(2M + Na)^+$); HRMS (pNSI): calcd $C_{30}H_{27}N_3O_6Na$ $[M + Na]^+$: 548.1792; observed: 548.1785.

3kk – benzyl (*R**)-6-(hydroxy(phenyl)amino)-8-methoxy-1,3-dioxo-2-phenyl-2,3,5,6-tetrahydro-1*H*,11*H*-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-11-carboxylate

To a stirred Schlenk flask was added benzyl 5-methoxy-3-vinyl-1*H*-indole-1-carboxylate (209 mg, 0.68 mmol) and DCM (10 mL). The solution was cooled to −78 °C and 4-phenyl-1,2,4-triazolidine-3,5-dione (120 mg, 0.68 mmol) was added. The reaction was stirred at −78 °C for 1.5 hours. The reaction was warmed to room temperature, nitrosobenzene (73 mg, 0.68 mmol) was added and the reaction was stirred for 20 hours. The solvent was removed under reduced pressure to leave the crude product as a pale yellow oil. The product was purified by column chromatography (petrol (40/60)–ethyl acetate 2 : 1, column diameter = 1 cm, silica = 16 cm) to give benzyl (*R**)-6-(hydroxy(phenyl)amino)-8-methoxy-1,3-dioxo-2-phenyl-2,3,5,6-tetrahydro-1*H*,11*H*-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]-indole-11-carboxylate (78%, 312 mg, 0.53 mmol) as a white powder.

Mp: 110.4–113.2 °C; R_f: 0.20 (Pet(40/60)–EA 2 : 1); ^{1}H NMR (400 MHz, CD_2Cl_2): δ_H 7.88 (1H, d, J = 9.1 Hz), 7.42–7.38 (5H, m), 7.36–7.32 (3H, m), 7.29–7.26 (2H, m), 7.24–7.20 (2H, m), 7.13 (2H, d, J = 8.1 Hz), 7.05 (1H, app t, J = 7.3 Hz). 6.76 (1H, dd, J = 9.1, 2.6 Hz), 6.24 (1H, s), 6.10 (1H, d, J = 2.5 Hz), 5.43 (1H, d, J = 12.0 Hz), 5.32–5.29 (1H, m), 5.25–5.18 (1H, m), 4.84–4.80 (1H, m), 3.64 (1H, dd, J = 14.0, 3.3 Hz), 3.55 (3H, s); ^{13}C NMR (101 MHz, CD_2Cl_2): δ_C 156.5, 151.1, 150.3, 149.4, 134.8, 131.2, 130.3, 129.2, 129.0, 129.0, 128.70, 128.7, 128.7, 128.6, 128.2, 126.9, 126.2, 124.6, 119.7, 115.3, 113.2, 101.0, 100.5, 69.9, 59.1, 55.5, 44.0; IR (neat): ν_{max}/cm^{-1} = 3336, 2935, 1716; MS (pNSI): 481.1 (17%, $(M - (N(OH)Ph))^+$), 588.2 (100%, $(M - (H_2) + H)^+$), 612.2 (15%, $(M + Na)^+$); HRMS (pNSI): calcd $C_{33}H_{27}N_5O_6Na$ $[M + Na]^+$: 612.1854; observed: 612.1838.

3ll – benzyl (*R**)-6-(hydroxy(*o*-tolyl)amino)-8-methoxy-1,3-dioxo-2-phenyl-2,3,5,6-tetrahydro-1*H*,11*H*-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-11-carboxylate

To a stirred Schlenk flask was added benzyl 5-methoxy-3-vinyl-1*H*-indole-1-carboxylate (209 mg, 0.68 mmol) and DCM (10 mL). The solution was cooled to −78 °C and 4-phenyl-1,2,4-triazolidine-3,5-dione (120 mg, 0.68 mmol) was added. The reaction was stirred at −78 °C for 1.5 hours. The reaction was warmed to room temperature, 1-methyl-2-nitrosobenzene (73 mg, 0.68 mmol) was added and the reaction was stirred for 24 hours. The solvent was removed under reduced pressure to leave the crude product as a pale orange oil. The product was purified by column chromatography (petrol (40/60)–ethyl acetate 2 : 1, column diameter = 2 cm, silica = 17 cm) to give benzyl (*R**)-6-(hydroxy(*o*-tolyl)amino)-8-methoxy-1,3-dioxo-2-phenyl-2,3,5,6-tetrahydro-1*H*,11*H*-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-11-carboxylate (82%, 338 mg, 0.56 mmol) as an off white powder.

Mp: 181.1–183.0 °C; R_f: 0.55 (Pet(40/60)–EA 2 : 1); ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 8.70 (1H, s), 7.84 (1H, d, J = 9.0 Hz), 7.55–7.48 (2H, m), 7.46–7.41 (3H, m), 7.41–7.33 (4H, m), 7.33–7.29 (2H, m), 7.13–7.03 (2H, m), 6.97 (1H, app td, J = 7.4, 1.3 Hz), 6.83 (1H, dd, J = 9.1, 2.6 Hz). 6.38 (1H, s), 5.43 (1H, d, J = 12.1 Hz), 5.33 (1H, d, J = 12.1 Hz), 4.80 (1H, dd, J = 13.7, 1.8 Hz), 4.71 (1H, dd, J = 3.3, 1.8 Hz), 3.68–3.61 (1H, dd, J = 13.7, 3.3 Hz), 3.58 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (101 MHz, CD_2Cl_2): δ_C 156.3, 151.6, 150.8, 150.3, 149.8, 135.3, 131.6, 130.9, 130.3, 130.0, 129.7, 129.2, 129.1, 129.1, 128.9, 128.0, 127.4, 127.1, 126.8, 125.2, 121.8, 115.3, 113.2, 103.1, 101.9, 69.9, 55.9, 55.6, 43.9, 18.2; IR (neat): ν_{max}/cm^{-1} = 3212, 2939, 1720; MS (pNSI): 481.2 (100%, $(M - N(OH)(o\text{-Tol}))^+$), 602.2 (34%, $(M - (H_2) + H)^+$), 626.2 (100%, $(M + Na)^+$); HRMS (pNSI): calcd $C_{34}H_{29}N_5O_6Na$ $[M + Na]^+$: 626.2010; observed: 626.2006.

4a – (3a*S**,5*S**,10b*S**)-5-methoxy-2-methyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione

To a stirred Schlenk flask was added benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-2-methyl-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate (120 mg, 0.24 mmol), platinum(IV) oxide (53 mg, 0.24 mmol) and methanol (5 mL). The resulting suspension was placed under an atmosphere of H_2 and stirred at room temperature for 18 hours. The suspension was filtered through celite and the solvent was removed under reduced pressure to leave the crude product as an orange solid, The crude product was purified by column chromatography (petrol (40/60)–ethyl acetate 1 : 1, column diameter = 2 cm, silica = 13 cm) to give (3a*S**,5*S**,10b*S**)-5-methoxy-2-methyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione (60%, 41 mg, 0.14 mmol) as a pale yellow powder.

Mp: 139.4–142.7 °C; R_f: 0.25 (Pet(40/60)–EA 1 : 1); ^{1}H NMR (400 MHz, CD_2Cl_2): δ_H 8.91 (1H, s), 7.56 (1H, d, J = 7.8 Hz), 7.34 (1H, d, J = 7.7 Hz), 7.14 (1H, app t, J = 7.5 Hz), 7.09 (1H, app t, J = 7.4 Hz), 4.73 (1H, app t, J = 2.7 Hz), 4.14 (1H, d, J = 8.8 Hz), 3.31–3.25 (1H, m), 3.22 (3H, s), 2.94 (1H, app t, J = 2.4 Hz), 2.90 (3H, s), 1.88 (1H, ddd, J = 14.2, 6.9, 2.2 Hz); ^{13}C NMR (101 MHz, CD_2Cl_2): δ_C 178.9, 176.1, 136.4, 128.8, 126.6, 122.3, 120.1, 118.2, 111.9, 111.3, 69.4, 56.1, 39.5, 37.3, 27.4, 25.1; IR (neat): ν_{max}/cm^{-1} 3398, 2931, 2870, 1689; MS (pNSI): 285.0 (29%), 355.1 (100%), 371.1 (57%), 560.0 (21%); HRMS (pNSI): calcd $C_{15}H_{13}N_2O_2$ $[M - OMe]^+$: 253.0972; observed: 253.0974.

4b – (3a*S**,5*S**,10b*S**)-5-ethoxy-2-methyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione

To a stirred Schlenk flask was added benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-2-methyl-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate (100 mg, 0.20 mmol), platinum(IV) oxide (45 mg, 0.20 mmol) and ethanol (5 mL). The resulting suspension was placed under an atmosphere of H_2 and stirred at room temperature for 18 hours. The suspension was filtered through celite and the solvent was removed under reduced pressure to leave the crude product as an yellow solid, The crude product was purified by column chromatography (petrol (40/60)–ethyl acetate 2 : 1, column diameter = 2 cm, silica = 15 cm) to give (3a*S**,5*S**,10b*S**)-5-

ethoxy-2-methyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione (24%, 20 mg, 0.04 mmol) as a brown powder.

Mp: 100.6–102.8 °C; R_f: 0.16 (Pet(40/60)–EA 2 : 1); ^{1}H NMR (400 MHz, CD_2Cl_2): δ_H 8.78 (1H, s), 7.54 (1H, d, J = 7.7 Hz), 7.35 (1H, d, J = 7.7 Hz), 7.17–7.12 (1H, m), 7.09 (1H, app t, J = 7.0 Hz), 4.83 (1H, app t, J = 2.8 Hz), 4.16 (1H, d, J = 8.8 Hz), 3.55 (1H, app td, J = 6.9, 1.8 Hz), 3.32–3.26 (2H, m), 2.93–2.91 (1H, m), 2.90 (3H, s), 1.88 (1H, ddd, J = 14.3, 7.1, 2.7 Hz), 0.97 (1H, t, J = 7.0 Hz); ^{13}C NMR (101 MHz, CD_2Cl_2): δ_C 178.9, 176.0, 136.3, 128.8, 126.5, 122.3, 120.1, 118.1, 112.5, 111.3, 67.4, 63.5, 39.5, 37.3, 27.9, 25.0, 15.2; IR (neat): ν_{max}/cm^{-1} 3300, 2969, 1690; MS (pAPCI): 108.1 (24%), 298.1 (6%, $(M)^+$), 299.1 (5%, $(M + H)^+$); HRMS (pAPCI): calcd $C_{17}H_{19}N_2O_3$ $[M + H]^+$: 299.1390; observed: 299.1387.

4c – (3a*S**,5*S**,10b*S**)-5-(hydroxy(phenyl)amino)-2-methyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione

To a stirred Schlenk flask was added benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(phenyl)amino)-2-methyl-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate (120 mg, 0.25 mmol), platinum(IV) oxide (57 mg, 0.25 mmol) and THF (5 mL). The resulting suspension was placed under an atmosphere of H_2 and stirred at room temperature for 5 hours. The suspension was filtered through celite and the solvent was removed under reduced pressure to leave the crude product as a yellow solid, The crude product was purified by trituration from DCM to give (3a*S**,5*S**,10b*S**)-5-(hydroxy(phenyl)amino)-2-methyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione (75%, 68 mg, 0.19 mmol) as a pale yellow powder.

Mp: 157.2–161.9 °C; R_f: 0.17 (Pet(40/60)–EA 1 : 1); ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 11.06 (1H, s), 8.20 (1H, s), 7.35 (1H, d, J = 8.0 Hz), 7.26 (1H, d, J = 8.0 Hz), 7.24–7.19 (2H, m), 7.17–7.08 (2H, m), 6.98 (1H, app ddd, J = 8.2, 7.0, 1.2 Hz), 6.91–6.81 (1H, m), 6.81 (1H, app ddd, J = 8.0, 6.9, 1.0 Hz), 4.88 (1H app t, J = 4.9 Hz), 4.27 (1H, d, J = 8.8 Hz), 3.64 (1H, app td, J = 8.8, 6.1 Hz), 2.81 (3H, s), 2.33 (1H, app dt, J = 13.7, 6.1 Hz), 1.84 (1H, ddd, J = 13.7, 8.8, 4.9 Hz); ^{13}C NMR (101 MHz, DMSO-d_6): δ_C 179.8, 176.3, 153.3, 137.0, 130.0, 129.0, 126.3, 121.5, 121.2, 119.9, 119.0, 117.2, 111.7, 110.0, 57.4, 39.6, 39.3, 25.8, 25.1; IR (neat): ν_{max}/cm^{-1} 3374, 3306, 2919, 1683; MS (pAPCI): 108.0 (28%), 251.1 (100%), 253.1 (68%, $(M - (N(OH)Ph) + H)^+$), 344.1 (13%, $(M - (OH) + H)^+$), 361.1 (3%, $(M + H)^+$); HRMS (pAPCI): calcd $C_{21}H_{20}N_3O_3$ $[M + H]^+$: 362.1499; observed: 362.1501.

Note: H^1 NMR ran at 40 °C.

4d – (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-2-methyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione

To a stirred Schlenk flask was added benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-2-methyl-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate (100 mg, 0.20 mmol), platinum(IV) oxide (45 mg, 0.20 mmol) and THF (5 mL). The resulting suspension was placed under an atmosphere of H_2 and stirred at room temperature for 7 hours. The suspension was filtered through celite and the solvent was removed under reduced pressure to leave the crude product as a yellow solid. The crude product was purified by column chromatography (petrol (40/60)–ethyl acetate 1 : 1, column diameter = 2 cm, silica = 16 cm) to give (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-2-methyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione (87%, 65 mg, 0.17 mmol) as a pale orange powder.

Mp: 179.3–181.0 °C; R_f: 0.60 (Pet(40/60)–EA 1 : 1); ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 11.08 (1H, s), 8.28 (1H, s), 7.50 (1H, d, J = 8.0 Hz), 7.29 (1H, d, J = 8.1 Hz), 7.14–7.10 (1H, m), 6.91–6.87 (4H, m), 6.67 (1H, app t, J = 7.4 Hz), 4.29 (1H, d, J = 8.2 Hz), 4.27 (1H, app t, J = 3.9 Hz), 3.83–3.74 (1H, m), 2.81 (3H, s), 2.65–2.56 (1H, m), 1.98 (3H, s), 1.67 (1H, ddd, J = 13.6, 10.5, 3.9 Hz); ^{13}C NMR (101 MHz, DMSO-d_6): δ_C 180.0, 176.3, 152.2, 136.7, 130.7, 130.5, 130.3, 126.5, 126.5, 124.5, 122.4, 121.2, 119.3, 118.9, 111.7, 109.7, 58.3, 40.0, 38.6, 27.3, 25.1, 18.3; IR (neat): ν_{max}/cm^{-1} 3379, 2955, 2873, 1691; MS (pAPCI): 108.1 (98%), 251.1 (100%), 253.1 (61%, $(M - (N(OH)(o\text{-Tol})) + H)^+$), 271.1 (6%, $(M - (N(OH)(o\text{-Tol})) + OH_2)^+$), 358.2 (13%, $(M - OH)^+$); HRMS (pAPCI): calcd $C_{22}H_{22}N_3O_3$ $[M + H]^+$: 376.1656; observed: 376.1658.

4e – (3a*S**,5*S**,10b*S**)-5-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-2-methyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione

To a stirred Schlenk flask was added benzyl (3a*S**,5*S**,10b*S**)-5-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-2-methyl-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate (110 mg, 0.20 mmol), platinum(IV) oxide (46 mg, 0.20 mmol) and THF (5 mL). The resulting suspension was placed under an atmosphere of H_2 and stirred at room temperature for 5 hours. The suspension was filtered through celite and the solvent was removed under reduced pressure to leave the crude product as a yellow solid. The product was purified by trituration from DCM to give (3a*S**,5*S**,10b*S**)-5-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-2-methyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3*aH*)-dione (91%, 79 mg, 0.18 mmol) as an off-white solid.

Mp: 262.4–264.0 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 11.43 (1H, s), 10.67 (1H, br s), 7.52–7.42 (4H, m), 7.39–7.37 (2H, m), 7.21 (1H, d, J = 7.9 Hz), 7.06 (1H, app t, J = 7.6 Hz), 6.94 (1H, app t, J = 7.5 Hz), 5.39 (1H, app t, J = 6.1 Hz), 4.33 (1H, d, J = 8.0 Hz), 3.72 (1H, app q, J = 6.8 Hz), 2.81 (3H, s), 2.35–2.31 (2H, m); ^{13}C NMR (101 MHz, DMSO-d_6): δ_C 178.9, 175.8, 152.7, 152.7, 137.2, 132.3, 130.7, 129.5, 128.5, 126.7, 125.3, 122.2, 119.9, 118.4, 112.3, 107.3, 48.1, 39.5, 38.3, 27.7, 25.3; IR (neat): ν_{max}/cm^{-1} 3229, 1693; MS (pAPCI): 178.1 (35%), 253.1 (100%, $(M - (PTAD) + H)^+$); HRMS (ASAP) calcd $C_{15}H_{13}N_2O_2$ $[M - PTAD + H]^+$: 253.0972; observed: 253.0969.

4f – (3a*S**,5*S**,10b*S**)-5-(hydroxy(phenyl)amino)-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione

To a stirred Schlenk flask was added benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(phenyl)amino)-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate (90 mg, 0.18 mmol), platinum(IV) oxide (41 mg, 0.18 mmol) and THF (5 mL). The

resulting suspension was placed under an atmosphere of H_2 and stirred at room temperature for 10 hours. The suspension was filtered through celite and the solvent was removed under reduced pressure to leave the crude product as an yellow solid, The crude product was purified by column chromatography (petrol (40/60)–ethyl acetate 1 : 1, column diameter = 2 cm, silica = 14 cm) to give (3a*S**,5*S**,10b*S**)-5-(hydroxy(phenyl) amino)-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione (41%, 26 mg, 0.07 mmol) as a yellow powder.

Mp: 150.0–153.1 °C; R_f: 0.33 (Pet(40/60)–EA 1 : 1); ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 11.22 (1H, s), 11.09 (1H, s), 8.24 (1H, s), 7.33 (1H, d, J = 8.1 Hz), 7.27–7.23 (1H, m), 7.20 (2H, app d, J = 7.3 Hz), 7.12 (2H, d, J = 7.7 Hz), 7.00–6.95 (1H, m), 6.85 (1H, app t, J = 7.2 Hz), 6.80 (1H app t, J = 7.3 Hz), 4.89 (1H, app t, J = 4.9 Hz), 4.25 (1H, d, J = 8.1 Hz), 3.63–3.52 (1H, m), 2.27 (1H, app dt, J = 13.6, 5.6 Hz), 1.80 (1H, ddd, J = 13.6, 9.2, 4.8 Hz); ^{13}C NMR (101 MHz, DMSO-d_6): δ_C 181.2, 177.6, 153.3, 137.0, 130.3, 129.0, 126.3, 121.4, 121.1, 119.9, 118.9, 117.2, 111.7, 109.9, 57.4, 40.9, 40.6, 25.7; IR (neat): ν_{max}/cm^{-1} 3302, 2924, 1706; MS (pAPCI): 108.1 (18%), 237.1 (100), 239.1 (46%, (M − (N(OH)Ph) + H)$^+$); HRMS (pAPCI): calcd $C_{14}H_{11}N_2O_2$ [M − (N(OH)Ph) + H]$^+$: 239.0815; observed: 239.0810.

4g – (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione

To a stirred Schlenk flask was added benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate (120 mg, 0.24 mmol), platinum(IV) oxide (54 mg, 0.24 mmol) and THF (5 mL). The resulting suspension was placed under an atmosphere of H_2 and stirred at room temperature for 6 hours. The suspension was filtered through celite and the solvent was removed under reduced pressure to leave the crude product as a yellow solid, The crude product was purified by column chromatography (petrol (40/60)–ethyl acetate 2 : 3, column diameter = 2 cm, silica = 17 cm) to give (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl) amino)-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione- (70%, 61 mg, 0.17 mmol) as an off white solid.

Mp: 149.9–153.2 °C; R_f: 0.52 (Pet(40/60)–EA 2 : 3); ^{1}H NMR (400 MHz, CD_2Cl_2): δ_H 8.81 (1H, s), 8.21 (1H, s), 7.56 (1H, d, J = 8.0 Hz), 7.30 (1H, d, J = 7.9 Hz), 7.18 (2H, d, J = 6.9 Hz), 7.06 (1H, app t, J = 7.6 Hz), 7.03–6.99 (2H, m), 6.91–6.85 (1H, m), 5.36 (1H, s), 4.51 (1H, app t, J = 4.5 Hz), 4.19 (1H, d, J = 8.6 Hz), 3.80 (1H, app td, J = 9.3, 6.4 Hz), 2.74 (1H, app dt, J = 13.6, 5.5 Hz), 2.15 (3H, s), 1.83 (1H, ddd, J = 13.6, 10.1, 4.1 Hz); ^{13}C NMR (101 MHz, DMSO-d_6): δ_C 181.5, 177.6, 152.2, 136.7, 130.6, 130.5, 130.5, 126.5, 126.5, 124.5, 122.4, 121.1, 119.3, 118.9, 111.6, 109.5, 58.3, 55.5, 40.9, 27.3, 18.3; IR (neat): ν_{max}/cm^{-1} 3372, 3298, 1683; MS (nNSI) = 186.0 (100%), 237.1 (97%, (M − (N(OH)(*o*-Tol)) − H)$^-$), 358.1 (35%, (M − H_2)$^-$), 394.1 (23%); HRMS (nNSI): calcd $C_{21}H_{18}N_3O_3$ [M − H]$^-$: 360.1354; observed: 360.1348.

4h – (3a*S**,5*S**,10b*S**)-5-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione

To a stirred Schlenk flask was added benzyl (3a*S**,5*S**,10b*S**)-5-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate (110 mg, 0.20 mmol), platinum(IV) oxide (46 mg, 0.20 mmol) and THF (5 mL). The resulting suspension was placed under an atmosphere of H_2 and stirred at room temperature for 5 hours. The suspension was filtered through celite and the solvent was removed under reduced pressure to leave the crude product as a white solid. The crude product was purified by trituration from DCM to give (3a*S**,5*S**,10b*S**)-5-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione (64%, 53 mg, 0.13 mmol) as a white powder.

Mp: 212.6–213.9 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 11.39 (1H, s), 11.36 (1H, s), 10.66 (1H, s), 7.51–7.44 (4H, m), 7.41–7.37 (2H, m), 7.23 (1H, d, J = 7.8 Hz), 7.07 (1H, app t, J = 7.5 Hz), 6.96 (1H, app t, J = 7.5 Hz), 5.42 (1H, app t, J = 6.0 Hz), 4.29 (1H, d, J = 8.0 Hz), 3.69 (1H, app q, J = 6.8 Hz), 2.37–2.21 (2H, m); ^{13}C NMR (101 MHz, DMSO-d_6): δ_C 180.3, 177.1, 152.7, 152.6, 137.2, 132.3, 131.0, 129.5, 128.5, 126.7, 125.3, 122.2, 119.9, 118.4, 112.3, 107.1, 55.5, 48.1, 40.9, 27.5; IR (neat): ν_{max}/cm^{-1} = 3310, 3155, 3077, 1719, 1674; MS (pAPCI): 239.1 (100%, (M − (PTAD) + H)$^+$), 414.1 (2%, (M − H)$^+$); HRMS (pAPCI): calcd $C_{22}H_{16}N_5O_4$ [M − H]$^+$: 414.1197; observed: 414.1185.

4i – (*R**)-6-(hydroxy(phenyl)amino)-2-phenyl-6,11-dihydro-1*H*,5*H*-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-1,3(2*H*)-dione

To a stirred Schlenk flask was added benzyl (*R**)-6-(hydroxy-(phenyl)amino)-1,3-dioxo-2-phenyl-2,3,5,6-tetrahydro-1*H*,11*H*-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-11-carboxylate (110 mg, 0.20 mmol), platinum(IV) oxide (46 mg, 0.20 mmol) and THF (5 mL). The resulting suspension was placed under an atmosphere of H_2 and stirred at room temperature for 5 hours. The suspension was filtered through celite and the solvent was removed under reduced pressure to leave the crude product as a yellow solid. The product was purified by trituration from DCM to give (*R**)-6-(hydroxy(phenyl)amino)-2-phenyl-6,11-dihydro-1*H*,5*H*-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-1,3(2*H*)-dione (65%, 55 mg, 0.13 mmol) as an off-white solid.

Mp: 174.3–175.2 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 11.63 (1H, s), 8.61 (1H, s), 7.54–7.38 (6H, m), 7.18 (2H, app t, J = 7.8 Hz), 7.10 (2H, app d, J = 7.8 Hz), 7.00–6.96 (2H, m), 6.91–6.83 (2H, m), 5.18–5.15 (1H, m), 4.48 (1H, dd, J = 13.0, 2.0 Hz), 3.77 (1H, dd, J = 13.0, 4.2 Hz); ^{13}C NMR (101 MHz, DMSO-d_6): δ_C 152.6, 149.6, 146.6, 134.2, 131.7, 129.8, 129.6, 128.9, 128.9, 127.0, 125.8, 122.3, 121.1, 120.2, 118.5, 118.3, 112.3, 92.4, 57.4, 43.4; IR (neat): ν_{max}/cm^{-1} 3431, 3054, 1698; MS (pAPCI): 317.1 (100%, (M − (N(OH) Ph) + H)$^+$), 407.1 (5%, (M − H_2O)$^+$); HRMS (pAPCI) calcd $C_{24}H_{19}N_5O_3$ [M − H]$^+$: 424.1404; observed: 424.1398.

4j – (*R**)-6-(hydroxy(*o*-tolyl)amino)-2-phenyl-6,11-dihydro-1*H*,5*H*-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-1,3(2*H*)-dione

To a stirred Schlenk flask was added benzyl (*R**)-6-(hydroxy(*o*-tolyl)amino)-1,3-dioxo-2-phenyl-2,3,5,6-tetrahydro-1*H*,11*H*-[1,2,4]-triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-11-carboxylate (140 mg, 0.24 mmol), platinum(IV) oxide (55 mg, 0.24 mmol) and THF (5 mL). The resulting suspension was placed under an

atmosphere of H_2 and stirred at room temperature for 5 hours. The suspension was filtered through celite and the solvent was removed under reduced pressure to leave the crude product as a white solid. The crude product was purified by trituration from DCM to give (*R**)-6-(hydroxy(*o*-tolyl)amino)-2-phenyl-6,11-dihydro-1*H*,5*H*-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-1,3(2*H*)-dione (44%, 46 mg, 0.11 mmol) as a white powder.

Mp: 188.1–189.6 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 11.65 (1H, s), 8.58 (1H, s), 7.59–7.51 (5H, m), 7.47–7.42 (1H, m), 7.36 (1H, d, J = 8.0 Hz), 7.17–7.13 (1H, m), 6.96–6.91 (3H, m), 6.79–6.69 (2H, m), 4.69 (1H, d, J = 12.8 Hz), 4.58 (1H, br s), 3.62 (1H, dd, J = 12.8, 3.3 Hz), 2.06 (3H, s); ^{13}C NMR (101 MHz, DMSO-d_6): δ_C 151.4, 150.4, 146.8, 134.0, 131.8, 131.2, 130.6, 129.8, 129.7, 128.9, 127.0, 126.7, 126.0, 125.1, 122.6, 121.0, 120.1, 118.1, 112.2, 92.3, 57.8, 43.5, 18.2; IR (neat): ν_{max}/cm^{-1} = 3426, 3380, 2950, 1712; MS (pAPCI): 108.1 (100%), 317.1 (37%, (M − (N(OH)(*o*-Tol)) + H)$^+$), 422.2 (4%, (M − (H_2O) + H)$^+$), 438.2 (6%, (M − H)$^+$); HRMS (pAPCI): calcd $C_{25}H_{20}N_5O_3$ [M − H]$^+$: 438.1561; observed: 438.1553.

4k – (3a*S**,5*S**,10b*S**)-5-(hydroxy(phenyl)amino)-7-methoxy-2-methyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione

To a stirred Schlenk flask was added benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(phenyl)amino)-7-methoxy-2-methyl-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate (130 mg, 0.25 mmol), platinum(IV) oxide (57 mg, 0.25 mmol) and THF (5 mL). The resulting suspension was placed under an atmosphere of H_2 and stirred at room temperature for 5 hours. The suspension was filtered through celite and the solvent was removed under reduced pressure to leave the crude product as an orange solid. The crude product was purified by column chromatography (petrol (40/60)–ethyl acetate 3 : 2, column diameter = 2 cm, silica = 14 cm) to give (3a*S**,5*S**,10b*S**)-5-(hydroxy(phenyl)amino)-7-methoxy-2-methyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione (70%, 69 mg, 0.18 mmol) as a pale yellow powder.

Mp: 149.1–151.2 °C; R_f: 0.19 (Pet(40/60)–EA 3 : 2); ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 10.95 (1H, s), 8.29 (1H, s), 7.23–7.19 (2H, m), 7.18 (1H, d, J = 2.8 Hz), 7.14–7.10 (2H, m), 6.87–6.83 (1H, m), 6.57 (1H, dd, J = 8.7, 2.5 Hz), 6.51 (1H, d, J = 2.5 Hz), 4.83 (1H, app t, J = 4.8 Hz), 4.24 (1H, d, J = 8.2 Hz), 3.64 (1H, app td, J = 9.1, 6.1 Hz), 3.48 (3H, s), 2.80 (3H, s), 2.35 (1H, ddd, J = 13.7, 6.1, 4.8 Hz), 1.83 (1H, ddd, J = 13.7, 9.1, 4.8 Hz); ^{13}C NMR (101 MHz, DMSO-d_6): δ_C 179.9, 176.3, 153.6C[1], 153.4, 132.0, 130.6, 129.0, 126.6, 121.2, 117.4, 112.3, 111.5, 109.5, 101.7, 57.7, 55.5, 39.5, 39.1, 27.1, 25.1; IR (neat): ν_{max}/cm^{-1} = 3394, 2937, 2833, 1690; MS (pAPCI): 283.1 (100%, (M − (N(OH)Ph) + H)$^+$), 374.1 (18%, (M − (H_2O) + H)$^+$), 390.1 (2%, (M − H)$^+$), 392.2 (1%, (M + H)$^+$); HRMS (pAPCI): calcd $C_{22}H_{22}N_3O_4$ [M + H]$^+$: 392.1605; observed: 392.1597.

4l – (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-7-methoxy-2-methyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione

To a stirred Schlenk flask was added benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-7-methoxy-2-methyl-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate (108 mg, 0.20 mmol), platinum(IV) oxide (46 mg, 0.20 mmol) and THF (5 mL). The resulting suspension was placed under an atmosphere of H_2 and stirred at room temperature for 5 hours. The suspension was filtered through celite and the solvent was removed under reduced pressure to leave the crude product as a white solid. The crude product was purified by column chromatography (petrol (40/60)–ethyl acetate 1 : 1, column diameter = 2 cm, silica = 15 cm) to give (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-7-methoxy-2-methyl-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione (70%, 57 mg, 0.14 mmol) as an off white powder.

Mp: 139.7–142.5 °C; R_f: 0.36 (Pet(40/60)–EA 1 : 1); ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 10.89 (1H, s), 8.36 (1H, s), 7.52 (1H, d, J = 8.0 Hz), 7.15–7.11 (2H, d, J = 8.7 Hz), 6.93–6.85 (2H, m), 6.49 (1H, dd, J = 8.7, 2.4 Hz), 6.23–6.17 (1H, m), 4.28 (1H, d, J = 8.2 Hz), 4.22 (1H, app t, J = 3.8 Hz), 3.78 (1H, ddd, J = 10.8, 8.2, 6.1 Hz), 3.45 (3H, s), 2.81 (3H, s), 2.70–2.63 (1H, m), 1.89 (3H, s), 1.66 (1H, ddd, J = 14.1, 10.8, 3.8 Hz); ^{13}C NMR (101 MHz, DMSO-d_6): δ_C 180.1, 176.3, 153.2, 152.5, 131.6, 131.1, 130.7, 130.4, 126.8, 126.5, 124.7, 122.7, 112.2, 111.4, 109.2, 100.6, 58.8, 55.3, 39.6, 38.4, 28.3, 25.1, 18.1; IR (neat): ν_{max}/cm^{-1} = 3384, 2954, 2866, 1693; MS (pAPCI): 283.1 (100%, (M − (N(OH)(*o*-Tol)) + H)$^+$), 388.2 (34%, (M − (H_2O) + H)$^+$), 404.2 (13%, (M − H)$^+$), 406.2 (11%, (M + H)$^+$); HRMS (pAPCI): calcd $C_{23}H_{24}N_3O_4$ [M + H]$^+$: 406.1761; observed: 406.1750.

4m – (3a*S**,5*S**,10b*S**)-5-(hydroxy(phenyl)amino)-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione

To a stirred Schlenk flask was added benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(phenyl)amino)-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate (90 mg, 0.18 mmol), platinum(IV) oxide (41 mg, 0.18 mmol) and THF (5 mL). The resulting suspension was placed under an atmosphere of H_2 and stirred at room temperature for 10 hours. The suspension was filtered through celite and the solvent was removed under reduced pressure to leave the crude product as an yellow solid, The crude product was purified by column chromatography (petrol (40/60)–ethyl acetate 1 : 1, column diameter = 2 cm, silica = 14 cm) to give (3a*S**,5*S**,10b*S**)-5-(hydroxy(phenyl)amino)-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione (41%, 26 mg, 0.07 mmol) as a yellow powder.

Mp: 150.0–153.1 °C; R_f: 0.33 (Pet(40/60)–EA 1 : 1); ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 11.22 (1H, s), 11.09 (1H, s), 8.24 (1H, s), 7.33 (1H, d, J = 8.1 Hz), 7.27–7.23 (1H, m), 7.20 (2H, app d, J = 7.3 Hz), 7.12 (2H, d, J = 7.7 Hz), 7.00–6.95 (1H, m), 6.85 (1H, app t, J = 7.2 Hz), 6.80 (1H app t, J = 7.3 Hz), 4.89 (1H, app t, J = 4.9 Hz), 4.25 (1H, d, J = 8.1 Hz), 3.63–3.52 (1H, m), 2.27 (1H, app dt, J = 13.6, 5.6 Hz), 1.80 (1H, ddd, J = 13.6, 9.2, 4.8 Hz); ^{13}C NMR (101 MHz, DMSO-d_6): δ_C 181.2, 177.6, 153.3, 137.0, 130.3, 129.0, 126.3, 121.4, 121.1, 119.9, 118.9, 117.2, 111.7, 109.9, 57.4, 40.9, 40.6, 25.7; IR (neat): ν_{max}/cm^{-1} 3302, 2924, 1706; MS (pAPCI): 108.1 (18%), 237.1 (100), 239.1 (46%, (M − (N(OH)Ph) + H)$^+$); HRMS (pAPCI): calcd $C_{14}H_{11}N_2O_2$ [M − (N(OH)Ph) + H]$^+$: 239.0815; observed: 239.0810.

4n – (3a*S,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*,3a*H*)-dione**

To a stirred Schlenk flask was added benzyl (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl)amino)-1,3-dioxo-2,3,3a,4,5,10b-hexahydropyrrolo[3,4-*a*]carbazole-10(1*H*)-carboxylate (120 mg, 0.24 mmol), platinum(IV) oxide (54 mg, 0.24 mmol) and THF (5 mL). The resulting suspension was placed under an atmosphere of H_2 and stirred at room temperature for 6 hours. The suspension was filtered through celite and the solvent was removed under reduced pressure to leave the crude product as a yellow solid, The crude product was purified by column chromatography (petrol (40/60)–ethyl acetate 2 : 3, column diameter = 2 cm, silica = 17 cm) to give (3a*S**,5*S**,10b*S**)-5-(hydroxy(*o*-tolyl) amino)-4,5,10,10b-tetrahydropyrrolo[3,4-*a*]carbazole-1,3(2*H*, 3a*H*)-dione (70%, 61 mg, 0.17 mmol) as an off white solid.

Mp: 149.9–153.2 °C; R_f: 0.52 (Pet(40/60)–EA 2 : 3); ^{1}H NMR (400 MHz, CD_2Cl_2): δ_H 8.81 (1H, s), 8.21 (1H, s), 7.56 (1H, d, J = 8.0 Hz), 7.30 (1H, d, J = 7.9 Hz), 7.18 (2H, d, J = 6.9 Hz), 7.06 (1H, app t, J = 7.6 Hz), 7.03–6.99 (2H, m), 6.91–6.85 (1H, m), 5.36 (1H, s), 4.51 (1H, app t, J = 4.5 Hz), 4.19 (1H, d, J = 8.6 Hz), 3.80 (1H, app td, J = 9.3, 6.4 Hz), 2.74 (1H, app dt, J = 13.6, 5.5 Hz), 2.15 (3H, s), 1.83 (1H, ddd, J = 13.6, 10.1, 4.1 Hz); ^{13}C NMR (101 MHz, DMSO-d_6): δ_C 181.5, 177.6, 152.2, 136.7, 130.6, 130.5, 130.5, 126.5, 126.5, 124.5, 122.4, 121.1, 119.3, 118.9, 111.6, 109.5, 58.3, 55.5, 40.9, 27.3, 18.3; IR (neat): ν_{max}/cm^{-1} 3372, 3298, 1683; MS (nNSI) = 186.0 (100%), 237.1 (97%, (M − (N(OH)(*o*-Tol)) − H)$^-$), 358.1 (35%, (M − H_2)$^-$), 394.1 (23%); HRMS (nNSI): calcd $C_{21}H_{18}N_3O_3$ [M − H]$^-$: 360.1354; observed: 360.1348.

4o – (*R)-6-(hydroxy(phenyl)amino)-8-methoxy-2-phenyl-6,11-dihydro-1*H*,5*H*-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-1,3(2*H*)-dione**

To a stirred Schlenk flask was added benzyl (*R**)-6-(hydroxy (phenyl)amino)-8-methoxy-1,3-dioxo-2-phenyl-2,3,5,6-tetrahydro-1*H*,11*H*-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-11-carboxylate (118 mg, 0.20 mmol), platinum(IV) oxide (46 mg, 0.20 mmol) and THF (5 mL). The resulting suspension was placed under an atmosphere of H_2 and stirred at room temperature for 5 hours. The suspension was filtered through celite and the solvent was removed under reduced pressure to leave the crude product as a yellow solid. The product was purified by trituration from DCM to give (*R**)-6-(hydroxy(phenyl) amino)-8-methoxy-2-phenyl-6,11-dihydro-1*H*,5*H*-[1,2,4]triazolo [1′,2′:1,2]pyridazino[3,4-*b*]indole-1,3(2*H*)-dione (38%, 35 mg, 0.08 mmol) as an off-white solid.

Mp: 173.7–176.4 °C; R_f: 0.18 (Pet–EA 3 : 1); ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 11.44 (1H, s) 8.62 (1H, s), 7.54–7.47 (4H, m), 7.44–7.41 (1H, m) 7.25–7.18 (3H, m), 7.12 (2H, d, J = 7.7 Hz), 6.90 (1H, app t, J = 6.8 Hz), 6.56 (1H, d, J = 8.7 Hz), 6.26 (1H, s), 5.12 (1H, br s), 4.51 (1H, d, J = 13.0 Hz), 3.81 (1H, dd, J = 13.0, 3.3 Hz), 3.49 (3H, s); ^{13}C NMR (101 MHz, DMSO-d_6): δ_C 154.3, 152.9, 149.7, 146.4, 131.8, 130.1, 129.6, 129.6, 128.9, 128.9, 127.0, 126.3, 122.3, 118.4, 112.9, 110.7, 100.8, 92.3, 57.7, 55.5, 44.3; IR (neat): ν_{max}/cm^{-1} 3362, 3000, 1758, 1700; MS (pAPCI): 213.1 (70%), 347.1 (100%, (M − (N(OH)Ph) + H)$^+$); HRMS (pAPCI): calcd $C_{25}H_{20}N_5O_4$ [M − H]$^+$: 454.1510; observed: 454.1502.

4p – (*R)-6-(hydroxy(*o*-tolyl)amino)-8-methoxy-2-phenyl-6,11-dihydro-1*H*,5*H*-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-*b*]indole-1,3(2*H*)-dione**

To a stirred Schlenk flask was added benzyl (*R**)-6-(hydroxy(*o*-tolyl)amino)-8-methoxy-1,3-dioxo-2-phenyl-2,3,5,6-tetrahydro-1*H*,11*H*-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4 *b*]indole-11-carboxylate (120 mg, 0.20 mmol), platinum(IV) oxide (46 mg, 0.20 mmol) and THF (5 mL). The resulting suspension was placed under an atmosphere of H_2 and stirred at room temperature for 5 hours. The suspension was filtered through celite and the solvent was removed under reduced pressure to leave the crude product as a white solid. The crude product was purified by trituration from DCM to (*R**)-6-(hydroxy(*o*-tolyl)amino)-8-methoxy-2-phenyl-6,11-dihydro-1*H*,5*H*-[1,2,4]triazolo[1′,2′:1,2]-pyridazino[3,4 *b*]indole-1,3(2*H*)-dione (64%, 53 mg, 0.13 mmol) as a white powder.

Mp: 171.9–173.8 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ_H 11.44 (1H, s), 8.64 (1H, s), 7.59 (1H, d, J = 8.1 Hz), 7.54–7.50 (4H, m), 7.46–7.43 (1H, m), 7.19 (1H, d, J = 8.5 Hz), 7.15 (1H, d, J = 7.5 Hz), 6.97–6.91 (2H, m), 6.50 (1H, dd, J = 8.7, 2.2 Hz), 6.01 (1H, s), 4.73 (1H, d, J = 12.8 Hz), 4.52 (1H, s), 3.67–3.61 (1H, m), 3.47 (3H, s), 1.96 (3H, s); ^{13}C NMR (101 MHz, DMSO-d_6): δ_C 154.1, 151.8, 150.5, 146.4, 131.8, 131.6, 130.6, 130.0, 129.7, 128.9, 128.7, 127.0, 126.7, 126.5, 125.3, 122.8, 112.7, 110.7, 100.0, 91.8, 58.3, 55.4, 44.3, 18.0; IR (neat): ν_{max}/cm^{-1} = 3442, 3394, 2939, 1699; MS (pAPCI): 347.1 (68%, (M − (N(OH)(*o*-Tol) + H)$^+$)), 391.1 (100%), 452.2 (4%, (M − (H_2O) + H)$^+$), 468.2 (2%, (M − H)$^+$); HRMS (pAPCI): calcd $C_{26}H_{22}N_5O_4$ [M − H]$^+$: 468.1666; observed: 468.1658.

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