Synthesis of Homocarbonyltopsentine Derivatives

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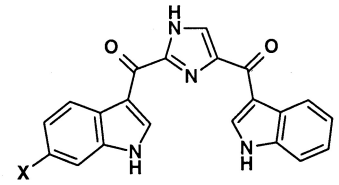
Abstract: Homocarbonyltopsentines **I** are known to exhibit interesting anti-inflammatory activity in vivo. In order to study the role of the heterocycles in the modulation of their activity, several analogues in which indoles were replaced either by substituted indoles or by bioisosteric heterocycles such as pyrrolo[2,3-*b*]pyridine, benzo[*b*]thiophene and pyridine were synthesised. The synthesis is based on selective halogen–metal exchange on triiodoimidazole **1** and subsequent addition to formylated heterocycles.

Key words: indoles, metalation, regioselectivity, addition reactions, palladium

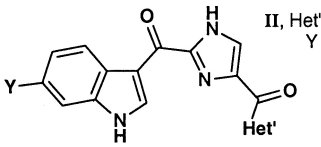
Many naturally occurring bis-indole alkaloids such as topsentins, dragmacidins, rhopaladins and hamacanthins, extracted from marine organisms and described to date, exhibit pharmacological properties.[1] Among them, a closely related structure called homocarbonyltopsentine **I** was reported in the literature, which showed potent anti-inflammatory activity in vivo.[2]

In a previous paper, we have described a general approach to prepare this bis-indole skeleton via selective halogen–metal exchange reactions on triiodoimidazole followed by addition to formylated indoles.[3] In our ongoing research work, we investigated the synthesis of compounds displaying the general structure **II**, in order to determine the importance of the nature of the substituent on the indole moiety and the nature of the heterocycle linked to the position 4 of the imidazole nucleus through a carbonyl function (Figure 1).

By this synthetic methodology, which allowed us to switch easily from one heterocycle to another, a wide range of homocarbonyltopsentine derivatives or analogues can be prepared in sufficient amount for biological assays (Scheme 1). Thus, selective halogen–metal exchange reactions were performed on triiodoimidazole **1**[4] (EOM = ethoxymethyl) in order to prepare highly nucleophilic species which can then react with conveniently substituted and protected formylated heterocycles (Het-CHO and Het′-CHO). According to literature procedures, 3-formylindoles **2a**,**b** and **2c**[5] were prepared in our laboratory (Scheme 1). Other aldehydes such as 3-formylpyridine (**2d**) and 3-formylbenzothiophene (**2e**) are commercially available.



Ia, X = OH : Homocarbonyltopsentine
Ib, X = OCOMe : Homocarbonyltopsentine monoacetate



II, Het' = indole, pyridine, benzothiophene
Y = H, OH, OMe, OBn

Figure 1

The first step of the synthesis was realised by reaction of *n*-BuLi with triiodoimidazole **1** which produced selectively the carbanion at C-2.[6] Addition of formylated heterocycles **2** to the carbanion intermediate afforded alcohols **3** in good yields (Scheme 2). Only in the case of 1-*tert*-butyloxycarbonyl-3-formylpyrrolo[2,3-*b*]pyridine, low reaction yield was observed (24%, not described). Alcohols **3** were then oxidised with MnO_2 to produce the corresponding ketones **4** (Table 1). After the first part of the synthesis was achieved, the derivatives **4a–c** were selected to reach the final compounds **II**.

Table 1 Yields of Compounds **3** and **4**

Aldehyde	Product **3**	Yield (%)	Product **4**	Yield (%)
2a	**3a**	75	**4a**	91
2b	**3b**	68	**4b**	90
2c	**3c**	73	**4c**	90
2d	**3d**	90	**4d**	85
2e	**3e**	43	**4e**	92

Using the same conditions as for the first substitution, the alcohols **5** were obtained in good yields from **4a–c** by selective iodine–lithium exchange at C-4 and reaction with aldehydes **2c–e** (Scheme 3, Table 2).[6] The alcohols were subsequently oxidised to produce the diketones **6** in fair yields (Table 2).

The last iodine on compounds **6** was then removed by hydrogenolysis in the presence of palladium on charcoal as

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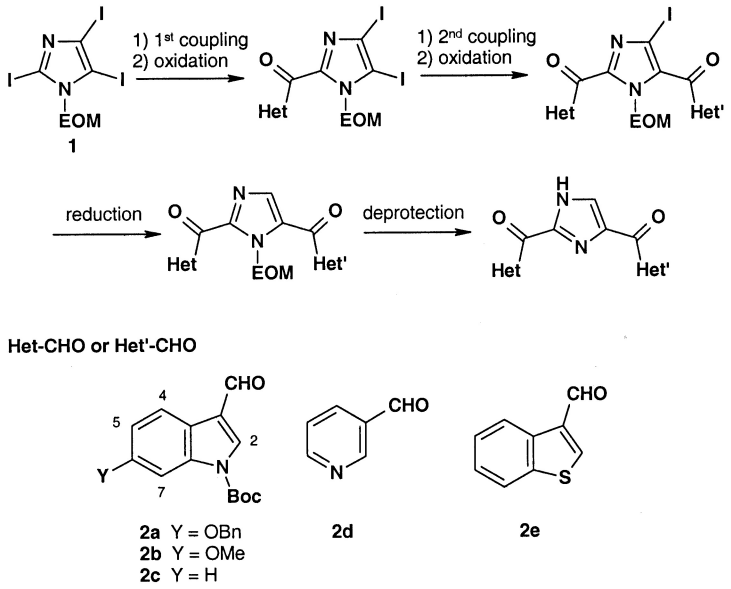
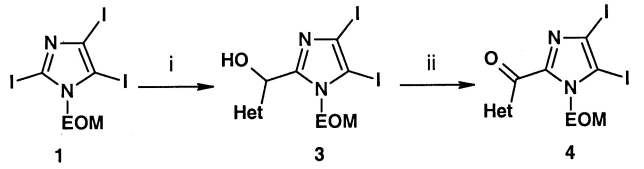


Scheme 1



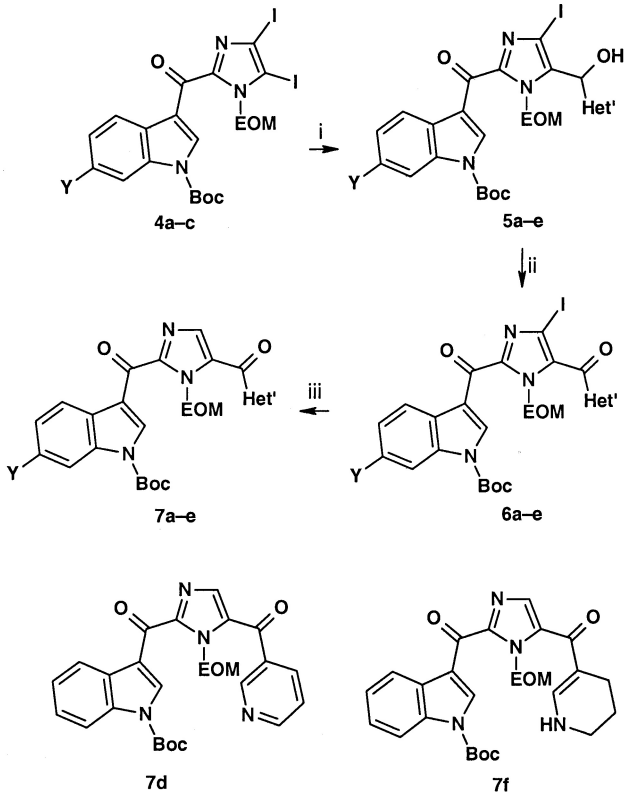
Scheme 2 *Reagents and conditions*: i. *n*-BuLi (1 equiv), THF, –78 °C, 5 min then **2** (1.1 equiv), 45 min; ii. MnO_2, CH_2Cl_2, r.t., 4 h.

catalyst and potassium carbonate as proton scavenger (Scheme 3). Under these conditions, the benzyl group of **6a** was not affected. For **6d**, we isolated **7d** in 55% yield along with the by-product **7f** (20%) in which the pyridine nucleus was reduced into 1,2,3,4-tetrahydropyridine (Scheme 3). Except this example, compounds **7** were isolated in 80–89% yields.

Final compounds **9** were obtained by successive deprotection of the *tert*-butyloxycarbonyl and the ethoxymethyl groups (Scheme 4). Thus, derivatives **7a–e** were, first treated with aqueous 1 N NaOH in 1,4-dioxane at 70 °C for 30 minutes to afford compounds **8a–e** in good yields (Table 3). The latter, when heated in the presence of aqueous 1 N HCl in 1,4-dioxane for 30 minutes gave **9a–e**.

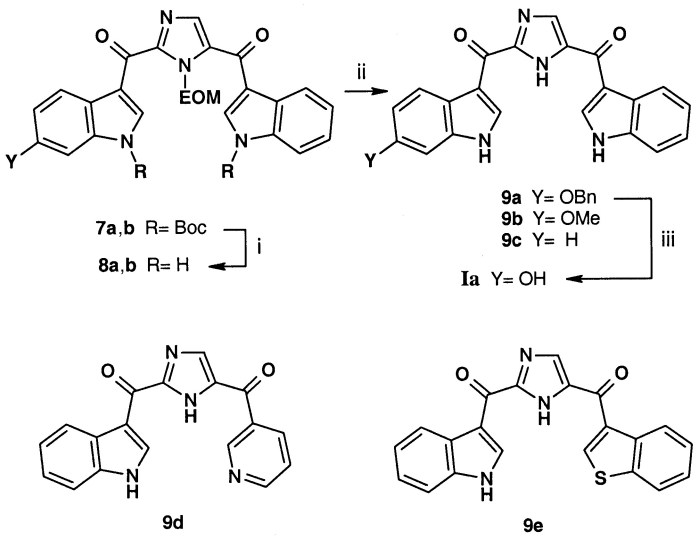
Table 2 Yields of Compounds **5–7**

Het′	Y	Yield (%)		
		5	**6**	**7**
2c	OBn	**5a** 61	**6a** 84	**7a** 89
2c	OMe	**5b** 61	**6b** 99	**7b** 93
2c	H	**5c** 71	**6c** 84	**7c** 85
2d	H	**5d** 70	**6d** 82	**7d** 55
2e	H	**5e** 65	**6e** 65	**7e** 80



Scheme 3 *Reagents and conditions*: i. *n*-BuLi (1 equiv), THF, –78 °C, 5 min then **2** (1.1 equiv), 45 min; ii. MnO_2, CH_2Cl_2, r.t., 5 h; iii. H_2 (15 bar), 10% Pd/C, K_2CO_3, EtOH–CH_2Cl_2, overnight, r.t.

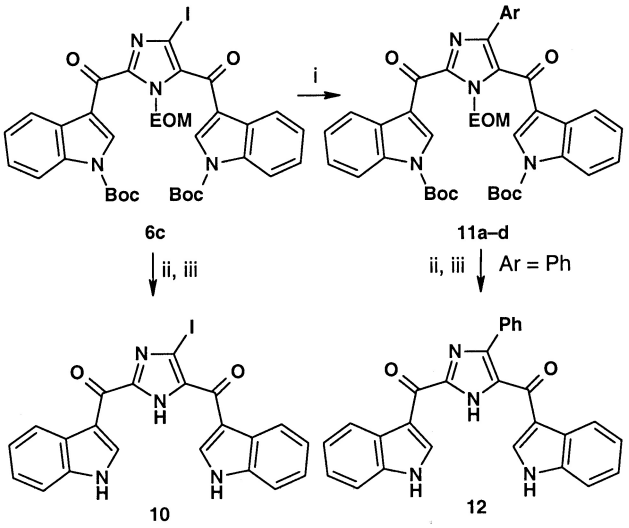
Close derivatives of **9d** have been reported as potent anticancer agents.[7] Synthesis of homocarbonyltopsentine **Ia** was finally achieved by hydrogenolysis (HCO_2NH_4, 10% Pd/C, EtOH, reflux, 1 h) of the benzyl protecting group of **9a** in 91% yield.



Scheme 4 *Reagents and conditions*: i. 1 N NaOH, 1,4-dioxane, 70 °C, 30 min; ii. 1 N HCl, 1,4-dioxane, 70 °C, 30 min; iii. 10% Pd/C, HCO_2NH_4, EtOH, reflux, 1 h, 91%.

Iodo derivative **10** was also prepared from **6c** in 56% yield (Scheme 5). Taking advantage of iodine on the imidazole ring of compounds **6**, introduction of a third substituent on the imidazole by palladium-mediated cross-coupling reaction can be done giving access to a wide variety of derivatives. From our part, only a Suzuki reaction[8] was explored in our laboratory (Scheme 5). According to the classical method, commercially available boronic acids (phenylboronic acid, 2-thienylboronic acid, 2-furylboronic acid and 1-*tert*-butyloxycarbonyl-2-pyrrolylboronic acid[9]) were coupled to derivative **6c** in the presence of tetrakis(triphenylphosphine)palladium to afford **11a–d** in good yields (Table 4). As a final example, two successive deprotection reactions were performed on **11a** to afford **12** in 83% yield (Scheme 5). Surprisingly, we observed a complete degradation of **11d** when submitted to the deprotection reactions.

In summary, we have prepared homocarbonyltopsentine **Ia** and several analogues or derivatives. These compounds are currently evaluated for anti-inflammatory activity and the results will be reported in due course.



Scheme 5 *Reagents and conditions*: i. $ArB(OH)_2$, $Pd(PPh_3)_4$, Na_2CO_3, toluene–EtOH, 80 °C, 1.5–48 h; ii. aq 1 N NaOH, 1,4-dioxane, 70 °C, 30 min; iii. aq 1 N HCl, 1,4-dioxane, 70 °C, 45 min, **10**: 56%, **12**: 83%.

Melting points were obtained on a Büchi capillary instrument and are uncorrected. IR spectra were recorded on a Perkin-Elmer 681 IR spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance 300 spectrometer. Chemical shifts are expressed in parts per million (ppm) relative to TMS. Mass spectra were recorded on a Perkin-Elmer SCIEX API spectrometer. Elemental analyses were performed on a Thermoquest Flash 1112 series EA analyser. TLC was conducted on precoated silica gel plates (Merck $60F_{254}$)

Table 3 Yields of Compounds **8** and **9**

8	Yield (%)	**9**	Yield (%)
8a	85	**9a**	83
8b	89	**9b**	85
8c	89	**9c**	90
8d	97	**9d**	96
8e	80	**9e**	88

Table 4 Yields of Compounds **11**

Ar	**11**	Yield (%)
Ph	**11a**	92
2-thienyl	**11b**	95
2-furyl	**11c**	96
2-(1-Boc)pyrrolyl	**11d**	89

and the spots were visualised under UV light. Flash chromatography was carried out on column using flash silica gel 60 Merck (40–63 μm) using the indicated solvents [petroleum ether (PE): bp 40–60 °C]. All reactions requiring anhydrous conditions were conducted in flame-dried apparatus. Boronic acids were purchased from Lancaster or Sigma-Aldrich.

tert-Butyl 6-Benzyloxy-3-formyl-1*H*-indole-1-carboxylate (2a); Typical Procedure

A solution of 6-benzyloxyindole-3-carboxaldehyde[10] (232 mg, 0.92 mmol), Boc_2O (409 mg, 1.86 mmol) and a catalytic amount of DMAP (5 mg) in MeCN (15 mL) was stirred overnight at r.t. After evaporation of the solvent, the residue was partitioned between EtOAc (20 mL) and H_2O (20 mL). The two layers were separated and the aqueous phase was extracted with EtOAc (10 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated in vacuo. The oily residue crystallised upon addition of pentane to give **2a** (321 mg, 99%); mp 118–119 °C (pentane).

IR (KBr): 3140, 2800, 2720, 1740, 1670 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.69 (s, 9 H, 3 CH_3), 5.14 (s, 2 H, OCH_2), 7.08 (dd, 1 H, *J* = 2.1, 8.7 Hz, H-5), 7.31–7.48 (m, 5 H, C_6H_5), 7.82 (d, 1 H, *J* = 2.1 Hz, H-7), 8.12 (s, 1 H, H-2), 8.15 (d, 1 H, *J* = 8.7 Hz, H-4), 10.05 (s, 1 H, CHO).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.1 (3 CH_3), 70.4 (OCH_2), 85.6 (C) , 100.5 (CH), 114.4 (CH), 120.0 (C), 121.7 (C), 122.7 (CH), 127.6 (2 CH), 128.1 (CH), 128.6 (2 CH), 135.6 (CH), 136.9 (C), 137.1 (C), 148.9 (C), 158.0 (C=O), 185.8 (C=O).

MS (ESI): *m*/*z* = 352 ($M + H^+$).

Anal. Calcd for $C_{21}H_{21}NO_4$ (351.41): C, 71.78; H, 6.02; N, 3.91. Found: C, 72.06; H, 5.91; N, 4.12.

tert-Butyl 3-Formyl-6-methoxy-1*H*-indole-1-carboxylate (2b)

According to the procedure described for **2a**, compound **2b** was prepared from 6-methoxyindole-3-carboxaldehyde[11] in 97% yield as a solid; mp 111–112 °C (pentane).

IR (KBr): 3140, 2800, 2720, 1740, 1670 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.71 (s, 9 H, 3 CH_3), 3.89 (s, 3 H, OCH_3), 6.99 (dd, 1 H, *J* = 2.1, 8.7 Hz, H-5), 7.72 (d, 1 H, *J* = 2.1 Hz, H-7), 8.11 (s, 1 H, H-2), 8.14 (d, 1 H, *J* = 8.7 Hz, H-4), 10.04 (s, 1 H, CHO).

^{13}C NMR ($CDCl_3$): δ = 28.2 (3 CH_3), 55.7 (OCH_3), 85.6 (C), 99.3 (CH), 113.8 (CH), 119.8 (C), 121.8 (C), 122.7 (CH), 135.6 (CH), 137.2 (C), 149.0 (C), 159.0 (C=O), 185.9 (C=O).

MS (ESI): *m*/*z* = 276 ($M + H^+$).

Anal. Calcd for $C_{15}H_{17}NO_4$ (275.31): C, 65.44; H, 6.22; N, 5.09. Found: C, 65.21; H, 6.12; N, 4.99.

First Coupling: Reaction of Triiodoimidazole 1 with Formylated Heterocycles 2; General Procedure

At –78 °C and under N_2, a solution of 2.3 M of *n*-BuLi in hexanes (1.1 mmol) was added dropwise to a solution of **1** (504 mg, 1 mmol) in anhyd THF (10 mL). After stirring for 5 min, compound **2** (1.1 mmol) in anhyd THF (5 mL) was added. The final solution was stirred at –78 °C for 1 h. The reaction was hydrolysed by the addition of sat. aq NH_4Cl solution. The solution was extracted with CH_2Cl_2 (2 × 10 mL). The organic phases were combined, dried ($MgSO_4$), and evaporated in vacuo. The crude residue was purified by column chromatography to afford derivative **3**.

tert-Butyl 3-[(1-Ethoxymethyl-4,5-diiodo-1*H*-imidazol-2-yl)hydroxymethyl]-6-benzyloxy-1*H*-indole-1-carboxylate (3a)

Chromatography eluent: PE–EtOAc (7:3); yield: 75%; foam.

IR (film): 3400, 1730, 1620 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.06 (t, 3 H, *J* = 7.0 Hz, CH_3), 1.66 (s, 9 H, 3 CH_3), 3.36 (d, 2 H, *J* = 7.0 Hz, CH_2), 4.89 (br s, 1 H, OH), 5.13 (s, 2 H, CH_2O), 5.32 (AB system, 2 H, *J* = 11.9 Hz, CH_2N), 6.25 (br s, 1 H, C*H*OH), 6.91 (dd, 1 H, *J* = 2.2, 8.7 Hz, H-5), 7.26 (d, 1 H, *J* = 8.7 Hz, H-4), 7.33–7.48 (m, 5 H, C_6H_5), 7.59 (s, 1 H, H-2), 7.83 (br s, 1 H, H-7).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.8 (CH_3), 28.2 (3 CH_3), 64.5 (CH_2), 70.4 (CH_2), 76.7 (CH_2), 84.0 (C), 84.8 (C), 94.9 (C), 100.8 (CH), 112.9 (CH), 119.9 (C), 120.3 (CH), 122.1 (C), 122.7 (CH), 127.6 (2 CH), 127.9 (CH), 128.6 (3 CH), 136.9 (C), 137.1 (C), 149.7 (C), 153.7 (C), 157.3 (C=O).

MS (ESI): *m*/*z* = 730 ($M + H^+$).

Anal. Calcd for $C_{27}H_{29}I_2N_3O_5$ (729.36): C, 44.46; H, 4.01; N, 5.76. Found: C, 44.13; H, 4.17; N, 5.90.

tert-Butyl 3-[(1-Ethoxymethyl-4,5-diiodo-1*H*-imidazol-2-yl)hydroxymethyl]-6-methoxy-1*H*-indole-1-carboxylate (3b)

Chromatography eluent: PE–EtOAc (6:4); yield: 68%; foam.

IR (film): 3420, 1730, 1615 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.12 (t, 3 H, *J* = 7.0 Hz, CH_3), 1.66 (s, 9 H, 3 CH_3), 3.40–3.50 (m, 2 H, CH_2), 3.85 (s, 3 H, OCH_3), 3.86 (br s, 1 H, OH), 5.16–5.27 (m, 2 H, CH_2N), 6.17 (d, 1 H, *J* = 8.5 Hz, C*H*OH), 6.81 (d, 1 H, *J* = 8.7 Hz, H-5), 7.24 (d, 1 H, *J* = 8.7 Hz, H-4), 7.52 (s, 1 H, H-2), 7.69 (br s, 1 H, H-7).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.7 (CH_3), 28.1 (3 CH_3), 55.5 (CH_3), 64.2 (CH_2), 64.4 (CH), 76.5 (CH_2), 83.7 (C), 84.8 (C), 94.6 (C), 99.3 (CH), 112.1 (CH), 119.9 (C), 120.2 (CH), 121.8 (C), 122.2 (CH), 136.7 (C), 149.6 (C), 153.7 (C), 157.9 (C=O).

MS (ESI): *m*/*z* = 654 ($M + H^+$).

Anal. Calcd for $C_{21}H_{25}I_2N_3O_5$ (653.26): C, 38.61; H, 3.86; N, 6.43. Found: C, 38.88; H, 3.92; N, 6.28.

tert-Butyl 3-[(1-Ethoxymethyl-4,5-diiodo-1*H*-imidazol-2-yl)hydroxymethyl]indole-1-carboxylate (3c)

Chromatography eluent: PE–EtOAc (85:15); yield: 73%; solid; mp 168–169 °C (Et_2O).

IR (KBr): 3218, 1734, 1611 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.11 (t, 3 H, *J* = 7.0 Hz, CH_3), 1.67 (s, 9 H, 3 CH_3), 3.44 (q, 2 H, *J* = 7.0 Hz, CH_2), 3.82 (d, 1 H, *J* = 7.1 Hz, OH), 5,22 (AB system, 2 H, *J* = 7.0 Hz, CH_2N), 6.22 (d, 1 H, *J* = 7.1 Hz, C*H*OH), 7.18 (t, 1 H, *J* = 8.0 Hz, H-5), 7.31 (t, 1 H, *J* = 8.0 Hz, H-6), 7.42 (d, 1 H, *J* = 8.0 Hz, H-4), 7.65 (s, 1 H, H-2), 8.11 (d, 1 H, *J* = 8.0 Hz, H-7).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.7 (CH_3), 28.2 (3 CH_3), 64.5 (CH_2 + CH), 77.0 (CH_2), 84.1 (C), 84.8 (C), 94.8 (C), 115.3 (CH), 119.8 (CH + C), 123.0 (CH), 123.9 (CH), 124.8 (CH), 128.1 (C), 135.8 (C), 149.6 (C), 153.6 (C).

MS (ESI): *m*/*z* = 624 ($M + H^+$).

Anal. Calcd for $C_{20}H_{23}I_2N_3O_4$ (623.23): C, 38.54; H, 3.72; N, 6.74. Found: C, 38.86; H, 3.90; N, 6.87.

(1-Ethoxymethyl-4,5-diiodo-1*H*-imidazol-2-yl)pyridin-3-ylmethanol (3d)

Chromatography eluent: CH_2Cl_2–MeOH (97:3); yield: 90%; foam.

IR (film): 3150, 1580, 1479 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.94 (t, 3 H, *J* = 7.0 Hz, CH_3), 3.24 (q, 2 H, *J* = 7.0 Hz, CH_2), 5.28 (AB system, 2 H, *J* = 10.7 Hz, CH_2N), 6.07 (s, 1 H, C*H*OH), 7.23 (dd, 1 H_{pyr}, *J* = 4.9, 7.9 Hz), 7.70 (d, 1 H_{pyr}, *J* = 7.9 Hz), 8.40 (d, 1 H_{pyr}, *J* = 4.9 Hz), 8.56 (br s, 1 H_{pyr}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.7 (CH_3), 64.2 (CH_2), 67.4 (CH), 76.6 (CH_2), 85.3 (C), 95.1 (C), 123.4 (CH), 134.7 (CH), 136.3 (C), 147.4 (CH), 148.4 (CH), 153.7 (C).

MS (ESI): *m*/*z* = 486 ($M + H^+$).

Anal. Calcd for $C_{12}H_{13}I_2N_3O_2$ (485.07): C, 29.71; H, 2.70; N, 8.66. Found: C, 29.55; H, 2.65; N, 8.75.

Benzo[*b*]thiophen-3-yl-(1-ethoxymethyl-4,5-diiodo-1*H*-imidazol-2-yl)methanol (3e)
Chromatography eluent: PE–EtOAc (85:15); yield: 43%; solid; mp 159–161 °C (EtOAc–PE).

IR (KBr): 3480, 1596, 1485 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.04 (t, 3 H, *J* = 7.0 Hz, CH_3), 3.33 (q, 2 H, *J* = 7.0 Hz, CH_2), 4.26 (d, 1 H, *J* = 7.0 Hz, OH), 5.17 (s, 2 H, CH_2N), 6.33 (d, 1 H, *J* = 7.0 Hz, C*H*OH), 7.31–7.37 (m, 2 H, H-5, H-6), 7.49 (s, 1 H, H-2), 7.73–7.78 (m, 1 H, H-4), 7.81–7.87 (m, 1 H, H-7).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.8 (CH_3), 64.5 (CH_2), 66.4 (CH), 76.8 (CH_2), 84.9 (C), 95.0 (C), 122.5 (CH), 122.9 (CH), 124.6 (2 CH), 124.8 (CH), 124.7 (C), 136.9 (C), 141.0 (C), 153.5 (C).

MS (ESI): *m*/*z* = 541 ($M + H^+$).

Anal. Calcd for $C_{15}H_{14}I_2N_2O_2S$ (540.16): C, 33.35; H, 2.61; N, 5.19. Found: C, 33.30; H, 2.75; N, 5.30.

Oxidation of Alcohols 3 to Ketones 4; General Procedure
A solution of **3** (0.65 mmol) and MnO_2 (2.14 g, 24.64 mmol) in CH_2Cl_2 (18 mL) was stirred at r.t. for 4 h. MnO_2 was removed by filtration on Celite and the filtrate was evaporated in vacuo. Product **4** was isolated either by crystallisation or by column chromatography.

***tert*-Butyl 3-(1-Ethoxymethyl-4,5-diiodo-1*H*-imidazole-2-carbonyl)-6-benzyloxy-1*H*-indole-1-carboxylate (4a)**
Chromatography eluent: PE–EtOAc (8:2); yield: 91%; foam.

IR (film): 1745, 1625, 1530, 1420 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.18 (t, 3 H, *J* = 7.1 Hz, CH_3), 1.70 (s, 9 H, 3 CH_3), 3.60 (q, 2 H, *J* = 7.1 Hz, CH_2), 5.15 (s, 2 H, CH_2O), 6.00 (s, 2 H, CH_2N), 7.08 (dd, 1 H, *J* = 2.2, 8.8 Hz, H-5), 7.30–7.49 (m, 5 H, C_6H_5), 7.87 (d, 1 H, *J* = 2.2 Hz, H-7), 8.32 (d, 1 H, *J* = 8.8 Hz, H-4), 9.01 (s, 1 H, H-2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.0 (CH_3), 28.1 (3 CH_3), 64.6 (CH_2), 70.3 (CH_2), 77.7 (CH_2N), 85.1 (C), 92.2 (C), 97.7 (C), 100.3 (CH), 114.1 (CH), 117.4 (C), 122.1 (C), 123.1 (CH), 127.5 (2 CH), 127.9 (CH), 128.5 (2 CH), 136.1 (C), 136.3 (CH), 136.9 (C), 148.2 (C), 148.9 (C), 157.5 (C=O), 176.3 (C=O).

MS (ESI): *m*/*z* = 728 ($M + H^+$).

Anal. Calcd for $C_{27}H_{27}I_2N_3O_5$ (727.34): C, 44.59; H, 3.74; N, 5.78. Found: C, 44.74; H, 3.66; N, 5.70.

***tert*-Butyl 3-(1-Ethoxymethyl-4,5-diiodo-1*H*-imidazole-2-carbonyl)-6-methoxy-1*H*-indole-1-carboxylate (4b)**
Chromatography eluent: PE–EtOAc (9:1); yield: 90%; solid; mp 147–148 °C (Et_2O–pentane).

IR (KBr): 1745, 1620, 1530 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.18 (t, 3 H, *J* = 7.1 Hz, CH_3), 1.71 (s, 9 H, 3 CH_3), 3.60 (q, 2 H, *J* = 7.1 Hz, CH_2), 3.89 (s, 3 H, OCH_3), 5.99 (s, 2 H, CH_2N), 6.99 (dd, 1 H, *J* = 2.2, 8.7 Hz, H-5), 7.75 (d, 1 H, *J* = 2.2 Hz, H-7), 8.29 (d, 1 H, *J* = 8.7 Hz, H-4), 9.00 (s, 1 H, H-2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.0 (CH_3), 28.1 (3 CH_3), 55.6 (OCH_3), 64.7 (CH_2), 77.7 (CH_2N), 85.2 (C), 92.2 (C), 97.7 (C), 99.0 (CH), 113.6 (CH), 117.5 (C), 121.8 (C), 123.0 (CH), 136.3 (CH + C), 148.3 (C), 149.1 (C), 158.4 (C=O), 176.9 (C=O).

MS (ESI): *m*/*z* = 652 ($M + H^+$).

Anal. Calcd for $C_{21}H_{23}I_2N_3O_5$ (651.24): C, 38.73; H, 3.56; N, 6.45. Found: C, 39.01; H, 3.46; N, 6.52.

***tert*-Butyl 3-(1-Ethoxymethyl-4,5-diiodo-1*H*-imidazole-2-carbonyl)indole-1-carboxylate (4c)**
Chromatography eluent: PE–EtOAc (9:1); yield: 90%; solid; mp 160–161 °C (Et_2O).

IR (KBr): 1726, 1626, 1606, 1452 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.19 (t, 3 H, *J* = 7.0 Hz, CH_3), 1.72 (s, 9 H, 3 CH_3), 3.61 (q, 2 H, *J* = 7.0 Hz, CH_2), 6.01 (s, 2 H, CH_2), 7.38–7.40 (m, 2 H, H-5, H-6), 8.17–8.20 (m, 1 H, H-4), 8.43–8.47 (m, 1 H, H-7), 9.14 (s, 1 H, H-2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.0 (CH_3) 28.1 (3 CH_3), 64.7 (CH_2), 77.8 (CH_2), 85.4 (C), 92.3 (C), 97.8 (C), 115.1 (CH), 117.5 (C), 122.6 (CH), 124.6 (CH), 125.6 (CH), 128.4 (C), 135.3 (C), 137.5 (CH), 148.4 (C), 149.0 (C), 176.9 (C=O).

MS (ESI): *m*/*z* = 622 ($M + H^+$).

Anal. Calcd for $C_{20}H_{21}I_2N_3O_4$ (621.22): C, 38.67; H, 3.41; N, 6.76. Found: C, 38.34; H, 3.28; N, 6.73.

(1-Ethoxymethyl-4,5-diiodo-1*H*-imidazol-2-yl)-pyridin-3-yl-methanone (4d)
Chromatography eluent: CH_2Cl_2; yield: 85%; solid; mp 133–134 °C (Et_2O).

IR (KBr): 1632, 1595, 1574, 1479 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.20 (t, 3 H, *J* = 7.0 Hz, CH_3), 3.61 (q, 2 H, *J* = 7.0 Hz, CH_2), 5.96 (s, 2 H, CH_2N), 7.43 (dd, 1 H_{pyr}, *J* = 4.9, 8.0 Hz), 7.70 (d, 1 H_{pyr}, *J* = 8.0 Hz), 8.79 (dd, 1 H_{pyr}, *J* = 1.6, 4.9 Hz), 9.40 (d, 1 H_{pyr}, *J* = 1.6 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.0 (CH_3), 64.9 (CH_2), 78.2 (CH_2), 95.3 (C), 98.9 (C), 123.2 (CH), 132.0 (CH), 138.4 (2 CH), 147.2 (C), 153.3 (C), 180.6 (C=O).

MS (ESI): *m*/*z* = 484 ($M + H^+$).

Anal. Calcd for $C_{12}H_{11}I_2N_3O_2$ (483.05): C, 29.84; H, 2.30; N, 8.70. Found: C, 30.11; H, 2.44; N, 8.56.

Benzo[*b*]thiophen-3-yl-(1-ethoxymethyl-4,5-diiodo-1*H*-imidazol-2-yl)methanone (4e)
Chromatography eluent: CH_2Cl_2; yield: 92%; foam.

IR (film): 1635, 1490 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.18 (t, 3 H, *J* = 7.0 Hz, CH_3), 3.61 (q, 2 H, *J* = 7.0 Hz, CH_2), 5.94 (s, 2 H, CH_2N), 7.41 (t, 1 H, *J* = 7.5 Hz, H_5), 7.50 (t, 1 H, *J* = 7.5 Hz, H-6), 7.87 (d, 1 H, *J* = 7.5 Hz, H-4), 8.75 (d, 1 H, *J* = 7.5 Hz, H-7), 9.26 (s, 1 H, H-2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.0 (CH_3), 64.7 (CH_2), 78.0 (CH_2), 93.0 (C), 98.1 (C), 122.4 (CH), 125.3 (CH), 125.5 (CH), 125.9 (CH), 132.1 (C), 137.5 (C), 139.3 (C), 143.5 (C), 148.4 (C), 175.8 (C=O).

MS (ESI): *m*/*z* = 539 ($M + H^+$).

Anal. Calcd for $C_{15}H_{12}I_2N_2O_2S$ (538.15): C, 33.48; H, 2.25; N, 5.21. Found: C, 33.23; H, 2.27; N, 5.15.

Second Coupling: Reaction of Diodoimidazoles 4 with Formylated Heterocycles 2; General Procedure
At –78 °C and under argon, a solution of 2.3 M of *n*-BuLi in hexanes (0.64 mmol) was added dropwise to a solution of **4** (0.64 mmol) in anhyd THF (10 mL). After stirring for 5 min, compound **2** (0.70 mmol) in anhyd THF (5 mL) was added. The final solution

was stirred at –78 °C for 45 min. The reaction was hydrolysed by addition of sat. aq NH_4Cl solution and the mixture was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic phases were dried ($MgSO_4$) and evaporated in vacuo. The crude residue was purified by column chromatography to afford derivative **5**.

***tert*-Butyl 3-{5-[(1-*tert*-Butoxycarbonyl-1*H*-indol-3-yl)hydroxymethyl]-1-ethoxymethyl-4-iodo-1*H*-imidazole-2-carbonyl}-6-benzyloxy-1*H*-indole-1-carboxylate (5a)**
Chromatography eluent: PE–EtOAc (85:15); yield: 61%; foam.

IR (KBr): 3440, 1735, 1630 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.20 (t, 3 H, *J* = 7.0 Hz, CH_3), 1.75 (s, 9 H, 3 CH_3), 1.79 (s, 9 H, 3 CH_3), 3.65 (br q, 2 H, *J* = 7.0 Hz, CH_2), 4.73 (d, 1 H, *J* = 9.4 Hz, OH), 5.17 (s, 2 H, CH_2O), 5.42 (d, 1 H, *J* = 10.5 Hz, CH_2N), 6.33 (d, 1 H, *J* = 9.4 Hz, C*H*OH), 6.38 (d, 1 H, *J* = 10.5 Hz, CH_2N), 7.10 (dd, 1 H_{arom}, *J* = 2.2, 8.8 Hz), 7.18–7.52 (m, 8 H, C_6H_5 + H_{arom}), 7.83 (s, 1 H_{arom}), 7.91 (d, 1 H_{arom}, *J* = 2.2 Hz), 8.22 (d, 1 H_{arom}, *J* = 8.3 Hz), 8.33 (d, 1 H_{arom}, *J* = 8.8 Hz), 9.20 (s, 1 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.7 (CH_3), 28.0 (3 CH_3), 28.2 (3 CH_3), 63.9 (CH), 64.9 (CH_2), 70.3 (CH_2O), 73.7 (CH_2N), 84.0 (C), 85.1 (C), 88.2 (C), 100.3 (CH), 114.0 (CH), 115.4 (CH), 118.0 (C), 119.7 (CH), 120.4 (C), 122.1 (C), 122.1 (CH), 123.0 (CH), 123.4 (CH), 124.8 (CH), 127.5 (2 CH), 127.6 (C), 127.9 (CH), 128.5 (2 CH), 136.0 (C), 136.2 (C), 136.6 (CH), 136.8 (C), 138.2 (C), 146.2 (C), 148.9 (C), 149.5 (C=O), 157.5 (C=O), 178.0 (C=O).

MS (ESI): *m*/*z* = 847 ($M + H^+$).

Anal. Calcd for $C_{41}H_{43}IN_4O_8$ (846.73): C, 58.16; H, 5.12; N, 6.62. Found: C, 57.80; H, 4.96; N, 6.44.

***tert*-Butyl 3-{5-[(1-*tert*-Butoxycarbonyl-1*H*-indol-3-yl)hydroxymethyl]-1-ethoxymethyl-4-iodo-1*H*-imidazole-2-carbonyl}-6-methoxy-1*H*-indole-1-carboxylate (5b)**
Chromatography eluent: PE–EtOAc (85:15); yield: 61%; solid; mp 161–163 °C (dec.) (Et_2O–pentane).

IR (KBr): 3410, 1730, 1620, 1530 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.18 (t, 3 H, *J* = 7.0 Hz, CH_3), 1.70 (s, 9 H, 3 CH_3), 1.75 (s, 9 H, 3 CH_3), 3.60–3.65 (m, 2 H, CH_2), 3.88 (s, 3 H, OCH_3), 4.70 (d, 1 H, *J* = 10.0 Hz, OH), 5.29 (d, 1 H, *J* = 10.6 Hz, CH_2N), 6.27 (d, 1 H, *J* = 10.0 Hz, C*H*OH), 6.35 (d, 1 H, *J* = 10.6 Hz, CH_2N), 6.97 (dd, 1 H, *J* = 2.1, 8.7 Hz, H-5), 7.12–7.34 (m, 3 H_{arom}), 7.75–7.77 (m, 2 H_{arom}), 8.15 (br d, 1 H_{arom}, *J* = 8.0 Hz), 8.24 (d, 1 H_{arom}, *J* = 8.7 Hz), 9.11 (s, 1 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.8 (CH_3), 28.1 (3 CH_3), 28.3 (3 CH_3), 55.6 (OCH_3), 64.0 (CH), 65.1 (CH_2), 73.8 (CH_2N), 84.2 (C), 85.3 (C), 88.5 (C), 99.0 (CH), 113.6 (CH), 115.5 (CH), 118.1 (C), 119.8 (CH), 120.3 (CH), 121.8 (C), 122.9 (CH), 123.1 (CH), 123.5 (CH), 124.9 (CH), 127.5 (C), 136.0 (C), 136.3 (C), 136.6 (CH), 138.3 (C), 146.3 (C), 149.1 (C), 149.6 (C=O), 158.4 (C=O), 178.2 (C=O).

MS (ESI): *m*/*z* = 771 ($M + H^+$).

Anal. Calcd for $C_{35}H_{39}IN_4O_8$ (770.63): C, 54.55; H, 5.10; N, 7.27. Found: C, 54.59; H, 4.97; N, 7.37.

***tert*-Butyl 3-{5-[(1-*tert*-Butoxycarbonyl-1*H*-indol-3-yl)hydroxymethyl]-1-ethoxymethyl-4-iodo-1*H*-imidazole-2-carbonyl}indole-1-carboxylate (5c)**
Chromatography eluent: PE–EtOAc (85:15); yield: 71%; foam.

IR (KBr): 3432, 1739, 1633, 1479 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.19 (t, 3 H, *J* = 7.0 Hz, CH_3), 1.70 (s, 9 H, 3 CH_3), 1.75 (s, 9 H, 3 CH_3), 3.61–3.72 (m, 2 H, CH_2), 4.57 (d, 1 H, *J* = 10.4 Hz, OH), 5.26 (d, 1 H, *J* = 10.7 Hz, CH_2N), 6.25 (dd, 1 H, *J* = 1.5, 10.4 Hz, C*H*OH), 6.37 (d, 1 H, *J* = 10.7 Hz, CHN), 7.17–7.19 (m, 2 H_{arom}), 7.29–7.42 (m, 3 H_{arom}), 7.74 (d, 1 H_{arom}, *J* = 1.5 Hz), 8.14–8.23 (m, 2 H_{arom}), 8.39–8.43 (m, 1 H_{arom}), 9.24 (s, 1 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.9 (CH_3), 28.2 (3 CH_3), 28.3 (3 CH_3), 64.1 (CH), 65.2 (CH_2), 73.9 (CH_2N), 84.3 (C), 85.5 (C), 88.5 (C), 115.1 (CH), 115.5 (CH), 118.1 (C), 119.8 (CH), 120.4 (C), 122.5 (CH), 123.2 (CH), 123.6 (CH), 124.6 (CH), 125.0 (CH), 125.6 (CH), 127.6 (C), 128.4 (C), 135.3 (C), 136.1 (C), 137.8 (CH), 138.5 (C), 146.4 (C), 149.1 (C=O), 149.7 (C=O), 178.3 (C=O).

MS (ESI): *m*/*z* = 741 ($M + H^+$).

Anal. Calcd for $C_{34}H_{37}IN_4O_7$ (740.60): C, 55.14; H, 5.04; N, 7.57. Found: C, 54.79; H, 4.89; N, 7.46.

3-{5-[(1-*tert*-Butoxycarbonyl-1*H*-indol-3-yl)hydroxymethyl]-1-ethoxymethyl-4-iodo-1*H*-imidazole-2-carbonyl}pyridine (5d)
Chromatography eluent: PE–EtOAc (6:4); yield: 70%; solid; mp 174–176 °C (dec.) (Et_2O).

IR (KBr): 3360, 1740, 1630 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.15 (t, 3 H, *J* = 7.0 Hz, CH_3), 1.73 (s, 9 H, 3 CH_3), 3.62 (q, 2 H, *J* = 7.0 Hz, CH_2), 4.51 (d, 1 H, *J* = 9.4 Hz, OH), 5.07 (d, 1 H, *J* = 10.9 Hz, CH_2N), 6.20 (d, 1 H, *J* = 9.4 Hz, C*H*OH), 6.32 (d, 1 H, *J* = 10.9 Hz, CH_2N), 7.32–7.41 (m, 3 H, H_{arom} + H_{pyr}), 7.75 (br d, 1 H_{pyr}, *J* = 7.9 Hz), 8.18–8.21 (m, 1 H_{arom}), 8.39–8.42 (m, 1 H_{arom}), 8.59 (br d, 1 H_{pyr}, *J* = 4.1 Hz), 8.65 (s, 1 H_{pyr}), 9.19 (s, 1 H_{arom}).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 14.4 (CH_3), 27.5 (3 CH_3), 63.2 (CH_2), 64.6 (CH), 73.5 (CH_2), 85.5 (C), 87.7 (C), 114.8 (CH), 117.1 (C), 122.0 (CH), 123.1 (CH), 124.4 (CH), 125.5 (CH), 127.7 (C), 133.4 (CH), 134.4 (C), 136.8 (C), 137.1 (CH), 139.3 (C), 145.2 (C), 147.2 (CH), 148.3 (CH), 148.4 (C=O), 177.2 (C=O).

MS (ESI): *m*/*z* 603 ($M + H^+$).

Anal. Calcd for $C_{26}H_{27}IN_4O_5$ (602.43): C, 51.84; H, 4.52; N, 9.30. Found: C, 51.90; H, 4.45; N, 9.15.

3-{5-[(1-*tert*-Butoxycarbonyl-1*H*-indol-3-yl)hydroxymethyl]-1-ethoxymethyl-4-iodo-1*H*-imidazole-2-carbonyl}benzo[*b*]thiophene (5e)
Chromatography eluent: PE–EtOAc (9:1); yield: 65%; solid; mp 162–164 °C (dec.) (Et_2O).

IR (KBr): 3375, 1740, 1630 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.19 (t, 3 H, *J* = 7.0 Hz, CH_3), 1.75 (s, 9 H, 3 CH_3), 3.57–3.66 (m, 2 H, CH_2), 4.62 (d, 1 H, *J* = 10.2 Hz, OH), 5.12 (d, 1 H, *J* = 10.7 Hz, CH_2N), 6.31 (d, 1 H, *J* = 10.2 Hz, C*H*OH), 6.29–6.35 (d, 1 H, *J* = 10.7 Hz, CH_2N), 7.28–7.42 (m, 4 H_{arom}), 7.52 (dd, 1 H_{arom}, *J* = 2.0, 6.8 Hz), 7.65 (d, 1 H_{arom}, *J* = 1.5 Hz), 7.87 (dd, 1 H_{arom}, *J* = 2.0, 6.8 Hz), 8.18 (dd, 1 H_{arom}, *J* = 2.0, 6.8 Hz), 8.38 (dd, 1 H_{arom}, *J* = 1.8, 6.8 Hz), 9.23 (s, 1 H_{arom}).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 15.0 (CH_3), 28.2 (3 CH_3), 65.3 (CH_2), 66.0 (CH), 73.8 (CH_2N), 85.6 (C), 89.0 (C), 115.2 (CH), 118.1 (C), 122.5 (CH), 122.6 (CH), 123.2 (CH), 123.8 (CH), 124.6 (CH), 124.7 (CH), 124.8 (CH), 125.7 (CH), 128.4 (C), 135.0 (C), 135.3 (C), 136.3 (C), 137.9 (CH), 138.4 (C), 141.3 (C), 146.4 (C), 149.1 (C), 178.4 (C=O).

MS (ESI): *m*/*z* = 658 ($M + H^+$).

Anal. Calcd for $C_{29}H_{28}IN_3O_5S$ (657.53): C, 52.97; H, 4.29; N, 6.39. Found: C, 53.27; H, 4.25; N, 6.50.

***tert*-Butyl 3-[5-(1-*tert*-Butoxycarbonyl-1*H*-indole-3-carbonyl)-1-ethoxymethyl-4-iodo-1*H*-imidazole-2-carbonyl]-6-benzyloxy-1*H*-indole-1-carboxylate (6a)**
According to the procedure described for **4**, compound **6a** was prepared from **5a** in 84% yield as a foam (chromatography eluent: PE–EtOAc, 85:15).

IR (KBr): 1745, 1640 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.05 (t, 3 H, *J* = 7.0 Hz, CH_3), 1.72 (s, 9 H, 3 CH_3), 1.75 (s, 9 H, 3 CH_3), 3.57 (q, 2 H, *J* = 7.0 Hz, CH_2), 5.17 (s, 2 H, CH_2O), 6.10 (s, 2 H, CH_2N), 7.13 (dd, 1 H_{arom}, *J* = 2.3, 8.8 Hz), 7.31–7.51 (m, 7 H, C_6H_5 + H_{arom}), 7.92 (d, 1 H_{arom}, *J* = 2.3 Hz), 8.23 (dd, 1 H_{arom}, *J* = 2.0, 6.5 Hz), 8.28 (s, 1 H_{arom}), 8.36 (dd, 1 H_{arom}, *J* = 2.0, 6.5 Hz), 8.40 (d, 1 H_{arom}, *J* = 8.7 Hz), 9.15 (s, 1 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.8 (CH_3), 28.1 (6 CH_3), 65.0 (CH_2), 70.4 (CH_2O), 74.9 (CH_2N), 85.3 (C), 85.9 (C), 87.5 (C), 100.4 (CH), 114.3 (CH), 115.3 (CH), 118.3 (C), 119.5 (C), 122.0 (C), 122.4 (CH), 123.1 (CH), 124.9 (CH), 126.1 (CH), 127.1 (C), 127.6 (2 CH), 128.0 (CH), 128.6 (2 CH), 135.9 (C), 136.4 (C), 136.7 (C), 136.8 (CH), 136.9 (C + CH), 146.3 (C), 148.8 (C), 149.0 (C=O), 157.7 (C=O), 177.9 (C=O), 181.3 (C=O).

MS (ESI): *m*/*z* = 845 ($M + H^+$).

Anal. Calcd for $C_{41}H_{41}IN_4O_8$ (844.71): C, 58.30; H, 4.89; N, 6.63. Found: C, 58.15; H, 4.95; N, 6.51.

tert-Butyl 3-[5-(1-*tert*-Butoxycarbonyl-1*H*-indole-3-carbonyl)-1-ethoxymethyl-4-iodo-1*H*-imidazole-2-carbonyl]-6-methoxy-1*H*-indole-1-carboxylate (6b)

According to the procedure described for **4**, compound **6b** was prepared from **5b** in 99% yield as a solid; mp 157–158 °C (EtOAc–pentane).

IR (KBr): 1740, 1630, 1530 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.01 (t, 3 H, *J* = 7.0 Hz, CH_3), 1.70 (s, 9 H, 3 CH_3), 1.73 (s, 9 H, 3 CH_3), 3.53 (q, 2 H, *J* = 7.0 Hz, CH_2), 3.91 (s, 3 H, OCH_3), 6.05 (s, 2 H, CH_2N), 7.02 (dd, 1 H_{arom}, *J* = 2.2, 8.7 Hz), 7.40–7.49 (m, 2 H_{arom}), 7.78 (d, 1 H_{arom}, *J* = 2.2 Hz), 8.19 (d, 1 H_{arom}, *J* = 7.0 Hz), 8.24 (s, 1 H_{arom}), 8.31–8.35 (m, 2 H_{arom}), 9.07 (s, 1 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.9 (CH_3), 28.1 (3 CH_3), 28.2 (3 CH_3), 55.6 (OCH_3), 65.1 (CH_2), 75.0 (CH_2N), 85.4 (C), 86.0 (C), 87.6 (C), 99.1 (CH), 113.7 (CH), 115.3 (CH), 118.4 (C), 119.5 (C), 121.7 (C), 122.4 (CH), 123.1 (CH), 124.9 (CH), 126.1 (CH), 127.1 (C), 135.9 (C), 136.5 (C), 136.7 (C), 136.8 (CH), 137.0 (CH), 146.4 (C), 148.9 (C), 149.1 (C=O), 149.5 (C=O), 178.5 (C=O), 181.9 (C=O).

MS (ESI): *m*/*z* = 769 ($M + H^+$).

Anal. Calcd for $C_{35}H_{37}IN_4O_8$ (768.61): C, 54.69; H, 4.85; N, 7.29. Found: C, 54.89; H, 4.66; N, 7.11.

tert-Butyl 3-[5-(1-*tert*-Butoxycarbonyl-1*H*-indole-3-carbonyl)-1-ethoxymethyl-4-iodo-1*H*-imidazole-2-carbonyl]indole-1-carboxylate (6c)

According to the procedure described for **4**, compound **6c** was prepared from **5c** in 84% yield as a solid; mp 162–164 °C (dec.) (EtOH).

IR (KBr): 1750, 1640, 1530 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.02 (t, 3 H, *J* = 7.0 Hz, CH_3), 1.71 (s, 9 H, 3 CH_3), 1.74 (s, 9 H, 3 CH_3), 3.54 (q, 2 H, *J* = 7.0 Hz, CH_2), 6.06 (s, 2 H, CH_2N), 7.40–7.50 (m, 4 H_{arom}), 8.18–8.23 (m, 2 H_{arom}), 8.23 (s, 1 H_{arom}), 8.33 (d, 1 H_{arom}, *J* = 6.6 Hz), 8.48–8.51 (m, 1 H_{arom}), 9.22 (s, 1 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.9 (CH_3), 28.1 (3 CH_3), 28.2 (3 CH_3), 65.1 (CH_2), 75.0 (CH_2N), 85.5 (C), 86.0 (C), 87.5 (C), 115.1 (CH), 115.3 (CH), 118.2 (C), 119.6 (C), 122.4 (CH), 122.6 (CH), 124.7 (CH), 124.9 (CH), 125.7 (CH), 126.1 (CH), 127.1 (C), 128.3 (C), 135.3 (C), 135.9 (C), 136.8 (C), 136.9 (CH), 138.0 (CH), 146.4 (C), 148.9 (C=O), 149.0 (C=O), 178.0 (C=O), 181.4 (C=O).

MS (ESI): *m*/*z* = 739 ($M + H^+$).

Anal. Calcd for $C_{34}H_{35}IN_4O_7$ (738.59): C, 55.29; H, 4.78; N, 7.59. Found: C, 54.96; H, 4.63; N, 7.68.

tert-Butyl 3-[1-Ethoxymethyl-4-iodo-5-(pyridine-3-carbonyl)-1*H*-imidazole-2-carbonyl]indole-1-carboxylate (6d)

According to the procedure described for **4**, compound **6d** was prepared from **5d** in 82% yield as a solid; mp 168–169 °C (EtOH).

IR (KBr): 1745, 1657, 1628 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.01 (t, 3 H, *J* = 7.0 Hz, CH_3), 1.72 (s, 9 H, 3 CH_3), 3.50 (q, 2 H, *J* = 7.0 Hz, CH_2), 6.10 (s, 2 H, CH_2N), 7.37–7.45 (m, 2 H_{arom}), 7.51 (dd, 1 H_{pyr}, *J* = 4.9, 7.9 Hz), 8.16–8.20 (m, 2 H, H_{arom} + H_{pyr}), 8.45–8.49 (m, 1 H_{arom}), 8.88 (d, 1 H_{pyr}, *J* = 4.9 Hz), 9.06 (s, 1 H_{pyr}), 9.20 (s, 1H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.8 (CH_3), 28.1 (3 CH_3), 65.1 (CH_2), 75.2 (CH_2N), 85.7 (C), 90.4 (C), 115.2 (CH), 118.2 (C), 122.6 (CH), 123.9 (CH), 124.8 (CH), 125.9 (CH), 128.2 (C), 132.4 (C), 134.7 (C), 135.4 (C), 137.3 (CH), 138.2 (CH), 147.4 (C), 149.0 (C), 151.6 (CH), 154.3 (C=O), 178.0 (C=O), 186.2 (C=O).

MS (ESI): *m*/*z* = 601 ($M + H^+$).

Anal. Calcd for $C_{26}H_{25}IN_4O_5$ (600.42): C, 52.01; H, 4.20; N, 9.33. Found: C, 52.34; H, 4.25; N, 9.21.

tert-Butyl 3-[5-(Benzo[*b*]thiophene-3-carbonyl)-1-ethoxymethyl-4-iodo-1*H*-imidazole-2-carbonyl]indole-1-carboxylate (6e)

According to the procedure described for **4**, compound **6e** was prepared from **5e** in 65% yield as a solid (chromatography eluent: PE–EtOAc, 9:1); mp 169–171 °C (dec.) (Et_2O).

IR (KBr): 1740, 1630 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.00 (t, 3 H, *J* = 7.1 Hz, CH_3), 1.73 (s, 9 H, 3 CH_3), 3.52 (q, 2 H, *J* = 7.1 Hz, CH_2), 6.08 (s, 2 H, CH_2N), 7.38–7.48 (m, 2 H_{arom}), 7.50–7.60 (m, 2 H_{arom}), 7.93 (d, 1 H_{arom}, *J* = 7.9 Hz), 8.19–8.22 (m, 1 H_{arom}), 8.26 (s, 1 H_{arom}), 8.47–8.50 (m, 1 H_{arom}), 8.66 (d, 1 H_{arom}, *J* = 8.1 Hz), 9.22 (s, 1 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.9 (CH_3), 28.2 (3 CH_3), 65.0 (CH_2), 75.2 (CH_2N), 85.6 (C), 88.6 (C), 115.2 (CH), 118.3 (C), 122.6 (2 CH), 124.8 (CH), 125.2 (CH), 125.8 (CH), 126.2 (CH), 126.4 (CH), 128.3 (C), 134.6 (C), 135.4 (C), 136.2 (C), 136.7 (C), 138.1 (CH), 140.4 (C), 142.8 (CH), 146.7 (C), 149.0 (C=O), 178.1 (C=O), 181.1 (C=O).

MS (ESI): *m*/*z* = 656 ($M + H^+$).

Anal. Calcd for $C_{29}H_{26}I_2N_3O_5S$ (655.52): C, 53.14; H, 4.00; N, 6.41. Found: C, 52.88; H, 3.90; N, 6.32.

Hydrogenolysis of Iodoimidazoles 6; General Procedure

A suspension of **6** (0.20 mmol), K_2CO_3 (1 mmol) and 10% Pd/C (15 mg) in CH_2Cl_2–MeOH (12 mL, 1:1) was stirred in a stainless steel reactor under 15 bar of H_2 overnight at r.t. The catalyst was removed by filtration and the filtrate was evaporated in vacuo. The crude residue was purified by column chromatography to afford derivative **7**.

tert-Butyl 3-[5-(1-*tert*-Butoxycarbonyl-1*H*-indole-3-carbonyl)-1-ethoxymethyl-1*H*-imidazole-2-carbonyl]-6-benzyloxy-1*H*-indole-1-carboxylate (7a)

Chromatography eluent: PE–EtOAc (85:15); yield: 89%; solid; mp 154–156 °C (dec.) (EtOAc–pentane).

IR (KBr): 1740, 1640 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.14 (t, 3 H, *J* = 7.0 Hz, CH_3), 1.72 (s, 9 H, 3 CH_3), 1.73 (s, 9 H, 3 CH_3), 3.64 (q, 2 H, *J* = 7.0 Hz, CH_2), 5.16 (s, 2 H, CH_2O), 6.35 (s, 2 H, CH_2N), 7.13 (dd, 1 H_{arom}, *J* = 2.2, 8.8 Hz), 7.31–7.50 (m, 7 H, C_6H_5 + H_{arom}), 7.77 (s, 1 H_{imid}), 7.88 (d, 1 H_{arom}, *J* = 2.2 Hz), 8.20 (br d, 1 H_{arom}, *J* = 7.0 Hz), 8.30 (s, 1 H_{arom}), 8.40 (dd, 1 H_{arom}, *J* = 2.0, 7.0 Hz), 8.43 (d, 1 H_{arom}, *J* = 8.8 Hz), 9.03 (s, 1 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.1 (CH_3), 28.1 (3 CH_3), 28.1 (3 CH_3), 64.9 (CH_2), 70.3 (CH_2O), 74.5 (CH_2N), 85.3 (C), 85.7 (C), 100.4 (CH), 114.2 (CH), 115.2 (CH), 118.8 (C), 120.7 (C), 122.1 (C), 122.4 (CH), 123.2 (CH), 124.5 (CH), 126.0 (CH), 127.5 (2 CH), 127.8 (C), 127.9 (CH), 128.5 (2 CH), 133.2 (CH + C), 135.7 (C), 136.2 (CH), 136.3 (CH), 136.4 (C), 136.9 (C), 146.8 (C), 149.0 (C), 149.1 (C=O), 157.7 (C=O), 179.3 (C=O), 180.1 (C=O).

MS (ESI): *m*/*z* = 719 (M + H$^+$).

Anal. Calcd for $C_{41}H_{42}N_4O_8$ (718.81): C, 68.51; H, 5.89; N, 7.79. Found: C, 68.33; H, 6.01; N, 7.88.

tert-Butyl 3-[5-(1-_tert_-Butoxycarbonyl-1*H*-indole-3-carbonyl)-1-ethoxymethyl-1*H*-imidazole-2-carbonyl]-6-methoxy-1*H*-indole-1-carboxylate (7b)

Chromatography eluent: PE–EtOAc (85:15); yield: 93%; solid; mp 155–156 °C (dec.) (EtOAc–pentane).

IR (KBr): 1740, 1625, 1530 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.11 (t, 3 H, *J* = 7.0 Hz, CH_3), 1.71 (s, 9 H, 3 CH_3), 1.72 (s, 9 H, 3 CH_3), 3.61 (q, 2 H, *J* = 7.0 Hz, CH_2), 3.91 (s, 3 H, OCH_3), 6.31 (s, 2 H, CH_2N), 7.03 (dd, 1 H_{arom}, *J* = 2.2, 8.8 Hz), 7.38–7.48 (m, 2 H_{arom}), 7.74 (s, 1 H_{imid}), 7.77 (d, 1 H_{arom}, *J* = 2.2 Hz), 8.19 (br d, 1 H_{arom}, *J* = 7.0 Hz), 8.27 (s, 1 H_{arom}), 8.36–8.40 (m, 2 H_{arom}), 8.97 (s, 1 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.1 (CH_3), 28.1 (3 CH_3), 28.2 (3 CH_3), 55.7 (OCH_3), 65.0 (CH_2), 74.6 (CH_2N), 85.4 (C), 85.9 (C), 99.2 (CH), 113.7 (CH), 115.3 (CH), 118.9 (C), 120.8 (C), 121.9 (C), 122.5 (CH), 123.3 (CH), 124.7 (CH), 126.2 (CH), 127.9 (C), 133.3 (C + CH), 135.8 (C), 136.3 (2 CH), 136.5 (C), 146.9 (C), 149.1 (C), 149.3 (C=O), 158.6 (C=O), 179.5 (C=O), 180.2 (C=O).

MS (ESI): *m*/*z* = 643 (M + H$^+$).

Anal. Calcd for $C_{35}H_{38}N_4O_8$ (642.72): C, 65.41; H, 5.96; N, 8.72. Found: C, 65.25; H, 6.10; N, 8.63.

tert-Butyl 3-[5-(1-_tert_-Butoxycarbonyl-1*H*-indole-3-carbonyl)-1-ethoxymethyl-1*H*-imidazole-2-carbonyl]indole-1-carboxylate (7c)

Chromatography eluent: PE–EtOAc (85:15); yield: 85%; solid; mp 162–163 °C (dec.) (EtOAc–PE).

IR (KBr): 1750, 1740, 1640, 1530 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.12 (t, 3 H, *J* = 7.0 Hz, CH_3), 1.72 (s, 18 H, 6 CH_3), 3.62 (q, 2 H, *J* = 7.0 Hz, CH_2), 6.33 (s, 2 H, CH_2N), 7.40–7.50 (m, 4 H_{arom}), 7.75 (s, 1 H_{imid}), 8.18–8.21 (m, 2 H_{arom}), 8.21 (s, 1 H_{arom}), 8.36–8.39 (m, 1 H_{arom}), 8.52–8.55 (m, 1 H_{arom}), 9.12 (s, 1 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.1 (CH_3), 28.2 (6 CH_3), 65.0 (CH_2), 74.7 (CH_2N), 85.6 (C), 85.8 (C), 115.2 (CH), 115.3 (CH), 118.8 (C), 120.8 (C), 122.5 (CH), 122.8 (CH), 124.7 (2 CH), 125.7 (CH), 126.2 (CH), 127.9 (C), 128.4 (C), 133.3 (CH), 133.4 (C), 135.4 (C), 135.8 (C), 136.3 (CH), 137.6 (CH), 146.9 (C), 149.1 (C=O), 149.2 (C=O), 179.5 (C=O), 180.2 (C=O).

MS (ESI): *m*/*z* = 613 (M + H$^+$).

Anal. Calcd for $C_{34}H_{36}N_4O_7$ (612.69): C, 66.75; H, 5.92; N, 9.14. Found: C, 66.40; H, 5.76; N, 8.99.

tert-Butyl 3-[1-Ethoxymethyl-5-(pyridine-3-carbonyl)-1*H*-imidazole-2-carbonyl]indole-1-carboxylate (7d)

Chromatography eluent: PE–EtOAc (85:15); yield: 55%; solid; mp 157–159 °C (dec.) (EtOH).

IR (KBr): 1732, 1655, 1630 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.13 (t, 3 H, *J* = 7.0 Hz, CH_3), 1.71 (s, 9 H, 3 CH_3), 3.61 (q, 2 H, *J* = 7.0 Hz, CH_2), 6.34 (s, 2 H, CH_2N), 7.40–7.44 (m, 2 H_{arom}), 7.50 (dd, 1 H_{pyr}, *J* = 4.9, 7.9 Hz), 7.66 (s, 1 H_{imid}), 8.16–8.24 (m, 2 H, H_{arom} + H_{pyr}), 8.50–8.54 (m, 1 H_{arom}), 8.88 (dd, 1 H_{pyr}, *J* = 1.7, 4.9 Hz), 9.08 (s, 1 H_{arom}), 9.14 (d, 1 H_{pyr}, *J* = 1.7 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.1 (CH_3), 28.2 (3 CH_3), 65.0 (CH_2O), 74.9 (CH_2N), 85.7 (C), 115.2 (CH), 118.7 (C), 122.7 (CH), 123.7 (CH), 124.8 (CH), 125.9 (CH), 128.2 (C), 131.7 (C), 134.1 (C), 135.4 (C), 136.8 (CH), 137.9 (CH), 139.6 (CH), 147.8 (C), 149.1 (C), 150.4 (CH), 153.6 (C=O), 179.4 (C=O), 184.1 (C=O).

MS (ESI): *m*/*z* = 475 (M + H$^+$).

Anal. Calcd for $C_{26}H_{26}N_4O_5$ (474.52): C, 65.81; H, 5.52; N, 11.81. Found: C, 65.99; H, 5.55; N, 11.90.

tert-Butyl 3-[1-Ethoxymethyl-5-(1,4,5,6-tetrahydropyridine-3-carbonyl)-1*H*-imidazole-2-carbonyl]indole-1-carboxylate (7f)

Yield: 20%; amorphous solid.

IR (KBr): 1750, 1630 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.09 (t, 3 H, *J* = 7.0 Hz, CH_3), 1.70 (s, 9 H, 3 CH_3), 1.86–1.94 (m, 2 H, CH_2), 2.56 (t, 2 H, *J* = 6.2 Hz, CH_2), 3.32 (br s, 2 H, CH_2), 3.53 (q, 2 H, *J* = 7.0 Hz, CH_2), 5.13 (br s, 1 H, NH), 6.08 (s, 2 H, CH_2N), 7.23 (s, 1 H_{imid}), 7.35–7.42 (m, 2 H_{arom}), 7.54 (d, 1 H, *J* = 6.6 Hz, =CH), 8.14–8.17 (m, 1 H_{arom}), 8.48–8.51 (m, 1 H_{arom}), 9.05 (s, 1 H_{arom}).

MS (ESI): *m*/*z* = 479 (M + H$^+$).

Anal. Calcd for $C_{26}H_{30}N_4O_5$ (478.55): C, 65.26; H, 6.32; N, 11.71. Found: C, 65.43; H, 6.19; N, 11.86.

tert-Butyl 3-[5-(Benzo[*b*]thiophene-3-carbonyl)-1-ethoxymethyl-1*H*-imidazole-2-carbonyl]indole-1-carboxylate (7e)

Chromatography eluent: PE–EtOAc (9:1); yield: 80%; solid; mp 173-175 °C (dec.) (Et_2O).

IR (KBr): 1740, 1630 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.12 (t, 3 H, *J* = 7.0 Hz, CH_3), 1.71 (s, 9 H, 3 CH_3), 3.62 (q, 2 H, *J* = 7.0 Hz, CH_2), 6.34 (s, 2 H, CH_2N), 7.40–7.57 (m, 4 H_{arom}), 7.69 (s, 1 H_{imid}), 7.93 (d, 1 H_{arom}, *J* = 8.1 Hz), 8.17–8.20 (m, 1 H_{arom}), 8.29 (s, 1 H_{arom}), 8.51–8.55 (m, 1 H_{arom}), 8.60 (d, 1 H_{arom}, *J* = 7.0 Hz), 9.11 (s, 1 H_{arom}).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 15.2 (CH_3), 28.2 (3 CH_3), 65.1 (CH_2), 74.8 (CH_2N), 85.7 (C), 115.2 (CH), 118.8 (C), 122.6 (CH), 122.8 (CH), 124.8 (CH), 125.1 (CH), 125.8 (CH), 126.0 (CH), 126.1 (CH), 128.4 (C), 133.5 (C), 135.4 (C), 135.9 (C), 137.0 (C), 137.6 (CH), 137.7 (CH), 138.2 (CH), 140.2 (C), 147.3 (C), 149.2 (C=O), 179.5 (C=O), 180.0 (C=O).

MS (ESI): *m*/*z* = 530 (M + H$^+$).

Anal. Calcd for $C_{29}H_{27}N_3O_5S$ (529.62): C, 65.77; H, 5.14; N, 7.93. Found: C, 65.98; H, 4.97; N, 8.06.

Boc Deprotection of 7; General Procedure

A solution of **7** (0.17 mmol), and aq 1 N NaOH (2 mL) in 1,4-dioxane (4 mL) was stirred at 70 °C for 30 min. After cooling, the solution was neutralised by aq 1 N HCl (pH 6–7) and extracted with CH_2Cl_2 (2 × 5 mL). The combined organic phases were dried ($MgSO_4$) and evaporated in vacuo. Product **8** was isolated either by crystallisation or by column chromatography.

[1-Ethoxymethyl-5-(1*H*-indole-3-carbonyl)-1*H*-imidazol-2-yl](6-benzyloxy-1*H*-indol-3-yl)methanone (8a)

Yield: 85%; solid; mp >210 °C (dec.) (EtOAc–pentane).

IR (KBr): 3415, 3285, 1612 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.09 (t, 3 H, *J* = 7.0 Hz, CH_3), 3.64 (q, 2 H, *J* = 7.0 Hz, CH_2), 4.98 (s, 2 H, CH_2O), 6.31 (s, 2 H, CH_2N), 6.83 (s, 1 H_{arom}), 7.07 (dd, 1 H_{arom}, *J* = 2.1, 8.7 Hz), 7.28–7.39 (m, 8

H, C_6H_5 + H_{arom}), 7.44 (s, 1 H_{arom}), 7.67 (s, 1 H_{imid}), 8.42–8.45 (m, 3 H_{arom}), 8.97 (s, 1 H, NH), 9.00 (s, 1 H NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 14.8 (CH_3), 63.6 (CH_2), 69.5 (CH_2O), 73.7 (CH_2N), 97.1 (CH), 112.4 (CH), 112.6 (CH), 115.2 (C), 116.5 (C), 120.5 (C), 121.4 (CH), 122.1 (CH), 122.2 (CH), 123.4 (CH), 126.0 (C), 127.6 (2 CH), 127.7 (CH), 128.4 (2 CH), 133.2 (C), 134.5 (CH), 135.8 (CH), 136.9 (C), 137.2 (C), 137.3 (C), 137.7 (CH), 146.8 (C), 155.7 (C), 178.3 (C=O), 179.3 (C=O).

MS (ESI): *m*/*z* = 519 (M + H$^+$).

Anal. Calcd for $C_{31}H_{26}N_4O_4$ (518.58): C, 71.80; H, 5.05; N, 10.80. Found: C, 71.98; H, 4.93; N, 10.67.

[1-Ethoxymethyl-5-(1*H*-indole-3-carbonyl)-1*H*-imidazol-2-yl](6-methoxy-1*H*-indol-3-yl)methanone (8b)
Yield: 89%; solid; mp 169–171 °C (dec.) (EtOAc).

IR (KBr): 3340, 1615, 1510 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 0.91 (t, 3 H, *J* = 7.0 Hz, CH_3), 3.40 (q, 2 H, *J* = 7.0 Hz, CH_2), 3.82 (s, 3 H, OCH_3), 6.15 (s, 2 H, CH_2N), 6.91 (dd, 1 H_{arom}, *J* = 2.1, 8.7 Hz), 7.04 (d, 1 H_{arom}, *J* = 2.1 Hz), 7.23–7.32 (m, 2 H_{arom}), 7.54 (br d, 1 H_{arom}, *J* = 7.0 Hz), 7.77 (s, 1 H_{imid}), 8.19 (d, 1 H_{arom}, *J* = 8.7 Hz), 8.25–8.29 (m, 2 H_{arom}), 8.62 (s, 1 H_{arom}), 12.05 (br s, 1 H, NH), 12.22 (br s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 14.9 (CH_3), 55.3 (OCH_3), 63.7 (CH_2), 73.7 (CH_2N), 95.7 (CH), 112.0 (CH), 112.4 (CH), 115.3 (C), 116.5 (C), 120.3 (C), 121.4 (CH), 122.2 (2 CH), 123.5 (CH), 126.0 (CH), 133.2 (C), 134.5 (CH), 135.9 (CH), 136.9 (C), 137.4 (C), 137.6 (CH), 146.9 (C), 156.7 (C), 178.3 (C=O), 179.4 (C=O).

MS (ESI): *m*/*z* = 443 (M + H$^+$).

Anal. Calcd for $C_{25}H_{22}N_4O_4$ (442.48): C, 67.86; H, 5.01; N, 12.66. Found: C, 67.99; H, 4.95; N, 12.80.

[1-Ethoxymethyl-5-(1*H*-indole-3-carbonyl)-1*H*-imidazol-2-yl](1*H*-indol-3-yl)methanone (8c)
Yield: 89%; solid; mp 209–210 °C ($CHCl_3$).

IR (KBr): 3400, 1610, 1520 cm^{-1}.

^{1}H NMR (300 MHz, CD_3OD): δ = 0.99 (t, 3 H, *J* = 7.0 Hz, CH_3), 3.50 (q, 2 H, *J* = 7.0 Hz, CH_2), 6.20 (s, 2 H, CH_2N), 7.20–7.32 (m, 4 H_{arom}), 7.49–7.53 (m, 2 H_{arom}), 7.67 (s, 1 H_{imid}), 8.12 (s, 1 H_{arom}), 8.31–8.34 (m, 1 H_{arom}), 8.38–8.42 (m, 1 H_{arom}), 8.52 (s, 1 H_{arom}).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 14.8 (CH_3), 63.7 (CH_2), 73.8 (CH_2N), 112.4 (CH), 112.5 (CH), 115.2 (C), 116.6 (C), 121.4 (CH), 121.6 (CH), 122.2 (CH), 122.4 (CH), 123.4 (CH), 123.5 (CH), 126.0 (C), 126.4 (C), 133.3 (C), 134.5 (CH), 135.8 (CH), 136.4 (C), 136.9 (C), 138.4 (CH), 146.9 (C), 178.5(C=O), 179.4 (C=O).

MS (ESI): *m*/*z* = 413 (M + H$^+$).

Anal. Calcd for $C_{24}H_{20}N_4O_3$ (412.45): C, 68.89; H, 4.89; N, 13.58. Found: C, 68.98; H, 5.01; N, 13.77.

1-Ethoxymethyl-5-(pyridine-3-carbonyl)-1*H*-imidazol-2-yl](1*H*-indol-3-yl)methanone (8d)
Yield: 97%; solid; mp 170–172 °C (EtOH).

IR (KBr): 1650, 1610 cm^{-1}.

^{1}H NMR (300 MHz, acetone-d_6): δ = 1.01 (t, 3 H, *J* = 7.0 Hz, CH_3), 3.54 (q, 2 H, *J* = 7.0 Hz, CH_2), 6.33 (s, 2 H, CH_2N), 7.28–7.34 (m, 2 H_{arom}), 7.57–7.64 (m, 2 H, H_{arom} + H_{pyr}), 7.73 (s, 1 H_{imid}), 8.27–8.30 (m, 1 H_{pyr}), 8.49–8.51 (m, 1 H_{arom}), 8.86–8.88 (m, 2 H, H_{arom} + H_{pyr}), 9.08 (br s, 1 H_{pyr}).

^{13}C NMR (75 MHz, acetone-d_6): δ = 15.3 (CH_3), 64.9 (CH_2O), 75.3 (CH_2N), 113.1 (CH), 116.9 (C), 122.9 (CH), 123.4 (CH), 124.5 (2 CH), 127.7 (C), 132.2 (C), 137.4 (CH), 137.6 (C), 139.3 (CH + C), 140.2 (CH), 149.7 (C), 150.9 (CH), 154.2 (CH), 179.5 (C=O), 185.0 (C=O).

MS (ESI): *m*/*z* = 375 (M + H$^+$).

Anal. Calcd for $C_{21}H_{18}N_4O_3$ (374.40): C, 67.37; H, 4.85; N, 14.96. Found: C, 66.98; H, 5.00; N, 15.10.

[5-(Benzo[*b*]thiophene-3-carbonyl)-1-ethoxymethyl-1*H*-imidazol-2-yl](1*H*-indol-3-yl)methanone (8e)
Chromatography eluent: PE–EtOAc (6:4); yield: 80%; foam.

IR (KBr): 3375, 1630 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.11 (t, 3 H, *J* = 7.0 Hz, CH_3), 3.63 (q, 2 H, *J* = 7.0 Hz, CH_2), 6.37 (s, 2 H, CH_2N), 7.32–7.56 (m, 5 H_{arom}), 7.66 (s, 1 H_{imid}), 7.94 (br d, 1 H_{arom}, *J* = 7.4 Hz), 8.26 (s, 1 H_{arom}), 8.57–8.61 (m, 2 H_{arom}), 8.73 (s, 1 H, NH), 8.78 (d, 1 H_{arom}, *J* = 3.0 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.1 (CH_3), 65.1 (CH_2), 74.7 (CH_2N), 111.8 (CH), 116.7 (C), 122.6 (2 CH), 123.3 (CH), 124.1 (CH), 125.0 (CH), 126.0 (CH), 126.1 (CH), 126.6 (C), 133.0 (C), 135.8 (C), 136.3 (C), 137.0 (C), 137.5 (CH), 137.6 (CH), 138.0 (CH), 140.2 (C), 148.2 (C), 178.8 (C=O), 179.9 (C=O).

MS (ESI): *m*/*z* = 430 (M + H$^+$).

Anal. Calcd for $C_{24}H_{19}N_3O_3S$ (429.50): C, 67.12; H, 4.46; N, 9.78. Found: C, 66.80; H, 4.33; N, 9.75.

EOM Deprotection of Imidazoles 8; General Procedure
A solution of **8** (0.11 mmol) and aq 1 N HCl (1 mL) in 1,4-dioxane (2 mL) was stirred at 70 °C for 30 min. After cooling, the solution was neutralised by sat. aq $NaHCO_3$ and extracted with CH_2Cl_2 (2 × 5 mL). The combined organic phases were dried ($MgSO_4$) and evaporated in vacuo. The crude residue was recrystallised (or washed) to afford **9**.

[5-(1*H*-Indole-3-carbonyl)-1*H*-imidazol-2-yl](6-benzyloxy-1*H*-indol-3-yl)methanone (9a)
Yield: 83%; solid; mp >210 °C (EtOH).

IR (KBr): 3395, 3340, 1605, 1575 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 5.18 (s, 2 H, CH_2O), 7.00 (dd, 1 H, *J* = 2.2, 8.7 Hz, H-5), 7.14 (d, 1 H, *J* = 1.9 Hz, H-7), 7.20–7.56 (m, 8 H, C_6H_5 + H_{arom}), 8.01 (d, 1 H_{imid}, *J* = 1.9 Hz), 8.24 (d, 1 H_{arom}, *J* = 8.7 Hz), 8.37–8.40 (m, 1 H_{arom}), 8.96 (br d, 1 H_{arom}, *J* = 2.5 Hz), 9.01 (d, 1 H_{arom}, *J* = 3.0 Hz), 11.99 (br s, 2 H, NH), 13.67 (s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 69.5 (CH_2O), 96.9 (CH), 112.1 (CH), 112.5 (CH), 113.5 (C), 114.9 (C), 120.6 (C), 121.7 (CH), 121.8 (CH), 122.2 (CH), 122.9 (CH), 126.7 (C), 127.6 (2 CH), 127.8 (CH), 128.4 (2 CH), 135.5 (CH), 136.2 (C), 136.3 (2 CH), 137.1 (C), 137.3 (C), 155.6 (C), 176.3 (C=O), 181.6 (C=O).

MS (ESI): *m*/*z* = 461 (M + H$^+$).

Anal. Calcd for $C_{28}H_{20}N_4O_3$ (460.50): C, 73.03; H, 4.38; N, 12.17. Found: C, 72.74; H, 4.19; N, 12.00.

[5-(1*H*-Indole-3-carbonyl)-1*H*-imidazol-2-yl](6-methoxy-1*H*-indol-3-yl)methanone (9b)
Yield: 85%; solid; mp >210 °C (EtOAc–pentane).

IR (KBr): 3205, 1592, 1510 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 3.82 (s, 3 H, OCH_3), 6.91 (d, 1 H_{arom}, *J* = 8.7 Hz), 7.07 (s, 1 H_{arom}), 7.23–7.28 (m, 2 H_{arom}), 7.54 (d, 1 H_{arom}, *J* = 7.0 Hz), 8.01 (s, 1 H_{imid}), 8.23 (d, 1 H_{arom}, *J* = 8.7 Hz), 8.38 (d, 1 H_{arom}, *J* = 8.0 Hz), 8.96–9.01 (m, 2 H_{arom}), 11.98 (s, 2 H, NH), 13.67 (s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 55.3 (CH_3), 95.5 (CH), 111.9 (CH), 112.2 (CH), 113.5 (C), 114.8 (C), 120.4 (C), 121.7 (CH),

121.8 (CH), 122.2 (CH), 122.9 (CH), 124.3 (CH), 126.7 (C), 135.7 (CH), 136.2 (CH), 137.3 (C), 143.3 (C), 145.5 (C), 156.6 (2 C), 176.4 (C=O), 181.6 (C=O).

MS (ESI): m/z = 385 ($M + H^+$).

Anal. Calcd for $C_{22}H_{16}N_4O_3$ (384.40): C, 68.74; H, 4.20; N, 14.58. Found: C, 68.86; H, 4.02; N, 14.68.

[5-(1*H*-Indole-3-carbonyl)-1*H*-imidazol-2-yl](1*H*-indol-3-yl)methanone (9c)

Yield: 90%; solid; mp >210 °C (purified by washing with hot MeOH).

IR (KBr): 3198, 1609, 1590, 1512 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 7.22–7.30 (m, 4 H_{arom}), 7.53–7.59 (m, 2 H_{arom}), 8.02 (s, 1 H_{imid}), 8.37–8.40 (m, 2 H_{arom}), 8.97 (s, 1 H_{arom}), 9.14 (s, 1 H_{arom}), 12.00 (s, 1 H, NH), 12.21 (s, 1 H, NH), 13.70 (s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 112.2 (CH), 112.5 (CH), 113.4 (C), 114.9 (C), 121.6 (CH), 121.7 (2 CH), 122.3 (CH), 122.9 (CH), 123.2 (CH), 124.3 (CH), 126.5 (C), 126.7 (C), 135.7 (CH), 136.2 (C), 136.3 (C), 137.1 (CH), 143.3 (C), 145.5 (C), 176.5 (C=O), 181.6 (C=O).

MS (ESI): m/z = 355 ($M + H^+$).

Anal. Calcd for $C_{21}H_{14}N_4O_2$ (354.37): C, 71.18; H, 3.98; N, 15.81. Found: C, 70.93; H, 4.12; N, 15.77.

(1*H*-Indol-3-yl)[5-(pyridine-3-carbonyl)-1*H*-imidazol-2-yl]methanone (9d)

Yield: 96%; solid; mp >210 °C (dioxane–H_2O).

IR (KBr): 3280, 1610 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 7.24–7.26 (m, 2 H_{arom}), 7.51–7.53 (m, 1 H_{arom}), 7.57–7.61 (dd, 1 H_{pyr}, J = 4.9, 7.9 Hz), 8.10 (s, 1 H_{imid}), 8.42–8.46 (m, 1 H_{arom}), 8.55 (d, 1 H_{pyr}, J = 7.5 Hz), 8.79 (br s, 1 H_{arom}), 9.17 (s, 1 H_{pyr}), 9.44 (br s, 1 H_{pyr}), 12.13 (s, 1 H, NH), 14.10 (s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 112.4 (CH), 113.6 (C), 121.7 (CH), 122.0 (CH), 123.0 (CH), 123.4 (CH + C), 126.7 (C), 134.2 (C), 136.2 (C), 137.1 (CH), 137.4 (CH), 149.1 (C), 150.6 (CH), 152.0 (CH), 185.6 (2 C=O).

MS (EI): m/z = 316 (M^+);

Anal. Calcd for $C_{18}H_{12}N_4O_2$ (316.32): C, 68.35; H, 3.82; N, 17.71. Found: C, 68.01; H, 3.90; N, 17.66.

[5-(Benzo[*b*]thiophene-3-carbonyl)-1*H*-imidazol-2-yl](1-indol-3-yl)methanone (9e)

Chromatography eluent: EtOAc; yield: 88%; solid; mp >210 °C (Et_2O).

IR (KBr): 3375, 1740, 1630 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 7.25–7.31 (m, 2 H_{arom}), 7.47–7.58 (m, 3 H_{arom}), 8.14 (d, 1 H_{arom}, J = 7.2 Hz), 8.20 (s, 1 H_{imid}), 8.37–8.40 (m, 1 H_{arom}), 8.64 (br d, 1 H_{arom}, J = 7.8 Hz), 9.18 (s, 1 H_{arom}), 9.49 (s, 1 H_{arom}), 12.2 (s, 1 H, NH), 13.9 (s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 112.5 (CH), 113.2 (C), 121.5 (CH), 122.3 (CH), 122.9 (CH), 123.2 (CH), 124.6 (CH), 125.3 (CH), 125.5 (CH), 126.5 (C), 126.6 (CH), 133.2 (C), 136.3 (C), 137.4 (C), 137.6 (CH), 139.2 (C), 140.8 (CH), 142.1 (C), 146.1 (C), 176.2 (C=O), 181.4 (C=O).

MS (ESI): m/z = 372 ($M + H^+$).

Anal. Calcd for $C_{21}H_{13}N_3O_2S$ (371.42): C, 67.91; H, 3.53; N, 11.31. Found: C, 68.27; H, 3.44; N, 11.15.

[5-(1*H*-Indole-3-carbonyl)-1*H*-imidazol-2-yl](6-hydroxy-1*H*-indol-3-yl)methanone (Ia)

A suspension of **9a** (46 mg, 0.10 mmol), HCO_2NH_4 (63 mg, 1.00 mmol) and 10% Pd/C (5 mg) in EtOH (5 mL) was refluxed for 1 h. The catalyst was removed by filtration and the filtrate was evaporated in vacuo. The crude residue was washed with hot EtOAc and filtered to afford **Ia** (34 mg, 91%) as a yellow solid; mp >210 °C (purified by washing with hot EtOAc).

IR (KBr): 3380, 3200, 1592, 1572, 1525 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 6.78 (dd, 1 H_{arom}, J = 1.7, 8.6 Hz), 6.92 (br s, 1 H_{arom}), 7.20–7.28 (m, 2 H_{arom}), 7.53–7.56 (m, 1 H_{arom}) 8.01 (s, 1 H_{imid}), 8.15 (d, 1 H_{arom}, J = 8.6 Hz), 8.38–8.41 (m, 1 H_{arom}), 8.96 (br s, 2 H_{arom}), 9.33 (s, 1 H, OH), 11.84 (s, 1 H, NH), 11.99 (s, 1 H, NH), 13.63 (s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 97.6 (CH), 112.2 (CH), 112.3 (CH), 113.6 (C), 114.9 (C), 119.4 (C), 121.7 (CH), 121.8 (CH), 122.1 (CH), 122.9 (CH), 124.2 (CH), 126.8 (C), 135.7 (CH), 135.9 (CH), 136.2 (C), 137.6 (C), 143.3 (C), 145.6 (C), 154.4 (C), 176.3 (C=O), 181.6 (C=O).

MS (ESI): m/z = 371 ($M + H^+$).

Anal. Calcd for $C_{21}H_{14}N_4O_3$ (370.37): C, 68.10; H, 3.81; N, 15.13. Found: C, 67.90; H, 3.87; N, 15.23.

[5-(1*H*-Indole-3-carbonyl)-4-iodo-1*H*-imidazol-2-yl](1*H*-indol-3-yl)methanone (10)

Compound **10** was prepared in 56% overall yield from **6c** by two successive deprotection reactions; mp >210 °C (purified by washing with MeOH).

IR (KBr): 3390, 3200, 1610, 1590, 1510 cm^{-1}.

^1H NMR (300 MHz, acetone-d_6): δ = 7.25–7.31 (m, 4 H_{arom}), 7.53–7.60 (m, 2 H_{arom}), 8.45–8.55 (m, 2 H_{arom}), 8.97 (s, 1 H_{arom}), 9.27 (s, 1 H_{arom}), 11.01 (s, 1 H, NH), 11.22 (s, 1 H, NH), 13.09 (s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 90.2 (C), 112.2 (CH), 112.5 (CH), 113.1 (C), 115.1 (C), 121.5 (CH), 121.7 (CH), 121.8 (CH), 122.3 (CH), 122.9 (CH), 123.3 (CH), 126.5 (2 C), 126.7 (C), 136.1 (C), 136.4 (CH + C), 136.9 (CH), 142.5 (C), 175.7 (C=O), 181.6 (C=O).

HRMS (ESI): m/z = 481 ($M + H^+$).

Anal. Calcd for $C_{21}H_{13}IN_4O_2$ (480.27): C, 52.52; H, 2.73; N, 11.67. Found: C, 52.53; H, 2.85; N, 11.79.

Suzuki Reaction of 6c with Arylboronic Acids; General Procedure

To a stirred solution of **6c** (131 mg, 0.18 mmol) in anhyd toluene (5 mL) was added freshly prepared $Pd(PPh_3)_4$ (12 mg, 6% mol). The solution was stirred for 30 min at r.t. The appropriate arylboronic acid (0.27 mmol) diluted with EtOH (2 mL) was then added, followed immediately by sat. aq $NaHCO_3$ solution (2 mL). The heterogeneous solution was stirred at 80 °C for t h. The Pd catalyst was removed by filtration. Brine was then added, the two layers were separated and the aqueous phase was extracted with EtOAc (3 × 5 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated in vacuo. The crude residue was purified by column chromatography to give the desired compound **11**.

***tert*-Butyl 3-[5-(1-*tert*-Butoxycarbonyl-1*H*-indole-3-carbonyl)-1-ethoxymethyl-4-phenyl-1*H*-imidazole-2-carbonyl]indole-1-carboxylate (11a)**

t = 1.5 h; chromatography eluent: PE–EtOAc (9:1); yield: 92%; amorphous solid.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.00 (t, 3 H, J = 7.0 Hz, CH_3), 1.56 (s, 9 H, 3 CH_3), 1.74 (s, 9 H, 3 CH_3), 3.54 (q, 2 H, J = 7.0 Hz, CH_2), 6.16 (s, 2 H, CH_2N), 7.20–23 (m, 3 H, C_6H_5), 7.40–7.43 (m, 4

H_{arom}), 7.60–7.63 (m, 2 H, C_6H_5), 7.73 (s, 1 H_{arom}), 8.08–8.11 (m, 1 H_{arom}), 8.24–8.26 (m, 1 H_{arom}), 8.43–8.46 (m, 1 H_{arom}), 8.53–8.56 (m, 1 H_{arom}), 9.54 (s, 1 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.9 (CH_3), 28.0 (3 CH_3), 28.2 (3 CH_3), 64.8 (CH_2), 74.9 (CH_2N), 85.2 (C), 85.5 (C), 115.1 (2 CH), 118.6 (C), 120.0 (C), 122.5 (CH), 122.7 (CH), 124.7 (CH), 124.8 (CH), 125.6 (CH), 126.0 (CH), 127.3 (C), 128.0 (CH), 128.4 (2 CH), 128.5 (2 CH), 130.1 (C), 133.2 (C), 135.4 (C), 135.7 (C), 136.3 (CH), 138.0 (CH), 142.9 (C), 144.0 (C), 148.5 (C), 149.1 (C), 179.1 (C=O), 183.1 (C=O).

MS (ESI): *m*/*z* = 689 ($M + H^+$).

Anal. Calcd for $C_{40}H_{40}N_4O_7$ (688.79): C, 69.75; H, 5.85; N, 8.13. Found: C, 69.66; H, 5.90; N, 8.04.

tert-Butyl 3-[5-(1-_tert_-Butoxycarbonyl-1*H*-indole-3-carbonyl)-1-ethoxymethyl-4-(2-thienyl)-1*H*-imidazole-2-carbonyl]indole-1-carboxylate (11b)

t = 15 h; chromatography eluent: PE–EtOAc (9:1); yield: 95%; solid; mp 142–144 °C (dec.).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.01 (t, 3 H, *J* = 7.0 Hz, CH_3), 1.61 (s, 9 H, 3 CH_3), 1.75 (s, 9 H, 3 CH_3), 3.54 (q, 2 H, *J* = 7.0 Hz, CH_2), 6.10 (s, 2 H, CH_2N), 6.85 (dd, 1 $H_{thienyl}$, *J* = 3.6, 5.1 Hz), 7.04 (dd, 1 $H_{thienyl}$, *J* = 1.0, 3.6 Hz), 7.22 (dd, 1 $H_{thienyl}$, *J* = 1.0, 5.0 Hz), 7.40–7.45 (m, 4 H_{arom}), 7.96 (s, 1 H_{arom}), 8.13–8.17 (m, 1 H_{arom}), 8.25–8.28 (m, 1 H_{arom}), 8.40–8.43 (m, 1 H_{arom}), 8.53–8.56 (m, 1 H_{arom}), 9.50 (s, 1 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.9 (CH_3), 28.1 (3 CH_3), 28.2 (3 CH_3), 64.9 (CH_2), 75.2 (CH_2N), 85.3 (C), 85.8 (C), 115.2 (CH), 115.3 (CH), 118.5 (C), 120.2 (C), 122.5 (CH), 122.7 (CH), 124.7 (CH), 124.9 (CH), 125.7 (CH), 125.9 (CH), 126.1 (CH), 126.5 (CH), 127.2 (C), 127.8 (CH), 128.5 (C), 129.1 (C), 135.5 (C), 135.9 (C+CH), 136.0 (C), 137.0 (C), 138.1 (CH), 143.5 (C), 148.7 (C), 149.1 (C), 178.8 (C=O), 182.7 (C=O).

MS (ESI): *m*/*z* = 695 ($M + H^+$).

Anal. Calcd for $C_{38}H_{38}N_4O_7S$ (694.81): C, 65.59; H, 5.51; N, 8.06. Found: C, 65.65; H, 5.46; N, 7.95.

tert-Butyl 3-[5-(1-_tert_-Butoxycarbonyl-1*H*-indole-3-carbonyl)-1-ethoxymethyl-4-(2-furyl)-1*H*-imidazole-2-carbonyl]indole-1-carboxylate (11c)

t = 48 h; chromatography eluent: PE–EtOAc (9:1); yield: 96%; amorphous solid.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.00 (t, 3 H, *J* = 7.0 Hz, CH_3), 1.62 (s, 9 H, 3 CH_3), 1.74 (s, 9 H, 3 CH_3), 3.53 (q, 2 H, *J* = 7.0 Hz, CH_2), 6.09 (s, 2 H, CH_2N), 6.35 (dd, 1 H_{furyl}, *J* = 1.7, 3.2 Hz), 6.66 (d, 1 H_{furyl}, *J* = 3.2 Hz), 7.21 (br s, 1 H_{furyl}), 7.39–7.44 (m, 4 H_{arom}), 7.92 (s, 1 H_{arom}), 8.14–8.17 (m, 1 H_{arom}), 8.22–8.25 (m, 1 H_{arom}), 8.41–8.44 (m, 1 H_{arom}), 8.51–8.54 (m, 1 H_{arom}), 9.42 (s, 1 H_{arom}).

MS (ESI): *m*/*z* = 679 ($M + H^+$).

Anal. Calcd for $C_{38}H_{38}N_4O_8$ (678.75): C, 67.24; H, 5.64; N, 8.25. Found: C, 66.99; H, 5.77; N, 8.30.

tert-Butyl 3-[5-(1-tert-Butoxycarbonyl-1*H*-indole-3-carbonyl)-1-ethoxymethyl-4-(2-(1-_tert_-butoxycarbonyl)pyrrolyl)-1*H*-imidazole-2-carbonyl]indole-1-carboxylate (11d)

t = 4 h; chromatography eluent: PE–EtOAc (85:15); yield: 89%; solid; mp 114–116 °C (dec.) (EtOH).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.05 (t, 3 H, *J* = 7.0 Hz, CH_3), 1.33 (s, 9 H, 3 CH_3), 1.66 (s, 9 H, 3 CH_3), 1.70 (s, 9 H, 3 CH_3), 3.56 (q, 2 H, *J* = 7.0 Hz, CH_2), 6.10–6.12 (m, 1 H_{pyr}), 6.29 (s, 2 H, CH_2N), 6.45–6.47 (m, 1 H_{pyr}), 7.10–7.11 (m, 1 H_{pyr}), 7.35–7.42 (m, 4 H_{arom}), 7.91 (s, 1 H_{imid}), 8.05–8.08 (m, 1 H_{arom}), 8.18–8.21 (m, 1 H_{arom}), 8.36–8.39 (m, 1 H_{arom}), 8.54–8.57 (m, 1 H_{arom}), 9.36 (s, 1 H_{arom}).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 14.5 (CH_3), 27.0 (3 CH_3), 27.4 (6 CH_3), 63.7 (CH_2), 73.9 (CH_2N), 83.3 (C), 84.4 (C), 84.6 (C), 110.1 (CH), 114.5 (2 CH), 116.2 (CH), 117.6 (C), 118.8 (C), 121.9 (CH), 122.2 (CH), 122.3 (CH), 123.8 (CH), 123.9 (CH), 124.9 (CH), 125.1 (CH), 126.1 (C), 126.9 (C), 127.9 (C), 130.5 (C), 134.2 (CH), 134.5 (C), 134.6 (C), 136.6 (C), 137.3 (CH), 142.9 (C), 147.6 (C), 147.8 (C), 148.1 (C), 177.9 (C=O), 180.2 (C=O).

MS (ESI): *m*/*z* = 778 ($M + H^+$).

Anal. Calcd for $C_{43}H_{47}N_5O_9$ (777.88): C, 66.40; H, 6.09; N, 9.00. Found: C, 66.75; H, 5.95; N, 8.88.

[5-(1*H*-Indole-3-carbonyl)-4-phenyl-1*H*-imidazol-2-yl](1*H*-indol-3-yl)methanone (12)

Compound **12** was prepared in 83% overall yield from **11a** by two successive deprotection reactions; pp 144–146 °C (dec.).

IR (KBr): 3200, 1701, 1595, 1509 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.21–7.30 (m, 4 H, C_6H_5 + H_{arom}), 7.43–7.58 (m, 5 H_{arom}), 7.78 (br d, 2 H, *J* = 6.0 Hz, C_6H_5), 8.30 (d, 1 H_{arom}, *J* = 7.9 Hz), 8.39–8.41 (m, 1 H_{arom}), 8.57 (s, 1 H_{arom}), 9.09 (s, 1 H_{arom}), 11.96 (s, 1 H, NH), 12.12 (s, 1 H, NH), 13.81 (s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 112.2 (CH), 112.4 (CH), 113.6 (C), 115.8 (C), 121.6 (CH), 121.7 (CH), 121.8 (CH), 122.2 (CH), 122.8 (CH), 123.2 (CH), 126.5 (C), 126.6 (C), 128.0 (CH), 129.2 (C), 129.3 (CH), 134.2 (CH), 136.2 (C), 136.3 (C), 136.5 (C), 136.6 (CH), 137.0 (CH), 138.3 (C), 144.4 (C), 176.4 (C=O), 183.6 (C=O).

MS (ESI): *m*/*z* = 431 ($M + H^+$).

Anal. Calcd for $C_{27}H_{18}N_4O_2$ (430.47): C, 75.34; H, 4.21; N, 13.02. Found: C, 75.03; H, 4.09; N, 12.88.

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