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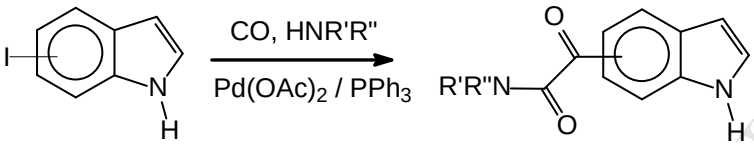
Graphical abstract



Functionalization of Indole at C-5 or C-7 via Palladium-Catalysed Double Carbonylation. A Facile Synthesis of Indole Ketocarboxamides and Carboxamide Dimers.

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Abstract: Palladium-catalysed aminocarbonylation of 7-iodoindole derivatives (the parent compound and 5-bromo-7-iodoindole), as well as 5-iodoindole with various primary and secondary amines, including amino acid esters and chiral diamines, was carried out. In this way, a highly selective double carbonylation reaction at the C-7 was performed resulting in the formation of the corresponding indol-7-ylglyoxylamides when monoamines were used. The bromoarene moiety remained intact, so bromo-substituted glyoxylamides of practical importance have been synthesised in moderate to high yields. The use of chiral alkyl and aryl diamines as nucheophiles allowed the synthesis of a new family of dimeric 7-indole derivatives under moderate reaction conditions (10 bar, 100 ºC). The aminocarbonylation at the C-5 position led to much lower chemoselectivities toward indol-5-ylglyoxylamides under similar conditions (40 bar CO, 50^{o}C).

The aminocarbonylation of iodoindoles shows a strikingly different chemoselectivity depending on the basicity of the amine while primary and secondary amines of high basicity gave 2-ketocarboxamides in up to 98% chemoselectivity, aniline resulted in almost exclusive formation of the corresponding carboxamide product.

Key-words: carbonylation**,** 2-ketocarboxamide**,** palladium**,** carbon monoxide, iodoindole.

1. Introduction

Carbonylation reactions are among the most widely used homogeneous catalytic reactions with several practical applications reported.[1-3] In addition to the parent hydroformylation used for the functionalization of alkenes, [4-6] aminocarbonylation [7-9] has also gained several synthetic applications.

In this reaction, alkenyl and aryl triflates or their corresponding synthetic surrogates (iodoalkenes and iodoaromatics, respectively) served as substrates. The seminal work of Heck *et al.* showed that this methodology provides an excellent route to carboxamides of varying structure using carbon monoxide and primary/secondary amines as N-nucleophiles.[10] Moreover, Yamamoto *et al.* published a double carbonylation process, where aromatic triflates and iodides insert two molecules of carbon monoxide resulting in the formation of 2-ketocarboxamides.[11]

Among the number of substrates tested in aminocarbonylation,[7-9] the functionalization of the indole nucleus has been the topic of interest for many years.[12,13] Special efforts have been devoted to the introduction of functionalities at C-2. The palladium-catalysed alkoxycarbonylation and carbonylation (in the presence of tributylstannane) of 2-iodoindole resulted in the formation of the corresponding 2-ester and 2-formyl compounds, respectively.[14] *N*-Protected and unprotected 2-iodoindole derivatives underwent aminocarbonylation with various *N*-nucleophiles. This way, the efficiency of palladium-catalysed aminocarbonylation for the introduction of amide side-chain was demonstrated.[15] A carbonylative alkoxycarbonylation-cyclocondensation reaction sequence based on 3-iodoindoles was developed leading to compounds with protein kinase inhibitor activity.[16] As direct preliminary work to our present research, the aminocarbonylation of 7-iodoindole with piperidine in the presence of palladium(I)-dimers,[17] as well as the high-yielding palladium-catalysed aminocarbonylation of unprotected bromoindoles[18] should be mentioned. In the latter work, carboxamide functionalities were introduced at all positions within the benzene fragment of the indoles, *i.e.*, 4-, 5-, 6- and 7-carboxamides (among them amphetamine derivatives) were synthesised.

Furthermore, the synthesis of indole dimers is of great importance, since *bis*-indole derivatives are relevant compounds that can be found in many natural products and pharmaceuticals.[19] In particular, the synthesis of bis-indole carboxamides remains a challenge for which the use of diamines as nucleophiles in aminocarbonylation reactions was recently described as a promising synthetic approach.[20]

Although the double carbonyl insertion providing 2-ketocarboxamides is general in palladium-catalysed aminocarbonylation of iodoaromatics,[21] only the selective formation of carboxamides was observed using iodo-N-heteroaromatics with an iodo substituent adjacent to the ring-nitrogen.[22] 2-Carboxamidopyridines and carboxamidopyrazines were formed, while the corresponding 2-ketocarboxamides were not observed. The aim of the selective synthesis of indoleketocarboxamides, *i.e.*, a prevailing double carbonylation in C-7 position being far from the 'indole nitrogen', seemed to be quite plausible, which is the primary aim of this work.

Prompted by the previous investigations of our group in the aminocarbonylation of iodoarenes,[23-27] a systematic study was carried out imploying unprotected iodoindoles. The most important achievement of this work was the direct one-step synthesis of functionalised indoles bearing 2-ketocarboxamide functionalities and the synthesis of chiral dimeric indole carboxamides.

2. Results and discussion

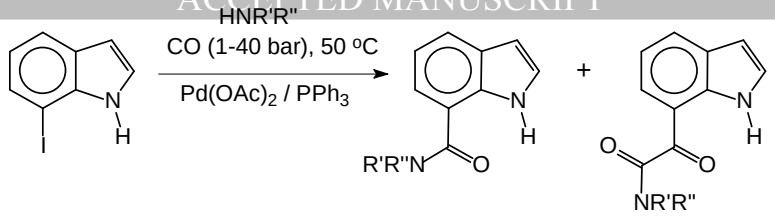
2.1. Aminocarbonylation of 7-iodoindole in the presence of various N-nucleophiles

Palladium(0) catalytic systems, formed *in situ* in the reaction of $Pd(OAc)_2$ and two molar equivalents of triphenylphosphine, have been used for the aminocarbonylation of 7-iodoindole (**1**) (*Scheme 1*). Primary (**a**, **b**, **e-h**) and secondary amines (**c**, **d**) including functionalised amines (amino acid methylesters) have been used as *N*-nucleophiles.

According to the generally accepted mechanism,[7-10] palladium(0) catalysts are necessary to oxidatively add the starting iodoalkene substrate. As in several cases before, instead of the coordinatively saturated 'pre-formed' Pd(0) catalyst, $Pd(PPh_3)_4$, a highly active 'phosphine-deficient' $Pd(OAc)_2$/2 PR_3–type *in situ* catalyst has been used. In fact, the catalytically active palladium intermediates contain one PR_3 ligand only, since one of the two equivalents of phosphine ligands is oxidized to the corresponding phosphine oxide.[28-30]

The aminocarbonylation of 7-iodoindole (**1**) (*Scheme1*), carried out *at atmospheric carbon monoxide pressure*, resulted in the formation of indol-7-ylglyoxylamides (**3**) and the corresponding carboxamides (**2**), in case of all the amines (*Table 1, entries 1, 2 ,7, 9, 10, 14, 15*), except for aniline (**b**). As observed previously, the less basic aniline (**b**) and the sterically crowded methyl prolinate (**h**) exhibited lower reactivity, so no reasonable conversion was obtained (*entry 4 and entry 20*, respectively). Surprisingly, the 2-ketocarboxamide-type products (**3**), formed by double CO insertion, prevail in all cases. The chemoselectivity toward **3** was found to be in the range of 60-90%, depending on the *N*-nucleophile. In spite of the formation of carboxamides as minor products, we have been able to isolate **2a**, **2c**, **2d**, **2g** and characterise them as analytically pure compounds.

The aminocarbonylations carried out *at high (40 bar) carbon monoxide pressure* showed high chemoselectivity towards ketocarboxamides (**3**), *i.e.*, the ketocarboxamide/carboxamide (**3**/**2**) ratios observed at atmospheric pressure (*vide supra*) were substantially improved. These chemoselectivity values fall typically in the range of 70-90%, in some cases up to 97% selectivities towards ketocarboxamides (*entries 3, 8, 11, 13, 17, 21*). A strikingly different behavior was observed for **b**. In spite of the high CO pressure, the high-yielding formation of carboxamide **2b** was observed, *i.e.*, the ketocarboxamide-type product formed via double CO insertion was detected in trace amounts by GC-MS (*entries 5 and 6*).



1 **2** **3**

	R'	R"
a	H	*t*Bu
b	H	Ph
c	-$(CH_2)_5$-	
d	-$(CH_2)_2O(CH_2)_2$-	
e	H	CH_2COOCH_3
f	H	$CH(CH_3)COOCH_3$
g	H	$CH(CH(CH_3)_2)COOCH_3$
h	H	-$CH(COOCH_3)(CH_2)_3$-

Scheme 1. Aminocarbonylation of 7-iodoindole

Table 1. Aminocarbonylation of 7-iodoindole (**1**) in the presence of $Pd(OAc)_2$ + 2 PPh_3 'in situ' catalyst [a)]

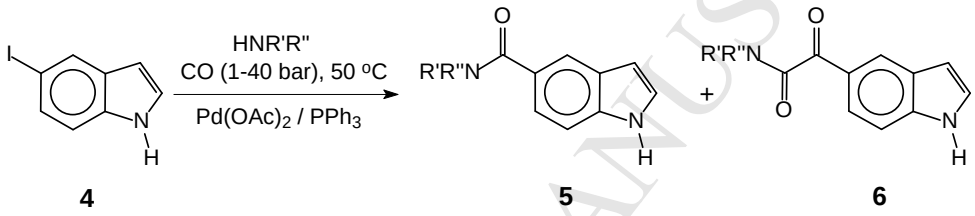
Entry	Amine	Reaction time [h]	p(CO) [bar]	Conv. [b)] [%]	Ratio of the carbonylated products [b)]; (isolated yield [c)]) [%]	
					Carboxamide (**2**)	Ketocarboxamide (**3**)
1	*t*-$BuNH_2$ (**a**)	24	1	70	17 (**2a**)	83 (**3a**)
2	*t*-$BuNH_2$ (**a**)	48	1	>98	33 (**2a**); (25)	67 (**3a**); (36)
3	*t*-$BuNH_2$ (**a**)	24	40	>98	5 (**2a**)	95 (**3a**); (58)
4	aniline (**b**)	48	1	<2	n.d.	n.d.
5	aniline (**b**)	24	40	95	>99 (**2b)**	<1 (**3b)**
6	aniline (**b**)	94	40	>98	>99 (**2b)**; (51)	<1 (**3b)**
7	piperidine (**c**)	24	1	>98	40 (**2c**); (33)	60 (**3c**); (40)
8	piperidine (**c**)	24	40	>98	6 (**2c**)	94 (**3c**); (66)
9	morpholine (**d**)	24	1	71	7 (**2d**)	93 (**3d**); (65)
10	morpholine (**d**)	48	1	82	22 (**2d**); (12)	78 (**3d**); (51)
11	morpholine (**d**)	24	40	94	3 (**2d**)	97 (**3d**); (52)
12	GlyOMe (**e**)	24	40	81	6 (**2e**)	94 (**3e**)
13	GlyOMe (**e**)	46	40	>98	6 (**2e**)	94 (**3e**); (68)
14	AlaOMe (**f**)	24	1	2	35 (**2f**)	65 (**3f**)
15	AlaOMe (**f**)	94	1	61	33 (**2f**)	67 (**3f**)
16	AlaOMe (**f**)	24	40	82	20 (**2f**)	80 (**3f**)
17	AlaOMe (**f**)	94	40	>98	21 (**2f**)	79 (**3f**)
18	ValOMe (**g**)	24	40	89	42 (**2g**)	58 (**3g**)
19	ValOMe (**g**)	94	40	>98%	45 (**2g**); (39)	55 (**3g**); (45)
20	ProOMe (**h**)	48	1	<2	n.d.	n.d.
21	ProOMe (**h**)	24	40	95	3 (**2h**)	97 (**3h**); (57)

a) Reaction conditions (unless otherwise stated): 1 mmol substrate (**1**), amine nucleophile: 3 mmol of **a** (or 2 mmol of **b** / 1.5 mmol of **c**, **d** / 1.1 mmol of **e**, **f**, **g**, **h**), 0.025 mmol of $Pd(OAc)_2$ (2.5 mol%), 0.05 mmol of PPh_3 (5 mol%), 0.5 mL of Et_3N, 10 mL of DMF, 50 ^oC
b) determined by GC-MS
c) yields of the isolated target compound (based on the substrate (**1**))

*2.2. Aminocarbonylation of 5-iodoindole (**4**) in the presence of various N-nucleophiles*

Surprisingly, the aminocarbonylation of 5-iodoindole (**4**) carried out using atmospheric carbon monoxide pressure gave the corresponding carboxamide and 2-ketocarboxamide in only trace amounts (<1%).

The aminocarbonylations carried out at high (40 bar) carbon monoxide pressure showed moderate to high chemoselectivities toward 2-ketocarboxamides (**6**) falling typically in the range of 79-94% (*Table 2*). There are two exceptions: *i)* the use of the arylamine **b** with lower basicity resulted in a formation of the corresponding carboxamide **5b** (*entry 3*), *i.e.* no carbon monoxide insertion into Pd-amide bond took place, *ii)* methyl valinate (**g**) gave a mixture of **5g** and **6g** with the prevailance of the carboxamide (**5g**) (*entries 10, 11*). It is worth noting that close to an equimolar mixture of carbonylated products was obtained using 7-iodoindole (**1**) as the substrate with this *N*-nucleophile (*Table 1, entries 18, 19*), the formation of 2-ketocarboxamide (**3g**) is slightly favoured in this case.



4 **5** **6**

Scheme 2. Aminocarbonylation of 5-iodoindole (for the *N*-nucleophiles used see *Scheme 1*)

Table 2. Aminocarbonylation of 5-iodoindole (**4**) in the presence of $Pd(OAc)_2$ + 2 PPh_3 'in situ' catalyst [a)]

Entry	Amine	Reaction time [h]	Conv. [b)] [%]	Ratio of the carbonylated products [b)]; (isolated yield [c)]) [%]	
				Carboxamide (**5**)	Ketocarboxamide (**6**)
1	*t*-$BuNH_2$ (**a**)	24	95	21 (**5a**); (11)	79 (**6a**); (46)
2	aniline (**b**)	24	90	>99 (**5b**)	<1 (**6b**)
3	aniline (**b**)	48	>98	>99 (**5b**); (47)	<1 (**6b**)
4	piperidine (**c**)	24	95	14 (**5c**); (15)	86 (**6c**); (66)
5	morpholine (**d**)	24	95	6 (**5d**)	94 (**6d**); (50)
6	GlyOMe (**e**)	24	51	10 (**5e**)	90 (**6e**)
7	GlyOMe (**e**)	140	>98	10 (**5e**)	90 (**6e**); (74)
8	AlaOMe (**f**)	24	63	20 (**5f**)	80 (**6f**)
9	AlaOMe (**f**)	48	94	36 (**5f**)	64 (**6f**); (46)
10	ValOMe (**g**)	24	77	65 (**5g**)	35 (**6g**)
11	ValOMe (**g**)	96	>98	60 (**5g**); (25)	40 (**6g**); (24)
12	ProOMe (**h**)	24	70	17 (**5h**)	83 (**6h**)
13	ProOMe (**h**)	72	>98	21 (**5h**)	79 (**6h**); (36)

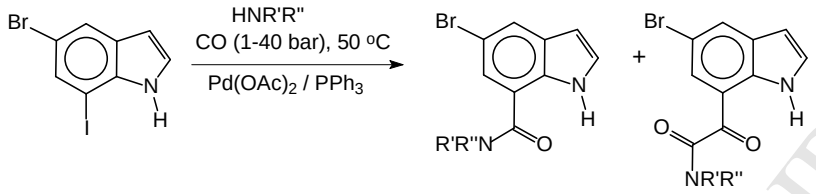
a) Reaction conditions (unless otherwise stated): 1 mmol substrate (**4**), amine nucleophile: 3 mmol of **a** (or 2 mmol of **b** / 1.5 mmol of **c**, **d** / 1.1 mmol of **e**, **f**, **g**, **h**), 0.025 mmol of $Pd(OAc)_2$ (2.5 mol%), 0.05 mmol of PPh_3 (5 mol%), 0.5 mL of Et_3N, 10 mL of DMF, 50 ^oC, 40 bar of CO.
b) determined by GC-MS
c) yields of the isolated target compound (based on the substrate (**4**))
d) 1 bar of CO

*2.3. Aminocarbonylation of 5-bromo-7-iodoindole (**7**) in the presence of various N-nucleophiles*

As a part of the systematic functionalization of the indole ring, the aminocarbonylation of 5-bromo-7-iodoindole (**7**) was carried out. As above (see reactions in *Scheme 1 and 2*), a mixture of the corresponding carboxamide (**8**) and 2-ketocarboxamide (**9**) was obtained (*Scheme 3*). It has been determined by MS and NMR investigations that the bromoaryl moiety remained intact under the conditions used. This behaviour is of practical importance, since the bromoarene functionality can potentially be further reacted in other cross-coupling reactions, enabling further selective functionalization of the parent indole.

Although aminocarbonylation can be carried out even at atmospheric carbon monoxide pressure (*Table 3, entries 1,2*), giving rise to the formation of 2-ketocarboxamde (**9a**), in general, high selectivities (>98%)

towards ketoamides (**9**) can be achieved at high CO pressure (*entries 3, 6, 7, 10*). Even under these conditions, methyl alaninate (**f**) and methyl valinate (**g**) gave lower chemoselectivities (*entries 8 and 9*, respectively). Based on the aforementioned results, the almost exclusive formation of carboxamide (**8b**) was observed with **b** as nucleophile (*entry 4*).



7 **8** **9**

Scheme 3. Aminocarbonylation of 5-bromo-7-iodoindole (for the *N*-nucleophiles used see *Scheme 1*)

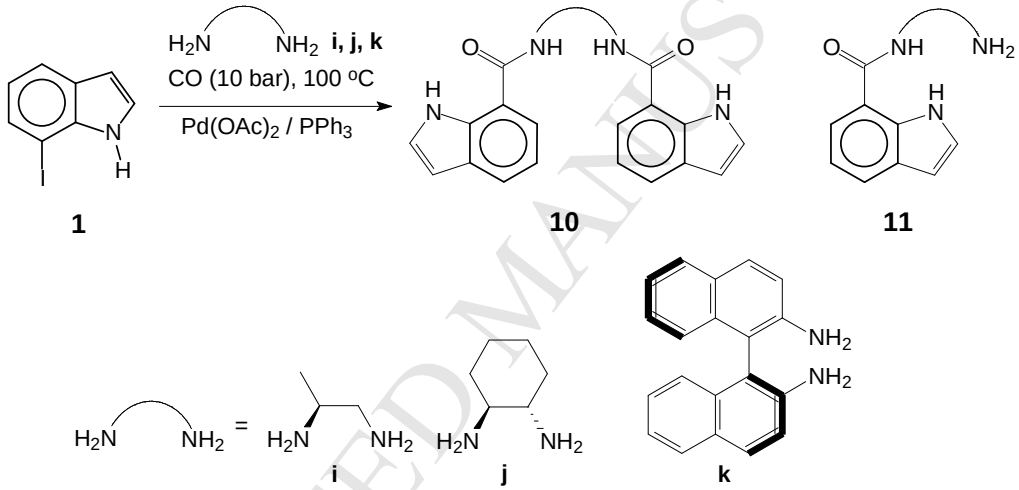
Table 3. Aminocarbonylation of 5-bromo-7-iodoindole (**7**) in the presence of $Pd(OAc)_2$ + 2 PPh_3 'in situ' catalyst [a)]

Entry	Amine	Reaction time [h]	Pressure [bar]	Conv. [b)] [%]	Ratio of the carbonylated products [b)]; (isolated yield [c)]) [%]	
					Carboxamide (**8**)	Ketocarboxamide (**9**)
1	*t*-BuNH_2 (**a**)	24	1	65	13 (**8a**)	87 (**9a**)
2	*t*-BuNH_2 (**a**)	48	1	>98	16 (**8a**)	84 (**9a**) (53)
3	*t*-BuNH_2 (**a**)	24	40	>98	3 (**8a**)	97 (**9a**) (53)
4	aniline (**b**)	48	40	>98	>98 (**8b**) (68)	<2 (**9b**)
5	piperidine (**c**)	24	40	>98	8 (**8c**)	92 (**9c**) (54)
6	morpholine (**d**)	24	40	94	<2 (**8d**)	>98 (**9d**) (66)
7	GlyOMe (**e**)	70	40	95	<2 (**8e**)	>98 (**9e**) (45)
8	AlaOMe (**f**)	24	40	82	18 (**8f**)	82 (**9f**) (38)
9	ValOMe (**g**)	96	40	>98	26 (**8g**)	74 (**9g**) (46)
10	ProOMe (**h**)	24	40	>98	<2 (**8h**)	>98 (**9h**) (66)

a) Reaction conditions (unless otherwise stated): 1 mmol substrate (**7**), amine nucleophile: 3 mmol of **a** (or 2 mmol of **b** / 1.5 mmol of **c**, **d** / 1.1 mmol of **e**, **f**, **g**, **h**), 0.025 mmol of $Pd(OAc)_2$ (2.5 mol%), 0.05 mmol of PPh_3 (5 mol%), 0.5 mL of Et_3N, 10 mL of DMF, 50 °C.
b) determined by GC-MS
c) yields of the isolated target compound (based on the substrate (**7**))

*2.4. Aminocarbonylation of 7-iodoindole (**1**) in the presence of chiral diamines as N-nucleophiles*

In order to obtain new chiral bis-indole derivatives bearing carboxamide moieties, the scope of the aminocarbonylation reaction of 7-iodoindole (**1**) was expanded to the use of several chiral diamines as *N*-nucleophiles: (*S*)-propane-1,2-diamine (**i**), (1*S*,2*S*)-(+)-1,2-diaminocyclohexane(**j**) and the axially chiral aromatic (*S*)-1,1'-binaphthyl-2,2'-diamine (**k**) (*Scheme 4*). The reactions were carried out under 10 bar CO, at 100 °C for 24 h. After work-up, the conversions were calculated based on NMR analysis of crude mixtures, and the dimeric-indole derivatives (**10i**, **10j**, **10k**) were purified by column chromatography. In all cases, the substrate was fully converted, with the dimeric indole derivatives being the main products. It should be noted that the monomeric product (**11**) was only observed and isolated when the less nucheophilic aromatic diamine (**k**) was used (*Table 4, entry 3*).



Scheme 4. Aminocarbonylation of 7-iodoindole using chiral diamines (**i**, **j**, **k**) as *N*-nucleophiles

Table 4. Synthesis of 7-carboxamide indole dimers *via* aminocarbonylation of 7-iodoindole (**1**), using chiral diamines as nucleophiles, in the presence of $Pd(OAc)_2$ + 2 PPh_3 'in situ' catalyst [a]

Entry	Diamine	Conv. [b)]	Dicarboxamide (**10**) (isolated yields)	Monoarboxamide (**11**) (isolated yields)
1	**i**	>97	46[b] (**10i**) (39)	-
2	**j**	>98	31 [b] (**10j**) (16)	-
3	**k**	>96	40 [b] (**10k**) (32)	34[b] (**11k**) (29)

a) Reaction conditions: 0.9 mmol substrate (**1**), 0.45 mmol amine nucleophile (**i-k**), 0.025 mmol $Pd(OAc)_2$ (2.8 mol%) 0.05 mmol PPh_3 (5.6 mol%), 0.5 mL Et_3N, 9 mL DMF, 100°C, 10 bar of CO; 24 h.

b) determined by NMR on the crude mixture.

Conclusions

The synthesis of ketocarboxamide-functionalised indoles with double CO insertion at C-7 and C-5 was achieved using a highly reactive, low-ligated Pd(0) catalyst generated from $Pd(OAc)_2/2PPh_3$. The coordination of the $PPh_3(O)$ in the catalytically active intermediate to form $Pd(PPh_3)(P(O)Ph_3)$ species cannot be excluded. The importance of the coordination of strong and weak donor ligands was emphasized in the aminocarbonylation of 2-bromopyridine derivatives using Bedford palladacycle and dppf (1,1'-bis(diphenylphosphinoferrocene) as catalyst.[31]

The formation of indole-2-ketocarboxamides is of particular note. The 2-ketocarboxamides were obtained as major products for most N-nucleophiles, with the only exception being aniline of low basicity. In the latter case, the corresponding carboxamides formed via simple carbon monoxide insertion, prevailed under the reaction conditions used (50 ^{o}C, 1-40 bar CO). The aminocarbonylation reaction enabled the facile preparation of the target compounds.

Considering the high relevance and large bio-aplications of dimeric indole-derivatives the *bis*-aminocarbonylation reaction herein described provides an efficient and versatile synthetic methodology to obtain a new family of chiral *bis*-indole carboxamide in a one-pot reaction.

3. Experimental

3.1. General procedures

^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker Avance III 500 spectrometer at 500 and 125.7 MHz, respectively. Chemical shifts δ are reported in ppm relative to $CHCl_3$ (7.26 and 77.00 ppm for ^{1}H and ^{13}C, respectively). Elemental analyses were measured on a 1108 Carlo Erba apparatus. Samples of the catalytic reactions were analysed with a Hewlett Packard 5830A gas chromatograph fitted with a capillary column coated with OV-1 (internal standard: naphthalene; injector temp 250 ˚C, oven: starting temp 50 ˚C (hold-time 1 min), heating rate 15 ˚C min^{-1}, final temp 320 ˚C (hold-time 11 min); detector temp 280 ˚C, carrier gas: helium (rate: 1 mL min^{-1})). The FT-IR spectra were taken in KBr pellets using an IMPACT 400 spectrometer (Nicolet) applying a DTGS detector in the region of 400-4000 cm^{-1}, the resolution was 4 cm^{-1}. The amount of the samples was *ca*. 0.5 mg.

The iodoarene substrates, 7-iodoindole, 5-iodoindole, 5-bromo-7-iodoindole, as well as the amine nucleophiles were purchased from Sigma-Aldrich and were used without further purification.

3.2. Aminocarbonylation of 7-iodoindole in the presence of various amines as N-nucleophiles under atmospheric carbon monoxide pressure

In a typical experiment $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), triphenylphosphine (13.1 mg, 0.05 mmol), 7-iodoindole (243 mg, 1 mmol) or 5-bromo-7-iodindole (322 mg, 1mmol), amine nucleophile (3 mmol of **a** / 2 mmol of **b** / 1.5 mmol of **c**, **d** / 1.1 mmol of **e**, **f**, **g**, **h**) and triethylamine (0.5 mL) were dissolved in DMF (10 mL) under argon in a three-necked flask equipped with a gas inlet, reflux condenser with a ballon (filled with

argon) at the top. The atmosphere was changed to carbon monoxide. The reaction was conducted for the given reaction time upon stirring at 50 ˚C and analysed by GC-MS (internal standard: naphthalene). The mixture was then concentrated and evaporated to dryness. The residue was dissolved in chloroform (20 mL) and washed with water (3 20 mL). the organic phase was dried over Na_2SO_4, filtered and evaporated to a crystalline material or a waxy residue. All compounds were subjected to column chromatography (Silicagel 60 (Merck), 0.063-0.200 mm), EtOAc/$CHCl_3$, or EtOAc/toluene, or hexane/EtOAc/MeOH (the exact ratios are specified in Section Characterization (3.4) for each compound).

3.3. Aminocarbonylation of 7-iodoindole in the presence of various amines as N-nucleophiles under high carbon monoxide pressure

In a typical experiment, $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), triphenylphosphine (13.1 mg, 0.05 mmol), 7-iodoindole (243 mg, 1 mmol) or 5-bromo-7-iodindole (322 mg, 1mmol), amine nucleophile (3 mmol of **a** / 2 mmol of **b** / 1.5 mmol of **c**, **d** / 1.1 mmol of **e**, **f**, **g**, **h**) and triethylamine (0.5mL) were dissolved in DMF (10 mL) under argon in a 100 mL autoclave. The atmosphere was changed to carbon monoxide and the autoclave was pressurized to the given pressure by carbon monoxide. The reaction was conducted for the given reaction time upon stirring at 50 ˚C and analysed by GC-MS (internal standard: naphthalene). The mixture was then concentrated and evaporated to dryness and worked-up as described in Section 3.2.

The analogous procedures (same molar ratios, identical reaction conditions, similar work-up) were used in the aminocarbonylation of 5-iodoindole and 5-bromo-7-iodoindole.

3.4. Carbonylation of 7-iodoindole using chiral diamines as N-nucleophiles

In a typical experiment, $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), triphenylphosphine (13.1 mg, 0.05 mmol), 7-iodoindole (224 mg, 0.9 mmol), the desired diamine nucleophile (0.45 mmol) were placed in a stainless steel autoclave. After degassing the autoclave, triethylamine (0.5 ml) and DMF (9 mL) were added *via* cannula. The autoclave was then pressurized with 10 bar CO and the reaction was conducted for 24 h at 100 °C. The mixture was then concentrated and evaporated to dryness, with the crude being analysed by ^{1}H-NMR spectroscopy. The residue was dissolved in chloroform (20 ml) and washed with water (3x20 mL) and BRINE (3x20 mL). The organic phase was dried over Na_2SO_4, filtered and the solvent was evaporated. All compounds were subjected to column chromatography (Silicagel 60 (Merck), 0.063-0.200 mm) using EtOAc/$CHCl_3$ (the exact ratios are specified in Section Characterization (3.5) for each compound).

3.5. Characterization of the products

7-(*N*-*tert*-Butylcarboxamido)indole (**2a**). Yield: 54 mg (25 %); brown viscous material [Found: C, 72.26; H, 7.58; N, 12.65; $C_{13}H_{16}N_2O$ requires C, 72.19; H, 7.46; N, 12.95 %]; R_f (20 % toluene, 80 % $CHCl_3$) 0.72; δ_H (500 MHz, $CDCl_3$) 10.37 (1 H, brs, indole-NH), 7.80 (1 H, d, 7.8 Hz, Ar-H), 7.34-7.31 (2 H, overlap, m, Ar-H and indole-H), 7.12 (1 H, t, 7.7 Hz, Ar-H), 6.58 (1 H, dd, 3.0 Hz, 2.3 Hz, indole-H), 6.21 (1 H, brs,

NH), 1.55 (9 H, s, $(CH_3)_3$). δ_C (125.7 MHz, $CDCl_3$) 167.5, 135.5, 129.6, 125.5, 124.4, 118.6, 118.5, 117.2, 101.8, 51.5, 29.01. IR (KBr, ν (cm^{-1})): 3422 (indole-NH), 3336 (NH), 1632 (CON); MS m/z (rel int.): 216 (58, M^+), 201 (2), 185 (2), 160 (33), 144 (100), 116 (31), 89 (16), 63 (4).

7-(*N*-*tert*-Butylglyoxylamido)indole (**3a**). Yield: 142 mg (58 %); off-white solid material, mp. 104 ˚C; [Found: C, 68.70; H, 6.75; N, 11.25; $C_{14}H_{16}N_2O_2$ requires C, 68.83; H, 6.60; N, 11.47 %]; R_f (20 % toluene, 80 % $CHCl_3$) 0.58; δ_H (500 MHz, $CDCl_3$) 10.44 (1 H, brs, indole-NH), 8.79 (1 H, d, 7.8 Hz, Ar-H), 7.98 (1 H, d, 7.8 Hz, Ar-H), 7.86 (1 H, dd, 3.0 Hz, 2.3 Hz, indole-H), 7.23 (1 H, t, 7.8 Hz, Ar-H), 6.99 (1 H, brs, NH), 6.65 (1 H, dd, 3.0 Hz, 2.3 Hz, indole-H), 1.52 (9 H, s, $(CH_3)_3$). δ_C (125.7 MHz, $CDCl_3$) 188.8, 162.1, 135.9, 129.4, 129.3, 129.2, 125.4, 119.3, 116.7, 103.1, 51.7, 29.01. IR (KBr, ν (cm^{-1})): 3381 (indole-NH), 3246 (NH), 1656 (CO), 1640 (CON); MS m/z (rel int.): 244 (36, M^+), 144 (100), 116 (36), 89 (14), 57 (14).

7-(*N*-Phenylcarboxamido)indole (**2b**). Yield: 120 mg (51 %); brown solid material, mp. 145 ˚C; [Found: C, 76.16; H, 5.30; N, 11.69; $C_{15}H_{12}N_2O$ requires C, 76.25; H, 5.12; N, 11.86 %]; R_f (5 % EtOAc, 95 % $CHCl_3$) 0.53; δ_H (500 MHz, $CDCl_3$) 10.33 (1 H, brs, indole-NH), 8.11 (1 H, brs, NH), 7.89 (1 H, d, 7.5 Hz, Ar-H), 7.68 (2H, d, 8.0 Hz, Ph (*ortho*)), 7.55 (1 H, d, 7.5 Hz, Ar-H), 7.68 (2H, d, 8.0 Hz, Ph (*meta*)), 7.36 (1 H, dd, 3.0 Hz, 2.3 Hz, indole-H), 7.21 (2 H, overlap, m, Ar-H and Ph(*para*)), 6.64 (1 H, dd, 3.0 Hz, 2.3 Hz, indole-H). δ_C (125.7 MHz, $CDCl_3$) 166.1, 137.7, 135.6, 129.8, 129.2, 125.9, 125.4, 124.7, 120.6, 119.0, 118.8, 116.1, 102.1. IR (KBr, ν (cm^{-1})): 3418 (indole-NH), 3295 (NH), 1643 (CON); MS m/z (rel int.): 236 (64, M^+), 206 (3), 144 (100), 116 (47), 89 (19), 63 (5).

7-(*N*,*N*-Pentane-1,5-diylcarboxamido)indole (**2c**). Yield: 76 mg (33 %); pale brown solid material, mp. 121 ˚C; [Found: C, 73.49; H, 7.14; N, 12.05; $C_{14}H_{16}N_2O$ requires C, 73.66; H, 7.06; N, 12.27 %]; R_f (5 % EtOAc, 95 % $CHCl_3$) 0.46; δ_H (500 MHz, $CDCl_3$) 9.29 (1 H, brs, indole-NH), 7.71 (1 H, d, 7.8 Hz, Ar-H), 7.26 (1 H, s, indole-H), 7.22 (1 H, d, 7.3 Hz, Ar-H), 7.11 (1 H, t, 7.6 Hz, Ar-H), 6.56 (1 H, s, indole-H), 3.69 (4 H, brs, 2x N-CH_2), 1.73-1.66 (6 H, m, 3x CH_2). δ_C (125.7 MHz, $CDCl_3$) 169.4, 134.9, 129.1, 125.2, 122.8, 120.9, 118.5, 117.6, 102.4, 47.0, 26.3, 24.7. IR (KBr, ν (cm^{-1})): 3244 (indole-NH), 1623 (CON); MS m/z (rel int.): 228 (87, M^+), 144 (100), 116 (60), 89 (22), 84 (16), 63 (5).

7-(*N*,*N*-Pentane-1,5-diylglyoxylamido)indole (**3c**). Yield: 170 mg (66 %); beige solid material, mp. 125 ˚C; [Found: C, 70.16; H, 6.41; N, 10.75; $C_{15}H_{16}N_2O_2$ requires C, 70.29; H, 6.29; N, 10.93 %]; R_f (5 % EtOAc, 95 % $CHCl_3$) 0.71; δ_H (500 MHz, $CDCl_3$) 10.34 (1 H, brs, indole-NH), 7.97 (1 H, d, 7.8 Hz, Ar-H), 7.68 (1 H, d, 7.6 Hz, Ar-H), 7.38 (1 H, dd, 3.0 Hz, 2.3 Hz, indole-H), 7.22 (1 H, t, 7.7 Hz, Ar-H), 6.66 (1 H, dd, 3.0 Hz, 2.3 Hz, indole-H), 3.82-3.76 (2 H, m, N-CH_2), 3.38-3.33 (2 H, m, N-CH_2), 1.79-1.70 (4 H, m, 2x

CH_2), 1.62-1.55 (2 H, m, CH_2). δ_C (125.7 MHz, $CDCl_3$) 193.9, 165.3, 134.7, 129.7, 128.9, 127.1, 126.1, 119.4, 116.7, 102.85, 47.2, 42.2, 26.2, 25.5, 24.4. IR (KBr, ν (cm^{-1})): 3359 (indole-NH), 1661 (CO), 1630 (CON); MS m/z (rel int.): 256 (42, M^+), 144 (100), 116 (35), 89 (30), 84 (3), 69 (30), 63 (3).

7-(*N,N*-Pentane-3-oxa-1,5-diylcarboxamido)indole (**2d**). Yield: 28 mg (12 %); brown solid material, mp. 107 ˚C; [Found: C, 67.76; H, 6.30; N, 12.01; $C_{13}H_{14}N_2O_2$ requires C, 67.81; H, 6.13; N, 12.17 %]; R_f (5 % EtOAc, 95 % $CHCl_3$) 0.36; δ_H (500 MHz, $CDCl_3$) 9.27 (1 H, brs, indole-NH), 7.75 (1 H, d, 7.8 Hz, Ar-H), 7.28 (1 H, s, indole-H), 7.23 (1 H, d, 7.3 Hz, Ar-H), 7.11 (1 H, t, 7.3 Hz, Ar-H), 6.59 (1 H, s, indole-H), 3.81-3,76 (8 H, overlap, m, 2x O-*CH_2* and 2x N-*CH_2*), 1.73-1.66 (6 H, m, 3x CH_2). δ_C (125.7 MHz, $CDCl_3$) 169.6, 135.0, 129.3, 125.4, 123.4, 121.2, 118.5, 116.3, 102.6, 67.1, 45.6. IR (KBr, ν (cm^{-1})): 3253 (indole-NH), 1615 (CON); MS m/z (rel int.): 230 (65, M^+), 215 (3), 186 (5), 144 (100), 116 (45), 89 (17), 63 (5).

7-(*N,N*-Pentane-3-oxa-1,5-diylglyoxylamido)indole (**3d**). Yield: 170 mg (65 %); beige solid material, mp. 166 ˚C; [Found: C, 65.16; H, 5.40; N, 10.66; $C_{14}H_{14}N_2O_3$ requires C, 65.11; H, 5.46; N, 10.85 %]; R_f (5 % EtOAc, 95 % $CHCl_3$) 0.63; δ_H (500 MHz, $CDCl_3$) 10.32 (1 H, brs, indole-NH), 7.99 (1 H, d, 5.6 Hz, Ar-H), 7.70 (1 H, d, 5.6 Hz, Ar-H), 7.39 (1 H, s, indole-H), 7.23 (1 H, t, 5.6 Hz, Ar-H), 6.67 (1 H, s, indole-H), 3.85 (4 H, brs, 2x O-*CH_2*), 3.66 (2 H, brs, N-*CH_2*), 3.42 (2 H, brs, N-*CH_2*). δ_C (125.7 MHz, $CDCl_3$) 193.0, 165.3, 134.7, 129.8, 129.3, 127.1, 126.3, 119.4, 116.5, 103.0, 66.8, 66.7, 46.4, 41.7. IR (KBr, ν (cm^{-1})): 3360 (indole-NH), 1661 (CO), 1634 (CON); MS m/z (rel int.): 258 (30, M^+), 144 (100), 116 (35), 89 (12), 63 (4).

7-(*N*-(1'-Methoxycarbonylmethyl)carboxamido)indole (**2e**) (identified as minor component in **3e**). MS m/z (rel int.): 232 (76, M^+), 200 (6), 185 (4), 173 (4), 144 (100), 116 (50), 89 (22), 63 (7). δ_H (500 MHz, $CDCl_3$) 10.28 (1 H, brs, indole-NH), 7.83 (1 H, d, 7.8 Hz, Ar-H), 7.48 (1 H, d, 7.8 Hz, Ar-H), 7.33 (1 H, overlapping brs, indole-H), 7.15 (1 H, t, 7.8 Hz, Ar-H), 6.95 (1 H, brs NH), 6.59 (1 H, dd, 3.0 Hz, 2.3 Hz, indole-H), 4.31 (2 H, d, 5.6 Hz, N-*CH_2*), 3.83 (3 H, s, O-*CH_3*).

7-(*N*-(1'-Methoxycarbonylmethyl)glyoxylamido)-indole (**3e**). Yield: 176 mg (68 %); yellow solid material, mp. 98 ˚C; [Found: C, 60.14; H, 4.77; N, 10.55; $C_{13}H_{12}N_2O_4$ requires C, 60.00; H, 4.65; N, 10.76 %]; R_f (5 % EtOAc, 95 % $CHCl_3$) 0.62; δ_H (500 MHz, $CDCl_3$) 10.42 (1 H, brs, indole-NH), 8.77 (1 H, d, 7.7 Hz, Ar-H), 7.98 (1 H, d, 7.7 Hz, Ar-H), 7.72 (1 H, brs NH), 7.34 (1 H, dd, 3.0 Hz, 2.3 Hz, indole-H), 7.21 (1 H, t, 7.7 Hz, Ar-H), 6.67 (1 H, dd, 3.0 Hz, 2.3 Hz, indole-H), 4.24 (2 H, d, 5.6 Hz, N-*CH_2*), 3.83 (3 H, s, O-*CH_3*). δ_C (125.7 MHz, $CDCl_3$) 186.9, 169.6, 162.7, 135.8, 129.6, 129.4, 129.3, 125.6, 119.4, 116.5, 103.2, 52.6, 41.1. IR (KBr, ν (cm^{-1})): 3434 (indole-NH), 3302 (NH), 1771 (COO), 1663 (CO), 1636 (CON); MS m/z (rel int.): 260 (33, M^+), 201 (2), 144 (100), 116 (46), 89 (15), 63 (4).

7-(*N*-(1'-Methoxycarbonylethyl)carboxamido)indole (**2f**) (isolated in a 2/8 mixture of **2f**/**3f**). δ_H (500 MHz, $CDCl_3$) 10.29 (1 H, brs, indole-NH), 7.83 (1 H, d, 7.8 Hz, Ar-H), 7.48 (1 H, d, 7.8 Hz, Ar-H), 7.34 (1 H, dd, 3.0 Hz, 2.3 Hz, indole-H), 7.15 (1 H, t, 7.8 Hz, Ar-H), 6.98 (1 H, d, 5.7 Hz, NH), 6.59 (1 H, dd, 3.0 Hz, 2.3 Hz, indole-H), 4.87 (1 H, qi, 7.2 Hz, N-*CH*) 3.83 (3 H, s, O-*CH_3*), 1.58 (3 H, d, 7.2 Hz, CH*CH_3*). δ_C (125.7 MHz, $CDCl_3$) 173.7, 167.4, 135.8, 129.6, 129.3, 125.1, 119.3, 118.7, 115.3, 102.0, 52.6, 48.3, 18.6. MS m/z (rel int.): 246 (48, M^+), 187 (9), 171 (5), 144 (100), 116 (33), 102 (2), 89 (14), 63 (4).

7-(*N*-(1'-Methoxycarbonylethyl)glyoxylamido)indole (**3f**) (isolated in a 2/8 mixture of **2f**/**3f**). R_f (5 % MeOH, 20 % EtOAc, 75 % hexane) 0.40; δ_H (500 MHz, $CDCl_3$) 10.43 (1 H, brs, indole-NH), 8.78 (1 H, d, 7.8 Hz, Ar-H), 7.98 (1 H, d, 7.8 Hz, Ar-H), 7.72 (1 H, d, 6.1 Hz, NH), 7.34 (1 H, dd, 3.0 Hz, 2.3 Hz, indole-H), 7.21 (1 H, t, 7.8 Hz, Ar-H), 6.65 (1 H, dd, 3.0 Hz, 2.3 Hz, indole-H), 4.76 (1 H, qi, 7.3 Hz, N-*CH*) 3.83 (3 H, s, O-*CH_3*), 1.57 (3 H, d, 7.3 Hz, CH*CH_3*). δ_C (125.7 MHz, $CDCl_3$) 187.1, 167.4, 162.1, 135.9, 129.6, 129.4, 129.3, 125.1, 119.4, 116.6, 103.2, 52.7, 48.1, 18.2. IR (KBr, ν (cm^{-1})): 3402 (indole-NH), 3261 (NH), 1745 (COO), 1664 (CO), 1636 (CON); MS m/z (rel int.): 274 (31, M^+), 215 (4), 144 (100), 116 (36), 102 (6), 89 (15), 63 (4).

7-(*N*-(1'-Methoxycarbonyl-2'-methylpropyl)carboxamido)indole (**2g**), Yield: 107 mg (39 %); pale yellow viscous material; [Found: C, 65.46; H, 6.47; N, 10.05; $C_{15}H_{18}N_2O_3$ requires C, 65.68; H, 6.61; N, 10.21 %]; R_f (5 % MeOH, 15 % EtOAc, 80 % hexane) 0.64; δ_H (500 MHz, $CDCl_3$) 10.28 (1 H, brs, indole-NH), 7.84 (1 H, d, 7.8 Hz, Ar-H), 7.51 (1 H, d, 7.8 Hz, Ar-H), 7.34 (1 H, dd, 3.0 Hz, 2.3 Hz, indole-H), 7.16 (1 H, t, 7.7 Hz, Ar-H), 6.91 (1 H, d, 8.3 Hz, NH), 6.59 (1 H, dd, 3.0 Hz, 2.3 Hz, indole-H), 4.84 (1 H, dd, 8.6 Hz, 5.1 Hz, N-*CH*) 3.82 (3 H, s, O-*CH_3*), 2.37-2.30 (1 H, m, *CH*(CH_3)$_2$), 1.06 (3 H, d, 6.9 Hz, CH*CH_3*), 1.04 (3 H, d, 6.9 Hz, CH*CH_3*). δ_C (125.7 MHz, $CDCl_3$) 172.7, 167.7, 135.4, 129.6, 125.6, 125.1, 119.2, 118.7, 115.5, 102.0, 57.2, 52.3, 31.7, 19.1, 18.1. IR (KBr, ν (cm^{-1})): 3427 (NH), 1734 (COO), 1646 (CON); MS m/z (rel int.): 274 (29, M^+), 215 (7), 171 (11), 160 (17), 144 (100), 130 (2), 116 (37), 89 (13), 63 (2).

7-(*N*-(1'-Methoxycarbonyl-2'-methylpropyl)glyoxylamido)indole (**3g**), Yield: 136 mg (45 %); yellow solid material, mp. 71 ˚C; [Found: C, 63.46; H, 6.12; N, 9.03; $C_{16}H_{18}N_2O_4$ requires C, 63.56; H, 6.00; N, 9.27 %]; R_f (5 % MeOH, 15 % EtOAc, 80 % hexane) 0.52; δ_H (500 MHz, $CDCl_3$) 10.46 (1 H, brs, indole-NH), 8.77 (1 H, d, 7.7 Hz, Ar-H), 7.98 (1 H, d, 7.7 Hz, Ar-H), 7.69 (1 H, d, 8.8 Hz, NH), 7.36 (1 H, dd, 3.0 Hz, 2.3 Hz, indole-H), 7.21 (1 H, t, 7.7 Hz, Ar-H), 6.59 (1 H, dd, 3.0 Hz, 2.3 Hz, indole-H), 4.71 (1 H, dd, 9.1 Hz, 5.1 Hz, N-*CH*) 3.82 (3 H, s, O-*CH_3*), 2.39-2.30 (1 H, m, *CH*(CH_3)$_2$), 1.06 (3 H, d, 6.9 Hz, CH*CH_3*), 1.03 (3 H, d, 6.9 Hz, CH*CH_3*). δ_C (125.7 MHz, $CDCl_3$)187.3 171.7, 162.4, 135.9, 129.6, 129.4, 129.3, 125.6, 119.4, 116.6,

103.2, 57.3, 52.4, 61.5, 19.1, 17.8. IR (KBr, ν (cm^{-1})): 3427 (overlap indole-NH and NH), 3284 (NH), 1742 (COO), 1665 (CO), 1636 (CON); MS m/z (rel int.): 302 (29, M^+), 243 (4), 144 (100), 130 (9), 116 (35), 89 (13), 63 (2).

7-(*N*-(2'-Methoxycarbonylbutane-1,4-diyl)glyoxylamido)indole (**3h**), (ca. 1/3 mixture of two C(O)N rotamers). Yield: 171 mg (57%); beige solid material, mp. 94 ˚C; [Found: C, 64.12; H, 5.40; N, 9.12; $C_{16}H_{16}N_2O_4$ requires C, 63.99; H, 5.37; N, 9.33 %]; R_f (5 % EtOAc, 95 % $CHCl_3$) 0.68; δ_H (500 MHz, $CDCl_3$) 10.33/10.28 (major/minor) (1 H, brs, indole-NH), 7.99-7.94 (major + minor) (2 H, overlap, m, 2x Ar-H), 7.38/7.35 (major/minor) (1 H, dd, 3.00 Hz, 2.34 Hz, indole-H), 7.26/7.21 (major/minor) (1 H, t, 7.70 Hz, Ar-H), 6.66/6.64 (major/minor) (1 H, dd, 3.00 Hz, 2.34 Hz, indole-H), 4.73/4.69 (major/minor) (1 H dd, 8.82 Hz, 4.15 Hz, N-*CH*), 3.89/3.43 (major/minor) (3 H, s, O-CH_3), 3.84-3.78/3.64-3.55 (minor/major) (2 H, m, N-CH_2), 2.39-1.94 (major/minor) (4 H, m, 2x CH_2). δ_C (125.7 MHz, $CDCl_3$) 192.7/191.9 (major/minor), 172.0, 165.3/164.5 (major/minor), 135.2/134.9 (minor/major), 129.5/129.4 (major/minor), 129.1/128.9 (major/minor), 128.3/127.9 (minor/major), 126.0/125.8 (major/minor), 119.7/119.2 (major/minor), 116.5/116.3 (minor/major), 102.9, 59.5/58.3 (minor/major), 52.6/52.3 (major/minor), 47.3/46.4 (major/minor), 31.1/29.2 (minor/major), 24.7/22.4 (major/minor). IR (KBr, ν (cm^{-1})): 3410 (indole-NH), 3410 (indole-NH), 1745 (COO), 1653 (CO), 1636 (CON); MS m/z (rel int.): 300 (35, M^+), 241 (4), 144 (100), 128 (33), 116 (37), 89 (15), 63 (4).

5-(*N*-*tert*-Butylcarboxamido)indole (**5a**). Yield: 25 mg (11 %); brow viscous material, [Found: C, 72.01; H, 7.30; N, 12.75; $C_{13}H_{16}N_2O$ requires C, 72.19; H, 7.46; N, 12.95 %]; R_f (5 % EtOAc, 95 % $CHCl_3$) 0.28; δ_H (500 MHz, $CDCl_3$) 9.11 (1 H, brs, indole-NH), 8.04 (1 H, s, Ar-H), 7.6 (1 H, d, 8.5 Hz, Ar-H), 7.38 (1 H, d, 8.5 Hz, Ar-H), 7.26 (1 H, s, indole-H), 6.59 (1 H, s, indole-H), 6.1 (1 H, brs, indole-NH), 1.52 (9 H, s, $(CH_3)_3$). δ_C (125.7 MHz, $CDCl_3$) 168.5, 137.5, 132.1, 127.5, 125.8, 120.7, 119.6, 111.1, 103.1, 51.5, 29.0. IR (KBr, ν (cm^{-1})): 3357 (indole-NH and NH (overlapping)), 1638 (CON); MS m/z (rel int.): 216 (20, M^+), 201 (2), 160 (20), 144 (100), 116 (34), 89 (14), 63 (4).

5-(*N*-*tert*-Butylglyoxylamido)indole (**6a**). Yield: 113 mg (46 %); beige solid material, mp. 175 ˚C; [Found: C, 68.96; H, 6.40; N, 11.25; $C_{14}H_{16}N_2O_2$ requires C, 68.83; H, 6.60; N, 11.47 %]; R_f (5 % EtOAc, 95 % $CHCl_3$) 0.60; δ_H (500 MHz, $CDCl_3$) 8.90 (1 H, s, Ar-H), 8.73 (1 H, brs, indole-NH), 8.12 (1 H, dd, 8.7 Hz, 1.5 Hz, Ar-H), 7.40 (1 H, d, 8.68 Hz, Ar-H), 7.24 (1H, dd, 3.02 Hz, 2.35 Hz, indole-H), 7.01 (1 H, brs, NH), 6.67 (1 H, d, 1.97 Hz, indole-H), 1.51 (9 H, s, $(CH_3)_3$). δ_C (125.7 MHz, $CDCl_3$) 188.3, 162.5, 139.1, 127.4,

127.1, 125.8, 125.7, 124.6, 111.2, 104.9, 51.6, 28.5. IR (KBr, ν (cm^{-1})): 3357 (indoleNH), 3212 (NH), 1661 (CO), 1647 (CON); MS m/z (rel int.): 244 (7, M^+), 144 (100), 116 (35), 89 (13), 57 (8).

5-(*N*-Phenylcarboxamido)indole (**5b**). Yield: 111 mg (47 %); brown solid material, mp. 180 ˚C; [Found: C, 76.16; H, 5.30; N, 11.75; $C_{15}H_{12}N_2O$ requires C, 76.25; H, 5.12; N, 11.86 %]; R_f (20 % EtOAc, 80 % $CHCl_3$) 0.53; δ_H (500 MHz, $CDCl_3$) 8.55 (1 H, brs, indole-NH), 8.23 (1 H, s, Ar-H), 7.93 (1 H, s, NH), 7.77 (1H, dd, 8.51 Hz, 1.65 Hz, Ar-H), 7.70 (2H, d, 7.67 Hz, Ph (*ortho*)), 7.48 (1 H, d, 8.5 Hz, Ar-H), 7.45 (2H, t, 8.2 Hz, Ph (*meta*)), 7.32 (1 H, t, 3.0 Hz, indole-H), 7.16 (1 H, t, 7.4 Hz, Ph(*para*)), 6.68 (1 H, s, indole-H). δ_C (125.7 MHz, $CDCl_3$) 166.8, 138.4, 137.7, 129.1, 127.7, 126.9, 125.8, 124.2, 121.2, 120.3, 120.1, 111.3, 103.7. IR (KBr, ν (cm^{-1})): 3418 (indole-NH), 3178 (NH), 1643 (CON); MS m/z (rel int.): 236 (26, M^+), 144 (100), 116 (40), 89 (17), 63 (7).

5-(*N,N*-Pentane-1,5-diylcarboxamido)indole (**5c**). Yield: 35 mg (15 %); brown viscous material, [Found: C, 73.50; H, 7.23; N, 12.01; $C_{14}H_{16}N_2O$ requires C, 73.66; H, 7.06; N, 12.27 %]; R_f (30 % EtOAc, 70 % $CHCl_3$) 0.37; δ_H (500 MHz, $CDCl_3$) 9.41 (1 H, brs, indole-NH), 7.67 (1 H, s, Ar-H), 7.35 (1 H, d, 8.3 Hz, Ar-H), 7.23 (1 H, s, indole-H), 77.11 (1 H, d, 8.2 Hz, Ar-H), 6.52 (1 H, s, indole-H), 3.58-3.56 (2 H, m, N-*CH_2*), 3.38-3.29 (2 H, m, N-*CH_2*), 1.67-1.59 (2H, m, CH_2), 1.59-1.53 (4H, m, 2x CH_2). δ_C (125.7 MHz, $CDCl_3$) 172.09, 136.52, 128.59, 127.3, 125.66, 120.92, 119.81, 111.19, 102.61, 47.19, 41.74, 26.39, 25.28, 24.37. IR (KBr, ν (cm^{-1})): 3487 (indole-NH), 1653 (CON); MS m/z (rel int.): 228 (68, M^+), 144 (100), 116 (47), 89 (18), 63 (5).

5-(*N,N*-Pentane-1,5-diylglyoxylamido)indole (**6c**). Yield: 170 mg (66 %); beige solid material, mp. 198 ˚C; [Found: C, 70.16; H, 6.41; N, 10.70; $C_{15}H_{16}N_2O_2$ requires C, 70.29; H, 6.29; N, 10.93 %]; R_f (30 % EtOAc, 70 % $CHCl_3$) 0.52; δ_H (500 MHz, $CDCl_3$) 9.03 (1 H, brs, indole-NH), 8.25 (1H, s, Ar-H), 7.80 (1H, d, 8.6 Hz, Ar-H), 7.40 (1H, d, 8.6 Hz, Ar-H), 7.28 (1 H, t, 3 Hz, indole-H), 6.65 (1 H, s, indole-H), 3.77-3.75 (2 H, m, N-CH_2), 3.35-3.33 (2H, m, N-CH_2), 1.73-1.71 (4H, m, 2x CH_2), 1.56-1.55 (2H, m, CH_2). δ_C (125.7 MHz, $CDCl_3$) 192.5, 166.6, 139.5, 127.7, 126.4, 125.7, 125.1, 122.6, 111.8, 104.5, 47.2, 42.1, 26.2, 25.5, 24.4. IR (KBr, ν (cm^{-1})): 3172 (indole-NH), 1656 (CO), 1625 (CON); MS m/z (rel int.): 256 (4, M^+), 144 (100), 116 (35), 89 (14), 69 (7).

5-(*N,N*-Pentane-3-oxa-1,5-diylcarboxamido)indole (**5d**). MS m/z (rel int.): 230 (22, M^+), 144 (100), 116 (43), 89 (17), 56 (5).

5-(*N,N*-Pentane-3-oxa-1,5-diylglyoxylamido)indole (**6d**). Yield: 129 mg (50 %); beige solid material, mp. 187 ˚C; [Found: C, 65.19; H, 5.30; N, 10.71; $C_{14}H_{14}N_2O_3$ requires C, 65.11; H, 5.46; N, 10.85 %]; R_f (40

% EtOAc, 60 % $CHCl_3$) 0.40; δ_H (500 MHz, $CDCl_3$) 8.81 (1 H, brs, indole-NH), 8.28 (1 H, s, Ar-H), 7.84 (1 H, dd, 8.61 Hz, 1.38 Hz, Ar-H), 7.45 (1 H, d, 8.58 Hz, Ar-H), 7.31 (1 H, t, 2.6 Hz, indole-H), 6.69 (1 H, s, indole-H), 3.85 (4 H, s, 2x O-*CH_2*), 3.67 (2 H, t, N-*CH_2*), 3.43 (2 H, t, N-*CH_2*). δ_C (125.7 MHz, $CDCl_3$) 191.6, 166.6, 139.5, 127.7, 126.4, 125.6, 125.3, 122.8, 111.8, 104.7, 66.8, 66.7, 46.4, 41.6. IR (KBr, ν (cm^{-1})): 3260 (indole-NH), 1664 (CO), 1631 (CON); MS m/z (rel int.): 258 (3, M^+), 144 (100), 116 (40), 89 (15), 63 (5).

5-(*N*-(1'-Methoxycarbonylmethyl)carboxamido)indole (**5e**) (identified as a minor component in **6e**). MS m/z (rel int.): 232 (42, M^+), 200 (3), 144 (100), 116 (28), 89 (19), 63 (7). δ_H (500 MHz, $CDCl_3$) 8.85 (1 H, s, Ar-H), 8.65 (1 H, brs, indole-NH), 8.36 (1 H, d, 8.8 Hz, Ar-H), 8.31 (1 H, d, 8.7 Hz, Ar-H), 7.37 (1 H, brs NH), 7.29 (1 H, s, indole-H), 6.70 (1 H, s, indole-H), 4.23 (2 H, d, 5.6 Hz, N-*CH_2*), 3.84 (3 H, s, O-*CH_3*).

5-(*N*-(1'-Methoxycarbonylmethyl)glyoxylamido)indole (**6e**). Yield: 196 mg (74 %); brown solid material, mp. 117 ˚C; [Found: C, 60.17; H, 4.70; N, 10.55; $C_{13}H_{12}N_2O_4$ requires C, 60.00; H, 4.65; N, 10.76 %]; R_f (40 % EtOAc, 60 % $CHCl_3$) 0.57; δ_H (500 MHz, $CDCl_3$) 8.91 (1 H, s, Ar-NH), 8.58 (1 H, brs, indole-NH), 8.15 (1 H, d, 8.7 Hz, Ar-H), 7.62 (1 H, brs NH), 7.43 (1 H, d, 8.7 Hz, Ar-H), 7.28 (1 H, s, indole-H), 6.70 (1 H, s, indole-H), 4.23 (2 H, d, 5.6 Hz, N-*CH_2*), 3.83 (3 H, s, O-*CH_3*). δ_C (125.7 MHz, $CDCl_3$) 186.4, 169.5, 163.1, 139.3, 127.5, 127.3, 125.8, 125.5, 124.5, 111.3, 105.1, 52.5, 41.1. IR (KBr, ν (cm^{-1})): 3376 (indole-NH), 3337 (NH), 1739 (COO), 1670 (CO), 1652 (CON); MS m/z (rel int.): 260 (10, M^+), 144 (100), 116 (49), 89 (19), 63 (5).

5-(*N*-(1'-Methoxycarbonylethyl)carboxamido)indole (**5f**). MS m/z (rel int.): 246 (12, M^+), 187 (7), 144 (100), 116 (33), 89 (12), 63 (4).

5-(*N*-(1'-Methoxycarbonylethyl)glyoxylamido)indole (**6f**). Yield: 126 mg (46 %); brown solid material, mp. 135 ˚C; [Found: C, 61.20; H, 5.41; N, 10.01; $C_{14}H_{14}N_2O_4$ requires C, 61.31; H, 5.14; N, 10.21 %];R_f (30 % EtOAc, 70 % $CHCl_3$) 0.60; δ_H (500 MHz, $CDCl_3$) 8.89 (1 H, s, Ar-H), 8.73 (1 H, brs, indole-NH), 8.12 (1 H, dd, 8.70 Hz, 1.5 Hz, Ar-H), 7.63 (1 H, d, 7.02 Hz, NH), 7.41 (1 H, d, 8.7 Hz, Ar-H), 7.26 (1 H, t, 3.0 Hz, indole-H), 6.67 (1 H, s, indole-H), 4.73 (1 H, qi, 7.26 Hz, N-*CH*) 3.81 (3 H, s, O-*CH_3*), 1.56 (3 H, d, 7.2 Hz, CH*CH_3*). δ_C (125.7 MHz, $CDCl_3$186.7, 172.6, 162.6, 139.3, 127.5, 127.2, 125.9, 125.5, 124.5, 111.3, 104.9, 52.6, 48.2, 18.1. IR (KBr, ν (cm^{-1})): 3363 (indole-NH), 3289 (NH), 1733 (COO), 1664 (CO), 1646 (CON); MS m/z (rel int.): 274 (7, M^+), 144 (100), 116 (37), 89 (14), 63 (4).

5-(*N*-(1'-Methoxycarbonyl-2'-methylpropyl)carboxamido)indole (**5g**), Yield: 70 mg (25 %); brown viscous material; [Found: C, 65.77; H, 6.40; N, 10.05; $C_{15}H_{18}N_2O_3$ requires C, 65.68; H, 6.61; N, 10.21 %]; R_f (20 % EtOAc, 80 % $CHCl_3$) 0.47; δ_H (500 MHz, $CDCl_3$) 9.52 (1 H, brs, indole-NH), 8.15 (1 H, s, Ar-H), 7.65

(1 H, dd, 8.53 Hz, 1.5 Hz, Ar-H), 7.38 (1 H, d, 8.52 Hz, Ar-H), 7.25 (1 H, t, 2.8 Hz, indole-H), 6.81 (1 H, d, 8.65 Hz, NH), 6.59 (1 H, s, indole-H), 4.84 (1 H, dd, 8.56 Hz, 5.17 Hz, N-*CH*) 3.77 (3 H, s, O-CH_3), 2.27-2.34 (1 H, m, *CH*(CH_3)$_2$), 1.04 (3 H, d, 6.87 Hz, CHCH_3), 1.03 (3 H, d, 6.9 Hz, CHCH_3). δ_C (125.7 MHz, $CDCl_3$) 173.9, 168.9, 137.9, 127.5, 126.1, 125.5, 120.8, 120.2, 111.3, 103.1, 57.6, 52.1, 31.6, 19.1, 18.1. IR (KBr, ν (cm^{-1})): 3341 (indole-NH), 3217 (NH), 1737 (COO), 1634 (CON); MS m/z (rel int.): 274 (9, M^+), 215 (3), 160 (28), 144 (100), 116 (37), 89 (12), 63 (3).

5-(*N*-(1'-Methoxycarbonyl-2'-methylpropyl)glyoxylamido)indole (**6g**), Yield: 74 mg (24 %); brown viscous material; [Found: C, 63.78; H, 5.80; N, 9.05; $C_{16}H_{18}N_2O_4$ requires C, 63.56; H, 6.00; N, 9.27 %]; R_f (20 % EtOAc, 80 % $CHCl_3$) 0.68; δ_H (500 MHz, $CDCl_3$) 10.04 (1 H, brs, indole-NH), 8.88 (1 H, s, Ar-H), 8.11 (1 H, dd, 8.69 Hz, 1.53 Hz, Ar-H), 7.61 (1 H, d, 9.3 Hz, NH), 7.39 (1 H, d, 8.7 Hz, Ar-H), 7.24 (1 H, t, 2.86 Hz, indole-H), 6.65 (1 H, s, indole-H), 4.67 (1 H, dd, 9.02 Hz, 5.08 Hz, N-*CH*) 3.80 (3 H, s, O-CH_3), 2.37-2.27 (1 H, m, *CH*(CH_3)$_2$), 1.05 (3 H, d, 6.86 Hz, CHCH_3), 1.01 (3 H, d, 6.88 Hz, CHCH_3). δ_C (125.7 MHz, $CDCl_3$)186.8 171.6, 163.0, 139.4, 127.5, 127.1, 126.0, 125.5, 124.4, 111.4, 104.9, 57.4, 52.3, 31.4, 19.1, 17.7. IR (KBr, ν (cm^{-1})): 3332 (indole-NH and NH (overlapping)), 1742 (COO), 1652 (CO), 1636 (CON); MS m/z (rel int.): 302 (9, M^+), 144 (100), 116 (30), 89 (9), 63 (2).

5-(*N*-(2'-Methoxycarbonylbutane-1,4-diyl)carboxamido)indole (5h). MS m/z (rel int.): 272 (16, M^+), 213 (12), 144 (100), 116 (30), 89 (11), 63 (3).

5-(*N*-(2'-Methoxycarbonylbutane-1,4-diyl)glyoxylamido)indole (**6h**) (ca. 1/3 mixture of two C(O)N rotamers). Yield: 112 mg (36%); brown viscous material; [Found: C, 64.17; H, 5.40; N, 9.11; $C_{16}H_{16}N_2O_4$ requires C, 63.99; H, 5.37; N, 9.33 %]; R_f (20 % EtOAc, 80 % $CHCl_3$) 0.34; δ_H (500 MHz, $CDCl_3$) 9.78/9.71 (minor/major) (1 H, brs, indole-NH), 8.40/8.36 (major/minor) (1H, s, Ar-H), 7.86/7.84 (1 H, d, 8.5 Hz, Ar-H), 7.38/7.36 (1 H, d, 8.6 Hz, Ar-H), 7.20/7.15 (major/minor) (1 H, m, indole-H), 6.61/6.58 (major/minor) (1 H, s, indole-H), 4.71/4.54 (major/minor) (1 H dd, 8.73 Hz, 4.24 Hz, N-*CH*), 3.82/3.75 (major/minor) (3 H, s, O-CH_3), 3.73-3.69/3.63-3.50 (major/minor) (2 H, m, N-CH_2), 2.35-1.86 (minor/major) (4 H, m, 2x CH_2). δ_C (125.7 MHz, $CDCl_3$) 191.7/190.9 (major/minor), 172.1, 166.8/165.9 (major/minor), 139.8/139.6 (major/minor), 127.8/127.5 (major/minor), 126.7/126.5 (major/minor), 126.0/125.7 (minor/major), 125.1/124.9 (minor/major), 123.2/122.27 (minor/major), 112.1/111.6 (major/minor), 104.3/102.6 (major/minor), 59.5/58.4 (minor/major), 52.5/52.4 (major/minor), 47.3/46.4 (major/minor), 31.2/29.5 (minor/major), 24.9/22.4 (major/minor). IR (KBr, ν (cm^{-1})): 3292 (indole-NH), 1744 (COO), 1661 (CO), 1636 (CON); MS m/z (rel int.): 300 (3, M^+), 144 (100), 128 (11), 116 (31), 89 (11), 63 (3).

5-Bromo-7-(*N*-*tert*-butylcarboxamido)indole (**8a**). MS m/z (rel int.): 294/296 (55, M^+), 279/281 (5), 238/240 (59), 222/234 (100), 194/196 (19), 115 (53), 88 (9), 57 (12).

5-Bromo-7-(*N*-*tert*-butylglyoxylamido)indole (**9a**). Yield: 170 mg (53%); yellow solid material, mp. 120 ˚C; [Found: C, 52.17; H, 4.80; N, 8.55; $C_{14}H_{15}N_2O_2Br$ requires C, 52.03; H, 4.68; N, 8.67 %]; R_f (2 % EtOAc, 98 % $CHCl_3$) 0.90; δ_H (500 MHz, $CDCl_3$) 10.45 (1 H, brs, indole-NH), 8.95 (1 H, d, 1.60 Hz, Ar-H), 8.06 (1 H, d, 1.60 Hz, Ar-H), 7.34 (1 H, dd, 3.00 Hz, 2.34 Hz, indole-H), 7.06 (1 H, brs, NH), 6.58 (1 H, dd, 3.00 Hz, 2.34 Hz, indole-H), 1.51 (9 H, s, $(CH_3)_3$). δ_C (125.7 MHz, $CDCl_3$) 187.5, 161.3, 134.7, 131.3, 131.2, 131.0, 126.7, 117.6, 112.0, 102,6, 51.8, 28.4. IR (KBr, ν (cm^{-1})): 3313 (NH), 1661 (CO), 1649 (CON); MS m/z (rel int.): 322/324 (34, M^+), 222/224 (100), 194/196 (25), 115 (48), 88 (5), 57 (43).

5-Bromo-7-(*N*-phenylcarboxamido)indole (**8b**). Yield: 214 mg (68%); yellow solid material, mp. 187 ˚C; [Found: C, 57.30; H, 3.40; N, 8.03; $C_{15}H_{11}N_2OBr$ requires C, 57.16; H, 3.52; N, 8.19 %]; R_f (10 % EtOAc, 90 % $CHCl_3$) 0.90; δ_H (500 MHz, $CDCl_3$) 10.28 (1 H, brs, indole-NH), 7.98 (2 H, brs, 1 Hz, overlap NH, Ar-H), 7.67 (2H, dd, 8.39 Hz, 0,87 Hz, Ph (*ortho*)), 7.64 (1 H, d, 2 Hz, Ar-H), 7.43 (2H, t, 7.95 Hz, Ph (*meta*)), 7.36 (1 H, t, 2.7 Hz, indole-H), 7.23 (1H, t, 7.43 Hz, Ph (*para*)), 6.57 (1 H, dd, 3.07 Hz, 2.31 Hz, indole-H). δ_C (125.7 MHz, $CDCl_3$) 164.8, 137.3, 134.2, 131.3, 129.2, 127.5, 127.1, 125.0, 121.6, 120.7, 117.5, 111,5 101.8. IR (KBr, ν (cm^{-1})): 3409 (indole-NH), 3342 (NH), 1653 (CON); MS m/z (rel int.): 314/316 (64, M^+), 222/224 (100), 194/196 (30), 115 (69), 92 (9), 88 (7), 77 (3), 65 (9), 51 (3).

5-Bromo-7-(*N*-phenylglyoxylamido)indole (**9b**). MS m/z (rel int.): 342/344 (36, M^+), 222/224 (100), 194/196 (26), 115 (60), 77 (12), 63 (7), 51 (3).

5-Bromo-7-(*N,N*-pentane-1,5-diyl-carboxamido)indole (**8c**). MS m/z (rel int.): 306/308 (100, M^+), 222/224 (79), 194/194 (40), 115 (88), 88 (12), 84 (51), 63 (5), 56 (5).

5-Bromo-7-(*N,N*-pentane-1,5-diylglyoxylamido)indole (**9c**). Yield: 167 mg (54%); yellow solid material, mp. 183 ˚C; [Found: C, 53.66; H, 4.40; N, 8.07; $C_{15}H_{15}N_2O_2Br$ requires C, 53.75; H, 4.51; N, 8.36 %]; R_f (5 % EtOAc, 95 % $CHCl_3$) 0.50; δ_H (500 MHz, $CDCl_3$) 10.37 (1 H, brs, indole-NH), 8.07 (1 H, d, 1.25 Hz, Ar-H), 7.76 (1 H, d, 1.55 Hz, Ar-H), 7.39 (1 H, dd, 3.00 Hz, 2.34 Hz, indole-H), 6.66 (1 H, dd, 3.00 Hz, 2.34 Hz, indole-H), 3.76 (2 H, brs, N-CH_2), 3.35-3.27 (2 H, m, N-CH_2), 1.77-1.72 (4 H, m, 2x CH_2), 1.58 (2 H, brs, CH_2). δ_C (125.7 MHz, $CDCl_3$) 192.8, 164.5, 133.5, 131.4, 131.0, 128.9, 127.4, 117.7, 111.9, 102.4, 47.3, 42.4, 26.2, 25.5, 24.4. IR (KBr, ν (cm^{-1})): 1653 (CO), 1629 (CON); MS m/z (rel int.): 334/336 (35, M^+), 222/224 (56), 194/196 (19), 115 (50), 112 (100), 88 (7), 84 (13), 69 (43), 56 (9).

5-Bromo-7-(*N,N*-pentane-3-oxa-1,5-diylcarboxamido)indole (**8d**). MS m/z (rel int.): 308/310 (75, M^+), 293/295 (5), 264/266 (11), 222/224 (100), 194/196 (38), 115 (80), 88 (11), 86 (20), 63 (5), 56 (13).

5-Bromo-7-(*N,N*-pentane-3-oxa-1,5-diylglyoxylamido)indole (**9d**). Yield: 222 mg (66%); yellow solid material, mp. 134 ˚C; [Found: C, 50.02; H, 3.70; N, 8.05; $C_{14}H_{13}N_2O_3Br$ requires C, 49.87; H, 3.89; N, 8.31 %]; R_f (10 % EtOAc, 95 % $CHCl_3$) 0.50; δ_H (500 MHz, $CDCl_3$) 10.29 (1 H, brs, indole-NH), 8.09 (1 H, d, 1.23 Hz, Ar-H), 7.70 (1 H, d, 1.55 Hz, Ar-H), 7.39 (1 H, dd, 3.00 Hz, 2.34 Hz, indole-H), 6.61 (1 H, dd, 3.00 Hz, 2.34 Hz, indole-H), 3.85 (4 H, brs, 2x O-*CH*$_2$), 3.74-3.68 (2 H, m, N-*CH*$_2$), 3.48-3.42 (2 H, m, N-*CH*$_2$). δ_C (125.7 MHz, $CDCl_3$) 191.8, 164.5, 133.5, 131.5, 131.4, 129.0, 127.5, 117.5, 111.9, 102.6, 66.7, 66.6, 46.4, 41.8. IR (KBr, ν (cm^{-1})): 1669 (CO), 1636 (CON); MS m/z (rel int.): 336/338 (30, M^+), 222/224 (100), 194/196 (23), 115 (50), 88 (7), 70 (25), 63 (4), 56(4).

5-Bromo-7-(*N*-(1'-Methoxycarbonylmethyl)carboxamido)indole (8e). MS m/z (rel int.): 310/312 (89, M^+), 222/224 (100), 194/196 (34), 143 (17), 115 (96), 88 (18), 56 (9).

5-Bromo-7-(*N*-(1'-Methoxycarbonylmethyl)glyoxylamido)indole (9e). Yield: 152 mg (45 %); yellow solid material, mp. 166 ˚C; [Found: C, 46.19; H, 3.40; N, 8.22; $C_{13}H_{11}N_2O_4Br$ requires C, 46.04; H, 3.27; N, 8.36 %]; R_f (10 % EtOAc, 90 % $CHCl_3$) 0.52; δ_H (500 MHz, $CDCl_3$) 10.41 (1 H, brs, indole-NH), 8.96 (1 H, d, 1.69 Hz, Ar-H), 8.10 (1 H, d, 1.51 Hz, Ar-H), 7.66 (1 H, brs NH), 7.37 (1 H, t, 2.76 Hz, indole-H), 6.61 (1 H, t, 2.91 Hz, indole-H), 4.24 (2 H, d, 5.54 Hz, N-*CH*$_2$), 3.85 (3 H, s, O-*CH*$_3$). δ_C (125.7 MHz, $CDCl_3$) 185.8, 169.4, 161.8,134.7, 131.7, 131.3, 131.0, 126.8, 117.3, 112.1, 102.7, 52.6, 41.1. IR (KBr, ν (cm^{-1})): 3408 (indole-NH), 3293 (NH), 1746 (COO), 1663 (CO), 1637 (CON); MS m/z (rel int.): 338/340 (26, M^+), 222/224 (100), 194/196 (34), 143 (7), 115 (76), 88 (26), 56 (12).

5-Bromo-7-(*N*-(1'-methoxycarbonyl-ethyl)carboxamido)indole (**8f**) (identified as a minor component in **9f**). MS m/z (rel int.): 324/326 (41, M^+), 265/267 (12), 249/251 (6), 222/224 (100), 194/196 (24), 115 (49), 102 (2), 88 (6), 63 (2).δ_H (500 MHz, $CDCl_3$) 10.24 (1 H, brs, indole-NH), 7.89 (1 H, d, 0.97 Hz, Ar-H), 7.55 (1 H, d, 1.43 Hz, Ar-H), 7.31 (1 H, dd, 3.00 Hz, 2.34 Hz, indole-H), 6.95 (1 H, d, 6.75 Hz, NH), 6.49 (1 H, dd, 3.00 Hz, 2.34 Hz, indole-H), 4.84 (1 H, qi, 7.14 Hz, N-*CH*), 3.84 (3 H, s, O-*CH*$_3$), 1.57 (3 H, d, 7.20 Hz, CH*CH*$_3$).

5-Bromo-7-(*N*-(1'-methoxycarbonylethyl)glyoxylamido)indole (**9f**). Yield: 134 mg (38%); yellow solid material, mp. 148 ˚C; [Found: C, 47.55; H, 3.80; N, 7.70; $C_{14}H_{13}N_2O_4Br$ requires C, 47.61; H, 3.71; N, 7.93 %]; R_f (5 % EtOAc, 95 % $CHCl_3$) 0.71; δ_H (500 MHz, $CDCl_3$) 10.41 (1 H, brs, indole-NH), 8.89 (1 H, d, 1.62 Hz, Ar-H), 8.05 (1 H, d, 1.35 Hz, Ar-H), 7.75 (1 H, d, 7.25 Hz, NH), 7.35 (1 H, dd, 3.00 Hz, 2.34 Hz,

indole-H), 6.57 (1 H, dd, 3.00 Hz, 2.34 Hz, indole-H), 4.74 (1 H, qi, 7.27 Hz, N-*CH*) 3.84 (3 H, s, O-CH_3), 1.57 (3 H, d, 7.20 Hz, CHCH_3). δ_C (125.7 MHz, $CDCl_3$) 186.1, 172.6161.4, 134.6, 131.6, 131.1, 131.0, 126.9, 117.3, 112.0, 102.7, 52.8, 48.2, 18.1. IR (KBr, ν (cm^{-1})): 3276 (NH), 1747 (COO), 1664 (CO), 1636 (CON); MS m/z (rel int.): 352/354 (31, M^+), 293/265 (4), 222/224 (100), 194/196 (36), 115 (55), 102 (28), 88 (8), 70 (8), 63 (6).

5-Bromo-7-(*N*-(1'-Methoxycarbonyl-2'-methylpropyl)carboxamido)indole (8g). MS m/z (rel int.): 352/354 (28, M^+), 293/295 (13), 249/251 (13), 238/240 (25), 222/224 (100), 194/196 (29), 143 (7), 115 (61), 88 (6), 59 (4).

5-Bromo-7-(*N*-(1'-Methoxycarbonyl-2'-methyl-propyl)glyoxylamido)indole (9g). Yield: 176 mg (46%); yellow solid material, mp. 115 ˚C; [Found: C, 50.19; H, 4.40; N, 7.15; $C_{16}H_{17}N_2O_4Br$ requires C, 50.41; H, 4.49; N, 7.35 %]; R_f (5 % EtOAc, 95 % $CHCl_3$) 0.81; δ_H (500 MHz, $CDCl_3$) 10.45 (1 H, brs, indole-NH), 8.92 (1 H, d, 1.6 Hz, Ar-H), 8.08 (1 H, d, 1.4 Hz, Ar-H), 7.70 (1 H, d, 8.84 Hz, NH), 7.37 (1 H, t, 2.8 Hz, Ar-H), 6.59 (1 H, dd, 3.1 Hz, 2.2 Hz, indole-H), 4.68 (1 H, dd, 9.1 Hz, 4.9 Hz, N-*CH*), 3.83 (3 H, s, O-CH_3), 2.41-2.28 (1 H, m, *CH*(CH_3)$_2$), 1.06 (3 H, d, 6.86 Hz, CHCH_3), 1.05 (3 H, d, 6.89Hz, CHCH_3). δ_C (125.7 MHz, $CDCl_3$) 186.2, 171.6, 161.7, 134.6, 131.6, 131.2, 126.9, 121.8, 117.4, 112.0, 102.7, 57.3, 52.4, 31.5, 19.1, 17.8. IR (KBr, ν (cm^{-1})): 3393 (indole-NH), 3298 (NH), 1741 (COO), 1667 (CO), 1640 (CON); MS m/z (rel int.): 380/382 (34, M^+), 321/323 (6), 222/224 (100), 194/196 (34), 115 (67), 98 (15), 88 (9), 59 (9).

5-Bromo-7-(*N*-(2'-methoxycarbonylbutane-1,4-diyl)glyoxylamido)indole (**9h**). (ca. 2/5 mixture of two C(O)N rotamers). Yield: 250 mg (66%); yellow viscous material; [Found: C, 50.70; H, 4.12; N, 7.12; $C_{16}H_{15}N_2O_4Br$ requires C, 50.61; H, 3.99; N, 7.39 %]; R_f (5 % EtOAc, 95 % $CHCl_3$) 0.34; δ_H (500 MHz, $CDCl_3$) 10.32/10.25 (major/minor) (1 H, brs, indole-NH), 8.08 (major + minor) (1 H, overlap, d, 1.35 Hz, Ar-H), 8.05/8.03 (minor/major) (1 H, d, 1.20 Hz, Ar-H), 7.39/7.35 (major/minor) (1 H, dd, 3.00 Hz, 2.34 Hz, indole-H), 7.26/7.21 (major/minor) (1 H, t, 7.70 Hz, Ar-H), 6.60/6.58 (major/minor) (1 H, dd, 3.00 Hz, 2.34 Hz, indole-H), 4.74/4.70 (major/minor) (1 H dd, 8.85 Hz, 4.31 Hz, N-*CH*), 3.90/3.49 (major/minor) (3 H, s, O-CH_3), 3.82-3.76/3.64-3.54 (minor/major) (2 H, m, N-CH_2), 2.39-1.96 (major/minor) (4 H, m, 2x CH_2). δ_C (125.7 MHz, $CDCl_3$) 191.5/190.7 (major/minor), 171.9/171.7 (minor/major), 164.6/163.8 (major/minor), 134.0/133.7 (minor/major), 131.4/131.2 (major/minor), 131.1/129.9 (major/minor), 130.1/129.6 (minor/major), 127.4/127.1 (major/minor), 117.4/117.3 (minor/major), 112.1/111.8 (major/minor), 102.4, 59.6/58.5 (minor/major), 52.4/52.1 (major/minor), 47.3/46.6 (major/minor), 31.1/29.2 (minor/major),

24.7/22.3 (major/minor). IR (KBr, ν (cm^{-1})): 1757 (COO), 1742 (CO), 1636 (CON); MS m/z (rel int.): 378/380 (23, M^+), 222/224 (58), 194/196 (20), 156, (3); 128 (100), 115 (43), 88 (5), 59 (5).

(*S*)-*N*,*N*'-(propane-1,2-diyl)bis(1*H*-indole-7-carboxamide) (10i). Yield: 63 mg (39 %), beige solid, m.p. 45-147 °C. $[\alpha]_D^{20}$ = -20.0 (*c* 0.25, CH_2Cl_2). R_f (25 % $CHCl_3$, 75 % EtOAc) 0.66. δ_H (400 MHz, $CDCl_3$) 10.26 (1H, brs, indole-NH), 10.24 (1H, brs, indole-NH), 7.74–7.70 (2H, m, indole-H), 7.48-7.30 (4H, m, indole-H), 7.22 (2H, brs, indole-H), 7.02–6.96 (2H, m, indole-Ar), 6.51 (2H, brs, NH), 4.42–4.40 (1H, m, alkyl-CH_2), 3.69–3.64 (1H, m, alkyl-CH_2), 3.52–3.48 (1H, m, alkyl-CH_2), 1.29 (3H, d, 6.6 Hz, CH_3). δ_C (100.6 MHz, $CDCl_3$) 169.5, 168.9, 135.40, 135.43, 129.61, 129.63, 125.7 (double intensity), 125.00, 125.02, 119.5 (double intensity), 118.80, 118.84, 115.8, 115.7, 102.11, 102.13, 47.1, 46.2, 18.5. HRMS (ESI): *m*/*z* calcd. for $C_{21}H_{20}N_4O_2Na$ $[M+Na]^+$ 383.1478; found 383.1477.

***N*,*N*'-((1*S*,2*S*)-cyclohexane-1,2-diyl)bis(1*H*-indole-7-carboxamide) (10j).** Yield: 39 mg (16 %), yellow oil. $[\alpha]_D^{20}$ = + 10.0 (*c* 0.5, CH_2Cl_2). R_f (75 % $CHCl_3$, 25 % EtOAc) 0.45. δ_H (400 MHz, $CDCl_3$) 10.13 (2H, brs, indole-NH), 7.73 (2H, d, 7.8 Hz, indole-H), 7.42 (2H, d, 7.4 Hz, indole-H), 7.24–7.20 (2H, m, indole-H), 7.17–7.11 (2H, brs, indole-H), 7.04 (2H, t, 7.7 Hz, indole-H), 6.49–6.48 (2H, m, NH), 4.05 (2H, brs, alkyl-$(CH)_2$, 2.29 (2H, d, 7.6 Hz, alkyl-$(CH)_2$), 1.86-1.84 (2H, m, alkyl-$(CH)_2$), 1.45–1.44 (4H, m, alkyl-$(CH)_2$). δ_C (100.6 MHz, $CDCl_3$) 168.9, 135.4, 129.6, 125.6, 125.0, 119.4, 118.8, 115.9, 102.0, 54.6, 32.6, 24.9. HRMS (ESI): m/z calcd. for $C_{24}H_{24}N_4O_2Na$ $[M+Na]^+$ 423.1797; found 423.1797.

***N*,*N*'-(1,1'-binaphthyl-2,2'-diyl)bis(1*H*-indole-7-carboxamide) (10k).** 82 mg (32 %), beige solid, m.p. > 250 °C. $[\alpha]_D^{20}$ = - 70.0 (*c* 1.0, CH_2Cl_2). R_f (90 % $CHCl_3$, 10 % EtOAc) 0.92. δ_H (400 MHz, $CDCl_3$) 10.04 (2H, brs, indole-NH), 8.72 (2H, d, 9.0 Hz,), 8.16 (2H, d, 9.0 Hz,), 8.04–8.00 (4H, m,), 7.68 (2H, d, 7.8 Hz,), 7.49 (2H, t, J = 7.6 Hz,), 7.35 (2H, t, J = 7.6 Hz,), 7.28 (2H, d, J = 8.7 Hz,), 7.23–7.20 (2H, m,), 6.82 (2H, t, J = 7.7 Hz,), 6.49-6.45 (4H, m,). δ_C (100.6 MHz, $CDCl_3$) 166.4, 135.5, 135.2, 132.5, 131.5, 130.3, 129.6, 128.7, 127.9, 125.9, 125.8, 125.5, 125.2, 121.7, 121.1, 119.1, 118.9, 115.8, 102.2. HRMS (ESI): m/z calcd. for $C_{38}H_{27}N_4O_2$ $[M+H]^+$ 571.2129; found 571.2131.

***N*-(2'-amino-1,1'-binaphthyl-2-yl)-1*H*-indole-7-carboxamide (11k).** Yield: 55 mg (29 %), beige solid, m.p 118-120 °C. $[\alpha]_D^{20}$: - 50.0 (*c* 1.0, CH_2Cl_2). R_f (90 % $CHCl_3$, 10 % EtOAc) 0.75. δ_H (400 MHz, $CDCl_3$) 10.20 (1H, brs, indole-NH), 8.90 (1H, d, 9.0 Hz,), 8.18 (1H, brs, indole-NH), 8.09 (1H, d, 9.2 Hz,), 7.96 (1H, d, 8.0 Hz,), 7.91 (1H, d, 8.7 Hz,), 7.85 (1H, d, 8.0 Hz,), 7.68 (1H, d, 7.8 Hz,), 7.48–7.43 (1H, m,), 7.33–7.27 (4H, m,), 7.24–7.16 (m, 2H), 7.02 (1H, d, 8.2 Hz,), 6.81 (1H, t, 7.7 Hz,), 6.51 (1H, brs, amide-NH), 6.44 (1H, d, 7.5 Hz,), 3.75 (2H, s,). δ_C (100.6 MHz, $CDCl_3$) 166.1, 156.5, 142.9, 135.5, 135.2, 133.7, 132.8, 131.4,

130.8, 129.60, 129.64, 128.51, 128.53, 127.7, 127.1, 125.8, 125.7, 125.3, 125.2, 123.8, 123.1, 120.9, 120.5, 119.0, 118.9, 118.2, 116.4, 110.5, 102.2. HRMS (ESI): m/z calcd. for $C_{29}H_{22}N_3O$ $[M+H]^+$ 428.1757; found 428.1756.

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