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Substrate scope in the copper-mediated construction of bis-oxindoles via a double C–H/Ar–H coupling process

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Dedicated to the memory of Alan Katritzky: inspirational giant of heterocyclic chemistry, collaborator, and friend

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ABSTRACT

The synthesis of bis-oxindoles via the copper(II)-mediated double cyclisation of linear bis-anilides is described. $Cu(OAc)_2 \cdot H_2O$ was identified as an efficient and inexpensive catalyst for this process. In contrast to previous methods, which rely on the synthesis of the central core from existing oxindole building blocks, this new approach focusses on concurrent formation of both oxindole rings from a simple linear precursor, allowing the formation of bis-oxindoles containing a diverse range of cyclic and acyclic linkers using a single synthetic method.

1. Introduction

The oxindole motif has long been the subject of considerable attention due to its prevalence in natural and unnatural compounds with varied and extensive biological activities.[1] More recently, bis-oxindoles have emerged as interesting yet synthetically challenging targets owing to their complex polycyclic architecture. Some biologically active spirocyclic bis-oxindoles include the synthetic anti-bacterial/anti-cancer spirooxindole-pyrrolidine **1**,[2] naturally occurring anti-inflammatory geleganimine B **2**,[3] and cholinesterase inhibitor **3** (Fig. 1).[4] Non-spirocyclic bis-oxindole **4** has also been shown to possess potent anti-bacterial activity against both Gram positive and Gram negative organisms.[5] Moreover, bis-oxindoles (e.g., **5**) have been used extensively as key intermediates in the total synthesis of the cyclotryptamine[6] and related[7] alkaloids.

Given the demonstrated utility of bis-oxindoles, coupled with the synthetic challenge of preparing complex polycyclic scaffolds containing multiple stereogenic centres, it is not surprising that a number of approaches to these intriguing heterocycles have been reported.[8] Some representative examples of bis-spirooxindoles, containing various core ring sizes and linkers, are shown in Fig. 2. These have been prepared by cascade reactions[9] (e.g., **6**, **8**, and **9**), photochemical [2+2]-cycloadditions[10] (e.g., **7**), and by condensation onto isatin-based imines[11] (e.g., **10**). It is noteworthy that excellent control over both relative and absolute stereochemistry can often be achieved in such systems.

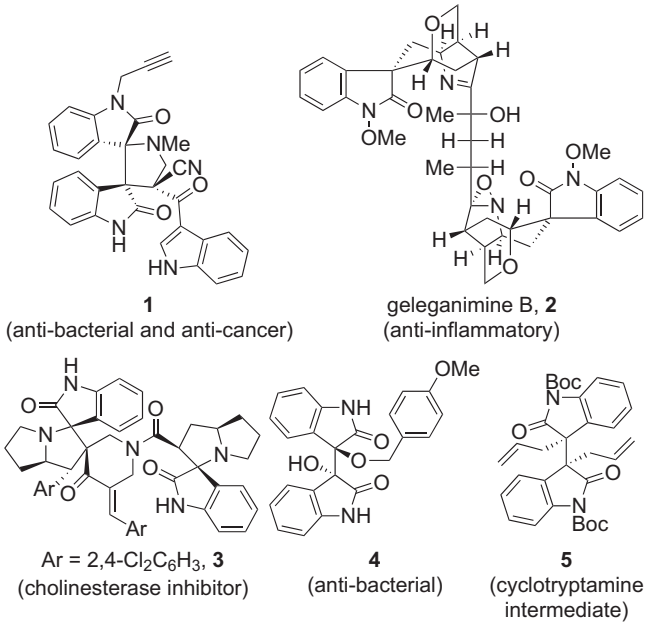

Fig. 1. Examples of valuable bis-oxindoles.

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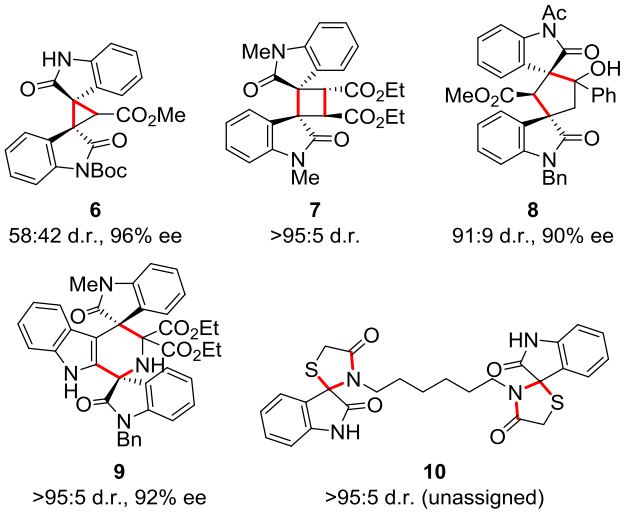
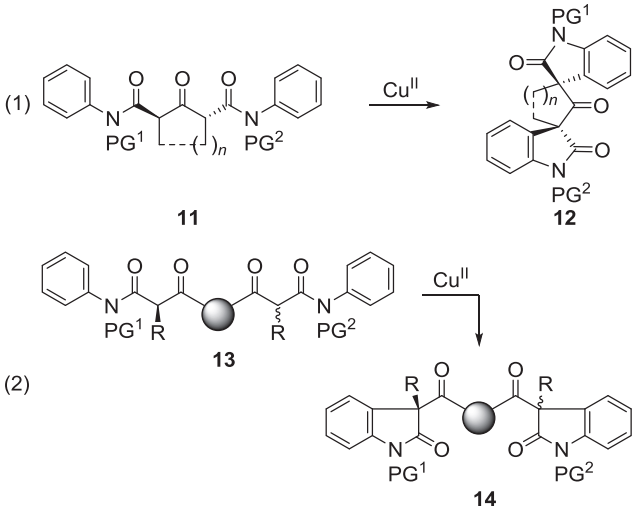


Fig. 2. Examples of bis-spirooxindoles prepared by elaboration of pre-formed oxindoles. Bonds formed in the cyclisation process are shown in red.

However, regardless of the structural diversity of bis-oxindoles that can be accessed via these different synthetic manifolds, the previous approaches all rely on a single overall strategy: i.e., synthesis of the central core from pre-existing oxindole building blocks, often derived from isatin.

We have previously demonstrated the efficient synthesis of oxindoles from linear anilides in high yield via a copper(II)-mediated formal C–H/Ar–H coupling reaction,[12] and subsequently reported preliminary studies, which took advantage of this method to provide access to bis-spirooxindoles with complete control of diastereoselectivity (Scheme 1, Eq. 1).[13] We now wish to disclose full results on the copper(II)-mediated double cyclisation of readily available linear bis-anilides, which offers a fundamentally different approach to the synthesis of bis-oxindoles by simultaneous formation of both oxindole rings around an existing central linker (Scheme 1, Eqs. 1 and 2). In addition to detailed experimental procedures, 15 previously unreported cyclisations are included in this publication.

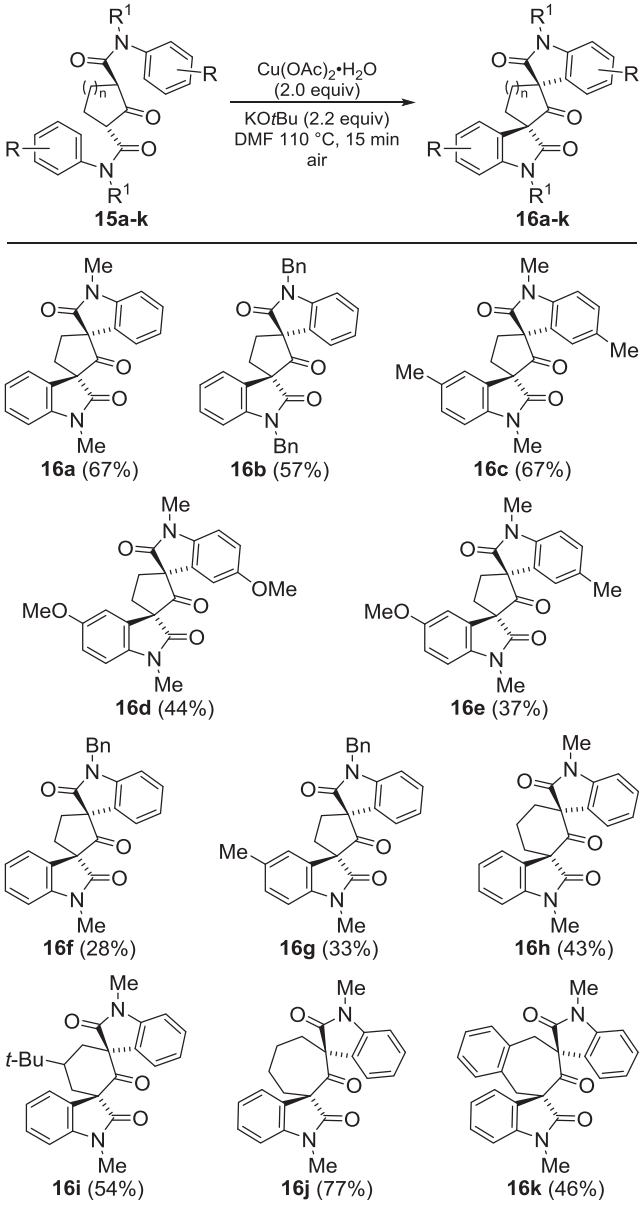


Scheme 1. Bis-anilide double cyclisation strategy for the synthesis of bis-oxindoles.

2. Results and discussion

2.1. Synthesis of spirocyclic bis-oxindoles

In our preliminary studies,[13] we focussed on the synthesis of spirocyclic bis-oxindoles **16a**–**k** by the copper-mediated double cyclisation of linear bis-anilides **15a**–**k** in moderate to good yields (Scheme 2). These results are reproduced here, and warrant only brief comment. Optimisation studies carried out for the cyclisation of cyclopentanone 2,5-dicarboxamide **15a** showed that the preferred reaction conditions involved $Cu(OAc)_2 \cdot H_2O$ (2.2 equiv) and KO*t*Bu (2.2 equiv) in DMF at 110 °C for 15 min, delivering the desired bis-spirooxindole **16a** in 67% isolated yield and as a single diastereomer. The *trans*-relationship of the carboxamides present in both the linear bis-anilide **15a** and bis-oxindole **16a** was confirmed unambiguously by X-ray crystallography (Fig. 3). We also examined the scope of this copper-mediated double cyclisation, exemplified by the synthesis of symmetrical (**16b**–**d**) and un-



Scheme 2. Substrate scope in the synthesis of spirocyclic bis-oxindoles. All compounds were isolated as single diastereomers.

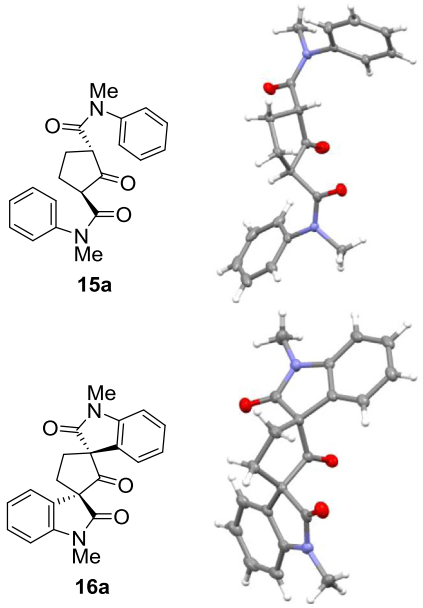


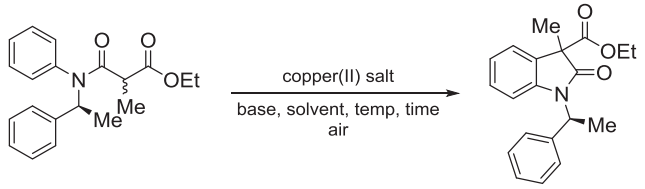
Fig. 3. Crystal structures of *trans*-cyclopentanone 2,5-dicarboxamide **15a** and spirocyclic bis-oxindole **16a** (50% probability ellipsoids).

symmetrical (**16e**–**g**, differentiated by both ring substitution and nitrogen protecting group) bis-oxindoles, as well as those containing varying core ring sizes (**16h**–**k**). Key features of this method include the inexpensive copper salt used, the short reaction time, broad diversity in the cyclic linker, and high diastereoselectivity observed in the cyclisation.

2.2. Towards a copper-mediated cyclisation approach to enantioenriched spirocyclic bis-oxindoles

In a new aspect to this work, we wished to explore the potential of extending the diastereoselective copper-mediated double cyclisation to the enantioselective synthesis of spirocyclic bis-oxindoles. Jones and McCarthy have reported the use of the α-methylbenzyl group as a chiral auxiliary on nitrogen in the radical cyclisation of *N*-arylacrylamides to give enantioenriched 3,3-disubstituted oxindoles, albeit in a moderate 39% ee after removal of the auxiliary.[14] It was anticipated that a similar approach might be successful in our process. To test this hypothesis, model linear anilide **17** bearing an (*S*)-α-methylbenzyl group was prepared in 68% yield via Mukaiyama coupling of the requisite aniline and carboxylic acid. The copper-mediated cyclisation of **17** was then carried out under several different sets of conditions to examine the effect on the diastereoselectivity of the reaction (Table 1). In the event, the highest chemical yield of **18** was observed in toluene at 110 °C (entry 2). Of greater import, a slight bias in favour of one diastereomer was observed in all cases, providing encouragement for the potential success of this approach in the synthesis of the sterically more encumbered bis-spirooxindoles.

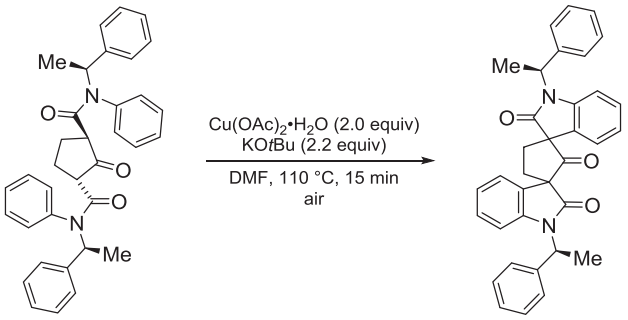
Table 1
Cyclisation of linear anilide **17**



17 **18**

Entry	Conditions	Yield (%)	dr
1	$Cu(OAc)_2 \cdot H_2O$ (1 equiv), KO*t*Bu, DMF, 110 °C, 1 h	26	44:56
2	$Cu(OAc)_2 \cdot H_2O$ (1 equiv), toluene, 110 °C, 18 h	76	44:56
3	$Cu(OAc)_2 \cdot H_2O$ (1 equiv), mesitylene, 170 °C, 1.5 h	55	45:55

The linear bis-anilide precursor **19** containing the (*S*)-α-methylbenzyl chiral auxiliary on both nitrogen atoms was therefore prepared in analogous fashion to **15a**. Cyclisation of **19** under the optimised conditions for bis-spirooxindole formation delivered **20** in 46% yield as an inseparable mixture of diastereomers in a 44:56 ratio (Scheme 3), similar to **18** above.



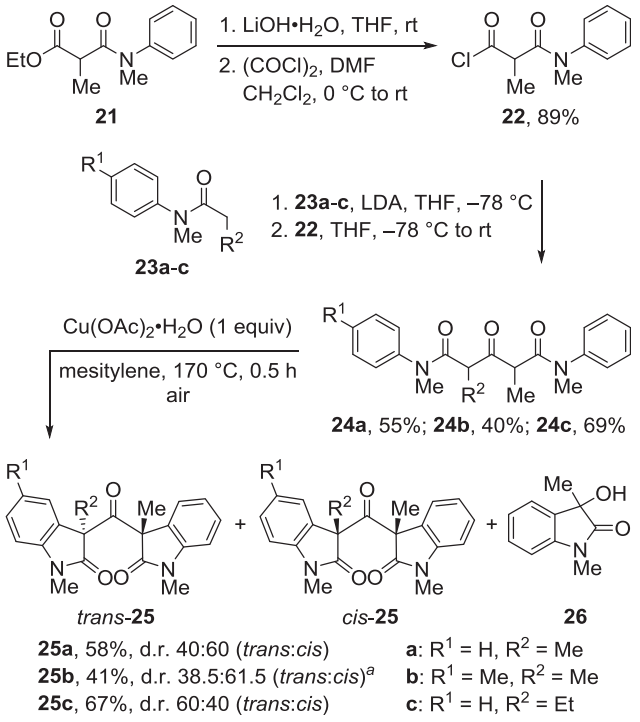
Scheme 3. Cyclisation of linear bis-anilide **19**.

Despite the rather disappointing diastereoselectivity imparted by the (*S*)-α-methylbenzyl group, these preliminary results show promise for future improvement through optimisation of the chiral auxiliary and reaction conditions.

2.3. Synthesis of bis-oxindoles with an acyclic monoketone linker

Having established the utility of the double cyclisation of linear bis-anilides for the synthesis of spirocyclic bis-oxindoles, attention turned to expanding the scope of this method to include substrates containing an acyclic linker. The required cyclisation precursors were easily prepared in three steps from known ester **21** (Scheme 4).[12a] Thus, saponification of the ester moiety in **21** followed by treatment with oxalyl chloride delivered acid chloride **22**, which was sufficiently stable to allow storage at −10 °C for several months without degradation. Treatment of anilides **23a**–**c** with LDA, followed by addition of the acid chloride **22** delivered the target linear bis-anilides **24a**–**c** in 40–69% yield. Crucially, this stepwise strategy provided access to unsymmetrical substrates differentiated by ring substitution (**24b**, R^1=Me), and at the carbonyl α-position (**24c**, R^2=Et).

Cyclisation of **24a** in the presence of $Cu(OAc)_2 \cdot H_2O$ (2 equiv) and KO*t*Bu (2.2 equiv) in DMF at 110 °C for 1 h delivered the desired bisoxindole **25a** as a mixture of diastereomers, along with significant quantities of an oxidative cleavage by-product, namely *N*-methyl 3-hydroxy-3-methyloxindole **26** (*trans*-**25a**/*cis*-**25a**/**26** molar ratio=1:3:1). Pleasingly, formation of this by-product can be minimised by performing the reaction without base in mesitylene at 170 °C for 30 min, giving bis-oxindole **25a** as a separable 40:60 mixture of *trans*/*cis*-diastereomers in 58% combined yield. The small amount of hydroxyindole **26** formed in this reaction was easily removed during the workup by washing with 4 M NaOH solution. Unsymmetrical bisoxindole **25b** was prepared in similar fashion. Interestingly, changing one of the α-methyl groups to the bulkier ethyl group (**25c**, R^2=Et) prompted a change in selectivity,



Scheme 4. Synthesis of bis-oxindoles with an acyclic monoketone linker. [a]2 equiv of $Cu(OAc)_2 \cdot H_2O$ was used with a reaction time of 3 h.

with *trans*-**25c** isolated as the major product. The relative stereochemistries in *trans*-**25a**, *trans*-**25c** and *cis*-**25c** were all confirmed by X-ray crystallography (Fig. 4).

The moderate diastereoselectivities observed in the synthesis of bis-oxindoles **25a**–**c** containing a flexible acyclic linker highlights the key role played by the more rigid cyclic core in spirocyclic bis-oxindoles **16a**–**k**, which serves to more efficiently relay stereochemical information during the cyclisation, leading to the complete diastereoselectivity observed in the latter case.

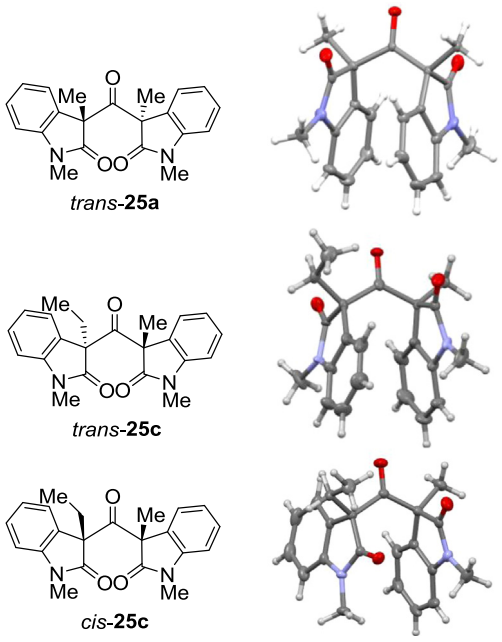


Fig. 4. Crystal structures of *trans*-**25a**, *trans*-**25c** and *cis*-**25c** (50% probability ellipsoids).

2.4. Synthesis of bis-oxindoles with diketone linkers

With the synthesis of bis-oxindoles separated by a one-carbon ketone linker established via this copper-mediated double cyclisation, we next sought to extend the scope to incorporate linkers of varying chain lengths. The required linear substrates were easily prepared via reaction of diacid chlorides **27** with 2.4 equiv of the enolate derived from anilides **23** (Scheme 5). This flexible approach provided rapid access to cyclisation precursors containing a diverse array of central linkers incorporating various aliphatic chains (**28a**–**d**), an adamantane (**28e**) and aromatic rings (**28f**–**j**). In most cases an inseparable 50:50 mixture of *dl*/*meso*-diastereomers was obtained, which is inconsequential for the subsequent cyclisation. The exception was malonate-derived substrate **28a**, where the diastereomers were separable by column chromatography, giving *meso*-**28a** and *dl*-**28a** in 32% and 27% yields, respectively. The relative stereochemistry in *meso*-**28a** and *dl*-**28a** was assigned based on the characteristic signals for the *gem*-dimethyl group in the ^{1}H NMR spectrum (2×3H singlets at δ_H 1.42 and 1.23 for *meso*-**28a**, 1×6H singlet at δ_H 1.21 for *dl*-**28a**). In addition, the structure of *dl*-**28a** was confirmed by X-ray crystallography (Fig. 5).

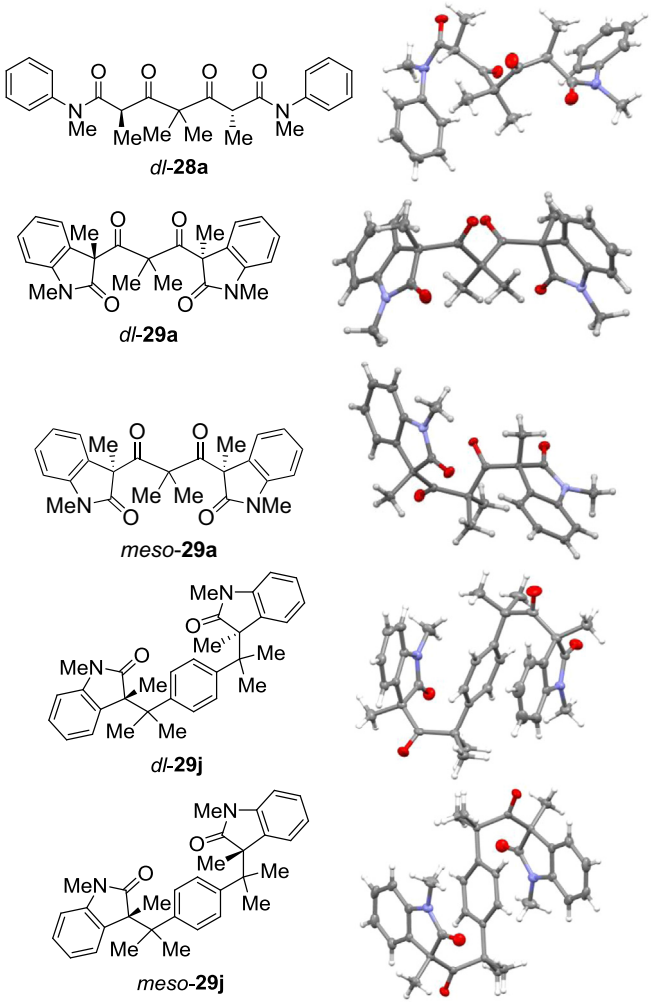
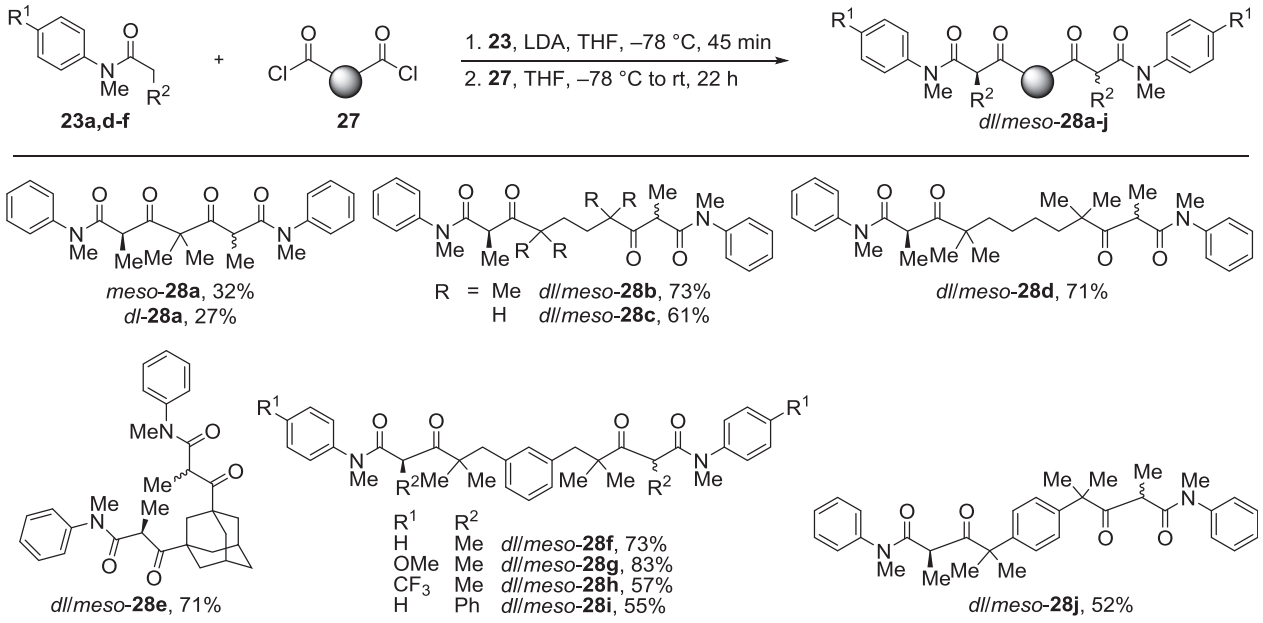


Fig. 5. Crystal structures of *dl*-**28a**, *dl*-**29a**, *meso*-**29a**, *dl*-**29j** and *meso*-**29j** (50% probability ellipsoids).

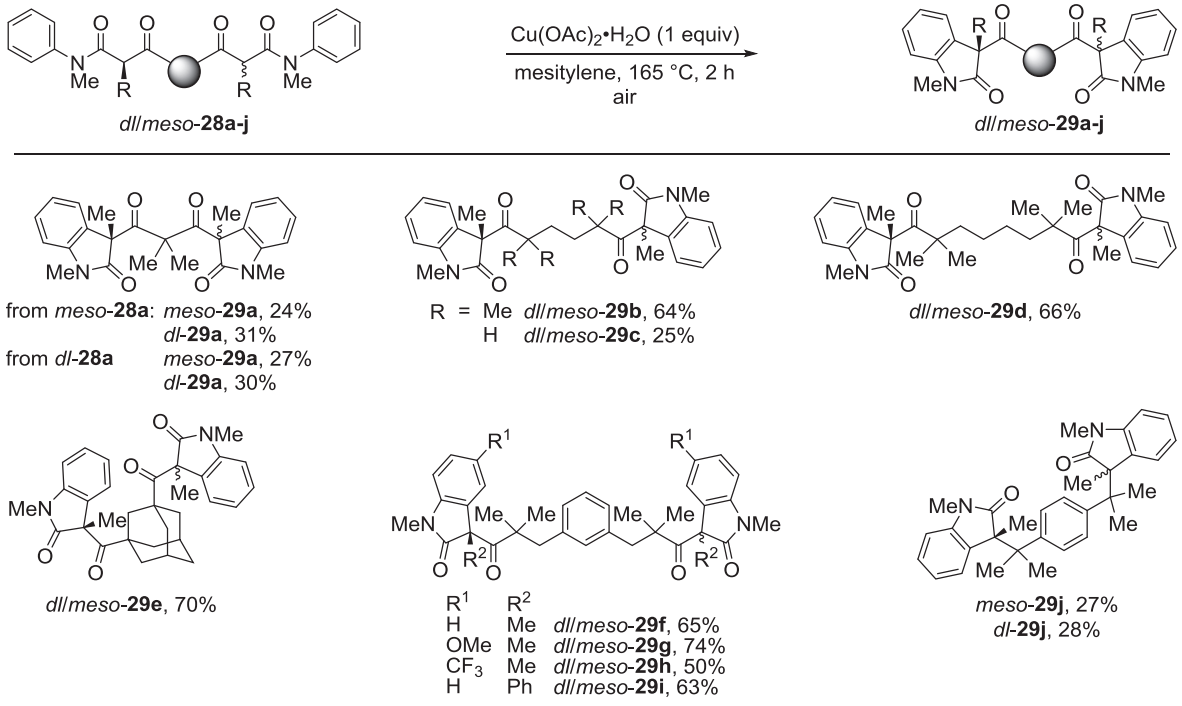
As expected, cyclisation of *meso*-**28a** occurred smoothly on heating in the presence of $Cu(OAc)_2 \cdot H_2O$ (1 equiv) in mesitylene, giving a separable 44:56 mixture of *meso*-**29a** and *dl*-**29a** in a combined 55% yield (Scheme 6). The same result was obtained



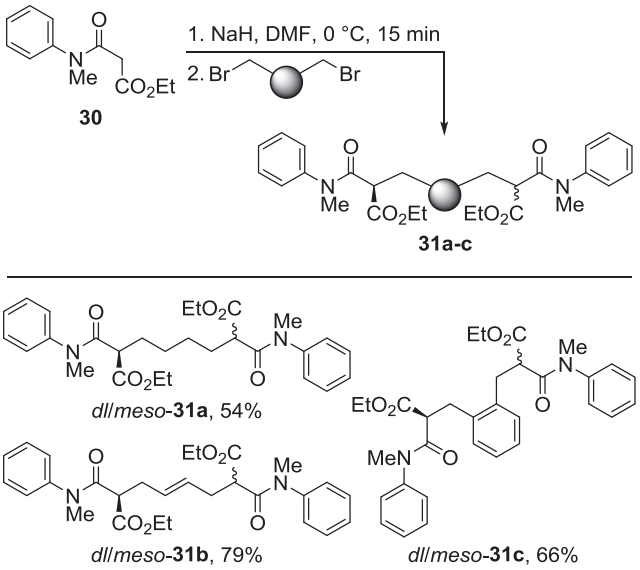
Scheme 5. Synthesis of bis-oxindole linear precursors. With the exception of **28a**, all compounds were isolated as an inseparable 50:50 mixture of *dl*/*meso*-diastereomers.

when *dl*-**28a** was used as the substrate. Once again, the structures of *meso*-**29a** and *dl*-**29a** were confirmed by the characteristic ^{1}H NMR signals for the *gem*-dimethyl group, as well as by X-ray crystallography (Fig. 5). Variation in the aliphatic linker chain length was also tolerated, delivering bis-oxindoles **29b**–**d** as mixtures of diastereomers. Replacement of the *gem*-dimethyl groups in **29b** with methylene groups (**29c**, R=H) results in a significant reduction in yield, highlighting the preference for substitution at the carbonyl α-positions to avoid decomposition.

More complex linkers were also well tolerated, exemplified by the synthesis of adamantane **29e** in 70% yield. Bis-oxindoles **29f**–**i**, incorporating an aromatic linker derived from the well-known rhodium ligand α,α,α′,α′-tetramethyl-1,3-benzenedipropionic acid (H_2esp),[15] could be also prepared in similar fashion. It is noteworthy that substitution on the aromatic ring with both electron-donating (**29g**, R^1=OMe) and electron-withdrawing groups (**29h**, R^1=CF_3), or replacement of the oxindole C-3/C-3′ methyl groups with an aromatic ring (**29i**, R^2=Ph) all resulted in successful cyclisation reactions. Aromatic-linked bis-oxindoles *meso*-**29j** and *dl*-**29j** proved separable by column chromatography. However, determination of the relative stereochemistry proved difficult by NMR spectroscopy alone, necessitating their characterisation by X-ray crystallography (Fig. 5).



Scheme 6. Synthesis of bis-oxindoles with diketone linkers. With the exception of **29a** and **29j**, all compounds were isolated as an inseparable 50:50 mixture of *dl*/*meso*-diastereomers.

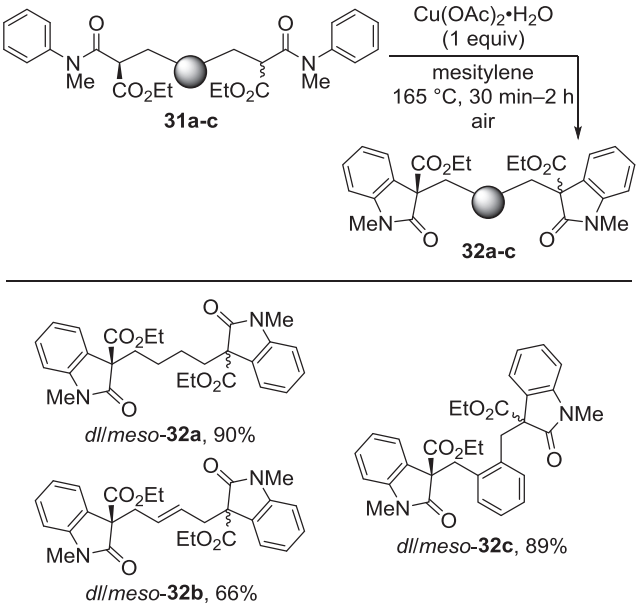


Scheme 7. Synthesis of ester-containing linear precursors. All compounds were isolated as an inseparable 50:50 mixture of *dl*/*meso*-diastereomers.

2.5. Synthesis of ester-containing bis-oxindoles

In a final new aspect to this work, we wished to explore the effect of moving the required electron-withdrawing group from the linker into the C-3 position of the oxindole. The required linear precursors **31a**–**c** were rapidly prepared from anilide **30** by deprotonation with NaH followed by introduction of the requisite dibromide (Scheme 7).

In the event, cyclisation of **31a**–**c** under the optimised conditions delivered bis-oxindoles containing aliphatic (**32a**), olefinic (**32b**) and aromatic (**32c**) linkers in good to excellent yield (Scheme 8).



Scheme 8. Synthesis of ester-containing bis-oxindoles. All compounds were isolated as an inseparable 50:50 mixture of *dl*/*meso*-diastereomers.

3. Conclusions

In conclusion, we have developed a concise synthesis of bis-oxindoles from linear bis-anilides via a copper(II)-mediated formal C–H/Ar–H coupling process. Highlights of this method include the inexpensive copper salt used, the short reaction times and the complete diastereoselectivity observed in the synthesis of spirocyclic bis-oxindoles containing various core ring sizes. Furthermore, we are able to prepare bis-oxindoles connected by diverse acyclic linkers using this single synthetic method.

This simple double cyclisation represents a fundamentally different approach to the synthesis of bis-oxindoles by simultaneous formation of both oxindole rings around an existing central linker. We anticipate that this method should find ready application in the synthesis of complex bis-oxindoles, efforts towards which are underway in our laboratory.

4. Experimental

4.1. General information

Except where stated, all reagents were purchased from commercial sources and used without further purification. Anhydrous solvents (CH_2Cl_2, toluene, DMF) were obtained from an Innovative Technologies solvent purification system. Anhydrous THF was obtained by distillation over sodium benzophenone ketyl immediately before use. NMR spectra were recorded on a JEOL spectrometer operating at 400 MHz (^{1}H) and 100 MHz (^{13}C). All spectral data were acquired at 295 K. Chemical shifts (δ) are quoted in parts per million (ppm). The residual solvent peak, δ_H 7.26 ($CHCl_3$) and δ_C 77.0 ($CDCl_3$) was used as a reference. Coupling constants (J) are reported in hertz (Hz) to the nearest 0.1 Hz. The multiplicity abbreviations used are: s singlet, d doublet, t triplet, q quartet, m multiplet, br broad. Signal assignment was achieved by analysis of DEPT, COSY, NOESY, HMBC and HSQC experiments where required. Infrared (IR) spectra were recorded neat on a Perkin–Elmer Spectrum Two FTIR-ATR spectrometer. Mass-spectra (low- and high-resolution) were obtained using electrospray ionisation (ESI) on a Micro-TOF spectrometer. Melting points were recorded in capillary tubes on a Gallenkamp apparatus and are uncorrected. Thin layer chromatography was carried out on silica gel 60F254 pre-coated aluminium foil sheets and were visualised using UV light (254 nm) and stained with either basic aq potassium permanganate, ethanolic *p*-anisaldehyde or ammonium molybdate as appropriate. Flash column chromatography was carried out using slurry packed silica gel (SiO_2), 35–75 Dm particle size, 60 Å pore size, under a light positive pressure, eluting with the specified solvent system.

4.2. General procedure 1 for the formation of spirocyclic bis-oxindoles 16a–k

To a stirred solution of the bis-anilide **15** (1 equiv) in DMF (0.02–0.06 M) were added $Cu(OAc)_2 \cdot H_2O$ (2 equiv) and KO*t*Bu (2.2 equiv). The reaction mixture was stirred at 110 °C for 15 min under an atmosphere of air and allowed to cool to room temperature. An aq solution of 10% NH_4OH (2×5 mL) was added and the aqueous phase was extracted with EtOAc (2×5 mL). The combined organic phases were washed with water (4×5 mL), and brine (5 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. The ^{1}H NMR spectrum of the crude reaction mixture showed only the *trans*-diastereoisomer present. The residue was purified by column chromatography (SiO_2, hexane/EtOAc) to give the *title compound* **16**.

*4.2.1. (trans)-1,1″-Dimethyl-1,1″,2,2″-tetrahydrodispiro[indole-3,1′-cyclopentane-3′,3″-indole]-2,2′,2″-trione (**16a**).* Bis-anilide **15a** (27.4 mg, 0.078 mmol), $Cu(OAc)_2 \cdot H_2O$ (32.2 mg, 0.161 mmol) and KO*t*Bu (18.8 mg, 0.168 mmol) in DMF (3 mL) were subjected to general procedure 1. The residue was purified by column chromatography (SiO_2, hexane/EtOAc, 4:1) to give the *title compound* **16a** (18.2 mg, 67%) as a colourless solid, mp 184–186 °C; R_f 0.42 (hexane/EtOAc, 1:1); ν_{max} (ATR, cm^{-1}) 1751, 1704, 1612, 1493, 1471, 1370, 1347, 1266, 1070, 885, 752; δ_H (400 MHz, $CDCl_3$) 7.43 (2H, dd, J=7.6,

1.2 Hz, C*H*), 7.31 (2H, td, *J*=7.6, 1.2 Hz, C*H*), 7.10 (2H, td, *J*=7.6, 1.2 Hz, C*H*), 6.84 (2H, d, *J*=7.6 Hz, C*H*), 3.21 (6H, s, CH_3), 3.15–3.10 (2H, m, CH_2), 2.78–2.72 (2H, m, CH_2); δ_C (100 MHz, $CDCl_3$) 208.0 (*C*), 175.0 (*C*), 144.4 (*C*), 129.8 (*C*), 129.1 (CH), 124.3 (*C*H), 123.6 (*C*H), 108.4 (*C*H), 63.7 (*C*), 32.4 (CH_2), 26.6 (CH_3); HRMS (ESI): MNa^+, found 369.1213. $[C_{21}H_{18}N_2NaO_3]^+$ requires 369.1210. CCDC 1004040 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

*4.2.2. (trans)-1,1″-Dibenzyl-1,1″,2,2″-tetrahydrodispiro[indole-3,1′-cyclopentane-3′,3″-indole]-2,2′,2″-trione (**16b**).* Bis-anilide **15b** (14.7 mg, 0.029 mmol), $Cu(OAc)_2 \cdot H_2O$ (11.6 mg, 0.058 mmol) and KO*t*Bu (7.22 mg, 0.064 mmol) in DMF (1.5 mL) were subjected to general procedure 1. The residue was purified by column chromatography (SiO_2, hexane/EtOAc, 4:1) to give the *title compound* **16b** (8.2 mg, 57%) as a pale yellow solid, mp 115–117 °C; R_f 0.50 (hexane/EtOAc, 2:1); ν_{max} (ATR, cm^{-1}) 1740, 1703, 1612, 1488, 1467, 1455, 1359, 1311, 1178, 873, 752, 734; δ_H (400 MHz, $CDCl_3$) 7.48 (2H, dd, *J*=7.6, 1.0 Hz, C*H*), 7.34–7.30 (4H, m, C*H*), 7.30–7.27 (6H, m, C*H*), 7.19 (2H, td, *J*=7.6, 1.0 Hz, C*H*), 7.07 (2H, td, *J*=7.6, 1.0 Hz, C*H*), 6.70 (2H, d, *J*=7.6 Hz, C*H*), 5.02 (2H, d, *J*=15.9 Hz, CH_2), 4.83 (2H, d, *J*=15.9 Hz, CH_2), 3.26–3.15 (2H, m, CH_2), 2.93–2.81 (2H, m, CH_2); δ_C (100 MHz, $CDCl_3$) 208.0 (*C*), 175.2 (*C*), 143.5 (*C*), 135.3 (*C*), 129.8 (*C*), 129.1 (CH), 129.0 (CH), 127.8 (CH), 127.1 (CH), 124.4 (CH), 123.7 (CH), 109.5 (CH), 63.8 (*C*), 43.9 (CH_2), 32.5 (CH_2); HRMS (ESI): MNa^+, found 521.1825. $[C_{33}H_{26}N_2NaO_3]^+$ requires 521.1836.

*4.2.3. (trans)-1,1″,5,5″-Tetramethyl-1,1″,2,2″-tetrahydrodispiro[indole-3,1′-cyclopentane-3′,3″-indole]-2,2′,2″-trione (**16c**).* Bis-anilide **15c** (39.8 mg, 0.105 mmol), $Cu(OAc)_2 \cdot H_2O$ (43.7 mg, 0.219 mmol) and KO*t*Bu (25.8 mg, 0.230 mmol) in DMF (4 mL) were subjected to general procedure 1. The residue was purified by column chromatography (SiO_2, hexane/EtOAc, 4:1) to give the *title compound* **16c** (26.2 mg, 67%) as a colourless solid, mp 197–199 °C; R_f 0.60 (hexane/EtOAc, 1:2); ν_{max} (ATR, cm^{-1}) 1751, 1701, 1624, 1602, 1499, 1349, 1271, 1069, 918, 811; δ_H (400 MHz, $CDCl_3$) 7.24 (2H, dd, *J*=1.3, 0.6 Hz, C*H*), 7.10 (2H, ddd, *J*=7.9, 1.3, 0.6 Hz, C*H*), 6.72 (2H, d, *J*=7.9 Hz, C*H*), 3.19 (6H, s, CH_3), 3.17–3.04 (2H, m, CH_2), 2.77–2.64 (2H, m, CH_2), 2.33 (6H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 208.4 (*C*), 175.0 (*C*), 142.1 (*C*), 133.3 (*C*), 129.8 (*C*), 129.3 (CH), 125.1 (CH), 108.1 (CH), 63.8 (*C*), 32.5 (CH_2), 26.6 (CH_3), 21.2 (CH_3); HRMS (ESI): MNa^+, found 397.1506. $[C_{23}H_{22}N_2NaO_3]^+$ requires 397.1523.

*4.2.4. (trans)-5,5″-Dimethoxy-1,1″-dimethyl-1,1″,2,2″-tetrahydrodispiro[indole-3,1′-cyclopentane-3′,3″-indole]-2,2′,2″-trione (**16d**).* Bis-anilide **15d** (41.7 mg, 0.102 mmol), $Cu(OAc)_2 \cdot H_2O$ (41.1 mg, 0.206 mmol) and KO*t*Bu (25.6 mg, 0.228 mmol) in DMF (4 mL) were subjected to general procedure 1. The residue was purified by column chromatography (SiO_2, hexane/EtOAc, 4:1 to hexane/EtOAc, 2:1) to give the *title compound* **16d** (18.3 mg, 44%) as a colourless solid, mp 180–182 °C; R_f 0.46 (hexane/EtOAc, 1:2); ν_{max} (ATR, cm^{-1}) 1749, 1701, 1600, 1497, 1469, 1435, 1354, 1288, 1039, 811; δ_H (400 MHz, $CDCl_3$) 7.07 (2H, d, *J*=2.6 Hz, C*H*), 6.83 (2H, dd, *J*=8.4, 2.6 Hz, C*H*), 6.74 (2H, d, *J*=8.4 Hz, C*H*), 3.79 (6H, s, CH_3), 3.18 (6H, s, CH_3), 3.15–3.03 (2H, m, CH_2), 2.79–2.67 (2H, m, CH_2); δ_C (100 MHz, $CDCl_3$) 207.9 (*C*), 174.7 (*C*), 156.7 (*C*), 137.9 (*C*), 130.8 (*C*), 114.1 (CH), 111.1 (CH), 108.8 (CH), 64.1 (*C*), 56.0 (CH_3), 32.5 (CH_2), 26.6 (CH_3); HRMS (ESI): MNa^+, found 429.1433. $[C_{23}H_{22}N_2NaO_5]^+$ requires 429.1421.

*4.2.5. (trans)-5-Methoxy-1,1″,5″-trimethyl-1,1″,2,2″-tetrahydrodispiro[indole-3,1′-cyclopentane-3′,3″-indole-2,2′,2″-trione (**16e**).* Bis-anilide **15e** (51.0 mg, 0.130 mmol), $Cu(OAc)_2 \cdot H_2O$ (52.0 mg, 0.260 mmol), and KO*t*Bu (32.0 mg, 0.286 mmol) in DMF (4 mL) were subjected to general procedure 1. The crude product was purified by column chromatography (SiO_2, hexane/EtOAc, 4:1 to 1:1) to give the *title compound* **16e** (19.0 mg, 37%) as a colourless solid, mp 176–178 °C; R_f 0.48 (hexane/EtOAc, 3:2); ν_{max} (ATR, cm^{-1}) 2940, 1749, 1691, 1601, 1496, 1465, 1433, 1349, 1310, 1287, 1216, 1172, 1067, 1040, 1022, 845; δ_H (400 MHz, $CDCl_3$) 7.23–7.22 (1H, m, C*H*), 7.12–7.09 (2H, m, C*H*), 6.84 (1H, dd, *J*=8.4, 2.5 Hz, C*H*), 6.74 (1H, d, *J*=8.4 Hz, C*H*), 6.72 (1H, d, *J*=7.9 Hz, C*H*), 3.80 (3H, s, CH_3), 3.19 (3H, s, CH_3), 3.18 (3H, s, CH_3), 3.16–3.06 (2H, m, CH_2), 2.77–2.68 (2H, m, CH_2), 2.34 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 208.1 (*C*), 174.8 (*C*), 174.7 (*C*), 156.6 (*C*), 142.0 (*C*), 137.7 (*C*), 133.1 (*C*), 130.8 (*C*), 129.5 (*C*), 129.3 (CH), 124.9 (CH), 113.9 (CH), 111.1 (CH), 108.7 (CH), 108.0 (CH), 63.9 (*C*), 63.7 (*C*), 55.9 (CH_3), 32.4 (CH_2), 32.3 (CH_2), 26.5 (CH_3), 26.4 (CH_3), 21.1 (CH_3); HRMS (ESI): MH^+, found 391.1655. $[C_{23}H_{23}N_2O_4]^+$ requires 391.1652.

*4.2.6. (trans)-1-Benzyl-1″-methyl-di-1,1″,2,2″-tetrahydrodispiro[indole-3,1′-cyclopentane-3′,3″-indole]-2,2′,2″-trione (**16f**).* Bis-anilide **15f** (0.107 g, 0.250 mmol), $Cu(OAc)_2 \cdot H_2O$ (0.100 g, 0.500 mmol), and KO*t*Bu (62.0 mg, 0.550 mmol) in DMF (4 mL) were subjected to general procedure 1. The crude product was purified by column chromatography (SiO_2, hexane/EtOAc, 9:1 to 4:1) to give the *title compound* **16f** (29.1 mg, 28%) as a colourless solid, mp 92–94 °C; R_f 0.53 (hexane/EtOAc, 3:2); ν_{max} (ATR, cm^{-1}) 2934, 1752, 1697, 1610, 1488, 1466, 1345, 1309, 1253, 1176, 1079, 1030; δ_H (400 MHz, $CDCl_3$) 7.47 (1H, dd, *J*=7.4, 0.7 Hz, C*H*), 7.46 (1H, dd, *J*=7.4, 0.7 Hz, C*H*), 7.36–7.23 (6H, m, C*H*), 7.19 (1H, td, *J*=7.8, 1.2 Hz, C*H*), 7.12 (1H, td, *J*=7.6, 0.8 Hz, C*H*), 7.07 (1H, td, *J*=7.6, 0.8 Hz, C*H*), 6.86 (1H, d, *J*=7.7 Hz, C*H*), 6.70 (1H, d, *J*=7.7 Hz, C*H*), 4.99 (1H, d, *J*=15.9 Hz, CH_2), 4.85 (1H, d, *J*=15.9 Hz, CH_2), 3.23 (3H, s, CH_3), 3.20–3.12 (2H, m, CH_2), 2.87–2.77 (2H, m, CH_2); δ_C (100 MHz, $CDCl_3$) 207.9 (*C*), 175.2 (*C*), 174.8 (*C*), 144.3 (*C*), 143.4 (*C*), 135.2 (*C*), 129.7 (*C*), 129.6 (*C*), 129.0 (CH), 128.90 (CH), 128.86 (CH), 127.6 (CH), 127.0 (CH), 124.3 (CH), 124.2 (CH), 123.52 (CH), 123.49 (CH), 109.3 (CH), 108.3 (CH), 63.65 (*C*), 63.61 (*C*), 43.8 (CH_2), 32.4 (CH_2), 32.3 (CH_2), 26.5 (CH_3); HRMS (ESI): MNa^+, found 445.1516. $[C_{27}H_{22}N_2NaO_3]^+$ requires 445.1523.

*4.2.7. (trans)-1″-Benzyl-1,5-dimethyl-1,1″,2,2″-tetrahydrodispiro[indole-3,1′-cyclopentane-3′,3″-indole]-2,2′,2″-trione (**16g**).* Bis-anilide **15g** (0.116 g, 0.263 mmol), $Cu(OAc)_2 \cdot H_2O$ (0.105 g, 0.526 mmol), and KO*t*Bu (65.0 mg, 0.579 mmol) in DMF (8 mL) were subjected to general procedure 1. The crude product was purified by column chromatography (SiO_2, hexane/EtOAc, 1:4 to 1:1) to give the *title compound* **16g** (37.8 mg, 33%) as a colourless solid, mp 102–104 °C; R_f 0.51 (hexane/EtOAc, 3:2); ν_{max} (ATR, cm^{-1}) 2942, 1753, 1701, 1605, 1498, 1466, 1348, 1310, 1253, 1175, 1080, 1059, 1030; δ_H (400 MHz, $CDCl_3$) 7.51 (1H, dd, *J*=7.3, 0.6 Hz, C*H*), 7.34–7.29 (4H, m, C*H*), 7.27–7.23 (2H, m, C*H*), 7.19 (1H, td, *J*=7.7, 1.3 Hz, C*H*), 7.14–7.11 (1H, m, C*H*), 7.07 (1H, td, *J*=7.7, 0.9 Hz, C*H*), 6.74 (1H, d, *J*=7.9 Hz, C*H*), 6.68 (1H, d, *J*=7.7 Hz, C*H*), 5.00 (1H, d, *J*=16.0 Hz, CH_2), 4.85 (1H, d, *J*=16.0 Hz, CH_2), 3.25–3.09 (2H, m, CH_2), 3.20 (3H, s, CH_3), 2.86–2.74 (2H, m, CH_2), 2.35 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 208.1 (*C*), 175.3 (*C*), 174.7 (*C*), 143.4 (*C*), 141.9 (*C*), 135.1 (*C*), 133.2 (*C*), 129.8 (*C*), 129.5 (*C*), 129.3 (CH), 128.8 (CH), 127.6 (CH), 126.9 (CH), 124.8 (CH), 124.3 (CH), 123.5 (CH), 109.3 (CH), 108.0 (CH), 63.7 (*C*), 63.6 (*C*), 43.7 (CH_2), 32.4 (CH_2), 32.3 (CH_2), 26.4 (CH_3), 21.1 (CH_3); HRMS (ESI): MNa^+, found 459.1662. $[C_{28}H_{24}N_2NaO_3]^+$ requires 459.1679.

*4.2.8. (trans)-1,1″-Dimethyl-1,1″,2,2″-tetrahydrodispiro[indole-3,1′-cyclohexane-3′,3″-indole]-2,2′,2″-trione (**16h**).* Bis-anilide **15h** (33.3 mg, 0.091 mmol), $Cu(OAc)_2 \cdot H_2O$ (37.4 mg, 0.187 mmol) and KO*t*Bu (22.7 mg, 0.202 mmol) in DMF (3 mL) were subjected to general procedure 1. The residue was purified by column chromatography (SiO_2, hexane/EtOAc, 4:1) to give the *title compound* **16h** (14.2 mg, 43%) as a colourless solid, mp 210–212 °C; R_f 0.64 (hexane/EtOAc, 1:4); ν_{max} (ATR, cm^{-1}) 1705, 1688, 1610, 1494, 1471, 1372, 1348, 1266, 1105, 753; δ_H (400 MHz, $CDCl_3$) 7.57 (2H, dd, *J*=7.4, 1.2 Hz, C*H*), 7.28 (2H, dd, *J*=7.4, 1.2 Hz, C*H*), 7.07 (2H, td, *J*=7.4, 1.2 Hz, C*H*), 6.79 (2H,

d, J=7.4 Hz, C*H*), 3.17 (6H, s, CH_3), 2.50 (6H, s, CH_2); δ_C (100 MHz, $CDCl_3$) 203.2 (*C*), 175.8 (*C*), 143.9 (*C*), 132.9 (*C*), 128.7 (*C*H), 124.4 (*C*H), 123.4 (*C*H), 108.3 (*C*H), 62.3 (*C*), 33.5 (CH_2), 26.6 (CH_3), 17.1 (CH_2); HRMS (ESI): MNa^+, found 383.1370. $[C_{22}H_{20}N_2NaO_3]^+$ requires 383.1366.

*4.2.9. 5-tert-Butyl-(trans)-1,1″-dimethyl-1,1″,2,2″-tetrahydrodispiro[indole-3,1′-cyclohexane-3′,3″-indole]-2,2′,2″-trione (**16i**).* Bis-anilide **15i** (45.4 mg, 0.108 mmol), $Cu(OAc)_2 \cdot H_2O$ (43.8 mg, 0.219 mmol) and KO*t*Bu (25.6 mg, 0.228 mmol) in DMF (4.5 mL) were subjected to general procedure 1. The residue was purified by column chromatography (SiO_2, hexane/EtOAc, 4:1) to give the *title compound* **16i** (24.1 mg, 54%) as a colourless solid, mp 152–154 °C; R_f 0.48 (hexane/EtOAc, 1:2); ν_{max} (ATR, cm^{-1}) 1707, 1690, 1651, 1610, 1494, 1470, 1371, 1346, 1263, 753; δ_H (400 MHz, $CDCl_3$) 7.86 (1H, dd, J=7.6, 1.2 Hz, C*H*), 7.34 (1H, dd, J=7.6, 1.2 Hz, C*H*), 7.28 (1H, dd, J=7.6, 1.2 Hz, C*H*), 7.28 (1H, dd, J=7.6, 1.2 Hz, C*H*), 7.08 (1H, td, J=7.6, 1.2 Hz, C*H*), 7.07 (1H, td, J=7.6, 1.2 Hz, C*H*), 6.81 (1H, d, J=7.6 Hz, C*H*), 6.78 (1H, d, J=7.6 Hz, C*H*), 3.19 (3H, s, CH_3), 3.14 (3H, s, CH_3), 3.05–2.95 (1H, m, C*H*), 2.48 (1H, t, J=13.1 Hz, CH_2), 2.34 (2H, d, J=8.8 Hz, CH_2), 2.19 (1H, d, J=14.9 Hz, CH_2), 0.96 (9H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 203.9 (*C*), 176.4 (*C*), 175.5 (*C*), 143.9 (*C*), 143.8 (*C*), 133.9 (*C*), 132.7 (*C*), 128.8 (*C*H), 128.6 (*C*H), 124.7 (*C*H), 124.0 (*C*H), 123.5 (*C*H), 123.3 (*C*H), 108.4 (*C*H), 108.2 (*C*H), 63.3 (*C*), 61.9 (*C*), 37.5 (*C*H), 35.8 (CH_2), 35.6 (CH_2), 32.6 (*C*), 27.3 (CH_3), 26.7 (CH_3), 26.5 (CH_3); HRMS (ESI): MNa^+, found 439.2011. $[C_{26}H_{28}N_2NaO_3]^+$ requires 439.1992.

*4.2.10. (trans)-1,1″-Dimethyl-1,1″,2,2″-tetrahydrodispiro[indole-3,1′-cycloheptane-3′,3″-indole]-2,2′,2″-trione (**16j**).* Bis-anilide **15j** (24.5 mg, 0.065 mmol), $Cu(OAc)_2 \cdot H_2O$ (27.5 mg, 0.138 mmol) and KO*t*Bu (16.4 mg, 0.146 mmol) in DMF (2.5 mL) were subjected to general procedure 1. The residue was purified by column chromatography (SiO_2, hexane/EtOAc, 4:1) to give the *title compound* **16j** (18.8 mg, 77%) as a colourless solid, mp 196–198 °C; R_f 0.69 (hexane/EtOAc, 1:2); ν_{max} (ATR, cm^{-1}) 1701, 1682, 1608, 1493, 1470, 1373, 1347, 1260, 1126, 1079, 947, 753, 729; δ_H (400 MHz, $CDCl_3$) 7.36 (2H, d, J=7.6 Hz, C*H*), 7.23 (2H, td, J=7.6, 1.2 Hz, C*H*), 7.02 (2H, td, J=7.6, 1.2 Hz, C*H*), 6.76 (2H, d, J=7.6 Hz, C*H*), 3.20 (6H, s, CH_3), 2.85 (2H, br s, CH_2), 2.43 (2H, br t, J=9.0 Hz, CH_2), 2.07–1.94 (4H, m, CH_2); δ_C (100 MHz, $CDCl_3$) 174.9 (*C*), 142.8 (*C*), 132.0 (*C*), 128.5 (*C*H), 125.3 (*C*H), 122.9 (*C*H), 108.2 (*C*H), 67.9 (*C*), 33.9 (CH_2), 26.5 (CH_3), 24.2 (CH_2); HRMS (ESI): MNa^+, found 397.1510. $[C_{23}H_{22}N_2NaO_3]^+$ requires 397.1523.

*4.2.11. (trans)-1,1″-Dimethyl-1,1″,2,2″,7′,9′-hexahydro-5′H-dispiro[indole-3,6′-benzo[7]annulene-8′,3″-indole]2,2″,7′-trione (**16k**).* Bis-anilide **15k** (31.1 mg, 0.073 mmol), $Cu(OAc)_2 \cdot H_2O$ (30.2 mg, 0.151 mmol) and KO*t*Bu (19.1 mg, 0.170 mmol) in DMF (2 mL) were subjected to general procedure 1. The residue was purified by column chromatography (SiO_2, hexane/EtOAc, 4:1) to give the *title compound* **16k** (14.3 mg, 46%) as a yellow solid, mp 214–216 °C; R_f 0.50 (hexane/EtOAc, 1:1); ν_{max} (ATR, cm^{-1}) 1710, 1678, 1609, 1493, 1471, 1370, 1347, 1261, 1077, 1023, 910, 798, 752; δ_H (400 MHz, $CDCl_3$) 7.33 (2H, dd, J=5.4, 3.3 Hz, C*H*), 7.26 (2H, td, J=7.6, 1.2 Hz, C*H*), 7.16 (2H, dd, J=5.4, 3.3 Hz, C*H*), 7.04 (2H, d, J=7.6 Hz, C*H*), 6.98 (2H, td, J=7.6, 1.2 Hz, C*H*), 6.81 (2H, d, J=7.6 Hz, C*H*), 3.65 (2H, d, J=14.7 Hz, CH_2), 3.46 (2H, d, J=14.7 Hz, CH_2), 3.17 (6H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 205.2 (*C*), 174.9 (*C*), 143.9 (*C*), 135.9 (*C*), 132.5 (*C*), 130.8 (*C*H), 128.8 (*C*H), 127.7 (*C*H), 125.0 (*C*H), 123.1 (*C*H), 108.3 (*C*H), 65.7 (*C*), 38.0 (CH_2), 26.5 (CH_3); HRMS (ESI): MNa^+, found 445.1527. $[C_{27}H_{22}N_2NaO_3]^+$ requires 445.1523.

4.3. Synthesis of bis-oxindoles 18 and 20 bearing chiral auxiliaries

*4.3.1. Ethyl 3-methyl-2-oxo-1-[(1S)-1-phenylethyl]-2,3-dihydro-1H-indole-3-carboxylate (**18**).* To a stirred solution of anilide **17** (27.7 mg, 0.085 mmol) in toluene (2 mL) was added $Cu(OAc)_2 \cdot H_2O$ (17.7 mg, 0.089 mmol). The reaction mixture was stirred at 110 °C for 18 h under an atmosphere of air and allowed to cool to room temperature. The copper salt was removed by addition of an aq soln of NH_4OH (5 mL). The aqueous phase was extracted with EtOAc (2×5 mL). The combined organic extracts were washed with water (5 mL), and brine (5 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. The crude product was purified by column chromatography (SiO_2, hexane/EtOAc, 9:1) to give the *title compound* **18** (44:56, 21.0 mg, 76%) as a yellow oil; R_f 0.23 (hexane/EtOAc, 6:1); ν_{max} (ATR, cm^{-1}) 2982, 2936, 1741, 1714, 1607, 1484, 1467, 1350, 1237, 1190, 1112, 1019, 752, 698; δ_H (400 MHz, $CDCl_3$) 7.41–7.37 (1H, m, C*H*), 7.35–7.26 (4H, m, C*H*), 7.23 (0.45H, d, J=7.4 Hz, C*H*), 7.22 (0.55H, d, J=7.4 Hz, C*H*), 7.08–7.01 (1H, m, C*H*), 6.96 (0.45H, td, J=7.6, 1.0 Hz, C*H*), 6.96 (0.55H, td, J=7.6, 1.0 Hz, C*H*), 6.49 (0.45H, d, J=7.6 Hz, C*H*), 6.45 (0.55H, d, J=7.6 Hz, C*H*), 5.92 (0.55H, q, J=7.2 Hz, C*H*), 5.83 (0.45H, q, J=7.2 Hz, C*H*), 4.24–4.13 (1.1H, m, CH_2), 4.12–4.02 (0.9H, m, CH_2), 1.85 (1.35H, d, J=7.2 Hz, CH_3), 1.82 (1.65H, d, J=7.2 Hz, CH_3), 1.72 (1.35H, s, CH_3), 1.71 (1.65H, s, CH_3), 1.20 (1.65H, t, J=7.1 Hz, CH_3), 1.15 (1.35H, t, J=7.1 Hz, CH_3); δ_C (100 MHz, $CDCl_3$) 175.5 and 175.4 (*C*), 171.4 and 170.0 (*C*), 141.7 and 141.5 (*C*), 139.1 and 139.0 (*C*), 130.6 and 130.5 (*C*), 128.8 and 128.7 (*C*H), 128.56 and 128.55 (*C*H), 127.54 and 127.45 (*C*H), 126.7 and 126.6 (*C*H), 123.01 and 122.97 (*C*H), 122.52 and 122.50 (*C*H), 111.4 and 111.1 (*C*H), 62.1 and 62.0 (CH_2), 55.01 and 54.99 (*C*), 49.5 and 48.8 (*C*H), 20.0 and 19.7 (CH_3), 16.2 and 16.1 (CH_3), 13.94 and 13.92 (CH_3); HRMS (ESI): MNa^+, found 346.1406. $[C_{20}H_{21}NNaO_3]^+$ requires 346.1414.

*4.3.2. 1,1″-Bis[(1S)-1-phenylethyl]-1,1″,2,2″-tetrahydrodispiro[indole-3,1′-cyclopentane-3′,3″-indole]-2,2′,2″-trione (**20**).* To a stirred solution of bis-anilide **19** (35.9 mg, 0.068 mmol) in DMF (2 mL) was added $Cu(OAc)_2 \cdot H_2O$ (27.7 mg, 0.139 mmol) and KO*t*Bu (16.7 mg, 0.149 mmol). The reaction mixture was stirred at 110 °C for 15 min under an atmosphere of air and allowed to cool to room temperature. An aq solution of 10% NH_4OH (2×5 mL) was added and the aqueous phase was extracted with EtOAc (2×5 mL). The combined organic phases were washed with water (4×5 mL), and brine (5 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by column chromatography (SiO_2, hexane/EtOAc, 8:1) to give the *title compound* **20** (44:56, 16.4 mg, 46%) as a colourless solid, mp 66–68 °C; R_f 0.31 (hexane/EtOAc, 4:1); ν_{max} (ATR, cm^{-1}) 2981, 1755, 1700, 1608, 1484, 1466, 1348, 1310, 1254, 1052, 850, 752, 697; δ_H (400 MHz, $CDCl_3$) 7.50–7.45 (2H, m, C*H*), 7.36–7.26 (10H, m, C*H*), 7.10–7.00 (4H, m, C*H*), 6.51 (1.1H, d, J=7.1 Hz, C*H*), 6.44 (0.9H, dd, J=7.1, 0.7 Hz, C*H*), 5.78 (2H, pent, J=7.1 Hz, C*H*), 3.26–3.16 (2H, m, CH_2), 2.94–2.83 (2H, m, CH_2), 1.84 (3H, d, J=7.2 Hz, CH_3), 1.84 (3H, d, J=7.2 Hz, CH_3); δ_C (100 MHz, $CDCl_3$) 208.1 and 208.0 (*C*), 175.2 and 175.1 (*C*), 142.5 and 142.4 (*C*), 139.0 and 138.6 (*C*), 130.2 and 130.1 (*C*), 128.8 (*C*H), 128.6 (*C*H), 127.6 and 127.5 (*C*H), 126.6 (*C*H), 124.4 and 124.3 (*C*H), 123.24 and 123.19 (*C*H), 111.2 and 111.0 (*C*H), 63.8 and 63.6 (*C*), 49.6 and 49.2 (*C*H), 32.7 and 32.3 (CH_2), 16.5 and 16.3 (CH_3); HRMS (ESI): MNa^+, found 549.2162. $[C_{35}H_{30}N_2NaO_3]^+$ requires 549.2149.

4.4. General procedure 2 for the synthesis of monoketone linked bis-oxindoles 25a–c

To a stirred solution of bis-anilide **24** (1 equiv) in mesitylene (0.03–0.1 M) was added $Cu(OAc)_2 \cdot H_2O$ (1 equiv). The reaction mixture was stirred for 30 min at 170 °C (Drysyn heating block) under an atmosphere of air. Mesitylene was removed in vacuo. The resulting residue was diluted with EtOAc (5 mL) and washed twice with a 10% aq solution of NH_4OH (2×5 mL) and 4 M solution of NaOH (3×5 mL). The ^1H NMR spectrum of the crude reaction showed a mixture of diastereoisomers present. Purification by column chromatography (SiO_2, hexane/EtOAc) gave the *title compound* **25**.

*4.4.1. dl-3-(1,3-Diethyl-2-oxo-2,3-dihydro-1H-indole-3-carbonyl)-1,3-dimethyl-2,3-dihydro-1H-indol-2-one (dl-**25a**) and meso-3-(1,3-dimethyl-2-oxo-2,3-dihydro-1H-indole-3-carbonyl)-1,3-dimethyl-2,3-dihydro-1H-indol-2-one (meso-**25a**).* Bis-anilide **24a** (35.7 mg, 0.101 mmol), and $Cu(OAc)_2 \cdot H_2O$ (21.0 mg, 0.105 mmol) in mesitylene (3.5 mL) were submitted to general procedure 2. The ^1H NMR spectrum of the crude reaction showed a mixture of diastereoisomers in a ratio of 40:60 *dl*-**25a**/*meso*-**25a**. Purification by column chromatography (SiO_2, hexane/EtOAc, 4:1) gave first *dl*-**25a** (9.6 mg, 27%) as a white solid, mp 262–264 °C; R_f 0.42 (hexane/EtOAc, 1:1); ν_{max} (ATR, cm^{-1}) 2932, 1728, 1706, 1611, 1492, 1469, 1446, 1374, 1345, 1120, 1028, 988, 768, 752; δ_H (400 MHz, $CDCl_3$) 7.10 (2H, td, *J*=7.6, 1.1 Hz, C*H*), 7.06 (2H, dd, *J*=7.6, 1.1 Hz, C*H*), 6.98 (2H, td, *J*=7.6, 1.1 Hz, C*H*), 6.31 (2H, d, *J*=7.6 Hz, CH), 2.78 (6H, s, CH_3), 1.48 (6H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 196.3 (*C*), 174.1 (*C*), 144.1 (*C*), 129.0 (CH), 127.8 (*C*), 125.5 (CH), 122.2 (CH), 107.9 (CH), 62.1 (*C*), 26.3 (CH_3), 22.7 (CH_3); HRMS (ESI): MNa^+, found 371.1350. $[C_{21}H_{20}N_2NaO_3]^+$ requires 371.1366. CCDC 1004039 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

The diastereoisomer *meso*-**25a** (10.9 mg, 31%) was then isolated by column chromatography (SiO_2, hexane/EtOAc, 4:1) as a white solid, mp 170–172 °C; R_f 0.25 (hexane/EtOAc, 1:1); ν_{max} (ATR, cm^{-1}) 1731, 1717, 1608, 1490, 1468, 1374, 1344, 1120, 1032, 761, 542; δ_H (400 MHz, $CDCl_3$) 7.20 (2H, td, *J*=7.6, 1.2 Hz, C*H*), 6.76 (2H, td, *J*=7.6, 1.2 Hz, C*H*), 6.63 (2H, d, *J*=7.6 Hz, C*H*), 6.55 (2H, dd, *J*=7.6, 1.2 Hz, C*H*), 2.91 (6H, s, CH_3), 1.50 (6H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 197.9 (*C*), 174.2 (*C*), 144.4 (*C*), 129.1 (CH), 128.6 (*C*), 123.9 (CH), 122.3 (CH), 108.3 (CH), 61.3 (*C*), 26.4 (CH_3), 22.9 (CH_3); HRMS (ESI): MNa^+, found 371.1372. $[C_{21}H_{20}N_2NaO_3]^+$ requires 371.1366.

*4.4.2. trans/cis-3-(1,3-Dimethyl-2-oxo-2,3-dihydro-1H-indole-3-carbonyl)1,3,5-trimethyl-2,3-dihydro-1H-indol-2-one (trans/cis-**25b**).* Bis-anilide **24b** (89.0 mg, 0.243 mmol), and $Cu(OAc)_2 \cdot H_2O$ (97.0 mg, 0.486 mmol) in mesitylene (2.4 mL) were submitted to general procedure 2, with a reaction time of 3 h. The crude product was purified by column chromatography (SiO_2, hexane/EtOAc, 9:1 to 4:1) to give *trans*/*cis*-**25b** (38.5:61.5, 36.2 mg, 41%) as a colourless solid, mp 143–145 °C; R_f 0.20 (hexane/EtOAc, 3:2); ν_{max} (ATR, cm^{-1}) 2929, 1714, 1694, 1604, 1502, 1490, 1468, 1445, 1421, 1368, 1342, 1257, 1185, 1146, 1118, 1027; δ_H (400 MHz, $CDCl_3$) 7.22 (0.615H, td, *J*=7.8, 1.1 Hz, C*H*), 7.19 (0.385H, td, *J*=7.8, 1.1 Hz, C*H*), 7.00–6.96 (1H, m, C*H*), 6.84 (0.615H, td, *J*=7.5, 0.8 Hz, C*H*), 6.75 (0.385H, td, *J*=7.5, 0.8 Hz, C*H*), 6.71 (0.615H, dd, *J*=7.4, 0.8 Hz, C*H*), 6.62 (0.385H, d, *J*=7.8 Hz, C*H*), 6.58 (0.615H, d, *J*=7.8 Hz, C*H*), 6.54 (1H, d, *J*=7.9 Hz, C*H*), 6.51 (0.385H, d, *J*=7.9 Hz, C*H*), 6.34 (0.385H, s, C*H*), 6.17 (0.615H, s, C*H*), 2.96 (1.85H, s, CH_3), 2.90 (1.15H, s, CH_3), 2.87 (1.15H, s, CH_3), 2.81 (1.85H, s, CH_3), 2.12 (1.15H, s, CH_3), 2.05 (1.85H, s, CH_3), 1.50 (1.85H, s, CH_3), 1.49 (1.15H, s, CH_3), 1.48 (1.15H, s, CH_3), 1.47 (1.85H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 197.9 (*C*), 174.3 and 174.09 (*C*), 174.06 and 173.9 (*C*), 144.3 and 144.1 (*C*), 142.2 and 142.0 (*C*), 131.63 and 131.58 (*C*), 129.4 and 129.3 (CH), 129.0 and 128.9 (CH), 128.8 and 128.51 (*C*), 128.48 and 128.2 (*C*), 124.9 and 124.7 (CH), 123.7 and 123.6 (CH), 122.22 and 122.19 (CH), 108.2 and 108.1 (CH), 107.8 and 107.7 (CH), 61.4 and 61.2 (*C*), 61.1 and 61.0 (*C*), 26.5 and 26.34 (CH_3), 26.29 and 26.2 (CH_3), 22.73 and 22.71 (2×CH_3), 20.91 and 20.87 (CH_3); HRMS (ESI): MNa^+, found 385.1514. $[C_{22}H_{22}N_2NaO_3]^+$ requires 385.1523.

*4.4.3. trans-3-(3-Ethyl-1-methyl-2-oxo-2,3-dihydro-1H-indole-3-carbonyl)-1,3-dimethyl-2,3-dihydro-1H-indol-2-one (trans-**25c**) and cis-3-(3-ethyl-1-methyl-2-oxo-2,3-dihydro-1H-indole-3-carbonyl)-1,3-dimethyl-2,3-dihydro-1H-indol-2-one (cis-**25c**).* Bis-anilide **24c** (51.3 mg, 0.140 mmol) and $Cu(OAc)_2 \cdot H_2O$ (28.0 mg, 0.140 mmol) in mesitylene (4 mL) were subjected to general procedure 2. The ^1H NMR spectrum of the crude reaction showed a mixture of diastereoisomers in a ratio of 60:40 *trans*-**25c**/*cis*-**25c**. Purification by column chromatography (SiO_2, hexane/EtOAc, 4:1 to hexane/EtOAc, 1:1) gave first *trans*-**25c** (20.8 mg, 41%) as a colourless solid, mp 200–202 °C; R_f 0.42 (hexane/EtOAc, 1:1); ν_{max} (ATR, cm^{-1}) 1724, 1701, 1609, 1489, 1461, 1369, 1346, 1259, 1160, 1101, 765; δ_H (400 MHz, $CDCl_3$) 7.11–7.05 (3H, m, C*H*), 7.03 (1H, dd, *J*=7.6, 1.2 Hz, C*H*), 7.01–6.93 (2H, m, C*H*), 6.29 (2H, d, *J*=7.6 Hz, C*H*), 2.80 (3H, s, CH_3), 2.79 (3H, s, CH_3), 2.21 (1H, dq, *J*=14.8, 7.4 Hz, CH_2), 2.10 (1H, dq, *J*=14.8, 7.4 Hz, CH_2), 1.47 (3H, s, CH_3), 0.42 (3H, t, *J*=7.4 Hz, CH_3); δ_C (100 MHz, $CDCl_3$) 196.1 (*C*), 174.2 (*C*), 173.2 (*C*), 144.9 (*C*), 144.0 (*C*), 129.0 (CH), 128.9 (CH), 127.9 (*C*), 126.0 (CH), 125.4 (*C*), 125.2 (CH), 122.1 (CH), 121.9 (CH), 107.9 (CH), 107.7 (CH), 67.2 (*C*), 62.3 (*C*), 29.1 (CH_2), 26.4 (CH_3), 26.2 (CH_3), 22.8 (CH_3), 7.8 (CH_3); HRMS (ESI): MNa^+, found 385.1525. $[C_{22}H_{22}N_2NaO_3]^+$ requires 385.1523. CCDC 1016758 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

The diastereoisomer *cis*-**25c** (13 mg, 26%) was then isolated by column chromatography (SiO_2, hexane/EtOAc, 1:1) as a colourless solid, mp 155–157 °C; R_f 0.23 (hexane/EtOAc, 1:1); ν_{max} (ATR, cm^{-1}) 1727, 1712, 1611, 1493, 1470, 1372, 1347, 1259, 1161, 1102, 755; δ_H (400 MHz, $CDCl_3$) 7.20 (1H, td, *J*=7.6, 1.2 Hz, C*H*), 7.19 (1H, td, *J*=7.6, 1.2 Hz, C*H*), 6.78 (1H, td, *J*=7.6, 1.2 Hz, C*H*), 6.73 (1H, td, *J*=7.6, 1.2 Hz, C*H*), 6.65 (1H, d, *J*=7.6 Hz, C*H*), 6.60 (1H, d, *J*=7.6 Hz, C*H*), 6.57 (1H, dd, *J*=7.6, 1.2 Hz, C*H*), 6.48 (1H, dd, *J*=7.6, 1.2 Hz, C*H*), 2.94 (3H, s, CH_3), 2.85 (3H, s, CH_3), 2.18 (1H, dq, *J*=14.8, 7.4 Hz, CH_2), 2.09 (1H, dq, *J*=14.8, 7.4 Hz, CH_2), 1.48 (3H, s, CH_3), 0.47 (3H, t, *J*=7.4 Hz, CH_3); δ_C (100 MHz, $CDCl_3$) 197.7 (*C*), 174.2 (*C*), 173.3 (*C*), 145.0 (*C*), 144.6 (*C*), 129.12 (CH), 129.10 (CH), 128.6 (*C*), 126.6 (*C*), 124.3 (CH), 123.7 (CH), 122.2 (CH), 108.4 (CH), 108.1 (CH), 66.2 (*C*), 61.6 (*C*), 29.6 (CH_2), 26.5 (CH_3), 26.2 (CH_3), 22.9 (CH_3), 7.7 (CH_3); HRMS (ESI): MNa^+, found 385.1518. $[C_{22}H_{22}N_2NaO_3]^+$ requires 385.1523. CCDC 1004041 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

4.5. General procedure 3 for the formation of diketone linked bis-oxindoles 29a–j

A solution of bis-anilide **28** (1 equiv) and $Cu(OAc)_2 \cdot H_2O$ (1 equiv) in mesitylene (0.1 M) was heated at 165 °C for 2 h under an atmosphere of air, then cooled to room temperature. Saturated NH_4Cl (15 mL) was added and the aqueous phase extracted with EtOAc (3×15 mL). The combined organics were washed with 10% NH_4OH (15 mL), 4 M NaOH (3×15 mL), and saturated brine (15 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography (SiO_2, hexane/EtOAc) to give the *title compound* **29**.

*4.5.1. meso-1,3-Bis(1,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-3-yl)-2,2-dimethylpropane-1,3-dione (meso-**29a**) and dl-1,3-bis(1,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-3-yl)-2,2-dimethylpropane-1,3-dione (dl-**29a**)*

*4.5.1.1. From dl-N,N′-2,4,4,6-hexamethyl-3,5-dioxo-N,N′-diphenylheptanedicarboxamide (dl-**28a**).* Bis-anilide *dl*-**28a** (0.180 g, 0.426 mmol) and $Cu(OAc)_2 \cdot H_2O$ (85.0 mg, 0.426 mmol) in mesitylene (4.3 mL) were subjected to general procedure 3. The crude product was purified by column chromatography (SiO_2, hexane/EtOAc, 9:1 to 4:1) to give *meso*-**29a** (47.6 mg, 27%) as a colourless solid, mp 159–161 °C; R_f 0.50 (hexane/EtOAc, 3:2); ν_{max} (ATR, cm^{-1}) 2936, 1721, 1705, 1694, 1667, 1607, 1492, 1470, 1445, 1366, 1343, 1256, 1121, 1099, 1082, 1027, 990; δ_H (400 MHz, $CDCl_3$) 7.40 (2H, dd, *J*=7.5, 0.8 Hz, C*H*), 7.34 (2H, td, *J*=7.8, 1.1 Hz, C*H*), 7.06 (2H, td, *J*=7.5,

0.8 Hz, C*H*), 6.88 (2H, d, *J*=7.8 Hz, C*H*), 3.25 (6H, s, CH_3), 1.57 (6H, s, CH_3), 0.98 (3H, s, CH_3), 0.94 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 203.4 (*C*), 175.6 (*C*), 142.9 (*C*), 130.2 (*C*), 128.9 (*C*H), 124.8 (*C*H), 122.9 (*C*H), 108.3 (*C*H), 64.5 (*C*), 60.4 (*C*), 26.6 (*C*H_3), 24.3 (*C*H_3), 23.4 (*C*H_3), 22.7 (*C*H_3); HRMS (ESI): MH^+, found 419.1972. $[C_{25}H_{27}N_2O_4]^+$ requires 419.1965. CCDC 1013389 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

The diastereoisomer *dl*-**29a** (53.7 mg, 30%) was then isolated as a colourless solid, mp 128–130 °C; R_f 0.40 (hexane/EtOAc, 3:2); ν_{max} (ATR, cm^{-1}) 2930, 1697, 1657, 1609, 1492, 1470, 1447, 1372, 1346, 1260, 1117, 1094, 1028, 976; δ_H (400 MHz, $CDCl_3$) 7.33 (2H, td, *J*=7.7, 1.2 Hz, C*H*), 7.29 (2H, dd, *J*=7.5, 0.7 Hz, C*H*), 7.10 (2H, td, *J*=7.6, 0.9 Hz, C*H*), 6.85 (2H, d, *J*=7.7 Hz, C*H*), 3.24 (6H, s, CH_3), 1.57 (6H, s, CH_3), 0.89 (6H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 204.0 (*C*), 175.8 (*C*), 142.8 (*C*), 129.7 (*C*), 128.9 (*C*H), 124.4 (*C*H), 123.1 (*C*H), 108.3 (*C*H), 64.5 (*C*), 60.5 (*C*), 26.5 (*C*H_3), 23.8 (*C*H_3), 21.2 (*C*H_3); HRMS (ESI): MH^+, found 419.1975. $[C_{25}H_{27}N_2O_4]^+$ requires 419.1965. CCDC 1013390 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

*4.5.1.2. From meso-N,N′-2,4,4,6-hexamethyl-3,5-dioxo-N,N′-diphenylheptanedicarboxamide (meso-**28a**).* Bis-anilide *meso*-**28a** (0.148 g, 0.350 mmol) and $Cu(OAc)_2 \cdot H_2O$ (70.0 mg, 0.350 mmol) in mesitylene (3.5 mL) were subjected to general procedure 3. The crude product was purified by column chromatography (SiO_2, hexane/EtOAc, 9:1 to 4:1) to give *meso*-**29a** (35.4 mg, 24%) as a colourless solid, followed by *dl*-**29a** (45.2 mg, 31%) as a colourless solid.

*4.5.2. dl/meso-1,6-Bis(1,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-3-yl)-2,2,5,5-tetramethylhexane-1,6-dione (dl/meso-**29b**).* Bis-anilide *dl*/*meso*-**28b** (0.215 g, 0.436 mmol) and $Cu(OAc)_2 \cdot H_2O$ (87.0 mg, 0.436 mmol) in mesitylene (4.4 mL) were subjected to general procedure 3. The crude product was purified by column chromatography (SiO_2, hexane/EtOAc, 1:9 to 1:4) to give the *title compound dl*/*meso*-**29b** (50:50, 0.136 g, 64%) as a colourless solid, mp 182–184 °C; R_f 0.57 (hexane/EtOAc, 3:2); ν_{max} (ATR, cm^{-1}) 2972, 1706, 1688, 1608, 1491, 1471, 1373, 1346, 1259, 1118, 1098, 1029, 983; δ_H (400 MHz, $CDCl_3$) 7.34–7.29 (2H, m, C*H*), 7.05–7.02 (4H, m, C*H*), 6.88 (2H, d, *J*=7.9 Hz, C*H*), 3.27 (6H, s, CH_3), 1.50 (6H, s, CH_3), 1.31–1.25 (2H, m, CH_2), 1.09–0.99 (2H, m, CH_2), 0.90 (3H, s, CH_3), 0.89 (3H, s, CH_3), 0.77 (3H, s, CH_3), 0.76 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 207.66 and 207.65 (*C*), 176.3 and 176.2 (*C*), 143.4 (*C*), 129.8 and 129.7 (*C*), 128.9 (*C*H), 123.50 and 123.46 (*C*H), 122.80 and 122.78 (*C*H), 108.6 (*C*H), 60.8 (*C*), 49.5 and 49.4 (*C*), 35.7 and 35.5 (*C*H_2), 26.5 (*C*H_3), 24.3 (*C*H_3), 24.0 (*C*H_3), 23.44 and 23.43 (*C*H_3), 23.4 (*C*H_3); HRMS (ESI): MH^+, found 489.2746. $[C_{30}H_{37}N_2O_4]^+$ requires 489.2748.

*4.5.3. dl/meso-1,6-Bis(1,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-3-yl)hexane-1,6-dione (dl/meso-**29c**).* Bis-anilide *dl*/*meso*-**28c** (0.218 g, 0.500 mmol) and $Cu(OAc)_2 \cdot H_2O$ (0.100 g, 0.500 mmol) in mesitylene (5 mL) were subjected to general procedure 3. The crude product was purified by column chromatography (SiO_2, hexane/EtOAc, 9:1 to 4:1) to give the *title compound dl*/*meso*-**29c** (50:50, 52.9 mg, 25%) as a colourless solid, mp 120–122 °C; R_f 0.19 (hexane/EtOAc, 3:2); ν_{max} (ATR, cm^{-1}) 2937, 1719, 1689, 1608, 1491, 1475, 1374, 1348, 1258, 1160, 1119, 1099, 1061, 1035, 985; δ_H (400 MHz, $CDCl_3$) 7.34–7.28 (2H, m, C*H*), 7.08–7.02 (4H, m, C*H*), 6.89 (2H, d, *J*=8.0 Hz, C*H*), 3.263 (3H, s, CH_3), 3.259 (3H, s, CH_3), 2.28–2.21 (2H, m, CH_2), 1.97–1.89 (2H, m, CH_2), 1.51 (3H, s, CH_3), 1.50 (3H, s, CH_3), 1.24–1.16 (4H, m, CH_2); δ_C (100 MHz, $CDCl_3$) 202.8 and 202.7 (*C*), 175.9 (*C*), 143.6 (*C*), 129.3 (*C*), 129.0 (*C*H), 123.33 and 123.31 (*C*H), 123.134 and 123.129 (*C*H), 108.52 and 108.51 (*C*H), 61.6 (*C*), 37.8 and 37.7 (*C*H_2), 26.5 (*C*H_3), 22.4 and 22.3 (*C*H_2), 19.0 and 18.9 (*C*H_3); HRMS (ESI): MNa^+, found 455.1931. $[C_{26}H_{28}N_2NaO_4]^+$ requires 455.1941.

*4.5.4. dl/meso-1,8-Bis(1,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-3-yl)-2,2,7,7-tetramethyloctane-1,8-dione (dl/meso-**29d**).* Bis-anilide *dl*/*meso*-**28d** (0.250 g, 0.480 mmol) and $Cu(OAc)_2 \cdot H_2O$ (96.0 mg, 0.480 mmol) in mesitylene (4.8 mL) were subjected to general procedure 3. The crude product was purified by column chromatography (SiO_2, hexane/EtOAc, 9:1 to 4:1) to give the *title compound dl*/*meso*-**29d** (50:50, 0.164 g, 66%) as a colourless solid, mp 109–111 °C; R_f 0.25 (hexane/EtOAc, 3:1); ν_{max} (ATR, cm^{-1}) 2938, 1718, 1687, 1609, 1493, 1467, 1449, 1374, 1342, 1261, 1119, 1101, 1030, 981; δ_H (400 MHz, $CDCl_3$) 7.31 (2H, tdd, *J*=7.1, 2.0, 1.2 Hz, C*H*), 7.04–7.00 (4H, m, C*H*), 6.86 (2H, d, *J*=7.7 Hz, C*H*), 3.252 (3H, s, CH_3), 3.247 (3H, s, CH_3), 1.49 (6H, s, CH_3), 1.42–1.32 (2H, m, CH_2), 1.27–1.19 (2H, m, CH_2), 0.93–0.77 (4H, m, CH_2), 0.88 (3H, s, CH_3), 0.87 (3H, s, CH_3), 0.79 (6H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 208.0 and 207.9 (*C*), 176.2 (*C*), 143.3 (*C*), 129.8 (*C*), 128.8 (*C*H), 123.273 and 123.269 (*C*H), 122.8 (*C*H), 108.5 (*C*H), 60.8 (*C*), 49.7 (*C*), 40.89 and 40.86 (*C*H_2), 26.4 (*C*H_3), 24.91 and 24.87 (*C*H_2), 24.5 and 24.38 (*C*H_3), 24.36 and 24.28 (*C*H_3), 23.4 (*C*H_3); HRMS (ESI): MNa^+, found 539.2859. $[C_{32}H_{40}N_2NaO_4]^+$ requires 539.2880.

*4.5.5. dl/meso-3-[3-(1,3-Dimethyl-2-oxo-2,3-dihydro-1H-indole-3-carbonyl)adamantane-1-carbonyl]-1,3-dimethyl-2,3-dihydro-1H-indol-2-one (dl/meso-**29e**).* Bis-anilide *dl*/*meso*-**28e** (0.206 g, 0.400 mmol) and $Cu(OAc)_2 \cdot H_2O$ (80.0 mg, 0.400 mmol) in mesitylene (4 mL) were subjected to general procedure 3. The crude product was purified by column chromatography (SiO_2, hexane/EtOAc, 9:1 to 4:1) to give the *title compound dl*/*meso*-**29e** (0.143 g, 70%) as a colourless solid, mp 173–174.5 °C; R_f 0.34 (hexane/EtOAc, 1:3); ν_{max} (ATR, cm^{-1}) 2930, 1707, 1685, 1608, 1491, 1470, 1447, 1372, 1342, 1258, 1171, 1119, 1099, 1043, 1022; δ_H (400 MHz, $CDCl_3$) 7.34 (2H, tt, *J*=7.7, 1.5 Hz, C*H*), 7.07–6.99 (2H, m, C*H*), 6.94 (1H, dd, *J*=7.0, 0.6 Hz, C*H*), 6.91–6.88 (2H, m, C*H*), 6.82 (1H, d, *J*=7.3 Hz, C*H*), 3.29 (3H, s, CH_3), 3.27 (3H, s, CH_3), 1.80–1.76 (1H, m, C*H*), 1.74–1.68 (1H, m, C*H*), 1.64–1.52 (3H, m, CH_2), 1.46–1.43 (3H, m, CH_2), 1.45 (3H, s, CH_3), 1.44 (3H, s, CH_3), 1.38–1.30 (5H, m, CH_2), 1.27–1.23 (1H, m, CH_2); δ_C (100 MHz, $CDCl_3$) 206.7 and 206.6 (*C*), 176.1 and 176.0 (*C*), 143.6 and 143.4 (*C*), 129.71 and 129.66 (*C*), 129.0 and 128.9 (*C*H), 123.1 (*C*H), 122.97 and 122.95 (*C*H), 108.8 and 108.7 (*C*H), 60.58 and 60.55 (*C*), 49.1 and 48.9 (*C*), 39.2 and 39.1 (*C*H_2), 37.52 and 37.47 (*C*H_2), 36.9 (*C*H_2), 36.6 (*C*H_2), 34.99 and 34.98 (*C*H_2), 27.84, 27.82 and 27.80 (*C*H), 26.6 and 26.5 (*C*H_3), 23.13 and 23.05 (*C*H_3); HRMS (ESI): MNa^+, found 533.2421. $[C_{32}H_{34}N_2NaO_4]^+$ requires 533.2411.

*4.5.6. dl/meso-3-[2-({3-[3-(1,3-Dimethyl-2-oxo-2,3-dihydro-1H-indol-3-yl)-2,2-dimethyl-3-oxopropyl]phenyl}methyl)-2-methylpropanoyl]-1,3-dimethyl-2,3-dihydro-1H-indol-2-one (dl/meso-**29f**).* Bis-anilide *dl*/*meso*-**28f** (0.145 g, 0.255 mmol) and $Cu(OAc)_2 \cdot H_2O$ (51.0 mg, 0.255 mmol) in mesitylene (2.6 mL) were subjected to general procedure 3. The crude product was purified by column chromatography (SiO_2, hexane/EtOAc, 9:1 to 4:1) to give the *title compound dl*/*meso*-**29f** (50:50, 93.2 mg, 65%) as a colourless oil, R_f 0.60 (hexane/EtOAc, 3:2); ν_{max} (ATR, cm^{-1}) 2972, 2930, 1710, 1690, 1608, 1491, 1467, 1447, 1372, 1341, 1257, 1118, 1097, 1030, 984; δ_H (400 MHz, $CDCl_3$) 7.27 (2H, tt, *J*=7.8, 1.3 Hz, C*H*), 7.06 (1H, td, *J*=7.6, 3.3 Hz, C*H*), 6.90–6.83 (6H, m, C*H*), 6.69–6.63 (3H, m, C*H*), 3.27 (6H, s, CH_3), 2.89 (1H, d, *J*=13.2 Hz, CH_2), 2.88 (1H, d, *J*=13.2 Hz, CH_2), 2.56 (1H, d, *J*=13.2 Hz, CH_2), 2.55 (1H, d, *J*=13.2 Hz, CH_2), 1.53 (3H, s, CH_3), 1.52 (3H, s, CH_3), 0.94 (3H, s, CH_3), 0.93 (3H, s, CH_3), 0.74 (3H, s, CH_3), 0.72 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 207.38 and

207.37 (*C*), 176.3 (*C*), 143.09 and 143.08 (*C*), 136.7 (*C*), 133.62 and 133.59 (*C*H), 129.54 and 129.52 (*C*), 128.88 and 128.85 (*C*H), 128.63 and 128.62 (*C*H), 127.1 (*C*H), 123.02 and 122.98 (*C*H), 122.79 and 122.78 (*C*H), 108.4 (*C*H), 60.9 (*C*), 50.60 and 50.57 (*C*), 45.77 and 45.76 (CH_2), 26.4 (CH_3), 24.9 and 24.8 (CH_3), 23.4 (CH_3), 22.6 and 22.5 (CH_3); HRMS (ESI): MNa^+, found 587.2876. $[C_{36}H_{40}N_2NaO_4]^+$ requires 587.2880.

*4.5.7. dl/meso-5-Methoxy-3-[2-({3-[3-(5-methoxy-1,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-3-yl)-2,2-dimethyl-3-oxopropyl]phenyl}methyl)-2-methylpropanoyl]-1,3-dimethyl-2,3-dihydro-1H-indol-2-one (dl/meso-**29g**).* Bis-anilide *dl/meso*-**28g** (0.305 g, 0.485 mmol) and $Cu(OAc)_2 \cdot H_2O$ (97.0 mg, 0.485 mmol) in mesitylene (4.9 mL) were subjected to general procedure 3. The crude product was purified by column chromatography (SiO_2, hexane/EtOAc, 9:1 to 4:1) to give the *title compound dl/meso*-**29g** (50:50, 0.223 g, 74%) as a colourless solid, mp 60–62 °C; R_f 0.09 (hexane/EtOAc, 3:1); ν_{max} (ATR, cm^{-1}) 2970, 2931, 1703, 1689, 1598, 1497, 1469, 1433, 1369, 1348, 1288, 1235, 1202, 1173, 1106, 1036, 985; δ_H (400 MHz, $CDCl_3$) 7.04 (1H, td, *J*=7.7, 3.4 Hz, C*H*), 6.85–6.82 (2H, m, C*H*), 6.76 (2H, dt, *J*=8.6, 1.8 Hz, C*H*), 6.72 (2H, d, *J*=8.6 Hz, C*H*), 6.65 (0.5H, s, C*H*), 6.64 (0.5H, s, C*H*), 6.40 (1H, d, *J*=2.4 Hz, C*H*), 6.37 (1H, d, *J*=2.4 Hz, C*H*), 3.68 (3H, s, CH_3), 3.67 (3H, s, CH_3), 3.22 (6H, s, CH_3), 2.82 (2H, d, *J*=12.7 Hz, CH_2), 2.58 (2H, d, *J*=12.7 Hz, CH_2), 1.49 (6H, s, CH_3), 0.88 (3H, s, CH_3), 0.87 (3H, s, CH_3), 0.75 (3H, s, CH_3), 0.72 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 207.6 and 207.5 (*C*), 176.01 and 176.00 (*C*), 156.1 (*C*), 136.64 and 136.63 (*C*), 136.56 and 136.55 (*C*), 133.53 and 133.52 (*C*H), 130.90 and 130.87 (*C*), 128.92 and 128.89 (*C*H), 126.99 and 126.96 (*C*H), 113.0 (*C*H), 110.4 and 110.3 (*C*H), 108.8 (*C*H), 61.22 and 61.21 (*C*), 55.6 (CH_3), 50.59 and 50.56 (*C*), 45.53 and 45.52 (CH_2), 26.5 (CH_3), 24.4 and 24.2 (CH_3), 23.6 (CH_3), 23.0 and 22.8 (CH_3); HRMS (ESI): MNa^+, found 647.3106. $[C_{38}H_{44}N_2NaO_6]^+$ requires 647.3092.

*4.5.8. dl/meso-5-(Trifluoromethyl)-3-[2-({3-[3-(5-(trifluoromethyl)-1,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-3-yl)-2,2-dimethyl-3-oxopropyl]phenyl}methyl)-2-methylpropanoyl]-1,3-dimethyl-2,3-dihydro-1H-indol-2-one (dl/meso-**29h**).* Bis-anilide *dl/meso*-**28h** (0.211 g, 0.300 mmol) and $Cu(OAc)_2 \cdot H_2O$ (60.0 mg, 0.300 mmol) in mesitylene (3 mL) were subjected to general procedure 3. The crude product was purified by column chromatography (SiO_2, hexane/EtOAc, 9:1 to 4:1) to give the *title compound dl/meso*-**29h** (50:50, 0.106 g, 50%) as a colourless solid, mp 68–70 °C; R_f 0.12 (hexane/EtOAc, 3:1); ν_{max} (ATR, cm^{-1}) 2971, 1717, 1694, 1620, 1503, 1471, 1452, 1372, 1343, 1324, 1288, 1254, 1215, 1157, 1115, 1067, 1025, 984; δ_H (400 MHz, $CDCl_3$) 7.54 (2H, d, *J*=8.2 Hz, C*H*), 7.05–7.01 (2H, m, C*H*), 6.98 (1H, s, C*H*), 6.91 (2H, d, *J*=8.2 Hz, C*H*), 6.83–6.80 (2H, m, C*H*), 6.64–6.62 (1H, m, C*H*), 3.294 (3H, s, CH_3), 3.292 (3H, s, CH_3), 2.88 (2H, d, *J*=13.2 Hz, CH_2), 2.55 (1H, d, *J*=13.2 Hz, CH_2), 2.54 (1H, d, *J*=13.2 Hz, CH_2), 1.55 (3H, s, CH_3), 1.54 (3H, s, CH_3), 0.92 (3H, s, CH_3), 0.91 (3H, s, CH_3), 0.73 (3H, s, CH_3), 0.72 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 206.6 (*C*), 176.4 (*C*), 146.0 (*C*), 136.46 and 136.45 (*C*), 133.32 and 132.29 (*C*H), 130.22 and 130.18 (*C*), 128.9 (*C*H), 127.32 and 127.31 (*C*H), 126.6 (q, *J*=4.0 Hz, *C*H), 125.2 (q, *J*=32.1 Hz, *C*), 123.9 (q, *J*=272 Hz, *C*), 120.11 and 120.07 (q, *J*=3.7 Hz, *C*H), 108.3 (*C*H), 60.6 (*C*), 50.9 and 50.8 (*C*), 45.64 and 45.58 (CH_2), 26.7 (CH_3), 24.9 and 24.6 (CH_3), 23.7 (CH_3), 22.8 and 22.6 (CH_3); HRMS (ESI): MNa^+, found 723.2620. $[C_{38}H_{38}F_6N_2NaO_4]^+$ requires 723.2628.

*4.5.9. dl/meso-3-[2-({3-[3-(2,2-Dimethyl-3-(1-methyl)-2-oxo-3-phenyl-2,3-dihydro-1H-indol-3-yl)-3-oxopropyl]phenyl}methyl)-2-methylpropanoyl]-1-methyl-3-phenyl-2,3-dihydro-1H-indol-2-one (dl/meso-**29i**).* Bis-anilide *dl/meso*-**28i** (0.208 g, 0.300 mmol) and $Cu(OAc)_2 \cdot H_2O$ (60.0 mg, 0.300 mmol) in mesitylene (3 mL) were subjected to general procedure 3. The crude product was purified by column chromatography (SiO_2, hexane/EtOAc, 9:1 to 4:1) to give the *title compound dl/meso*-**29i** (50:50, 0.131 g, 63%) as a colourless solid, mp 105–107 °C; R_f 0.28 (hexane/EtOAc, 3:1); ν_{max} (ATR, cm^{-1}) 2970, 1709, 1693, 1608, 1490, 1469, 1446, 1368, 1341, 1253, 1129, 1076, 1055, 1022; δ_H (400 MHz, $CDCl_3$) 7.34 (1H, td, *J*=7.7, 1.2 Hz, C*H*), 7.33 (1H, td, *J*=7.7, 1.2 Hz, C*H*), 7.29–7.26 (6H, m, C*H*), 7.20–7.16 (4H, m, C*H*), 7.07 (0.5H, d, *J*=7.4 Hz, C*H*), 7.03 (0.5H, d, *J*=7.4 Hz, C*H*), 6.96 (1H, td, *J*=7.6, 0.6 Hz, C*H*), 6.93 (1H, td, *J*=7.6, 0.6 Hz, C*H*), 6.91–6.81 (6H, m, C*H*), 6.68–6.66 (1H, m, C*H*), 3.192 (3H, s, CH_3), 3.188 (3H, s, CH_3), 2.92 (1H, d, *J*=12.9 Hz, CH_2), 2.90 (1H, d, *J*=12.9 Hz, CH_2), 2.75 (1H, d, *J*=12.9 Hz, CH_2), 2.71 (1H, d, *J*=12.9 Hz, CH_2), 1.13 (3H, s, CH_3), 1.12 (3H, s, CH_3), 0.82 (3H, s, CH_3), 0.80 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 207.3 and 207.2 (*C*), 174.6 (*C*), 143.97 and 143.95 (*C*), 138.0 (*C*), 136.72 and 136.69 (*C*), 133.8 and 133.7 (*C*H), 129.5 and 129.4 (*C*H), 129.2 and 129.1 (*C*H), 128.5 (*C*H), 128.1 (*C*H), 127.8 (*C*H), 127.13 and 127.11 (*C*H), 126.00 and 125.99 (*C*H), 125.5 and 125.4 (*C*), 122.8 and 122.7 (*C*H), 108.63 and 108.61 (*C*H), 70.40 and 70.39 (*C*), 51.24 and 51.17 (*C*), 45.5 and 45.3 (CH_2), 26.66 and 26.65 (CH_3), 24.9 and 24.5 (CH_3), 22.5 and 22.2 (CH_3); HRMS (ESI): MNa^+, found 711.3170. $[C_{46}H_{44}N_2NaO_4]^+$ requires 711.3193.

*4.5.10. meso-3-(2-{4-[2-(1,3-Dimethyl-2-oxo-2,3-dihydro-1H-indol-3-yl)propan-2-yl]phenyl}propan-2-yl)-1,3-dimethyl-2,3-dihydro-1H-indol-2-one (meso-**29j**) and dl-3-(2-{4-[2-(1,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-3-yl)propan-2-yl]phenyl}propan-2-yl)-1,3-dimethyl-2,3-dihydro-1H-indol-2-one (dl-**29j**).* Bis-anilide *dl/meso*-**28j** (0.189 g, 0.350 mmol) and $Cu(OAc)_2 \cdot H_2O$ (70.0 mg, 0.350 mmol) in mesitylene (3.5 mL) were subjected to general procedure 3. The crude product was purified by column chromatography (SiO_2, hexane/EtOAc, 1:9 to 1:4) to give the *title compound meso*-**29j** (49.7 mg, 27%) as a colourless solid, mp 213–214 °C; R_f 0.34 (hexane/EtOAc, 3:1); ν_{max} (ATR, cm^{-1}) 2979, 1691, 1606, 1490, 1471, 1450, 1374, 1343, 1251, 1118, 1095, 1033, 999; δ_H (400 MHz, $CDCl_3$) 7.12 (2H, td, *J*=7.6, 1.2 Hz, C*H*), 6.98 (2H, dd, *J*=7.3, 0.9 Hz, C*H*), 6.89 (2H, td, *J*=7.5, 0.7 Hz, C*H*), 6.43 (4H, s, C*H*), 6.37 (2H, d, *J*=7.7 Hz, C*H*), 2.66 (6H, s, CH_3), 1.53 (6H, s, CH_3), 1.48 (6H, s, CH_3), 1.36 (6H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 206.9 (*C*), 175.7 (*C*), 142.4 (*C*), 139.1 (*C*), 130.3 (*C*), 128.4 (*C*H), 126.7 (*C*H), 123.2 (*C*H), 122.5 (*C*H), 107.9 (*C*H), 60.7 (*C*), 53.2 (*C*), 29.2 (CH_3), 25.9 (CH_3), 24.1 (CH_3), 24.0 (CH_3); HRMS (ESI): MNa^+, found 559.2565. $[C_{34}H_{36}N_2NaO_4]^+$ requires 559.2567. CCDC 1031379 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

The diastereoisomer *dl*-**29j** (53.1 mg, 28%) was then isolated as a colourless solid, mp 195–196 °C; R_f 0.22 (hexane/EtOAc, 3:1); ν_{max} (ATR, cm^{-1}) 2978, 1704, 1692, 1609, 1493, 1471, 1449, 1373, 1343, 1256, 1121, 1032, 997; δ_H (400 MHz, $CDCl_3$) 7.08 (2H, td, *J*=7.6, 1.2 Hz, C*H*), 6.93 (2H, dd, *J*=7.4, 0.6 Hz, C*H*), 6.83 (2H, td, *J*=7.4, 0.6 Hz, C*H*), 6.43 (4H, s, C*H*), 6.34 (2H, d, *J*=7.7 Hz, C*H*), 2.68 (6H, s, CH_3), 1.62 (6H, s, CH_3), 1.47 (6H, s, CH_3), 1.30 (6H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 206.9 (*C*), 175.8 (*C*), 142.3 (*C*), 139.2 (*C*), 130.1 (*C*), 128.3 (*C*H), 126.7 (*C*H), 123.2 (*C*H), 122.4 (*C*H), 107.9 (*C*H), 60.6 (*C*), 53.3 (*C*), 29.1 (CH_3), 25.9 (CH_3), 24.2 (CH_3), 23.8 (CH_3); HRMS (ESI): MNa^+, found 559.2566. $[C_{34}H_{36}N_2NaO_4]^+$ requires 559.2567. CCDC 1031380 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

4.6. General procedure 4 for the formation of di-ester-containing bis-oxindoles 32a–c

To a stirred solution of bis-anilide **31** (1 equiv) in mesitylene (0.04–0.06 M) was added $Cu(OAc)_2 \cdot H_2O$ (1 equiv). The reaction mixture was stirred for 30 min to 2 h at 170 °C under an atmosphere of air and allowed to cool to room temperature. Mesitylene

was removed, the residue was diluted with EtOAc (5 mL), and washed with an aq soln of NH_4OH (5 mL). The aqueous phase was extracted with EtOAc (2×5 mL). The combined organic extracts were washed with water (5 mL), and brine (5 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. The crude product was purified by column chromatography (SiO_2, hexane/EtOAc, 3:1) to give the *title compound* **32**.

*4.6.1. dl/meso-Ethyl 3-{4-[3-(ethoxycarbonyl)-1-methyl-2-oxo-2,3-dihydro-1H-indol-3-yl]butyl}-1-methyl-2-oxo-2,3-dihydro-1H-indole-3-carboxylate (dl/meso-**32a**).* Bis-anilide *dl/meso*-**31a** (60.1 mg, 0.121 mmol) and $Cu(OAc)_2 \cdot H_2O$ (24.2 mg, 0.121 mmol) in mesitylene (2 mL) were subjected to general procedure 4. The reaction mixture was stirred at 170 °C for 30 min. The crude product was purified by column chromatography (SiO_2, hexane/EtOAc, 3:1) to give the *title compound dl/meso*-**32a** (50:50, 53.9 mg, 90%) as a yellow solid, mp 145–147 °C; R_f 0.35 (hexane/EtOAc, 1:2); ν_{max} (ATR, cm^{-1}) 1736, 1709, 1609, 1492, 1470, 1372, 1346, 1223, 1081, 1020, 750, 727; δ_H (400 MHz, $CDCl_3$) 7.29 (1H, td, J=7.4, 1.2 Hz, C*H*), 7.28 (1H, td, J=7.4, 1.2 Hz, C*H*), 7.16 (1H, dd, J=7.4, 1.2 Hz, C*H*), 7.15 (1H, dd, J=7.4, 1.2 Hz, C*H*), 7.04 (1H, td, J=7.4, 1.2 Hz, C*H*), 7.02 (1H, td, J=7.4, 1.2 Hz, C*H*), 6.80 (2H, t, J=8.3 Hz, C*H*), 4.13–4.02 (4H, m, CH_2), 3.20 (3H, s, CH_3), 3.18 (3H, s, CH_3), 2.15–2.00 (4H, m, CH_2), 1.12 (3H, t, J=7.1 Hz, CH_3), 1.10 (3H, t, J=7.1 Hz, CH_3), 0.99–0.73 (4H, m, CH_2); δ_C (100 MHz, $CDCl_3$) 174.3 and 174.2 (*C*), 169.4 (*C*), 144.1 (*C*), 129.1 and 129.0 (CH), 128.1 and 128.0 (*C*), 123.37 and 123.36 (CH), 123.0 and 122.8 (CH), 108.3 (CH), 61.9 (CH_2), 59.5 and 59.4 (*C*), 34.0 and 33.9 (CH_2), 26.47 and 26.45 (CH_3), 23.63 and 23.55 (CH_2), 13.99 and 13.98 (CH_3); HRMS (ESI): MNa^+, found 515.2153. $[C_{28}H_{32}N_2NaO_6]^+$ requires 515.2153.

*4.6.2. dl/meso-Ethyl 3-[(2E)-4-[3-(ethoxycarbonyl)-1-methyl-2-oxo-2,3-dihydro-1H-indol-3-yl]but-2-en-1-yl]-1-methyl-2-oxo-2,3-dihydro-1H-indole-3-carboxylate (dl/meso-**32b**).* Bis-anilide *dl/meso*-**31b** (49.4 mg, 0.100 mmol), and $Cu(OAc)_2 \cdot H_2O$ (20.0 mg, 0.100 mmol) in mesitylene (2 mL) were subjected to general procedure 4. The reaction mixture was stirred at 170 °C for 2 h. The residue was purified by column chromatography (SiO_2, hexane/EtOAc, 2:1) to give the *title compound dl/meso*-**32b** (50:50, 32.3 mg, 66%) as a yellow solid, mp 130–132 °C; R_f 0.35 (hexane/EtOAc, 1:1); ν_{max} (ATR, cm^{-1}) 1736, 1711, 1609, 1493, 1470, 1372, 1347, 1223, 1086, 1021, 750, 729; δ_H (400 MHz, $CDCl_3$) 7.28 (2H, td, J=7.6, 1.1 Hz, C*H*), 7.14–7.09 (2H, m, C*H*), 7.04–6.98 (2H, m, C*H*), 6.79 (2H, d, J=7.6 Hz, C*H*), 5.02 (1H, dd, J=4.4, 3.6 Hz, C*H*), 4.94 (1H, d, J=3.6 Hz, C*H*), 4.11–4.00 (4H, m, CH_2), 3.21 (3H, s, CH_3), 3.14 (3H, s, CH_3), 2.80 (2H, td, J=14.1, 3.2 Hz, CH_2), 2.69–2.55 (2H, m, CH_2), 1.10 (3H, t, J=7.1 Hz, CH_3), 1.09 (3H, t, J=7.1 Hz, CH_3); δ_C (100 MHz, $CDCl_3$) 173.6 and 173.5 (*C*), 169.04 and 168.94 (*C*), 144.2 and 144.1 (*C*), 129.0 (CH), 127.9 and 127.61 (CH), 127.56 and 127.49 (*C*), 123.7 and 123.5 (CH), 122.8 and 122.7 (CH), 108.5 and 108.3 (CH), 61.9 and 61.8 (CH_2), 59.3 and 59.1 (*C*), 35.64 and 35.57 (CH_2), 26.6 and 26.5 (CH_3), 14.0 (CH_3); HRMS (ESI): MNa^+, found 513.1997. $[C_{28}H_{30}N_2NaO_6]^+$ requires 513.1996.

*4.6.3. dl/meso-Ethyl 3-[(2-{[(ethoxycarbonyl)-1-methyl-2-oxo-2,3-dihydro-1H-indol-3-yl]methyl}phenyl)methyl]-1-methyl-2-oxo-2,3-dihydro-1H-indole-3-carboxylate (dl/meso-**32c**).* Bis-anilide *dl/meso*-**31c** (60.2 mg, 0.111 mmol), and $Cu(OAc)_2 \cdot H_2O$ (24.0 mg, 0.120 mmol) in mesitylene (3 mL) were subjected to general procedure 4. The reaction mixture was stirred at 170 °C for 2 h. The residue was purified by column chromatography (SiO_2, hexane/EtOAc, 2:1) to give the *title compound dl/meso*-**32c** (50:50, 48.3 mg, 89%) as a white solid, mp 113–115 °C; R_f 0.42 (hexane/EtOAc, 1:2); ν_{max} (ATR, cm^{-1}) 1735, 1710, 1609, 1492, 1470, 1372, 1351, 1222, 1095, 1060, 1021, 751, 728; δ_H (400 MHz, $CDCl_3$) 7.24 (1H, d, J=7.4 Hz, C*H*), 7.18 (1H, t, J=7.4 Hz, C*H*), 7.14 (1H, t, J=7.4 Hz, C*H*), 7.08 (1H, d, J=7.4 Hz, C*H*), 6.98 (1H, t, J=7.4 Hz, C*H*), 6.95 (1H, t, J=7.4 Hz, C*H*), 6.74–6.68 (2H, m, C*H*), 6.68–6.63 (2H, m, C*H*), 6.54 (1H, d, J=7.4 Hz, C*H*), 6.50 (1H, d, J=7.4 Hz, C*H*), 4.15 (4H, dq, J=14.4, 7.2 Hz, CH_2), 3.64 (1H, d, J=14.2 Hz, CH_2), 3.39 (1H, d, J=14.2 Hz, CH_2), 3.33 (1H, d, J=14.2 Hz, CH_2), 3.18 (1H, d, J=14.2 Hz, CH_2), 2.93 (3H, s, CH_3), 2.91 (3H, s, CH_3), 1.17 (3H, t, J=7.1 Hz, CH_3), 1.15 (3H, t, J=7.1 Hz, CH_3); δ_C (100 MHz, $CDCl_3$) 173.8 and 173.7 (*C*), 169.3 and 169.2 (*C*), 144.0 and 143.4 (*C*), 134.1 and 133.8 (*C*), 129.9 and 129.7 (CH), 129.1 and 129.0 (CH), 127.4 and 127.1 (*C*), 126.1 and 126.0 (CH), 124.4 and 124.2 (CH), 122.4 and 122.3 (CH), 108.03 and 108.01 (CH), 62.1 and 62.0 (CH_2), 61.0 and 60.9 (*C*), 35.94 and 35.87 (CH_2), 26.2 (CH_3), 14.0 (CH_3); HRMS (ESI): MNa^+, found 563.2163. $[C_{32}H_{32}N_2NaO_6]^+$ requires 563.2153.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2015.02.060.

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