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Synthesis of new bis(tetrahydropyrrolo[3,4-*b*]carbazoles) with a functionalized diaryl spacer

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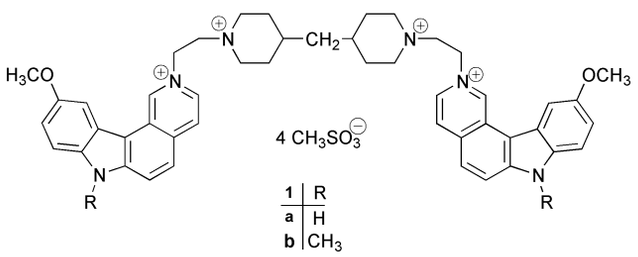
Some new bis(tetrahydropyrrolo[3,4-*b*]carbazoles) were synthesized by Diels–Alder reactions of *in-situ* generated indole-2,3-quinodimethanes with a variety of bismaleimides as dienophiles and also by reaction of dianilines with a succinic acid anhydride group incorporated into a biscarbazole. In a special reaction a spermine linker was introduced. The new biscarbazoles represent potential DNA ligands for the development of new antitumor active drugs.

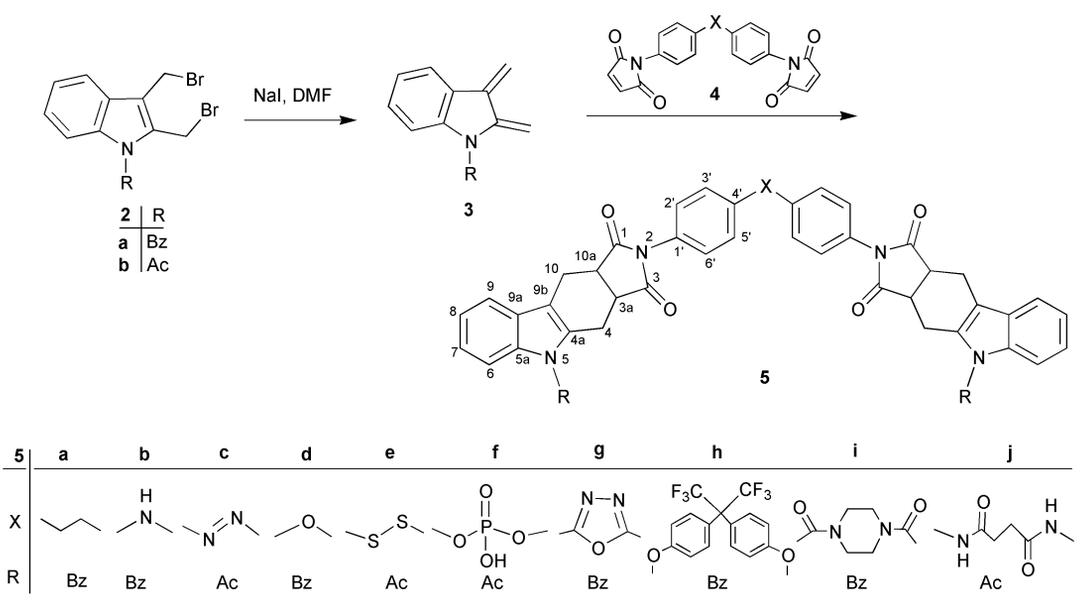
Introduction

Small molecules that target specific DNA sequences have the potential to control gene expression.[1,2] A variety of carbazoles and pyrido-annelated carbazoles represent DNA ligands with pronounced antitumor activity.[3] Among these compounds bis(pyridocarbazoles) linked with a piperidine tether are of special interest as sequence selective DNA-bisintercalators[3] (see for example compounds **1a**, **1b**).[4] In this context we have synthesized some new bis(pyrrolo[3,4-*b*]carbazoles) with a diaryl tether as a novel class of potential DNA ligands.[5] In continuation of our studies on pericyclic reactions with indole derivatives,[6] we have expanded our synthetic studies to include some further bis(pyrrolo[3,4-*b*]carbazoles) with a variety of linkage groups.[5] The synthetic strategies were dependent on the nature of the linking functionality. We used the Diels–Alder reactions of *in-situ* generated indole-2,3-quinodimethanes **3** with appropriate bismaleimide dienophiles linked with diaryl groups (Scheme 1). Moreover, we have extended the synthetic studies and have succeeded in synthesizing these types of



compounds by a polar reaction of the racemic tetrahydrofuro-[*b*]indoles **6** with some dianiline derivatives (Scheme 2).

In a further study we tried to combine two bis(pyrrolocarbazoles) with an aliphatic amine (or polyamine) and amide linker "X", according to the strategies outlined in the Schemes 1–4. In summary, our synthetic investigations allowed the introduction of a great variety of linkers "X" into the molecules with the aim of development of new antitumor active drugs with DNA binding ability.



Scheme 1 One pot synthesis of new bis(pyrrolo[*b*]carbazoles) linked with a functionalized diaryl spacer.

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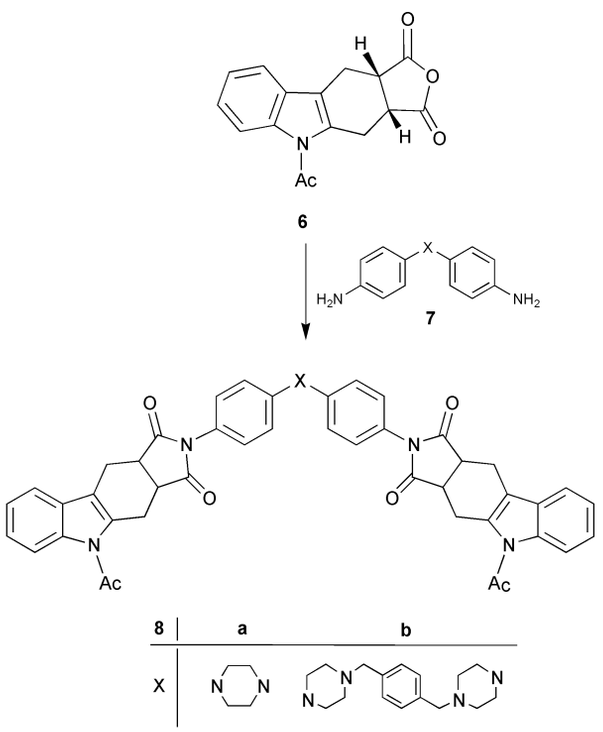
Results and discussion

Synthetic aspects

According to the Diels–Alder strategy in Scheme 1 a variety of appropriate dienophiles **4** were readily synthesized from the bisanilines and maleic acid anhydride in yields from 60–80% by optimization of known procedures.[7]

Thus, the reaction of *in-situ* generated indole-2,3-quinodimethane **3**[5] gave rise to a variety of new biscarbazoles **5** with yields of 50–70%. The compounds **5** were always formed as a mixture of C_2-symmetric enantiomers and a *meso* form, and so far the mixture has not been separated experimentally (stereoisomers: C3a-*S*, 10a-*R*, C3a′-*S*, 10a′-*R* and C3a-*R*, 10a-*S*–C3a′-*R*, 10a′-*S* enantiomeric form and C3a-*S*, 10a-*R*, C3a′-*R*, 10a′-*S meso* form). This synthetic method is in general suitable for the production of compounds with a variety of linkers from aliphatic chains to amide, ether, disulfite, phosphate and nitrogen containing heterocyclic systems with relatively low basicity.



Scheme 2 Reaction of dianilines **7** with the furo[*b*]carbazole **6**.

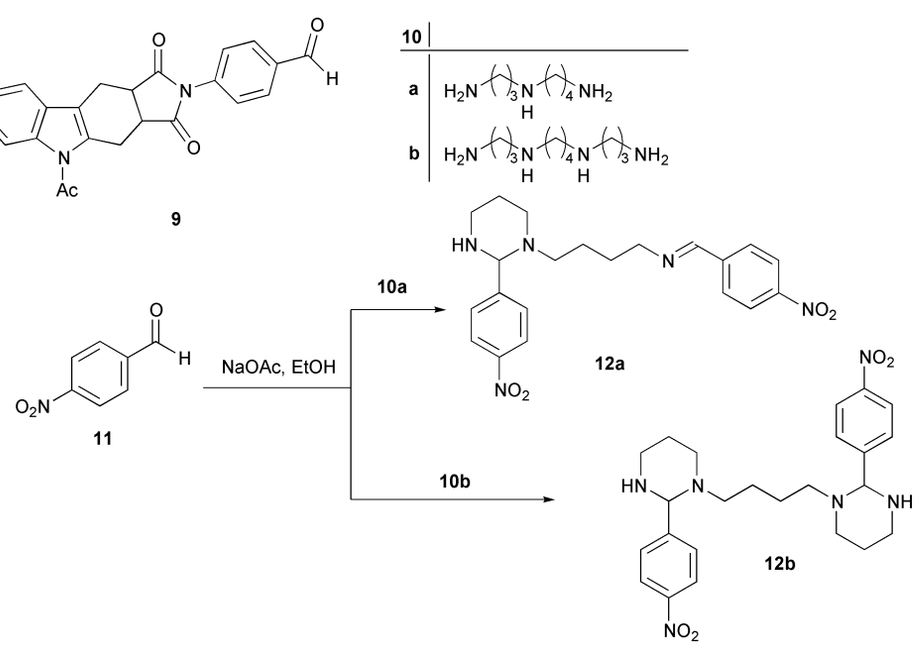
In the case of target compounds with the more basic linkers "X" the reaction of a furo[*b*]carbazole **6** with the appropriate dianilines **7** was more successful (Scheme 2). From this methodology the new biscarbazoles **8** were readily available in yields of 30–40% and the rest of the product mixture was reactant and undefinable polymer material. The racemic carbazole **6** also produced a mixture of *meso* form and a racemate of the biscarbazoles **8**.

It is reported in the literature that the aliphatic tetraamine spermine **10b** and its derivatives are potential candidates for the development of DNA binding drugs.[8–10] In this context we tried to synthesize a compound with two pyrrolocarbazole units and a spermine-like structural linker using reagent **7** and a variation of the procedure outlined in Scheme 2. After several experiments, it seemed reasonable to use a Schiff base reaction of the readily synthesized arylaldehyde **9** with the appropriate di- or polyamines.[11] However, the condensation reactions were very complicated and unselective. We were only able to isolate products by the reaction of spermidine **10a** and spermine **10b** with the arylaldehyde **11** (Scheme 3). The combined application of several ^{1}H- and ^{13}C-NMR techniques and FD-MS revealed that the polyamines **10a**, **10b** reacted with all the nucleophilic centers, inter- and intramolecular, to give the hexahydropyrimidine derivatives **12a** and **12b**. Further reaction of the corresponding dianilines obtained from **12** according to Scheme 2 was unsuccessful.

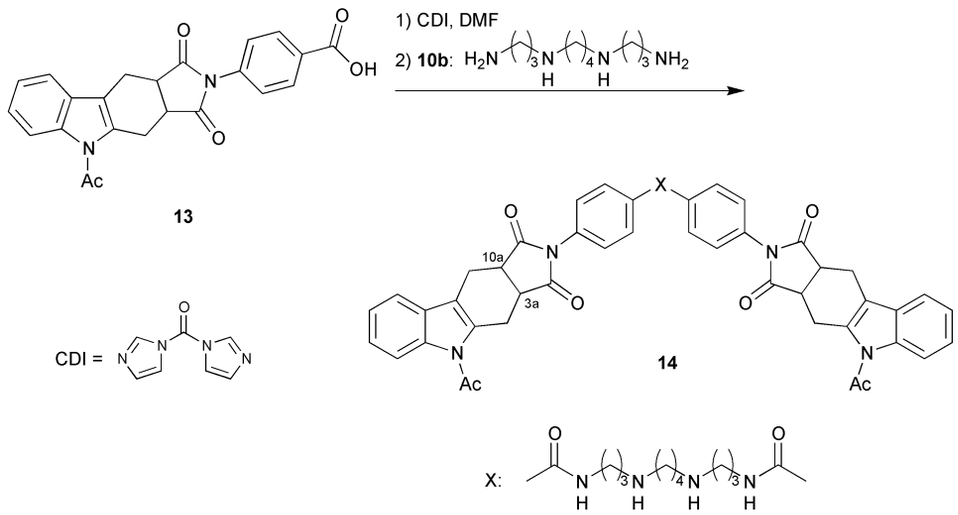
However, the introduction of a diamidic linker between two pyrrolocarbazole units was more successful (see compounds **5i** and **5j** Scheme 1). Thus, the carboxylic acid **13** could be coupled with spermine **10b** to give rise to the interesting diamidic bis(pyrrolocarbazole) **14** with DNA-intercalating and groove binding structural elements (Scheme 4).[12] Nevertheless, the yield was poor (20%) because during the extensive chromatographic purification loss of product was significant.

Structural aspects

The structures of the novel biscarbazoles **5**, **8** and **14** were unambiguously clarified by routine high resolution ^{1}H- and ^{13}C-NMR spectroscopy. In the ^{1}H-NMR spectra the protons of the



Scheme 3 Results of the synthetic concept of the Schiff base method in combination with the strategy of Scheme 2.



Scheme 4 Synthetic concept of carboxylic acid / diamidic formation.

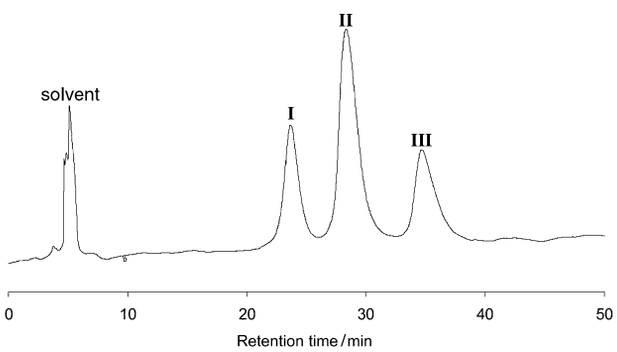


Fig. 1 Chiral HPLC analysis of **5b** (stationary phase: Whelk-O1, eluent: acetonitrile–MeOH–H_2O, 20 : 70 : 10, UV-detector: $\lambda = 254$ nm). I, III: enantiomeric form, II: *meso* form.

two coupled ABX systems of the tetrahydrocarbazole units were of higher diagnostic value than the protons of the linker group (for more details see Experimental). The *cis* configuration of the two protons (C3a–C10a) at the annelation site is obvious according to the vicinal coupling $J = 8.9$ Hz. The close structural similarity of the *meso* form and the racemate of the new biscarbazoles[5] did not allow any separation of the ^{1}H- and ^{13}C-NMR signals by application of the high resolution NMR (600 MHz) technique. The molar mass of compound **14** was additionally analyzed by MALDI-TOF-MS.

However in the case of the compounds **5b**, a chiral HPLC technique succeeded in separating the *meso* form from the enantiomeric forms of the biscarbazoles analytically (Fig. 1). From these important informative results we suggest that all the synthesized biscarbazoles **5**, **8** and **14** do indeed exist as a product mixture of the *meso* form and the C_2-symmetric racemate.

Biological evaluation

A variety of the new bis(tetrahydrocarbazoles) were tested at the National Cancer Institute (Bethesda) using a developmental therapeutics program involving tumor cell line cytotoxicity.[13] From these screenings GI_{50} values were obtained. The GI_{50} value is a response parameter and represents the concentration of the compound which induces 50% cell line growth inhibition (Table 1). However, the cytotoxicity of compound **5b** against some leukemia cell lines [CCRF-CEM and HL-60 (TB)] is significant. In comparison, the cytotoxicity data of the known cytostatic compound bis(pyridocarbazolium) (DMS)[13] for the leukemia cell lines CCRF-CEM, HL-60(TB), K-562, MOLT-4 and RPMI-8226 are −6.562, −6.391, −6.642, −6.461 and −6.734 (all values are in $\log_{10}GI_{50}$). These results have encouraged us to synthesize further new biscarbazoles by variation of the dianilino linker to form diarylalkylamine linker units.

Table 1 *in vitro* Growth inhibitory values of compound **5b** against a variety of leukemia cells lines; a mean graph is shown in the right side of the table

Panel/cell line (leukemia)	$\log_{10} GI_{50}$	GI_{50}
CCRF-CEM	–4.39	
HL-60 (TB)	–5.05	
K-562	>–4.00	
MOLT-4	>–4.00	
SR	–4.35	

Moreover, the compounds **5** are promising candidates for inhibition of several protein kinase enzymes.[14] Details will be published later. DNA-binding studies of the biscarbazoles are in progress.

Conclusion

We have developed convenient procedures for the synthesis of new bis(tetrahydropyrrolo[3,4-*b*]carbazoles) with a diaryl spacer with several functionalities. The synthetic concept outlined in Scheme 1 is highly suitable for the construction of biscarbazoles with a great variety of linkers and of linkers with relatively low N-basicity. However, the synthetic procedure starting with the furo[*b*]carbazole **6**, outlined in Scheme 2, is more appropriate for the synthesis of biscarbazoles with more basic linkers. For the introduction of a spermine linker a carboxylic acid amidation reaction was performed (Scheme 4).

Experimental

General details

^{1}H- and ^{13}C-NMR spectra were recorded at room temperature using Bruker AC 300 and 400 spectrometers and Me_4Si as an internal reference and J values are given in Hz. The FD mass spectra were measured with a Varian CH 7a spectrometer and the MALDI-TOF spectra with Bruker Reflex II (20 kV) instrument. Ionisation modes are indicated in parentheses. Elemental analyses were performed using a Carlo Erba Strumentazione 1106 apparatus. Mps were measured with an Electrothermal 8200 instrument. Flash column chromatography was performed on Merck 60 silica gel (particle size: 0.040–0.063 mm). Chiral HPLC was performed on a Merck Hitachi L-6200 instrument with a Whelk-O1 (5 μm), 250 × 4.6

mm analytical column using as eluent acetonitrile–methanol–water (20 : 70 : 10). A Hitachi L-4000 UV-detector was used at $\lambda = 254$ nm. The light petroleum used boiled in the range 40–60 °C. All reactions were performed in highly pure, anhydrous solvents under an argon atmosphere. The yields given refer to analytically pure compounds. In all cases, the biscarbazoles included some amount of pure solvent in a non-stoichiometric ratio.

General procedure for the preparation of compounds 4

Dianilines **7** (6.70 mmol) were added to a solution of maleic acid anhydride (14.08 mmol) in 50 ml dimethyl ketone and the solution was stirred at room temperature for 1 h. A slurry of the corresponding maleamic acid was mixed with 0.1 g $Co(OAc)_2 \cdot 4H_2O$ and (16.09 mmol) acetic anhydride and heated to 55 °C. Triethylamine (1 ml) was added over 10 min, and the mixture was further heated at 58–60 °C for 1.5 h and cooled to 25 °C to give *N*,*N*′-bismaleimide.[7]

General procedure for the preparation of compounds 5

To a solution of bismaleimide **4** (1.45 mmol) and 2,3-bis-(bromomethyl)indole **2** (2.9 mmol) in *N*,*N*′-dimethylformamide (DMF) or dimethoxyethane (DME) at 65 °C was added powdered sodium iodide (100 mg). The reaction mixture was stirred for 1 h. The crude product was treated with sodium thiosulfate and then filtered off. The solution was concentrated to a volume of 5–10 ml under reduced pressure and the residue obtained was washed with water, whereupon a precipitate was formed. The solid material was separated and washed with methanol. The resulting residue was purified by flash column chromatography using light petroleum and ethyl acetate as eluent (ratio 1 : 2).

Preparation of compound 6

To a solution of 1-acetyl-2,3-bis(bromomethyl)indole **2**, (R = Ac 5.8 mmol) and maleic acid anhydride (5.8 mmol) in *N*,*N*′-dimethylformamide or dimethoxyethane at 55–65 °C was added powdered sodium iodide (250 mg). The reaction mixture was stirred at 65 °C for 1 h. The crude product was treated with sodium thiosulfate and then filtered off. The solution was concentrated to a volume of 5–10 ml under reduced pressure and the residue obtained was washed with water, whereupon a precipitate was formed. The solid material was separated and the resulting residue was purified by flash column chromatography using light petroleum and ethyl acetate as eluent (ratio 1 : 4).

General procedure for the preparation of compounds 8

To a solution of a hexahydrofuro[3,4-*b*]carbazoledione **6** (1.6 mmol) in acetone (50 ml) was added the appropriate bisaniline **7** (0.8 mmol). The reaction mixture was stirred at room temperature for 1 h. A slurry of the corresponding maleimic acid was mixed with $Co(OAc)_2 \cdot 4H_2O$ (0.1 mmol) and acetic anhydride (1.9 mmol) and heated to 55 °C. After 10 min triethylamine (1.7 mmol) was added over a period of 10 min and then the reaction mixture was further heated to 58–60 °C for 1.5 h. The crude product was cooled to 25 °C and concentrated to a volume of 20 ml. Then the resulting residue was purified by flash column chromatography using light petroleum, ethyl acetate and diethylamine as eluent (ratio 1 : 2 : 1).

Preparation of compound 9

To a solution of 2,3-bis(bromomethyl)indole **2** (1.16 mmol) and pyrrolylbenzaldehyde (1.16 mmol) in *N*,*N*′-dimethylformamide or dimethoxyethane at 65 °C was added powdered sodium iodide (20 mg). The reaction mixture was stirred for 1 h. The crude product was treated with sodium thiosulfate and then filtered off. The solution was concentrated to a volume of 5–10 ml under reduced pressure and the residue obtained was washed with water, whereupon a precipitate was formed. The solid material was separated and washed with methanol. The resulting residue was purified by flash column chromatography using light petroleum and ethyl acetate as eluent (ratio 1 : 2).

General procedure for the preparation of compounds 12

In a 100 ml round-bottomed flask provided with an electromagnetic stirrer, a reflux condenser and an N_2-guard equipment were placed ethanol (30 ml, 40%), polyamine **10b** (4.9 mmol), and sodium acetate (0.01 mol) as a buffering agent. The flask was then heated to 60–70 °C on a water-bath. When the solid compounds dissolved, nitrobenzaldehyde **11** (9.8 mmol) was added. in an N_2-atmosphere The solution was refluxed with continuous stirring at 60–70 °C for 1.5 h. The crude product was cooled to 25 °C and concentrated to a volume of 20 ml, whereupon a precipitate was formed. The solid material was separated and the resulting residue was purified by flash column chromatography using light petroleum and ethyl acetate as eluent (ratio 1 : 4).

Preparation of compound 13

To a solution of 2,3-bis(bromomethyl)indole **2** (5.79 mmol) and pyrrolylbenzoic acid (5.79 mmol) in *N*,*N*′-dimethylformamide or dimethoxyethane at 65 °C was added powdered sodium iodide (50 mg). The reaction mixture was stirred for 1 h. The crude product was treated with sodium thiosulfate and then filtered off. The solution was concentrated to a volume of 5–10 ml under reduced pressure and the residue obtained was washed with water, whereupon a precipitate was formed. The solid material was separated and washed with methanol. The resulting residue was purified by flash column chromatography using light petroleum and ethyl acetate as eluent (ratio 1 : 2).

Preparation of compound 14

To a solution of a carboxylic acid **13** (2.56 mmol) in *N*,*N*′-dimethylformamide (50 ml) was added 1,1′-dicarbonyldiimidazole CDI (2.56 mmol) and the resulting suspension was stirred at rt for 30 min, then treated with spermine **10b** (1.28 mmol). The reaction mixture was stirred at room temperature for 1 day, then concentrated *in vacuo*. Then the resulting residue was purified by flash column chromatography using dichloromethane, methanol and ammonium hydroxide as eluent (ratio 7 : 3 : 1) to afford impure **14** containing acid **13**.

1,2-Bis[4-(5-benzoyl-1,3-dioxo-1,2,3,3a,4,5,10,10a-octahydropyrrolo[3,4-*b*]carbazol-2-yl)phenyl]ethane 5a

This compound was obtained from *in-situ* generated *N*-benzoylindole-2,3-quinodimethane **3** from *N*-benzoyl-2,3-bis(bromomethyl)indole **2** 418 mg (1.02 mmol) as starting material and bismaleimide **4** 191 mg (0.51 mmol). The crude product was purified by flash column chromatography using gradient light petroleum and ethyl acetate as eluent (ratio 1 : 2). Yield 60%, mp 260–265 °C (from ethanol); $C_{56}H_{42}N_4O_6$; δ_H (300 MHz, $CDCl_3$) 2.86 (4H, s, 2 × C_2H_4-H), 3.03–3.14 (4H, m, 2 × 10-Hα and 2 × 10-Hβ), 3.30–3.31 (2H, d, 2 × 10a-H), 3.36–3.39 (2H, m, 2 × 3a-H), 3.42–3.56 (4H, m, 2 × 4-Hβ and 2 × 4-Hα), 7.02–7.05 (4H, d, 2 × 3′,5′-H), 7.11–7.29 (10H, m, 2 × 2′,6′-H, 2 × 8-H, 2 × 7-H, 2 × Bz-H), 7.48–7.53 (6H, m, 2 × 9-H, 4 × Bz-H), 7.61–7.70 (6H, m, 4 × Bz-H, 2 × 6-H); δ_C (75 MHz, $CDCl_3$) 20.90 (2 × C-10), 23.80 (2 × C-4), 37.33 (2 × C-C_2H_4), 39.20 (2 × C-10a), 40.14 (2 × C-3a), 114.90 (2 × C-6), 115.49 (2 × C_q), 118.03 (2 × C-9), 123.15 (2 × C-8), 124.06 (2 × C-7), 126.22 (2 × C-3′, 2 × C-5′), 128.50 (2 × C_q), 128.96 (2 × 2 × C_t-Bz), 129.10 (2 × 2 × C_t-Bz), 129.56 (2 × C-2′, 2 × C-6′), 129.77 (2 × C_q), 132.96 (2 × 2 × C_t-Bz), 133.47 (2 × C_q), 135.40 (2 × C_q), 136.87 (2 × C_q), 142.10 (2 × C_q),

168.91 (2 × C=O, Bz), 177.98 (2 × C-1), 178.56 (2 × C-3); *m*/*z* (FD) 867.6 (M^+, 100%).

Bis[4-(5-benzoyl-1,3-dioxo-1,2,3,3a,4,5,10,10a-octahydropyrrolo[3,4-*b*]carbazol-2-yl)phenyl]amine 5b

This compound was obtained from *in-situ* generated *N*-benzoylindole-2,3-quinodimethane **3** from *N*-benzoyl-2,3-bis(bromomethyl)indole **2** 1200 mg (2.95 mmol) as starting material and bismaleimide **4** 529 mg (1.47 mmol). The crude product was purified by flash column chromatography using gradient light petroleum and ethyl acetate as eluent (ratio 1 : 2). Yield 45%, mp 243–249 °C (from ethanol); found: C, 75.53; H, 4.67; N, 7.98. $C_{54}H_{39}N_5O_6$ requires C, 75.98; H, 4.56; N, 8.20%; δ_H (400 MHz, DMSO) 2.94 (4H, br s, 2 × 10-Hα, 2 × 10-Hβ), 3.01–3.07 (2H, q, ^2J 7.92, 2 × 4-Hβ), 3.19–3.23 (2H, d, 2 × 4-Hα), 3.51–3.57 (4H, m, 2 × 10a-H, 2 × 3a-H), 6.88–6.90 (4H, d, ^2J 8.8, 2 × 3′-H, 2 × 5′-H), 7.04-7.07 (4H, d, 2 × 2′-H, 2 × 6′-H), 7.13–7.17 (2H, t, ^2J 7.20, 2 × 8-H), 7.20–7.23 (2H, t, ^2J 7.0, 2 × 7-H), 7.31–7.33 (2H, d, 2 × 9-H), 7.56–7.59 (6H, t, ^2J 8.0, 2 × Bz-H), 7.65–7.67 (4H, d, 2 × Bz-H), 7.70–7.73 (2H, d, 2 × 6-H), 8.51 (1H, s, N–H); δ_C (100.6 MHz, DMSO) 19.93 (2 × C-10), 23.52 (2 × C-4), 30.55 (2 × C-10a), 38.88 (2 × C-3a), 114.30 (2 × C-6), 115.47 (2 × C-9b), 116.63 (2 × 2 × C_t-Bz), 117.99 (2 × C-9), 122.90 (2 × C_t), 123.59 (2 × C-8), 124.04 (2 × C5a), 127.58 (2 × 2 × C_t-Bz), 128.30 (2 × 2 × C_t-3′, 5′), 128.95 (2 × C9a), 129.06 (2 × 2 × C_t-2′, 6′), 132.88 (2 × C-7), 133.78 (2 × C_q), 135.07 (2 × C_q), 136.16 (2 × C_q), 142.81 (2 × C_q), 168.36 (2 × C=O, C-Bz), 178.55 (2 × C-1), 178.89 (2 × C-3); *m*/*z* (FD) 854 (M^+, 100%).

Bis[4-(5-acetyl-1,3-dioxo-1,2,3,3a,4,5,10,10a-octahydropyrrolo-[3,4-*b*]carbazol-2-yl)phenyl]diazene 5c

This compound was obtained from *in-situ* generated *N*-acetylindole-2,3-quinodimethane **3** from *N*-acetyl-2,3-bis(bromomethyl)indole **2** 700 mg (2.03 mmol) as starting material and bismaleimide **4** 377 mg (1.01 mmol). The crude product was purified by flash column chromatography using gradient light petroleum and ethyl acetate as eluent (ratio 1 : 2). Yield 50%, mp 250–255 °C (from ethanol); $C_{44}H_{34}N_6O_6$; δ_H (300 MHz, DMSO) 2.72 (6H, s, 2 × CH_3), 3.09–3.21 (4H, m, 2 × 10-Hα, 2 × 10-Hβ), 3.40–3.49 (2H, dd, ^2J 17.2, ^3J 8.1, 2 × 4-Hβ), 3.60–3.75 (6H, m, 2 × 4-Hα, 2 × 10a-H, 2 × 3a-H), 7.22–7.30 (4H, d, 2 × 2H, 3′, 5′-H), 7.43–7.47 (4H, d, 2 × 2H, 2′, 6′-H), 7.54–7.60 (2H, d, 2 × 9-H), 7.93–7.98 (4H, t, 2 × 7-H, 2 × 8-H), 7.70–7.73 (2H, d, 2 × 6-H); δ_C (75 MHz, DMSO) 19.80 (2 × C-10), 23.82 (2 × C-4), 27.41 (2 × C-10a), 27.41 (2 × CH_3), 38.60 (2 × C-3a), 115.50 (2 × C-6), 118.25 (2 × C-9), 123.31 (2 × 2 × C_t), 123.41 (2 × C-8), 124.46 (2 × C-7), 127.47 (2 × C_q), 128.09 (2 × 2 × C_t), 128.82 (2 × C_q), 133.61 (2 × C_q), 135.23 (2 × C_q), 135.81 (2 × C_q), 151.24 (2 × C_q), 170.50 (2 × C=O, C-Ac), 178.73 (2 × C-1), 178.87 (2 × C-3); *m*/*z* (FD) 743.1 (M^+, 100%).

Bis[4-(5-benzoyl-1,3-dioxo-1,2,3,3a,4,5,10,10a-octahydropyrrolo[3,4-*b*]carbazol-2-yl)phenyl] ether 5d

This compound was obtained from *in-situ* generated *N*-benzoylindole-2,3-quinodimethane **3** from *N*-benzoyl-2,3-bis(bromomethyl)indole **2** 2370 mg (5.82 mmol) as starting material and bismaleimide **4** 1048 mg (2.91 mmol). The crude product was purified by flash column chromatography using gradient light petroleum and ethyl acetate as eluent (ratio 1 : 2). Yield 65%, mp 153–159 °C (from ethanol); $C_{54}H_{58}N_4O_7$; δ_H (300 MHz, $CDCl_3$) 3.03–3.14 (4H, m, 2 × 10-Hα, 2 × 10-Hβ), 3.31–3.32 (2H, d, 2 × 10a-H), 3.38–3.39 (2H, d, 2 × 3a-H), 3.44–3.56 (4H, m, 2 × 4-Hβ, 2 × 4-Hα), 6.97–7.00 (4H, d, 4 × Bz-H), 7.06–7.15 (8H, m, 2 × 9-H, 2 × 8-H, 2 × 7-H, 2 × Bz-H), 7.19–7.28 (2H, dd, ^2J 17.1, ^3J 7.4, 2 × Bz-H), 7.47–7.52 (6H, t, 2 × Bz-H, 2 × 3′-H, 2 × 5′-H), 7.61–7.69 (6H, dd, ^2J 17.1, ^3J 7.4, 2 × 2′-H, 2 × 6′-H, 2 × 6-H); δ_C (75 MHz, $CDCl_3$) 20.93 (2 × C-10), 23.82 (2 × C-4), 39.21 (2 × C-10a), 40.15 (2 × C-3a), 114.91 (2 × C-6), 115.47 (2 × C_q), 118.01 (2 × C-9), 119.42 (2 × C-8), 123.18 (2 × C-7), 124.09 (2 × C-3′, 2 × C-5′), 127.15 (2 × C_q), 127.86 (2 × 2 × C_t-Bz), 128.45 (2 × 2 × C_t-Bz), 128.98 (2 × C-2′, 2 × C-6′), 129.56 (2 × C_q), 132.99 (2 × 2 × C_t-Bz), 133.45 (2 × C_q), 135.37 (2 × C_q), 136.86 (2 × C_q), 156.58 (2 × C_q), 168.90 (2 × C=O, Bz), 177.97 (2 × C-1), 178.55 (2 × C-3); *m*/*z* (FD) 854.6 (M^+, 100%).

Bis[4-(5-acetyl-1,3-dioxo-1,2,3,3a,4,5,10,10a-octahydropyrrolo-[3,4-*b*]carbazol-2-yl)phenyl] disulfide 5e

This compound was obtained from *in-situ* generated *N*-acetylindole-2,3-quinodimethane **3** from *N*-acetyl-2,3-bis-(bromomethyl)indole **2** 1700 mg (4.93 mmol) as starting material and bismaleimide **4** 1006 mg (2.46 mmol). The crude product was purified by flash column chromatography using gradient light petroleum and ethyl acetate as eluent (ratio 1 : 2). Yield 55%, mp 130–145 °C (from methanol); $C_{44}H_{34}N_4O_6S_2$; δ_H (300 MHz, $CDCl_3$) 2.75 (6H, s, 2 × CH_3), 2.99–3.09 (2H, m, 2 × 10-Hβ), 3.30–3.40 (4H, m, 2 × 10-Hα, 2 × 4-Hβ), 3.50–3.56 (4H, m, 2 × 10a-H, 2 × 3a-H), 3.92–3.99 (2H, d, 2 × 4-Hα), 7.00–7.03 (4H, d, 2 × 3′-H, 2 × 5′-H), 7.07–7.09 (4H, d, 2 × 2′-H, 2 × 6′-H), 7.25–7.33 (2H, m, 2 × 9-H), 7.42–7.46 (4H, m, 2 × 7-H, 2 × 8-H), 7.90–7.95 (2H, m, 2 × 6-H); δ_C (75 MHz, $CDCl_3$) 20.66 (2 × C-10), 24.09 (2 × C-4), 27.40 (2 × CH_3), 38.77 (2 × C-10a), 40.10 (2 × C-3a), 115.20 (2 × C-6), 115.69 (2 × C_q), 118.15 (2 × C-9), 123.39 (2 × C_t), 124.69 (2 × C-8), 126.77 (2 × C-7), 127.09 (2 × 2 × C_t), 128.86 (2 × C_q), 130.81 (2 × C_q), 133.01 (2 × C_t), 133.10 (2 × C_q), 135.95 (2 × C_q), 137.17 (2 × C_q), 169.73 (2 × C=O, C-Ac), 177.95 (2 × C-1), 178.26 (2 × C-3); *m*/*z* (FD) 778.8 (M^+, 100%).

Bis[4-(5-acetyl-1,3-dioxo-1,2,3,3a,4,5,10,10a-octahydropyrrolo-[3,4-*b*]carbazol-2-yl)phenyl] hydrogen phosphate 5f

This compound was obtained from *in-situ* generated *N*-acetylindole-2,3-quinodimethane **3** from *N*-acetyl-2,3-bis(bromomethyl)indole **2** 500 mg (1.45 mmol) as starting material and bismaleimide **4** 319 mg (0.72 mmol). The crude product was purified by flash column chromatography using gradient light petroleum and ethyl acetate as eluent (ratio 1 : 2). Yield 30%, mp 140–147 °C (from ethanol); $C_{44}H_{35}N_4O_{10}P$; δ_H (300 MHz, $CDCl_3$) 2.71 (6H, s, 2 × CH_3), 2.89–2.90 (2H, d, 2 × 10-Hα), 2.97–3.02 (6H, m, 2 × 4-Hβ, 2 × 10a-H, 2 × 10-Hβ), 3.45–3.52 (4H, m, 2 × 4-Hα, 2 × 3a-H), 6.94–6.97 (2H, d, 2 × 3′-H or 5′-H), 7.01–7.06 (2H, t, 2 × 2′-H or 6′-H), 7.29–7.38 (6H, m, 2 × 3′-H or 5′-H, 2 × 2′-H or 6′-H, 2 × 7-H, or 8-H), 7.55–7.57 (2H, m, 2 × 7-H, or 8-H), 7.63–7.65 (2H, d, 2 × 9-H), 7.85–7.88 (2H, d, 2 × 6-H); δ_C (75 MHz, $CDCl_3$) 10.89 (2 × C-10), 22.42 (2 × C-4), 22.42 (2 × CH_3), 22.63 (2 × C-10a), 26.65 (2 × C-3a), 109.82 (2 × C-6), 112.48 (2 × C-9), 113.69 (2 × C_t), 114.83 (2 × C-8), 118.17 (2 × C-7), 118.35 (2 × C_q), 119.61 (2 × C_t), 120.99 (2 × C_t), 123.54 (2 × C_t), 124.64 (2 × C_q), 128.37 (2 × C_q), 130.98 (2 × C_q), 137.45 (2 × C_q), 146.57 (2 × C_q), 158.54 (2 × C=O, C-Ac), 164.82 (2 × C-1), 182.48 (2 × C-3); *m*/*z* (FD) 810.3 (M^+, 100%).

Bis[4-(5-benzoyl-1,3-dioxo-1,2,3,3a,4,5,10,10a-octahydropyrrolo-[3,4-*b*]carbazol-2-yl)phenyl]-1,3,4-oxadiazole 5g

This compound was obtained from *in-situ* generated *N*-benzoylindole-2,3-quinodimethane **3** from *N*-benzoyl-2,3-bis(bromomethyl)indole **2** 1240 mg (3.05 mmol) as starting material and bismaleimide **4** 628 mg (1.52 mmol). The crude product was purified by flash column chromatography using gradient light petroleum and ethyl acetate as eluent (ratio 1 : 2). Yield 57%, mp 144–150 °C (from ethanol); $C_{56}H_{38}N_6O_7$; δ_H (300 MHz, $CDCl_3$) 3.09–3.17 (4H, m, 2 × 10-Hα, 2 × 10-Hβ), 3.33–3.48 (4H, m, 2 × 10a-H, 2 × 3a-H), 3.53–3.65 (4H, m, 2 × 4-Hβ,

2 × 4-Hα), 7.12–7.19 (2H, m, 2 × Bz-H), 7.26–7.30 (2H, m, 2 × Bz-H), 7.38–7.43 (4H, d, 2 × 9-H, 2 × Bz-H), 7.46–7.54 (8H, m, 2 × 3′-H, 2 × 5′-H, 2 × 8-H, 2 × 7-H), 7.61–7.75 (8H, m, 2 × 2H-2′, 6′-H, 4 × Bz-H), 8.13–8.16 (2H, d, 2 × 6-H); δ_C (75 MHz, $CDCl_3$) 20.88 (2 × C-10), 23.73 (2 × C-4), 39.29 (2 × C-10a), 40.21 (2 × C-3a), 114.9 (2 × C-6), 115.39 (2 × C_q), 118.03 (2 × C-9), 118.38 (2 × C-8), 123.20 (2 × C_q), 123.60 (2 × C-7), 126.71 (2 × C-3′, 2 × C-5′), 127.67 (2 × 2 × C_t-Bz), 128.23 (2 × C_q), 128.38 (2 × 2 × C_t-Bz), 129.58 (2 × C-2′, 2 × C-6′), 133.05 (2 × C_t-Bz), 133.40 (2 × C_q), 134.86 (2 × C_q), 135.31 (2 × C_q), 136.87 (2 × C_q), 164.05 (2 × C_q), 168.91 (2 × C=O, Bz), 177.50 (2 × C-1), 178.07 (2 × C-3); *m*/*z* (FD) 906.7 (M^+, 100%).

Bis[4-(5-benzoyl-1,3-dioxo-1,2,3,3a,4,5,10,10a-octahydropyrrolo[3,4-*b*]carbazol-2-yl)phenoxyphenyl]bis(trifluoromethyl)methane 5h

This compound was obtained from *in-situ* generated *N*-benzoylindole-2,3-quinodimethane **3** from *N*-benzoyl-2,3-bis(bromomethyl)indole **2** 630 mg (1.54 mmol) as starting material and bismaleimide **4** 525 mg (0.77 mmol). The crude product was purified by flash column chromatography using gradient light petroleum and ethyl acetate as eluent (ratio 1 : 2). Yield 50%, mp 130–133 °C (from ethanol); $C_{69}H_{46}F_6N_4O_8$; δ_H (300 MHz, $CDCl_3$) 3.03–3.14 (4H, m, 2 × 10-Hα, 2 × 10-Hβ), 3.33–3.42 (4H, dd, *J* 8.8, *J* 2.8, 2 × 10a-H, 2 × 3a-H), 3.44–3.57 (4H, m, 2 × 4-Hβ, 2 × 4-Hα), 6.95–6.98 (4H, d, *J* 6.9, 2 × 2′′-H, 2 × 6′′-H), 6.99–7.04 (4H, d, *J* 15.9, 2 × 3′-H, 2 × 5′-H), 7.06–7.16 (6H, m, 2 × 3′′-H, 2 × 5′′-H, 2 × 9-H), 7.21–7.27 (4H, m, 2 × Bz-H, 2 × 2′-H), 7.30–7.35 (4H, m, 2 × Bz-H, 2 × 6′-H), 7.49–7.53 (6H, m, 2 × Bz-H, 2 × 8-H, 2 × 7-H), 7.68–7.70 (2H, d, *J* 8.7, 2 × Bz-H), 7.68–7.70 (4H, d, *J* 7.2, 2 × Bz-H, 2 × 6-H); δ_C (75 MHz, $CDCl_3$) 14.9 (CF_3), 15.6 (CF_3), 20.9 (2 × CH_2, C-10), 23.8 (2 × CH_2, C-4), 39.2 (2 × CH, C-10a), 40.1 (2 × CH, C-3a), 65.6 (C_q), 114.9 (2 × CH, C-6), 115.4 (2 × C_q), 118.0 (2 × CH, C-9), 118.1 (2 × 2CH), 119.8 (2 × 2CH), 123.2 (2 × CH, C-8), 124.1 (2 × CH, C-7), 127.4 (2 × C_q), 127.9 (6 × CH, 2 × C-3′, 2 × C-5′, 2 × CH), 128.2 (2 × C_q), 128.4 (2 × C_q), 128.9 (2 × 2 × CH, Bz), 129.5 (2 × 2 × CH, Bz), 131.8 (2 × CH, C-2′), 133.0 (2 × CH, C-6′), 133.4 (2 × C_q), 135.3 (2 × C_q), 136.8 (2 × C_q), 156.1 (2 × C_q), 157.4 (2 × C_q), 168.9 (2 × C=O, Bz), 177.9 (2 × C-1), 178.5 (2 × C-3).

Bis[4-(5-benzoyl-1,3-dioxo-1,2,3,3a,4,5,10,10a-octahydropyrrolo[3,4-*b*]carbazol-2-yl)benzoyl]piperazine 5i

This compound was obtained from *in-situ* generated *N*-benzoylindole-2,3-quinodimethane **3** from *N*-benzoyl-2,3-bis(bromomethyl)indole **2** 1000 mg (2.45 mmol) as starting material and bismaleimide **4** 593 mg (1.22 mmol). The crude product was purified by flash column chromatography using gradient light petroleum and ethyl acetate as eluent (ratio 1 : 2). Yield 47%, mp 170–185 °C (from ethanol); $C_{60}H_{46}N_6O_8$; δ_H (300 MHz, pyridine) 3.12–3.20 (6H, m, 2 × 10-Hα, 2 × 10-Hβ, 2 × 10a-H), 3.55–3.68 (6H, m, 2 × 3a-H, 2 × 4-Hβ, 2 × 4-Hα), 3.69–3.70 (8H, s, 4 × NCH_2), 7.15–7.20 (2H, m, 2 × 8-H), 7.23–7.30 (2H, m, 2 × 7-H), 7.40–7.45 (8H, m, 2 × 3′-H, 2 × 5′-H, 2 × 2H Bz-H), 7.51–7.57 (8H, m, 2 × 2′-H, 2 × 6′-H, 2 × 6-H, 2 × 9-H), 7.61–7.68 (2H, d, 2 × Bz-H), 7.72–7.75 (4H, d, 2 × 2H-Bz-H,); δ_C (75 MHz, pyridine) 20.94 (2 × C-10), 24.22 (2 × C-4), 39.84 (2 × C-10a), 40.74 (2 × C-3a), 49.74 (4 × NCH_2), 115.23 (2 × C-6), 115.97 (2 × C_q), 118.35 (2 × C-9), 124.13 (2 × 2 × C_t), 126.99 (2 × 2 × C_t), 128.16 (2 × C-3′, 2 × C-5′), 129.07 (2 × C_q), 129.16 (2 × 2 × C_t-Bz), 129.68 (2 × 2 × C_t-Bz), 133.02 (2 × C_t), 134.04 (2 × C_q), 134.28 (2 × C_q), 135.90 (2 × C_q), 136.17 (2 × C_q), 137.21 (2 × C_q), 168.92 (2 × C=O, Bz), 169.24 (2 × C=O), 178.50 (2 × C-1), 178.90 (2 × C-3); *m*/*z* (FD) 978.8 (M^+, 100%).

N^1,N^4-Bis[4-(5-acetyl-1,3-dioxo-1,2,3,3a,4,5,10,10a-octahydropyrrolo[3,4-*b*]carbazol-2-yl)phenyl]succinamide 5j

This compound was obtained from *in situ* generated *N*-acetylindole-2,3-quinodimethane **3** from *N*-acetyl-2,3-bis(bromomethyl)indole **2** 1000 mg (2.89 mmol) as starting material and bismaleimide **4** 660 mg (1.44 mmol). The crude product was purified by flash column chromatography using gradient light petroleum and ethyl acetate as eluent (ratio 1 : 2). Yield 50%, mp 180–185 °C (from ethanol); $C_{48}H_{40}N_6O_8$; δ_H (300 MHz, DMSO) 2.73 (4H, s, 2 × CH_2), 2.85 (6H, s, 2 × CH_3), 3.09–3.30 (2H, m, 2 × 10-Hβ), 3.36–3.42 (4H, m, 2 × 10-Hα, 2 × 4-Hβ), 3.55–3.70 (4H, m, 2 × 10a-H, 2 × 3a-H), 3.89–3.93 (2H, d, 2 × 4-Hα), 7.02–7.10 (4H, d, 2 × 3′-H, 2 × 5′-H), 7.22–7.34 (4H, m, 2 × 2′-H, 2 × 6′-H), 7.39–7.50 (2H, m, 2 × 9-H), 7.52–7.64 (4H, m, 2 × 7-H, 2 × 8-H), 8.09–8.12 (2H, m, 2 × 6-H), 8.90 (2H, s, 2 × N-H); δ_C (75 MHz, DMSO) 19.96 (2 × C-10), 22.99 (2 × C-4), 26.40 (2 × CH_3), 31.70 (2 × CH_2), 39.77 (2 × C-10a), 42.90 (2 × C-3a), 109.69 (2 × C_q), 115.20 (2 × C-6), 117.15 (2 × C-9), 122.99 (2 × C_t), 124.79 (2 × C-8), 126.90 (2 × C-7), 127.89 (2 × 2 × C_t), 128.86 (2 × C_q), 131.85 (2 × C_q), 132.31 (2 × C_t), 134.10 (2 × C_q), 135.95 (2 × C_q), 138.27 (2 × C_q), 168.86 (2 × C=O), 169.73 (2 × C=O, C-Ac), 178.65 (2 × C-1), 179.36 (2 × C-3); *m*/*z* (FD) 828.6 (M^+, 100%).

Bis[4-(5-acetyl-1,3-dioxo-1,2,3,3a,4,5,10,10a-octahydropyrrolo[3,4-*b*]carbazol-2-yl)phenyl]piperazine 8a

This compound was obtained from furocarbazole **6** 500 mg (1.76 mmol) as starting material and piperazinoaniline **7a** 236 mg (0.90 mmol). The crude product was purified by flash column chromatography using gradient light petroleum and ethyl acetate as eluent (ratio 1 : 2). Yield 37%, mp 173–178 °C (from ethyl acetate–hexane); $C_{48}H_{42}N_6O_6$; δ_H (300 MHz, DMSO) 2.86 (6H, s, 2 × CH_3), 2.94 (8H, s, 4 × NCH_2), 3.19–3.36 (6H, m, 2 × 10-Hα, 2 × 10-Hβ, 2 × 4-Hβ), 3.41–3.76 (6H, m, 2 × 3a-H, 2 × 10a-H, 2 × 4-Hα), 6.97–7.04 (4H, m, H-aromatic), 7.20–7.35 (4H, d, H-aromatic), 7.46–7.49 (4H, m, H-aromatic), 7.92–7.95 (2H, m, H-aromatic), 7.98–8.01 (2H, m, H-aromatic); δ_C (75 MHz, DMSO) 21.54 (2 × C-10), 23.32 (2 × C-4), 25.92 (2 × CH_3), 38.84 (2 × C-10a), 41.67 (2 × C-3a), 45.74 (4 × NCH_2), 115.23 (2 × C-aromatic), 115.97 (2 × C_q), 118.35 (2 × C-aromatic), 124.13 (2 × C-aromatic), 126.89 (2 × C-aromatic), 128.17 (4 × C-aromatic), 129.87 (2 × C_q), 133.09 (2 × C-aromatic), 134.48 (2 × C_q), 135.80 (2 × C_q), 136.07 (2 × C_q), 136.41 (2 × C_q), 168.80 (2 × C=O, Ac), 169.24 (2 × C=O), 177.90 (2 × C-1), 178.23 (2 × C-3); *m*/*z* (FD) 798.8 (M^+, 100%).

1,4-Bis{*N*-[4-(5-acetyl-1,3-dioxo-1,2,3,3a,4,5,10,10a-octahydropyrrolo[3,4-*b*]carbazol-2-yl)phenyl]piperazinylmethyl}benzene 8b

This compound was obtained from furocarbazole **6** 500 mg (1.76 mmol) as starting material and piperazinoaniline **7b** 401 mg (0.88 mmol). The crude product was purified by flash column chromatography using gradient light petroleum and ethyl acetate as eluent (ratio 1 : 2). Yield 30%, mp 137–144 °C (from ethyl acetate–hexane); $C_{60}H_{58}N_8O_6$; δ_H (300 MHz, DMSO) 2.78 (4H, s, 2 × CH_2), 2.85 (6H, s, 2 × CH_3), 2.93 (16H, s, 8 × NCH_2), 3.15–3.22 (6H, m, 2 × 10-Hα, 2 × 10-Hβ, 2 × 4-Hβ), 3.65–3.86 (6H, m, 2 × 3a-H, 2 × 10a-H, 2 × 4-Hα), 6.96–7.03 (4H, m, H-aromatic), 7.19–7.34 (4H, m, H-aromatic), 7.45–7.48 (2H, m, H-aromatic), 7.91–7.94 (4H, m, H-aromatic), 7.98–8.0 (2H, m, H-aromatic), 8.04 (4H, s, H-aromatic); δ_C (75 MHz, DMSO) 18.25 (2 × CH_2), 25.59 (2 × CH_3), 27.46 (2 × C-10a), 29.66 (2 × CH_2), 31.51 (2 × CH_2), 33.44 (4 × NCH_2), 36.57 (2 × C-3a), 47.48 (4 × NCH_2), 96.75 (2 × C_q), 115.07 (2 × C-6), 116.88 (2 × C_t), 117.67 (2 × C_q), 118.47 (2 × C-9), 123.23 (2 × C_t), 123.63 (2 × C_t), 124.33 (2 × 2 × C_t), 124.53 (2 × C_t), 128.09 (2 × 2 × C_t), 129.61 (2 × C_q), 134.43 (2 × C_q),

136.17 (2 × C_q), 136.65 (2 × C_q), 141.40 (2 × C_q), 154.86 (2 × C=O, Ac), 169.61 (2 × C-1), 169.85 (2 × C-3); *m*/*z* (FD) 986.6 (M^+, 100%).

1-[4-(4-Nitrophenyl)methyliminobutyl]-2-(nitrophenyl)hexahydropyrimidine 12a

This compound was obtained from 4-nitrobenzaldehyde **11** 4160 mg (24.90 mmol) as starting material and spermidine **10a** 1808 mg (12.44 mmol). The crude product was purified by flash column chromatography using gradient light petroleum, methanol and triethylamine as eluent (ratio 1 : 1 : 9). Yield 75%, mp 92–95 °C (from ethyl acetate–hexane); δ_H (300 MHz, $CDCl_3$) 1.44–1.48 (6H, m, 3 × NCH_2), 1.62–1.66 (2H, m, 2 × CH_2), 1.90–2.02 (2H, m, 2 × NCH_2), 2.25–2.29 (2H, m, 2 × CH_2), 3.52–3.56 (2H, m, 2 × CH_2), 4.04 (1H, s, CH), 7.60–7.63 (2H, d, 2 × H-aromatic), 7.81–7.84 (2H, d, 2 × H-aromatic), 8.14–8.17 (2H, d, 2 × H-aromatic), 8.22–8.24 (2H, d, 2 × H-aromatic), 8.25 (1H, s, N=CH); δ_C (75 MHz, $CDCl_3$) 24.38 (NCH_2), 26.76 (NCH_2), 28.35 (NCH_2), 45.54 (CH_2), 51.65 (CH_2), 53.32 (CH_2), 61.61 (NCH_2), 80.74 (NCH), 123.92 (4 × C_t-aromatic), 128.41 (4 × C_t-aromatic), 128.69 (C_q), 141.71 (C_q), 149.90 (C_q), 150.20 (C_q), 159.29 (N=CH); *m*/*z* (FD) 969.50 (M^+, 100%).

1,4-Bis[2-(*p*-dinitrophenyl)hexahydropyrimidin-1-yl]butane 12b

This compound was obtained from 4-nitrobenzaldehyde **11** 1490 mg (8.91 mmol) as starting material and spermine **10b** 902 mg (4.45 mmol). The crude product was purified by flash column chromatography using gradient light petroleum, methanol and triethylamine as eluent (ratio 1 : 1 : 9). Yield 50%, mp 150–155 °C (from ethyl acetate–hexane); δ_H (300 MHz, $CDCl_3$) 1.11–1.38 (6H, m, 2 × CH_2, NCH_2), 1.58–1.84 (6H, m, 2 × CH_2, NCH_2), 2.00–2.17 (4H, m, 2 × NCH_2), 2.64–2.74 (2H, m, 2 × NH), 3.07–3.17 (4H, m, 2 × NCH_2), 3.94–3.98 (4H, d, 2 × CH), 7.52–7.57 (4H, t, H-aromatic), 8.17–8.16 (4H, t, H-aromatic); δ_C (75 MHz, $CDCl_3$) 24.37 (2 × NCH_2), 26.74 (2 × NCH_2), 45.50 (2 × CH_2), 51.57 (2 × CH_2), 53.23 (2 × NCH_2), 80.73 (2 × CH), 123.91 (4 × C_t-aromatic), 128.76 (4 × C_t-aromatic), 147.69 (2 × C_q), 149.86 (2 × C_q); *m*/*z* (FD) 469.50 (M^+, 100%).

N,*N*′-Bis[4-(5-acetyl-1,3-dioxo-1,2,3,3a,4,5,10,10a-octahydropyrrolo[3,4-*b*]carbazol-2-yl)benzoyl]spermine 14

This compound was obtained from benzoic acid **13** 1000 mg (2.48 mmol) as starting material and spermine **10b** 251 mg (1.24 mmol). The crude product was purified by flash column chromatography using gradient dichloromethane, methanol and ammonium hydroxide as eluent (ratio 7 : 3 : 1). Yield 10%, mp 192–197 °C (from methanol); δ_H (300 MHz, DMSO) 1.73–1.75 (10H, m, 5 × CH_2), 1.80 (6H, s, 2 × CH_3), 1.88 (4H, s, 2 × CH_2), 3.04–3.10 (10H, m, 2 × 10-Hβ, 2×10-Hα, 2×10a-H, 2×CH_2), 3.23–3.35 (10H, m, 2 × 4-Hα, 2 × 4-Hβ, 2 × 3a-H, 2 × CH_2), 6.87–6.98 (4H, m, 2 × H-aromatic), 7.16–7.45 (4H, m, 2 × CH-aromatic), 7.57–7.94 (8H, m, 2 × 9-H, 2 × 7-H, 2 × 8-H, 2 × 6-H), 8.15–8.18 (2H, br s, 2 × NH-amide); δ_C (75 MHz, DMSO) 11.22 (4 × CH_2), 22.85 (2 × C-10), 26.17 (2 × CH_3), 26.09 (2 × C-4), 41.53 (6 × CH_2), 44.90 (2 × C-10a), 46.24 (2 × C-3a), 110.91 (2 × C_q), 112.86 (2 × 2 × C_t), 117.38 (2 × C_t), 118.37 (2 × C_q), 118.45 (2 × C_t), 118.56 (2 × 2 × C_t), 120.36 (2 × C_q), 127.25 (2 × C_q), 129.06 (2 × C_q), 130.51 (2 × C_t), 131.49 (2 × C_t), 136.28 (2 × C_q), 167.39 (2 × C=O, C-Ac), 169.94 (2 × C-3, 2 × C-1, 2 × C=O amide); *m*/*z* (MALDI, TOF) 969.50 (M^+, 100%).

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14 These biochemical assays are from a running project at Aventis pharma Frankfurt/M, Germany.