Pergamon

Tetrahedron 55 (1999) 6243–6260

TETRAHEDRON

Syntheses of 6-Substituted Indolo[3,2-*b*]carbazoles, Including 6-Formylindolo[3,2-*b*]carbazole, an Extremely Efficient Ligand for the TCDD (Ah) Receptor

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Received 5 January 1999; revised 4 March 1999; accepted 18 March 1999

Abstract:

A number of 6-substituted indolo[3,2-*b*]carbazoles have been synthesized using 2,3-diindolylmethane **5** as a crucial precursor. Most notably, 6-formylindolo[3,2-*b*]carbazole **3** has been synthesized, and thereby a previously assigned structure has been confirmed. 6-Formylindolo[3,2-*b*]carbazole **3** is an extremely efficient ligand for the TCDD (Ah) receptor. A much improved synthesis of 2,3-diindolylmethane **5** has also been developed.

Keywords: biologically active compounds; cyclisation; indoles; polycyclic heterocyclic compounds

1. Introduction

The TCDD (2,3,7,8-tetrachlorodibenzo-*p*-dioxin **1**) receptor is a ubiquitous, intracellular protein present in virtually all rodent tissues or human cells examined.[1] Another name for the same receptor commonly used in the literature is the aryl hydrocarbon (Ah) receptor protein. Upon binding to a proper ligand the resulting receptor-ligand complex is translocated to the nucleus where activation of transcription of several genes will take place. These genes encode proteins involved in the metabolism of xenobiotica and in cell growth and differentiation. Most notably, cytochrome P-4501A1 (CYP1A1), considered to play a major role in the activation of procarcinogens, is induced by TCDD-like substances.[1a,b, 2] The hitherto known ligands of the receptor include polychlorinated aromatic hydrocarbons, polycyclic aromatic hydrocarbons, and some compounds of dietary origin, e.g. indolo[3,2-*b*]carbazole **2**.[3] The importance of the signal pathways involving the TCDD receptor in mammals, including man, can hardly be overestimated. Recent data appear to favour a physiological role for the TCDD receptor in addition to its function in xenobiotic metabolism:[4] TCDD receptor deficient mice have a low survival rate and show impaired development of the liver and the immune system.[4]

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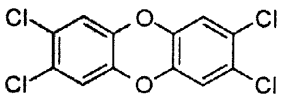
PII: S0040-4020(99)00268-9



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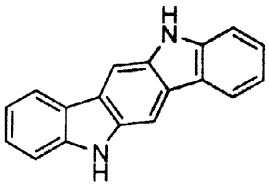
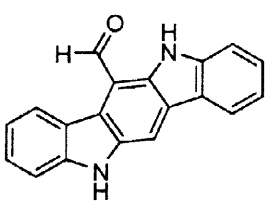


2

A physiological ligand for the receptor has not yet been found, but the search is on. Studies in rats have indicated that UV light induces CYP1A1 in the skin[5] and in the liver.[6] Of the UV-absorbing amino acids, tryptophan is among the most strongly-absorbing.[7] Two of the many products formed when UV-irradiating an aqueous solution of tryptophan possessed extremely high affinities for the TCDD receptor.[8] The compounds were assigned[9] the structures **3** and **4** and the identity of the former has recently been confirmed by synthesis.[10] The mono-formyl compound **3** is especially interesting, binding 5-8 times as strong to the receptor (K_d= 7×10^{-11}) as TCDD **1** itself. The synthesis of **3**[10] has now made animal studies possible, aiming at further investigating receptor function and discovering whether **3** might in fact be an endogenous ligand to the receptor.



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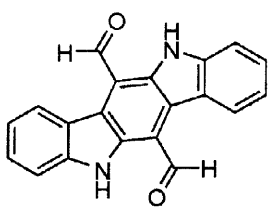
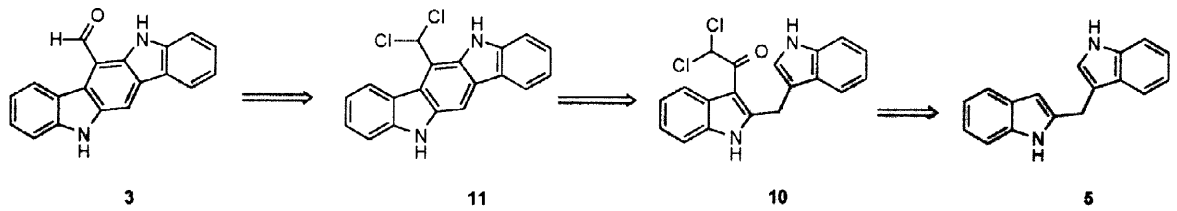


4

In this article we want to disclose the details of the synthesis of **3** as well as of a number of other 6-substituted indolo[3,2-*b*]carbazoles, all emanating from the crucial precursor 2,3-diindolylmethane **5**. Furthermore, two dramatic improvements of the synthesis of 2,3-diindolylmethane **5** since the previous letter[10] will also be presented.

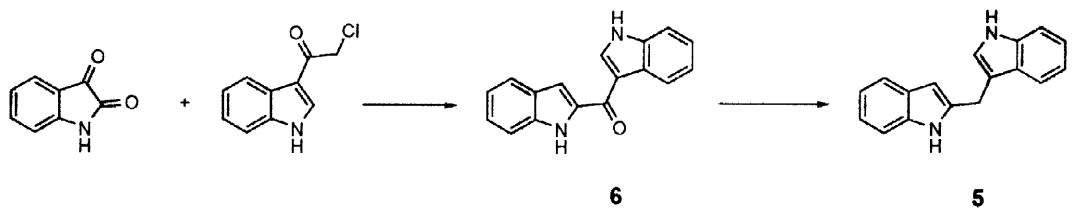
2. Results and discussion

Since indolo[3,2-*b*]carbazole **2** itself is readily available *via* Fischer indolization of the *bis*-phenylhydrazone of 1,4-cyclohexanedione,[11] direct formylation would seem to be a method of choice. However, neither Vilsmeier reagents (several variants) nor more powerful Duff conditions[12] (hexamethylene tetraamine-trifluoroacetic acid) showed any signs of the desired product, so we therefore decided to employ a different strategy involving construction of the indolo[3,2-*b*]carbazole ring system en route (Scheme 1).



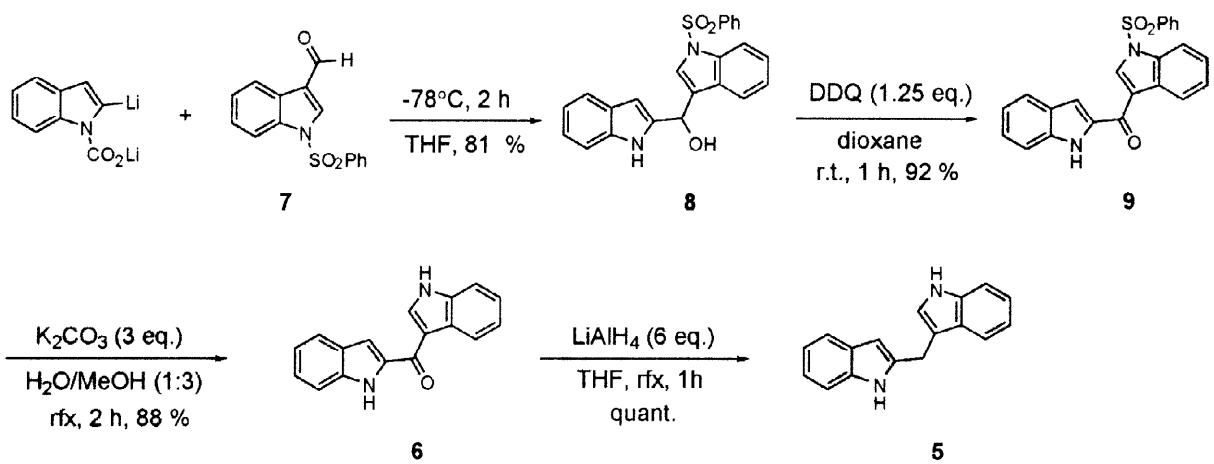
Scheme 1

The 2,3-diindolylmethane **5** has previously been prepared by Jackson and Shannon[13] starting from isatin and 3-chloroacetylindole giving 2,3-diindolylketone **6**, which was subsequently reduced with $LiAlH_4$ (Scheme 2).



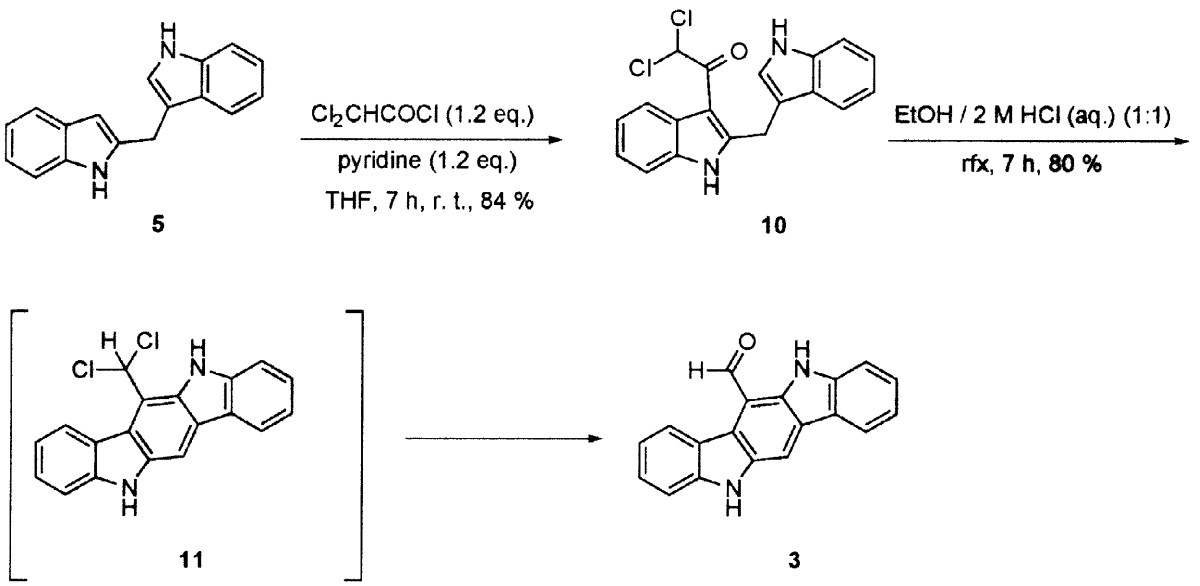
Scheme 2

However, in our hands this method was in many ways troublesome: obtaining sufficiently clean 3-chloroacetylindole in good yields was difficult and the reaction leading to ketone **6** was low-yielding (< 20 %). An alternative approach was therefore developed (Scheme 3), in which the first step was according to the Katritzky protocol,[14] using CO_2 as an easily removed protecting/directing group for lithiation of the indole 2-position. In our previous communication[10] we reported a mediocre 30 % yield for the addition of *N*-phenylsulfonyl-3-formylindole **7** to the doubly lithiated indole. A slight change of the conditions (quenching with saturated, aqueous NH_4Cl instead of aq. HCl) increased the yield of the alcohol **8** substantially. DDQ-oxidation of **8** gave mono-protected ketone **9** (92 %), which was then hydrolysed to the ketone **6** in 88 % yield. Finally, exhaustive $LiAlH_4$-reduction of **6** gave **5** quantitatively. The spectral data of **5** and **6** were in agreement with those already reported.[13]



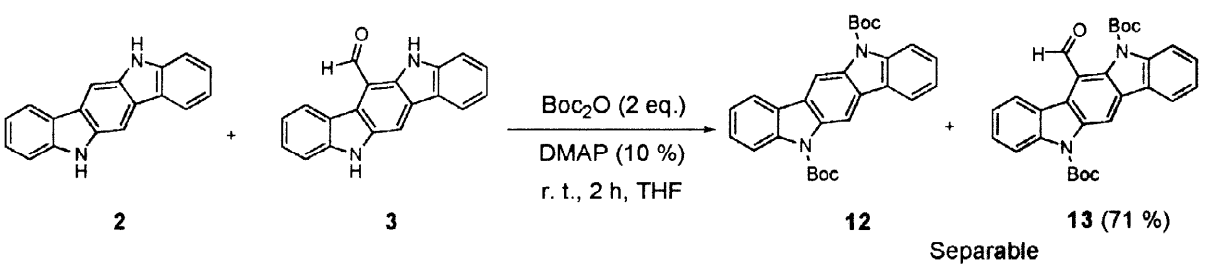
Scheme 3

Next, dichloroacetylation of **5** (Scheme 4) was performed using a modification of an existing technique[15] giving the dichloroacetyl compound **10** in 84 % yield. To our joy, the cyclization of **10** did not only work as planned, but also resulted in hydrolysis of the presumed, intermediate dichloromethyl compound **11**, which we so far have been unable to isolate.



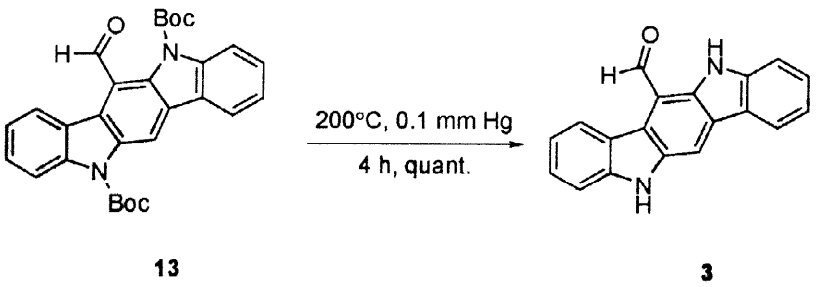
Scheme 4

Unfortunately, the formation of the desired 6-formylindolo[3,2-b]carbazole **3** was accompanied by small amounts of the parent indolo-[3,2-*b*]carbazole **2**, making the preparation of pure **3** difficult: no satisfactory solvent was found for recrystallization (the insolubility of the compounds requires large amounts of solvent, and then very little material is recovered) and **2** and **3** co-sublimed, actually enriching the sublimed material in **2**. Finally, a satisfactory solution was found whereby **2** and **3** were Boc-protected making separation (chromatography) possible (Scheme 5).



Scheme 5

The identity of **12** could be confirmed by independent Boc-ylation of **2** under similar reaction conditions, although the reaction time had to be prolonged due to the extreme insolubility of pure **2**. The desired compound **3** was obtained quantitatively by heating **13** at reduced pressure in order to remove the Boc groups (Scheme 6).

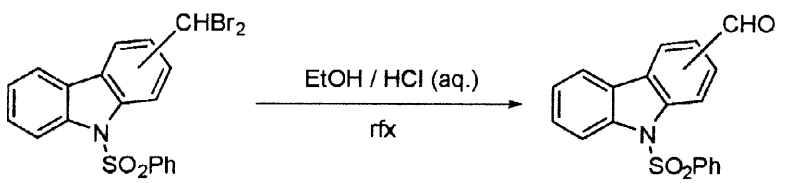


13 3

Scheme 6

The synthesized compound **3** was in all respects identical with the sample obtained by UV-irradiation.[9]

It is worth mentioning that a hydrolysis of a dibromomethyl group to an aldehyde in a similar carbazole system has been described previously in the literature[16] (Scheme 7).

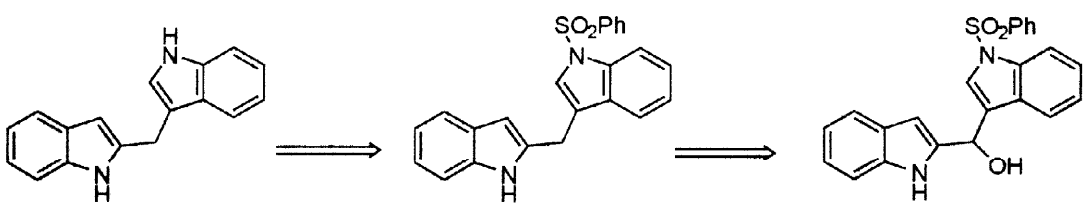


14a, 2-$CHBr_2$
b, 3-$CHBr_2$
c, 4-$CHBr_2$

Scheme 7

The dibromomethyl groups in the 2- and 4-positions were more susceptible to hydrolysis than the one in the 3-position. Thus, hydrolysis of **14a** and **14c** was complete after 5 h in a 3:1 EtOH/0.5 M HCl (aq.) mixture, whereas hydrolysis of **14b** required 24 h in a medium which was twice as acidic.

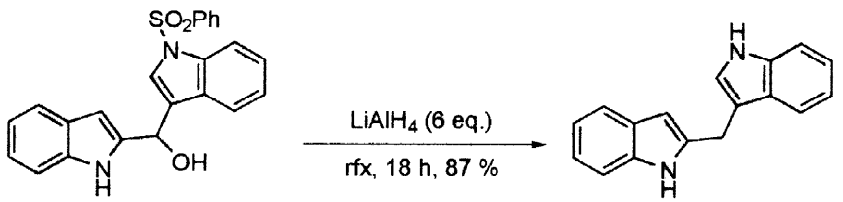
The 2,3-diindolylmethane **5** seemed to be a very promising candidate for synthesis of other 6-substituted indolo[3,2-*b*]carbazoles, but before initiating that investigation we felt that it should be possible to make the synthesis of **5** more efficient: we had hoped to save one step in the reaction sequence by first reducing the alcohol **8** exhaustively and then hydrolyze the potentially formed mono-phenylsulfonylated diindolylmethane **15** to the desired **5** (Scheme 8).



5 15 8

Scheme 8

As it turned out, refluxing the alcohol **8** for 2 h with 6 eq. of $LiAlH_4$ gave just one product (apart from unreacted starting material), namely diindolylmethane **5**. There was no sign of the mono-phenylsulfonyl-protected diindolylmethane **15**. Further experimentation led to **5** in 87 % yield by refluxing **8** for 18 h with 6 eq. of $LiAlH_4$, and thereby a shortening of the previous route to **5** by not one step, but two (Scheme 9).

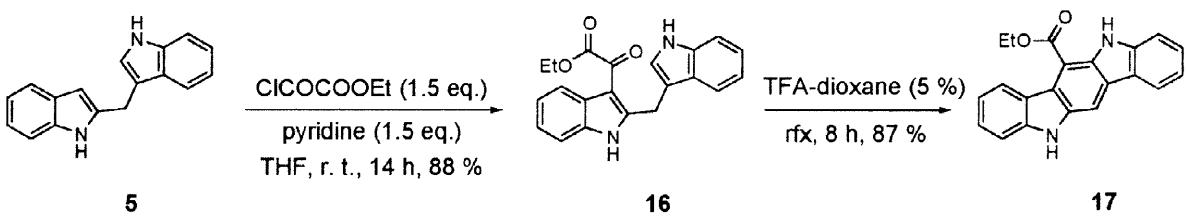


8 **5**

Scheme 9

Since the synthesis of the alcohol **8** had been substantially improved (*vide supra*), we now had an efficient route to diindolylmethane **5**.

With the objective of synthesizing further 6-substituted indolo[3,2-*b*]carbazoles we now turned our attention to reactions of **5** with various electrophiles. For example, **5** could be acylated with ethyl oxalyl chloride to give the α-keto ester **16** in 88 % yield. Cyclization of **16** in 5% TFA/dioxane then gave the ester **17** in high yield (Scheme 10).

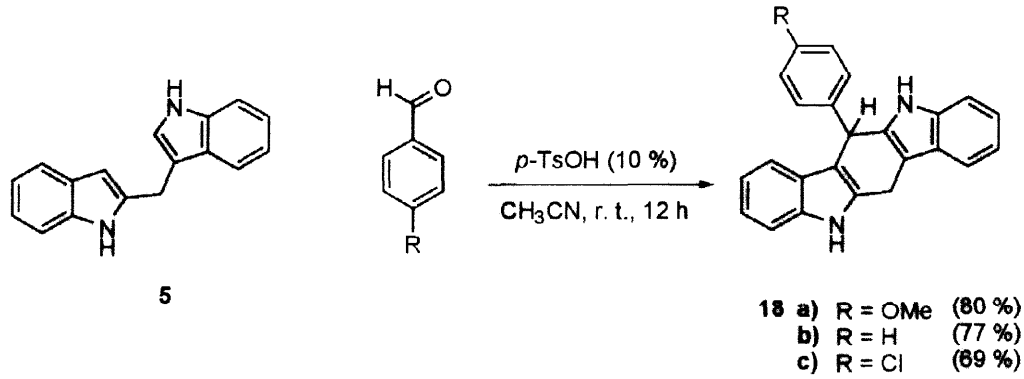


5 **16** **17**

Scheme 10

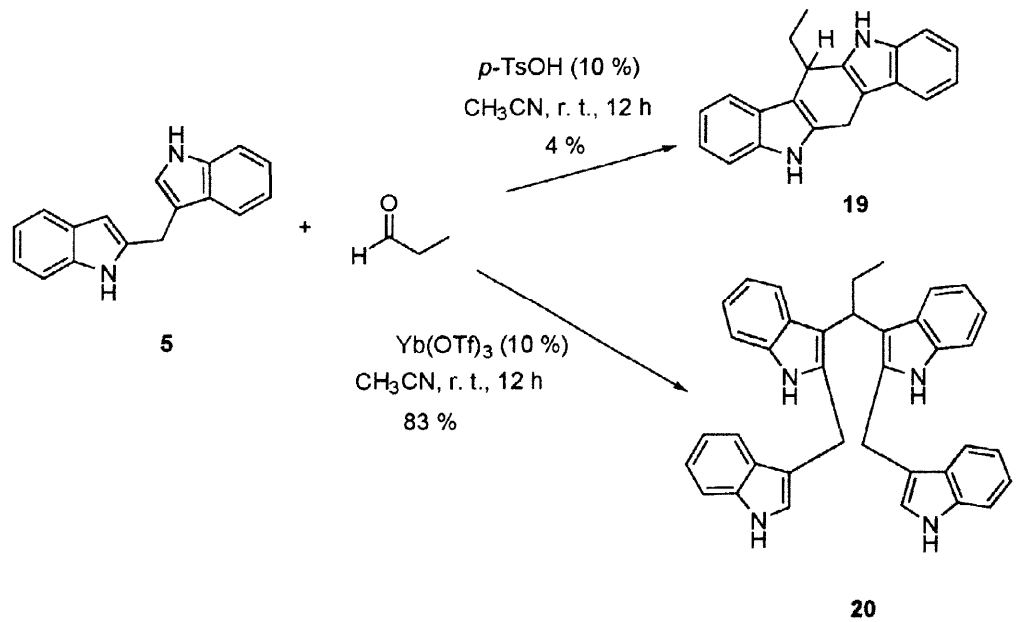
Interestingly, cyclization of the dichloroacetyl compound **10** under similar conditions (50 % TFA-dioxane was needed in this case) did not give the dichloromethyl compound **11**, but again the hydrolysis product, the aldehyde **3** (presumably during work-up). Under these condtions no indolo[3,2-*b*]carbazole **2** was formed, but the isolated yield of the aldehyde **3** was anyway much lower using this protocol.

Compound **5** reacted rapidly with various benzaldehydes in CH_3CN at room temperature with *p*-TsOH as catalyst (10 %) to give 6-aryl-6,12-dihydroindolo[3,2-*b*]carbazoles **15a-c** in good yields (Scheme 11). These dihydro compounds seem to be stable at room temperature for months without dehydrogenation.



Scheme 11

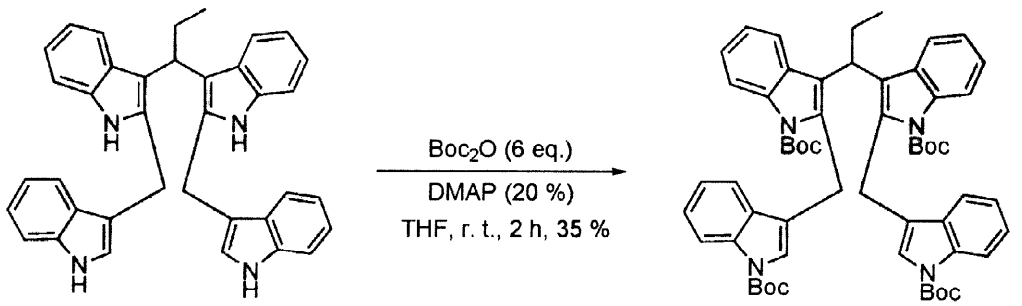
Next, we investigated the reactivity of **5** with an aliphatic aldehyde. At room temperature in CH_3CN with *p*-TsOH as catalyst, **5** reacted with propionaldehyde to give indolo[3,2-*b*]carbazole **19** in a very low yield (Scheme 12). Correspondingly, the reaction of **5** with dichloroacetaldehyde (as its diethyl acetal), to potentially obtain mono-aldehyde **3** in one step, was not successful. Since Wang *et al.* had used lanthanide triflates as efficient catalysts for the reaction of indoles with aldehydes and ketones,[17] we reacted **5** with propionaldehyde in CH_3CN in the presence of $Yb(OTf)_3$ in the hope of obtaining **19** in higer yields. The reaction now looked much cleaner, but instead of **19** the tetraindole **20** was obtained as practically the only product.



Scheme 12

Reasoning that the Yb catalyst might be too large to permit an intramolecular reaction giving **19**, we instead tried the smaller $ZnCl_2$ as catalyst. Using a 50 % catalyst load and higher temperature (50°C was needed) **5** was, however, once again converted into **20** as the practically only product after 12 h. In spite of considerable efforts, the tetraindole **20** could never be

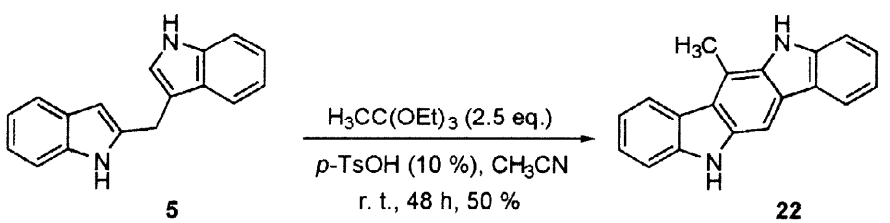
isolated in an analytically pure form: small amounts of a by-product could not be removed. Finally, we isolated **20** as its tetra-Boc derivative **21** (Scheme 13).



20 **21**

Scheme 13

In view of the reported reaction of 3,3-diindolylmethane with triethyl orthoformate in the presence of acid to give parent indolo[3,2-*b*]carbazole **2**,[18] one might expect a reaction with triethyl orthoacetate to give 6-methylindolo[3,2-*b*]carbazole **22**. In fact, no reaction at all took place under the same conditions, most probably as a result of steric hindrance. In contrast, 2,3-diindolylmethane **5** reacted with triethyl orthoacetate, albeit sluggishly, to give **22** in 50 % yield (Scheme 14).



5 **22**

Scheme 14

Reflux conditions actually gave a *lower* yield, but that as a result of product staying in solution. No product other than **22** was formed: the remaining material consisted entirely of unreacted starting material.

3. Conclusion

In summary, we have synthesized a number of 6-substituted indolo[3,2-*b*]carbazoles, most notably 6-formylindolo[3,2-*b*]carbazole **3**, an extremely efficient ligand for the TCDD (Ah) receptor. All the indolo[3,2-*b*]carbazoles emanated from the crucial precursor 2,3-diindolylmethane **5**.

4. Experimental section

With the following exceptions all reagents and solvents were purchased from commercial suppliers and used without further purification: indole-3-carboxaldehyde was kindly donated by Laboratoires Plan, Geneva; benzaldehyde was freshly distilled before use; indolo-[3,2-*b*]carbazole was synthesized according to Robinson;[11] THF was distilled from Na/benzophenone, and distilled solvents were used for flash chromatography. The petroleum ether used for chromatography had the boiling point range 60-80°C. Silica gel (230-400 mesh) for column chromatography as well as corresponding TLC plates were purchased from Merck. Experiments involving dry solvents were performed using oven-dried glassware. The expressions "evaporation of solvent(s)" and "concentration of solvent(s)" refer to the use of a rotatory evaporator at reduced pressure at 30°C. NMR experiments were performed on a Bruker DPX300 or AM400 instrument. IR spectra were recorded on a Perkin-Elmer FT-IR 1600 spectrophotometer. Melting points (uncorrected) were determined on an Electrothermal IA9020 digital melting point apparatus or on a Kofler Hotbench (Leica VM HB) when appropriate. Microanalyses were performed by H. Kolbe Mikroanalytisches Laboratorium, Mühlheim an der Ruhr, Germany. High resolution mass spectroscopy (HRMS) experiments were performed by Sveriges Lantbruksuniversitet (SLU), Uppsala, Sweden.

N-Benzenesulfonyl-3-formylindole, (7)

Indole-3-carboxaldehyde (10.16 g, 70 mmol), anhydrous K_2CO_3 (38.70 g, 280 mmol) and phenylsulfonyl chloride (24.73 g, 140 mmol) were suspended in 2-butanone (280 mL) and refluxed for 5 h. The reaction was monitored by TLC (50 % ethyl acetate-petroleum ether) since prolonged heating deteriorated the yield. The resulting mixture was filtered while hot and the solvent was evaporated to give a solid, off-white material. This was suspended in diethyl ether (100 mL) and stirred overnight to give a smooth mixture. The solid material was then filtered off to give 18.17 g (91 %) of pure **7** as an off-white powder. An analytical sample was obtained as white, shiny crystals by recrystallization from EtOH, mp 157.5-158.5°C (Lit. 156.5-158°C[19]).
^{1}H NMR ($CDCl_3$, 300 MHz) δ 10.11 (s, 1H), 8.27 (d, 1H, J= 7.7 Hz), 8.25 (s, 1H), 8.01-7.92 (m, 3H), 7.63 (t, 1H, J= 7.5 Hz), 7.52 (dd, 2H), 7.43 (dd, 1H), 7.37 (dd, 1H).
^{13}C NMR ($CDCl_3$, 75 MHz) δ 185.5 (d), 137.6 (s), 136.3 (d), 135.5 (s), 134.9 (d), 129.9 (d), 127.4 (d), 126.6 (d), 126.5 (s), 125.3 (d), 122.8 (d), 122.7 (s), 113.4 (d).
IR (KBr) 3129, 2844, 1678, 1543, 1479, 1445, 1392, 1377, 1271, 1228, 1186, 1179, 1123, 1100, 1083, 968, 780, 758, 747, 733, 682, 587, 572, 550 cm^{-1}.

(*N*-Benzenesulfonyl-1*H*-indol-3-yl)-(1*H*-indol-2-yl)-methanol, (8)

Indole (1.172 g, 10 mmol) was dissolved in dry THF (20 mL) under N_2. The solution was cooled to -78 °C and *n*-BuLi (12.5 mmol, 5.0 mL, c=2.5 M) was added dropwise during 10 minutes. The lithium salt precipitated within 5-10 minutes. 1.5 h after the last drop of n-BuLi had been added the solution was protected with a drying tube and CO_2 was bubbled through the mixture during 20 minutes; a clear solution was obtained almost immediately. After the CO_2-bubbling the solution was allowed to stir for 30 minutes to let most of the dissolved CO_2 evaporate. A vacuum pump was then connected to the system to distill off the solvent (to ensure complete removal of CO_2). After pumping for 30 minutes at -78 °C the CO_2-EtOH-bath was replaced with an ordinary ice-bath to remove the solvent completely. Freshly distilled THF

(20 mL) was added, the solid residue was redissolved, and the solution was once again cooled to -78 °C. *tert*-BuLi (12.5 mmol, 7.4 mL, c=1.7 M) was added dropwise during 10 minutes to the stirred solution, whose colour changed continuously from yellow to deep orange. One hour after the addition of *t*-BuLi *N*-benzenesulfonyl-3-formylindole **7** (3.567 g 12.5 mmol) was added in one portion. The obtained, milky mixture was then stirred for 2 h at -78°C before quenching with saturated, aqueous NH_4Cl (1 mL). The suspension was allowed to reach room temperature and diluted with CH_2Cl_2 (100 mL). The organic phase was washed consecutively with water (30 mL) and brine (40 mL) before drying ($MgSO_4$). Evaporation of the solvents gave a golden, fluffy, solid residue which was treated with CH_2Cl_2 (50 mL). The resulting suspension was stirred until smooth and 2.85 g (71 %) of **8** was collected as an analytically pure, shiny, white powder. In order to maximize the yield, the filtrate was purified by column chromatography (ethyl acetate-CH_2Cl_2, 0-5 %). The fractions containing **8** were isolated and the solvents evaporated. As before, the residue was treated with CH_2Cl_2 to give additional 0.40 g of **8.** Total yield: 81 %, mp 145-146°C (decomp.).
^{1}H NMR (DMSO-d_6, 300 MHz) δ 11.14 (s, 1H, N*H*), 8.00 (d, 2H, J= 7.5 Hz), 7.90 (d, 1H, J= 8.3 Hz), 7.77 (s, 1H), 7.69 (t, 1H, J= 7.4 Hz), 7.62-7.53 (m, 3H), 7.42 (d, 1H, J= 7.7 Hz), 7.30 (dd, 2H), 7.16 (dd, 1H), 7.02 (dd, 1H), 6.92 (dd, 1H), 6.27 (d, 1H, J= 2.8 Hz, O*H*), 6.23 (s, 1H), 6.14 (d, 1H, J= 2.8 Hz).
^{13}C NMR (DMSO-d_6, 75 MHz) δ 141.2 (s), 137.0 (s), 136.2 (s), 134.7 (s), 134.6 (d), 129.8 (d), 128.8 (s), 127.5 (s), 126.7 (d), 125.8 (s), 124.8 (d), 123.5 (d), 123.2 (d), 121.0 (d), 120.7 (d), 119.8 (d), 118.7 (d), 113.1 (d), 111. 2 (d), 98.6 (d), 63.0 (d).
IR (KBr) 3536, 3447, 3416, 1448, 1350, 1288, 1277, 1162, 1135, 1099, 1082, 1020, 988, 958, 799, 758, 746, 725, 686, 656, 604, 592, 570, 546 cm^{-1}.
Anal. calcd. for $C_{23}H_{18}N_2O_3S$: C: 68.64; H: 4.51; N: 6.96. Found: C: 68.44; H: 4.54; N: 7.05.

(*N*-Benzenesulfonyl-1*H*-indol-3-yl)-(1*H*-indol-2-yl)-methanone, (9)

The alcohol **8** (386 mg, 0.96 mmol) was dissolved in dioxane (20 mL) at room temperature. DDQ (0.272 g, 1.20 mmol) was added in portions during 5 minutes. A brick-red precipitate was formed and after 1 h the reaction was complete as judged by TLC (50 % ethyl acetate-petroleum ether). The mixture was filtered through a bed of Celite® and the solvent was evaporated. The residue was purified by column chromatography (CH_2Cl_2-petroleum ether, 0-100 %) to give 355 mg (92 %) of pure **9** as a yellowish powder. An analytical sample was obtained as yellowish crystals by recrystallization from *iso*-butyronitrile, mp 223-225°C.
^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.51 (br s, 1H, N*H*), 8.42 (s, 1H), 8.30 (d, 1H, J= 7.3 Hz), 8.04 (d, 1H, J= 7.5 Hz), 7.97 (d, 2H, J= 7.9 Hz), 7.81 (d, 1H, J= 7.9 Hz), 7.60 (t, 1H, J= 7.5 Hz), 7.52-7.37 (m, 6H), 7.34 (s, 1H), 7.21 (dd, 1H).
^{13}C NMR ($CDCl_3$, 100 MHz) δ 180.6 (s), 137.5 (s), 137.5 (s), 135.1 (s), 135.0 (s), 134.6 (d), 131.4 (d), 129.6 (d), 128.4 (s), 127.7 (s), 127.1 (d), 126.4 (d), 126.1 (d), 124.8 (d), 123.2 (d), 122.7 (d), 121.2 (d), 120.6 (s), 113.3 (d), 112.1 (d), 110.3 (d).
IR (KBr) 3396, 3057, 1606, 1535, 1520, 1445, 1387, 1370, 1343, 1311, 1208, 1186, 1171, 1136, 1118, 1094, 999, 960, 855, 780, 769, 757, 738, 685, 634, 598, 570 cm^{-1}.
Anal. calcd. for $C_{23}H_{16}N_2O_3S$: C: 68.98; H: 4.03; N: 7.00. Found: C: 68.89; H: 4.03; N: 6.98.

(1*H*-Indol-3-yl)-(1*H*-indol-2-yl)-methanone, (6)

The mono-phenylsulfonylated diindolylketone **9** (1.00g, 2.50 mmol) was suspended in a mixture of MeOH (60 ml) and H_2O (20 mL) and refluxed for 2 h. After cooling most of the

MeOH was evaporated and the off-white residue was collected and dried to give 573 mg (88 %) of pure **6** as a greyish powder. An analytical sample was obtained as white crystals by recrystallization from *iso*-butyronitrile, mp 260-261°C (Lit.[13] 260-261°C).
^{1}H NMR (DMSO-d_6, 400 MHz) δ 12.09 (br s, 1H, N*H*), 11.76 (s, 1H, N*H*), 8.46 (s, 1H), 8.31 (d, 1H, J= 6.7 Hz), 7.71 (d, 1H, J= 8.1 Hz), 7.54 (d, 1H, J= 6.7 Hz), 7.51 (d, 1H, J= 8.1 Hz), 7.36 (s, 1H), 7.29-7.22 (m, 3H), 7.09 (dd, 1H).
^{13}C NMR (DMSO-d_6, 100 MHz) δ 180.4 (s), 137.0 (s), 136.4 (s), 136.2 (s) 133. 7 (d), 127.3 (s), 126.3 (s), 124.2 (d), 122.9 (d), 122.2 (d), 121.6 (d), 121.4 (d), 119.8 (d), 115.0 (s), 112.4 (d), 112.1 (d), 107.1 (d).
IR (KBr) 3402, 1601, 1526, 1456, 1435, 1404, 1346, 1337, 1232, 1166, 1106, 858, 817, 778, 748, 740, 616, 594, 550, 502 cm^{-1}.

(1*H*-Indol-3-yl)-(1*H*-indol-2-yl)-methane, (5)

Method 1: The method of Jackson[13] (reflux of the diindolylketone **6** with 6 eq. of lithium aluminium hydride in THF for 1 h) gave a quantitative yield of **5**, which could be used without further purification in the next step.

Method 2: Lithium aluminium hydride (95 %) (0.719 g, 18 mmol) was suspended in THF (15 mL) under N_2. The alcohol **8** (0.739 g, 3.0 mmol) dissolved in THF (12 mL) was added during one minute to the mixture. The reactor was covered with aluminium foil to protect from light and the suspension was heated ro reflux. After refluxing the mixture for 18 h it was cooled in an ice-bath before being carefully quenched with a saturated solution of Rochelle's salt. After the quenching was complete the mixture was filtered through a bed of Celite®. The flask and the filter-cake was washed consecutively with THF (25 mL) and CH_2Cl_2 (100 mL). The filtrate was then washed with water (2×30 mL) and brine (60 ml) before drying ($MgSO_4$). After evaporation of the solvents the residue was dissolved in a minimal volume of CH_2Cl_2-petroleum ether (70 %) and rapidly purified by column chromatography (CH_2Cl_2-petroleum ether, 70-100 %) to give 0.645 g (87 %) of **5** as a pinkish powder, mp 138-139°C (Lit.[13] 141-142°C). Compound **5** appeared to be both light- and air-sensitive and was therefore stored in an air-tight container in a fridge. However, we recommend that compound **5** is used as soon as possible after preparation to reduce deterioration.
^{1}H NMR (DMSO-d_6, 400 MHz) δ 10.88 (s, 2H, 2×N*H*), 7.49 (d, 1H, J= 7.7 Hz), 7.39-7.34 (m, 2H), 7.26 (d, 1H, J= 7.7 Hz), 7.23 (s, 1H), 7.06 (dd, 1H), 6.99-6.88 (m, 3H), 6.15 (s, 1H), 4.18 (s, 2H).
^{13}C NMR (CD_3CN, 75 MHz) δ 140.9 (s), 138.0 (s), 137.6 (s), 130.1 (s), 128.6 (s), 124.5 (d), 122.9 (d), 121.8 (d), 120.7 (d), 120.4 (d), 120.2 (d), 119.9 (d), 113.7 (s), 112.7 (d), 111.8 (d), 100.5 (d), 25.3 (t). All peaks in the ^{13}C spectrum could not be resolved in DMSO. However, the ^{1}H NMR spektrum was clearer in DMSO than in CD_3CN.
IR (KBr) 3396, 1616, 1548, 1456, 1425, 1408, 1340, 1292, 1231, 1101, 1008, 787, 772, 746, 629, 623, 594, 578, 509 cm^{-1}.

2,2-Dichloro-1-[2-(1*H*-indol-3-ylmethyl)-1*H*-indol-3-yl]-ethanone, (10)

2,3-Diindolylmethane **5** (560 mg, 2.27 mmol) was dissolved in THF (25 mL) under N_2 and the reactor was covered with Al-foil to protect the reaction from light. Pyridine (216 mg, 2.73 mmol) was added and the solution was cooled to 0°C. Dichloroacetyl chloride (402 mg, 2.73 mmol) was added dropwise during 5 minutes and a white precipitate was formed almost

immediately. The ice-bath was removed and the mixture was stirred at room temperature for 7 h. The formed thick slurry was diluted with CH_2Cl_2 (100 mL) and extracted consecutively with aqueous HCl (2 M, 25 mL), saturated, aqueous $NaHCO_3$ (25 mL), and 75 % brine (50 mL) before drying ($MgSO_4$). After evaporation of the solvents the residue was purified by column chromatography (ethyl acetate-petroleum ether, 0-50 %) to give 678 mg (84 %) of **10** as a pinkish, fluffy solid, mp 80 °C. **10** appeared to be both light- and air-sensitive and was therefore stored in an air-tight container in a fridge. However, we recommend that compound **10** is used as soon as possible after preparation to reduce deterioration.
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.61 (br s, 1H, N*H*), 8.36 (br s, 1H, N*H*), 7.90 (d, 1H, J= 7.9 Hz), 7.47 (d, 1H, J= 8.3 Hz), 7.45 (d, 1H, J= 7.9 Hz), 7.34 - 7.08 (m, 6H), 6.91 (s, 1H), 4.76 (s, 2H).
^{13}C NMR ($CDCl_3$, 100 MHz) δ 182.0 (s), 151.6 (s), 136.6 (s), 134.5 (s), 127.1 (s), 125.5 (s), 124.1 (d), 124.1 (d), 123.1 (d), 123.0 (d), 120.7 (d), 120.4 (d), 118.8 (d), 111.9 (d), 111.6 (d), 109.4 (s), 108.2 (s), 69.9 (d, $CHCl_2$), 25.8 (t, CH_2).
IR (KBr) 3396, 1641, 1483, 1456, 742 cm^{-1}.
HRMS (FAB+), calcd. for $C_{19}H_{14}Cl_2N_2O$: 356.0483. Found: 356.0483.

6-Formylindolo[3,2-*b*]carbazole, (3)

Dichloroacetyl compound **10** (0.573 g, 1.60 mmol) was dissolved in a mixture of EtOH (15 mL) and aqueous HCl (2 M, 15 mL) and heated at reflux for 7h. After cooling the mixture was concentrated until the remaining liquid was colourless. The brown precipitate was collected and dried to give 0.399 g (88%) of crude 6-formyl-indolo[3,2-*b*]carbazole **3** as a brown powder, pure enough for our purposes (> 90 % as judged by ^{1}H NMR). However, the crude product contained indolo[3,2-*b*]carbazole **2** as major by-product, something which caused trouble when trying to obtain an analytical sample: **2** co-sublimed with formyl compound **3** and the insolubility of the crude product made large quantities of solvent necessary for crystallization (finally in solution very little, if any, material crystallized). Derivatization of the mixture with Boc groups ultimately made separation of **2** and **3** possible [see the preparation below of *N,N'*-di-*tert*-butoxycarbonyl-6-formylindolo[3,2-*b*]carbazole, (**13**) for the preparation of analytically pure **3**].

N,N'-di-*tert*-butoxycarbonyl-indolo[3,2-*b*]carbazole, (12)

Indolo[3,2-*b*]carbazole **2**[11] (0.320 g, 1.25 mmol) was suspended in dry THF (20 mL) under N_2. Boc_2O (0.600 g, 2.75 mmol) was added followed by DMAP (34 mg, 0.275 mmol). The suspension was stirred until the consumption of starting material was complete (12 h) as judged by TLC (ethyl acetate-petroleum ether, 10 %). The solvent was evaporated and the residue was redissolved in a minimal volume of a solution of CH_2Cl_2 and petroleum ether (1:3) and purified by column chromatography (CH_2Cl_2-petroleum ether, 50 %) to give 0.490 g (86 %) of di-Boc-protected indolo[3,2-*b*]carbazole **12** as a white powder, mp 249°C (de-Boc-protection; this process is gradual, so the melting point given was determined on a Kofler Hotbench in such a way that the crystals were rapidly moved towards ever-higher temperatures until a complete, immediate melt was observed).
^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.94 (s, 2H), 8.31 (d, 2H, J= 8.2 Hz), 8.09 (d, 2H, J= 7.5 Hz), 7.50 (dd, 2H), 7.39 (dd, 2H), 1.85 (s, 18H).
^{13}C NMR (CDCl3, 75 MHz) δ 151.5 (s), 139.5 (s), 135.4 (s), 127.4 (d), 126.6 (s), 126.1 (s), 123.3 (d), 119.9 (d), 116.6 (d), 107.1 (d), 84.2 (s), 28.7 (q).

IR (KBr) 2978, 1719, 1481, 1436, 1376, 1311, 1238, 1219, 1153, 1111, 1051, 768, 748 cm^{-1}.
HRMS (FAB+), calcd. for $C_{28}H_{28}N_2O_4$: 456.2049. Found: 456.2010.

N,N'-di-*tert*-butoxycarbonyl-6-formylindolo[3,2-*b*]carbazole, (13)

Crude 6-formylindolo[3,2-*b*]carbazole **3** (62 mg, 0.218 mmol) was suspended in dry THF (5 mL) in a dry flask equipped with a drying tube. Boc_2O (190 mg, 0.872 mmol) was added followed by DMAP (6 mg, 0.044 mmol) and the mixture was stirred until the consumption of starting material was complete (2 h) as judged by TLC (CH_2Cl_2). The solvent was evaporated and the residue was purified by column chromatography (CH_2Cl_2-petroleum ether, 0-100 %) to give 75 mg (71 %) of **13** as a light-yellow, fluffy solid, mp 176-177°C (de-Boc-protection).
^1H NMR ($CDCl_3$, 300 MHz) δ 10.91 (s, 1H), 9.21 (s, 1H), 8.60 (d, 1H, J= 7.7 Hz), 8.36 (d, 1H, J= 8.4 Hz), 8.15 (d, 1H, J= 8.3 Hz), 8.08 (d, 1H, J= 7.5 Hz), 7.58-7.48 (2×dd, 2H), 7.45-7.37 (2×dd, 2H), 1.85 (s, 9H), 1.73 (s, 9H).
^{13}C NMR ($CDCl_3$, 75 MHz) δ 189.7 (d), 152.0 (s), 151.2 (s), 140.8 (s), 139.9 (s), 136.4 (s), 134.5 (s), 128.2 (d), 127.9 (d), 127.0 (s), 126.2 (s), 125.0 (s), 124.9 (d), 123.9 (s), 123.8 (d), 123.5 (d), 120.4 (s), 120.1 (d), 116.5 (d), 116.2 (d), 110.7 (d), 85.5 (s), 84.8 (s), 28.7 (q), 28.4 (q).
IR (KBr) 2976, 1741, 1722, 1681, 1499, 1476, 1445, 1393, 1372, 1291, 1254, 1233, 1153, 1128, 1101, 842, 764, 743 cm^{-1}.
HRMS (FAB+), calcd. for $C_{29}H_{28}N_2O_5$: 484.1998. Found: 484.1972.

Analytically pure, yellow, flaky 6-formylindolo[3,2-*b*]carbazole **3** was obtained in quantitative yield by heating **13** at 200°C for 4 h at reduced pressure (0.1 mm Hg), mp 352.5-353.5°C (subl. / decomp.). By raising the temperature to 250°C, **3** began to sublime.
^1H NMR (DMSO-d_6, 300 MHz) δ 11.75 (s, 1H, N*H*), 11.63 (s, 1H, N*H*), 11.37 (s, 1H), 8.60 (s, 1H), 8.57 (d, 1H, J= 8.2 Hz), 8.30 (d, 1H, J= 7.7 Hz), 7.75 (d, 1H, J= 8.1 Hz), 7.60 (d, 1H, J= 8.1 Hz), 7.52 - 7.42 (m, 2H), 7.27 - 7.18 (m, 2H).
^{13}C NMR (DMSO-d_6, 75 MHz) δ 189.9 (d), 141.5 (s), 141.5 (s), 135.2 (s), 134.7 (s), 126.3 (d), 126.1 (d), 124.5 (d), 123.2 (s), 121.5 (s), 121.2 (s), 120.9 (s), 120.3 (d), 119.1 (d), 118.7 (d), 112.2 (s), 111.9 (d), 111.3 (d), 109.8 (d).
IR (KBr) 3382, 1655, 1616, 1520, 1459, 1322, 1288, 741 cm^{-1}.
Anal. calcd. for $C_{19}H_{12}N_2O$: C: 80.27; H: 4.25; N: 9.85. Found: C: 80.08; H: 4.36; N: 9.68.

[2-(1H-Indol-3-ylmethyl)-1H-indol-3-yl]-oxo-acetic acid, ethyl ester, (16)

2,3-Diindolylmethane **5** (345 mg, 1.4 mmol) was dissolved in THF (10 mL) under N_2 and the reactor was covered with Al-foil to protect the reaction from light. Pyridine (166 mg, 2.1 mmol) was added and the solution was cooled to 0°C. Ethyl oxalyl chloride (287 mg, 2.1 mmol) was added dropwise during 5 minutes and a white precipitate was formed almost immediately. The ice-bath was removed after the addition and the mixture was stirred at room temperature for 14 h. The thick slurry was diluted with CH_2Cl_2 (40 mL) and consecutively extracted with H_2O (15 mL) and brine (20 mL) before drying ($MgSO_4$). After evaporation of the solvents, the residue was purified by flash chromatography (ethyl acetate-petroleum ether,0-50 %) to give 428 mg (88 %) of **16** as an off-white powder. An analytical sample was obtained as off-white crystals by recrystallization from CH_3CN, mp 193-195°C (decomp.).

^{1}H NMR (DMSO-d_6, 400 MHz) δ 12.14 (br s, 1H, N*H*), 10.98 (br s, 1H, N*H*), 7.77 (dd, 1H), 7.45 (d, 1H, J= 8.1 Hz), 7.42 (dd, 1H), 7.36 (d, 1H, J= 8.1 Hz), 7.22-7.16 (m, 3H), 7.07 (dd, 1H), 6.94 (dd, 1H), 4.46 (s, 2H), 4.25 (q, 2H, J= 7.0 Hz), 1.19 (t, 3H, J= 7.0 Hz).
^{13}C NMR (DMSO-d_6, 100 MHz) δ 181.4 (s), 166.0 (s), 150.7 (s), 136.1 (s), 135.3 (s), 126.6 (s), 126.2 (s), 124.0 (d), 122.9 (d), 122.3 (d), 121.1 (d), 119.3 (d), 118.5 (d), 118.0 (d), 112.2 (d), 111.4 (d), 109.7 (s), 107.6 (s), 61.6 (d), 23.5 (t), 13.6 (q).
IR (KBr) 3380, 3228, 1732, 1590, 1569, 1489, 1458, 1422, 1379, 1268, 1240, 1187, 1169, 1030, 1011, 756, 743, 734, 714, 639 cm^{-1}.
Anal. calcd. for $C_{21}H_{18}N_2O_3$: C: 72.82; H: 5.24; N: 8.09. Found: C: 72.67; H: 5.24; N: 8.06.

Indolo[3,2-*b*]carbazole-6-carboxylic acid, ethyl ester, (17)

The α-keto ester **16** (50 mg, 0.14 mmol) was dissolved in a mixture of dioxane (4.75 mL) and TFA (0.25 ml) and refluxed for 8 h. After cooling the mixture was evaporated on silica gel (0.5 g) and purified by flash chromatography (CH_2Cl_2-petroleum ether, 0-100 %) to give 41 mg (87 %) of **17** as a yellow powder. An analytical sample was obtained as a yellow powder by recrystallization from toluene, mp 219-221°C (decomp.).
^{1}H NMR (DMSO-d_6, 300 MHz) δ 11.60 (s, 1H, N*H*), 10.97 (s, 1H, N*H*), 8.72 (d, 1H, J= 8.2 Hz), 8.48 (s, 1H), 8.27 (d, 1H, J= 7.7 Hz), 7.69 (d, 1H, J= 8.1 Hz), 7.54 (d, 1H, J= 8.0 Hz), 7.47-7.40 (m, 2H), 7.23-7.11 (m, 2H), 4.69 (q, 2H, J= 7.1 Hz), 1.52 (t, 3H, J= 7.1 Hz).
^{13}C NMR (DMSO-d_6, 75 MHz) δ 167.2 (s), 141.6 (s), 141.1 (s), 135.7 (s), 135.2 (s), 126.2 (d), 126.1 (d), 124.9 (d), 123.3 (s), 121.7 (s), 121.2 (s), 120.3 (d), 120.0 (s), 118.6 (d), 117.7 (d), 111.5 (d), 110.8 (d), 106.7 (d), 105.1 (s), 60.9 (t), 14.5 (q).
IR (KBr) 3391, 3050, 2974, 1677, 1615, 1515, 1458, 1421, 1321, 1299, 1274, 1228, 1178, 1148, 1110, 1060, 1030, 1018, 902, 870, 798, 755, 742, 695 cm^{-1}.
Anal. calcd. for $C_{21}H_{16}N_2O_2$: C: 76.81; H: 4.91; N: 8.53. Found: C: 76.99; H: 4.85; N: 8.44.

General procedure for condensation of (1*H*-Indol-3-yl)-(1*H*-indol-2-yl)-methane (5) with aromatic aldehydes:

2,3-Diindolylmethane **5** (99 mg, 0.4 mmol) was dissolved in CH_3CN (5 mL) at room temperature. The aromatic aldehyde (0.48 mmol) was added followed by *p*-toluene sulfonic acid monohydrate (9 mg, 0.048 mmol). The solution adopted a yellowish colour and after a few minutes a thick, white precipitate was formed. Although the reaction was complete within minutes as judged by TLC (10 % ethyl acetate-petroleum ether) the mixture was stirred for 12 h to maximize the amount of precipitate before the pure products were collected, washed, and dried.

6-*p*-Methoxyphenyl-6,12-dihydro-indolo[3,2-*b*]carbazole, (18a)
Yield: 80 % white powder, mp 320-322°C (decomp./subl.).
^{1}H NMR (DMSO-d_6, 300 MHz) δ 11.11 (s, 1H, N*H*), 10.64 (s, 1H, N*H*), 7.55 (d, 1H, J= 7.5 Hz), 7.32 (d, 1H, J= 8.0 Hz), 7.27 (d, 1H, J= 6.9 Hz), 7.20 (d, 2H, J= 8.6 Hz), 7.12 (d, 1H, J= 7.8 Hz), 7.08-6.96 (m, 3H), 6.85-6.77 (m, 3H), 5.43 (dd, 1H, J= 4.8, 4.8 Hz), 4.24 (dd, 1H, J= 4.8, 20.0 Hz), 4.10 (dd, 1H, J= 4.8, 20.0 Hz), 3.68 (s, 3H).
^{13}C NMR (DMSO-d_6, 75 MHz) δ 157.7 (s), 136.9 (s), 136.8 (s), 136.7 (s), 136.4 (s), 133.0 (s), 129.2 (d), 126.4 (s), 126.1 (s), 120.7 (d), 120.3 (d), 118.3 (d), 118.1 (d), 118.1 (d), 117.8 (d), 113.6 (d), 111.0 (d), 110.8 (d), 110.4 (s), 105.0 (s), 55.0 (q), 38.6 (d), 20.9 (t). The peaks at 118.1 had to be resolved with HMQC.

IR (KBr) 3396, 3058, 3028, 2955, 2859, 2830, 1611, 1509, 1460, 1320, 1301, 1259, 1237, 1173, 1027, 810, 749, 739 cm^{-1}.
HRMS (FAB+), calcd. for $C_{25}H_{20}N_2O$: 364.1576. Found: 364.1559.

6-Phenyl-6,12-dihydro-indolo[3,2-*b*]carbazole, (18b)
Yield: 77 % white powder, mp 312-314°C (decomp./subl.).
^1H NMR (DMSO-d_6, 300 MHz) δ 11.16 (s, 1H, N*H*), 10.70 (s, 1H, N*H*), 7.57 (d, 1H, J= 7.6 Hz), 7.34-7.21 (m, 6H), 7.14 (dd, 2H), 7.09-6.96 (m, 3H), 6.82 (dd, 1H), 5.48 (dd, 1H, J= 4.7, 4.7 Hz), 4.26 (dd, 1H, J= 4.7, 20.0 Hz), 4.12 (dd, 1H, J= 4.7, 20.0 Hz).
^{13}C NMR (DMSO-d_6, 75 MHz) δ 144.4 (s), 136.8 (s), 136.6 (s), 136.5 (s), 133.1 (s), 128.3 (d), 128.2 (d), 126.4 (s), 126.2 (d), 126.0 (s), 120.8 (d), 120.3 (d), 118.3 (d), 118.1 (d), 118.0 (d), 117.8 (d), 111.0 (d), 110.8 (d), 110.1 (s), 105.2 (s), 39.5 (d), 20.9 (t).
IR (KBr) 3384, 3055, 3026, 2862, 2821, 1458, 1320, 1139, 754, 744, 720, 702, 652 cm^{-1}.
HRMS (FAB+), calcd for $C_{24}H_{18}N_2$: 334.1470. Found: 334.1455.

6-*p*-Chlorophenyl-6,12-dihydro-indolo[3,2-*b*]carbazole, (18c)
Yield: 69 % white powder, mp 284-286°C (decomp./subl.).
^1H NMR (DMSO-d_6, 300 MHz) δ 11.19 (s, 1H, N*H*), 10.73 (s, 1H, N*H*), 7.57 (d, 1H, J= 7.5 Hz), 7.35-7.26 (m, 6H), 7.13-6.97 (m, 4H), 6.84 (dd, 1H), 5.52 (dd, 1H, J= 4.3, 5.0 Hz), 4.26 (dd, 1H, J= 4.3, 20.0 Hz), 4.11 (dd, 1H, J= 5.0, 20.0 Hz).
^{13}C NMR (DMSO-d_6, 75 MHz) δ 143.4 (s), 136.9 (s), 136.7 (s), 136.1 (s), 133.3 (s), 130.8 (s), 130.2 (d), 128.2 (d), 126.4 (s), 125.9 (s), 121.0 (d), 120.5 (d), 118.5 (d), 118.3 (d), 118.0 (d), 118.0 (d), 111.1 (d), 110.9 (d), 109.7 (s), 105.5 (s), 38.8 (d), 20.9 (t). The peaks at 118.0 had to be resolved with HMQC.
IR (KBr) 3391, 3055, 2860, 2820, 1488, 1460, 1321, 1138, 1089, 1014, 808, 746 cm^{-1}.
HRMS (FAB+), calcd for $C_{24}H_{17}ClN_2$: 368.1080. Found: 368.1058.

6-Ethyl-6,12-dihydro-indolo[3,2-*b*]carbazole, (19)

2,3-Diindolylmethane **5** (148 mg, 0.60 mmol) was dissolved in CH_3CN (6 mL) at room temperature. Propionaldehyde (42 mg, 0.72 mmol) was added followed by *p*-toluene sulfonic acid monohydrate (14 mg, 0.072 mmol). The solution slowly became dark-red, but after a couple of hours a white precipitate started to form. After 24 h the solid material was collected and dried to give 7 mg (4 %) of **19** as a pinkish powder, mp 358-360°C (decomp.). It is important to note that to avoid the formation of dark-red by-products the excess of aldehyde should not be too large.
^1H NMR (DMSO-d_6, 300 MHz) δ 10.93 (s, 1H, N*H*), 10.28 (s, 1H, N*H*), 7.47 (2×d, 2H, J= 8.4 Hz), 7.19 (d, 1H, J= 8.0 Hz), 7.04 (m, 2H), 6.95 (dd, 1H), 6.83 (dd, 1H), 6.65 (dd, 1H), 4.06 (d, 1H, J= 16.3 Hz), 3.88 (dd, 1H), 3.59 (d, 1H, J= 16.3 Hz), 2.17 (m, 1H), 1.88 (m, 1H), 0.54 (t, 3H)
^1H NMR (DMSO-d_6, 300 MHz, 70°C), d 10.68 (s, 1H, N*H*) 10.05 (s, 1H, N*H*), 7.49-7.44 (m, 2H), 7.20 (d, 1H, J=8.0 Hz), 7.12 (d, 1H, J=8.0 Hz), 7.03 (dd, 1H), 6.95 (dd, 1H), 6.84 (dd, 1H), 6.68 (dd, 1H), 4.07 (d, 1H, J=16.4 Hz), 3.97 (dd, 1H, J=6.8, 8.9 Hz), 3.68 (d, 1H, J=16.4 Hz), 2.20 (m, 1H), 1.92 (m, 1H), 0.56 (t, 3H).
^{13}C NMR (DMSO-d_6, 75 MHz, 70°C) δ 138.8 (s), 135.7 (s), 135.2 (s), 134.7 (s), 128.9 (s), 126.1 (s), 119.3 (d), 119.1 (d), 118.1 (d), 117.9 (d), 117.4 (d), 116.8 (d), 110.9 (s), 110.8 (d), 110.6 (d), 106.7 (s), 35.0 (d), 25.5 (t), 20.9 (t), 11.8 (q). The solubility of the subtance was so low, that heating was necessary to obtain a ^{13}C spectrum in reasonable time.

IR (KBr) 3442, 3398, 3054, 2962, 2928, 2872, 1459, 1435, 1338, 1298, 744 cm^{-1}.
HRMS (FAB+), calcd. for $C_{20}H_{17}N_2$ (M-H): 285.1392. Found: 285.1353.

1-*Bis*-[2-(1*H*-indol-3-ylmethyl)-1*H*-indol-3-yl]-propane, (20)

2,3-Diindolylmethane **5** (369 mg, 1.50 mmol) was dissolved in CH_3CN (15 mL) and the flask was wrapped in Al-foil to protect the solution from light. Propionaldehyde (105 mg, 1.8 mmol) was added followed by $Yb(OTf)_3$ (93 mg, 0.15 mmol). The solution was stirred until the consumption of starting material was complete (12 h) as judged by TLC (CH_2Cl_2). The solution was then diluted with CH_2Cl_2 (60 mL) and washed with H_2O (15 mL) before drying ($MgSO_4$). After evaporation of the solvents the residue was purified by flash chromatography (CH_2Cl_2-petroleum ether, 0-100 %) to give 333 mg (83 %) of a shiny, brownish, fluffy solid, mp 176-177°C (decomp.), pure enough to characterize it as **20**. To obtain an analytical sample **20** was derivatized with Boc-groups to give **21** (see below).
^1H NMR (DMSO-d_6, 300 MHz) δ 10.86 (s, 2H, N*H*), 10.51 (s, 2H, N*H*), 7.64 (d, 2H, J= 7.9 Hz), 7.35 (d, 2H, J= 8.2 Hz), 7.25 (d, 2H, J= 8.0 Hz), 7.19 (d, 2H, J= 7.9 Hz), 7.05 (dd, 2H), 6.97-6.80 (m, 8H), 4.63 (dd, 1H), 4.23 (d, 2H, J= 16.3 Hz), 4.14 (d, 2H, J= 16.3 Hz), 2.50-2.30 (m, 2H), 0.91 (t, 3H).
^{13}C NMR (DMSO-d_6, 75 MHz) δ 136.3 (s), 135.5 (s), 134.6 (s), 127.7 (s), 127.0 (s), 123.2 (d), 120.9 (d), 119.4 (d), 119.2 (d), 118.4 (d), 118.2 (d), 117.9 (d), 113.7 (s), 112.0 (s), 111.3 (d), 110.8 (d), 36.3 (d), 27.8 (t), 22.5 (t), 13.5 (q).
IR (KBr) 3404, 3051, 2960, 2868, 1617, 1486, 1457, 1421, 1339, 1223, 1090, 1010, 741 cm^{-1}.

***N,N′N″N‴*-tetra-*tert*-butyloxycarbonyl-[1-*bis*-[2-(1*H*-indol-3-ylmethyl)-1*H*-indol-3-yl]-propane], (21)**

Tetraindole **20** (56 mg, 0.105 mmol) was dissolved in dry THF (5 mL) at room temperature. Boc_2O (276 mg, 1.26 mmol) was added followed by DMAP (5 mg, 0.042 mmol) and the solution was stirred until the consumption of starting material was complete (2 h) as judged by TLC. Silica gel (1 g) was then added and the solvent was evaporated. The residue was purified by column chromatography (ethyl acetate-petroleum ether, 0-20 %) to give 34 mg (35 %) of analytically pure, shiny, greenish, crystalline **21**, mp 107-108°C.
^1H NMR ($CDCl_3$, 300 MHz) δ 8.16 (d, 2H, J= 8.2 Hz), 8.08 (br d, 2H, J= 7.7 Hz), 7.75 (d, 2H, J= 7.8 Hz), 7.33-7.24 (m, 4H), 7.18-7.07 (m, 6H), 6.81 (s, 2H), 4.44 (t, 1H), 4.34 (d, 2H, J= 17.1 Hz), 4.15 (d, 2H, J= 17.1 Hz), 2.41 (m, 2H), 1.59 (s, 18H), 1.31 (s, 18H), 0.91 (t, 3H).
^{13}C NMR ($CDCl_3$, 75 MHz) δ 150.3 (s), 149.9 (s), 136.5 (s), 135.5 (s), 134.2 (s), 130.3 (s), 129.5 (s), 124.4 (d), 123.7 (d), 122.7 (d), 122.5 (d), 122.4 (d), 121.6 (s), 120.0 (d), 119.5 (s), 118.9 (d), 115.7 (d), 115.3 (d), 83.7 (s), 83.5 (s), 37.2 (d), 28.4 (q), 28.0 (q), 27.4 (t), 23.5 (t), 13.8 (q).
IR (KBr) 2976, 2931, 1732, 1455, 1370, 1325, 1256, 1160, 1119, 1074, 744 cm^{-1}.
Anal. calcd. for $C_{57}H_{64}N_4O_8$: C: 73.37; H: 6.91; N: 6.00. Found: C: 73.18; H: 6.87; N: 5.96.

6-Methylindolo[3,2-*b*]carbazole, (22)

2,3-Diindolylmethane **5** (99 mg, 0.4 mmol) was dissolved in CH_3CN (4 mL) at room temperature. Triethyl orthoacetate (162 mg, 1.0 mmol) was added followed by *p*-toluene sulfonic acid monohydrate (9 mg, 0.048 mmol). The solution first became orange-coloured and

after a couple of hours a yellowish precipitate started to form. After stirring for 48 h 54 mg (50 %) of **22** as a slightly yellow powder, mp 294-296°C (decomp./subl.), was collected.
^{1}H NMR (DMSO-d_6, 300 MHz), δ 11.08 (s, 1H, N*H*), 10.97 (s, 1H, N*H*), 8.24 (d, 1H, J= 7.8 Hz), 8.17 (d, 1H, J= 7.7 Hz), 7.96 (s, 1H), 7.49 (d, 1H, J= 8.1 Hz), 7.47 (d, 1H, J= 7.9 Hz), 7.40-7.34 (m, 2H), 7.17-7.08 (m, 2H), 3.04 (s, 3H).
^{13}C NMR (DMSO-d_6, 75 MHz) δ 141.2 (s), 141.1 (s), 135.3 (s), 134.4 (s), 125.4 (d), 124.8 (d), 123.2 (s), 122.9 (s), 122.1 (d), 120.8 (s), 120.3 (d), 117.6 (d), 117.6 (d), 112.8 (s), 110.6 (d), 110.2 (d), 97.7 (d), 14.6 (q). One carbon signal (s) could not be resolved. It has coalesced with either a doublet or another singlet carbon. Microanalysis, however, showed that the assumed elemental composition was correct.
IR (KBr) 3413, 3393, 3050, 1614, 1529, 1458, 1415, 1333, 1325, 1282, 1269, 739, 690 cm^{-1}.
Anal. calcd. for $C_{19}H_{14}N_2$: C: 84.42; H: 5.22; N: 10.36. Found: C: 84.54; H: 5.21; N: 10.29.

5. References and Notes:

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