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In memory of Professor Nicholas Alexandrou

Some new acylation and cyclization reactions of 2,2'-bisindolyls **1**, **2** are described. The product patterns constitute acyl derivatives **3**, **4**, **5** and an aldehyde **7**, indolo[2,3-*a*]carbazoles **6**, **14**, **17**, **19**, **20** and cyclopentadiindoles **22** and **24**. In the reaction with aryl or diazotated anthranilic acid, a 3-benzoylindole derivative **9** and phenylindolyl azo dye **10** are formed. *N*-methylmaleimide reacts with 2,2'-bisindolyl **2** via Michael type addition, dehydrogenation and cyclization to several functionalized or anellated indole derivatives **11**, **12**, **13** and **14**, respectively.

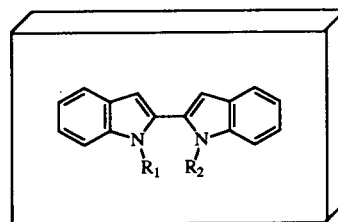
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Introduction.

The interesting biological activities of indolo[2,3-*a*]carbazole alkaloids such as the tumor growth inhibitor rebeccamycin and the protein kinase C inhibitor staurosporine [1] have stimulated the development of synthetic analogs [2]. Among these compounds some functionalized bisindolyl derivatives exhibit pronounced inhibitory activity against protein kinase C and thus represent interesting lead substances for the design of new drugs with antitumor activity [3]. In this context, we have synthesized a variety of potential protein kinase C inhibitors starting from 2,2'-bis(*N*-methylindolyl) (**2**) by reaction with some electrophiles and appropriate dienophiles [3-5]. We have now continued these experiments systematically with the aim of obtaining more information concerning the scope and limitations of one pot functionalization reactions of 2,2'-bisindolyls [5].

In the present study, we now report on some new reactions of the 2,2'-bisindolyls **1** and **2** - readily obtained by an indole coupling procedure [3,6] - with a variety of acid chlorides and some carbodienophiles. In this context, the synthesis of further new acyl functionalized and cyclized 2,2'-bisindolyl derivatives is described.

Formula 1 and 2



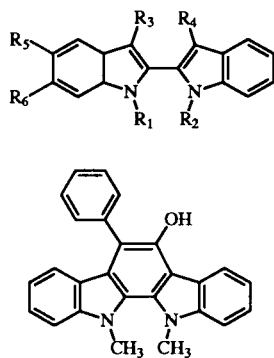
	R ₁	R ₂
1	PhSO ₂	PhSO ₂
2	CH ₃	CH ₃

Results and Discussion.

Synthetic Aspects.

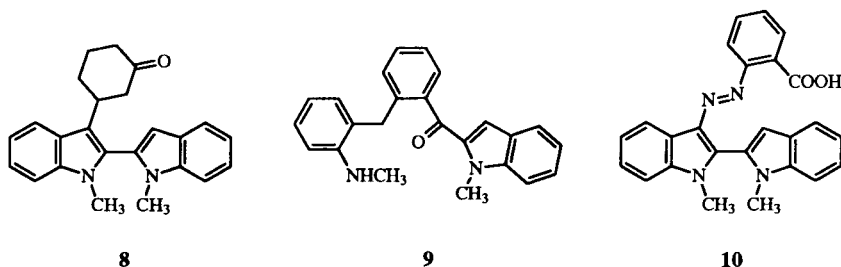
Competitive electrophilic substitution experiments entailing reaction of 2,2'-bisindolyls **1**, **2** with α -chloroacetyl chloride revealed that 2,2'-bisindolyl **1** is significantly less nucleophilic than the *N*-methyl derivative **2**. Only in one case were we able to realize a Friedel-Crafts acylation of compound **1**, namely with acetyl chloride/aluminum trichloride, which gives rise to the 3-acetyl derivative **3**, respectively. In contrast to the bis(*N*-phenylsulfonyl) derivative **1**, the 2,2'-bis(*N*-methylindolyl) (**2**) reacts successfully with a variety of acid chlorides under Friedel-Crafts conditions. Thus, in the reaction with **2**

Formula 3



	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆
3	PhSO ₂	PhSO ₂	COCH ₃	H	H	H
4a	CH ₃	CH ₃	COCH ₃	H	H	H
4b	CH ₃	CH ₃	H	H	COCH ₃	H
4c	CH ₃	CH ₃	COCH ₃	COCH ₃	H	H
5a	CH ₃	CH ₃	H	H	COCHClCH ₃	H
5b	CH ₃	CH ₃	H	H	H	COCHClCH ₃
5c	CH ₃	CH ₃	COCHClCH ₃	COCHClCH ₃	H	H
7	CH ₃	CH ₃	CHO	H	H	H

Formula 4



acetyl chloride yields the 3-acetyl and 5-acetyl derivatives **4a**, **4b** and the 3,3'-bisacetylated compound **4c**. The reaction of **2** with racemic α -chloropropionic acid chloride produces a similar product pattern (compounds **5**). However, a substitution of the electrophilic reagent at the position C6 instead of the C3-position was observed in this case. The electrophilic acylation of **2** with racemic α -chloro- α -phenyl acetyl chloride gave rise to the cyclization product **6**. The formation of product **6** reflects the binucleophilic reactivity of this acid chloride. Vilsmeier formylation (*N,N*-dimethylformamide/phosphoryl chloride) of **2** produces the formyl derivative **7**.

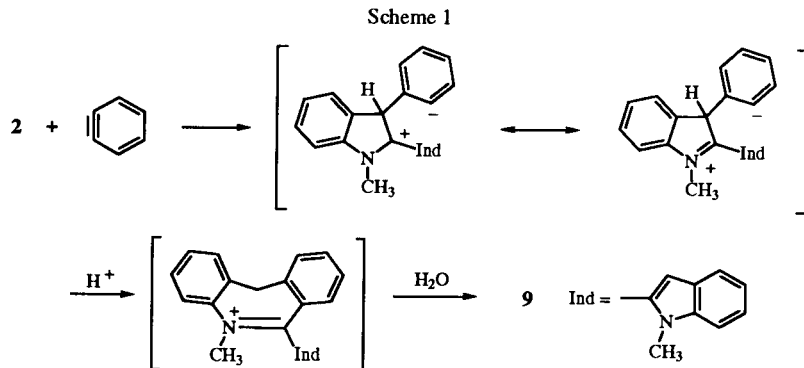
The extremely low nucleophilicity of 2,2'-bisindolyl **1** towards electrophiles was also documented by our investigations with electrophilic dienophiles, generally used as Diels-Alder reagents. In no case were electrophilic substitution products nor Diels-Alder products detected in the reaction with **1** and dienophiles. Therefore we focused our studies on reactions of 2,2'-bis(*N*-methylindolyl) (**2**) with further carbodienophiles [3-5].

Cyclohexenone reacts with **2** in the presence of aluminum trichloride to form the 3-substituted cyclohexanone **8**. Aryne generated *in situ* from diazotated anthranilic acid [7a] yielded the 2-benzoylindole derivative **9** and the bisindolyl azo dye **10**, respectively. We suggest that compound **9** is probably formed by an electrophilic addition of aryne to the indole-3-position (Michael type), followed by ring-closure and subsequent hydrolytic ring-opening reaction (Scheme 1). However, an alternative mechanism *via* an indolo-benzo-anellated cyclobutane as an intermediate is also possible [7b].

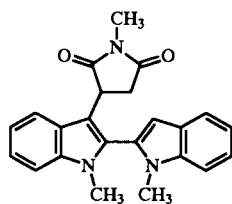
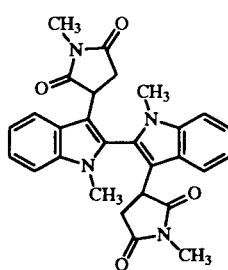
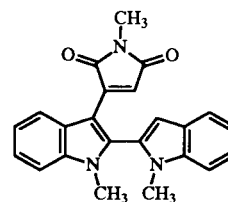
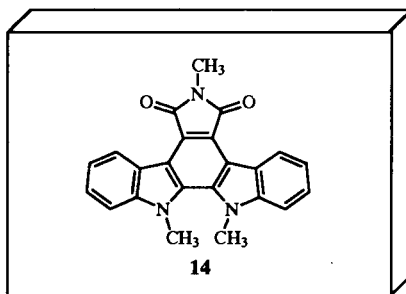
The formation of azo dye **10** is the result of a classical azo coupling reaction of the aryne precursor diazotated anthranilic acid as diazonium salt at the highly nucleophilic indole 3-position of **2**. The diazonium salt is always present in the reaction mixture [7].

We have already described some first electrophilic reactions of maleimide and *N*-phenylmaleimide with 2,2'-bisindolyl **2** [3-5]. Here, we investigate the more reactive *N*-methylmaleimide. In the presence of aluminum trichloride, compound **2** reacts with this electrophilic dienophile to form the Michael type adducts **11** and **12**. The 'ortho'-tetrasubstituted product **12** possesses central and axial chirality elements and exists as a mixture of atropisomers as a consequence of severely restricted rotation about the central C2sp²-C2'sp²-sigma bond [3,8]. The "mono" substituted product **11** was dehydrogenated in the presence of Pd/C in a one pot procedure to compound **13** and to indolo[*a*]pyrrolo[*c*]carbazole **14**, possessing the rebeccamycin aglycone unite [3,5], respectively.

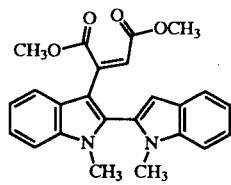
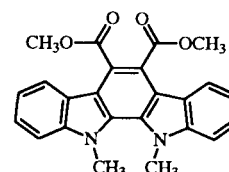
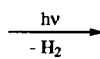
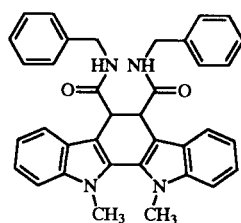
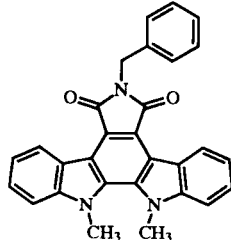
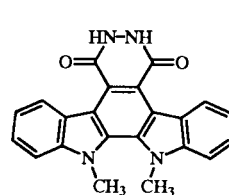
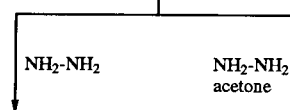
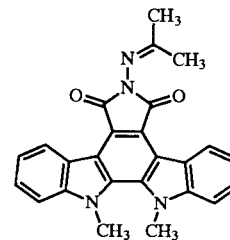
In our previous papers [3-5], we described the electrophilic reaction of 2,2'-bisindolyl **2** with dimethyl acetylenedicarboxylate, which gave rise to a variety of substituted products bearing a vinyl function. Among these products, first of all the 3-dimethyl maleoyl substituted 2,2'-bisindolyl **15** is of general interest for intramolecular cyclization reactions. In this context, we have recently reported that photochemically induced 1,6- π -electrocyclization gave rise to indolo[2,3-*a*]carbazole **16** and aluminum trichloride catalyzed cyclization to cyclopenta[2,1*b*:3,4-*b'*]diindole derivative **21** [5]. Meanwhile, we have varied the reaction conditions and were



Formula 5

**11****12****13****14**

Formula 6

**15** [3]**16** [5]**17****18** [5]**19****20**

able to expand the product pattern resulting from transformation reactions of compound 15.

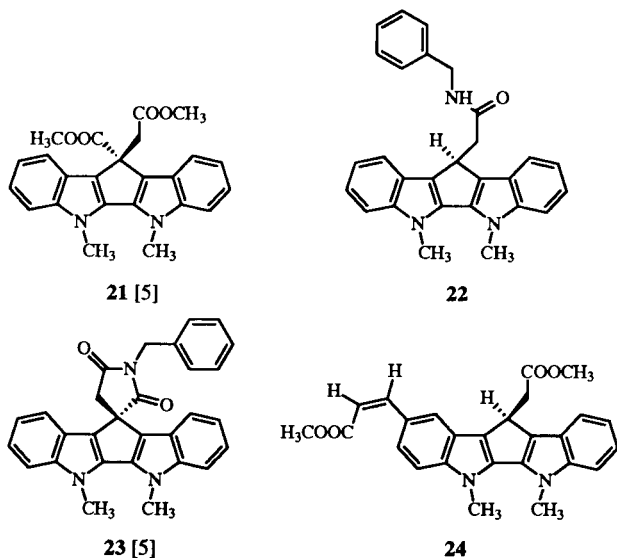
Thus, compound 15 reacts in refluxing benzyl amine to form dibenzylamide 17 besides the indolo[*a*]pyrrolo[*c*]carbazole 18 [5] already described. The indolo[2,3-*a*]carbazole 16 was transformed with hydrazine to the indolo-

[*a*]tetrahydropyridazino[*c*]carbazoledione 19 and in the presence of acetone to the indolo[*a*]pyrrolo[*c*]carbazole 20. The 3-vinylindole 15 was cyclized in an ionic reaction in presence of aluminum trichloride (for mechanism see reference [5]) to diester 21. Compound 21 underwent aminolysis with benzylamine and produced the new amide 22 and

the spiro compound **23** [5]. In an analogous way, 2,2'-bisindolyl **2** reacts with methyl propynoate in the presence of aluminum trichloride to form the cyclopentadiindole **24**. In this reaction, regioselective electrophilic addition of the unsaturated ester at the indole phenyl group has occurred.

On the basis of a biological assay for investigation of protein kinase C α inhibition activity [9], compound **20** was the most active ($IC_{50} = 89 \mu M$) in the series of new bisindolyl-derivatives reported in our previous publications [3-5] and in this paper.

Formula 7



Structural Aspects.

The constitutions of compounds **3-14**, **17**, **19**, **20**, **22** and **24** were clarified by routine 400 MHz and/or 200 MHz 1H nmr spectroscopy (see Experimental). In addition, the structures of compounds **6**, **8**, **9**, **16** and **21** [3] were unambiguously supported by X-ray crystallographic analyses [10]. The 3,3'-bisindolyl derivatives **5c**, **8**, **11** and **12** reveal a double set of signals in the 400 MHz 1H nmr spectra at 20°C and thus represent a mixture of diastereomeric atropisomers [8].

EXPERIMENTAL

Materials and Techniques.

All reactions were carried out in highly pure and anhydrous solvents under an argon atmosphere. Merck silica gel (grain size: 0.063-0.200 mm) was used for column chromatography and Merck silica gel (grain size: 0.040-0.063 mm) for "flash" chromatography. The petroleum ether used had the boiling range 40-60°. Melting points were determined on Büchi SMP-20 and Electrothermal IA 920 instruments and are not corrected. Elemental analyses were performed with a Carlo Erba Strumenatazione 1106 apparatus. The infrared spectra were

recorded on a Beckmann IR 4220 spectrophotometer. The electron impact (70 eV) and field desorption mass spectra were obtained using a Varian MAT CH 7A spectrometer. The 1H and ^{13}C nmr spectra were recorded on Bruker AC 200 and Bruker AM 400 spectrometer. C_p = primary, C_s = secondary, C_t = tertiary, C_q = quaternary carbon atoms.

3-Acetyl-1-phenylsulfonyl-2-(1-phenylsulfonyl-1*H*-indol-2-yl)-1*H*-indole (**3**).

To a suspension of aluminum trichloride (240 mg, 1.8 mmoles) in 10 ml of 1,2-dichloroethane, 240 μ l of acetyl chloride (3.3 mmoles) were slowly added at 0°. The mixture was then allowed to warm up to room temperature. After 20 minutes, 300 mg of 2,2'-bis(*N*-phenylsulfonylindolyl) **1** (0.59 mmole) [6a], dissolved in 5 ml of 1,2-dichloroethane, were added within 20 minutes. After stirring for 2 hours at room temperature the mixture was poured into ice/water. The organic layer was separated, and the aqueous phase was extracted several times with dichloromethane. The combined organic phases were dried with sodium sulfate, concentrated and the residue was purified by column chromatography (petroleum ether/ethyl acetate, 2:1). The product **3** was obtained as colorless crystals in 46% yield (151 mg), mp 185-188° (petroleum ether/ethyl acetate); ms: m/z (%) 554 (M^{++} , 9), 414 (18), 413 (63), 273 (29), 272 (100), 271 (14), 243 (23); 1H nmr (400 MHz, deuteriochloroform): δ 1.71 (s, 3H, -CH₃), 6.56 (s, 1H, indole C3'-H), 7.34-7.88 (m, 15H, aromatic H), 8.28-8.36 (m, 3H, aromatic H); ^{13}C nmr (100.6 MHz, deuteriochloroform): δ 29.9 (COCH₃), 114.4(8) (C_t), 114.5(4) (C_t), 114.8 (C_t), 121.4 (C_t), 123.1 (C_t), 123.6 (C_t), 125.0 (C_t), 126.1 (C_t), 126.5 (C_t), 126.9 (2 x C_t), 127.3 (C_q), 127.4 (2 x C_t), 127.9 (C_q), 129.0 (2 x C_t), 129.2 (2 x C_t), 132.5 (C_q), 134.05 (C_t), 134.12 (C_t), 136.3 (C_q), 137.0 (C_q), 138.6 (C_q), 138.8 (C_q), 195.2 (CO), two peaks are overlapped.

Anal. Calcd. for $C_{30}H_{22}N_2O_5S_2$ (554.65): C, 64.97; H, 4.00; N, 5.05. Found: C, 64.70; H, 4.06; N, 5.03.

3-Acetyl-1-methyl-2-(1-methyl-1*H*-indol-2-yl)-1*H*-indole (**4a**).

Compound **4a** was synthesized analogous to the procedure for **3**, using 650 mg of aluminum trichloride (4.89 mmoles), 330 μ l (4.5 mmoles) acetyl chloride and 520 mg of 2,2'-bis(*N*-methylindolyl) **2** (2 mmoles) [3]. Purification was performed by column chromatography (petroleum ether/ethyl acetate 1:1). The product **4a** was obtained as colorless crystals in 20% yield (121 mg), mp 178-180° (petroleum ether/ethyl acetate); ms: m/z (%) 303 ($M^{++} + 1$, 23), 302 (M^{++} , 100), 288 (18), 287 ($M^{++} - CH_3$, 82), 285 (23), 270 (16), 260 ($M^{++} - COCH_3$, 16), 259 (55), 258 (15), 257 (21), 244 (19), 243 (25), 217 (10), 151 (16), 144 (11), 130 (13); 1H nmr (200 MHz, dideuteriodichloromethane): δ 1.97 (s, 3H, CO-CH₃), 3.57 (s, 3H, N-CH₃), 3.58 (s, 3H, N-CH₃), 6.77 (s, 1H, indole C3'-H), 7.17-7.50 (m, 6H, aromatic H), 7.73 (d, $^3J = 7.84$ Hz, 1H, indole C4'-or C7-H), 8.45-8.49 (m, 1H, indole C4-H).

Anal. Calcd. for $C_{20}H_{18}N_2O$ (302.38): C, 79.44; H, 6.00; N, 9.26. Found: C, 79.40; H, 6.05; N, 9.21.

5-Acetyl-1-methyl-2-(1-methyl-1*H*-indol-2-yl)-1*H*-indole (**4b**).

Compound **4b** represents the second product from the reaction of **2** with acetyl chloride. Purification was performed by column chromatography (petroleum ether/ethyl acetate 1:1). Compound **4b** was obtained as colorless crystals in 30% yield (181 mg), mp 187-189° (methanol and dichloromethane); ir (potassium bromide): ν 1660, 1600, 1560, 1465, 1435, 1415, 1350, 1320, 1300, 1250, 1235, 1220, 1155, 1140, 1105, 1055, 1005, 950, 925, 880,

805, 750, 670, 630 cm^{-1} ; ms: m/z (%) 303 ($M^{++} + 1$, 22), 302 (M^{++} , 100), 301 (12), 287 ($M^{++} - \text{CH}_3$, 27), 259 (19), 243 (10), 144 (19); ^1H nmr (200 MHz, dideuteriodichloromethane): δ 2.70 (s, 3H, CO- CH_3), 3.73 (s, 3H, N- CH_3), 3.75 (s, 3H, N- CH_3), 6.69 (s, 1H indole C3- or C3'-H), 6.77 (s, 1H, indole C3- or C3'-H), 7.16-7.44 (m, 4H, aromatic H), 7.70 (d, $^3J = 7.71$ Hz, 1H, indole C7-H), 7.98 (dd, $^3J = 8.72$ Hz and $^4J = 1.40$ Hz, 1H, indole C6-H), 8.36 (s, 1H, indole C4-H).

Anal. Calcd. for $\text{C}_{20}\text{H}_{18}\text{N}_2\text{O}$ (302.38): C, 79.44; H, 6.00; N, 9.26. Found: C, 79.37; H 5.92; N, 9.18.

3,3'-Diacetyl-1,1'-dimethyl-1*H*,1'*H*-2,2'-bisindolyl (4c).

Compound **4c** represents the third product obtained from reaction of **2** with acetyl chloride. Compound **4c** was isolated by column chromatography (petroleum ether/ethyl acetate 1:1) and obtained as colorless crystals in 15% yield (103 mg), mp 179-180° (petroleum ether/ethyl acetate); ir (potassium bromide): ν 3060, 2930, 1640, 1610, 1570, 1460, 1440, 1400, 1380, 1360, 1335, 1255, 1225, 1200, 1155, 1130, 1100, 1010, 1000, 950, 930, 810, 760, 700, 665, 640, 610 cm^{-1} ; ms: m/z (%) 344 (M^{++} , 12), 302 (22), 301 ($M^{++} - \text{COCH}_3$, 100); ^1H nmr (400 MHz, dideuteriodichloromethane): δ 2.06 (s, 6H, 2 x CO- CH_3), 3.57 (s, 6H, 2 x N- CH_3), 7.38-7.54 (m, 6H, aromatic H), 8.44 (d, $^3J = 7.23$ Hz, 2H, indole C4-H and C4'-H); ^{13}C nmr (100.6 MHz, dideuteriodichloromethane): δ 29.4 (C_p , 2 x CO- CH_3), 31.3 (C_p , 2 x N- CH_3), 110.7 (2 x C_l), 118.8 (2 x C_q), 123.2 (2 x C_l), 123.6 (2 x C_l), 124.7 (2 x C_l), 126.8 (2 x C_q), 135.2 (2 x C_q), 138.0 (2 x C_q), 193.3 (C_q , 2 x CO).

Anal. Calcd. for $\text{C}_{22}\text{H}_{20}\text{N}_2\text{O}_2$ (344.41): C, 76.72; H, 5.85; N, 8.13. Found: C, 76.51; H, 5.82; N, 8.09.

5-(2-Chlorpropionyl)-1-methyl-2-(1-methyl-1*H*-indol-2-yl)-1*H*-indole (5a).

To a suspension of aluminum trichloride (490 mg, 3.7 mmoles) in 15 ml of dichloromethane, 940 mg of α -chlorpropionic acid chloride (7.4 mmoles) were slowly added at 0°. After stirring for 20 minutes at this temperature, 325 mg of compound **2** (1.25 mmoles), dissolved in 15 ml of dichloromethane, were added slowly. The mixture was stirred for 2 hours at 0° and then 3 hours at room temperature. Then the mixture was poured into ice/water. The organic layer was separated, and the aqueous phase was extracted with dichloromethane. The combined organic phases were dried with sodium sulfate, concentrated and the residue was purified by "flash" chromatography (petroleum ether/ethyl acetate, 3:1) to furnish the compound **5a** in 40% yield (175 mg), mp 167-168° (petroleum ether/ethyl acetate); ir (potassium bromide): ν 2920, 1660, 1600, 1555, 1450, 1430, 1410, 1360, 1345, 1320, 1280, 1250, 1180, 1155, 1140, 1080, 1050, 990, 960, 910, 880, 780, 745, 695, 665, 650 cm^{-1} ; ms: m/z (%) 350 (M^{++} , 22), 287 (40), 232 (10), 230 (10); ^1H nmr (400 MHz, dideuteriodichloromethane): δ 1.78 (d, $^3J = 6.62$ Hz, 3H, CHCl-CH_3), 3.73 (s, 3H, N- CH_3), 3.76 (s, 3H, N- CH_3), 5.49 (q, $^3J = 6.63$ Hz, 1H, $-\text{CHCl-CH}_3$), 6.72 (s, 1H, indole C3- or C3'-H), 6.83 (s, 1H, indole C3- or C3'-H), 7.19 (pt, 1H, $J = 7.86$ Hz and 7.08 Hz, indole C5'- or C6'-H), 7.30-7.35 (m, 1H, indole C5'- or C6'-H), 7.45 (d, $^3J = 8.85$ Hz, 1H, C7'-H), 7.50 (d, $^3J = 8.76$ Hz, 1H, aromatic H), 7.70 (d, $^3J = 7.88$ Hz, 1H, aromatic H), 8.00 (dd, $^3J = 8.75$ Hz, $^4J = 1.74$ Hz, 1H, indole C6-H), 8.42 (d, $^4J = 1.50$ Hz, 1H, indole C4-H); ^{13}C nmr (100.6 MHz, dideuteriodichloromethane): δ 20.8 (C_p ; CHCl-CH_3), 31.3 (C_p ; N- CH_3), 31.6 (C_p ; N- CH_3), 53.8 (C_i ; $-\text{CHCl-CH}_3$), 105.2

(C_l), 106.6 (C_l), 110.3 (C_l), 110.5 (C_l), 120.6 (C_l), 121.3 (C_l), 123.0 (C_l), 123.5 (C_l), 123.9 (C_l), 127.2 (C_q), 127.8 (C_q), 128.2 (C_q), 131.1 (C_q), 134.4 (C_q), 138.7 (C_q), 141.2 (C_q), 194.0 (C_q ; CO).

Anal. Calcd. for $\text{C}_{21}\text{H}_{19}\text{N}_2\text{OCl}$ (350.85): C, 71.89; H 5.46; N, 7.98. Found: C, 71.91; H, 5.50; N, 7.97.

6-(2-Chlorpropionyl)-1-methyl-2-(1-methyl-1*H*-indole-2-yl)-1*H*-indole (5b).

The product **5b** was obtained from the reaction to **5a** with α -chlorpropionic acid chloride as yellow crystals in 7% yield (31 mg), mp 186-188° (petroleum ether/ethyl acetate); ir (potassium bromide): ν 2910, 1660, 1595, 1440, 1410, 1385, 1370, 1340, 1325, 1235, 1185, 1150, 1095, 1060, 1050, 995, 970, 900, 880, 825, 795, 740, 670, 655, 630, 610 cm^{-1} ; ms: m/z (%) 352 (isotope peak 19), 351 (isotope peak 13), 350 (M^{++} , 55), 288 (21), 287 (100), 259 (14), 144 (15); ^1H nmr (400 MHz, dideuteriodichloromethane): δ 1.78 (d, $^3J = 6.67$ Hz, 3H, CHCl-CH_3), 3.74 (s, 3H, N- CH_3), 3.82 (s, 3H, N- CH_3), 5.50 (q, $^3J = 6.65$ Hz, 1H, CHCl-CH_3), 6.72 (s, 1H, indole C3-H or C3'-H), 6.74 (s, 1H, indole C3-H or C3'-H), 7.16-7.20 (m, 1H, C6'-H), 7.29-7.33 (m, 1H, C5'-H), 7.44 (d, $^3J = 8.25$ Hz, 1H, C7'-H), 7.68 (d, $^3J = 7.91$ Hz, 1H, C4'-H), 7.74 (d, $^3J = 8.33$ Hz, 1H, C4-H), 7.82 (dd, $^3J = 8.40$ Hz, $^4J = 1.45$ Hz, 1H, C5-H), 8.16 (s, 1H, C7-H); ^{13}C nmr (100.6 MHz, dideuteriodichloromethane): δ 20.7 (C- CH_3), 31.3 (N'- CH_3), 31.5 (N- CH_3), 105.1 (C_l), 105.3 (C_l), 110.3 (C_l), 112.1 (C_l), 120.6 (C_l), 120.9 (2 x C_l), 121.3 (C_l), 123.1 (C_l), 128.1 (C_q), 128.7 (C_q), 131.1 (C_q), 132.5 (C_q), 136.8 (C_q), 138.1 (C_q), 138.8 (C_q), 194.1 (CO). The CHCl signal is overlapped with the solvent peak.

Anal. Calcd. for $\text{C}_{21}\text{H}_{19}\text{N}_2\text{OCl}$ (350.85): C, 71.89; H, 5.46; N, 7.98. Found: C, 71.68; H, 5.54; N, 7.76.

3,3'-Bis(2-chlorpropionyl)-1,1'-dimethyl-1*H*,1'*H*-2,2'-bisindolyl (5c).

The compound **5c** was obtained from the electrophilic substitution of compound **2** with α -chlorpropionic acid chloride beside the monosubstituted products **5a** and **5b** as a mixture of diastereomeric atropisomers in the ratio of 1:1 (^1H nmr) in 29% yield (160 mg), mp 240-245° (petroleum ether/ethyl acetate); ms: m/z (%) 442 (isotope peak, 15), 441 (M^{++} , 5), 440 (22), 379 (28), 378 (20), 377 (81), 352 (34), 350.3 (24), 349.6 (100), 315 (16), 314 (14), 313 (13), 287 (25), 286 (47), 285 (12), 271 (12), 257 (11), 256 (10), 157 (21), 143 (28), 125 (11), 107 (29), 99 (25), 98 (16), 91 (35); ^1H nmr (400 MHz, deuteriochloroform): δ 1.52 (d, $^3J = 6.60$ Hz, 6H, 2 x CHCl-CH_3), 1.56 (d, $^3J = 6.58$ Hz, 6H, 2 x CHCl-CH_3), 3.51 (s, 6H, 2 x N- CH_3), 3.58 (s, 6H, 2 x N- CH_3), 4.60 (q, $^3J = 6.58$ Hz, 2H, 2 x CHCl), 4.75 (q, $^3J = 6.60$ Hz, 2H, 2 x CHCl), 7.40-7.52 (m, 12H, aromatic H), 8.25-8.29 (m, 2H, C4- and C4'-H), 8.42-8.44 (m, 2H, C4- and C4'-H).

Anal. Calcd. for $\text{C}_{24}\text{H}_{22}\text{N}_2\text{O}_2\text{Cl}_2$ (441.36): C, 65.31; H, 5.02; N, 6.35. Found: C, 65.21; H, 4.96; N, 6.05.

11,12-Dimethyl-5-hydroxy-6-phenyl-11,12-dihydroindolo[2,3*a*]-carbazole (6).

To a suspension of aluminum trichloride (370 mg, 2.8 mmoles) in 10 ml of dichloromethane, 786 mg of α -chlor- α -phenylacetyl chloride (4.2 mmoles) were slowly added at 0°. After stirring for 20 minutes at this temperature 260 mg of compound **2** (1 mmole), dissolved in 10 ml of dichloromethane, were added slowly. The mixture was stirred 30 minutes at 0° and then 2 hours at room

temperature. Then the mixture was poured into ice/water. The organic layer was separated, and the aqueous phase was extracted with dichloromethane. The combined organic phases were dried with sodium sulfate, concentrated and the residue was purified by column chromatography (petroleum ether/ethyl acetate, 5:1) to furnish the compound **6** in 25% yield (94 mg), mp 237-238° (petroleum ether/ethyl acetate); ir (potassium bromide): ν 3520, 1620, 1600, 1450, 1430, 1380, 1360, 1320, 1265, 1220, 1150, 1100, 1020, 900, 800, 740, 725, 700, 665 cm^{-1} ; ms: m/z (%) 377 ($M^{++} + 1$, 27), 376 (M^{++} , 100), 362 (10), 361 (28), 188 (11); ^1H nmr (400 MHz, dideuteriodichloromethane): δ 4.14 (s, 3H, N11-CH₃ or N12-CH₃), 4.21 (s, 3H, N11-CH₃ or N12-CH₃), 5.50 (s, 1H, OH), 6.87-6.94 (m, 2H, aromatic H), 7.30-7.39 (m, 2H, aromatic H), 7.45-7.59 (m, 3H, aromatic H), 7.60-7.70 (m, 5H, aromatic H), 8.42 (d, $^3J = 7.77$ Hz, 1H, C4-H or C7-H); ^{13}C nmr (100.6 MHz, dideuteriodichloromethane): δ 36.7 (N-CH₃), 37.3 (N-CH₃), 110.0 (C_D), 110.7 (C_D), 112.6 (C_q), 113.3 (C_q), 119.6 (C_D), 120.6 (C_D), 121.9 (C_D), 122.3 (C_q), 123.2 (C_D), 124.5 (C_q), 125.2 (2 x C_q), 125.3 (C_D), 125.4 (C_D), 129.0 (C_D), 130.3 (2 x C_D), 130.6 (C_q), 131.9 (2 x C_D), 135.6 (C_q), 143.8 (C_q), 143.9 (C_q), 145.3 (C_q).

Anal. Calcd. for C₂₆H₂₀N₂O (376.46): C, 82.95; H, 5.35; N, 7.44. Found: C, 82.77; H, 5.52; N, 7.19.

3-Formyl-1-methyl-2-(1-methyl-1*H*-indol-2-yl)-1*H*-indole (**7**).

Under stirring and cooling in ice/water, 0.4 ml of phosphoryl chloride were added to a mixture of compound **2** (1040 mg, 4 mmoles) and dimethylformamide (15 ml) in such a way, that the inside temperature didn't increase over 20°. After stirring for 1 hour at 20° and then 1.5 hours at 35° the mixture was poured into ice/water. Upon addition of 5*N* sodium hydroxide (pH = 6), an amorphous precipitate was formed. It was crystallized from methanol and dichloromethane. The product **7** was obtained as colorless crystals in 98% yield (1135 mg), mp 171-172° (petroleum ether/ethyl acetate); ir (potassium bromide): ν 3050, 2930, 2800, 2720, 1700, 1610, 1575, 1500, 1460, 1435, 1420, 1405, 1380, 1330, 1250, 1235, 1160, 1125, 1100, 1060, 1030, 1010, 930, 820, 790, 770, 750 cm^{-1} ; ms: m/z (%) 289 ($M^{++} + 1$, 21), 288 (M^{++} , 100), 287 (18), 273 (12), 272 (12), 271 (47), 260 (25), 258 (43), 245 (14), 244 (15), 243 (15), 217 (17), 144 (21), 131 (10), 130 (15); ^1H nmr (200 MHz, dideuteriodichloromethane): δ 3.65 (s, 3H, N-CH₃), 3.68 (s, 3H, N-CH₃), 6.83 (s, 1H, indole C3'-H), 7.21-7.46 (m, 6H, aromatic H), 7.74 (d, $^3J = 7.08$ Hz, indole C4'- or C7-H), 8.45-8.48 (m, 1H, indole C4-H), 9.79 (s, 1H, -CHO).

Anal. Calcd. for C₁₉H₁₆N₂O (288.35): C, 79.14; H, 5.59; N, 9.72. Found: C, 79.37; H, 5.47; N, 9.67

3-[2-(1-Methyl-1*H*-indol-2-yl)-1-methyl-1*H*-indol-3-yl]cyclohexanone (**8**).

To a solution of aluminum trichloride (310 mg, 2.3 mmoles) in dichloromethane, 500 μl of cyclohexenone (5.1 mmoles) in 10 ml of dichloromethane were added slowly at 0°. After 20 minutes 340 mg of compound **2** (1.31 mmoles) was added and the resulting mixture was stirred for 4 hours at 0°. Then the mixture was poured into ice/water, the organic layer separated and the aqueous phase extracted with dichloromethane. The combined organic phases were dried with sodium sulfate, concentrated and the residue purified by "flash" chromatography (petroleum ether/ethyl acetate, 4:1). The product **8** was obtained as a mixture of diastereomeric atropisomer in the ratio of 1:1 (^1H nmr) in approximately 41% yield (190 mg), mp 205-206° (petroleum ether/ethyl acetate); ir (potassium bromide): ν 2930, 1695, 1455,

1415, 1390, 1360, 1315, 1240, 1215, 1160, 1090, 1010, 945, 800, 790, 745 cm^{-1} ; ms: m/z (%) 357 ($M^{++} + 1$, 26), 356 (M^{++} , 100), 299 (20), 286 (19), 285 (45), 271 (21), 270 (18), 269 (11), 256 (11), 178 (13); ^1H nmr (400 MHz, deuteriochloroform): δ 1.62-1.70 (m, 3H, aliphatic H), 1.96-2.53 (m, 11H, aliphatic H), 2.77 (pt, $J = 13.78$ Hz and 13.67 Hz, 1H, aliphatic H), 3.00 (pt, $J = 13.73$ Hz and 13.74 Hz, 1H, aliphatic H), 3.12-3.23 (m, 2H, aliphatic H), 3.47 (s, 3H, N-CH₃), 3.48 (s, 3H, N-CH₃), 3.52 (s, 3H, N-CH₃), 3.53 (s, 3H, N-CH₃), 6.60 (s, 1H, indole C3'-H), 6.64 (s, 1H, indole C3'-H), 7.17-7.42 (m, 12H, aromatic H), 7.68-7.71 (m, 2H, aromatic H), 7.79-7.81 (m, 2H, aromatic H).

Anal. Calcd. for C₂₄H₂₄N₂O (356.47): C, 80.87; H, 6.79; N, 7.86. Found: C, 80.77; H, 6.65; N, 7.65.

2-[2-(2-Methylaminobenzyl)benzoyl]-1-methyl-1*H*-indole (**9**).

Anthranilic acid (475 mg, 3.46 mmoles) and 4.2 mg of trichloro acetic acid (0.026 mmole) were solved in 10 ml of tetrahydrofuran and the mixture was cooled to 0°. Then 0.8 ml of isoamyl nitrite (5.9 mmoles) were added within 2 minutes and the resulting mixture was stirred for 1.5 hours at 20°. The precipitate was filtered off and alternatively washed with tetrahydrofuran and dichloroethane until the washing-liquid was colorless. This freshly prepared precipitate (Caution! Explosive in the dried state!) was then suspended in dichloroethane and finally added to a boiling solution of compound **2** (325 mg, 1.25 mmoles) in 25 ml of dichloroethane. After refluxing for 3 hours the mixture was allowed to cool to room temperature and then concentrated. The residue was purified by "flash" chromatography (petroleum ether/ethyl acetate, 10:1) to furnish the compound **9** in 15% yield (66 mg), mp 124-125° (petroleum ether/ethyl acetate); ir (potassium bromide): ν 3340, 3030, 2800, 1610, 1600, 1590, 1575, 1520, 1500, 1460, 1430, 1415, 1380, 1350, 1320, 1300, 1255, 1250, 1220, 1150, 1130, 1115, 1075, 1030, 935, 915, 900, 880, 830, 810, 780, 735, 720, 655, 615 cm^{-1} ; ms: m/z (%) 355 ($M^{++} + 1$, 12), 354 (M^{++} , 45), 337 (35), 336 (100), 247 (12), 223 (18), 208 (13), 204 (10), 194 (20), 180 (13), 165 (16), 132 (12), 118 (14), 106 (21); ^1H nmr (400 MHz, deuteriochloroform): δ 2.73 (s, 3H, -NH-CH₃), 3.93 (s, 2H, benzyl-CH₂), 4.20 (s, 3H, indole N-CH₃), 4.50 (br, 1H, -NH-CH₃), 6.54 (d, $^3J = 8.06$ Hz, 1H, aromatic H), 6.65 (pt, $J = 7.31$ Hz and 7.33 Hz, 1H, aromatic H), 6.87 (s, 1H, indole C3-H), 7.05 (d, $^3J = 7.30$ Hz, 1H, aromatic H), 7.13 - 7.49 (m, 8H, aromatic H), 7.63 (d, $^3J = 8.09$ Hz, 1H, indole C4-H); ^{13}C nmr (100.6 MHz, deuteriochloroform): δ 30.5 (C_p, -NH-CH₃ or indole N-CH₃), 32.2 (C_p, -NH-CH₃ or indole N-CH₃), 34.6 (C_s, benzyl-CH₂), 109.6 (C_D), 110.4 (C_D), 116.1 (C_D), 116.5 (C_D), 120.9 (C_D), 123.2 (C_D), 123.7 (C_q), 125.4 (C_D), 125.8 (C_q), 126.5 (C_D), 128.0 (C_D), 128.6 (C_D), 129.5 (C_D), 130.3 (C_D), 131.1 (C_D), 135.6 (C_q), 138.6 (C_q), 139.7 (C_q), 140.8 (C_q), 147.4 (C_q), 191.5 (CO).

Anal. Calcd. for C₂₄H₂₂N₂O (354.45): C, 81.33; H, 6.26; N, 7.90. Found: C, 80.89; H, 5.87; N, 8.05.

2-[(1-Methyl-1*H*-indol-2-yl)-1-methyl-1*H*-indol-3-ylazo]benzoic Acid (**10**).

To a stirred solution of 760 mg of anthranilic acid (5.5 mmoles) and 500 mg of trichloroacetic acid in 18 ml of tetrahydrofuran, 1.35 ml of isoamyl nitrite were added at 0°. The mixture was allowed to warm up to room temperature and stirred for 2 hours. The formed precipitate was filtered off and washed alternatively with dichloromethane and tetrahydrofuran, until the washing-liquid was colorless. The washed precipitate was suspended in 25 ml of

tetrahydrofuran and stirred. To this suspension a solution of compound **2** (400 mg, 1.54 mmoles) in 5 ml of tetrahydrofuran was added slowly. After refluxing for 5 hours the mixture was allowed to cool to room temperature and then concentrated. The residue was purified by "flash" chromatography (petroleum ether/ethyl acetate, 2:1) to furnish the compound **10** in 12% yield (75 mg), mp 255-258° (petroleum ether/ethyl acetate); ir (potassium bromide): ν 1700, 1590, 1510, 1450, 1415, 1400, 1375, 1325, 1310, 1280, 1255, 1235, 1130, 1110, 1070, 1030, 920, 890, 845, 800, 770, 735, 690, 665, 630 cm^{-1} ; ms: m/z (%) 409 ($M^{++} + 1$, 26), 408 (M^{++} , 95), 407 (20), 363 ($M^{++} - \text{COOH}$, 12), 287 (M^{++} benzoic acid, 13), 273 (24), 272 (100), 271 (19), 260 (13), 259 (48), 258 (22), 257 (32), 256 (10), 244 (36), 243 (38), 242 (15), 230 (10), 218 (11), 217 (20), 216 (16), 196 (10) 195 (34), 130 (17), 129 (10); ^1H nmr (400 MHz, deuteriodimethyl sulfoxide): δ , 3.73 (s, 3H, N-CH₃), 3.84 (s, 3H, N-CH₃), 6.98 (s, 1H, indole C3'-H), 7.16 (pt, $J = 7.22$ Hz and 7.31 Hz, 1H, aromatic H), 7.29-7.48 (m, 6H, aromatic H), 7.61-7.74 (m, 4H, aromatic H), 8.51 (d, $^3J = 7.62$ Hz, 1H, indole C4-H), 13.28 (br, 1H, COOH); ^{13}C nmr (100.6 MHz, deuteriochloroform): δ , 31.9 (C_q , N-CH₃), 32.1 (C_q , N-CH₃), 107.9 (C_t), 110.1 (C_t), 110.7 (C_t), 115.3 (C_t), 117.4 (C_q), 120.6 (C_t), 121.5 (C_t), 121.6 (C_t), 123.6 (C_t), 124.8 (C_q), 125.7 (C_t), 125.9 (C_t), 127.5 (C_q), 127.6 (C_q), 129.4 (C_t), 132.6 (C_t), 133.6 (C_t), 134.8 (C_q), 138.7 (C_q), 138.9 (C_q), 142.4 (C_q), 151.9 (C_q), 167.2 (COOH).

Anal. Calcd. for $\text{C}_{25}\text{H}_{20}\text{N}_4\text{O}_2$ (408.46): C, 73.51; H, 4.94; N, 13.72. Found: C, 73.59; H, 5.00; N, 13.58.

3-(5-Methylsuccinimido-2-yl)-1-methyl-2-(1-methyl-1*H*-indol-2-yl)-1*H*-indole (**11**).

A suspension of aluminum trichloride (420 mg, 3.15 mmoles) and *N*-methylmaleimide (360 mg, 3.24 mmoles) in 60 ml dichloromethane was stirred at room temperature for 20 minutes. The 2,2-bisindolyl **2** (780 mg, 3 mmoles) was added, and the reaction mixture was stirred at room temperature for 5 hours and then poured into water. The organic layer was separated, and the aqueous phase washed with dichloromethane. The combined organic layers were dried with sodium sulfate, concentrated, and the residue purified by "flash" chromatography (petroleum ether/ethyl acetate, 2:1) to furnish the mixture of diastereomeric atropisomer in the ratio of 18:16 in 75% yield (836 mg), mp 178-179° (petroleum ether/ethyl acetate); ms: m/z (%) 371 (M^{++} , 100), 287 (15), 286 (69), 285 (40), 284 (12), 272 (10), 271 (47), 270 (38), 269 (30), 268 (12), 260 (12), 259 (21), 257 (13), 256 (31), 255 (32), 241 (10), 135 (10), 128 (14); ^1H nmr (400 MHz, deuteriochloroform): δ 2.65 (s, 3H, succinimido N-CH₃, b), 2.89-3.13 (m, 4H, aliphatic H), 3.05 (s, 3H, succinimido N-CH₃, a), 3.53 (s, 3H, N-CH₃), 3.56 (s, 3H, N-CH₃), 3.57 (s, 3H, N-CH₃), 3.67 (s, 3H, N-CH₃), 4.07 (dd, $^3J = 9.50$ Hz, $^3J = 5.48$ Hz, 1H, aliphatic H, b), 4.25 (dd, $^3J = 9.69$ Hz, $^3J = 4.86$ Hz, 1H, aliphatic H, a), 6.63 (s, 1H, C3'-H, b), 6.70 (s, 1H, C3'-H, a), 7.14-7.42 (m, 14H, aromatic H, a and b), 7.66-7.70 (m, 2H, aromatic H, a and b); ^{13}C nmr (100.6 MHz, deuteriochloroform): δ 24.8 (C_t ; succinimido C2, a), 25.0 (C_t ; succinimido C2, b), 30.5 (C_p ; N-CH₃), 30.6 (3 x N-CH₃), 36.4 (C_s ; succinimido C3, a), 37.49 (C_s ; succinimido C3, b), 37.54 (C_p ; succinimido N-CH₃, b), 38.4 (C_p ; succinimido N-CH₃, a), 105.9 (C_t), 106.4 (C_t), 109.6 (C_t), 109.9 (C_t), 110.1 (C_t), 110.2 (C_t), 112.4 (C_q), 113.4 (C_q), 118.3 (C_t), 118.4 (C_t), 120.2 (2 x C_t), 120.3 (C_t), 120.4 (C_t), 120.9 (C_t), 121.1 (C_t), 122.7 (C_t), 122.8 (C_t), 123.0 (C_t), 123.1 (C_t), 124.8 (C_q), 125.9 (C_q), 127.5 (C_q), 127.6 (C_q), 129.1 (C_q), 129.0 (C_q), 129.8 (C_q), 130.8 (C_q), 137.4

(C_q), 137.7 (C_q), 138.08 (C_q), 138.12 (C_q), 176.3 (CO), 176.5 (CO), 178.1 (CO), 178.3 (CO).

Anal. Calcd. for $\text{C}_{23}\text{H}_{21}\text{N}_3\text{O}_2$ (371.44): C, 74.37; H, 5.70; N, 11.31. Found: C, 74.04; H, 5.70; N, 10.87.

3,3'-Bis(5-methylsuccinimido-2-yl)-1,1'-dimethyl-1*H*,1'*H*-2,2'-bisindolyl (**12**).

The product **12** was obtained beside the formation of **11** as a diastereomeric mixture in the ratio of approximately 1:1 (^1H nmr), yield 27% (390 mg), mp 285-288° (petroleum ether/ethyl acetate); ms: m/z (%) 482.4 (M^{++} , 100); ^1H nmr (400 MHz, deuteriochloromethane): δ 2.99-3.08 (m, 6H, aliphatic H), 3.01 (s, 6H, 2 x succinimido N-CH₃), 3.03 (s, 6H 2 x succinimido N-CH₃), 3.25 (m, 2H, 2 x succinimido C3-H), 3.52 (s, 6H, 2 x indole N-CH₃), 3.64 (s, 6H, 2 x indole N-CH₃), 3.93 (dd, $^3J = 8.60$ Hz, $^3J = 6.51$ Hz, 2H, aliphatic H), 4.21 (dd, $^3J = 9.72$ Hz, $^3J = 5.40$ Hz, 2H, aliphatic H), 7.13-7.50 (m, 16H, aromatic H).

Anal. Calcd. for $\text{C}_{28}\text{H}_{26}\text{N}_4\text{O}_4$: (482.54): C, 69.70; H, 5.43; N, 11.61. Found: C, 69.67; H, 5.38; N, 11.41.

3-(5-Methylmaleimido-2-yl)-1-methyl-2-(1-methyl-1*H*-indol-2-yl)-1*H*-indole (**13**) and 12,13-Dimethyl-6-methyl-5,7,12,13-tetrahydro-6*H*-indolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione (**14**).

Compound **11** (240 mg, 0.65 mmole) was dissolved in 15 ml of *o*-dichlorobenzene and stirred for 30 minutes at room temperature. Then 10% Pd/C (240 mg) was added and the mixture was heated for 72 hours under reflux. The reaction mixture was concentrated, the residue dried over silica gel and then separated by "flash" chromatography (petroleum ether/ethyl acetate, 3:1). After separation of **13**, the column was washed with 1 liter of dichloromethane. The dichloromethane fraction was concentrated and the residue crystallized from dichloromethane to furnish compound **14** as orange-yellow filmy plates. Yield of **13**, 51% (122 mg), mp 177-180° (petroleum ether/ethyl acetate); ms: m/z (%) 370 ($M^{++} + 1$, 26), 369 (M^{++} , 100), 352 (13), 311 (16), 284 (23), 283 (22), 269 (30), 268 (24), 267 (12), 156 (12), 142.1 (10), 141.6 (10), 141 (12); ^1H nmr (400 MHz, deuteriochloroform): δ 2.94 (s, 3H, maleimido N-CH₃), 3.60 (s, 3H, indole N-CH₃), 3.62 (s, 3H, indole N-CH₃), 6.13 (s, 1H, maleimido C3-H), 6.60 (s, 1H, indole C3'-H), 7.18 (pt, $J = 7.78$ Hz and 7.14 Hz, 1H, aromatic H), 7.29-7.44 (m, 5H, aromatic H), 7.65 (d, $^3J = 7.91$ Hz, 1H, indole C4'-H), 8.01 (d, $^3J = 8.03$ Hz, 1H, indole C4-H); ^{13}C nmr (100.6 MHz, deuteriochloroform): δ , 23.8 (maleimido N-CH₃), 30.7 (indole N-CH₃), 30.9 (indole N-CH₃), 106.1 (C_t), 107.4 (C_q), 109.9 (C_t), 110.1 (C_t), 120.3 (C_t), 121.2 (C_t), 121.4 (C_t), 122.0 (C_t), 122.5 (C_t), 123.0 (C_t), 123.8 (C_t), 125.9 (C_q), 127.7 (C_q), 129.3 (C_q), 133.9 (C_q), 137.9 (C_q), 138.2 (C_q), 141.3 (C_q), 170.5 (CO), 171.5 (CO).

Anal. Calcd. for $\text{C}_{23}\text{H}_{19}\text{N}_3\text{O}_2$ (369.42): C, 74.78; H, 5.18; N, 11.37. Found: C, 74.67; H, 5.18; N, 11.36.

The yield of **14** was 25% (60 mg), mp 325-326° (dichloromethane); ms: m/z (%) 368 ($M^{++} + 1$, 26), 367 (M^{++} , 100), 352 ($M^{++} - \text{CH}_3$, 33), 268 (13), 267 (46), 266 (24), 265 (11), 240 (15); ^1H nmr (400 MHz, deuteriochloroform): δ 3.25 (s, 3H, N6-CH₃), 4.19 (s, 6H, N12- and N13-CH₃), 7.41-7.45 (m, 2H, C2- and C10- respectively, C3- and C9-H), 7.51 (d, $^3J = 8.17$ Hz, 2H, C1- and C11-H), 7.59-7.63 (m, 2H, C2- and C10- respectively, C3 and C9-H), 9.25 (d, $^3J = 7.86$ Hz, 2H, C4- and C8-H); ^{13}C nmr (100.6 MHz, deuteriochloroform): δ 23.7 (N6-CH₃), 36.9 (N12- and N13-CH₃), 110.0, 120.0, 120.2,

121.5, 122.9, 125.7, 127.5, 133.0, 145.1, 170.0 (2 x CO).

Anal. Calcd. for $C_{23}H_{17}N_3O_2$: (367.41): C, 75.19; H, 4.66; N, 11.44. Found: C, 74.91; H, 4.68; N, 11.50.

11,12-Dimethyl-5,6,11,12-tetrahydro-indolo[2,3-*a*]carbazole-5,6-dicarboxylic Acid Dibenzylamide (17).

Compound 15 (510 mg, 1.27 mmoles) [3] was dissolved in 15 ml of benzylamine and heated for 10 hours under reflux. After cooling to room temperature the mixture was dried over silica gel and then separated by "flash" chromatography (petroleum ether/ethyl acetate, 5:4) to furnish compound 17 in 25% yield (175 mg), mp 209° (petroleum ether/ethyl acetate); ir (potassium bromide): ν 3400, 3250, 3060, 2920, 1645, 1550, 1510, 1450, 1415, 1355, 1325, 1255, 1235, 1205, 1155, 1130, 1080, 1010, 735, 695 cm^{-1} ; ms: m/z (%) 553 ($M^{++} + 1$, 14), 552 (M^{+} , 31), 419 (26), 418 (81), 311 (19), 286 (21), 285 (100), 284 (41), 270 (29), 269 (34), 267 (11); 1H nmr (400 MHz, dideuterio-dichloromethane): δ , 3.88 (s, 6H, 2 x N-CH₃), 3.97 (dd, $^2J = 15.55$ Hz, $^3J = 5.06$ Hz, 2H, 2 x Ha from -NH-CH₂-), 4.38 (dd, $^2J = 15.52$ Hz, $^3J = 7.32$ Hz, 2H, 2 x Hb from -NH-CH₂-), 4.82 (s, 2H, 2 x CH), 6.16 (pt, 2H, 2 x -NH-CH₂-), 6.56 (d, $^3J = 7.61$ Hz, 4H, 2 x phenyl C2- and C6-H), 6.88 (pt, $J = 7.59$ Hz, $J = 7.72$ Hz, 4H, 2 x phenyl C3- and C5-H), 7.04 (pt, $J = 7.44$ Hz, $J = 7.33$ Hz, 2H, 2 x phenyl C4-H), 7.24-7.28 (m, 2H, C2- and C9-H respectively, C3- and C8-H), 7.33-7.37 (m, 2H, C2- and C9-H respectively, C3- and C8-H), 7.48 (d, $^3J = 8.20$ Hz, 2H, C1- and C10-H), 7.70 (d, $^3J = 7.81$ Hz, 2H, C4- and C7-H); ^{13}C nmr (100.6 MHz, dideuterio-dichloromethane): δ 34.6 (C_t or C_p, 2 x CH or 2 x N-CH₃), 43.3 (C_s, 2 x -NH-CH₂-), 44.3 (C_t or C_p, 2 x CH or 2 x N-CH₃), 110.9 (2 x C_t), 119.2 (2 x C_t), 121.8 (2 x C_t), 123.5 (2 x C_t), 126.8 (4 x phenyl C_t), 127.2 (2 x C_t), 128.0 (2 x C_q), 128.6 (4 x phenyl C_t), 131.4 (2 x C_q), 139.1 (2 x C_q), 140.3 (2 x C_q), 172.5 (2 x CO). One C_q peak for 2 aromat C is overlapped.

Anal. Calcd. for $C_{36}H_{32}N_4O_2$: (552.68): C, 78.24; H, 5.84; N, 10.14. Found: C, 78.17; H, 5.88; N, 10.17.

13,14-Dimethyl-5,6,7,8,13,14-hexahydroindolo[2,3-*a*]pyridazino[4,5-*c*]carbazole-5,8-dione (19).

Compound 16 (100 mg, 0.25 mmole) [5] and hydrazine hydrate (6 ml) were heated for 8 hours under reflux. Then the mixture was stirred again for 5 hours at room temperature, whereupon an amorphous orange-yellow precipitate was formed. The precipitate was separated and crystallized from tetrahydrofuran and ethyl acetate, yield 68% (63 mg), mp 308-309° (tetrahydrofuran/ethyl acetate); ir (potassium bromide): ν 3320, 3040, 2910, 1750, 1700, 1600, 1570, 1470, 1440, 1425, 1410, 1380, 1345, 1320, 1265, 1235, 1150, 1100, 1075, 1010, 910, 870, 840, 800, 760, 730, 710, 640 cm^{-1} ; ms: m/z (%) 369 ($M^{++} + 1$, 26), 368 (M^{+} , 100), 354 (10), 353 (30), 267 (12), 141 (11); 1H nmr (400 MHz, deuteriodimethyl sulfoxide): δ 4.22 (s, 6H, 2 x N-CH₃), 4.88 (s, 2H, 2 x NH), 7.36 (pt, $J = 7.27$ and 7.41 Hz, 2H, C2- and C11-H respectively, C3- and C10-H), 7.62 (pt, $J = 7.41$ and 7.19 Hz, 2H, C2- and C11-H respectively, C3- and C10-H), 7.74 (d, $^3J = 8.10$ Hz, 2H, C1- and C12-H), 9.09 (d, $^3J = 7.79$ Hz, 2H, indole C4- and C9-H).

Anal. Calcd. for $C_{22}H_{16}N_4O_2$ (368.39): C, 71.73; H, 4.38; N, 15.21. Found: C, 71.95; H, 4.21; N, 15.63.

12,13-Dimethyl-6-isopropylideneamino-5,7,12,13-tetrahydro-6-*H*-indolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione (20).

Compound 20 was synthesized according to the procedure to obtain 19. Compound 16 (100 mg, 0.31 mmole) and 6 ml of hydrazine hydrate were used as starting materials. After addition of 3 ml of acetone, a precipitate was formed. The precipitate was crystallized from hot tetrahydrofuran, to furnish the compound 20 in 38% yield (39 mg), mp 312-315° (tetrahydrofuran); ir (potassium bromide): ν 2930, 1740, 1690, 1625, 1515, 1460, 1430, 1365, 1335, 1315, 1285, 1265, 1235, 1150, 1110, 1075, 1055, 1010, 975, 930, 870, 815, 800, 740, 730, 710, 635 cm^{-1} ; ms: m/z (%) 409 ($M^{++} + 1$, 29), 408 (M^{+} , 100), 383 (15), 382 (58), 353 (19), 352 (11), 282 (33), 267 (17), 266 (13); 1H nmr (400 MHz, deuteriochloroform): δ 2.10 (s, 3H, C-CH₃), 2.37 (s, 3H, C-CH₃), 4.20 (s, 6H, 2 x N-CH₃), 7.36 (pt, $J = 7.83$ and 7.16 Hz, 2H, C2- and C10- respectively, C3- and C9-H), 7.50 (d, $^3J = 8.01$ Hz, 2H, C1- and C11-H), 7.56-7.60 (m, 2H, C2- and C10- respectively, C3- and C9-H), 9.17 (d, $^3J = 7.60$ Hz, 2H, C4- and C8-H).

Anal. Calcd. for $C_{25}H_{20}N_4O_2$: (408.46): C, 73.51; H, 4.94; N, 13.72. Found: C, 73.01; H, 4.91; N, 13.45.

N-Benzyl 2-(5,6-Dimethyl-6,11-dihydro-5*H*-cyclopenta[2,1-*b*]-3,4-*b'*]diindol-11-yl)acetamide (22).

Compound 15 (210 mg, 0.52 mmole) was dissolved in 6 ml of benzyl amine and the mixture was refluxed for 19 hours. After cooling to room temperature the mixture was dried over silica gel. The purification was performed by "flash" chromatography (petroleum ether/ethyl acetate, 2:1), to furnish the compound 22 in 40% yield (87 mg), mp 215° (petroleum ether/ethyl acetate); ms: (fd) m/z (%) 419.6 (M^{++} , 100); ir (potassium bromide): ν 3260, 3025, 2900, 1625, 1600, 1530, 1440, 1400, 1375, 1315, 1250, 1145, 1120, 1105, 1005, 720, 690 cm^{-1} ; 1H nmr (400 MHz, dideuteriodichloromethane): δ 2.66 (d, $^3J = 7.32$ Hz, 2H, -COCH₂-), 4.02 (s, 6H, 2 x N-CH₃), 4.34 (t, $^3J = 7.31$ Hz, 1H, -CH-), 4.40 (d, $^3J = 5.72$ Hz, 2H, -NH-CH₂-), 5.63 (pt, br, 1H, -NH-), 7.08-7.18 (m, 6H, aromatic H), 7.23-7.27 (m, 3H, aromatic H), 7.37 (d, $^3J = 8.18$ Hz, 2H, indole C7-H and C7'-H), 7.55 (d, $^3J = 7.72$ Hz, 2H, indole C4-H and C4'-H); ^{13}C nmr (100.6 MHz, dideuteriodichloromethane): δ 33.4 (C_p, 2 x N-CH₃), 35.1 (C_t, -CH₂-), 40.4 (C_s, -CO-CH₂- or -NH-CH₂-), 44.1 (C_s, -CO-CH₂- or -NH-CH₂-), 110.5 (2 x C_t), 118.8 (2 x C_t), 120.5 (2 x C_t), 121.0 (2 x C_t), 124.9 (2 x C_q), 127.7 (C_t), 128.2 (2 x C_t), 128.3 (2 x C_q), 128.9 (2 x C_t), 138.6 (2 x C_q), 139.0 (C_q, -benzyl C), 141.4 (2 x C_q), 171.9 (CO).

Anal. Calcd. for $C_{28}H_{25}N_3O$ (419.53): C, 80.16; H, 6.01; N, 10.02. Found: C, 79.68; H, 6.54; N, 9.87.

Methyl[3-(5,6-Dimethyl-11-methoxycarbonylmethyl-6,11-dihydro-5*H*-cyclopenta[2,1-*b*]-3,4-*b'*]diindol-2-yl)acrylate (24).

To a suspension of aluminum trichloride (280 mg, 2.1 mmoles) in 20 ml of bromobenzene, 450 μ l of methyl propynoate (5 mmoles) were added. After 20 minutes 260 mg of 2,2'-bisindolyl 2 (1 mmoles) were added in 10 ml of bromobenzene. The mixture was stirred for 55 hours at room temperature and then poured into ice/water. The organic layer was separated, and the aqueous phase washed with dichloromethane. The combined organic layers were dried with sodium sulfate, concentrated and purified by "flash" chromatography (petroleum ether/ethyl acetate, 3:1) to furnish the compound 24 in 10% yield (42 mg), mp 183° (petroleum ether/ethyl acetate); ms: m/z (%) 428 (M^{+} , 7), 356 (25), 356 (100), 339 (17); 1H nmr (400 MHz, deuteriochloroform): δ 2.33 (d, $^3J = 8.07$ Hz, 2H, -CH₂-), 3.42 (s, 3H, N- or O-CH₃), 3.74 (s, 3H, N- or O-CH₃), 3.84 (s, 3H, N- or O-CH₃), 3.96 (s, 3H, N- or O-CH₃), 5.39 (m, 1H, aliphatic H),

7.22-7.47 (m, 6H, aromatic H), 7.82 (d, $^3J = 7.84$ Hz, 1H, vinyl H), 7.94 (d, $^3J = 7.86$ Hz, 1H, vinyl H), 8.12 (dd, $^4J = 0.93$ Hz, 1H, C1-H); ^{13}C nmr (100.6 MHz, deuteriochloroform): δ 29.3 (-CH₂-), 33.1 (indole N-CH₃), 33.6 (indole N-CH₃), 33.9 (-CH₂-), 51.2 (O-CH₃), 52.0 (O-CH₃), 109.9 (C₁), 110.1 (C₁), 114.3 (C_q), 119.2 (C₁), 119.5 (C_q), 119.6 (C₁), 120.5 (C₁), 121.3 (C₁), 123.5 (C₁), 123.8 (C₁), 126.7 (C_q), 127.0 (C_q), 127.4 (C_q), 128.7 (C₁), 134.0 (C_q), 139.3 (C_q), 142.0 (C_q), 167.3 (CO), 172.2 (CO), one C_q signal is overlapped.

Anal. Calcd. for C₂₆H₂₄N₂O₄ (428.49): C, 72.88; H, 5.65; N, 6.54. Found: C, 72.61; H, 5.21; N, 6.27.

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