Synthesis of symmetric and non-symmetric indolo[2,3-*c*]carbazole derivatives: preparation of indolo[2,3-*c*]pyrrolo[3,4-*a*]carbazoles

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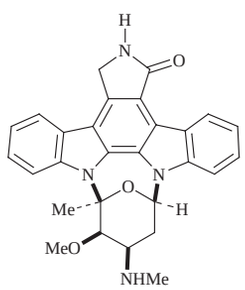
Symmetric and non-symmetric indolo[2,3-*c*]carbazoles have been prepared from 3,3′-biindolyls 9a–d by two strategies; step by step, by thermal electrocyclic reaction, or directly. Indolo[2,3-*c*]pyrrolo-[3,4-*a*]carbazoles 28aa–db, a new class of indolopyrrolocarbazoles, have been obtained in a one step reaction from readily available precursors.

Introduction

The indolocarbazole family is composed of five possible isomeric compounds and possess a wide range of biological activities. Thus, staurosporine **1** [1] (inhibits protein Kinase C) and rebeccamycin **2** [2] (exhibits antibiotic and antitumor activities) certainly are the most well-known of the indolo[2,3-*a*]carbazole derivatives. Three general methods exist to prepare the [2,3-*a*] framework; Fischer indolization,[3,4] Diels–Alder reaction,[5–7] or oxidative cyclization of bisindolylmaleimides.[8–11] The latter method is the one most frequently used. Indolo[3,2-*b*]carbazole **3** has recently attracted considerable interest due to its affinity



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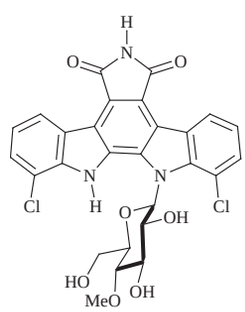

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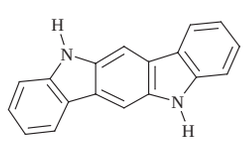

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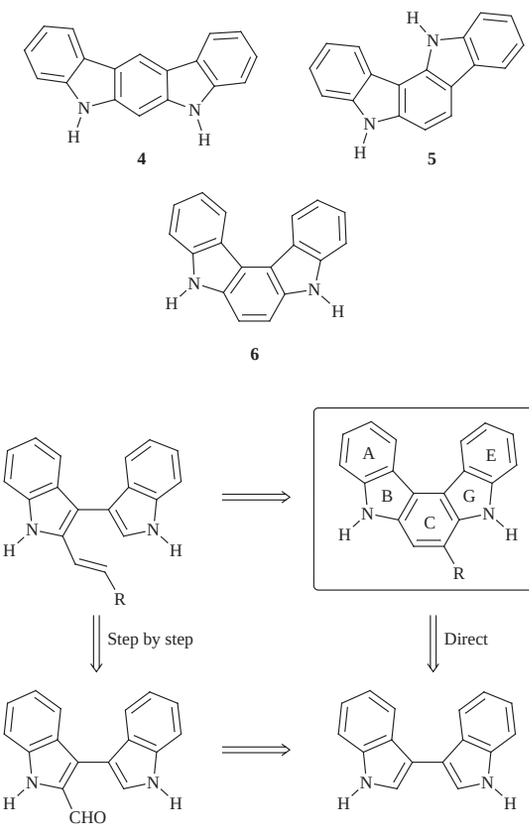
to the TCDD receptor.[12,13] However no generally applicable synthetic methods are available for these systems.[14–18]

The other indolocarbazoles **4**–**6** have been scantily studied. This is probably due to the lack of connection with any sort of biological activities or natural compounds. Indolo[2,3-*b*]carbazole **4** [19] is sometimes obtained during the preparation of **3** and the synthesis of indolo[3,2-*a*]carbazole **5** has only been reported by Mann and Willcox.[20]

In the case of the indolo[2,3-*c*]carbazole **6**, only the preparation of *N*,*N*′-dimethylindolo[2,3-*c*]carbazole has been described from *N*,*N*′-dimethyl-*N*,*N*′-diphenyl-1,4-phenylenediamine by irradiation.[21] Now, we have developed three general methods to prepare indolo[2,3-*c*]carbazoles **6** [22] by C-ring construction from readily available 3,3′-biindolyl derivatives.[23,24] Two routes could be expected as outlined in the retrosynthetic Scheme 1; step by step, which uses thermal electrocyclic reaction, or by direct synthesis.



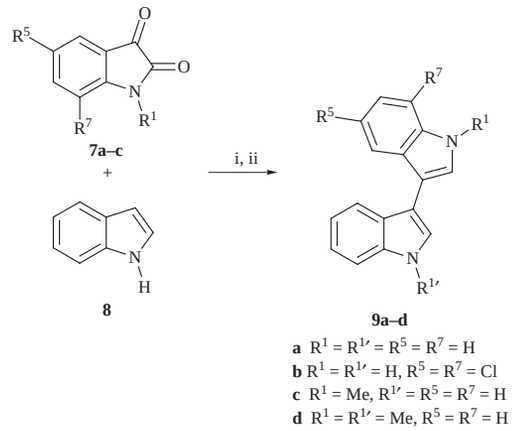
Scheme 1

These two routes capitalize on 3,3′-biindolyl as a readily available starting material as it can be prepared by condensation of isatin **7** and indole **8**, followed by reduction with lithium aluminium hydride. Symmetric or non-symmetric 3,3′-biindolyl derivatives **9a**–**c** have been prepared according to ref. 23 or 24 (Scheme 2).

Results and discussion

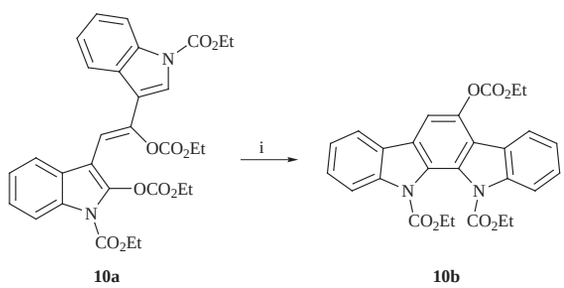
Synthesis of indolo[2,3-*c*]carbazoles: step by step

Thermal electrocyclic reactions [25] have previously been used to form aromatic rings during various preparations of carbazoles,[26–29] carbolines [30,31] or ellipticine [32,33] derivatives. Only a few workers have described this type of strategy to obtain the indolocarbazole framework. Thus, Wallace and co-workers [7] and Pindur *et al.*[6] have prepared indolo[2,3-*a*]carbazole derivatives from 2,2′-biindolyl by irradiation or by Lewis acid



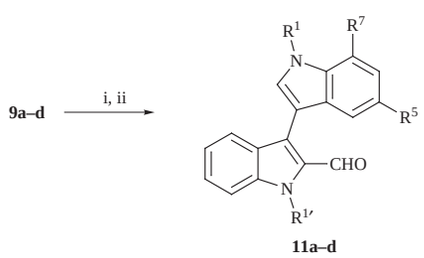
Scheme 2 *Reagents and conditions*: i, Et_2NH (cat), EtOH; ii, $LiAlH_4$ or $NaBH_4$, BF_3, Et_2O, DME; iii dimethyl oxalate, Bu′OK

catalysis. Marchesini and co-workers[34] have performed a 6π-electrocyclisation to obtain **10b** from **10a** (Scheme 3).



Scheme 3 *Reagents and conditions*: i, HPK 125 W, *hv*

The first step of our approach was to prepare 2-formyl-3,3′-biindolyls **11**. By treating the appropriate 3,3′-biindolyl derivatives **9a**–**d** with *N*,*N*-dimethylchloromethaniminium chloride[35] (1.3 equiv.) in CH_3CN at room temperature; the desired compounds **11a**–**d** were obtained in good yields (Scheme 4). The

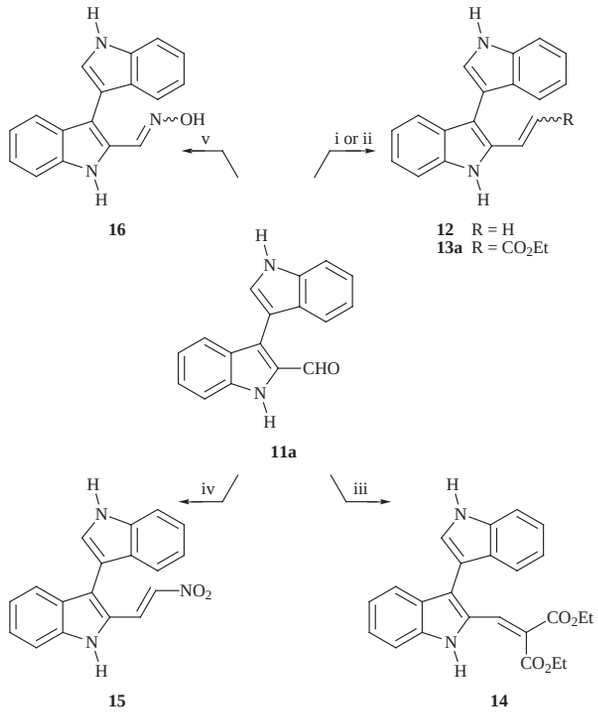


Scheme 4 *Reagents and conditions*: i, $ClCH{=}N(Me)_2^+\ Cl^-$ (1.3 equiv.), MeCN, RT; ii, $NaHCO_3$ sat.

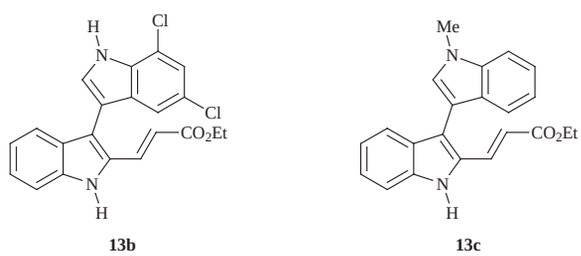
structures of compounds **11b** and **11c** have been studied by 2D-NMR to establish the correct position of the formyl group on the 3,3′-biindolyl framework. No 2,2′-diformyl derivatives were observed as side-products and were not even formed on attempted formylation of **11a** under forcing conditions. The electronic withdrawing effect of the formyl group in the 2-position exerts its lowering effect on the nucleophilic nature of the 2′-position.

From **11a**, many 2-substituted-3,3′-biindolyls could be prepared. Wittig or Horner–Emmons reactions led to compounds **12** or (*E*)-**13a** in 85% and 80% yield. The (*Z*) isomer of **13a** was isolated in 10% yield as a side-product (Scheme 5). Similarly, 2-formyl-3,3′-biindolyls **9b**,**c** yielded α,β-ethylenic esters (*E*)-**13b** and (*E*)-**13c** in 95% yield each.

The aldehyde **11a** led to the *gem*-diethyl ester **14** in 75% yield, by aldolisation in the presence of diethyl malonate in toluene at reflux with piperidine as catalyst or to the nitrovinyl derivative

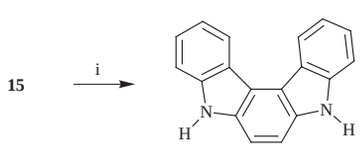


Scheme 5 *Reagents and conditions*: i, $Ph_3P^+CH_3Br^-$, K_2CO_3, triglyme; ii, $(EtO)_2POCH_2CO_2Et$, NaH, THF; iii diethylmalonate, piperidine (cat.), toluene; iv, $MeNO_2$, $MeCO_2NH_4$; v, NH_2OH, HCl, EtOH



15 in 81% yield by the classic Henry reaction. The ratio between the two isomeric oximes **16**, obtained in 95% yield in ethanol at reflux in the presence of NH_2OH and HCl was 1 : 1 (Scheme 5).

The construction of the C-ring was effected by heating the precursor **15** during 8 h at 190 °C in Ph_2O under an inert atmosphere which resulted in the formation of **17** in only 30% yield (Scheme 6). The reaction performed with Pd/C led to the

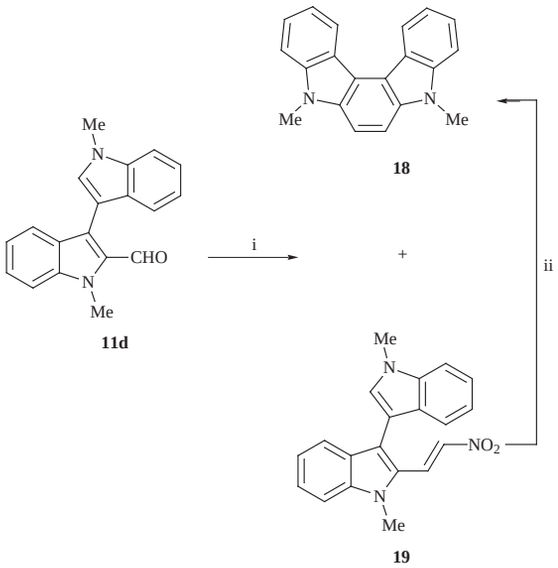


Scheme 6 *Reagents and conditions*: i, Ph_2O, 190 °C

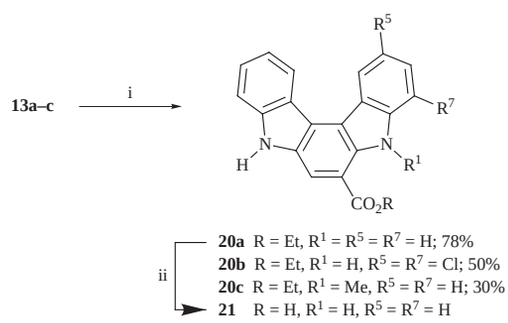
desired compound **17** in 28% yield as well. The low yield was due to a quick degradation of the compound observed during the reaction.

The stability of the *N*,*N*′-dimethylindolo[2,3-*c*]carbazole **18** contrasts with its non-substituted analog **17**. Henry aldolisation with the formyl compound **11d** during 48 h gave compound **19**[21] in 20% yield, whereas the expected compound **18** was obtained in only 8% yield. A large amount (69%) of starting material was recovered. From **19**, in Ph_2O at 160 °C, *N*,*N*′-dimethylindolo[2,3-*c*]carbazole **18**[21] could be prepared in 58% yield (Scheme 7).

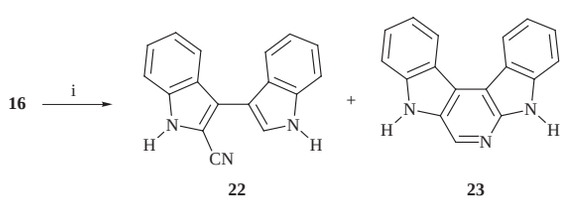
Other electrocyclisations have been executed under the same conditions (Ph_2O at 190 °C); either from (*E*)-**13a**–**c** to obtain



Scheme 7 *Reagents and conditions*: i, $MeNO_2$, $MeCO_2NH_4$; ii, Ph_2O, 160 °C



Scheme 8 *Reagents and conditions*: i, Ph_2O, 190 °C; ii, KOH, MeOH



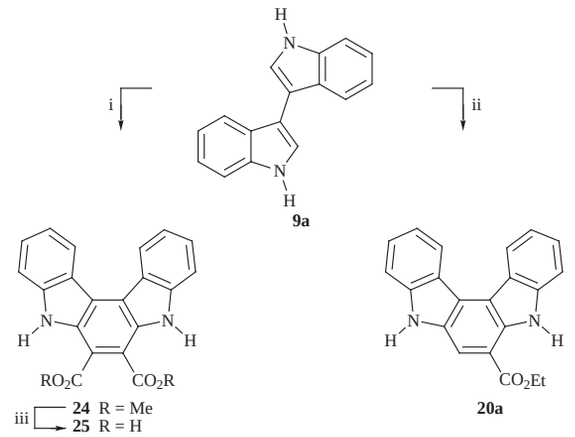
Scheme 9 *Reagents and conditions*: i, Ph_2O, 190 °C

indolocarbazoles **20a**–**c** in respectable yields (30–78%) (Scheme 8) or from any isomer of the oxime **16** which gave 2-cyano-3,3′-biindolyl **22** (31 %) and pyridodiindolyl **23** (51%) (Scheme 9). During the formation of **20a**, we have followed (*Z*)-**13a** on the mixture by TLC control. Attempts to cyclize (*E*)-**13a** at lower temperatures (reflux in xylene or acetic acid, 110 °C in Ph_2O) failed or gave **20a** in low yields (less than 5%) and using a Lewis acid was unsuccessful. Saponification of **20a** led to the parent acid **21** in 96% yield.

In connection with the studies of staurosporine and rebeccamycin derivatives, the direct synthesis of indolo[2,3-*c*]pyrrolo-[3,4-*a*]carbazoles has also been expected.

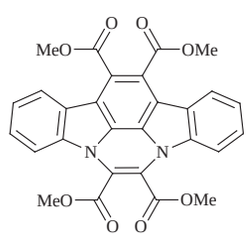
Indolo[2,3-*c*]pyrrolo[3,4-*a*]carbazoles: direct synthesis

In the 2,2′-biindolyl series, attempts to prepare directly indolo[2,3-*a*]carbazoles *via* Diels–Alder cycloaddition is fraught with difficulties and low yields. Michael addition products have been obtained but only traces of 1 : 1 cycloadducts have been identified.[5,7] We have studied the behaviour of 3,3′-biindolyl in the presence of certain dienophiles. Thus, the 3,3′-biindolyl **9a**, when heated in neat dimethyl acetylenedicarboxylate, gave directly the expected 1 : 1 adduct **24** in 75% yield (Scheme 10). Steric hindrance of the ester groups in **24** will



Scheme 10 *Reagents and conditions*: i, diethyl acetylenedicarboxylate, neat 210 °C; ii, ethyl propiolate, neat, 120 °C ; iii, MeOH, KOH

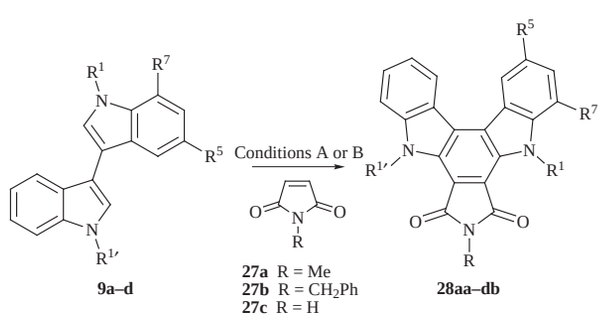
prevent further attack of dimethyl acetylenedicarboxylate and no 2 : 1 adduct was formed. However, in the 2,2′-biindolyl series the adduct **26** is formed when the reactants are heated in



o-dichlorobenzene.[5] Saponification of **24** led to the diacid **25** in 97% yield (Scheme 10). The monoester **20a** was analogously obtained in 23% yield when 3,3′-biindolyl **9a** was heated in ethyl propiolate (Scheme 10).

The results outlined in Scheme 10 induced us to carry out this similar procedure in the presence of maleimide derivatives **27** to obtain the framework involved in rebeccamycin compounds. Unfortunately, attempted generation of a maleimide ring from the diacid **25** to lead to **28ac** gave complex mixtures which were impossible to purify.

Nevertheless, heating of **9a**–**c** in Ph_2O at 200 °C (condition A) in the presence of *N*-methyl- or *N*-phenyl-maleimide **27a**–**d** resulted in the formation of the indolo[2,3-*c*]pyrrolo[3,4-*a*]-carbazoles **28** indicated in Scheme 11, Table 1. The starting



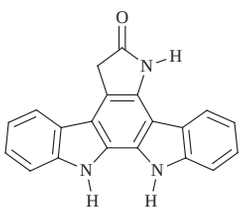
Scheme 11 *Reagents and conditions*: conditions A, Ph_2O, 190 °C; Conditions B, AcOH, 100 °C

material **9a** remained unchanged when maleic anhydride was used instead of an *N*-substituted maleimide.

Recently, treatment of 2,2′-biindolyl with maleimide **27c** in toluene in presence of TFA has been reported to yield the unnatural indolo[2,3-*a*]carbazole **29**.[36] In our case, at 100 °C in acetic acid (condition B, Scheme 11), 3,3′-biindolyl **9a** and maleimide derivative **27b** did not give the expected compound

Table 1 Preparation of indolo[2,3-*c*]pyrrolo[3,4-*a*]carbazoles **28aa**–**db**

Entry	**28**	R^1	$R^{1'}$	R^5	R^7	R	Conditions	Reaction time/h	Yield(%)
1	**aa**	H	H	H	H	Me	A	12	42
							B	36	44
2	**ab**	H	H	H	H	CH_2Ph	A	12	69
							B	24	55
3	**ac**	H	H	H	H	H	B	24	55
4	**bb**	H	H	Cl	Cl	CH_2Ph	A	24	53
5	**bc**	H	H	Cl	Cl	H	B	36	41
6	**cb**	H	Me	H	H	CH_2Ph	A	6	56
7	**db**	Me	Me	H	H	CH_2Ph	A	12	37



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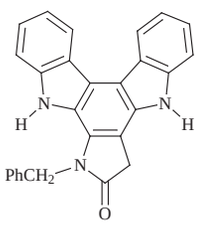

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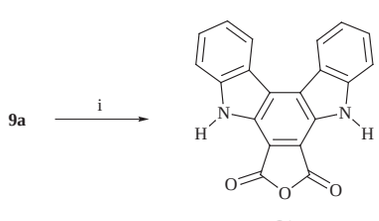
30 but the indolocarbazole **28ab** in 55% yield. The indolocarbazoles **28aa**,**ac**,**bc** could be similarly prepared. These results have further established that formal cycloaddition reactions are easier to control with 3,3′-biindolyls compared with 2,2′-biindolyls.

Compound **24** was obtained in 55% yield when **9a** was heated in acetic acid at 100 °C in the presence of dimethyl acetylenedicarboxylate. The reaction, performed in the presence of maleic anhydride during 2 days, yielded compound **31** in 46% yield (Scheme 12).



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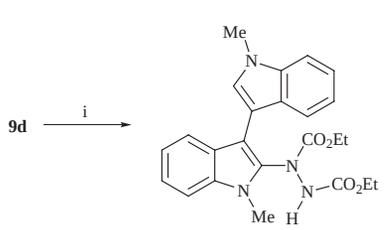
Scheme 12 *Reagents and conditions*: i, maleic anhydride, AcOH, 100 °C

The mechanism of formation of **28** in these two conditions is not clear. Nevertheless, for protic as well as aprotic conditions, it is reasonable to assume that a Michael addition occurs at the 2-position on the 3,3′-biindolyl. In accord with this, diethyl azodicarboxylate (DEAD), a good dienophile for Diels–Alder reactions, has been heated in toluene at 110 °C in the presence of 1,1′-dimethyl-3,3′-biindolyl **9d** and the Michael adduct **32** has been isolated in 87% yield (Scheme 13). This fact probably



Scheme 13 *Reagents and conditions*: i, DEAD, toluene, 110 °C

eliminates the hypothesis of a [4 + 2] cycloaddition mechanism for the aprotic conditions. However, in neither solvent, have any intermediates have been clearly isolated and the conditions of cyclization and aromatization of the C-ring have not been determined and are still under investigation.

Conclusions

A new class of indolocarbazoles have been prepared by two general methods; step by step *via* 2-formyl-3,3′-biindolyl or by direct synthesis to prepare symmetric and non-symmetric indolo[2,3-*c*]pyrrolo[3,4-*a*]carbazoles. Both routes, started with readily available 3,3′-biindolyl derivatives, led to different compounds in respectable yields. This easy access to indolo[2,3-*c*]-carbazole derivatives will help us to look for any kind of structural or conformational similarities with known receptor ligands.

Experimental

Melting points were determined on a Reichert WME Kofler hot stage and are uncorrected. IR spectra were recorded on a Perkin-Elmer 1600 FTIR instrument. NMR spectra were obtained on a Varian UNITY plus (400 MHz) or on a Bruker AM400 (400 MHz) instrument. *J* Values are given in Hz. Mass spectra were obtained on a Finnigan MAT SSQ710 instrument with a direct inlet at 70 eV. The ^{13}C NMR spectra of compounds **28bb,bc** could not be recorded due to their low solubility.

3,3′-Biindolyl derivatives 9a–c

3,3′-Biindolyl derivative **9a**–**c** was prepared according to procedures reported in refs. 23 or 24. Yields of **9a**–**c** were calculated from starting indoles or isatins.

3,3′-Biindolyl 9a. Yield 61%; mp >250 °C (lit.,[24] mp 285–287 °C); IR and NMR spectra data were identical with previous publications.

5,7-Dichloro-3,3′-biindolyl 9b. Yield 31%; mp 174–176 °C; ν_{max}(KBr)/cm^{-1} 3398, 3081, 1556, 1454, 1067, 747, 574; δ_H([$^2H_6$]DMSO) 7.08 (1 H, t, *J* 7.3, ArH), 7.16 (1 H, t, *J* 7.3, ArH), 7.33 (1 H, d, *J* 1.2, ArH), 7.47 (1 H, d, *J* 7.3, ArH), 7.65–7.78 (4 H, m, ArH), 11.26 (1 H, s, NH), 11.80 (1 H, s, NH); δ_C([$^2H_6$]DMSO) 108.0 (s), 111.1 (d), 111.6 (s), 116.7 (s), 117.9 (d), 119.0 (d), 119.1 (d), 120.3 (d), 121.3 (d), 122.6 (d), 123.4 (s), 124.7 (d), 125.8 (s), 128.3 (s), 131.8 (s), 136.3 (s).

1-Methyl-3,3′-biindolyl 9c. Yield 29%; mp 138–141 °C; ν_{max}(KBr)/cm^{-1} 3421, 3410, 3046, 1612, 1456, 1333, 1231, 742, 736; δ_H([$^2H_6$]DMSO) 3.87 (3 H, s, CH_3), 7.04–7.25 (4 H, m, ArH), 7.44–7.50 (2 H, m, ArH), 7.66 (1 H, d, *J* 2.0, ArH), 7.68 (1 H, s, ArH), 7.79–7.85 (2 H, m, ArH), 11.18 (1 H, s, NH); δ_C([$^2H_6$]DMSO) 32.3 (q), 108.9 (s), 109.3 (s), 109.6 (d), 111.5 (d), 118.7 (d), 118.8 (d), 119.5 (d), 119.7 (d), 121.1 (d), 121.2 (d), 121.7 (d), 125.8 (s), 126.2 (d), 126.3 (s), 136.3 (s), 136.6 (s).

1,1′-Dimethyl-3,3′-biindolyl 9d

1,1′-Dimethyl-3,3′-biindole **9d** was prepared from **9a** according to a procedure reported in ref. 37. Yield 65%; mp 185–187 °C (lit.,[38] mp 186–188 °C); ν_{max}(KBr)/cm^{-1} 2922, 2851, 1466, 1327, 1241, 739; δ_H([$^2H_6$]DMSO) 3.87 (3 H, s, CH_3), 7.11 (1 H, t, *J* 7.3, ArH), 7.22 (1 H, t, *J* 7.3, ArH), 7.48 (1 H, d, *J* 7.3, ArH), 7.69 (1 H, s, ArH), 7.85 (1 H, d, *J* 7.3, ArH); δ_C([$^2H_6$]DMSO) 32.3 (q), 108.5 (s), 109.7 (d), 118.8 (d), 119.7 (d), 121.3 (d), 126.1 (d), 136.6 (s).

3,3′-Biindolyl-2-carboxaldehyde derivatives 11a-d: general procedure

To a stirred suspension of 3,3′-biindolyl derivative **9a**–**d** (1 mmol) in CH_3CN (10 ml), *N*,*N*-dimethylchloromethaniminium chloride (1.3 mmol) was added at room temperature. After dissolution, a new precipitate soon appeared. The solvent was evaporated *in vacuo* after TLC control of the total disappearance of the starting material (2–12 h). Saturated aqueous $NaHCO_3$ (15 ml) was added and the aqueous phase was extracted with EtOAc (3 × 15 ml). The combined organic phases were dried ($MgSO_4$), filtered and evaporated *in vacuo*. The residue, chromatographed on a silica gel column (CH_2Cl_2), gave compound **11a**–**d** as a yellow solid.

3,3′-Biindolyl-2-carboxaldehyde 11a. Yield 85%; mp 189–191 °C (Found: C, 78.34; H, 4.68; N, 10.74. $C_{17}H_{12}N_2O$ requires C, 78.44; H, 4.65; N, 10.76%); ν_{max}(KBr)/cm^{-1} 3385, 3278, 2923, 1645, 1612, 748; δ_H($CDCl_3$) 7.12–7.25 (2 H, m, ArH), 7.31(1 H, t, *J* 8.1, ArH), 7.41–7.54 (4 H, m, ArH), 7.71 (1 H, d, *J* 8.1, ArH), 7.80 (1 H, d, *J* 8.1, ArH), 8.51 (1 H, s, NH), 9,12 (1 H, s, NH), 9.92 (1 H, s, CHO); δ_C([$^2H_6$]DMSO) 105.9 (s), 111.1 (d), 112.9 (d), 119.0 (d), 119.5 (d), 120.1 (d), 121.7 (d), 122.2 (s), 122.4 (d), 126.1 (d), 126.5 (s), 126.7 (d), 126.8 (s), 131.8 (s), 136.5 (s), 138.1 (s), 182.0 (d); *m*/*z* 260 (M^+, 100%).

5′,7′-Dichloro-3,3′-biindolyl-2-carboxaldehyde 11b. Yield 85%; mp 188–190 °C; ν_{max}(KBr)/cm^{-1} 3422, 3286, 2849, 1640, 1613, 744; δ_H([$^2H_6$]DMSO) 7.14 (1 H, t, *J* 8.1, ArH), 7.34–7.45 (3 H, m, ArH), 7.53 (1 H, d, *J* 8.1, ArH), 7.59 (1 H, d, *J* 8.1, ArH), 7.90 (1 H, s, ArH), 9.80 (1 H, s, CHO), 12.05 (1 H, s, NH), 12.20 (1 H, s, NH); δ_C([$^2H_6$]DMSO) 107.1 (s), 113.0 (d), 117.2 (s), 117.4 (d), 119.9 (s), 120.4 (d), 120.8 (s), 121.9 (d), 124.0 (s), 126.3 (s), 126.8 (d), 128.9 (d), 129.1 (s), 132.1 (s) 137.8 (s), 182.0 (d).

1′-Methyl-3,3′-biindolyl-2-carboxaldehyde 11c. Yield 95%; mp 166–168 °C; ν_{max}(KBr)/cm^{-1} 3325, 2925, 1640, 1612, 740; δ_H([$^2H_6$]DMSO) 3.91 (3 H, s, CH_3), 7.07–7.16 (2 H, m, ArH), 7.27 (1 H, t, *J* 8.1, ArH), 7.39 (1 H, t, *J* 8.1, ArH), 7.51–7.59 (3 H, m, ArH), 7.68 (1 H, d, *J* 8.1, ArH), 7.74 (1 H, s, ArH), 9.86 (1 H, s, CHO), 11.94 (1 H, s, NH); δ_C([$^2H_6$]DMSO) 32.6 (q), 105.0 (s), 110.2 (d), 112.9 (d), 119.2 (d), 119.7 (d), 120.1 (d), 121.7 (s), 121.8 (d), 122.3 (d), 126.4 (s), 126.8 (d), 127.0 (s), 130.2 (d), 131.7 (s) 136.9 (s), 138.1 (s) 182.0 (d).

1,1′-Dimethyl-3,3′-biindolyl-2-carboxaldehyde 11d. Yield 80%; mp 172–174 °C; ν_{max}(KBr)/cm^{-1} 2925, 2825, 1643, 1387, 744; δ_H([$^2H_6$]DMSO) 3.91 (3 H, s, CH_3), 4.12 (3 H, s, CH_3), 7.11 (1 H, t, *J* 7.3, ArH), 7.16 (1 H, t, *J* 7.3, ArH), 7.26 (1 H, t, *J* 8.1, ArH), 7.44–7.52 (2 H, m, ArH), 7.56 (1 H, d, *J* 7.3, ArH), 7.62–7.72 (3 H, m, ArH), 9.90 (1 H, s, CHO); δ_C([$^2H_6$]DMSO) 31.5 (q), 32.6 (q), 104.5 (s), 110.2 (d), 110.9 (d), 119.1 (d), 119.7 (d), 120.4 (d), 121.8 (d), 122.3 (d), 124.1 (s), 125.4 (d), 127.2 (s), 127.2 (s), 130.4 (s), 130.5 (d), 136.8 (s), 139.6 (s), 183.0 (d).

2-Vinyl-3,3′-biindolyl 12

A solution of triglyme (2,5,8,11-tetraoxadodecane) (1 ml) containing aldehyde **11a** (90 mg, 0.34 mmol), methyltriphenylphosphonium bromide (154 mg, 0.43 mmol) and K_2CO_3 (72 mg, 0.52 mmol) was heated during 4.5 h at 120 °C. After cooling, the solution was chromatographed on a silica gel column [CH_2Cl_2–light petroleum 50 : 50 (v/v)] affording 75 mg (85%) of **12**; mp 207–209 °C (dec.); ν_{max}(KBr)/cm^{-1} 3398, 2919, 1602, 1454, 741; δ_H($CDCl_3$) 5.22 (1 H, d, *J* 11.3, H_{eth}), 5.52 (1 H, d, *J* 17.7, H_{eth}), 6.89 (1 H, dd, *J* 11.3, 17.7, H_{eth}), 7.10 (1 H, t, *J* 8.0, ArH), 7.15 (1 H, t, *J* 8.0, ArH), 7.20–7.32 (3 H, m, ArH), 7.40 (1 H, d, *J* 8.0, ArH), 7.46 (1 H, d, *J* 8.0, ArH), 7.57–7.66 (2 H, m, ArH), 8.29 (2 H, s, NH); δ_C($CDCl_3$) 109.6 (s), 110.6 (d), 110.9 (t), 111.0 (s), 111.1 (d), 119.7 (d), 119.8 (d), 120.6 (d), 120.7 (d), 122.2 (d), 123.2 (d), 123.5 (d), 126.9 (d), 127.6 (s), 129.0 (s) 132.8 (s), 136.2 (s), 136.3 (s).

Ethyl 3-(3,3′-biindolyl-2-yl)propenoate derivatives 13a–c: general procedure

To a suspension of NaH (1.3 mmol) in dried THF (10 ml) under an inert atmosphere was added at 0 °C diethyl phosphonoethylacetate (1.3 mmol). The NaH suspension disappeared and, after 5 min, a solution of THF (10 ml) containing **11a**–**c** (1 mmol) was slowly added at 0 °C. The resulting solution was stirred during 15 min at 0 °C and 1 h at room temperature. The THF solution was quenched with water (40 ml) and the mixture was extracted with CH_2Cl_2 (4 × 20 ml). The combined organic phases were dried ($MgSO_4$), filtered and the solvent evaporated *in vacuo*. The residue was chromatographed on a silica gel column (CH_2Cl_2) giving yellow compound **13a**–**c**.

Ethyl (*E*)-3-(3,3′-biindolyl-2-yl)propenoate 13a. Yield 80%; mp 232–234 °C (Found: C, 76.25; H, 5.55; N, 8.59. $C_{21}H_{18}N_2O_2$ requires C, 76.34; H, 5.49; N, 8.48%); ν_{max}(KBr)/cm^{-1} 3425, 3304, 2978, 1684, 1625, 1193, 750; δ_H([$^2H_6$]DMSO) 1.21 (3 H, t br, CH_3), 4.14 (2 H, q br, CH_2), 6.59 (1 H, d, *J* 15.9, H_{eth}), 6.95–7.10 (2 H, m, ArH), 7.20 (1 H, t, *J* 7.3, ArH), 7.28 (1 H, t, *J* 7.3, ArH), 7.35–7.55 (5 H, m, ArH), 7.69 (1 H, d, *J* 15.9, H_{eth}), 11.48 (1 H, s, NH), 11.64 (1 H, s, NH); δ_C([$^2H_6$]DMSO) 14.1 (q), 59.7 (t), 107.1 (s), 111.4 (d), 111.8 (d), 114.3 (d), 116.6 (s), 119.1 (d), 119.2 (d), 119.5 (d), 120.6 (d), 121.4 (d), 124.6 (d), 124.9 (d), 126.8 (s), 127.5 (s), 130.0 (s), 133.4 (d), 136.4 (s) 137.8 (s), 166.4 (s); *m*/*z* 330 (M^+, 100%), 257 (40%).

Ethyl (*Z*)-3-(3,3′-biindolyl-2-yl)propenoate 13a. Yield 10%; mp 226–228 °C; ν_{max}(KBr)/cm^{-1} 3410, 2975, 1690, 1620, 740; δ_H($CDCl_3$) 1.37 (3 H, t, *J* 7.3, CH_3), 4.31 (2 H, q, *J* 7.3, CH_2), 5.71 (1 H, d, *J* 12.8, H_{eth}), 7.08 (1 H, t, *J* 7.0, ArH), 7.12 (1 H, d, *J* 12.8, H_{eth}), 7.15 (1 H, t, *J* 7.0, ArH), 7.28 (1 H, t, *J* 7.0, ArH), 7.30–7.35 (2 H, m, ArH), 7.46–7.53 (2 H, m, ArH), 7.59 (1 H, d, *J* 7.0, ArH), 7.62 (1 H, d, *J* 7.0, ArH), 8.39 (1 H, s, NH), 8.77 (1 H, s, NH).

Ethyl (*E*)-3-(5′,7′-dichloro-3,3′-biindolyl-2-yl)propenoate 13b. Yield 95%; mp 150–152 °C (Found: C, 63.28; H, 4.10; N, 7.14. $C_{21}H_{16}Cl_2N_2O_2$ requires C, 63.17; H, 4.04; N, 7.02%); ν_{max}(KBr)/cm^{-1} 3468, 3313, 2972, 1693, 1681, 1610, 1281, 750; δ_H([$^2H_6$]DMSO) 1.22 (3 H, t, *J* 7.0, CH_3), 4.15 (2 H, q, *J* 7.0, CH_2), 6.61 (1 H, d, *J* 16.2, H_{eth}), 7.07 (1 H, t, *J* 7.3, ArH), 7.25–7.31 (2 H, m, ArH), 7.37 (1 H, d, *J* 1.5, ArH), 7.44 (1 H, d, *J* 7.3, ArH), 7.46 (1 H, d, *J* 7.3, ArH), 7.55 (1 H, d, *J* 16.2, H_{eth}), 7.69 (1 H, d, *J* 2.6, ArH), 11.76 (1 H, s, NH), 12.13 (1 H, s, NH); δ_C([$^2H_6$]DMSO) 14.1 (q), 59.8 (t), 108.3 (s), 111.6 (d), 114.5 (s), 115.2 (d), 117.2 (s), 117.4 (d), 119.8 (d), 120.2 (d), 120.7 (d), 123.8 (s), 124.7 (d), 127.3 (s), 127.8 (d), 129.2 (s), 130.5 (s), 132.0 (s), 132.7 (d), 137.7 (s), 166,3 (s).

Ethyl (*E*)-3-(1-methyl-3,3′-biindolyl-2-yl)propenoate 13c. Yield 95%; mp 198–200 °C (Found: C, 76.67; H, 6.02; N, 8.27. $C_{22}H_{20}N_2O_2$ requires C, 76.72; H, 5.85; N, 8.13%); ν_{max}(KBr)/cm^{-1} 3330, 2921, 1682, 1609, 1277, 742, 733; δ_H([$^2H_6$]DMSO) 1.21 (3 H, t, *J* 7.0, CH_3), 3.92 (3 H, s, CH_3), 4.14 (2 H, q, *J* 7.0, CH_2), 6.59 (1 H, d, *J* 16.0, H_{eth}), 7.07–7.12 (2 H, m, ArH), 7.20–7.32 (2 H, m, ArH), 7.38–7.46 (2 H, m, ArH), 7.48–7.58 (3 H, m, ArH), 7.65 (1 H, d, *J* 16.0, H_{eth}), 11.65 (1 H, s, NH); δ_C([$^2H_6$]DMSO) 14.1 (q), 32.5 (q), 59.7 (t), 106.3 (s), 110.1 (d), 111.4 (d), 114.4 (d), 116.1 (s), 119.3 (d), 119.5 (d), 120.6 (d), 121.6 (d), 124.6 (d), 127.1 (s), 127.4 (s), 129.0 (d), 130.0 (s), 133.3 (d), 136.8 (s), 137.8 (s), 166.4 (s).

Diethyl 3,3′-biindolyl-2-ylmethylenemalonate 14

A mixture of compound **11a** (130 mg, 0.5 mmol) and diethyl malonate (0.091 µl, 0.6 mmol) was heated in toluene at reflux during 5 h. After evaporation of toluene *in vacuo*, the residue was chromatographed on a silica gel column (CH_2Cl_2) affording 152 mg (75%) of **14** as an orange solid; mp 160–162 °C (Found: C, 71.54; H, 5.51; N, 6.87. $C_{24}H_{22}N_2O_4$ requires C, 71.63; H, 5.51; N, 6.96%); ν_{max}(KBr)/cm^{-1} 3425, 2972, 1689, 1585, 1202, 741, 738; δ_H($CDCl_3$) 1.23 (3 H, t, *J* 7.1, CH_3), 1.41 (3 H, t, *J* 7.1, CH_3), 4.21 (2 H, q, *J* 7.1, CH_2), 4.44 (2 H, q, *J* 7.1, CH_2), 7.11 (1 H, t, *J* 8.0, ArH), 7.16 (1 H, t, *J* 8.0, ArH), 7.28 (1 H, t, *J* 8.0, ArH), 7.32 (1 H, t, *J* 2.4, ArH), 7.36 (1 H, t, *J* 8.0, ArH), 7.45–7.51 (2 H, m, ArH), 7.64 (1 H, d, *J* 8.0, ArH), 7.69 (1 H, d, *J* 8.0, ArH), 7.98 (1 H, s, H_{eth}), 8.45 (1 H, s, NH), 10.50 (1 H, s, NH);

$\delta_C(CDCl_3)$ 14.1 (q, 2C), 61.3 (t), 61.9 (t), 109.3 (s), 111.4 (d), 112.1 (d), 118.1 (s), 120.3 (d), 120.4 (d), 120.6 (d), 122.2 (d), 122.8 (d), 124.6 (d), 126.4 (d), 127.4 (s), 128.8 (s), 135.5 (d), 136.4 (s), 138.2 (s), 166.4 (s), 168.3 (s); *m/z* 402 (M^+, 100%), 286 (30%), 257 (35%).

2-(2-Nitroethenyl)-3,3′-biindolyl 15

A mixture of CH_3NO_2 (5 ml), **11a** (260 mg, 1 mmol) and NH_4OAc (58 mg, 0.75 mmol) was heated at reflux during 3 h. After evaporation *in vacuo*, the residue was chromatographed on a silica gel column (CH_2Cl_2) affording 245 mg (81%) of **15** as brownish solid; mp 205–207 °C (Found: C, 70.63; H, 4.81; N, 13.67. $C_{18}H_{15}N_3O_2$ requires C, 70.81; H, 4.95; N, 13.76%); ν_{max}(KBr)/cm^{-1} 3399, 3364, 1588, 1308, 1292, 1256, 1203, 746; δ_H([$^2H_6$]DMSO) 7.05–7.15 (2 H, m, ArH), 7.21 (1 H, m, ArH), 7.37 (1 H, m, ArH), 7.45–7.65 (5 H, m, ArH), 8.03 (1 H, d, *J* 13.3, H_{eth}), 8.09 (1 H, d, *J* 13.3, H_{eth}), 11.63 (1 H, s, NH), 11.84 (1 H, s, NH); δ_C([$^2H_6$]DMSO) 106.7 (s), 111.8 (d), 112.0 (d), 118.9 (d), 119.6 (d), 120.1 (d), 121.4 (d), 121.8 (d), 122.5 (s), 125.7 (d), 125.8 (s), 126.4 (s), 126.5 (d), 127.1 (s), 128.5 (d), 133.6 (d), 136.6 (s), 139.0 (s); *m/z* 303 (M^+, 100%), 231 (24%).

3,3′-Biindolyl-2-carbaldehyde oxime 16

A solution of EtOH (2 ml) containing **11a** (130 mg, 0.5 mmol), NaOAc (82 mg, 1 mmol) and NH_2OH·HCl (69.5 mg, 1 mmol) was heated at reflux during 1.5 h. After evaporation of EtOH *in vacuo*, the residue was chromatographed on a silica gel column [99.5 : 0.5, CH_2Cl_2–MeOH, (v/v)] affording 65 mg of (*E*)-**16** and 65 mg (*Z*)-**16** (95%).

(*E*)-3,3′-Biindolyl-2-carbaldehyde oxime 16. Mp 82–84 °C (dec.) (Found: C, 74.24; H, 4.78; N, 15.12. $C_{17}H_{13}N_3O$ requires C, 74.17; H, 4.76; N, 15.26%); ν_{max}(KBr)/cm^{-1} 3401, 2919, 1602, 1451, 1408, 955, 738; $\delta_H(CDCl_3)$ 7.09–7.20 (2 H, m, ArH), 7.24–7.33 (3 H, m, ArH), 7.38 (1 H, d, *J* 8.2, ArH), 7.47 (1 H, d, *J* 8.2, ArH), 7.62–7.68 (2 H, m, ArH), 8.29 (1 H, s, CH), 8.32 (1 H, s, NH), 8.98 (1 H, s, NH); $\delta_C(CDCl_3)$ 108.7 (s), 111.2 (d), 111.4 (d), 120.2 (d), 120.3 (d), 120.4 (d), 121.2 (d), 122.7 (d), 123.7 (d), 124.8 (d), 126.8 (s), 127.5 (s), 128.2 (s), 136.4 (s), 137.0 (s), 142.8 (d); *m/z* 275 (M^+, 100%), 257 (54%).

(*Z*)-3,3′-Biindolyl-2-carbaldehyde oxime 16. Mp 108–110 °C; ν_{max}(KBr)/cm^{-1} 3401, 2919, 1610, 1451, 1409, 914, 738; $\delta_H(CDCl_3)$ 7.11–7.20 (2 H, m, ArH), 7.27–7.38 (3 H, m, ArH), 7.46–7.52 (2 H, m, ArH), 7.63 (1 H, d, *J* 8.1, ArH), 7.66–7.70 (2 H, m, ArH), 8.40 (1 H, s, NH), 10.12 (1 H, s, NH).

5,8-Dihydroindolo[2,3-*c*]carbazole 17

A suspension of compound **15** (182 mg, 0.6 mmol) and Pd/C (10 mg) in Ph_2O (5 ml) was heated at 200 °C for 12 h. After cooling, the solution was chromatographed on a silica gel column [50 : 50 CH_2Cl_2–light petroleum (v/v)] affording 47 mg (30%) of **17**; mp 155–157 °C (dec.); ν_{max}(KBr)/cm^{-1} 3384, 2923, 2853, 1457, 1328, 737; δ_H([$^2H_6$]DMSO) 7.31 (2 H, t, *J* 7.4, ArH), 7.44 (2 H, t, *J* 7.4, ArH), 7.61 (2 H, d, *J* 7.4, ArH), 7.65 (2 H, s, ArH), 8.73 (2 H, d, *J* 7.4, ArH), 11.48 (2 H, s, NH); δ_C([$^2H_6$]DMSO) 110.2 (d), 111.0 (d), 115.1 (s), 118.1 (d), 122.0 (s), 122.4 (d), 124.2 (d), 134.4 (s), 139.3 (s); *m/z* 256 (M^+, 100%).

5,8-Dimethyl-5,8-dihydroindolo[2,3-*c*]carbazole 18 and 1,1′-dimethyl-2-(2-nitroethenyl)-3,3′-biindolyl 19 from compound 11d

A mixture of CH_3NO_2 (3 ml), **11d** (144 mg, 0.5 mmol) and NH_4OAc (19 mg, 0.25 mmol) was heated at reflux during 48 h. After evaporation *in vacuo*, the residue was chromatographed on a silica gel column (CH_2Cl_2) affording 29 mg (20%) of **19**, 15 mg (8%) of **18** and 100 mg (69%) of starting material **11d**.

5,8-Dimethyl-5,8-dihydroindolo[2,3-*c*]carbazole 18. Mp 240–244 °C (lit.,[21] mp 257.6–258.2 °C); ν_{max}(KBr)/cm^{-1} 2925, 1449, 1320, 738; δ_H([$^2H_6$]DMSO) 4.03 (6 H, s, CH_3), 7.37 (2 H, t, *J* 7.5, ArH), 7.55 (2 H, t, *J* 7.5, ArH), 7.73 (2 H, d, *J* 7.5, ArH), 7.87 (2 H, s, ArH), 8.79 (2 H, d, *J* 7.4, ArH); δ_C([$^2H_6$]DMSO) 29.3 (q), 108.3 (d), 109.2 (d), 115.0 (s), 118.3 (d), 121.2 (s), 122.6 (d), 124.7 (d), 135.8 (s), 140.2 (s).

1,1′-Dimethyl-2-(2-nitroethenyl)-3,3′-biindolyl 19. Mp 195–197 °C; ν_{max}(KBr)/cm^{-1} 2922, 1557, 1318, 738; δ_H([$^2H_6$]DMSO) 3.95 (3 H, s, CH_3), 4.03 (3 H, s, CH_3), 7.07–7.16 (2 H, m, ArH), 7.28 (1 H, t, *J* 7.4, ArH), 7.38 (1 H, d, *J* 7.4, ArH), 7.42 (1 H, t, *J* 7.4, ArH), 7.56 (1 H, d, *J* 7.4, ArH), 7.60 (1 H, d, *J* 7.4, ArH), 7.63 (1 H, s, ArH), 7.68 (1 H, d, *J* 7.4, ArH), 7.82 (1 H, d, *J* 14.0, H_{eth}), 8.21 (1 H, d, *J* 14.0, H_{eth}).

Conversion of 1,1′-dimethyl-2-(2-nitroethenyl)-3,3′-biindolyl 19 to compound 18

A suspension of compound **19** (35 mg, 0.1 mmol) in Ph_2O (1 ml) was heated at 160 °C during 3 h. After cooling, the solution was chromatographed on a silica gel column [50 : 50 CH_2Cl_2–light petrolum (v/v)] affording 16 mg (58%) of **18**; mp, IR, NMR spectral data were identical with the descriptions reported above.

Ethyl 5,8-dihydroindolo[2,3-*c*]carbazole-6-carboxylate 20a–c: general procedure

A suspension of compound **13a**–**c** (0.5 mmol) in Ph_2O (3 ml) was heated at 190–200 °C during 24–72 h. After cooling, the solution was chromatographed on a silica gel column [75 : 25, CH_2Cl_2–light petroleum (v/v)] giving compound **20a**–**c**.

Ethyl 5,8-dihydroindolo[2,3-*c*]carbazole-6-carboxylate 20a. Yield 78%; mp 240–242 °C (Found: C, 76.65; H, 4.91; N, 8.38. $C_{21}H_{16}N_2O_2$ requires C, 76.81; H, 4.91; N, 8.53%); ν_{max}(KBr)/cm^{-1} 3401, 2978, 1672, 1254, 1202, 741; δ_H([$^2H_6$]DMSO) 1.48 (3 H, t, *J* 7.0, CH_3), 4.53 (2 H, q, *J* 7.0, CH_2), 7.37 (2 H, t, *J* 7.4, ArH), 7.50 (1 H, t, *J* 7.4, ArH), 7.56 (1 H, t, *J* 7.4, ArH), 7.67 (1 H, d, *J* 7.4, ArH), 7.91 (1 H, d, *J* 7.4, ArH), 8.32 (1 H, s, ArH), 8.78 (1 H, d, *J* 7.4, ArH), 8.83 (1 H, d, *J* 7.4, ArH), 11.50 (1 H, s, NH) 11.70 (1 H, s, NH); δ_C([$^2H_6$]DMSO) 14.3 (q), 60.6 (t), 109.8 (s), 111.3 (d), 111.4 (d), 112.3 (d), 116.5 (s), 118.7 (d), 118.9 (d), 120.1 (s), 121.0 (s), 121.1 (s), 122.4 (d), 123.6 (d), 125.0 (d), 126.4 (d), 133.5 (s), 133.6 (s), 139.7 (s), 141.2 (s), 166.4 (s); *m/z* 328 (M^+, 100%), 282 (68%), 254 (37%).

Ethyl 2,4-dichloro-5,8-dihydroindolo[2,3-*c*]carbazole-6-carboxylate 20b. Yield 50%; mp 244–246 °C (Found: C, 63.39; H, 3.65; N, 6.94. $C_{21}H_{14}Cl_2N_2O_2$ requires C, 63.49; H, 3.55; N, 7.05%); ν_{max}(KBr)/cm^{-1} 3465, 3318, 2975, 1692, 1623, 1273, 1223, 767; δ_H([$^2H_6$]DMSO) 1.45 (3 H, t, *J* 7.0, CH_3), 4.44 (2 H, q, *J* 7.0, CH_2), 7.34 (1 H, t, *J* 7.4, ArH), 7.54 (1 H, t, *J* 7.4, ArH), 7.59 (1 H, d, *J* 1.2, ArH), 7.63 (1 H, d, *J* 7.4, ArH), 8.16 (1 H, s, ArH), 8.33 (1 H, d, *J* 1.2, ArH), 8.39 (1 H, d, *J* 7.4, ArH), 10.23 (1 H, s, NH); 11.71 (1 H, s, NH); δ_C([$^2H_6$]DMSO) 14.3 (q), 61.2 (t), 109.5 (s), 111.8 (d), 113.3 (d), 115.7 (s), 118.8 (s), 119.3 (d), 119.7 (d), 120.6 (s), 120.7 (s), 123.3 (d), 123.4 (s), 123.6 (d), 124.0 (s), 126.9 (d), 130.2 (s), 134.1 (s), 134.2 (s), 141.2 (s), 166.4 (s); *m/z* 400 (10%), 398 (61%), 396 (M^+, 100%), 352 (33%), 350 (61%).

Ethyl 5-methyl-5,8-dihydroindolo[2,3-*c*]carbazole-6-carboxylate 20c. Yield 30%; mp 180–182 °C; ν_{max}(KBr)/cm^{-1} 3348, 2922, 2852, 1686, 1621, 1267, 1206, 741; δ_H([$^2H_6$]DMSO) 1.44 (3 H, t, *J* 7.0, CH_3), 3.90 (3 H, s, CH_3), 4.50 (2 H, q, *J* 7.0, CH_2), 7.37 (1 H, t, *J* 7.4, ArH), 7.44 (1 H, t, *J* 7.4, ArH), 7.55 (1 H, t, *J* 7.4, ArH), 7.60 (1 H, t, *J* 7.4, ArH), 7.68 (1 H, d, *J* 7.4, ArH), 7.77 (1 H, d, *J* 7.4, ArH), 8.04 (1 H, s, ArH), 8.80–8.86 (2 H, m, ArH), 11.72 (1 H, s, NH); δ_C([$^2H_6$]DMSO) 14.1 (q), 33.6 (q), 61.1 (t), 109.9 (d), 111.4 (d), 111.8 (d), 114.4 (s), 118.2 (s), 118.7 (d), 119.3 (d), 121.0 (s), 121.3 (s), 122.5 (d), 123.4 (d), 125.5 (d), 126.0 (d), 133.5 (s), 140.8 (s), 141.6 (s), 167.4 (s); *m/z* 342 (M^+, 100%), 296 (52%).

Preparation of ethyl 5,8-dihydroindolo[2,3-*c*]carbazole-6-carboxylate 20a from compound 9a

Ethyl propiolate (2 ml) and **9a** (116 mg, 0.5 mmol) were heated at 120 °C during 24 h. After evaporation *in vacuo*, the residue was chromatographed on a silica gel column (CH_2Cl_2) affording 37 mg (23%) of **20a**; mp, IR and NMR spectra data were identical with the descriptions reported above.

5,8-Dihydroindolo[2,3-*c*]carbazole-6-carboxylic acid 21

The ester **20a** (148 mg, 0.45 mmol), EtOH (9 ml) and a solution of aq. NaOH (10%) (9 ml) were heated at reflux during 1 h. After cooling and acidification (pH 2–3), the precipitate was collected affording 130 mg (96%) of the yellow acid **21**; mp >250 °C (Found: C, 76.04; H, 4.03; N, 9.49. $C_{19}H_{12}N_2O_2$ requires C, 75.99; H, 4.03; N, 9.33%); ν_{max}(KBr)/cm^{-1} 3584, 3395, 1661, 1623, 1586, 1415, 1327, 1219, 740; δ_H([$^2H_6$]DMSO) 7.37 (2 H, t, *J* 7.4, ArH), 7.48 (1 H, t, *J* 7.4, ArH), 7.55 (1 H, t, *J* 7.4, ArH), 7.67 (1 H, d, *J* 7.4, ArH), 7.93 (1 H, d, *J* 7.4, ArH), 8.30 (1 H, s, ArH), 8.78 (1 H, d, *J* 7.4, ArH), 8.83 (1 H, d, *J* 7.4, ArH), 11.47 (1 H, s, NH), 11.74 (1 H, s, NH), 13.22 (1 H, s, CO_2H); δ_C([$^2H_6$]DMSO) 110.7 (s), 111.4 (d), 111.9 (d), 112.3 (d), 116.3 (s), 118.6 (d), 118.8 (d), 119.7 (s), 121.1 (s), 121.2 (s), 122.3 (d), 123.5 (d), 124.3 (d), 126.2 (d), 133.5 (s), 133.8 (s), 139.6 (s), 141.1 (s), 168.2 (s).

3,3′-Biindolyl-2-carbonitrile 22 and 5,8-dihydropyrido[2,3-*b*:5,4-*b*′]diindole 23

A suspension of **16** (138 mg, 0.5 mmol) in Ph_2O (4 ml) was heated during 5 h at 190–200 °C. After cooling, the solution was chromatographed on a silica gel column [99 : 1 CH_2Cl_2–MeOH, (v/v)] affording 40 mg (31%) of **22** and 65 mg (51%) of **23**.

3,3′-Biindolyl-2-carbonitrile 22. Mp 222–224 °C (Found: C, 79.26; H, 4.47; N, 16.25. $C_{17}H_{11}N_3$ requires C, 79.36; H, 4.31; N, 16.33%); ν_{max}(KBr)/cm^{-1} 3378, 2922, 2215, 1337, 1095, 745; δ_H([$^2H_6$]DMSO) 7.09 (1 H, t, *J* 7.3, ArH), 7.15–7.24 (2 H, m, ArH), 7.40 (1 H, t, *J* 7.3, ArH), 7.48–7.55 (2 H, m, ArH), 7.57 (1 H, d, *J* 7.3, ArH), 7.65–7.72 (2 H, m, ArH), 11.56 (1 H, s, NH), 12.34 (1 H, s, NH); δ_C([$^2H_6$]DMSO) 103.0 (s), 105.7 (s), 111.9 (d), 112.3 (d), 115.2 (s), 119.2 (d), 119.4 (d), 120.6 (d), 121.1 (d), 121.6 (d), 121.8 (s), 124.7 (d), 125.0 (s), 125.7 (s), 125.8 (d), 136.4 (s), 137.2 (s).

5,8-Dihydropyrido[2,3-*b*:5,4-*b*′]diindole 23. Mp >250 °C; ν_{max}(KBr)/cm^{-1} 3383, 2915, 2841, 1623, 1415, 1331, 740; δ_H([$^2H_6$]DMSO) 7.33–7.43 (2 H, m, ArH), 7.50 (1 H, t, *J* 7.4, ArH), 7.58–7.65 (2 H, m, ArH), 7.70 (1 H, d, *J* 7.4, ArH), 8.68 (1 H, d, *J* 7.4, ArH), 8.77 (1 H, d, *J* 7.4, ArH), 8.85 (1 H, s, ArH), 11.75 (1 H, s, NH), 11.88 (1 H, s, NH); δ_C([$^2H_6$]DMSO) 106.9 (s), 111.1 (d), 111.9 (d), 118.8 (d), 118.9 (d), 120.1 (s), 120.3 (s), 122.1 (s), 122.9 (d), 123.9 (d), 125.1 (d), 127.3 (d), 131.1 (d), 131.5 (s), 138.2 (s), 140.8 (s), 145.8 (s); *m*/*z* 257 (M$^+$, 100%).

Dimethyl 5,8-dihydroindolo[2,3-*c*]carbazole-6,7-dicarboxylate 24

3,3′-Biindolyl **9a** (2.32 g, 10 mmol) was heated together with dimethyl acetylenedicarboxylate (5 ml) during 2 h at 210 °C under nitrogen atmosphere. TLC analysis showed the absence of **9a** and the excess of ester was removed under reduced pressure. The residue, chromatographed on silica gel with CH_2Cl_2 as eluent, gave 2.80 g (75%) of the title compound **24** as yellow crystals; mp 180–182 °C (Found: C, 70.95; H, 4.41; N, 7.39. $C_{22}H_{16}N_2O_2$ requires C, 70.96; H, 4.33; N, 7.52%); ν_{max}(KBr)/cm^{-1} 3464, 3351, 2953, 1713, 1618, 1404, 1212, 1133, 738; δ_H([$^2H_6$]DMSO) 4.05 (6 H, s, CH_3), 7.42 (2 H, t, *J* 8.1, ArH), 7.59 (2 H, t, *J* 8.1, ArH), 7.83 (2 H, d, *J* 8.1, ArH), 8.85 (2 H, d, *J* 8.1, ArH), 11.54 (2 H, s, NH); δ_C([$^2H_6$]DMSO) 52.7 (q), 112.0 (d), 112.2 (s), 118.9 (s), 119.3 (d), 120.6 (s), 123.2 (d), 126.5 (d), 131.7 (s), 141.1 (s), 167.1 (s); *m*/*z* 372 (M$^+$, 100%), 341 (47%).

5,8-Dihydroindolo[2,3-*c*]carbazole-6,7-dicarboxylic acid 25

A suspension of compound **24** (186 mg, 0.5 mmol) in MeOH (12 ml) and aqueous KOH (5 M, 5 ml) was heated during 90 min. After cooling and acidification (pH 2–3), a precipitate appeared which was collected, affording 170 mg (98%) of **25** as an orange solid; mp >250 °C; ν_{max}(KBr)/cm^{-1} 3587, 3392, 3199, 1706, 1671, 1461, 1321, 1233, 1146, 728; δ_H([$^2H_6$]DMSO) 7.37 (2 H, t, *J* 8.1, ArH), 7.52 (2 H, t, *J* 8.1, ArH), 7.87 (2 H, d, *J* 8.1, ArH), 8.82 (2 H, d, *J* 8.1, ArH), 11.65 (2 H, s, NH); δ_C([$^2H_6$]DMSO) 112.1 (d), 114.8 (s), 118.1 (s), 118.8 (d), 120.6 (s), 123.0 (d), 125.8 (d), 133.2 (s), 140.6 (s), 169.2 (s).

Preparation of indolo[2,3-*c*]pyrrolo[3,4-*a*]carbazole derivatives 28 using Ph_2O as solvent (conditions A)

7-Methyl-6,7,8,9-tetrahydro-5*H*-indolo[2,3-*c*]pyrrolo[3,4-*a*]-carbazole-6,8-dione 28aa. A suspension of compound **9a** (0.5 mmol) and maleimide **27a** (0.6 mmol) in Ph_2O (3 ml) was heated at 190–200 °C for 12 h. The solution was chromatographed on a silica gel column (CH_2Cl_2) to give **28aa**; yield 42%; mp >250 °C (Found: C, 74.18; H, 3.80; N, 11.89. $C_{21}H_{13}N_3O_2$ requires C, 74.33; H, 3.86; N, 12.38%); ν_{max}(KBr)/cm^{-1} 3367, 2922, 2849, 1731, 1667, 1381, 1325, 1090, 736; δ_H([$^2H_6$]-DMSO) 3.16 (3 H, s, CH_3), 7.42 (2 H, t, *J* 8.1, ArH), 7.59 (2 H, t, *J* 8.1, ArH), 7.80 (2 H, d, *J* 8.1, ArH), 8.82 (2 H, d, *J* 8.1, ArH), 12.05 (2 H, s, NH); δ_C([$^2H_6$]DMSO) 23.5 (q) 110.4 (s), 112.4 (d), 119.7 (d), 120.6 (s), 122.5 (s). 123.4 (d), 127.0 (d), 128.5 (s), 142.4 (s), 168.6 (s); *m*/*z* 339 (M$^+$, 100%), 254 (20%).

7-Benzyl-6,7,8,9-tetrahydro-5*H*-indolo[2,3-*c*]pyrrolo[3,4-*a*]-carbazole-6,8-dione 28ab. A suspension of compound **9a** (0.5 mmol) and maleimide **27b** (0.6 mmol) in Ph_2O (3 ml) was heated at 190–200 °C for 12 h. The solution was chromatographed on a silica gel column (CH_2Cl_2) to give **28ab**; yield 69%; mp >250 °C; ν_{max}(KBr)/cm^{-1} 3403, 2922, 2850, 1741, 1691, 1682, 1613, 1461, 1325, 1224, 742; δ_H([$^2H_6$]DMSO) 4.90 (2 H, s, CH_2), 7.25–7.46 (7 H, m, ArH), 7.60 (2 H, t, *J* 8.1, ArH), 7.80 (2 H, d, *J* 8.1, ArH), 8.84 (2 H, d, *J* 8.1, ArH), 12.09 (2 H, s, NH); δ_C([$^2H_6$]DMSO) 40.5 (t), 110.1 (s), 112.4 (d), 119.8 (d), 120.6 (s), 122.8 (s), 123.5 (d), 127.2 (d), 127.3 (d), 128.5 (d), 128.6 (d), 128.7 (s), 137.5 (s), 142.5 (s), 168.2 (s); *m*/*z* 415 (M$^+$, 100%), 254 (32%).

7-Benzyl-2,4-dichloro-6,7,8,9-tetrahydro-5*H*-indolo[2,3-*c*]-pyrrolo[3,4-*a*]carbazole-6,8-dione 28bb. A suspension of compound **9b** (0.5 mmol) and maleimide **27b** (0.6 mmol) in Ph_2O (3 ml) was heated at 190–200 °C during 24 h. Table 1. After cooling, Et_2O was added and the resulting precipitate was filtered and washed with Et_2O to give **28bb**; yield 53%; mp >250 °C (Found: C, 67.09; H, 3.10; N, 8.57. $C_{27}H_{15}Cl_2N_3O_2$ requires C, 66.96; H, 3.12; N, 8.68%); ν_{max}(KBr)/cm^{-1} 3448, 3378, 3060, 1752, 1681, 1399, 1281, 720; δ_H([$^2H_6$]DMSO) 4.91 (2 H, s, CH_2), 7.26–7.51 (7 H, m, ArH), 7.63 (1 H, t, *J* 8.1, ArH), 7.81–7.85 (2 H, m, ArH), 8.66 (1 H, d, *J* 8.1, ArH), 8.69 (1 H, d, *J* 1.2, ArH), 11.94 (1 H, s, NH), 12.28 (1 H, s, NH).

7-Benzyl-5-methyl-6,7,8,9-tetrahydro-5*H*-indolo[2,3-*c*]-pyrrolo[3,4-*a*]carbazole-6,8-dione 28cb. A suspension of compound **9c** (0.5 mmol) and maleimide **27b** (0.6 mmol) in Ph_2O (3 ml) was heated at 190–200 °C during 6 h. After cooling, Et_2O was added and the resulting precipitate was filtered and washed with Et_2O to give **28cb**; yield 56%; mp >250 °C (Found: C, 78.31; H, 4.44; N, 9.78. $C_{28}H_{19}N_3O_2$ requires C, 78.31; H, 4.46; N, 9.78%); ν_{max}(KBr)/cm^{-1} 3342, 3031, 2928, 1737, 1684, 1609, 1396, 1343, 1322, 739; δ_H([$^2H_6$]DMSO) 4.49 (3 H, s, CH_3), 4.90 (2 H, s, CH_2), 7.26–7.46 (6 H, m, ArH), 7.49 (1 H, t, *J* 8.1, ArH), 7.61 (1 H, t, *J* 8.1, ArH), 7.70 (1 H, t, *J* 8.1, ArH), 7.79 (1 H, d, *J* 8.1, ArH), 7.83 (1 H, d, *J* 8.1, ArH), 8.86 (1 H, d, *J* 8.1, ArH), 8.91 (1 H, d, *J* 8.1, ArH), 12.05 (1 H, s, NH); *m*/*z* 325 (M$^+$, 100%), 278 (34%), 254 (23%).

7-Benzyl-5,9-dimethyl-6,7,8,9-tetrahydro-5*H*-indolo[2,3-*c*]-pyrrolo[3,4-*a*]carbazole-6,8-dione 28db. A suspension of compound **9d** (0.5 mmol) and maleimide **27b** (0.6 mmol) in Ph_2O (3 ml) was heated at 190–200 °C during 12 h. After cooling, Et_2O was added and the resulting precipitate was filtered and washed with Et_2O to give **28db**; yield mp >250 °C (Found: C, 78.60; H, 4.84; N, 9.34. $C_{29}H_{21}N_3O_2$ requires C, 78.54; H, 4.77; N, 9.47%); ν_{max}(KBr)/cm^{-1} 3051, 2934, 1744, 1694, 1589, 1480, 1393, 1333, 1128, 737, 698; δ_H($CDCl_3$) 4.26 (6 H, s, CH_3), 4.75 (2 H, s, CH_2), 7.25–7.39 (7 H, m, ArH), 7.50 (2 H, d, *J* 7.3, ArH), 7.56 (2 H, t, *J* 7.3, ArH), 8.62 (2 H, d, *J* 7.3, ArH); δ_C($CDCl_3$) 34.2 (q), 41.5 (t), 109.5 (d), 119.5 (d), 121.2 (s), 123.2 (s), 123.9 (d), 127.5 (d), 127.7 (d), 128.6 (d), 128.7 (d), 129.8 (s), 132.5 (s), 137.1 (s), 143.7 (s), 167.8 (s); *m*/*z* 443 (M$^+$, 100%), 352 (38%).

Preparation of indolo[2,3-*c*]pyrrolo[3,4-*a*]carbazole derivatives 28 using acetic acid as solvent (conditions B)

7-Methyl-6,7,8,9-tetrahydro-5*H*-indolo[2,3-*c*]pyrrolo[3,4-*a*]-carbazole-6,8-dione 28aa. A solution of AcOH (5 ml) containing compound **9a** (0.5 mmol) and maleimide **27a** (1 mmol) was heated at 90–100 °C during 36 h. After evaporation, the residue was treated with Et_2O and the resulting precipitate was filtered and washed with Et_2O to give compound **28aa**; yield 44%; mp, IR and NMR spectra data were identical with the descriptions reported above.

7-Benzyl-6,7,8,9-tetrahydro-5*H*-indolo[2,3-*c*]pyrrolo[3,4-*a*]-carbazole-6,8-dione 28ab. A solution of AcOH (5 ml) containing compound **9a** (0.5 mmol) and maleimide **27b** (1 mmol) was heated at 90–100 °C during 24 h. After evaporation, the residue was treated with Et_2O and the resulting precipitate was filtered and washed with Et_2O to give compound **28ab**; yield 55%; mp, IR and NMR spectra data were identical with the descriptions reported above.

6,7,8,9-Tetrahydro-5*H*-indolo[2,3-*c*]pyrrolo[3,4-*a*]carbazole-6,8-dione 28ac. A solution of AcOH (5 ml) containing compound **9a** (0.5 mmol) and maleimide **27c** (1 mmol) was heated at 90–100 °C during 24 h. After evaporation, the residue was treated with Et_2O the resulting precipitate was filtered and washed with Et_2O to lead to compound **28ac**; yield 55%; mp >250 °C (Found: C, 73.65; H, 3.53; N, 12.82. $C_{20}H_{11}N_3O_2$ requires C, 73.84; H, 3.41; N, 12.92%); ν_{max}(KBr)/cm^{-1} 3416, 3351, 3175, 1742, 1712, 1688, 1613, 1461, 1415, 1312, 1245, 742; δ_H([$^2H_6$]DMSO) 7.42 (2 H, t, *J* 8.1, ArH), 7.59 (2 H, t, *J* 8.1, ArH), 7.80 (2 H, d, *J* 8.1, ArH), 8.84 (2 H, d, *J* 8.1, ArH), 11.10 (1 H, s, NH), 12.06 (2 H, s, NH); δ_C([$^2H_6$]DMSO) 111.4 (s), 112.4 (d), 119.7 (d), 120.6 (s), 122.5 (s). 123.4 (d), 126.9 (d), 128.4 (s), 142.3 (s), 170.0 (s); *m*/*z* 325 (M$^+$, 100%), 254 (45%).

2,4-Dichloro-6,7,8,9-tetrahydro-5*H*-indolo[2,3-*c*]pyrrolo-[3,4-*a*]carbazole-6,8-dione 28bc. A solution of AcOH (5 ml) containing compound **9b** (0.5 mmol) and maleimide **27c** (1 mmol) was heated at 90–100 °C during 36 h. After evaporation, the residue was treated with Et_2O and the resulting precipitate was filtered and washed with Et_2O to lead to compound **28bc**; yield 41%; mp >250 °C (Found: C, 63.39; H, 3.65; N, 6.94. $C_{21}H_{14}Cl_2N_2O_2$ requires C, 63.49; H, 3.55; N, 7.05%); ν_{max}(KBr)/cm^{-1} 3416, 3222, 1749, 1709, 1613, 1453, 1314, 1309, 1272, 1237, 762, 642; δ_H([$^2H_6$]DMSO) 7.45 (1 H, t, *J* 7.7, ArH), 7.61 (1 H, t, *J* 7.7, ArH), 7.79 (1 H, s, ArH), 7.82 (1 H, t, *J* 7.7, ArH), 8.59 (1 H, t, *J* 7.7, ArH), 8.63 (1 H, s ArH), 11.20 (1 H, s, NH), 11.68 (1 H, s, NH), 12.17 (2 H, s, NH).

6,7,8,9-Tetrahydro-5*H*-indolo[2,3-*c*]carbazole-6,7-dicarboxylic anhydride 31. Similarly prepared as for compounds **28** using acetic acid as solvent and maleic anhydride (conditions B) during 2 days, yield 46%; mp >250 °C (Found: C, 73.01; H, 3.74; N, 8.10. $C_{20}H_{10}N_2O_3$ requires C, 73.62; H, 3.09; N, 8.58%); ν_{max}(KBr)/cm^{-1} 3402, 3361, 3206, 1808, 1740, 1715, 1613, 1460, 1329, 1208, 737; δ_H([$^2H_6$]DMSO) 7.44 (2 H, t, *J* 8.1, ArH), 7.63 (2 H, t, *J* 8.1, ArH), 7.79 (2 H, d, *J* 8.1, ArH), 8.82 (2 H, d, *J* 8.1, ArH), 12.38 (2 H, s, NH); δ_C([$^2H_6$]DMSO) 109.2 (s), 112.5 (d), 120.2 (d), 120.3 (s), 123.8 (d), 127.8 (d), 129.1 (s), 142.5 (s), 163.5 (s); *m*/*z* 326 (M$^+$, 100%), 254 (38%).

Diethyl (1,1′-dimethyl-3,3′-biindolyl-2-yl)hydrazine-1,2-dicarboxylate 32. A suspension of **9d** (130 mg, 0.5 mmol) in toluene (3 ml) and diethyl azodicarboxylate (115 µl, 0.6 mmol) was heated at 130 °C under an inert atmosphere. After 1 h, the green–brown solution was evaporated and the residue, chromatographed on a silica gel column (CH_2Cl_2), gave 190 mg (87%) of **32**; mp 168–170 °C; ν_{max}(KBr)/cm^{-1} 3258, 2984, 2926, 2909, 1757, 1703, 1510, 1478, 1329, 1235, 1075, 739; δ_H([$^2H_6$]DMSO) 1.10–1.30 (6 H, m, CH_3), 3.75–4.30 (10 H, m, CH_2 + CH_3), 7.01 (1 H, t, *J* 7.3, ArH), 7.07 (1 H, t, *J* 7.3, ArH), 7.19 (1 H, t, *J* 7.3, ArH), 7.26 (1 H, t, *J* 8.1, ArH), 7.31–7.54 (5 H, m, ArH), 9.90 (1 H, s, NH); δ_C([$^2H_6$]DMSO) 13.7 (q), 14.3 (q), 29.2 (q), 32.5 (q), 61.0 (t), 68.5 (t), 104.3 (s), 105.5 (s), 109.7 (d), 110.1 (d), 118.5 (d), 119.3 (d), 119.6 (d), 120.2 (d), 121.0 (d), 122.2 (d), 125.3 (s), 127.2 (s), 128.1 (d), 132.1 (s), 134.1 (s), 136.7 (s) 154.5 (s), 156.3 (s); *m*/*z* 434 (M$^+$, 100%), 346 (46%), 272 (23%), 259 (17%).

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