# SYNTHESIS AND CHARACTERIZATION OF NEW INDOLE TRIMERS AND TETRAMERS

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Abstract - A new method has been achieved to synthesize indole trimers and tetramers starting from indoles and 3-bromoindoles. Unusual open and cyclic trimers have been isolated and characterized, and the mechanism of formation is proposed.

Syntheses of 2,3'-biindolyls and indole trimers and tetramers have been recently reported through reaction of indolin-2-ones with phosphoryl chloride<sup>1</sup> and by other routes, such as cyclotrimerization of the indolyl-0-acetate<sup>2</sup>. We also described a new selective synthesis of 3-bromoindoles<sup>3</sup>, which under acid conditions react with 3-unsubstituted indoles to give 2,3'-biindolyls in good yield<sup>4,5</sup>. Now we extende our synthetic method to the preparation of open and cyclic indole trimers, to indole tetramers and pentamers, and we propose the mechanism of formation of a series of new indole trimers carrying an aniline function.

# RESULTS AND DISCUSSION

The reaction of 3-bromoindole with indole in dry dichloromethane in the presence of acid leads to 2,3'-biindolyl, which further reacts, under mild acid conditions, with the 3-bromoindole to give the indole trimer I. An excess of the acid increases the amount of secondary products which are mainly the trimer II, carrying an aniline function, and the symmetric cyclic derivative III. The structure of the unusual trimer II was confirmed by considering the spectroscopic data of the product and of the methyl derivatives obtained by reacting II with methyl iodide in DMF, as reported in Scheme 1.



Methylation of II occurs preferentially on the NH of indole, giving IV; trimethyl- and tetramethylderivatives V and VI were also observed by  $^{1}$ H NMR. The yield in trimers such as II increases by starting from 2-substituted indoles. A reasonable mechanism for their formation is proposed in Scheme 2.



 $R', R''' = H, CH_3$ ;  $R'' = H, CH_3$ , C6H5

Trimeric indoles X (2,3'-2',3"-triindolyls) undergo protonation at the 3" position, leading to an intramolecular electrophilic attack on the 3-unsubstituted indole position, which give a hypothetic cyclic indoline trimer XI. The probable easy protonation at the indoline nitrogen of XI originates the leaving group, with the opening of the pyrrole ring. The final deprotonation to XII is favoured by the formation of a new benzene ring. With R" = H, the intermediate XI is readily oxidisable to the more stable symmetric cyclic trimer XIII. With R" = methyl or phenyl, a major amount of the aniline trimer XII was isolated, as protonation of X is favoured by electronic effects, and the cyclization reaction to XIII is no longer feasible.

Moreover the reaction of indole with 3-bromoindole gives minor amounts of the indoline dimer VII, and of the trimers VIII and IX (Scheme 1.), the last probably originated from VIII through an acid catalyzed  $3 \longrightarrow 2$  rearrangement. Dimers and trimers such as VII and VIII come from reaction of protonated indole on indole itself, as previously reported<sup>b</sup>.

Indole tetramers were observed only in traces, probably because of the secondary reactions, which mainly lead to unusual trimers II and III. Poor yields of oligomers could also be attributed to the tendency of 3-bromoindole to self condense<sup>4</sup> giving 2,3'-biindoly1 and III, and to the low solubility of the oligomer intermediates which must be soluble and unprotonated to further react with the bromoindolinium cation as reported in Scheme 3.



 $XIV_{a}: R^{n} = CH_{3}, R^{m} = H; XIV_{b}: R^{n}, R^{m} = CH_{3}$ 

The yield of oligomers increases when starting from 2-substituted indoles, the cyclization reaction to trimers such as III being unfavoured, and when 3-bromo-1-methylindole is used in place of 3-bromoindole, as more soluble intermediates are formed. So tetramers XIVa and XIVb were obtained in moderate yields starting from 2-methylindole (a) and 1,2-dimethylindole (b) respectively, and pentamers (probably XV) were formed when 1-methylindole was treated with an excess of 3-bromo-1-methylindole.

The formation of trimers X and of oligomers such as XIV and XV can be explained by extending the mechanism proposed for the synthesis of 2,3'-biindolyls, that is an attack of the bromoindolinium cation on the indole substrate to give an intermediate which rearomatizes with the loss of a proton and of hydrogen bromide, as reported for the synthesis of the tetramers XIV (Scheme 3).

### EXPERIMENTAL

M.ps were determined on Buchi apparatus and are uncorrected. IR spectra were recorded with a Perkin Elmer 298 instrument, as KBr disks. UV spectra were obtained on a Jasco Uvidec 505 instrument, in EtoH. H and <sup>13</sup>C NMR were taken on Bruker CXP 200 and VarianEM-360 instruments, in DMSO-d, or in CDCl<sub>3</sub>. Chemical shifts are related to TMS ( $\delta$ H, $\delta$ C = 0); J are given in Hz. Mass spectra were performed on a 1020-Finnigan quadruple instrument (direct inlet, 70 eV), and relative intensities of major peaks are reported in brackets. Microanalyses were carried out by Istituto di Chimica Farmaceutica - Universita' di Parma.

Synthesis and characteristics of indole trimers from indole and 3-bromo indole. Indole (0.4 g) and 3-bromoindole (0.6 g) were dissolved in dichloromethane dried on calcium chloride (100 ml), treated with 0.2 ml of trifluoroacetic acid and kept under stirring at room temperature for 1 hour. The sample was then diluted with 50 ml of dichloromethane, treated with other 0.6 g of 3-bromoindole and stirred overnight. The sample was treated with aqueous ammonia and the basic solution was evaporated to dryness. The residue was dissolved with ethyl acetate and fractionated on a silica gel column (30 x 2.5 cm I.D.), eluting with hexane and ethyl acetate mixtures (7/3, v/v). The following products were recovered: 2,3'-biindolyl (80 mg), 2,3'-2',3"-triindolyl I (320 mg), cyclic indole trimer II (120 mg), symmetrical cyclic indolg trimer III (110 mg), the known indole dimer VII (40 mg)', the known indole trimer VIII (90 mg)', a new indole open trimer (IX) (20 mg), trace amounts of indole tetramers, and other minor amounts of not identified products. The main characteristics of the isolated products are reported.

2,3'-biindoly1: spectral data have been previously reported<sup>2</sup>.

 $\frac{2,3'-2,3''-triindolyl I}{2} \text{ m.p. } 239-243^{\circ}; \text{ IR (KBr, cm}^{-1}: 3400, 3410 (NH); UV $\lambda$ max nm ($\epsilon:): 297 (22, 800); NMR (DMSO-d,): $\delta$ H 5.42 [1, =CH-(3)s], 6.8-7.5 (11, arom m), 7.55 [1, =CH-(2'') d, J = 2.0], 7.6-7.8 (1, arom m), 10.85 [1, NH(1')s], 11.40 [1, NH(1')s], 11.45 1, [NH(1'')s]; shifts of NH protons were assigned by selective irradiation of protons at $\delta$ = 6.42 (H-3) and at 7.55 (H-2''); 6^{-3}C: 99.9 [=CH-(3)d], singlets: 104.2, 107.2, 125.3, 127.9, 128.5, 131.4, 133.4, 135.8, 136.0, 136.1; doublets: 110.9, 111.1, 111.7, 118.5, 118.6, 119.0, 119.3, 119.5, 120.0, 121.2, 121.5, 125.1; MS [m/e(% rel. int.)]: 347(M, 100), 345(39), 172(23), (Found: C, 82.07; H, 4.82; N, 12.01. C_{24}H_1N_3 requires: C, 82.97; H, 4.93; N, 12.10%).$ 

Indole trimer II: m.p. > 320°C (after elimination of included ethyl acetate by heating a few minutes at 120°C); IR (KBr, cm<sup>-1</sup>): 3430, 3360 (NH, NH<sub>2</sub>), 1710 (C=O) (ethyl acetate (1:1) was included, as shown by <sup>1</sup>H NMR; after heating this band disappeared); UV  $\lambda$  max rm (E): 242(28,600), 272(24,000), 285(25,200), 340(7,000), 358(5,400); NMR (DMSO-d<sub>2</sub>):  $\delta$ H 4.70(2,NH<sub>2</sub>s), 6.78(1 arom, t, J = 7.3), 6.90(1, arom, d, J = 8.0), 7.1-7.8(8, arom, m), 8.05(1, arom, s), 8.15(1, arom, d, J = 7.3), 8.68(1, arom, d, J = 7.3), 10.82(1,NH s), 11.75(1,NH,s); MS [m/e(% rel. int.)]: 347(M,100), 345(48), 330(11), 172(45), 159(11) (Found: C, 82.48; H, 4.88; N, 11.94. C<sub>24</sub>H<sub>17</sub>N<sub>3</sub> requires: C, 82.97; H, 4.93; N, 12.10%).

<u>Symmetrical cyclic indole trimer III</u>: m.p. >  $320^{\circ}$ C; IR(KBr, cm<sup>-1</sup>): 3440(NH); UV  $\lambda$  max nm (c): 224(30,400), 280(6,900); NMR (DMSO-d.):  $\beta$ H 7.33-7.43(6,arom, m), 7.79(3,arom, d, J = 7.7), 8.75(3,arom, d, J = 7.1), 11.93(3,NH s);  $\delta^{12}$ C, singlets: 110.5, 122.1, 133.6, 138.4, doublets: 110.7, 118.8, 119.6, 122.1; MS [m/e(% rel. int.)]: 345(M,100), 172(48), 158(22), 144(11), 132(11) (Found: C, 83.22; H, 4.31; N, 12.01.  $C_{24}H_{15}N_3$  requires: C, 83.45; H, 4.38; N, 12.17%).

Indoline dimer VII: m.p.  $110-111^{\circ}$ C; IR(KBr, cm<sup>-1</sup>): 3400(NH); UV  $\lambda$  max nm (E): 223(54,500), 282(10,200); NMR (CDC1<sub>3</sub>):  $\delta$ H 3.37(2,  $-CH_2-d$ , J = 7.3), 4.82(1, -CH t, J = 7.3), 6.52(1, arom,  $d_{13}$ J = 7.6), 6.60(1, arom, t, J = 7.5), 6.8-7.6(7, arom, m), 7.8(2, NH<sub>2</sub>, s broad); NMR (DMSO-d.):  $\delta$  c singlets: 118.9, 125.5, 127.9, 136.6, 151.7; doublets: 55.6, 107.8, 111.3, 110.6, 118.6, 120.8, 121.7, 123.8, 126.8, triplet: 37.3; MS [m/e(% rel. int.)]: 234(M,48), 233(52), 117(100) (Found: C, 81.87; H, 5.99; N, 11.83. C<sub>16</sub>H<sub>14</sub>N<sub>2</sub> requires: C, 82.02; H, 6.02; N, 11.96%).

Indole trimer VIII: m.p.  $167-169^{\circ}$ C; IR (KBr, cm<sup>-1</sup>): 3440(NH, NH<sub>2</sub>); UV  $\lambda$  max nm (C): 220(42,200), 282(8,700); NMR (DMSO-d<sub>2</sub>):  $\delta$  H 3.35 (2 -CH<sub>2</sub>- d, J = 7.5), 4.65 (2, NH<sub>2</sub>s), 4.86(1, -CH t, J = 7.5), 6.33(1 arom t, J = 7.5), 6.58 (1, arom d, J = 7.5), 6.7-7.1 (6, arom m), 7.26 2, arom s, 7.28(2, arom d, J = 7.6), 7.52(2, arom d, J = 7.6), 10.70(2, NH s);  $\delta^{13}$ C singlets: 118.5, 124.5, 126.4, 136.2, 145.8, doublets: 32.4, 111.2, 114.8, 116.4, 117.8, 118.8, 120.5, 121.9, 126.0, 129.1, triplet: 35.8; MS [m/e (% rel. int.)]: 351(M,3), 245(100), 217(21), 130(12), 117(28), 106(28); (Found: C, 81.79; H, 5.96; N, 11.78. C<sub>24</sub>H<sub>21</sub>N<sub>3</sub> requires: C, 82.02; H, 6.02; N, 11.90X).

New indole trimer IX: m.p. 166-168°C, IR (KBr,  $cm^{-1}$ ): 3440(NH, NH<sub>2</sub>); UV  $\lambda$  max mm (E): 220(42,800), 282(8,200); NMR (DMSO-d<sub>6</sub>):  $\delta$  H 3.35(2, -CH<sub>2</sub>- d, J = 7.5), 4.82 (l, -CH- t, J = 7.5), 4.85(2, NH<sub>2</sub>- s), 6.22(1, =CH-(3)s), 6.32(1, arom t, J = 7.5), 6.60(1, arom d, J = 7.5), 6.7-7.1(6, arom m), 7.2-7.4(3, arom m), 7.52(2, arom d, J = 7.6), 10.84(1, NH s), 10.88 (l, NH s); MS [m/e (X rel. int.)]: 351(M,2), 245(100), 233(8), 217(10), 117(8) (Found: C, 81.33; H, 6.01; N, 11.78.  $C_{24}H_{21}N_3$ , requires: C, 82.02; H, 6.02; N, 11.96X).

Indole tetramer: MS [m/e (% rel. int)]: 462(M,4), 360(18), 358(20), 245(42), 117(71), 106(100).

Methylation of the indole trimer II to IV, V and VI. Trimer II (0.1 g) was dissolved in DMF (5 ml) and treated with methyl iodide (0.5 ml) in the presence of solid KOH (0.2 g). The solution was stirred for 1 hour at room temperature, then filtered and evaporated to dryness. The residue was recovered with ethyl acetate and fractionated on preparative silica plates (25x25 cm) eluting with hexane/ethylacetate (85/15, v/v). Two bands were recovered, containing respectively the dimethylated product IV and a 2/1 mixture of trimethylated and tetramethylated products V and VI. Spectroscopic data of compounds are reported.

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 $\begin{array}{l} \underline{\text{Dimethylated indole trimer IV}: \ UV \ \lambda \ \max \ \min \ (\varepsilon): \ 242(30,700), \ 287(20,100), \ 355(3,900), \ 370(6,100); \ \text{NMR (DMSO-d_): } \tilde{\mathbf{O}} \ \text{H} \ 3.53 \ (3, \ CH_3-N \ s), \ 4.50 \ (3, \ CH_3-N \ s), \ 4.55 \ (2, \ NH_2 \ s), \ 6.74 \ (1, \ arom \ t, \ J = 7.5), \ 6.83 \ (1, \ arom \ d, \ J = 7.6), \ 7.1-7.8 \ (8, \ arom \ m), \ 7.98 \ (1, \ arom \ s), \ 8.18 \ (1, \ arom \ d, \ J = 7.6), \ 8.70 \ (1, \ arom \ d, \ J = 7.6); \ \text{MS } \left[ m/e \ (\ \ rel \ int.) \right]: \ 375(M,92), \ 188(73), \ 171(100), \ 133(52) \ (\text{Found: C, } 82.75; \ \text{H}, \ 5.68; \ \text{N}, \ 11.11. \ C_{26} \ H_{21} \ \text{N}_3 \ requires: \ C, \ 83.17, \ \text{H}, \ 5.64, \ \text{N}, \ 11.192). \end{array}$ 

<u>Trimethylated aniline cyclic trimer V</u>: UV (mixture of trimers V and VI)  $\lambda$  max nm ( $\varepsilon$ ): 243(30,200), 287(22,200), 355(3,900), 370(6,100); NMR (DMSO-d<sub>6</sub>):  $\delta$  H 2.66 (3, <u>CH<sub>3</sub>NH-</u> d, J = 5.6), 3.40 (3, CH<sub>3</sub>N s), 4.32 (1, CH<sub>3</sub>NH- q, J = 5.6), 4.50 (3, NCH<sub>3</sub> s), 6.65-6.83 (2, arom m), 7.05-7.75 (8, arom m), 7.97 (1, arom s), 8.16 (1, arom d, J = 7.6), 8.70 (1, arom d, J = 7.6); MS [m/e ( $\chi$  rel. int.)]: 389(M,18), 202(8), 185(9), 84(100).

 $\frac{\text{Tetramethylated aniline cyclic trimer VI: NMR (DMSO-d_): \delta H 2.38 [6, N(CH_3)_2 s], 3.45 (3, NCH_3 s), 4.50 (3, NCH_3 s), 6.65-6.85 (2, arom m), 7.05-7.75 (8, arom m), 8.07 (1, arom s), 8.10 (1, arom d, J = 7.6), 8.70 (1, arom d, J = 7.6); MS [m/e (% rel. int.)]: 403(M,20).$ 

Synthesis of indole trimers from 1-methylindole and 3-bromo-1-methylindole. The reaction has been carried out at room temperature, by dissolving 1-methylindole (130 mg) and 3-bromo-1-methylindole (400 mg), prepared as previously described<sup>2</sup>, in 20 ml of dry dichloromethane. 0.1 Ml of trifluoroacetic acid were added and the reaction was kept under stirring for three hours. The solution was made basic with aqueous ammonia and evaporated. The residue was recovered with ethyl acetate and fractionated on a silica gel column (30x1.5 cm I.D.) using hexane and ethyl acetate mixture (9/1, v/v). Known 1,1'-dimethyl-2,3'-bindolyl (35 mg)<sup>2</sup> and 1,1',1"-trimethyl-2,3'-2'-3"-triindolyl (150 mg)<sup>3</sup> were isolated, together with the brominated trimer 1,1',1"-trimethyl-3-bromo-2,3'-2'-3"-triindolyl (80 mg), and minor amounts of tetramers (M<sup>2</sup> = 518) and pentamers (M<sup>2</sup> = 647). Spectroscopic characteristics of the main products are reported.

 $\frac{1,1'1''-\text{Trimethy}_{2,3'-2'-3''-\text{triindo}_{1}_{1}: \text{ m.p. }199-201^{\circ}\text{C}; \text{ IR (KBr, cm}^{-1}): \text{ no absorption at }3400 \\ \text{cm}^{-1} \frac{1,1'1''-\text{Trimethy}_{2,3'-2'-3''-\text{triindo}_{1}_{1}_{1}: \text{ m.p. }199-201^{\circ}\text{C}; \text{ IR (KBr, cm}^{-1}): \text{ no absorption at } 3400 \\ \text{cm}^{-1} \frac{1}{(\text{NH}); \text{ UV } \lambda \text{max nm}(\epsilon): 220(31,000), 297(15,400): \text{ NMR (CDC1}_{3}) (60 \text{ MHz}): \delta \text{ H } 3.15 (3, \text{ CH}_{3}\text{N-s}), \\ 3.62 (3, \text{ CH}_{3}\text{N-s}), 3.71 (3, \text{ CH}_{3}\text{N s}), 6.57 [1, \text{ "CH}_{-}(3) \text{ s}], 6.8-7.7 (12, \text{ arom m}); \text{ MS [m/e (X rel. int.)]: } 389(\text{M},100), 373(21), 180(11) (Found: C, 82.58; \text{ H, } 6.11; \text{ N, } 10.62. \text{ } C_{27}\text{H}_{23}\text{N}_{3} \text{ requires: C, } \\ 83.26; \text{ H, } 5.95; \text{ N, } 10.79\text{X}. \end{cases}$ 

 $\frac{1,1',1''-Trimethyl-3-bromo-2,3'-2',3''-triindolyl: m.p. 208-210^{\circ}C; IR (KBr, cm<sup>-1</sup>): no absorption at 3400 cm<sup>-1</sup> (NH); UV ) max nm (<math>\varepsilon$ ): 220(33,000), 295(13,500); NMR (CDCl<sub>3</sub>) (60 MHz):  $\delta$  H 3.18 (3, CH<sub>3</sub>N- s), 3.65 (3, CH<sub>3</sub>N- s), 3.75 (3, CH<sub>3</sub>N- s), 6.8-7.7 (12, arom m) (no signal at 6.4-6.6  $\delta$ ); MS [m/e (X rel. int.)]: 469-467(M,23), 388(46), 387(48), 473(34), 194(78), 179(100).

Synthesis of indole trimers X and XII from 2-phenylindole and 3-bromoindole: 0.2 g of 2-phenylindole and 0.4 g of 3-bromoindole were dissolved in dichloromethane (20 ml), acidified with 0.1 ml of trifluoroacetic acid and stirred overnight at room temperature, made basic with aqueous ammonia, evaporated to dryness, recovered with ethylacetate and fractionated on a silica gel column (30x1.5 cm I.D.) eluting with hexane/ethylacetate (8/2, v/v). The indole trimer XII (R" = phenyl) was isolated (130 mg), together with the known indole trimer X (75 mg)<sup>4</sup>, the dimer 2'-phenyl-2, 3'-biindolyl (80 mg)<sup>2</sup> and other unknown minor compounds. Characteristics of trimers X and XII are reported.

Indole trimer X (R" = phenyl; R', R'''= H): m.p. 263-265°C; IR (KBr, cm<sup>-1</sup>): 3400 (NH); UV  $\lambda \max nm (\epsilon)$ : 303(14,300); NMR (DMSO-d,):  $\delta$ H 6.04 (1, =CH-(3) s), 6.70-7.65 (16, arom m), 7.90-8.05 (1, arom m), 10.76 (1, NH s broad), 11.34 (1, NH s), 11.79 (1, NH s); MS [m/e (X rel. int.)]: 423(M,100), 345(22), 260(87), 212(28) (Found: C, 84.81; H, 5.04; N, 9.76. C<sub>30</sub>H<sub>21</sub>N<sub>3</sub> requires: C, 85.08; H, 5.00; N, 9.92X).

 $\frac{\text{Indole trimer XII (R" = phenyl; R', R''' = H): m.p. > 320^{\circ}C; IR (KBr, cm<sup>-1</sup>): 3440 (NH, NH<sub>2</sub>), 1730 (C=0 caused by ethyl acetate inclusion); UV <math>\lambda$  max nm ( $\varepsilon$ ): 237(50,500), 265(42,800), 280(38,000), 336(12,900), 353(14,300); NMR (DMSO-d\_):  $\delta$  H 4.45 (2, NH<sub>2</sub> s broad), 6.4-7.1 (6, arom m), 7.10-7.45 (8, arom m), 7.55-7.70 (2, arom m), 8.70 (1, arom d, J = 7.6), 10.55 (1, NH s), 11.80 (1, NH s); MS [m/e (X rel. int.)]: 423(M,100), 202(46), 173(85) (Found: C, 84.71; H, 5.09; N, 9.76. C<sub>30</sub>H<sub>21</sub>N<sub>3</sub> requires: C, 85.08; H, 5.00; N, 9.92X).

Synthesis of oligomers from 2-methylindole and 3-bromoindole: 130 mg of 2-methylindole were dissolved in dichloromethane (20 ml) and mixed with 400 mg of 3-bromoindole and 0.1 ml of trifluoroacetic acid. The mixture was treated as reported above for the reaction of 2-phenylindole with 3-bromoindole. Two new products were isolated: the indole trimer XII (R" = methyl; R', R''' = H) (120 mg) and the regular tetramer XIVa (R" = CH<sub>3</sub>, R''' = H) (85 mg), which spectroscopic characteristics are reported. The known 2'-methyl-2,3'-biindolyl<sup>2</sup> was also isolated (60 mg).

 $\frac{1 \text{ ndole trimer XII: m.p. 215-218}^{\circ}\text{C}; \text{ IR (KBr, cm}^{-1}); 3400 (NH, NH_2); UV <math>\lambda \max nm(\varepsilon); 242(28,200), 268(24,400), 283(22,000), 338(3,300), 353(5,200); NMR (DMSO-d_2); \delta H 2.72 (3, CH_3 s), 4.70 (2, NH_2 s broad), 6.80 (1, arom t, J = 7.4), 6.94 (1, arom d, J = 7.5), 7.00-7.45 (6, arom m), 7.57 (1, arom d, J = 7.8), 7.70 (1, arom d, J = 7.8), 8.18 (1, arom d, J = 7.8), 8.65 (1, arom d, J = 7.2), 10.48 (1, NH, s), 11.76 (1, NH s); MS [m/e (X re1. int.)]: 361(M,100), 345(31), 180(27), 171(63) (Found: C, 82.71; H, 5.36; N, 11.53. C_{25}H_{19}N_3 requires: C, 83.07; H, 5.30; N, 11.63X).$ 

Indole tetramer XIVa (R" = CH<sub>1</sub>, R'' = H) (2'''-methyl-2,3'-2',3" -2",3''' -tetraindolyl): m.p. 278-280°C; IR (KBr, cm<sup>-1</sup>): 340°0 (NH); UV  $\lambda$  max nm (C): 295(8,800); NMR (DMSO-d<sub>1</sub>):  $\delta$  H 2.08 (3, CH<sub>2</sub> s), 6.15 (1, =CH- (3) d, J = 1.8), 6.75-7.60 (15, arom m), 7.75-7.60 (15, arom m), 7.75-7.90 (1, arom m), 10.30 (1, NH s broad), 11.06 (1, NH s), 11.17 (1, NH s), 11.43 (1, NH s); MS [m/e (X rel. int.)]: 476(M,12), 347(8), 260(8), 205(8), 57(100) (Found: C, 83.02; H, 5.11; N, 11.71. C<sub>33</sub>H<sub>24</sub>N<sub>4</sub> requires: C, 83.17; H, 5.08; N, 11.76X).

Synthesis of oligomers from 1', 2'-dimethy 1-2, 3'-biindoly1 and 3-bromoindole: 1', 2'-dimethy 1-2, 3'-biindoly1 was synthesized by reacting equimolecular amounts of 1,2-dimethylindole and 3-bromoindole in presence of acids, as previously reported for the synthesis of other biindoly1s<sup>2</sup>. The biindoly1 (0.26 g) was dissolved in dichloromethane (20 m1) containing 200 mg of 3-bromoindole, was acidified with 0.1 ml of trifluoroacetic acid and stirred overnight at room temperature. The reaction mixture was made basic and evaporated. The residue was chromatographed on a silica gel column (hexane/ethyl acetate, <math>8/2, v/v). The following three main products were isolated and identified: the indole trimer X (R' = H; R", R''' = methyl) (90 mg), the cyclic trimer XII (120 mg) and the indole tetramer XIVD (R", R''' = methyl) (50 mg). The characteristics of the products are reported:

 $\frac{1',2'-\text{dimethy1-2,3'-biindoly1: m.p. 165-166}^{\circ}C; IR (KBr, cm<sup>-1</sup>): 3360 (NH); UV \qquad \lambda \max (c): 220(28,200), 283(9,400); NMR, (DMSO-d): \delta H 2.60 (3, C-CH<sub>3</sub> s), 3.78 (3, NCH<sub>3</sub> s), 6.46 [1, =CH-(3) s], 6.95-7.30 (4, arom m), 7.40-7.65 (3, arom m), 7.76 (I, arom d, J = 7.57, 11.08 (1, NH s); \delta^{12}C 11.1 (CH<sub>3</sub>-C g), 29.4 (CH<sub>3</sub>-N q), singlets: 104.9, 125.8, 128.5, 133.2, 134.8, 136.1, 136.2; doublets: <math>99.1$  [=CH-(3) d], 109.1, 110.8, 118.4, 118.5, 118.8, 119.2, 119.8, 120.7: MS [m/e (X re1. int.)]: 260(M,100), 245(18), 217(15), 130(17) (Found: C, 83.01; H, 6.21; N, 10.71. C<sub>18</sub>H<sub>16</sub>N<sub>2</sub> requires: C, 83.04; H, 6.20; N, 10.76X).

Indole trimer X (R' = H; R', R''' = methyl): m.p. 108-110<sup>o</sup>C; IR (KBr, cm<sup>-1</sup>): 3380 (NH); UV  $\lambda \max \max (c): 290(11,600); NHR (DMSO-d_): \delta H 2.14 (3, CH_3-C s), 3.70 (3, CH_3N s), 6.32 [1, =CH (3)$ s], 6.80-7.60 (11, arom m), 7.88 (1, arom d, J = 7.5), 10.65 (1, NH s broad), 11.35 (1, NH s); MS[m/e (X rel. int.)]: 375(M,100), 360(18), 283(24), 270(38), 188(44), 180(94) (Found: C, 83.18; H,5.68: N. 11.14. C W N contained and the second second5.68; N, 11.14. C<sub>26</sub>H<sub>21</sub>N<sub>3</sub> requires: C, 83.17; H, 5.64; N, 11.19X).

Indole trimer XII (R' = H; R'', R''' = methyl): m.p. 153-155°C; IR (KBr, cm<sup>-1</sup>): 3400 (MH, NH<sub>2</sub>); UV  $\lambda \max \max (\epsilon)$ : 243(27,500), 260(24,600), 287(21,500), 338(4,100), 353(5,200); NMR (DNSO-d\_): 6 H 2.70 (3, CH<sub>2</sub>-C s), 2.74 (3, CH<sub>2</sub>NH d, J = 5.0), 4.20 (1, NH-CH<sub>2</sub> d, J = 5.0), 6.70-6.90 (2, arom m), 7.00-7.80 (8, arom m), 8.18 (1, arom d, J = 7.5), 8.64 (1, arom d, J = 7.5), 10.45 (1, NH s), 11.77 (1, NH s); MS [m/e (% rel. int.)]: 375(H,100), 360(38), 343(39), 188(27), 171(52) (Found: C, 83.02; H, 5.70; N, 11.11. C<sub>26</sub>H<sub>21</sub>N<sub>3</sub> requires: C, 83.17; H, 5.64; N, 11.19%).

Indole tetramer XIVb (R",R''' = methyl): m.p., the product became brown by heating and apparently did not melt under 320°C; IR (KBr, cm<sup>-1</sup>): 3380 (NH); UV  $\lambda$  max nm ( $\varepsilon$ ): 298(8,800); NMR (DMSO-d<sub>2</sub>):  $\delta$ H 2.10 (3, CH<sub>2</sub>-C s), 3.48 (3, CH<sub>2</sub>N s), 5.88 [1, =CH- (3) s], 6.75-7.90 (16, arom m), 10.23 (1, NH s broad), 11.12 (1, NH s), 11.35 (1, NH s); MS [m/e ( $\lambda$  rel. int.)]: 490(M,16), 210(100) (210(10 361(12), 260(100) (Found: C, 82.74; H, 5.41. N, 11.83. C<sub>34</sub>H<sub>26</sub>N<sub>4</sub> requires: C, 83.24; H, 5.34; N, 11.42%).

Synthesis of the cyclic trimer XII from 1',2'-dimethy1-2,3'-biindoly1 and 3-bromo-1-methylindole: Equimolecular amounts (1 mM) of the reagents were dissolved in dry dichloromethane, acidified with trifluoroacetic acid and stirred overnight. The reaction mixture was made basic with aqueous ammonia, and fractionated on a silica gel column eluting with hexane/ethyl acetate (8/2, v/v). The indole trimer XII (R',R'',R''' = methyl) (130 mg) was isolated together with unreacted dimer. Characteristics of the trimer are reported.

Indole trimer **XII** (R', R'', R''' = methyl): m.p. 203-205<sup>o</sup>C; IR (KBr, cm<sup>-1</sup>): 3360 (NH); UV  $\lambda$  max nm (c): 242(24,000), 270(21,500), 284(19,200), 338(3,900), 353(5,400); (DMSO-d<sub>b</sub>):  $\delta$ H 2.66 (3, CH<sub>3</sub>-C s), 2.68 (3, CH<sub>3</sub>-NH d, J = 5.0), 4.20 (1, CH<sub>3</sub>NH- q, J = 5.0), 4.52 (3, CH<sub>3</sub>N- s), 6.7-6.9 (2, arom m), 7.0-7.8 (B, arom m), 8.20 (1, arom d, J = 7.5), 8.58 (1, arom d, J = 7.6), 10.54 (1, NH s); MS [m/e (X rel. int.)]: 389(M,100), 374(18), 357(27), 269(13), 186(21), 171(31) (Found: C, 82, 56, N, 10, 57) 82.56; H, 5.98; N, 10.63. C<sub>27H23N3</sub> requires: C, 83.26; H, 5.95; N, 10.7Z).

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