Eco-friendly and efficient synthesis of bis(indolyl)methanes under microwave irradiation

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Abstract
Treatment of 2-arylindole derivatives with structurally diverse aldehydes in the presence of glacial acetic acid as an efficient, mild, and inexpensive catalyst under microwave irradiation condition compared with the conventional method afforded excellent yields of biologically important bis(indolyl)methane and tetraindolyl(terephthalyl)dimethane derivatives.

Keywords: Microwave irradiation, bis(indolyl)methanes, 2-arylindoles, aldehydes

Introduction

The indole moiety is featured in a variety of pharmacologically and biologically active compounds.[1] Among various indole derivatives, di(1-*H*-indolyl-3-yl)methanes (DIM) and 1,4-bis[di(1*H*-indol-3-yl)methyl]benzenes display diverse pharmacological activities and are useful in the treatment of fibromyalgia, chronic fatigue and irritable bowel syndrome.[2] These compounds also inhibit the proliferation of both estrogen dependent and independent cultured breast tumor cells.[3,4] Thus, the development of high-throughput methods for the synthesis of bis(indolyl)methanes remains a topic of paramount importance in view of their versatile biological and pharmacological activities. Numerous methods describing the synthesis of bis(indolyl)methanes were reported in the literature employing protic acids[5] and Lewis acids.[6,7] However, there are still some drawbacks in these catalytic systems including the requirement of large,[8,9] or stoichiometric amount of catalysts,[10,11] long reaction times,[8,9] low yields of products[11] and drastic condition for catalyst preparation.[12] Recently, metal triflate in ionic liquid,[13] Fe(III) salts in ionic liquids[14] and ionic liquids[15] were reported to be efficient for this transformation. Although ionic liquids are reusable they are very expensive.

During the past two decades many publications have described the successful combination of microwave irradiation as a nonclassical energy source with alternative reaction media. Microwave irradiation is well known to promote the synthesis of a variety of compounds,[16,17]

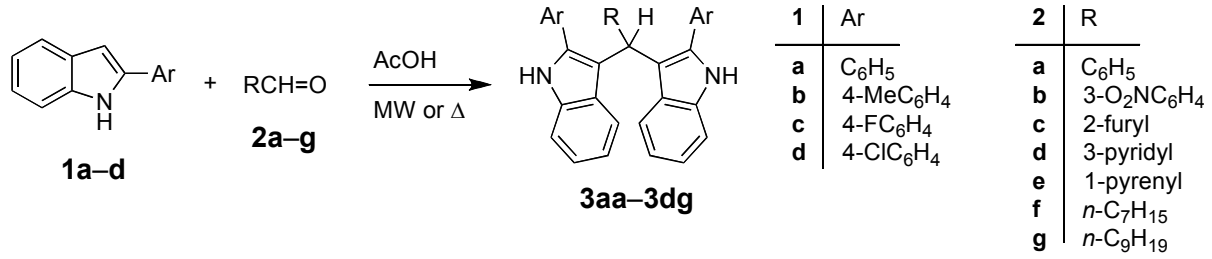
where chemical reactions are accelerated because of selective absorption of microwaves by polar molecules.

Recently, the coupling of microwave irradiation with polar organic molecules under solvent-free conditions has received notable attention.[17] A literature survey reveals examples of specific reactions, which do not occur under conventional heating, but could be possible by microwave irradiation.[18]

In continuation of our interest on indole derivatives[19] as well as the utility of microwave synthesis under solvent-free conditions,[20] we focus in this article on an efficient and facile microwave irradiation synthesis of pharmacologically interesting di(1*H*-indol-3-yl)methane and 1,4-bis[di(1*H*-indol-3-yl)methyl]benzene derivatives.

Results and Discussion

In the present article, a facile route using glacial acetic acid as a mild and highly efficient catalyst for a comparative synthesis of di(1*H*-indol-3-yl)methanes **3** by conventional heating and under microwave irradiation condition were described (Scheme 1).



Scheme 1. Glacial acetic acid catalyzed synthesis of di(1*H*-indol-3-yl)methanes **3**.

Attempts to synthesize some known di(1*H*-indol-3-yl)methane derivatives using catalysts such as I_2,[21] silica sulfuric acid,[22] $HClO_4$-SiO_2[23] under thermal conditions, revealed that the reactions took very long, required a huge amount of catalyst more than the reported, afforded low to moderate yields, and in some cases many by-products were formed.

In comparison with the reported methods, glacial acetic acid turned out to be an efficient medium in terms of handling, yields, and reaction times when carrying out the reactions under microwave irradiation. Thus, a mixture of 2-arylindole derivative **1a**–**d** and aldehyde **2a**–**g** (2:1 mmol) in glacial acetic acid was subjected to microwave irradiation with successive 30 sec periods to avoid overheating of the catalyst. The resulting di(1*H*-indol-3-yl)methanes **3** were obtained in excellent yields especially with aromatic and heteroaromatic aldehydes, but in the case of aliphatic aldehydes the yields were moderate to good (Table 1).

The work-up of these reactions is easy because some of the products either crystallized directly from the acetic acid, or upon pouring the reaction mixture onto water the solid product precipitated and was obtained by filtration and recrystallization.

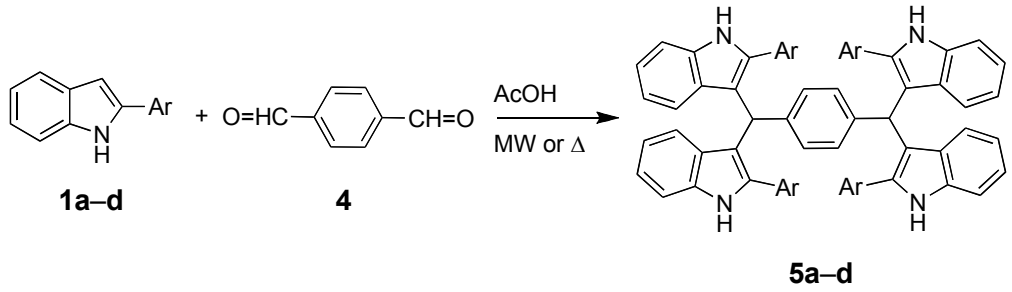
By conventional heating condition in acetic acid di(1*H*-indol-3-yl)methanes **3** and 1,4-bis[di(1*H*-indol-3-yl)methyl]benzene derivatives **5** were obtained in lower yields and required longer reaction times as compared with microwave irradiation (Table 1).

Table 1. Synthesis of di(1*H*-indol-3-yl)methanes **3** and tetraindolyl(terephthalyl)dimethanes **5** under thermal and microwave irradiation conditions

Indole	Aldehyde	Product	Thermal		Microwave (750 W)	
			Time [min]	Yield[a] [%]	Time [min]	Yield[a] [%]
1a	**2a**	**3aa**[c]	30	84	3	96
1b	**2a**	**3ba**	45	80	4	93
1c	**2a**	**3ca**[c]	15	63	1	91
1d	**2a**	**3da**	15	74	2	94
1a	**2b**	**3ab**	20	70	3	96
1b	**2b**	**3bb**	20	81	3	93
1c	**2b**	**3cb**	25	65	1	95
1d	**2b**	**3db**	30	66	5	84
1a	**2c**[b]	**3ac**[c]	10	82	2	96
1b	**2c**[b]	**3bc**[c]	10	81	2	96
1c	**2c**[b]	**3cc**[c]	15	80	2	90
1d	**2c**[b]	**3dc**	20	75	2	91
1a	**2d**	**3ad**	20	84	2	95
1b	**2d**	**3bd**	30	84	2	92
1c	**2d**	**3cd**	15	71	1	80
1d	**2d**	**3dd**	20	67	2	92
1a	**2e**	**3ae**	258	37	5	80
1b	**2e**	**3be**	300	35	10	77
1c	**2e**	**3ce**	720	53	5	79
1d	**2e**	**3de**	750	64	7	80
1a	**2f**	**3af**	480	43	10	63
1a	**2g**	**3ag**	600	45	5	56
1d	**2f**	**3df**	480	44	5	62
1d	**2g**	**3dg**	600	42	7	56
1a	**4**	**5a**	120	92	10	95
1b	**4**	**5b**	150	86	10	95
1c	**4**	**5c**	150	43	45	76
1d	**4**	**5d**	160	40	60	66

[a]Yield of isolated products. [b]Irradiation power was 350 W. [c]Known compounds.

The reaction was further explored, and under similar irradiation reaction conditions 1,4-bis[di(1*H*-indol-3-yl)methyl]benzene derivatives **5a**–**d** were synthesized in good to excellent yields (Table 1) by the electrophilic substitution reaction of 2-arylindole derivatives **1a**–**d** with terephthalaldehyde **4** (4**:**1 mmol**)** (Scheme 2).



Scheme 2. Reaction of 2-arylindoles **1a-d** with terephthaldehyde **4**.

All products **3** and **5** were characterized by spectroscopic and elemental analyses. The IR spectra of di(1*H*-indol-3-yl)methanes **3** and 1,4-bis[di(1*H*-indol-3-yl)methyl]benzene derivatives **5** show characteristic IR absorptions at 3747–3170 (N–H), 3062–3037 (aromatic C–H), 2860–2850 (aliphatic C–H), 1676–1660 (aromatic C=C), and 1613–1580 (C=C–N) cm^{-1}. In addition to substituent, aromatic and/or heteroaromatic proton signals, the ^{1}H NMR spectra display signals at δ 11.44–11.10 (br s, NH), and at δ 6.79–5.85 (s, >CH–R, R = aryl, hetaryl) or 4.78–4.77 (t, >CH–R, R = *n*-alkyl), respectively.

Melting points of di(1*H*-indol-3-yl)methanes 3aa,[24,26] 3ca,[25] 3ac,[27] 3bc,[27] and 3cc[27] closely match those reported in the literature. No spectral data have been reported in the literature for compounds 3ca,[25] 3bc,[27] and 3cc[27]; therefore, spectral data of these compounds are included in the Experimental Section.

All products 3 and 5 were obtained both by the microwave irradiation and conventional heating. Irrespective of these reaction conditions the IR spectra of each product are identical.

Experimental Section

General Procedures. All melting points were taken on a Stuart scientific melting point apparatus (Stuart Scientific, Stone, Staffordshire, UK). 1H NMR spectra of DMSO-d_6 solutions were recorded on a Varian Germini-2000 (300 MHz) spectrometer (Varian Inc., Palo Alto, CA, USA). IR spectra were recorded (KBr) on a Pye-Unicam Sp-883 spectrophotometer, Microanalytical Laboratory, Faculty of Science, Cairo University. Elemental analyses (C, H, N) were conducted using the Elemental Analyzer Yanaca CHN Corder MT-3. MS spectra were run on GC MS-QP 1000 EX Mass Spectrometer (Shimadzu). The microwave-induced reactions were carried out in an open Pyrex-glass vessel by using a domestic microwave oven (WhirlPool-

TALENT). The synthesized products and each reaction carried out under conventionally or microwave (MW) irradiation condition were monitored by thinlayer chromatography (TLC) on Merck silica gel 60 F254 plates (type E; Merck) using UV light (254 and 360 nm) for detection.

Di(1*H*-indol-3-yl)methane derivatives 3. General procedures

Microwave irradiation. A mixture of 2-arylindole **1a**–**d** (2 mmol), aldehyde **2a**–**g** (1 mmol) and glacial acetic acid (1 mL) in an open Pyrex-glass vessel was subjected to microwave irradiation (Table 1). Irradiation was carried out in successive 30 sec periods to avoid overheating of the catalyst. After completion of the reaction as monitored by TLC, the reaction mixture was cooled, and poured onto water. The precipitated solid was filtered off, washed with water, dried and recrystallized.

Thermal conditions. A mixture of 2-arylindole **1a**–**d** (2 mmol), aldehyde **2a**–**g** (1 mmol) and glacial acetic acid (1 mL) was refluxed for the appropriate time (Table 1). After completion of the reaction as monitored by TLC, work-up was performed as described above.

3,3'-(Phenylmethylene)bis(2-phenyl-1*H*-indole) (3aa). Colorless crystals; mp 272–274 °C (methanol) (lit.[24] 280 °C; lit.[26] 261 °C). IR (KBr): 3420, 3055, 2860, 1676, 1597 cm^{-1}, ^1H NMR (300 MHz, DMSO-d_6): δ 11.31 (br s, 2H, NH), 7.39–6.65 (m, 23H, ArH), 5.99 (s, 1H, CH). MS: m/z (%) 474 (100) [M^+]. All the spectroscopic data match those reported.[24,26]

3,3'-(Phenylmethylene)bis(2-*p*-tolyl-1*H*-indole) (3ba). Colorless crystals; mp 250–252 °C (methanol). IR (KBr): 3439, 3052, 2860, 1660, 1613 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.25 (br s, 2H, NH), 7.39–6.6 (m, 21H, ArH), 6.01 (s, 1H, CH), 2.56 (s, 6H, CH_3). MS: m/z (%) 502 (2.1) [M^+]. Anal. calcd. for $C_{37}H_{30}N_2$: C, 88.41; H, 6.02; N, 5.57. Found: C, 88.48; H, 6.28; N, 5.46.

3,3'-(Phenylmethylene)bis[2-(4-fluorophenyl)-1*H*-indole] (3ca). Colorless crystals; mp 220–221 °C ($CHCl_3$/petroleum ether) (lit.[25] 215 °C). IR (KBr): 3745, 3057, 2364, 1657, 1604 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.29 (s, 2H, NH), 7.36–6.67 (m, 21H, ArH), 5.89 (s, 1H, CH). MS: m/z (%) 510 (100) [M^+]. Anal. calcd. for $C_{35}H_{24}F_2N_2$: C, 82.33; H, 4.74; N, 5.49. Found: C, 82.48; H, 4.97; N, 5.22.

3,3'-(Phenylmethylene)bis[2-(4-chlorophenyl)-1*H*-indole] (3da). Colorless crystals; mp 270–272 °C ($CHCl_3$). IR (KBr): 3425, 3058, 1903, 1675, 1600 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.33 (s, 2H, NH), 7.36–6.68 (m, 21H, ArH), 5.95 (s, 1H, CH). MS: m/z (%) 542 (48.3) [M^+]. Anal. calcd. for $C_{35}H_{24}Cl_2N_2$: C, 77.35; H, 4.45; N, 5.15. Found: C, 77.22; H, 4.65; N, 5.21.

3,3'-(3-Nitrophenylmethylene)bis(2-phenyl-1*H*-indole) (3ab). Yellow crystals; mp 269–271 °C (methanol). IR (KBr): 3444, 3056, 2860, 1660, 1605 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.43 (br s, 2H, NH), 8.10–6.69 (m, 22H, ArH), 6.12 (s, 1H, CH). MS: m/z (%) 519 (100) [M^+]. Anal. calcd. for $C_{35}H_{25}N_3O_2$: C, 80.91; H, 4.85; N, 8.09. Found: C, 80.34; H, 5.11; N, 7.98.

3,3'-(3-Nitrophenylmethylene)bis(2-*p*-tolyl-1*H*-indole) (3bb). Yellow crystals; mp 247–249 °C (methanol). IR (KBr): 3246 2921, 2860, 1659, 1613 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.35 (br s, 2H, NH), 8.10–6.68 (m, 20H, ArH), 6.11 (s, 1H, CH), 2.25 (s, 6H, CH_3). MS: m/z

(%) 547 (100) [M^+]. Anal. calcd. for $C_{37}H_{29}N_3O_2$: C, 81.15; H, 5.34; N, 7.67. Found: C, 81.25; H, 5.60; N, 7.56.

3,3'-(3-Nitrophenylmethylene)bis[2-(4-fluorophenyl)-1*H*-indole] (3cb). Yellow crystals; mp 250–252 °C (ethanol). IR (KBr): 3746, 3060, 2363, 1647, 1613 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.40 (s, 2H, NH), 7.93–6.71 (m, 20H, ArH), 6.04 (s, 1H, CH). MS: m/z (%) 555 (100) [M^+]. Anal. calcd. for $C_{35}H_{23}F_2N_3O_2$: C, 75.67; H, 4.17; N, 7.56. Found: C, 75.82; H, 4.30; N, 7.29.

3,3'-(3-Nitrophenylmethylene)bis[2-(4-chlorophenyl)-1*H*-indole] (3db). Yellow crystals; mp >300 °C (methanol/DMF). IR (KBr): 3745, 3059, 2363, 1647, 1527 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.44 (s, 2H, NH), 7.97–6.72 (m, 20H, ArH), 6.10 (s, 1H, CH). MS: m/z (%) 587 (42.8) [M^+]. Anal. calcd. for $C_{35}H_{23}Cl_2N_3O_2$: C, 71.43; H, 3.94; N, 7.14. Found: C, 71.53; H, 4.07; N, 6.87.

3,3'-(2-Furylmethylene)bis(2-phenyl-1*H*-indole) (3ac). Colorless crystals; mp 256–257 °C (methanol) (Lit.[27] 255 °C). Spectroscopic data (IR, ^1H NMR, and MS) match those reported.[27]

3,3'-(2-Furylmethylene)bis(2-*p*-tolyl-1*H*-indole) (3bc). Colorless crystals; mp >300 °C (methanol) (Lit.[27] >360 °C). IR (KBr): 3422, 2861, 1915, 1669, 1449 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.21 (br s, 2H, NH), 7.95–5.92 (m, 19H, ArH), 5.84 (s, 1H, CH), 2.27 (s, 6H, CH_3). MS: m/z (%) 492 (100) [M^+]. Anal. calcd. for $C_{35}H_{28}N_2O$: C, 85.34; H, 5.73; N, 5.69. Found: C, 85.41; H, 5.99; N, 5.58.

3,3'-(2-Furylmethylene)bis[2-(4-fluorophenyl)-1*H*-indole] (3cc). Colorless crystals; mp >300 °C ($CHCl_3$) (Lit.[27] >360 °C). IR (KBr): 3745, 3056, 2362, 1647, 1603 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.29 (s, 2H, NH), 7.55–5.96 (m, 19H, ArH), 5.78 (s, 1H, CH). MS: m/z (%) 500 (100) [M^+]. Anal. calcd. for $C_{33}H_{22}F_2N_2O$: C, 79.19; H, 4.43; N, 5.60. Found: C, 79.34; H, 4.26; N, 5.33.

3,3'-(2-Furylmethylene)bis[2-(4-chlorophenyl)-1*H*-indole] (3dc). Colorless crystals; mp 256–258 °C ($CHCl_3$). IR (KBr): 3745, 3054, 1892, 1648, 1598 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.32 (s, 2H, NH), 7.57–5.98 (m, 19H, ArH), 5.85 (s, 1H, CH). MS: m/z (%) 532 (58.2) [M^+]. Anal. calcd. for $C_{33}H_{22}Cl_2N_2O$: C, 74.30; H, 4.16; N, 5.25. Found: C, 74.45; H, 4.39; N, 4.98.

3,3'-(3-Pyridylmethylene)bis(2-phenyl-1*H*-indole) (3ad). Colorless crystals; mp >300 °C (methanol). IR (KBr): 3387, 3161, 1890, 1663, 1578 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.40 (br s, 2H, NH), 8.44–6.69 (m, 22H, ArH), 6.06 (s, 1H, CH). MS: m/z (%) 475 (92.6) [M^+]. Anal. calcd. for $C_{34}H_{25}N_3$: C, 85.87; H, 5.30; N, 8.84. Found: C, 85.94; H, 5.58; N, 8.73.

3,3'-(3-Pyridylmethylene)bis(2-*p*-tolyl-1*H*-indole) (3bd). Colorless crystals; mp 299–300 °C (methanol). IR (KBr): 3170, 2924, 2850, 1661, 1580 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.30 (br s, 2H, NH), 8.43–6.66 (m, 20H, ArH), 6.03 (s, 1H, CH), 2.26 (s, 6H, CH_3). MS: m/z (%) 503 (100) [M^+]. Anal. calcd. $C_{36}H_{29}N_3$: C, 85.85; H, 5.80; N, 8.34. Found: C, 85.92; H, 6.06; N, 8.23.

3,3'-(3-Pyridylmethylene)bis[2-(4-fluorophenyl)-1*H*-indole] (3cd). Colorless crystals; mp >300 °C (methanol/DMF). IR (KBr): 3745, 2835, 1693, 1647, 1615 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.36 (s, 2H, NH), 8.44–6.68 (m, 20H, ArH), 5.96 (s, 1H, CH). MS: m/z (%) 511

(100) [M^+]. Anal. calcd. for $C_{34}H_{23}F_2N_3$: C, 79.83; H, 4.53; N, 8.21. Found: C, 79.98; H, 4.36; N, 7.94.

3,3'-(3-Pyridylmethylene)bis[2-(4-chlorophenyl)-1*H*-indole] (3dd). Colorless crystals; mp >300 °C (methanol/DMF). IR (KBr): 3401, 3049, 1900, 1667, 1576 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.39 (br s, 2H, NH), 8.38–6.72 (m, 20H, ArH), 6.03 (s, 1H, CH). MS: m/z (%) 543 (27.1) [M^+]. Anal. calcd. for $C_{34}H_{23}Cl_2N_3$: C, 75.00; H, 4.26; N, 7.72. Found: C, 75.15; H, 4.09; N, 7.45.

3,3'-(1-Pyrenylmethylene)bis(2-phenyl-1*H*-indole) (3ae). Colorless crystals; mp >300 °C (methanol). IR (KBr): 3288, 3049, 1676, 1640, 1597 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.38 (br s, 2H, NH), 8.28–6.51 (m, 27H, ArH), 6.26 (br s, 1H, CH). MS: m/z (%) 598 (42.9) [M^+]. Anal. calcd. for $C_{45}H_{30}N_2$: C, 90.27; H, 5.05; N, 4.68. Found: C, 90.34; H, 5.31; N, 4.57.

3,3'-(1-Pyrenylmethylene)bis(2-*p*-tolyl-1*H*-indole) (3be). Colorless crystals; mp 268–270 °C (methanol). IR (KBr): 3413, 3040, 1676, 1649, 1597 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.27 (br s, 2H, NH), 8.26–6.94 (m, 25H, ArH), 6.79 (s, 1H, CH), 2.19 (s, 6H, CH_3). MS: m/z (%) 626 (43.4) [M^+]. Anal. calcd. for $C_{47}H_{34}N_2$: C, 90.06; H, 5.47; N, 4.47. Found: C, 90.13; H, 5.73; N, 4.36.

3,3'-(1-Pyrenylmethylene)bis[2-(4-fluorophenyl)-1*H*-indole] (3ce). Pale yellow crystals; mp 248–250 °C (methanol). IR (KBr): 3745, 3047, 2362, 1693, 1647 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.43 (br s, 2H, NH), 8.27–7.00 (m, 25H, ArH), 6.70 (br s, 1H, CH). MS: m/z (%) 634 (32.2) [M^+]. Anal. calcd. for $C_{45}H_{28}F_2N_2$: C, 85.15; H, 4.45; N, 4.41. Found: C, 85.02; H, 4.65; N, 4.47.

3,3'-(1-Pyrenylmethylene)bis[2-(4-chlorophenyl)-1*H*-indole] (3de). Pale yellow crystals; mp 250–252 °C (methanol). IR (KBr): 3746, 3037, 2856, 1657, 1483 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.44 (br s, 2H, NH), 8.26–7.20 (m, 25H, ArH), 6.73 (br s, 1H, CH), 2.26 (s, 6H, CH_3). MS: m/z (%) 668 (25.2) [M^+]. Anal. calcd. for $C_{45}H_{28}Cl_2N_2$: C, 80.69; H, 4.23; N, 4.20. Found: C, 80.51; H, 4.43; N, 4.26.

3,3'-(1-Heptylmethylene)bis(2-phenyl-1*H*-indole) (3af). Colorless crystals; mp 134–136 °C (ethanol). IR (KBr): 3747, 3056, 2856, 1657, 1604 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.10 (s, 2H, NH), 7.54–6.78 (m, 18H, ArH), 4.78 (t, 1H, CH), 2.27 (q, 2H, CH_2), 1.08–1.00 (m, 8H, CH_2), 0.71 (t, 3H, CH_3). MS: m/z (%) 482 (18.04) [M^+]. Anal. calcd. for $C_{35}H_{34}N_2$: C, 87.10; H, 7.10; N, 5.80. Found: C, 87.17; H, 7.36; N, 5.82.

3,3'-(1-Nonylmethylene)bis(2-phenyl-1*H*-indole) (3ag). Colorless crystals; mp 138–140 °C (ethanol). IR (KBr): 3400, 3055, 2923, 2852, 1605 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.10 (s, 2H, NH), 7.54–6.77 (m, 18H, ArH), 4.77 (t, 1H, CH), 2.27 (q, 2H, CH_2), 1.17–1.03 (m, 12H, CH_2), 0.79 (t, 3H, CH_3). MS: m/z (%) 510 (9.7) [M^+]. Anal. calcd. for $C_{37}H_{38}N_2$: C, 87.02; H, 7.50; N, 5.48. Found: C, 87.09; H, 7.76; N, 5.37.

3,3'-(1-Heptylmethylene)bis[2-(4-chlorophenyl)-1*H*-indole] (3df). Colorless crystals; mp 196–198°C (ethanol). IR (KBr): 3744, 2953, 2855, 1693, 1647 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.09 (s, 2H, NH), 7.65–6.82 (m, 16H, ArH), 4.72 (t, 1H, CH), 2.38 (q, 2H, CH_2), 1.21–1.05

(m, 8H, CH_2), 0.78 (t, 3H, CH_3). MS: m/z (%) 550 (9.7) [M^+]. Anal. calcd. for $C_{35}H_{32}Cl_2N_2$: C, 76.22; H, 5.85; N, 5.08. Found: C, 76.09; H, 6.05; N, 5.14.

3,3'-(1-Nonylmethylene)bis[2-(4-chlorophenyl)-1*H*-indole] (3dg). Colorless crystals; mp 150–152 °C (ethanol). IR (KBr): 3744, 2923, 2852, 1693, 1647 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.09 (s, 2H, NH), 7.64–6.84 (m, 16H, ArH), 4.72 (t, 1H, CH), 2.35 (q, 2H, CH_2), 1.19–1.09 (m, 8H, CH_2), 0.83 (t, 3H, CH_3). MS: m/z (%) 578 (9.4) [M^+]. Anal. calcd. for $C_{35}H_{32}Cl_2N_2$: C, 76.67; H, 6.26; N, 4.83. Found: C, 76.54; H, 6.46; N, 4.89.

1,4-Bis[bis(2-aryl-1*H*-indol-3-yl)methyl]benzene derivatives 5. General procedures

Microwave irradiation. A mixture of 2-arylindole **1a-d** (4 mmol), terephthalaldehyde **4** (1 mmol) and glacial acetic acid (1 ml) was subjected to the same reaction conditions as described above for the preparation of **3**.

Thermal conditions. A mixture of 2-arylindole **1a-d** (4 mmol), terephthalaldehyde **4** (1 mmol) and glacial acetic acid (1 ml) was subjected to the same reaction conditions as described above for the preparation of **3**.

1,4-Bis[bis(2-phenyl-1*H*-indol-3-yl)methyl]benzene (5a). Colorless crystals; mp >300 °C (methanol). IR (KBr): 3297, 3060, 2860, 1661, 1602 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.31 (br s, 4H, NH), 7.95–6.67 (m, 40H, ArH), 5.92 (s, 2H, CH). MS: m/z (%) 870 (5.9) [M^+]. Anal. calcd. for $C_{64}H_{46}N_4$: C, 88.25; H, 5.32; N, 6.43. Found: C, 88.32; H, 5.58; N, 6.32.

1,4-Bis[bis[2-(4-methylphenyl)-1*H*-indol-3-yl]methyl]benzene (5b). Colorless crystals; mp >300 °C (methanol). IR (KBr): 3430, 3051, 2913, 1661, 1549 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.21 (br s, 4H, NH), 7.35–6.66 (m, 36H, ArH), 5.88 (s, 2H, CH), 2.27 (s, 12H, CH_3). MS: m/z (%) 927 (33.3) [M^+]. Anal. calcd. for $C_{68}H_{54}N_4$: C, 88.09; H, 5.87; N, 6.04. Found: C, 88.16; H, 6.13; N, 5.93.

1,4-Bis[bis[2-(4-fluorophenyl)-1*H*-indol-3-yl]methyl]benzene (5c). Colorless crystals; mp >300 °C (methanol/DMF). IR (KBr): 3746, 3056, 2912, 1694, 1647 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.39 (br s, 4H, NH), 8.38–6.72 (m, 36H, ArH), 6.03 (s, 2H, CH). MS: m/z (%) 942 (60) [M^+]. Anal. calcd. for $C_{64}H_{42}F_4N_4$: C, 81.51; H, 4.49; N, 5.94. Found: C, 81.38; H, 4.69; N, 6.00.

1,4-Bis[bis[2-(4-chlorophenyl)-1*H*-indol-3-yl]methyl]benzene (5d). Colorless crystals; mp >300 °C (methanol/DMF). IR (KBr): 3746, 3380, 2363, 1676, 1648 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 11.34 (br s, 4H, NH), 7.95–6.67 (m, 36H, ArH), 5.91 (s, 2H, CH). MS: m/z (%) 1006 (33) [M^+]. Anal. calcd. for $C_{64}H_{42}Cl_4N_4$: C, 76.19; H, 4.20; N, 5.55. Found: C, 76.06; H, 4.40; N, 5.61.

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