Benzenesulfonic Acid: A Versatile Catalyst for the Synthesis of Bis (indolyl)methanes as Antioxidants

Pulla Reddy Simha, Madhu Sekhar Mangali, Divya Kuppireddy Gari, Padmavathi Venkatapuram, and Padmaja Adivireddy*

Department of Chemistry, Sri Venkateswara University, Tirupati 517 502, Andhra Pradesh, India
*E-mail: adivireddyp@yahoo.co.in

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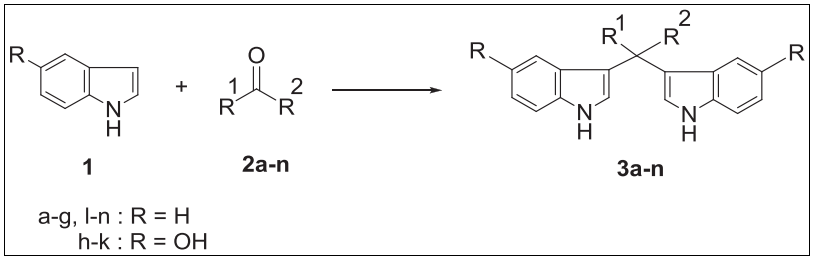

The reaction of indoles with carbonyl compounds in the presence of 5 mol% benzenesulfonic acid in acetonitrile was performed to synthesize bis(indolyl)methane derivatives adopting conventional and ultrasonication methodologies. The reaction proceeded in shorter reaction time in ultrasonication methodology leading to high yield of the products. All the synthesized compounds were tested for antioxidant activity. Among all the tested compounds, **3k** exhibited pronounced antioxidant activity.

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INTRODUCTION

Indole and their derivatives find important applications in the field of pharmaceuticals, agrochemicals, and materials science [1–3]. In fact bis(indolyl)alkanes exhibit a wide spectrum of biological activities *viz.,* cytotoxic [4,5], antitumor [6], antiviral [6], antimicrobial [7], anti-inflammatory [8], and antioxidant [9,10]. The bis(indolyl)methane is also a privileged scaffold in alkaloids including ramiflorine A and ramiflorine B, vibrindole A, streptindole, deoxytopsentin, bromodeoxytopsentin, and sponges. Besides, these compounds are the most active cruciferous substances for promoting beneficial estrogen metabolism and preventing cancer in human [11]. Some of the indole-based drugs are indomethacin [12], tenidap [13], sumatriptan, frovatriptan, and zolmitriptan [14]. Because of the unique pharmacological activities and the prevalence of indole moiety in many natural products, a great deal of interest has been focused on the development of efficient synthetic protocols for the preparation of bis(indolyl) alkanes. A number of synthetic methods for their preparation have been reported [15–19]. Among these methods, the acid catalyzed electrophilic addition of indole and carbonyl compounds is one of the most simple and straightforward approaches [20]. However, the use of toxic reagents, high temperature, and volatile organic solvents are among the drawbacks of most of these protocols [21]. Hence, there is a need for a new, efficient, and inexpensive synthetic methodologies based on green chemistry processes in organic synthesis. In the present communication, we herein report the use of benzenesulfonic acid as a catalyst for the synthesis of bis (indolyl)methane derivatives and studied their antioxidant properties.

RESULTS AND DISCUSSION

In recent years, benzenesulfonic acid has received considerable attention as an inexpensive and easily available catalyst for various organic reactions. In our initial attempts, the reaction of indole (**1**) (2 mmol) with 4-nitrobenzaldehyde (**2**) (1 mmol) in tetrahydrofuran was performed by using benzenesulfonic acid at room temperature for 6 h, and after work up, the product was obtained in 85% yield. Encouraged by these results, the catalytic activity of different Lewis acids in acetonitrile was examined in the reaction of compound **1** with compound **2**. Among the different catalysts, the reaction was completed in 15 min in the presence of benzenesulfonic acid (Table 1), which indicated its highest catalytic activity.

Furthermore, the effect of solvent was carried out to optimize the reaction conditions. The results presented in Table 2 revealed that acetonitrile was the better one than other solvents, and the reaction proceeded within 1 h at room temperature in high yield.

Table 1

The reaction of indole (**1**) with 4-nitrobenzaldehyde (**2**) in the presence of various catalysts.

Catalyst[a]	$C_6H_5SO_3H$	$Cu(OTf)_2$	$LiClO_4$	$FeCl_3$	$KHSO_4$	Sulphamic acid
Time (h)	0.25	3	12	12	13	10
Yield (%)[b]	95	90	30	59	60	67

[a]5 mol% of the catalyst was used.
[b]Yields referred to the isolated yield.

Table 2

Effect of solvents in the reaction of indole (**1**) with 4-nitrobenzaldehyde (**2**) catalyzed by benzenesulfonic acid.

Solvents	H_2O	MeOH	EtOH	THF	CH_3CN	DCM	Toluene
Time (h)	16	19	22	6	01	18	24
Yield (%)[a]	48	60	65	85	95	53	40

THF, tetrahydrofuran; DCM, Dichloromethane.
[a]Yields referred to the isolated yield.

Table 3

Effect of concentration of benzenesulfonic acid on the reaction of indole (**1**) with 4-nitrobenzaldehyde (**2**).

Mole % of catalyst	1	2.5	5	10	15
Time (min)	45	30	15	15	15
Yield (%)[a]	41	69	95	95	95

[a]Yields referred to the isolated yield.

Apart from these, to determine the influence of the catalyst concentration, the reaction of indole (**1**) and 4-nitrobenzaldehyde (**2**) was carried out with different concentrations of catalyst in acetonitrile at room temperature. The results presented in Table 3 indicated that 5 mol% of benzenesulfonic acid is optimum to achieve high yield in shorter reaction time.

Scheme 1. Synthesis of bis(indolyl)methane derivatives (**3a-n**).

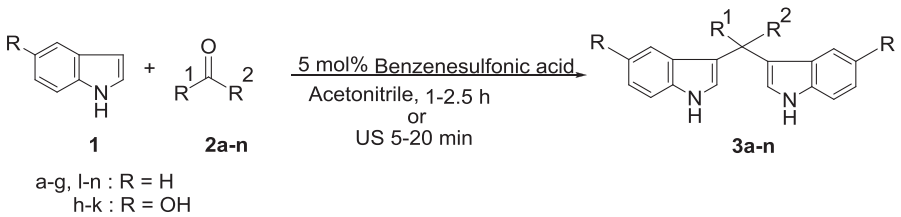
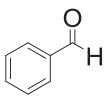
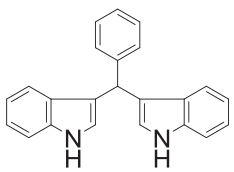
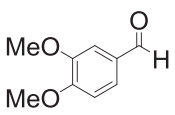
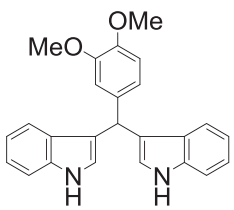


Table 4

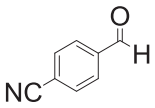
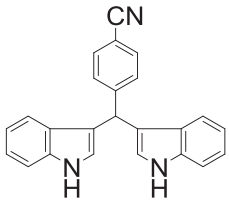
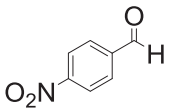
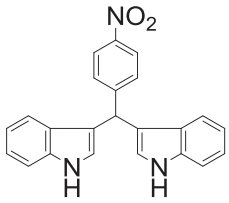
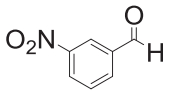
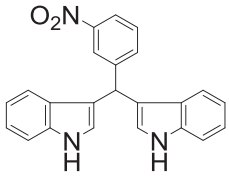
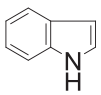
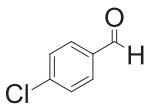
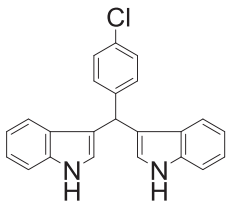
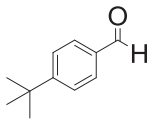
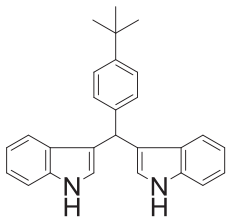
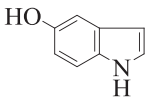
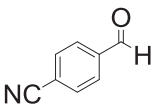
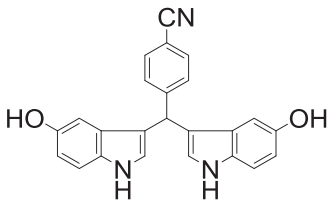
The preparation of compounds **3a-n** catalyzed by benzenesulfonic acid in acetonitrile under conventional and ultrasound irradiation methods.

				Conventional		Ultrasound	
Entry	Substituted Indole	Carbonyl compound	Product	Time (h)	Yield (%)	Time (min)	Yield (%)
3a				1.5	79	8	95
3b				1.0	86	17	90

(*Continued*)

Table 4

(*Continued*)

Entry	Substituted Indole	Carbonyl compound	Product	Conventional		Ultrasound	
				Time (h)	Yield (%)	Time (min)	Yield (%)
3c				1.4	80	16	92
3d				2.0	85	05	95
3e				1.1	81	18	92
3f				1.5	80	11	94
3g				2.0	83	20	90
3h				1.6	76	12	93

(*Continued*)

Table 4

(*Continued*)

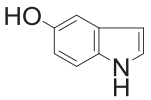
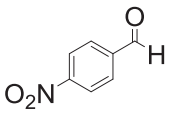
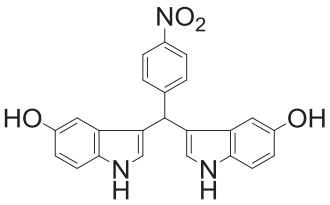
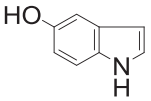
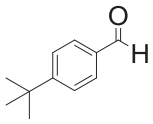
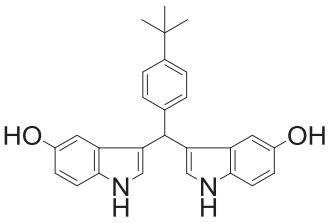
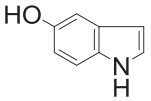
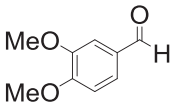
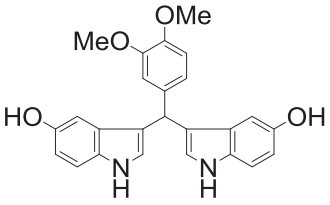
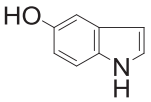
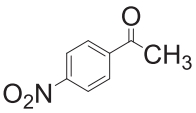
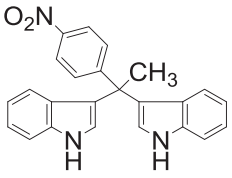
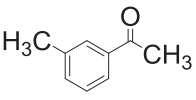
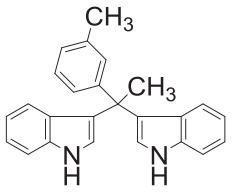
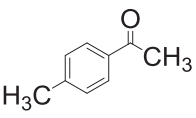
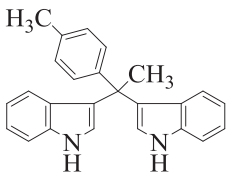
Entry	Substituted Indole	Carbonyl compound	Product	Conventional		Ultrasound	
				Time (h)	Yield (%)	Time (min)	Yield (%)
3i				1.4	68	10	95
3j				1.5	70	14	94
3k				1.3	84	10	90
3l				1.0	72	15	92
3m				1.6	68	20	88
3n				1.3	79	18	90

Table 5

The IC_{50} values of the compounds **3a-n** in DPPH, H_2O_2, and NO methods.

Compound. No.	IC_{50} values (μg/mL)		
	DPPH method	H_2O_2 method	NO method
3a	63.22	72.40	68.90
3b	52.45	61.83	54.70
3c	–	–	–
3d	–	–	–
3e	–	–	–
3f	79.14	82.72	80.14
3g	45.78	49.13	48.50
3h	81.48	89.25	84.52
3i	–	–	–
3j	42.70	49.62	46.80
3k	40.15	48.43	43.27
3l	–	–	–
3m	67.50	73.30	70.45
3n	54.18	61.83	60.02
Ascorbic Acid	33.50	39.97	37.56

DPPH, 2,2-diphenyl-1-picrylhydrazyl; NO, nitric oxide.

Thus, the reaction of indole (**1**) with carbonyl compounds (**2**) led to the formation of bis(indolyl) methane derivatives (**3a-n**) (Scheme 1) under the optimized reaction conditions in both conventional and ultrasonication methodologies (Table 4).

ANTIOXIDANT ACTIVITY

The compounds **3a-n** were tested for antioxidant activity by 2,2-diphenyl-1-picrylhydrazyl (DPPH) [22], nitric oxide (NO) [23], and H_2O_2 [24] methods. Ascorbic acid was used as standard control. This radical scavenging activity (RSA) was calculated using the following equation.

$$\%\mathrm{RSA} = [(A_C - A_S)/A_C] \times 100,$$

where A_C is the absorbance of the control and A_S is the absorbance of the tested compound. The antioxidant activity was also expressed as IC_{50} value that was defined as the concentration (in μg/mL**)** of which compound at which formation of DPPH, NO, and H_2O_2 radicals were inhibited by 50%.

The compounds **3g, 3j,** and **3k** proved to exhibit potent RSA; this may be due to the presence of electron donating groups such as OH, OMe, and Me in phenyl ring of bis (indolyl)methane derivatives as shown in Table 5 and Figures 1–3. In all three methods 3,3″-((3,4-dimethoxyphenyl)methylene)bis(1H-indol-5-ol) **(3k)** exhibited highest DPPH, NO, and H_2O_2 RSA with IC_{50} as 40.15, 43.27, and 48.43 when compared with other compounds. The compounds **3a, 3b, 3g**, **3m,** and **3n** showed good to moderate antioxidant activity, whereas the compounds **3f** and **3h** displayed least

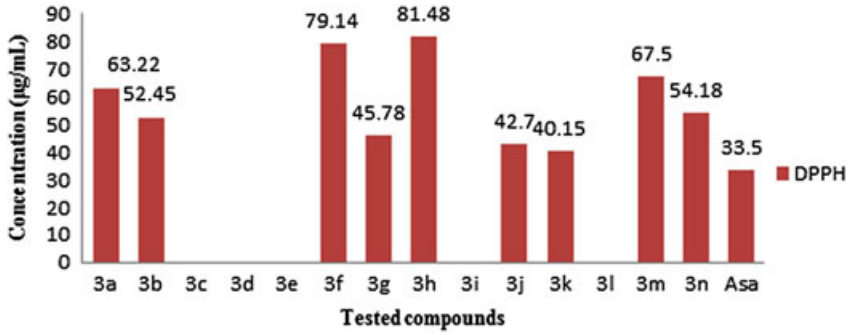


Figure 1. 2,2-Diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity IC_{50} values. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

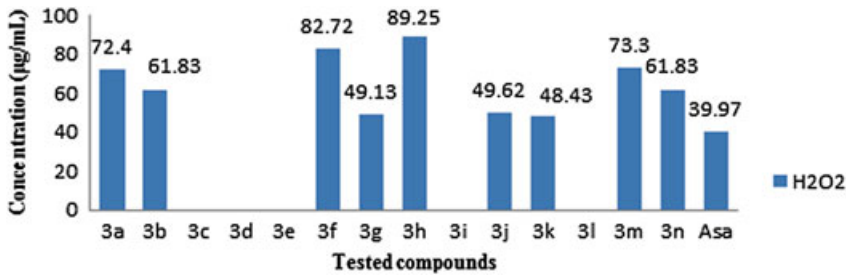


Figure 2. H_2O_2 radical scavenging activity IC_{50} values. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

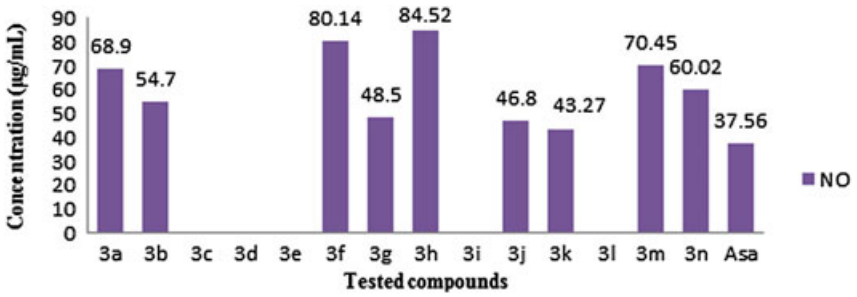


Figure 3. Nitric oxide (NO) radical scavenging activity IC_{50} values. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

activity. However, the compounds **3c, 3d, 3e, 3i,** and **3l** exhibited no activity.

CONCLUSIONS

The reaction of indole (**1**) with carbonyl compounds (**2**) in the presence of 5 mol% benzenesulfonic acid as catalyst in acetonitrile was carried out to obtain bis(indolyl) methane derivatives (**3a-n)** adopting conventional and ultrasonication methodologies. It was observed that the reaction proceeded in shorter reaction times and in high yield in ultrasonication methodology when compared with conventional method. All the synthesized compounds were tested for antioxidant activity. Among all the tested compounds, **3k** exhibited pronounced antioxidant activity.

EXPERIMENTAL

General. All the chemicals were purchased from commercial sources and used without further purification. Ultrasonication was performed in a Bandelin Sonorex RK 102H (ProfiLab24 GmbH, Berlin, Germany) ultrasonic bath operating at frequency of 35 KHz. Melting points were determined in open capillaries on a Mel-Temp apparatus and are uncorrected. The purity of the compounds was checked by thin-layer chromatography (TLC) (silica gel H, British Drug Houses (BDH), ethyl acetate/hexane, 1:3). Infrared (IR) spectra were recorded on a Thermo Nicolet IR 200 FT-IR spectrometer (Shimadzu Corporation, Kyoto, Japan) as KBr pellets, and the wave numbers are given in cm^{-1}. ^1H NMR spectra were recorded in $CDCl_3$/DMSO-d_6 on a Varian Mercury Plus spectrometer (Agilent Technology, California, USA) at 400 MHz. ^{13}C NMR spectra were recorded in $CDCl_3$/DMSO-d_6 on Varian Gemini spectrometer (Agilent Technology, California, USA) at 200 MHz. All chemical shifts are reported in δ (ppm) using tetramethylsilane as an internal standard. Mass spectra were recorded with PE Sciex model API 3000 spectrometer (Perkin Elmer, California, USA). The microanalyses were performed on a Perkin-Elmer 240C elemental analyzer (Massachusetts, USA). The progress of the reaction was monitored by TLC using silica gel plates (silica gel 60 F254 0.25 mm), and components were visualized by observation under ultraviolet (UV) light (254 and 365 nm).The antioxidant activity is carried out by measuring the absorbance of the test solution using UV–visible spectrometer, Shimadzu UV-2450 (Shimadzu Corporation, California, USA).

General procedure for the synthesis of bis(indolyl)methane derivatives (3a-n) under conventional method. To a stirred solution of substituted indole (**1**) (2.0 mmol) and carbonyl compound (**2**) (1.1 mmol) in acetonitrile (5 mL), benzenesulfonic acid (0.05 mmol) was added and continued the stirring at room temperature for 1–2.5 h. After completion of the reaction (monitored by TLC), the reaction mixture was extracted with dichloromethane. The organic layer was washed with brine solution, dried over an Na_2SO_4 and filtered. The solvent was removed under vacuum, and resultant crude product was purified by column chromatography (silica gel, 60–120 mesh) using ethyl acetate-hexane (1:3) as an eluent.

General procedure for the synthesis of bis(indolyl)methane derivatives (3a-n) under ultrasound irradiation method. To a solution of substituted indole (**1**) (2.0 mmol) and carbonyl compound (**2**) (1.1 mmol) in acetonitrile (3 mL), benzenesulfonic acid (0.05 mmol) was added and subjected to ultrasound irradiation at a frequency of 35 KHz at room temperature for 5–20 min. The progress of the reaction was monitored by TLC. After completion of the reaction, the contents of the flasks were extracted with dichloromethane. The dichloromethane layer was washed with brine solution, dried, and filtered. Removal of the solvent under reduced pressure gave crude product which was purified by column chromatography (silica gel, 60–120 mesh) using ethyl acetate-hexane (1:3) as an eluent.

3,3''-(Phenylmethylene)bis(1H-indole) (3a). Brick Red solid, mp 126–127°C; IR (KBr cm^{-1}): 3364 (NH), 1625 (C = C); ^1H NMR (400 MHz, DMSO-d_6): δ 5.87 (s, 1H, Ar-CH), 6.70–7.89 (m, 15H, Ar-H), 10.60 (bs, 2H, NH) ppm; ^{13}C NMR (200 MHz, DMSO-d_6): δ 39.2 (Ar-CH), 112.4, 116.4, 120.3, 121.7, 123.6, 124.7, 125.4, 126.2, 130.4, 135.6, 138.2, 139.7 ppm (aromatic carbons). MS

(ES): *m/z* 323.1473 $[M + H]^+$. *Anal*. Calcd. for $C_{23}H_{18}N_2$: C 85.68; H 5.63; N 8.69. Found: C 85.80; H 5.66; N 8.91%.

3,3"-((3,4-Dimethoxyphenyl)methylene)bis(1H-indole) (3b). Red solid, mp 196–198°C; IR (KBr cm^{-1}): 3358 (NH), 1621 (C = C); ^1H NMR (400 MHz, DMSO-d_6): δ 3.64 (s, 3H, $-OCH_3$), 3.70 (s, 3H, $-OCH_3$), 5.77 (s, 1H, Ar-CH), 6.80–7.38 (m, 13H, Ar-H), 10.76 (bs, 2H, NH) ppm; ^{13}C NMR (200 MHz, DMSO-d_6): δ 40.2 (Ar-CH), 55.4 (Ar-OCH_3), 111.3, 111.5, 112.5, 118.0, 118.3, 119.1, 120.1, 120.7, 123.4, 126.6, 136.5, 137.4, 146.8, 148.3 ppm (aromatic carbons). MS (ES): *m/z* 383.1672 $[M + H]^+$. *Anal*. Calcd. for $C_{25}H_{22}N_2O_2$: C 78.51; H 5.56; N 7.32. Found: C 78.61; H 5.55; N 7.48%.

4-(Di(1H-indol-3-yl)methyl)benzonitrile (3c). Slight brown solid, mp 205–207°C; IR (KBr cm^{-1}): 3374 (NH), 1633 (C = C); ^1H NMR (400 MHz, $CDCl_3$): δ 5.93 (s, 1H, Ar-CH), 6.66–7.59 (m, 14H, Ar-H), 7.97 (bs, 2H, NH) ppm; ^{13}C NMR (200 MHz, DMSO-d_6): δ 38.7 (Ar-CH), 108.5, 111.4, 116.7, 118.3, 118.8, 118.9, 120.9, 123.7, 126.3, 129.2, 132.0, 136.5, 150.7 ppm (aromatic carbons). MS (ES): *m/z* 348.1402 $[M + H]^+$. *Anal*. Calcd. for $C_{24}H_{17}N_3$: C 82.97; H 4.93; N 12.10. Found: C 83.08; H 4.95; N 12.30%.

3,3"-((4-Nitrophenyl)methylene)bis(1H-indole) (3d). Yellow solid, mp 217–219°C. IR (KBr cm^{-1}): 3372 (NH), 1629 (C = C); ^1H NMR (400 MHz, DMSO-d_6): δ 5.98 (s, 1H, Ar-CH), 6.72–8.12 (m, 14H, Ar-H), 10.90 (bs, 2H, NH) ppm; ^{13}C NMR (200 MHz, DMSO-d_6): δ 40.3 (Ar-CH), 111.5, 116.6, 118.3, 118.8, 121.0, 123.3, 123.9, 126.1, 129.4, 136.7, 145.6, 153.0 ppm (aromatic carbons). MS (ES): *m/z* 368.1325 $[M + H]^+$. *Anal.* Calcd. for $C_{23}H_{17}N_3O_2$: C 75.91; H 4.66; N 11.44. Found: C 76.05; H 4.70; N 11.61%.

3,3"-((3-Nitrophenyl)methylene)bis(1H-indole) (3e). Brick red solid, mp 154–156°C; IR (KBr cm^{-1}): 3378 (NH), 1635 (C = C); ^1H NMR (400 MHz, $CDCl_3$): δ 5.99 (s, 1H, Ar-CH), 7.98 (bs, 2H, NH), 6.68–8.21 (m, 14H, Ar-H) ppm; ^{13}C NMR (200 MHz, $CDCl_3$): δ 39.9 (Ar-CH), 111.2, 118.1, 119.4, 121.3, 122.1, 123.4, 123.6, 126.5, 129.0, 134.8, 136.6, 146.3, 148.3 ppm (aromatic carbons). MS (ES): *m/z* 368.1312 $[M + H]^+$. *Anal.* Calcd. for $C_{23}H_{17}N_3O_2$: C 75.91; H 4.66; N 11.44. Found: C 76.01; H 4.68; N 11.63%.

3,3"-((4-Chlorophenyl)methylene)bis(1H-indole) (3f). Brownish red solid, mp 101–103°C; IR (KBr cm^{-1}): 3380 (NH), 1626 (C = C); ^1H NMR (400 MHz, $CDCl_3$): δ 5.86 (s, 1H, Ar-CH), 6.66–7.39 (m, 14H, Ar-H), 7.95 (bs, 2H, NH) ppm; ^{13}C NMR (200 MHz, DMSO-d_6): δ 40.9 (Ar-CH), 111.4, 117.4, 118.1, 118.9, 120.8, 123.5, 126.4, 127.8, 130.0, 130.1, 136.5, 143.9 ppm (aromatic carbons). MS (ES): *m/z* 357.0977 $[M + H]^+$. *Anal.* Calcd. for $C_{23}H_{17}ClN_2$: C 77.41; H 4.80; N 7.85. Found: C 77.54; H 4.83; N 8.10%.

3,3"-((4-(Tert-butyl)phenyl)methylene)bis(1H-indole) (3g). Yellow soild, mp 70-72°C; IR (KBr cm^{-1}): 3375 (NH), 1622 (C = C); ^1H NMR (400 MHz, DMSO-d_6): δ 1.23 (s, 9H, CH_3), 5.78 (s, 1H, Ar-CH), 6.64–7.32 (m, 14H, Ar-H), 10.59 (bs, 2H, NH) ppm; ^{13}C NMR (200 MHz, DMSO-d_6): δ 31.5 (Ar-CH_3), 36.2 ($C(CH_3)_3$), 39.4 (Ar-CH), 102.3, 111.2, 111.4, 111.7 ,122.9 ,124.2, 126.9, 127.5, 131.2, 141.2, 146.2, 149.0 ppm (aromatic carbons). MS (ES): *m/z* 379.2099 $[M + H]^+$. *Anal*. Calcd. for $C_{27}H_{26}N_2$: C 85.68; H 6.92; N 7.40%. Found: C 85.79; H 6.90; N 7.61%.

4-(Bis(5-hydroxy-1H-indol-3-yl)methyl)benzonitrile (3h). Brick red solid, mp 209–211°C; IR (KBr cm^{-1}): 3456 (OH), 3384 (NH), 1631 (C = C), 1574 (C = N); ^1H NMR (400 MHz, DMSO-d_6): δ 5.69 (s, 1H, Ar-CH), 6.55–7.75 (m, 12H, Ar-H), 8.48 (s, 2H, OH), 10.54 (bs, 2H, NH) ppm; ^{13}C NMR (200 MHz, DMSO-d_6): δ 40.6 (Ar-CH), 102.9, 108.4, 111.3, 111.7, 115.7, 119.0, 124.1, 127.0, 129.2, 131.1, 131.9, 150.0, 150.8 ppm (aromatic carbons). MS (ES): *m/z* 380.1299 $[M + H]^+$. *Anal*. Calcd. for $C_{24}H_{17}N_3O_2$: C 75.97; H 4.52; N 11.08. Found: C 76.05; H 4.54; N 11.24%.

3,3"-((4-Nitrophenyl)methylene)bis(1H-indol-5-ol) (3i). Yellow solid, mp 218–220°C; IR (KBr cm^{-1}): 3446 (OH), 3380 (NH), 1628 (C = C); ^1H NMR (400 MHz, DMSO-d_6): δ 5.77 (s, 1H, Ar-CH), 6.55–8.16 (m, 12H, Ar-H), 8.48 (s, 2H, OH), 10.59 (bs, 2H, NH) ppm; ^{13}C NMR (200 MHz, DMSO-d_6): δ 41.0 (Ar-CH), 102.9, 111.3, 111.8, 115.6, 123.2, 124.2, 127.0, 129.3, 131.1, 145.6, 150.0, 153.0 ppm (aromatic carbons). MS (ES): *m/z* 400.1236 $[M + H]^+$. *Anal*. Calcd. for $C_{23}H_{17}N_3O_4$: C 69.17; H 4.29; N 10.52. Found: C 69.27; H 4.32; N 10.71%.

3,3"-((4-(Tert-butyl)phenyl)methylene)bis(1H-indol-5-ol) (3j). Pink solid, mp 144–146°C; IR (KBr cm^{-1}): 3448 (OH), 3388 (NH), 1634 (C = C); ^1H NMR (400 MHz, DMSO-d_6): δ 1.25 (s, 9H, CH_3), 5.52 (s, 1H, Ar-CH), 6.54–7.28 (m, 12H, Ar-H), 8.43 (s, 2H, OH) 10.40 (bs, 2H, NH) ppm; ^{13}C NMR (200 MHz, DMSO-d_6): δ 31.2 (CH_3), 34.0 ($C(CH_3)_3$), 55.4 (Ar-CH), 103.1, 111.0, 111.5, 117.1, 123.8, 124.5, 127.2, 127.7, 131.0, 141.8, 147.6, 149.7 ppm (aromatic carbons). MS (ES): *m/z* 411.1997 $[M + H]^+$. *Anal*. Calcd. for $C_{27}H_{26}N_2O_2$: C 79.00; H 6.38; N 6.82. Found: C 79.12; H 6.40; N 6.95%.

3,3"-((3,4-Dimethoxyphenyl)methylene)bis(1H-indol-5-ol) (3k). Brick red solid, mp 111–113°C; IR (KBr cm^{-1}): 3320 (NH), 1568 (C = N), 1633 (C = C); ^1H NMR (400 MHz, DMSO-d_6): δ 3.60 (s, 3H, $-OCH_3$), 3.64 (s, 3H, $-OCH_3$), 5.72 (s, 1H, Ar-CH), 6.85–7.36 (m, 11H, Ar-H), 8.42 (s, 2H, OH) 10.72 (bs, 2H, NH) ppm; ^{13}C NMR (200 MHz, DMSO-d_6): δ 40.1 (Ar-CH), 55.5 (Ar-OCH_3), 102.5, 111.8, 115.8, 120.1, 122.8, 123.8, 126.8, 129.7, 130.7, 137.2, 139.6, 144.9, 150.1, 153.5 ppm (aromatic carbons). MS (ES): *m/z* 415.1583 $[M + H]^+$. *Anal*. Calcd. for $C_{25}H_{22}N_2O_4$: C 72.45; H 5.35; N 6.76. Found: C 72.41; H 5.34; N 6.81%.

3,3''-(1-(4-Nitrophenyl)ethane-1,1-diyl)bis(1H-indole) (3l). Yellow solid, mp 246–248°C; IR (KBr cm^{-1}): 3342 (NH), 1642 (C = C); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.36 (s, 3H, CH_3), 6.71–8.05 (m, 14H, Ar-H), 10.72 (bs, 2H, NH) ppm; ^{13}C NMR (200 MHz, DMSO-d_6): δ 28.8 (Ar-CH_3), 39.4 (Ar-CH), 111.6, 118.1, 118.1, 120.6, 121.3, 122.8, 123.5, 125.6, 126.5 128.9, 137.0, 145.3 ppm (aromatic carbons). MS (ES): *m/z* 382.2473 $[M + H]^+$. *Anal.* Calcd. for $C_{24}H_{19}N_3O_2$: C 75.57; H 5.02; N 11.02. Found: C 75.52; H 5.00; N 10.84%.

3,3''-(1-(m-Tolyl)ethane-1,1-diyl)bis(1H-indole) (3m). White solid, mp 160–162°C; IR (KBr cm^{-1}): 3330 (NH), 1635 (C = C); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.16 (s, 3H, CH_3), 2.21(s, 3H, Ar-CH_3) 6.69–7.31 (m, 14H, Ar-H), 10.76 (bs, 2H, NH) ppm; ^{13}C NMR (200 MHz, DMSO-d_6): δ 21.3 (Ar-CH_3), 29.1 (Ar-CH_3), 38.4 (Ar-CH), 111.4, 117.7, 120.3, 120.9, 122.8, 123.2, 124.8, 125.3, 126.1, 127.2, 128.0, 129.3, 136.9, 148.1 ppm (aromatic carbons). MS (ES): *m/z* 351.1789 $[M + H]^+$. *Anal*. Calcd. for $C_{25}H_{22}N_2$: C 85.68; H 6.33; N 7.99%. Found: C 85.75; H 6.35; N 8.14%.

3,3''-(1-(p-Tolyl)ethane-1,1-diyl)bis(1H-indole) (3n). White solid, mp 173–175°C; IR (KBr cm^{-1}): 3352 (NH), 1645 (C = C); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.25 (s, 3H, CH_3), 2.28 (s, 3H, Ar-CH_3) 6.68–7.32 (m, 14H, Ar-H), 10.74 (bs, 2H, NH) ppm; ^{13}C NMR (200 MHz, DMSO-d_6): δ 20.4 (Ar-CH_3), 29.0 (Ar-CH_3), 42.7 (Ar-CH), 111.2, 120.5, 121.4, 122.6, 123.5, 125.9, 127.4, 128.5, 129.6, 134.3, 136.2, 145.2 ppm (aromatic carbons). MS (ES): *m/z* 351.2785 $[M + H]^+$. *Anal*. Calcd. for $C_{25}H_{22}N_2$: C 85.68; H 6.33; N 7.99. Found: C 85.79; H 6.36; N 8.20%.

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