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Glacial acetic acid as an efficient catalyst for simple synthesis of dindolylmethanes

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Glacial acetic acid as a protic acid was employed as a catalyst in a solvent free condition for facile preparation of di(indolyl)methanes (DIMs) via one-pot condensation of indole with aryl or heteroaryl aldehydes. Various aryl and heteroaryl aldehydes were efficiently converted to the corresponding di(indolyl)methanes (**1a-p**) in high yields. The described novel synthetic method proposes several advantages of safety, mild condition, short reaction times, high yields, simplicity and the inexpensively glacial acetic acid compared to other catalysts.

1. Introduction

Di(indolyl)methanes (DIMs) are molecules containing two indolyl moieties connected to the same carbon. Many advances in the strategy of DIMs synthesis were published as result of the variation of the catalyst. Other factors that prompted new research include the price of catalysts, yield of products, reaction rates, simplicity of the work up procedure, green chemistry, *etc*[1a]. Di(indolyl)alkanes and their derivatives are found in bioactive metabolites of terrestrial and marine origin[1b]. A recent patent describes the synthesis of DIMs forming complex compounds with radioactive metal ions (Gd^{3+}), which are found to be useful contrast agents for radio-imaging and visualization of various tissues and organs[2]. Recently, *Maciejewska* et al[3] used DNA-based electrochemical biosensors to demonstrate that bis(5-methoxyindol-3-yl)methane, considerably reduces the growth of the cancer cell lines such as HOP-92 (lung), A498 (renal) and MDAMB-231/1TCC (breast). Their results also indicated that BIMs could potentially be applied as chemotherapeutic agents against tumors[1,3]. BIMs and tris(indolyl)methanes (TIMs), have been used as legands for the synthesis of many complex

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molecules and different properties of these complex molecules have been investigated[4-9]. The electron rich indole nucleus shows an enhanced reactivity towards carbon electrophiles that generally results in the formation of three substituted indole derivatives[10]. The 3-position of the indole is the preferred site for the electrophilic substitution reactions. 3-Alkyl or 3-acyl indoles are versatile intermediates for the synthesis of a wide range of indole derivatives[11]. A simple and direct method for the synthesis of 3-alkylated indoles involves the condensation with aliphatic or aromatic aldehydes.

Normally these reactions occur in presence of several types of catalysts for example protic or Lewis acids or ionic liquids[12-39]. As seen from these reported literature numerous catalysts can promote the reaction of aldehydes or ketones and indoles to afford 3-alkylated indole compounds in good to high yields in a reasonable time.

2. Result and Discussion

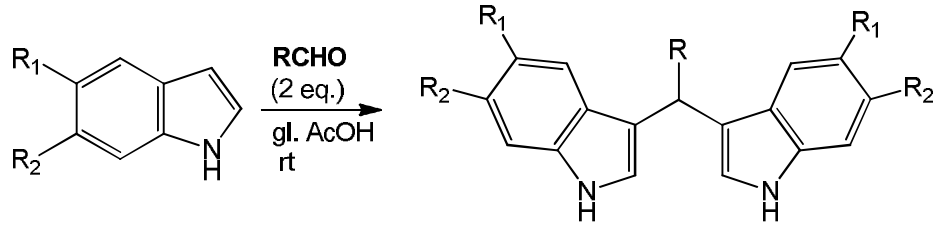
In the present work we wish to introduce AcOH as a mild and efficient catalyst for the promotion of the condensation reaction of indoles with aromatic aldehydes. In this paper we estimate the yield of BIMs *via* using glacial acetic acid in a solvent free condition with indoles and aromatic aldehydes. Some of these BIMs have been reported by using different types of catalysts as shown above. It has been found that, glacial acetic acid acts as a protic acid without solvent to catalyze the reaction of indoles (two equivalent moles) and aryl or heteroaryl aldehydes (one equivalent mole). Acetic acid has only been reported as a catalyst in the preparation of BIMs derived from 4-cyanoindole and formaldehyde solution. The reaction was done by using drops of acetic acid and finished after about 60 h[23,24]. In our present work *via* glacial acetic acid as a solvent (5 ml) the corresponding BIMs were given in high yields (73 - 98%) and after few hours (4 – 6 h) of stirring at room temperature. In comparison to the reported methods, glacial acetic acid under a solvent free condition was found to be an efficient catalyst in terms of handling, temperature, yields and reaction times, (**Scheme 1** and **Table 1**).

Table 1. Synthesized BIMs

Entry	Aldehydes	Indoles	Product	Reaction time (h)	Yield (%)
1	R = Ph	Indole	**1a**	5	90
2	R = *p*-NO2-Ph	"	**1b**	4	98
3	R = *p*-Br- Ph	"	**1c**	6	99
4	R = *p*-Cl- Ph	"	**1d**	5	76
5	R = *p*-N(Me)2- Ph	"	**1e**	5	91
6	R = *m*-Br-Ph	"	**1f**	4	88
7	R= *m*-OCH_2Ph- Ph	"	**1g**	5	87
8	R = *p,m*-OH- Ph	"	**1h**	6	73
9	R=*p*-MeO-*m*-OCH_2Ph-Ph	"	**1i**	4	89
10	R=*m*-MeO-*p*-OCH_2Ph-Ph	"	**1j**	5	92
11	R = *m*-Me,2,4,6-tri-F-Ph	"	**1k**	6	77
12	R = 1-naphthyl	"	**1l**	4	97
13	R = 3-pridyl	"	**1m**	6	95
14	R = 3-indolyl	"	**1n**	6	98
15	R=*p*-MeO-*m*-OCH_2Ph-Ph	5-Cl-indole	**1o**	4	91
16	R=*p*-MeO-*m*-OCH_2Ph-Ph	6-Cl-indole	**1p**	4	93

A series of substituted aryl or heteroaryl aldehydes were efficiently converted to the corresponding BIMs **1a-p**, as shown in **Table 1**, which give the reaction times and the formed yields. Concerning the substituent on the carbonyl compounds, we can summarize that the presence of either electron donating group (such as dimethylamino, methoxy, benzyloxy or hydroxy) or electron with-drawing group (e.g. nitro, chloro, bromo or trifluoro) has not noticeable effect on the reaction time or the percent of the yield. So we can conclude that glacial acetic acid promotes the electrophilic substitution reaction of indoles with aromatic aldehydes whatever the substituent on the aromatic aldehyde and this makes it different from all the catalysts used in these reactions. In addition the substituent on the indole phenyl ring (5-chloro and 6-chloro indole) plays a role in

the reaction which partially enhances the product formation as indicated by the same reaction time and higher yield (entry 15 and 16). BIMs **1a-f, and 1l-n** are known[12-39] and their identities were proven by means of MS, NMR, and IR spectra, and the other BIMs (**1g-k, 1o-p**), are novel and could not be found in the literature.



1a-p

Scheme 1. Synthesis of BIMs.

3. Conclusion

Glacial acetic acid was used as a catalyst and solvent for a facile synthesis of di(indolyl)methanes (DIMs) with high yields *via* one-pot condensation of indole with aryl or heteroaryl aldehydes. The described novel synthesis method proposes several advantages of safety, mild condition, short reaction times, high yields, simplicity and the inexpensively glacial acetic acid compared to other catalysts.

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4. Experimental

4.1. Materials and Methods

The melting points were measured on a Boetius-Mikroheiztisch the company "VEB weighing. Rapido Radebeul / VEB NAGEMA "measured and are uncorrected. TLC for the analyzes were with aluminium foil fluorescent indicator from Merck KGaA (silica gel 60 F254, layer thickness 0.2 mm). R_f -values (run level relative to the solvent front). The separations were with column chromatography at atmospheric pressure on silica gel 60 (Grain size from 0.063 to 0.200 mm) from Merck KGaA. NMR spectra were recorded on a "Gemini 2000" (400/100 MHz). The ATR spectra were recorded on a FT-IR spectrometer "IFS 28" by "Bruker. The ESI mass spectra were recorded on a "Finnigan LCQ Classic". The EI mass spectra were recorded on an "Intel 402".

4.2. General procedure for the preparation of compounds 1a-p : In a flask containing 5 ml of glacial acetic acid and 2 mmol of indole (0.234 gm) or 5-chloroindole 0.303 gm or 6-chloroindole 0.303 gm was added under stirring until all the indole was dissolved. Then 1 mmol of the appropriate aromatic or heterocyclic aldehyde was added under vigorous stirring. The reaction mixture was allowed to stir over 4 to 6 h, where the reaction solution turned from light yellow to light pink to dark red colour. The product was detected by TLC (100 % CH_2Cl_2), and when the reaction was finished 10 ml of water were added and the solution was extracted with ethyl acetate, washed with water and 100 ml brine, dried over anhydrous sodium sulphate and concentrated in vacuum. The product was purified by passing over a column and eluted with dichloromethane.

4.3. Physical and Spectral Data

3,3'-(Phenylmethylene)bis(1H-indole) (1a)*:* $C_{23}H_{18}N_2$, 322.40 g/mol, mp 126 - 127 ^{0}C, pink powder, ESI-MS: (m/z) = 321.32 [M^+-H], IR (ATR,cm^{-1}) = 3141 (NH), ^{1}H-NMR: (400 MHz, acetone-d_6) δ (ppm) = 5.90 (s, 1H, CH), 6.79 (d, 2H, *J*=1.5 Hz), 6.87 (t, 2H, *J*=7.2 Hz), 7.04 (t, 2H, *J*=7.6 Hz), 7.16 (d, 1H, *J*=7.3 Hz), 7.25 (t,

2H, *J*=7.5 Hz), 7.32 - 7.39 (m, 6H), 9.99 (s, 2H, 2NH), ^{13}C-NMR: (100 MHz, $CDCl_3$) δ (ppm) = 40.26 (CH), 110.94, 119.68, 120.59, 121.79, 121.85, 123.49, 123.99, 125.99, 126.98, 128.08, 128.59, 136.55, 143.88, EA: calcd. C, 85.68, H, 5.63, N, 8.69, found C, 85.72, H, 5.58, N, 8.66, R_f: 0.76 (CH_2Cl_2), yield: (580 mg), 90 %.

3,3′(4-Nitrophenyl)methylene)bis(1H-indole (1b)*:* $C_{23}H_{17}N_3O_2$, 367.40 g/mol, mp 219 - 221 ^{0}C, yellow powder, ESI-MS: (m/z) = 366.29 [M^+-H], IR (ATR, cm^{-1}) = 1456, 1507 (C-NO_2), 3052 (CH), 3455 (NH), ^{1}H-NMR: (400 MHz, DMSO-d_6) δ (ppm) = 5.98 (s, 1H, CH), 6.83 - 6.86 (m, 4H), 7.02 (d, 2H, *J*=8 Hz), 7.26 (d, 2H, *J*=7.9 Hz), 7.35 (d, 2H, *J*=8.1 Hz), 7.56 (d, 2H, *J*=8.72 Hz), 8.09 (d, 2H, *J*=8.92 Hz), 10.88 (s, br, 2H, 2NH), ^{13}C-NMR: (100 MHz, DMSO-d_6) δ (ppm) = 54.82 (CH), 111.51, 116.62, 118.36, 118.79, 121.04, 123.27, 123.74, 126.26, 129.32, 136.48, 145.65, 152.94, EA calcd. C, 75.19, H, 4.66, N, 11.44, found C, 75.28, H, 4.51, N, 11.60, R_f: 0.29 (CH_2Cl_2), yield: (720 mg), 98 %.

3,3'-((4-bromophenyl)methylene)bis(1H-indole) (1c): $C_{23}H_{17}BrN_2$, 401.30 g/mol, mp. 100 - 103 ^{0}C, yellow crystals, ESI-MS: (m/z) = 402 [M^++H], IR (ATR,cm^{-1}) = 4356 (NH), ^{1}H-NMR: (400 MHz, acetone-d_6) δ (ppm) = 5.91 (s, 1H, CH), 6.79 (d, 2H, *J*=7.2 Hz), 6.87 (t, 2H, *J*=7.5 Hz), 7.07 (t, 2H, *J*=7.4 Hz), 7.28 (d, 2H, *J*=8 Hz), 7.36 -7.40 (m, 6H), 10.93 (s, 2H, 2NH), ^{13}C-NMR: (400 MHz, acetone-d_6) = 57.50 (CH), 111.40, 117.48, 118.14, 118.99, 119.89, 120.80, 120.99, 123.48, 124.99, 127.89, 129.99, 136.50, 144.02, R_f 0.65 (CH_2Cl_2), yield: (700 mg), 99 %.

3,3'-((4-Chlorophenyl)methylene)bis(1H-indole) (1d)*:* $C_{23}H_{17}N_2Cl$, 356.85 g/mol, mp 104 - 106 ^{0}C, pink powder, ESI-MS: (m/z) = 355.11 [M^+-H], IR (ATR, cm^{-1}) = 3410 (NH), ^{1}H-NMR: (400 MHz, DMSO-d_6) δ (ppm) = 5.85 (s, 1H, CH), 6.83 (d, 2H, *J*=7.2 Hz), 6.86 (t, 2H, *J*=7.4 Hz), 7.04 (t, 2H, *J*=7.6 Hz), 7.28 (d, 2H, *J*=7.9 Hz), 7.29 - 7.36 (m, 6H), 10.83 (s, 2H, 2NH), ^{13}C-NMR: (100 MHz, DMSO-d_6) = 59.65 (CH), 111.38, 117.48, 118.14, 118.89, 119.85, 123.48, 124.99, 127.84, 129.97, 130.16, 136.49, 143.87, R_f 0.87 (CH_2Cl_2), yield: (649 mg), 76 %.

4-Di(1H-indol-3-yl)methyl)-N,N-dimethylaniline (1e)*:* $C_{25}H_{23}N_3$, 365.47 g/mol, mp. 225 - 226 ^{0}C, pink powder, ESI-MS: (m/z) = 366.25 [M^++H], 364.38 [M^+-H], IR (ATR, cm^{-1}) = 3314 (NH), ^{1}H-NMR: (400 MHz, DMSO-d_6) δ (ppm) = 4.60 (s,br., 6H, $2CH_3$), 5.89 (s, 1H, CH), 6.84 - 6.88 (m, 4H), 7.03 (t, 2H, *J*=7.99 Hz), 7.28 (d, 2H, *J*=7.9 Hz), 7.34 (d, 2H, *J*=8.1 Hz), 7.49 (t, 4H, *J*=10.6 Hz), 10.84 (s, 2H, 2NH), ^{13}C-NMR: (100 MHz, DMSO-d_6) δ (ppm) = 40.13 (CH_3), 43.62 (CH_3), 45.07 (CH), 111.39, 114.52, 117.43, 118.13, 118.85, 119.08, 120.83, 121.40, 123.47, 124.23, 126.37, 129.47, 136.46, 141.84, EA: calcd. C, 82.16; H, 6.34; N, 11.50, found C, 82.20, H, 6.37, N, 11.53, R_f 0.29 (CH_2Cl_2), yield: (665 mg), 91 %.

3,3'-((3-Bromophenyl)methylene)bis(1H-indole) (1f)*:* $C_{23}H_{17}BrN_2$, 401.30 g/mol, mp. 93 - 95 ^{0}C, red crystals, ESI-MS: (m/z) = 401.26 [M^++H], 399.31 [M^+-H], IR: (ATR, cm^{-1}) = 3405 (NH), ^{1}H-NMR: (400 MHz, DMSO-d_6) δ (ppm) = 5.86 (s, 1H, CH), 6.85 - 6.86 (m, 3H), 7.03 (t, 2H, *J*=7.6 Hz), 7.22 (t, 1H, *J*=7.8 Hz), 7.28 (d, 2H, *J*=7.9 Hz), 7.34 - 7.37 (m, 5H), 7.49 (s, 1H), 10.84 (s, 2H, 2NH), ^{13}C-NMR: (100 MHz, DMSO-d_6) δ (ppm) = 39.16 (CH), 111.38, 117.20, 118.16, 118.80, 120.84, 121.25, 123.51, 126.32, 127.23, 128.54, 130.08, 130.69, 136.42, 147.78, EA: calcd. C, 68.84, H, 4.27, Br, 19.91, N, 6.98, found C, 68.90, H, 4.30, Br, 19.95, N, 7.00, R_f-Value: 0.74 (CH_2Cl_2), yield: (787 mg), 88 %.

3,3′(3-Benzyloxy)phenyl)methylene)bis(1H-indole (1g)*:* $C_{30}H_{24}N_2O$, 428.52 g/mol, mp. 190 - 192 ^{0}C, white powder, ESI-MS: (m/z) = 428.24 [M^+-H], IR (ATR, cm^{-1}) = 1262 (C-O), 2852, 3034 (CH), 3425 (NH), ^{1}H-NMR: (400 MHz, acetone-d_6) δ (ppm) = 5.01 (s, 2H, CH_2), 5.90 (s, 1H, CH), 6.82 (d, 2H, *J*=7.5 Hz), 6.85 (d, 2H, *J*=7.2 Hz), 6.90 (t, 2H, *J*=7.5 Hz), 7.00 - 7.11 (m, 4H), 7.18 (t, 1H, *J*=7.9 Hz), 7.26 - 7.33 (m, 2H), 7.37 - 7.39 (m, 6H), 9.95 (s, br., 2H, 2NH), ^{13}C-NMR: (100 MHz, acetone-d_6) δ (ppm) = 41.18 (CH), 70.31 (CH_2-O), 112.06, 112.91, 116.41, 119.26, 119.63, 120.21, 121.98, 122.13, 123.51, 124.45, 128.04, 128.32, 128.37,

129.07, 129.23, 129.69, 137.98, 138.38, 147.55, 159.66 , EA: calcd. C, 84.08; H, 5.65; N, 6.54, found C, 84.12, H, 5.55, N, 6.58, R_f: 0.79 (CH_2Cl_2), yield: (746 mg), 87 %.

***4-(Di(1H-indol-3-yl)methyl)benzene-1,2-diol (1h)**:* $C_{23}H_{18}N_2O_2$, 354.40 g/mol, mp. 105 – 107 ^{0}C, light brown powder, ESI-MS: (m/z) = 392.89 [M^++K], 354.25 [M^+], 353.24 [M^+-H], IR: (ATR, cm^{-1}) = 1215 (C-O), 2922, 3051 (CH), 3400 (NH), ^{1}H-NMR: (400 MHz, acetone-d_6) δ (ppm) = 5.77 (s, 1H, CH), 6.45 (s, 1H), 6.76 (d, 2H, *J*=8.9 Hz), 6.86 - 6.89 (m, 2H), 7.04 (s, 2H), 7.29 (s, 1H), 7.35 (s, 4H), 7.55 (s, 1H), 9.89 (s, 2H, 2NH), EA: calcd. C, 77.95; H, 5.12; N, 7.90, found C, 78.01, H, 5.20, N, 7.96, R_f: 0.62 (CH_2Cl_2), yield: (517 mg), 73 %.

***3,3′-(3-Benzyloxy)-4-methoxyphenyl)methylene)bis(1H-indole (1i)**:* $C_{31}H_{26}N_2O_2$, 458.55 g/mol, mp 75 - 78 ^{0}C, orange crystals, ESI-MS: (m/z) = 481.16 [M^++Na], 457.24 [M^+-H], IR (ATR, cm^{-1}) = 1262 (C-O), 2850, 2925 (CH), 3398 (NH), ^{1}H-NMR: (400 MHz, DMSO-d_6) δ (ppm) = 3.71 (s, 3H, OMe), 4.95 (s, 2H, CH_2), 5.71 (s, 1H, CH), 6.74 - 6.76 (m, 2H), 6.81 - 6.86 (m, 4H), 7.02 (t, 2H, *J*=7.5 Hz), 7.06 (s, 1H), 7.23 (d, 2H, *J*=7.9 Hz), 7.29 - 7.31 (m, 6H), 7.34 (s, 1H), 10.73 (s, 2H, 2NH), ^{13}C-NMR:(100 MHz, DMSO-d_6) δ (ppm) = 55.59 (CH), 59.70 (OMe), 70.08 (OCH_2), 111.29, 111.98, 114.94, 118.00, 118.24, 119.03, 120.71, 123.29, 126.24, 126.56, 127.63, 127.75, 127.86, 128.18, 128.35, 136.49, 137.09, 137.39, 147.14, 147.38, EA: calcd. C, 81.20; H, 5.72; N, 6.11, found C, 81.22, H, 5.75, N, 6.14, R_f 0.79 (CH_2Cl_2), yield: (816 mg), 89 %.

***3,3′-((4-Benzyloxy)-3-methoxyphenyl)methylene)bis(1H-indole (1j)**:* $C_{31}H_{26}N_2O_2$, 458.55 g/mol, mp 215 – 219 ^{0}C, light orange crystals, ESI-MS: (m/z) = 457.20 [M^+-H], IR: (ATR, cm^{-1}) = 1245 (C-O), 2961, 3036 (CH), 3416 (NH), ^{1}H-NMR: (400 MHz, acetone-d_6) δ (ppm) = 3.70 (s, 3H, OMe), 5.04 (s, 2H, CH_2), 5.85 (s, 1H, CH), 6.81 (s, 2H), 6.85 - 6.92 (m, 4H), 7.04 (t, 2H, *J*=7.6 Hz), 7.09 (s, 1H), 7.29 (d, 1H, *J*=7.5 Hz), 7.33 - 7.37 (m, 6H), 7.47 (d, 2H, *J*=7.7 Hz), 9.95 (s, 2H, 2NH), ^{13}C-NMR: (400 MHz, acetone-d_6) δ (ppm) = 40.75 (CH), 56.19 (OMe), 71.61 (OCH_2), 112.05, 112.10, 114.33, 114.93, 119.23, 120.09, 120.32, 121.47, 121.98, 124.32, 124.47, 128.12, 128.45, 128.49, 129.12, 138.08, 138.83, 139.31, 147.72, 150.64, EA: calcd. C, 81.20; H, 5.72; N, 6.11, found C, 81.02, H, 5.90, N, 6.22, R_f: 0.71 (CH_2Cl_2), yield: (844 mg), 92 %.

***2,4,6-(3,3′-(Trifluoro-3-methylphenyl)methylene)bis(1H-indole) (1k)**:* $C_{24}H_{17}F_3N_2$, 390.40 g/mol, mp. >350 ^{0}C, white powder, ESI-MS: (m/z) = 391.90 [M^++H], 389.31 [M^+-H], IR-Spectrum: (ATR, cm^{-1}) = 2960, 3055 (CH), 3443 (NH), ^{1}H-NMR: (400 MHz, DMSO-d_6) δ (ppm) = 3.15 (s, 3H, Me), 5.73 (s, 1H, CH), 6.86 (t, 1H, *J*=10.9 Hz), 6.99 - 7.14 (m, 2H), 7.19 (d, 1H, *J*=8.2 Hz), 7.21 - 7.29 (m, 2H), 7.35 (t, 1H, *J*=7.7 Hz), 7.44 (s, 1H), 7.66 (d, 1H, *J*=8.2 Hz), 7.74 (t, 2H, *J*=10.4 Hz), 8.37 (s, 2H, 2NH), ^{13}C-NMR: (100 MHz, DMSO-d_6) δ (ppm) = 38.87 (Me), 52.77 (CH), 109.00, 110.02, 117.32, 119.88, 120.17, 122.73, 126.12, 126.21, 127.37, 128.25, 128.78, 129.21, 134.22, 142.00, EA: calcd. C, 73.84; H, 4.39; F, 14.60; N, 7.18, found C, 74.01, H, 4.52, F, 14.52, N, 7.23, R_f: 0.71 (CH_2Cl_2), yield: (390 mg), 77 %.

***3,3′-(Naphthalen-1-ylmethylene)bis(1H-indole (1l)**:* $C_{27}H_{20}N_2$, 372.46 g/mol, mp: 252 - 255 ^{0}C, White powder, ESI-MS: (m/z) = 371.30 [M^+-H], IR: (ATR, cm^{-1}) = 2834, 3048 (CH), 3407 (NH), ^{1}H-NMR: (400 MHz, DMSO-d_6) δ (ppm) = 5.71 (s, 1H, CH), 6.59 (s, 1H), 6.68 (d, 2H, *J*=7 Hz), 6.81 (t, 2H, *J*=7.5 Hz), 6.99 (t, 2H, *J*=7.6 Hz), 7.23 (d, 4H, *J*=8.1 Hz), 7.32 (t, 2H, *J*=9 Hz), 7.41 (t, 2H, *J*=7.7 Hz), 7.73 (d, 1H, *J*=8 Hz), 7.88 (d, 1H, *J*=7.5 Hz), 8.22 (d, 1H, *J*=8 Hz), 10.74 (s, 2H, 2NH), ^{13}C-NMR: (100 MHz, DMSO-d_6) δ (ppm) = 35.33 (CH), 111.41, 117.62, 118.15, 118.84, 120.77, 123.84, 124.13, 125.15, 125.19, 125.42, 125.68, 126.43, 126.54, 128.42, 131.23, 133.49, 136.56, 140.18, EA. calcd. C, 87.07; H, 5.41; N, 7.52, found C, 87.00, H, 5.51, N, 7.55, R_f: 0.87 (CH_2Cl_2), yield: (722 mg), 97 %.

***3,3′-(Pyridin-3-ylmethylene)bis(1H-indole (1m)**:* $C_{22}H_{17}N_3$, 323.39 g/mol, mp 98 - 101 ^{0}C, light pink powder, ESI-MS: (m/z) = 324.16 [M^++H], IR (ATR, cm^{-1}) = 2917, 3055 (CH), 3403 (NH), ^{1}H-NMR: (400 MHz, DMSO-d_6) δ (ppm) = 5.70 (s, 1H, CH), 5.88 (s, 1H, CH), 6.84 (t, 4H, *J*=7.1 Hz), 7.01 (t, 2H, *J*=7.6 Hz), 7.22 -

7.29 (m, 3H), 7.32 (d, 2H, *J*=8.1 Hz), 7.65 (d, 1H, *J*=7.9 Hz), 8.34 - 8.37 (m, 1H), 8.58 (d, 1H, *J*=7.9 Hz), 10.84 (s, 2H, 2NH), ^{13}C-NMR: (100 MHz, DMSO-d_6) δ (ppm) = 54.79 (CH), 54.78 (CH), 111.45, 117.07, 118.24, 118.83, 120.94, 123.15, 123.56, 126.29, 135.47, 136.51, 140.15, 146.99, 149.50, EA: calcd. C, 81.71; H, 5.30; N, 2.99, found C, 81.90, H, 5.35, N, 13.02, R_f 0.46 (7 % MeOH/CH_2Cl_2), yield: (614 mg), 95 %.

Tri(1H-indol-3-yl)methane (1n)*:* $C_{25}H_{19}N_3$, 361.44 g/mol, mp: 235 - 240 ^{0}C, light yellow powder, ESI-MS: (m/z) = 360.32 [M^+-H], IR (ATR, cm^{-1}) = 2882, 3054 (CH), 3424 (NH), ^{1}H-NMR: (400 MHz, acetone-d_6) δ (ppm) = 6.19 (s, 1H, CH), 6.85 - 6.93 (m, 6H), 7.03 (t, 4H, *J*=7.6 Hz), 7.37 (t, 3H, *J*=7.8 Hz), 7.48 (t, 2H, *J*=7.4 Hz), 9.88 (s, 3H, 3NH), ^{13}C-NMR: (100 MHz, acetone-d_6) δ (ppm) = 31.33 (CH), 111.13, 118.95, 119.08, 120.12, 121.09, 123.17, 124.60, 127.35, 128.17, 137.19, Elemental analysis: Calcd. C, 83.08; H, 5.30; N, 11.63, found C, 83.09, H, 5.33, N,11.71, R_f-Value: 0.73 (CH_2Cl_2), yield: (708 mg), 98 %.

3,3′-((3-Benzyloxy)-4-methoxyphenyl)methylene)bis(5-chloro-1H-indole (1o): $C_{31}H_{24}Cl_2N_2O_2$, 527.44 g/mol, mp. 82 - 85 ^{0}C, ESI-MS: (m/z) = 528.18 [M^++H], IR (ATR, cm^{-1}) = 1259 (C-O), 2850, 2924 (CH), 3369 (NH), ^{1}H-NMR: (400 MHz, $CDCl_3$) δ (ppm) = 3.77 (s, 3H, OMe), 4.93 (s, 2H, CH_2), 5.52 (s, 2H, CH), 6.41 (d, 2H, *J*=7.6 Hz), 6.73 (t, 4H, *J*=7.3 Hz), 7.02 (d, 2H, *J*=7 Hz), 7.13 (d, 2H, *J*=8.6 Hz), 7.18 (dd, 6H, *J*=3.1, 7.1 Hz), 7.88 (s, 2H, 2NH), ^{13}C-NMR: (100 MHz, acetone-d_6) δ (ppm) = 39.39 (CH), 55.99 (OMe), 71.03 (OCH_2), 111.51, 111.76, 112.12, 115.37, 119.15, 121.20, 122.31, 124.77, 124.99, 126.91, 127.46, 127.50, 127.66, 127.96, 128.64, 135.04, 135.74, 137.10, 147.63, 148.36, EA: calcd. C, 70.59; H, 4.59; Cl, 13.44; N, 5.31, found C, 70.62, H, 4.55, Cl, 13.55, N, 5.51, R_f: 0.68 (CH_2Cl_2), yield: (960 mg), 91 %.

3,3/-((3-(Benzyloxy)-4-methoxyphenyl)methylene)bis(6-chloro-1H-indole (1p): $C_{31}H_{24}Cl_2N_2O_2$, 527.44 g/mol, mp. 85 – 87 ^{0}C, light orange crystals, ESI-MS: (m/z) = 526.14 [M^+-H], IR (ATR, cm^{-1}) = 1253 (C-O), 2866, 2928 (CH), 3420 (NH), ^{1}H-NMR: (400 MHz, DMSO-d_6) δ (ppm) = 3.70 (s, 3H, OMe), 4.94 (s, 2H, OCH_2), 5.69 (s, 1H, CH), 6.77 (d, 2H, *J*=2 Hz), 6.79 (d, 1H, *J*=1.9 Hz), 6.84 (t, 2H, *J*=7.9 Hz), 7.00 (d, 1H, *J*=2 Hz), 7.17 (d, 2H, *J*=8.6 Hz), 7.30 (t, H, *J*=5.7 Hz), 7.37 (d, 2H, *J*=1.6 Hz), 10.91 (s, 2H, 2NH), ^{13}C-NMR: (100 MHz, DMSO-d_6) δ (ppm) = 26.78 (CH), 55.99 (OMe), 70.41 (OCH_2), 111.47, 112.41, 115.11, 118.79, 118.95, 120.83, 121.08, 125.02, 125.79, 126.10, 127.02, 128.17, 128.29, 128.71, 128.89, 137.22, 137.40, 137.59, 147.70, 147.99, Elemental analysis: calcd. C, 70.59; H, 4.59; Cl, 13.44; N, 5.31, found C, 70.63, H, 4.72, Cl, 13.53, N, 5.34, R_f 0.68 (CH_2Cl_2), yield: (960 mg), 93 %.

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