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PHOSPHORIC ACID-ON-SILICA GEL: A GREEN CATALYST FOR THE SYNTHESIS OF SYMMETRICAL BIS(INDOLYL)ALKANES

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Abstract – Orthophosphoric acid, adsorbed on TLC-grade silica gel, has been demonstrated to be an efficient green catalyst for an expeditious and solvent-free one-step synthesis of symmetrical bis(indolyl)alkanes from the reaction of indoles with aryl aldehydes at 60-70 °C.

INTRODUCTION

Bis(indolyl)alkanes (BIAs), primarily of synthetic origin, constitute an important group of bioactive metabolites isolated from terrestrial and marine sources.[1] The BIAs have emerged in recent years as a class of compounds with potent pharmaceutical activity. The symmetrical BIAs in particular are fast proving to be useful molecules. Thus, the symmetrical bis(indolyl)methane derivatives affect the central nervous system[2] and are used as tranquilizers.[3] Bis(indol-3-yl)methane itself[4] and bis(5-methoxyindol-3-yl)methane[5] have potent anti-carcinogenic properties. Recently, oxidised bis(indol-3-yl)phenylmethane has been used as a selective colorimetric sensor,[6] which makes the symmetrical BIAs even more important.

The symmetrical BIAs are mainly prepared by the reaction of indoles or indolyl Grignard reagents with carbonyl compounds or their masked forms using acids as catalysts.[7] Most of these methods have various disadvantages like the use of stoichiometric or larger amounts of acids, creation of toxic wastes, use of expensive Lewis acids and preformed reagents, very long reaction periods and very low or widely varying yields. The principles of Green Chemistry necessitate the use and generation of non-toxic and non-hazardous chemicals and methodologies.[8] Consequently, the symmetrical BIAs have been recently synthesised in ionic liquids,[9] using solid acids like Lewis acid-supported silica gel,[10] clay,[11] zeolite,[12] ion-exchange resin[13] and heteropoly acids,[14] sometimes using ultrasound, infrared or microwave irradiation, and even in water.[15] But

even these methods suffer from drawbacks, viz. the use of hazardous chemicals in preparing the reagents,[10c,15a] long reaction times (e.g. 24 h[9a] / 48 h[13c]) and low yields of the final products (e.g. 12%[9a] / 35%[13b]).

Except for reactions in aqueous medium, which have attracted considerable attention in recent years,[16] it is advisable to avoid the use of any volatile organic compound (voc) as solvent from the point of view of green chemistry.[8] Indeed, the use of solvent-free conditions in combination with heterogeneous catalysts represents one of the powerful green technology procedures.[17] Indoles and their derivatives have been our major synthetic targets in recent years.[18] In continuation of our interest, we wanted to develop a solvent-free and environmentally benign acidic catalyst for an expeditious synthesis of the symmetrical BIAs. We have achieved success and report herein that 10 mol% of orthophosphoric acid (H_3PO_4), adsorbed on TLC-grade silica gel (SiO_2), can efficiently catalyse the reaction of indoles with mainly aryl aldehydes to form expeditiously symmetrical BIAs in excellent yields.

RESULTS AND DISCUSSION

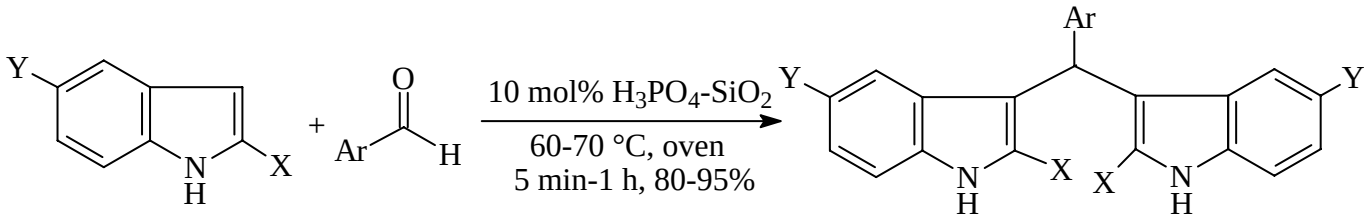
Since a solvent-free method was planned, we chose SiO_2 as the solid matrix, on which H_3PO_4 was to be adsorbed, because it possesses a large surface area but proved not to be acidic enough to catalyse the reaction of indole (**1a**) with benzaldehyde (**2a**) to form the expected symmetrical BIA, bis(indol-3-yl)phenylmethane (**3aa**) even at 60-70 °C (Entry 1; Table 1). In order to ascertain a suitable concentration of H_3PO_4, **1a** was treated with **2a** (0.75 equiv.) on SiO_2 containing 5, 10 and 20 mol% of H_3PO_4 at 60-70 °C (oven) in three separate experiments. The reactions were complete in 30, 10 and 10 min, respectively to furnish **3aa** as the sole product in comparable yields (Entries 2-4; Table 1) in each case. Just for comparison, **1a** was also treated with **2a** (0.75 equiv.) in ethyl acetate containing 10 mol% H_3PO_4 at rt and at 60-70 °C (oil bath) separately, which furnished **3aa** in 85% and 87% yields, respectively in 4.5 h and 1.5 h (Entry 5; Table 1). H_3PO_4 (10 mol%)-SiO_2 thus emerged to be the reagent of choice.

Table 1. Effect of catalysts and their concentrations on the formation of **3aa** at 60-70 °C

Entry	Catalyst	Reaction time	Yield of **3aa**
1	SiO_2[a]	2 h	Nil
2	H_3PO_4 (5 mol%)-SiO_2[a]	30 min	91%
3	H_3PO_4 (10 mol%)-SiO_2[a]	10 min / 1 h[b]	93% / 92%
4	H_3PO_4 (20 mol%)-SiO_2[a]	10 min	93%
5	H_3PO_4 (10 mol%) / EtOAc	1.5 h / 4.5 h[b]	87% / 85%

[a]Refers to TLC-grade silica gel; [b]Carried out at room temperature

In order to test the generality of the reaction, five different indoles (**1a**-**e**) were separately treated with 0.75-1.0 equiv.[19] of several benzaldehydes (**2a**-**j**) and three heteroaryl aldehydes (**2k**-**m**) on H_3PO_4 (10 mol%)-SiO_2 at 60-70 °C. For the reactions of indole with 2-formylpyrrole (**2m**) and of 5-nitroindole (**1d**) with benzaldehyde (**2a**) and vanillin (**2d**) (Entries 13, 18 and 19, respectively; Table 2), no reaction took place. In other cases, the indoles were fully consumed in 5-30 min (except for the reaction of **1a** with 4-dimethylaminobenzaldehyde (**2f**); Entry 6; Table 2), and the corresponding symmetrical BIAs (**3aa**-**al**, **bd**, **bg**, **cd**, **cg**, **ed**) were isolated as the sole products in 80-95% yields (Scheme 1, Table 2).



1a-e **2a-m** **3aa-al, bd, bg, cd, cg, ed**

X = H, Me
Y = OMe, Br, NO_2

Scheme 1

The results reflect the influence of the electronic nature of the substituents in both indoles and aryl aldehydes on the reaction periods and the yields of the BIAs. Thus, the reactions of indole (**1a**) and indoles (**1b**, **1c**, **1e**) bearing electron-donating groups with the benzaldehydes (**2a**-**e**) were quite fast (5-15 min) to furnish the BIAs (**3aa**-**ae**, **bd**, **cd**, **ed**) in excellent yields (92-95%). However, we are unable to explain why the reaction of **1a** with **2f** (Entry 6; Table 2) took a much longer period (1 h) for completion, which furnished the BIA (**3af**) in 85% yield. The reactions of 4-trifluoromethoxybenzaldehyde (**2g**) with the indoles (**1a**-**c**) were somewhat slower to furnish the BIAs (**3ag**-**cg**) in 89-93% yields. In contrast, the presence of a stronger electron-withdrawing group (NO_2) in aryl aldehydes or indole resulted in noticeably different results. Thus, whereas the reactions of 4/3/2-nitrobenzaldehydes (**2h**-**j**) with indole (**1a**) required slightly longer time (30-45 min) for completion to furnish the expected BIAs (**3ah**-**aj**) in somewhat lower yields (80-87%; Entries 8, 9, 10), 5-nitroindole (**1d**) did not react at all with benzaldehyde and vanillin (**2d**) (Entries 18, 19). The results of the reactions of the three heteroaryl aldehydes (**2k**-**m**) with indole (**1a**) using H_3PO_4-SiO_2 parallel the results obtained using silicotungstic acid (STA)[14b] as the catalyst but differed from those resulting from the use of the catalyst, montmorillonite K10 clay.[18c] Both these acidic solids had earlier been demonstrated by us to be effective catalysts for a similar synthesis of the symmetrical BIAs. Thus, in the present case, the 2-thienyl and 2-furyl aldehydes (**2k**, **2l**) required 20 min for completion to furnish the respective BIAs (**3ak**, **3al**) in 92% and 86% respective yields, whereas the 2-pyrrolyl aldehyde (**2m**) completely failed to react. A comparison of the results with **2k**-**m** using the three aforesaid catalysts is

presented in Table 3, which shows that H_3PO_4-SiO_2 is marginally better (than clay and STA) for 2-formylthiophene (**2k**), much better for furfural (**2l**) but ineffective for 2-formylpyrrole (**2m**).

Table 2. Formation of BIAs (**3**) using 10 mol% H_3PO_4-SiO_2 as the catalyst

Entry	Indole (**1**)	ArCHO (**2**) Ar =	Equiv of (**2**)	Time	BIA (**3**)	Yield (%)[a]
1	**a**: X=Y=H	**a**: Ph	0.75	10 min	**aa**	93
2	**a**	**b**: 4-$MeOC_6H_4$	0.75	10 min	**ab**	95
3	**a**	**c**: 4-HOC_6H_4	0.75	10 min	**ac**	95
4	**a**	**d**: 3-MeO-4-HOC_6H_3	0.75	15 min	**ad**	94
5	**a**	**e**: 3,4-$(MeO)_2C_6H_3$	0.75	15 min	**ae**	95
6	**a**	**f**: 4-$Me_2NC_6H_4$	1.0	1 h	**af**	85
7	**a**	**g**: 4-$CF_3OC_6H_4$	1.0	20 min	**ag**	89
8	**a**	**h**: 4-$NO_2C_6H_4$	1.0	30 min	**ah**	87
9	**a**	**i**: 3-$NO_2C_6H_4$	0.75	30 min	**ai**	80
10	**a**	**j**: 2-$NO_2C_6H_4$	0.75	45 min	**aj**	85
11	**a**	**k**: 2-Thienyl	1.0	20 min	**ak**	92
12	**a**	**l**: 2-Furyl	1.0	20 min	**al**	86
13	**a**	**m**: 2-Pyrrolyl	1.0	6 h[b]	-	-
14	**b**: X=H; Y=OMe	**d**	0.75	5 min	**bd**	95
15	**b**	**g**	1.0	15 min	**bg**	93
16	**c**: X=H; Y=Br	**d**	0.75	10 min	**cd**	95
17	**c**	**g**	1.0	20 min	**cg**	92
18	**d**: X=H; Y=NO_2	**a**	1.0	6 h[b]	-	-
19	**d**	**d**	1.0	6 h[b]	-	-
20	**e**: X=Me; Y=H	**d**	1.0	15 min	**ed**	92

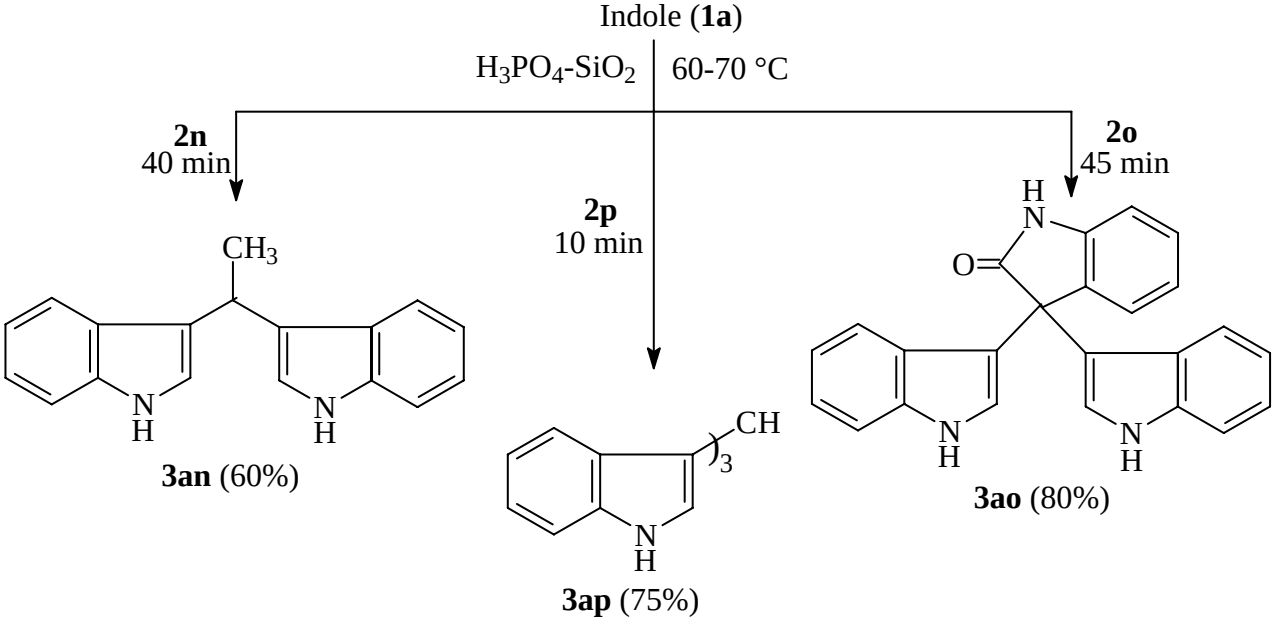
[a]Refer to isolated pure products; [b]No product was formed (TLC) even after 6 h.

Table 3. Reactions of **2k**-**m** with indole (**1a**) using different catalysts: A comparative evaluation

Araldehyde	Product, Reaction Time and Yield using			
	Clay[a]	STA[b]	H_3PO_4-SiO_2[c]	Conclusion
2k (X=S)	**3ak** 10 min, 80%	**3ak** 7 min, 90%	**3ak** 20 min, 92%	H_3PO_4-SiO_2: marginally better
2l (X=O)	**3al** 1 h, 81%	**3al** 30 min, 73%	**3al** 20 min, 86%	H_3PO_4-SiO_2: considerably better
2m (X=NH)	1,1,1-Tris(indol-3-yl)-methane (TIM)[18c] 4 h, 88%	No reaction 6 h	No reaction 6 h	TIM formed *via* expected product (**3am**) (*in situ* generated)

[a]Montmorillonite K10 clay (2 g) / 1 mmol indole / room temperature; [b]2 mol% silicotungstic acid / EtOAc / room temperature; [c]10 mol% H_3PO_4-SiO_2 / 60-70 °C (oven)

In order to test the applicability of H_3PO_4-SiO_2 to alkanals and ketones, indole was separately treated with each of formaldehyde, acetaldehyde (**2n**), propionaldehyde, glyceraldehyde, crotonaldehyde, ethyl methyl ketone, acetophenone, isatin (**2o**) (as an example of a ketone contained within a heteroarene) and finally 3-formylindole (**2p**). Interestingly, the reagent proved to be of success only in the cases of **2n**, **2o** and **2p** to furnish the respective symmetrical BIAs, vibrindole A[1e,1i] (**3an**), trisindoline[1i,20] (**3ao**) and tris(indol-3-yl)methane[1i] (**3ap**). All the three symmetrical molecules are natural products isolated from different strains of the bacteria *Vibrio parahaemolyticus* (Scheme 2).



Scheme 2

In conclusion, we have demonstrated that orthophosphoric acid (10 mol%)-on-silica gel (TLC-grade) is a highly efficient and eco-friendly catalyst for the solvent-free and fast one-step synthesis of symmetrical BIAs in excellent yields from the reaction of indoles with aryl aldehydes. Easy availability of the cheap reagent, mild reaction conditions and clean work-up of the present methodology make it a highly attractive protocol for the synthesis of diverse and new bioactive symmetrical BIAs.

EXPERIMENTAL

Mps were determined on a Toshniwal apparatus and are uncorrected. IR spectra (Nujol) were recorded on a Nicolet Impact 410 spectrophotometer, LR EI-MS on JEOL JMS-AX505HA and HR EI-MS on JEOL JMS-700 MStation mass spectrometers, ^{1}H (both 300 and 400 MHz) and ^{13}C (both 75 and 100 MHz) NMR spectra, both 1D and 2D, including DEPT 135, HMQC and HMBC spectra, on Varian MERCURY plus 300 and Varian UNITY-400 NMR spectrometers. Individual ^{1}H and ^{13}C NMR spectral assignments of **3bd, 3bg, 3cd, 3cg** and **3ed** were additionally based on HMQC and HMBC NMR spectra. TLCs were carried out on silica gel G (Merck, India) plates. PE refers to petroleum ether, bp 60-80 °C. Orthophosphoric acid Pure was used as procured from Merck, India.

Reaction in EtOAc solution at rt. A solution of indole (**1a**; 1 mmol) and benzaldehyde (**2a**; 0.75 equiv.) in EtOAc (5 mL) was treated with *ca.* 0.7 mL of H_3PO_4 from a stock solution (see below) and stirred at rt until (4.5 h) indole was fully consumed (TLC). The reaction mixture was then washed successively with 2% aq. $NaHCO_3$, water, dried (Na_2SO_4), filtered, solvent removed and the resulting residue directly purified by column chromatography (CC) over silica gel (grade SQ, Qualigens, India). 5% EtOAC/PE eluates furnished **3aa** in 85% yield. It was identified as stated below.

Reaction in EtOAc solution at 60-70 °C. The above reaction was repeated at 60-70 °C in an oil bath, when indole was consumed in 1.5 h. A similar work-up of reaction mixture and purification by CC over silica gel furnished **3aa** in 87% yield.

Preparation of H_3PO_4-SiO_2. Each time a reaction was carried out using 1.0 mmol of the indole, the catalyst was prepared by taking 0.7 mL of H_3PO_4 from a stock solution (0.15 mL H_3PO_4, made up to 15 mL with EtOAc) and adsorbing it on silica gel G (2 g). The solution was then allowed to evaporate off at rt inside a hood. Within few minutes it led to a free-flowing solid, which was H_3PO_4 (10 mol%)-SiO_2.

General experimental procedure. A solution of indole (1.0 mmol) and aldehyde (0.75-1.0 equiv.) in ≤0.5 mL of CH_2Cl_2 (or EtOAc for substrates insoluble in CH_2Cl_2) was adsorbed on freshly prepared H_3PO_4-SiO_2 (2 g). The solvent was then allowed to evaporate off at rt and then the contents heated in an oven at 60-70 °C. After the completion of the reaction (TLC), the reaction mixture was leached with CH_2Cl_2 (or EtOAc; 3×10 mL) and filtered. The filtrate was freed from acid by washing with 2% aq. $NaHCO_3$, washed with water until free from alkali, dried (Na_2SO_4) and the solvent removed. The resulting residue was purified by preparative

TLC using PE-EtOAc (except for **3ai** which was purified by direct crystallisation) to afford the pure BIAs. Unless otherwise stated, the BIAs were crystallised from PE-EtOAc.

The following BIAs were identified by direct comparison (for available samples) or by comparing their mps with the reported mps along with ^{1}H NMR spectroscopic data. **3aa**: mp 148-150 °C (PE-CH_2Cl_2) (lit.,[14b] 148 °C); **3ab**: mp 194-195 °C (PE-CH_2Cl_2) (lit.,[14b] 194-195 °C); **3ac**: mp 132-134 °C (lit.,[14b] 134-136 °C); **3ad**: mp 106-108 °C (lit.,[21] 110-112 °C); **3ae**: mp 194-196 °C (lit.,[22] 198-200 °C); **3af**: mp 142-144 °C (lit.,[23] not available); **3ag**: mp 270-272 °C (lit.,[14b] 272-274 °C); **3ah**: mp 236 °C (lit.,[14b] 240 °C); **3ai**: mp 216-218 °C (lit.,[14b] 218-220 °C); **3aj**: mp 142-144 °C (lit.,[14b] 141-143 °C); **3ak**: mp 162 °C (lit.,[14b] 160 °C); **3al**: mp >300 °C (lit.,[24] 325 °C); **3an**: mp 154-156 °C (lit.,[24] 156 °C); **3ao**: mp 312 °C (lit.,[25] 312-314 °C); **3ap**: mp 238-240 °C (lit.,[26] 242-244 °C).

Bis(5-methoxyindol-3-yl)(4′-hydroxy-3′-methoxyphenyl)methane (3bd): mp 124 °C (PE-CH_2Cl_2); IR: 3409, 1613, 1580, 1507, 1268, 1208, 1169, 1122, 1029, 923, 804, 771, 731 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 3.70 (6H, s, 2×5-OCH_3), 3.72 (3H, s, 3′- OCH_3), 5.70 (1H, s, Ar_3CH), 6.62 (2H, dd, J_1=2 Hz, J_2=1 Hz, 2×H-2), 6.82 (1H, d, *J*=9 Hz, H-5′), 6.83 (2H, d, *J*=2.5 Hz, 2×H-4), 6.80-6.86 (4H, m), 6.87 (1H, d, *J*=1.5 Hz, H-2′), 7.21 (2H, d, *J*=9 Hz, 2×H-7), 7.89 (2H, d, *J*=2 Hz, 2×NH); ^{13}C NMR: δ 39.9 (Ar_3CH), 55.81 (3′- OCH_3), 55.86 (2×5-OCH_3), 102.0 (2×CH-6), 111.4 (CH-2′), 111.6 (2×CH-7), 111.7 (2×CH-4), 113.9 (CH-5′), 119.3 (2×C-3), 121.2 (CH-6′), 124.3 (2×CH-2), 127.4 (2×C-3a), 131.8 (2×C-7a), 136.0 (C-1′), 143.7 (C-4′), 146.3 (C-3′), 153.5 (2×C-5); EI-MS: *m/z* (%) 428 (M^+, 100), 427 (23), 413 (4), 397 (6), 305 (26), 304 (5), 281 (8), 280 (7), 266 (3), 251 (2); HRMS (EI): calcd for $C_{26}H_{24}N_2O_4$, 428.1737; found 428.1732; Anal. Calcd for $C_{26}H_{24}N_2O_4$: C, 72.89; H, 5.60; N, 6.54. Found: C, 72.97; H, 5.61; N, 6.52.

Bis(5-methoxyindol-3-yl)(4′-trifluoromethoxyphenyl)methane (3bg): mp 136-138 °C; IR: 3404, 1622, 1581, 1513, 1493, 1260, 1208, 1167, 1101, 1056, 1016, 924, 804, 711 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 3.70 (6H, s, 2×5-OCH_3), 5.80 (1H, s, Ar_3CH), 6.63 (2H, d, *J*=1.5 Hz, 2×H-2), 6.78 (2H, d, *J*=2 Hz, 2×H-4), 6.85 (2H, dd, J_1=8.5 Hz, J_2=2 Hz, 2×H-6), 7.12 (2H, d, *J*=8 Hz, H-3′, 5′), 7.24 (2H, d, *J*=9 Hz, 2×H-7), 7.35 (2H, d, *J*=9 Hz, H-2′, 6′), 7.90 (2H, s, 2×NH); ^{13}C NMR: δ 39.6 (Ar_3CH), 55.8 (2×5-OCH_3), 101.7 (2×CH-4), 111.8 (2×CH-7), 111.9 (2×CH-6), 118.6 (2×C-3), 120.5 (q, *J*=255 Hz, 4′-OCF_3), 120.6 (CH-3′, 5′), 124.4 (2×CH-2), 127.2 (2×C-3a), 129.9 (CH-2′, 6′), 131.8 (2×C-7a), 142.6 (C-1′), 147.5 (q, *J*=1.7 Hz, C-4′), 153.7 (2×C-5); EI-MS: *m/z* (%) 466 (M^+, 100), 465 (23), 435 (8), 319 (9), 305 (35); HRMS (EI): calcd for $C_{26}H_{21}N_2O_3F_3$, 466.1504; found 466.1515; Anal. Calcd for $C_{26}H_{21}N_2O_3F_3$: C, 66.95; H, 4.50; N, 6.00. Found: C, 66.87; H, 4.49; N, 6.02.

Bis(5-bromoindol-3-yl)(4′-hydroxy-3′-methoxyphenyl)methane (3cd): mp 216 °C; IR: 3494, 3461, 3422, 1613, 1508, 1275, 1208, 1155, 1096, 1036, 883, 870, 797cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 3.65 (3H, s, 3′-OCH_3), 5.71 (1H, s, Ar_3CH), 6.66-6.68 (2H, s, H-5′, 6′), 6.86 (2H, d, *J*=2 Hz, 2×H-2), 6.93 (1H, s, H-2′), 7.13

(2H, dd, J_1=9 Hz, J_2=2 Hz, 2×H-6), 7.31 (2H, d, J=8 Hz, 2×H-7), 7.41 (2H, d, J=2 Hz, 2×H-4), 8.76 (1H, br s, 4′-OH), 11.03 (2H, d, J=2 Hz, 2×NH); ^{13}C NMR: δ 38.5 (Ar_3CH), 55.6 (3′- OCH_3), 110.7 (2×C-5), 112.7 (CH-2′), 113.5 (2×CH-7), 115.1 (CH-5′), 118.1 (2×C-3), 120.3 (CH-6′), 121.2 (2×CH-4), 123.3 (2×CH-6), 125.1 (2×CH-2), 128.4 (2×C-3a), 135.1 (C-1′), 135.2 (2×C-7a), 144.7 (C-4′), 147.2 (C-3′); EI-MS: *m/z* (%) 528 (M+4, 48), 526 (M+2, 100), 524 (M^+, 50), 511 (3), 509 (4), 507 (2), 405 (10), 403 (21), 401 (15); HRMS (EI): calcd for $C_{24}H_{18}N_2O_2{}^{79}Br_2$, 523.9735; found 523.9726; Anal. Calcd for $C_{24}H_{18}N_2O_2{}^{79+81}Br_2$: C, 54.75; H, 3.42; N, 5.32. Found: C, 54.84; H, 3.43; N, 5.33.

Bis(5-bromoindol-3-yl)(4′-trifluoromethoxyphenyl)methane (3cg): mp 126 °C; IR: 3418, 1719, 1606, 1566, 1503, 1420, 1255, 1218, 1162, 1102, 1029, 923, 883, 794 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 5.93 (1H, s, Ar_3CH), 6.91 (2H, d, J=2 Hz, 2×H-2), 7.14 (2H, dd, J_1=8.5 Hz, J_2=2 Hz, 2×H-6), 7.27 (2H, d, J=8.5 Hz, H-3′, 5′), 7.33 (2H, d, J=8.5 Hz, 2×H-7), 7.43 (2H, d, J=8.5 Hz, H-2′, 6′), 7.44 (2H, d, J=2 Hz, 2×H-4), 11.11 (2H, d, J=2 Hz, 2×NH); ^{13}C NMR: δ 47.5 (Ar_3CH), 120.5 (2×C-5), 123.1 (2×CH-7), 126.7 (2×C-3), 129.6 (q, J=256.5 Hz, 4′-OCF_3), 130.2 (CH-3′, 5′), 130.5 (2×CH-4), 133.0 (2×CH-6), 134.7 (2×CH-2), 137.7 (2×C-3a), 139.3 (CH-2′, 6′), 144.7 (2×C-7a), 153.3 (C-1′), 156.0 (q, J=1.5 Hz, C-4′); EI-MS: *m/z* (%) 566 (M+4, 53), 564 (M+2, 100), 562 (M^+, 52), 485 (9), 483 (13), 405 (14), 403 (30), 401 (17), 369 (11), 367 (10), 323 (5), 288 (15); HRMS (EI): calcd for $C_{24}H_{15}N_2O{}^{79}Br_2F_3$, 561.9503; found 561.9500; Anal. Calcd for $C_{24}H_{15}N_2O{}^{79+81}Br_2F_3$: C, 51.06; H, 2.66; N, 4.96. Found: C, 51.20; H, 2.67; N, 4.98.

Bis(2-methylindol-3-yl)(4′-hydroxy-3′-methoxyphenyl)methane (3ed): mp 184 °C; IR: 3546, 3379, 1613, 1508, 1241, 1122, 1023, 857, 824, 751 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.04 (6H, s, 2×2-CH_3), 3.55 (3H, s, 3′-OCH_3), 5.80 (1H, s, Ar_3CH), 6.51 (1H, dd, J_1=8 Hz, J_2=1.5 Hz, H-6′), 6.63 (1H, d, J=8 Hz, H-5′), 6.66 (2H, dt, J_1=8 Hz, J_2=1.5 Hz, 2×H-6), 6.80 (1H, d, J=1.5 Hz, H-2′), 6.84 (2H, dd, J_1=8 Hz, J_2=1.5 Hz, 2×H-7), 6.86 (2H, dt, J_1=8 Hz, J_2=1.5 Hz, 2×H-5), 7.18 (2H, d, J=8 Hz, 2×H-4), 8.70 (1H, s, 4′-OH), 10.66 (2H, s, 2×NH); ^{13}C NMR: δ 11.9 (2×2-CH_3), 38.1 (Ar_3CH), 55.6 (3′- OCH_3), 110.2 (2×CH-4), 112.7 (2×C-3), 113.4 (CH-2′), 114.9 (CH-5′), 117.8 (2×CH-6), 118.5 (2×CH-7), 119.4 (2×CH-5), 120.8 (CH-6′), 128.3 (2×C-7a), 131.8 (2×C-2), 135.0 (C-1′, 2×C-3a), 144.5 (C-4′), 147.3 (C-3′); EI-MS: *m/z* (%) 396 (M^+, 100), 395 (25), 381 (84), 365 (5), 273 (29), 265 (26), 264 (27), 257 (16), 130 (10); HRMS (EI): calcd for $C_{26}H_{24}N_2O_2$, 396.1837; found 396.1846; Anal. Calcd for $C_{26}H_{24}N_2O_2$: C, 78.78; H, 6.06; N, 7.07. Found: C, 78.89; H, 6.07; N, 7.08.

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