P_2O_5/SiO_2 as an efficient, mild, and heterogeneous catalytic system for the condensation of indoles with carbonyl compounds under solvent-free conditions

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Abstract

An efficient solvent-free procedure for the preparation of bis(indolyl)methanes via the condensation of indoles with aldehydes as well as ketones in the presence of catalytic amount of phosphorus pentoxide/silica gel (P_2O_5/SiO_2) at room temperature is described. The advantages of this method are generality, high yields, short reaction times, ease of product isolation, low cost and ecologically friendly.

Keywords: P_2O_5/SiO_2, indole, carbonyl compound, solvent-free, bis(indolyl)methane

Introduction

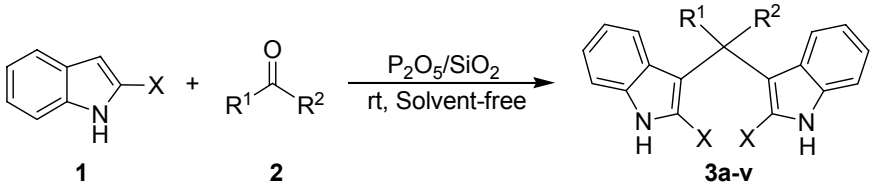
The condensation of indoles with carbonyl compounds is of importance as this reaction provides a direct and appealing route toward bis(indolyl)methanes.[1] Various biological and pharmaceutical activity has been reported for this class of compounds.[2] Bis(indolyl)methanes are cruciferous substances useful for promoting beneficial estrogen metabolism in men and women.[2a] They are also effective in the prevention of cancer due to their ability to modulate certain cancer causing estrogen metabolites.[2b] Moreover, these compounds may normalize abnormal cell growth associated with cervical dysplasia.[2c] As bis(indolyl)methanes are important compounds in pharmaceutical chemistry, their synthesis have received increasing attention. Several methods have been reported in the literature for the preparation of bis(indolyl)methanes from indoles and carbonyl compounds using protic acids[3] and Lewis acids.[4] Many Lewis acids like BF_3 and $AlCl_3$ promote this type of reaction but they generate harmful wastes, which pose environmental problems.[4a] Some Lewis acids are deactivated or sometimes decomposed by nitrogen of indoles. Even when the desired reactions proceed, more than stoichiometric amounts

of Lewis acids are required because they are trapped by nitrogen.[4b] Solid acid-catalysts such as zeolite have been also used for bis(indolyl)methanes synthesis, but they need very high temperature for reactivation.[4c] Recently, lanthanide triflates[4d] and lithium perchlorate[4e] have been also used as catalysts for condensation of indole with carbonyl compounds. However, these reactions require long reaction times and the process is expensive. Furthermore, the synthesis of bis(indolyl)methanes in the presence of surfactant has also been reported.[1a] But, this method can not be applied for the condensation of indoles with ketones. In addition, the reaction times reported in this work are long. Thus, there is a need for a new, efficient and eco-friendly catalysts for the synthesis of bis(indolyl)methanes.

Phosphorus pentoxide/silica gel is an inexpensive, heterogeneous and commercially available catalytic system which has been used in several transformations, such as esterification,[5a] oxidation of sulfides to sulfoxides,[5b] Schmidt reaction,[5c] Fries rearrangement,[5d] direct sulfonylation of aromatic rings,[5e] oxime preparation,[5f] conversion of aldehydes to acylals,[5g] selective deprotection of 1,1-diacetals,[5h] acetalization of carbonyl compounds,[5i] and acylation of alcohols, phenols and amines.[5j]

Solvent-free organic reactions have been applied as an useful protocol in organic synthesis.[6] Solvent-free conditions often lead to shorter reaction times, increased yields, easier workup, matches with green chemistry protocols, and may enhance the regio- and stereoselectivity of reactions.[6] Solvent-free condensation of indoles with carbonyl compounds is scarce in the literature.[4f,7]

Considering the above facts and also in extension of our previous studies on solvent-free organic reactions,[8] we now describe a new method for the condensation of indoles with aldehydes as well as ketones in the presence of silica-supported phosphorus pentoxide (P_2O_5/SiO_2) as an efficient, low cost and heterogeneous catalytic system in the absence of solvent at room temperature (Scheme 1).



Scheme 1. Condensation of indoles with carbonyl compounds.

Results and Discussion

To optimize the reaction conditions, at first the synthesis of compound **3a** was selected as a model reaction (Scheme 1), thus, to a mixture of benzaldehyde (1 mmol) and well ground P_2O_5

(0.4 mmol) was added indole (2.1 mmol) and the resulting mixture was ground at room temperature for 40 min; however, low yield of the product was obtained even by increasing the reaction time (Table 1). In these conditions, a highly sticky orange reaction mixture was obtained. The reaction yields were improved when supported P_2O_5 was used as catalyst (Table 1). Among the examined supports, silica gel showed the best results (Table 1, entry 3). Therefore, silica-supported P_2O_5 (P_2O_5/SiO_2) was used as catalyst for all reactions. The model reaction was also examined in the presence of silica gel without using P_2O_5 in which bis(indolyl)metane **3a** was obtained in 16% yield within 1 hour.

Table 1. The effect of different supports (0.8 g) on the condensation of indole (2.1 mmol) with benzaldehyde (1 mmol) in the presence of P_2O_5 (0.4 mmol) at room temperature

Entry	Support	Time (min)	Yield[a] (%)
1[b]	-	40	43
2[b]	-	60	43
3	Silica gel	30	94
4	Neutral Alumina	30	77
5	Acidic Alumina	30	80
6	Basic Alumina	30	56
7	Graphite	30	64
8	Molecular sieves	30	68

[a]Isolated yield. [b]Without support.

To compare the efficiency as well as capacity of the solvent-free conditions in comparison with solution conditions, the model reaction was examined in the presence of silica-supported P_2O_5 in several solvents (10 mL) at room temperature. The results are depicted in Table 2. As is shown in Table 2, higher yield and shorter reaction times were observed in the solvent-free conditions.

Table 2. Comparative synthesis of compound **3a** using solution conditions versus the solvent-free method

Entry	Solvent	Time (min)	Yield[a] (%)
1[b]	-	30	94
2	CH_3CN	120	53
3	THF	120	44
4	CH_2Cl_2	120	49
5	$CHCl_3$	120	41

[a]Isolated yield. [b]The solvent-free conditions.

In order to assess the capability of the present method with respect to the reported methods for the preparation of bis(indolyl)methanes from indoles and carbonyl compounds, the synthesis of compound **3a** was compared with the reported methods (Table 3). As it is clear from Table 3, the present method is more efficient.

Table 3. Comparative the condensation of indole with benzaldehyde using the reported methods versus the present method

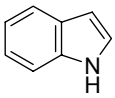
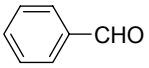
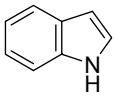
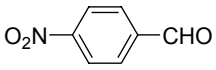
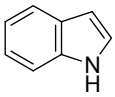
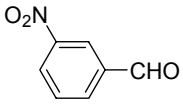
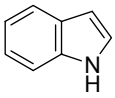
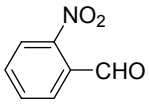
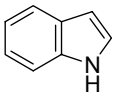
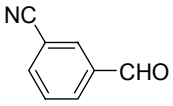
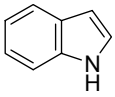
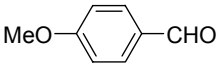
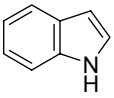
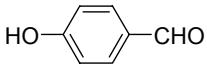
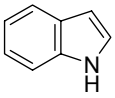
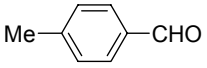
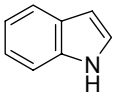
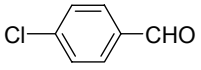
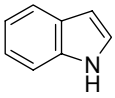
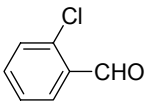
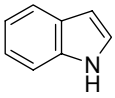
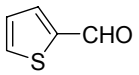
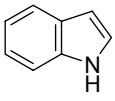
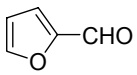
Entry	Reagent and Conditions	Time (min)	Yield[a] (%)	Ref.
1[b]	SiO_2/P_2O_5, Solvent-free, rt	30	94	-
2	$Zn(HSO_4)_2$	180	91	3a
3	$PPh_3.HClO_4/CH_3CN$	30	61	3b
4	$Ln(OTf)_3/EtOH.H_2O$	720	95	4d
5	$ZrOCl_2.8H_2O$, Solvent-free, 50 °C	40	84	4f
6	$In(OTf)_3/CH_3CN$	25	71	4g
7	Zeokarb-225/CH_3CN	450	95	4h
8	$La(PFO)_3$/EtOH	30	90	4i
9	$AlPW_{12}O_{40}$, CH_3CN, rt	15	92	4j

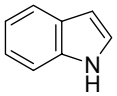
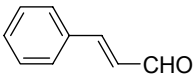
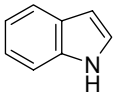
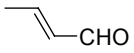
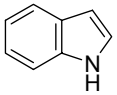
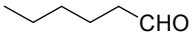
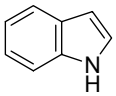
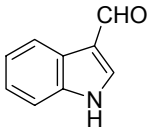
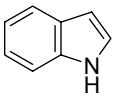
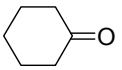
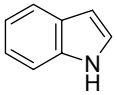
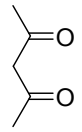
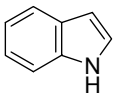
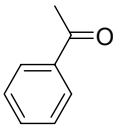
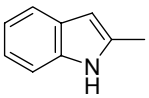
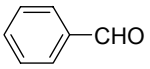
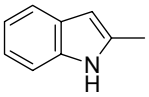
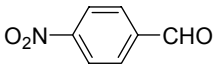
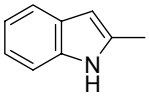
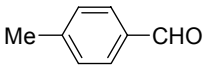
[a]Isolated yield. [b]The present method.

To establish the generality and applicability of this method, indoles were condensed with structurally diverse aldehydes and ketones to furnish bis(indolyl)methanes in high to excellent yields in short reaction times. The results are displayed in Table 4.

The influence of electron-withdrawing and electron-donating substituents on the aromatic ring of aldehydes upon results of the reaction was investigated. Interestingly, the results showed that both electron-withdrawing and electron-donating substituents had no significant effect on the reaction times and the yields (Table 4, entries 2, 3, 5-8, 21 and 22). Moreover, the presence of halogen (Cl) on the aromatic ring of aldehydes had negligible effect on the results of the reaction (Table 4, entry 9). The presence of substituent on ortho position of aromatic aldehydes raised the reaction times and decreased the yields (Table 4, entries 4 and 10). Aliphatic aldehydes as well as ketones afforded longer reaction times and lower yields in comparison with others (Table 4, entries 13-15 and 17-19). When 2-methyl-1*H*-indole instead of indole was applied in the reaction, the reaction times slightly increased and the yields decreased (Table 4, entries 20-22).

Table 4. Synthesis of bis(indolyl)methanes via the condensation of indoles with aldehydes as well as ketones using silica-supported P_2O_5 in solvent-free conditions at room temperature

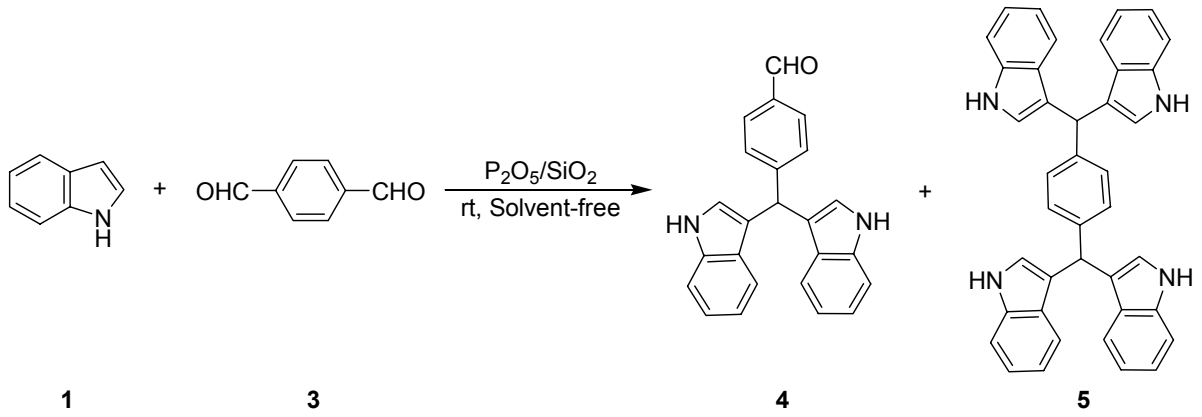
Entry	Indole	Carbonyl Compound	Product[a]	Time (min)	Yield[b] (%)	M.p. (Lit.)[a]
1			**3a**	30	94	140-142 (142-144)[1b]
2			**3b**	30	92	217-219 (217-220)[1a]
3			**3c**	30	93	220-222 (221-223)[1b]
4			**3d**	40	86	139-141 (140-142)[1c]
5			**3e**	30	91	98-100 (102-104)[1d]
6			**3f**	25	94	186-188 (185-187)[1b]
7			**3g**	25	88	119-121 (124-125)[4k]
8			**3h**	25	95	95-97 (93-94)[1a]
9			**3i**	30	92	78-80 (76-77)[1a]
10			**3j**	40	83	74-76 (70-71)[1a]
11			**3k**	25	89	147-149 (150-153)[1a]
12			**3l**	25	93	316-318 (>300)[1a]

13			**3m**	45	89	100-102 (98-99)[1a]
14			**3n**	45	86	126-128 (123-126)[1a]
15			**3o**	45	87	71-73 (68-70)[4k]
16[c]			**3p**	35	90	162, dec. (160, dec.)[4l]
17			**3q**	60	84	163-165 (162-164)[3c]
18			**3r**	60	75	226-228 (231)[3c]
19			**3s**	70	72	162-165 (165-167)[1b]
20			**3t**	35	89	244-246 (247-248)[1a]
21			**3u**	35	88	241-243 (240-242)[3d]
22			**3v**	30	91	175-177 (174-175)[1a]

[a]All compounds were identified by comparison of their melting points with the authentic samples and/or IR as well as ^{1}H NMR data. [b]Isolated yield. [c]In this reaction, tris(indolyl)methane was produced.

Interestingly, this method can be easily applied for condensation of indole with bis-aldehydes, such as terephthaldehyde (Scheme 2). The reaction of 2.1 equivalents of indole with terephthalaldehyde proceeded rapidly to give monomer **4** and dimer **5** in 93% and trace yields,

respectively. On the other hand, using 4.2 equivalents of indole afforded compounds **4** and **5** in trace and 90% yields, respectively, under similar reaction conditions (Scheme 2).



Scheme 2. Condensation of indole with terephthaldehyde.

Conclusions

In summary, we have developed an efficient, simple and rapid solventless method for the preparation of bis(indolyl)methanes as biologically interesting compounds via the condensation of indoles with carbonyl compounds using cheap and safe reagents.

Experimental Section

General Procedures. All chemicals were purchased from Merck or Fluka chemical companies. Silica gel 60, 0.063-0.200 mm (70-230 mesh ASTM) was used as support. Spectra were recorded on the following apparatus: ^{1}H NMR (250 MHz) and ^{13}C NMR (62.5 MHz) on a Bruker Avanced DPX-250, FT-NMR spectrometer (δ in ppm); and mass spectra on a Shimadzu GC MS-QP 1000 EX. Melting points were recorded on a Büchi B-545 apparatus in open capillary tubes.

Preparation of P_2O_5/SiO_2 catalytic system. A mixture of SiO_2 (2 g) and P_2O_5 (0.14 g, 1 mmol) was ground vigorously to give P_2O_5/SiO_2 catalytic system as a white powder (2.14 g).

Condensation of indoles with carbonyl compounds under solvent-free conditions at room temperature. To a mixture of carbonyl compound (1 mmol) and P_2O_5/SiO_2 (0.86 g) in a mortar was added indole (2.1 mmol) and the resulting mixture was ground at room temperature for the appropriate time (Table 4). Afterward, the reaction mixture was suspended in EtOAc (25 mL), filtered, and the filtrate was washed with saturated solution of $NaHCO_3$ (2×20 mL), saturated

solution of $NaHSO_4$ (2×20 mL) and water (2×20 mL). The organic layer was separated and dried with $CaCl_2$. The solvent was evaporated and the crude product was purified by recrystallization from EtOAc/petroleom ether (1/2) or plate chromatography on silica gel eluted with EtOAc/petroleom ether (1/2).

3-((1*H*-Indol-3-yl)(phenyl)methyl)-1*H*-indole (3a). Pink solid; mp 140-142 °C (Lit.[1b] mp 142-144 °C); ^{1}H NMR ($CDCl_3$): δ 5.86 (1H, s, ArCH), 6.66 (2H, s), 7.11 (2H, t, *J* = 6.9 Hz), 7.14-7.22 (3H, m), 7.28-7.31 (2H, m), 7.35-7.42 (6H, m), 7.93 (2H, br, NH); ^{13}C NMR ($CDCl_3$): δ 31.6, 110.9, 111.9, 118.4, 119.5, 121.2, 124.0, 126.3, 127.1, 128.5, 128.6, 137.0, 145.2; MS (m/z): 322 (M^+).

3-((1*H*-Indol-3-yl)(4-nitrophenyl)methyl)-1*H*-indole (3b). Yellow needles; mp 217-219 °C (Lit.[1a] mp 217-220 °C); ^{1}H NMR ($CDCl_3$): δ 6.01 (1H, s, ArCH), 6.72 (2H, s), 7.02-7.08 (4H, m), 7.36 (2H, d, *J* = 8.1 Hz), 7.41 (2H, d, *J* = 8.1 Hz), 7.49 (2H, d, *J* = 8.6 Hz), 8.05 (2H, br, NH), 8.17 (2H, d, *J* = 8.6 Hz).

3-((1*H*-Indol-3-yl)(3-nitrophenyl)methyl)-1*H*-indole (3c). Yellow solid; mp 220-222 °C (Lit.[1b] mp 221-223 °C); ^{1}H NMR ($CDCl_3$): δ 6.23 (1H, s, ArCH), 7.01 (2H, t, *J* = 7.3 Hz), 7.06 (2H, s), 7.22 (2H, t, *J* = 7.0 Hz), 7.45 (2H, d, *J* = 7.5 Hz), 7.53 (2H, d, *J* = 8.0 Hz), 7.75 (1H, m), 8.02 (1H, d, *J* = 7.6 Hz), 8.26 (1H, d, *J* = 7.7 Hz), 8.33 (1H, s), 8.09 (2H, s, NH).

3-((1*H*-Indol-3-yl)(2-nitrophenyl)methyl)-1*H*-indole (3d). Yellow solid; mp 139-141 °C (Lit.[1c] mp 140-142 °C); ^{1}H NMR ($CDCl_3$): δ 6.12 (1H, s, ArCH), 6.91 (2H, s), 7.08-7.17 (4H, m), 7.29 (2H, d, *J* = 7.8 Hz), 7.47 (2H, d, *J* = 7.9 Hz), 7.57-7.66 (2H, m), 7.79-7.90 (2H, m), 8.21 (2H, d, *J* = 8.6 Hz).

3-(Di(1*H*-indol-3-yl)methyl)benzonitrile (3e). Pink solid; mp 98-100 °C (Lit.[1d] mp 102-104 °C); ^{1}H NMR ($CDCl_3$): δ 6.09 (1H, s, ArCH), 6.83 (2H, s), 6.98-7.07 (4H, m), 7.19 (2H, d, *J* = 7.6 Hz), 7.42 (2H, d, *J* = 7.6 Hz), 7.65-7.87 (4H, m), 8.02 (2H, br, NH).

3-((1*H*-Indol-3-yl)(4-methoxyphenyl)methyl)-1*H*-indole (3f). Brown solid; mp 186-188 °C (Lit.[1b] mp 185-187 °C); ^{1}H NMR ($CDCl_3$): δ 3.76 (3H, s, OCH_3), 5.85, (1H, s, ArCH), 6.68 (2H, s), 6.91 (2H, d, *J* = 8.2 Hz), 7.02 (2H, t, *J* = 7.3 Hz), 7.16 (2H, t, *J* = 7.3 Hz), 7.20 (2H, m), 7.35-7.41 (4H, m), 7.95 (2H, br, NH).

4-(Di(1*H*-indol-3-yl)methyl)phenol (3g). Pink solid; mp 119-121 °C (Lit.[4k] mp 124-125 °C); ^{1}H NMR (DMSO-d_6): δ 5.74 (1H, s), 6.63 (4H, m), 6.87 (2H, t, *J* = 7.5 Hz), 7.03 (2H, t, *J* = 7.6 Hz), 7.13 (2H, d, *J* = 7.5 Hz), 7.34 (4H, m), 8.58 (1H, s, OH), 9.78 (2H, br, NH).

3-((1*H*-Indol-3-yl)(*p*-tolyl)methyl)-1*H*-indole (3h). Pink solid; mp 95-97 °C (Lit.[1a] mp 93-94 °C); ^{1}H NMR ($CDCl_3$): δ 2.33 (3H, s, $ArCH_3$), 5.87 (1H, s, ArCH), 6.69 (2H, s), 7.04 (2H, t, *J* = 7.1 Hz), 7.12 (2H, d, *J* = 7.1 Hz), 7.23-7.28 (6H, m), 7.41 (2H, d, *J* = 7.2 Hz), 7.94 (2H, br, NH).

3-((4-Chlorophenyl)(1*H*-indol-3-yl)methyl)-1*H*-indole (3i). Pink solid; mp 78-80 °C (Lit.[1a] mp 76-77 °C); ^{1}H NMR ($CDCl_3$): δ 5.86 (1H, s, ArCH), 6.65 (2H, s), 6.85-7.96 (12H, m), 8.00 (2H, br, NH).

3-((2-Chlorophenyl)(1*H*-indol-3-yl)methyl)-1*H*-indole (3j). Pink solid; mp 74-76 °C (Lit.[1a] (13) mp 70-71 °C); ^{1}H NMR ($CDCl_3$): δ 6.32 (1H, s, ArCH), 6.67 (2H, s), 7.02 (2H, t, *J* = 7.8 Hz), 7.10-7.22 (6H, m), 7.38-7.43 (4H, m), 7.98 (2H, br, NH).

3-((1*H*-Indol-3-yl)(thiophen-2-yl)methyl)-1*H*-indole (3k). Brown solid; mp 147-149 °C (Lit.[1a] mp 150-153 °C); ^{1}H NMR ($CDCl_3$): δ 6.08 (1H, s, ArCH), 6.86 (2H, s), 6.97-7.45 (11H, m), 7.94 (2H, br, NH).

3-(Furan-2-yl(1*H*-indol-3-yl)methyl)-1*H*-indole (3l). Brown solid; mp 316-318 °C (Lit.[1a] mp >300 °C); ^{1}H NMR ($CDCl_3$): δ 5.97 (1H, s, ArCH), 6.90 (2H, s), 7.08-7.43 (11H, m), 8.00 (2H, br, NH); ^{13}C NMR ($CDCl_3$): δ 34.8, 106.5, 110.2, 111.3, 112.2, 118.0, 119.3, 119.7, 121.7, 124.3, 126.3, 135.9, 142.0; MS (m/z): 312 (M^+).

(E)-3-(1-(1*H*-Indol-3-yl)-3-phenylallyl)-1*H*-indole (3m). Pale yellow solid; mp 100-102 °C (Lit.[1a] mp 98-99 °C); ^{1}H NMR ($CDCl_3$): δ 5.22 (1H, m), 6.19 (1H, m), 6.57 (1H, d, *J* = 15.4 Hz), 6.89 (2H, s), 7.02-7.09 (4H, m), 7.26-7.32 (7H, m), 7.49 (2H, d, *J* = 7.9 Hz), 7.92 (2H, br, NH).

(E)-3-(1-(1*H*-Indol-3-yl)but-2-enyl)-1*H*-indole (3n). Coloprless solid; mp 126-128 °C (Lit.[1a] mp 123-126 °C); ^{1}H NMR ($CDCl_3$): δ 1.66 (3H, m), 5.07 (m, 1H), 5.71 (2H, m), 6.93 (2H, s), 6.98-7.04 (4H, m), 7.27 (2H, d, *J* = 7.8 Hz), 7.48 (2H, d, *J* = 7.8 Hz), 7.90 (2H, br, NH).

3-(1-(1*H*-Indol-3-yl)hexyl)-1*H*-indole (3o). Colorless solid; mp 71-73 °C (Lit.[1a] mp 68-70 °C); ^{1}H NMR ($CDCl_3$, ppm) δ: 0.89 (3H, t, *J* = 6.7 Hz), 1.27-1.33 (6H, m), 1.52 (2H, m), 4.79 (1H, t, *J* = 6.6 Hz), 6.91 (2H, s), 6.99-7.07 (4H, m), 7.30 (2H, d, *J* = 7.8 Hz), 7.55 (2H, d, *J* = 7.8 Hz), 7.94 (2H, br, NH).

Tri(1*H*-indol-3-yl)methane (3p). Pale yellow solid; mp 162 °C (dec.) [Lit.[4l] mp 160 °C (dec.)]; ^{1}H NMR (DMSO-d_6): δ 6.11 (1H, s, ArCH), 6.86-6.91 (6H, m), 7.05 (3H, m), 7.35 (3H, d, *J* = 7.9 Hz), 7.52 (3H, d, *J* = 7.9 Hz), 10.59 (3H, s, NH).

3-(1-(1*H*-Indol-3-yl)cyclohexyl)-1*H*-indole (3q). Colorless solid; mp 163-165 °C (Lit.[3c] mp 162-164 °C); ^{1}H NMR ($CDCl_3$): δ 1.61 (2H, m), 1.69 (4H, m), 2.54-2.57 (4H, m), 6.91 (2H, s), 7.05-7.12 (4H, m), 7.34 (2H, d, *J* = 7.8 Hz), 7.58 (2H, d, *J* = 7.5 Hz), 7.94 (2H, br, NH).

4,4-Di(1*H*-indol-3-yl)pentan-2-one (3r). Colorless solid; mp 226-228 °C (Lit.[3c] 231 °C); ^{1}H NMR ($CDCl_3$): δ 1.58 (3H, s), 2.04 (3H, s), 3.13 (2H, s), 6.86 (2H, s), 7.02 (m, 2H), 7.28 (2H, d, *J* = 8.0 Hz), 7.37 (2H, m), 7.45 (2H, m), 7.96 (2H, br, NH).

3-(1-(1*H*-Indol-3-yl)-1-phenylethyl)-1*H*-indole (3s). Colorless solid; mp 162-165 °C (Lit.[1b] 165-167 °C); ^{1}H NMR ($CDCl_3$): δ 2.41 (3H, s, CH_3), 6.65 (2H, s), 6.95 (2H, t, *J* = 7.5 Hz), 7.16 (2H, t, *J* = 7.5 Hz), 7.27-7.44 (9H, m), 7.92 (2H, br, NH).

2-Methyl-3-((2-methyl-1*H*-indol-3-yl)(phenyl)methyl)-1*H*-indole (3t). Pink solid; mp 244-246 °C (Lit.[1a] 247-248 °C); ^{1}H NMR ($CDCl_3$): δ 2.05 (6H, s), 5.88 (1H, s, ArCH), 6.78-7.01 (6H, m), 7.14-7.22 (5H, m), 7.28-7.31 (2H, m), 8.02 (2H, br, NH).

2-Methyl-3-((2-methyl-1*H*-indol-3-yl)(4-nitrophenyl)methyl)-1*H*-indole (3u). Yellow solid; mp 241-243 °C (Lit.[3d] mp 240-242 °C); ^{1}H NMR ($CDCl_3$): δ 2.13 (6H, s), 5.96 (1H, s), 6.71-6.96 (6H, m), 7.21 (2H, d, *J* = 8.0 Hz), 7.47 (2H, d, *J* = 8.5 Hz), 8.00 (2H, d, *J* = 8.5 Hz), 8.07 (2H, br, NH); ^{13}C NMR ($CDCl_3$): δ 12.1, 39.0, 109.8, 111.9, 118.7, 119.1, 119.5, 121.5, 128.2, 129.4, 132.0, 135.0, 144.1, 152.4; MS (m/z): 395 (M^+).

2-Methyl-3-((2-methyl-1*H*-indol-3-yl)(*p*-tolyl)methyl)-1*H*-indole (3v). Pink solid; mp 175-177 °C (Lit.[1a] 174-175 °C); ^{1}H NMR ($CDCl_3$): δ 2.09 (6H, s), 2.29 (3H, s, $ArCH_3$), 5.92 (1H, s, ArCH), 6.71-6.96 (6H, m), 7.00-7.09 (4H, m), 7.18 (2H, d, *J* = 7.7 Hz), 7.98 (2H, br, NH).

4-(Di(1*H*-indol-3-yl)methyl)benzaldehyde (4). Pink solid; mp 257 °C (dec.);[41] ^{1}H NMR ($CDCl_3$): δ 6.08 (1H, s, ArCH), 6.67 (2H, s), 6.94-7.01 (4H, m), 7.21 (2H, d, *J* = 7.8 Hz), 7.34 (2H, d, *J* = 8.0 Hz), 7.43 (2H, d, *J* = 8.0 Hz), 7.60 (2H, d, *J* = 7.8 Hz).8.02 (2H, br, NH), 9.68 (1H, s, O=CH); ^{13}C NMR ($CDCl_3$): δ 36.1, 110.8, 112.4, 119.6, 120.0, 121.5, 124.7, 127.6, 130.0, 130.9, 134.8, 137.9, 146.7, 191.5; MS (m/z): 350 (M^+).

3-((4-(Di(1*H*-indol-3-yl)methyl)phenyl)(1H-indol-3-yl)methyl)-1H-indole (5). Pink solid, mp 191 °C (dec.) [Lit.[41] mp 194 °C (dec.)]; ^{1}H NMR (DMSO-d_6): δ 5.87 (2H, s, ArCH), 6.54 (4H, s), 7.09-7.18 (8H, m), 7.28-7.41 (12H, m), 8.14 (4H, br, NH); ^{13}C NMR ($CDCl_3$): δ 30.7, 111.8, 117.9, 118.1, 119.4, 121.1, 124.0, 126.6, 127.9, 137.0, 142.7; MS (m/z): 450 (M^+-C_8H_6N).

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