有机化学
DOI: 10.6023/cjoc201810011
研究论文
Chinese Journal of Organic Chemistry
ARTICLE

强酸性阳离子交换树脂催化水相法合成双吲哚甲烷类衍生物

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摘要　开发了一种通过强酸性离子交换树脂催化将苯甲醛和吲哚转化成双吲哚甲烷类衍生物的有效合成方法, 它是以水作为溶剂, 实现了催化剂可循环使用 6 次, 以较高收率得到了多种双吲哚甲烷化合物.

关键词　强酸性阳离子交换树脂; 吲哚; 双吲哚甲烷; 缩合

Strong-Acid Cation Exchange Resin Catalyzed Synthesis of Bis(indolyl)methanes in Water

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Abstract　An efficient protocol for conversion of aldehyde and indole into bis(indolyl)methanes derivatives catalyzed by strong-acid cation exchange resin has been developed. The H_2O was used as solution and recycle catalyst can be used six times. Various bis(indolyl)methanes derivatives were obtained in excellent yields.

Keywords　strong-acid cation exchange resin; indole; bis(indolyl)methanes; condensation

1　Introduction

The bis(indolyl)methanes (BIMs) have been widely found in various terrestrial and marine natural resources.[1] These compounds present various important biological and pharmacological activities,[2] such as antileishmanial,[3] antibacterial, anti-inflammatory,[4] antihyperlipidemic,[5] anxiolytic[6] and anticance.[7] They also are used as intermediates in agrochemicals,[8] electrochemical properties[9] and material science.[10] Due to the important pharmacological properties of BIMs, various methods have been reported for the synthesis of these derivatives in the literature.

Bisindolylmethanes have been synthesized in moderate to very good yields based on the reaction of indoles with aldehydes in the presence a wide range of catalysts. The most of these catalysts reported in the literature are Lewis acids, such as $FeSO_4$,[11] CdS,[12] sulfated anatase titania (TiO_2-SO_4^{2-}),[13] oxalic acid,[14] succinimide-*N*-sulfonic acid,[15] triethyl benzylammonium chloride,[16] trichloroisocyanuric acid,[17] $CeCl_3$,[18] Br_2[19] and sulfated polyborate.[20] And ion exchange resin,[21] montmorillonite,[22] tetranuclear Zn/4f coordination clusters,[23] magnetic solid acid nano-catalysts,[24] nano-catalyst,[25] polyacrylonitrile fiber,[26] bakers' yeast[27] all can catalyze this reaction. Also, the condensation occurs without the addition of catalysts under ultrasound irradiation[28] or high temperature.[29] The ion exchange resins, such as Amberlyst-15, Amberlyst-35 and Indion Ina 225H, with high specific surface area were found the most effective for reactions of indoles with aldehydes to afford the corresponding bis(indolyl)methanes in excellent yields.[21] It is a heterogeneous, selective, and eco-benign, and can be recovered and reused for several runs without loss of activity. They all react in an organic solvent such as acetonitrile, dichloroethane and acetone. As part of our ongoing interest in development of environmentally friendly synthetic methodologies[30] and aqueous-phase synthesis technology,[31] herein, we disclose a green and efficient synthetic strategy for preparation of bis(indolyl)methanes via the condensation of indoles with

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Received October 11, 2018; revised December 18, 2018; published online January 18, 2019.
Project supported by the Medical and Health Technology Development Program in Shandong Province (No. 2015WS0102).
山东省医药卫生科技发展计划(No. 2015WS0102)资助项目.

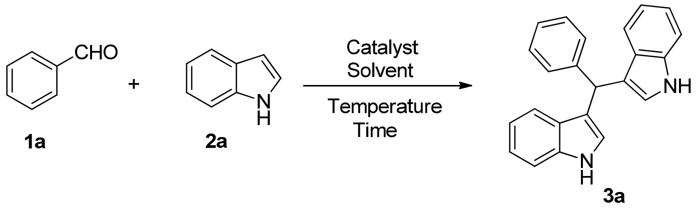
aldehydes in water catalyzed by strong-acid cation exchange resin.

2 Results and discussion

We initiated our investigation on the model reaction of benzaldehyde (**1a**) with indole (**2a**) to optimize the reaction parameters (Table 1). To our delight, the condensation took place in the presence of Amberlite 732 (10 mol%) in H_2O under N_2 for 4 h, the desired product was acquired in 97% yield (Entry 2, Table 1). Thus, Amberjet IMAC HP1110, Amberlite IR-120, Amberlite XAD 7HP, Amberlyst 15, Dowex 50WX8 and free catalyst were tested during this reaction, in which Amberlite 732 gave the best result (Entries 1～7, Table 1). Secondly, the effects of solvent were examined. Water was found to be effective solvent compared to EtOH, toluene, dichloroethane, *N*,*N*-dimethylformamide (DMF), CH_3CN and dimethyl sulfoxide (DMSO) (Entries 8～13, Table 1). When the temperature was reduced to room temperature or increased to 120 ℃, the yield decreased to 23% and 94% (Entries 14～18, Table 1). Finally, when the reaction times were shortened or delayed, the yield of **2a** decreased (Entries 1 and 19～23, Table 1). From the results shown above, the optimized condensation conditions were identified as follows: **1a** (0.5 mmol), indole (1.0 mmol), 10 mol% of amberlite 732 as catalyst, and H_2O (2.0 mL) as solvent, at 100 ℃ under an N_2 atmosphere for 4 h.

The representative results were summarized in Table 2, which the condensation of various aldehydes with indoles was obtained under the influence of the amberlite 732 in H_2O at 100 ℃ for 4 h. A series of aldehydes were allowed to react with indoles, affording bis(indolyl)methanes in moderate to good yields. Generally, no remarkable differences in reactivity were observed when electron-donor groups or electron-withdrawing were present in the aromatic ring (**3a**～**3j**). The reaction has slight impact on

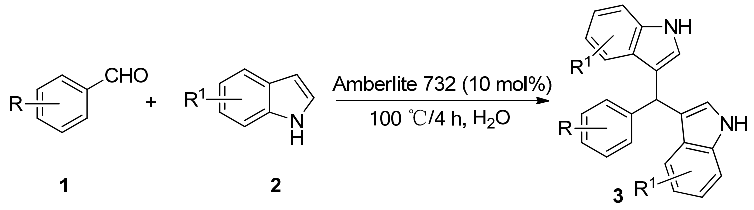
Table 1 Optimization of reaction conditions[a]

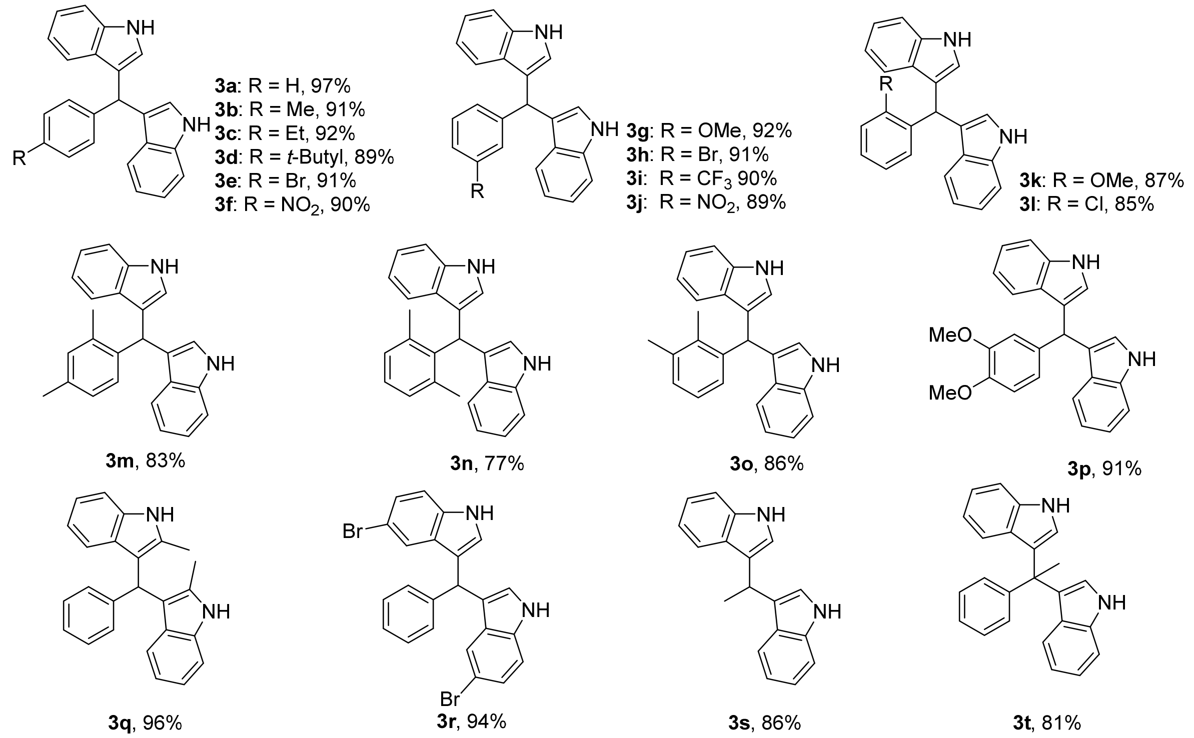


Entry	Catalyst	Solvent	Temperature/℃	Time/h	Yield[b]/%
1	—	H_2O	100	4	82
2	**Amberlite 732**	$\mathbf{H_2O}$	**100**	**4**	**97**, 81[c]
3	Amberjet IMAC HP1110	H_2O	100	4	93
4	Amberlite IR-120	H_2O	100	4	91
5	Amberlite XAD 7HP	H_2O	100	4	90
6	Amberlyst 15	H_2O	100	4	86
7	Dowex 50WX8	H_2O	100	4	88
8	HOAc	H_2O	100	4	90
9	Methanesulfonic acid	H_2O	100	4	92
10	*p*-toluenesulfonic acid	H_2O	100	4	87
11	Amberlite 732	EtOH	100	4	16
12	Amberlite 732	Toluene	100	4	9
13	Amberlite 732	Dichloroethane	100	4	27
14	Amberlite 732	DMF	100	4	25
15	Amberlite 732	CH_3CN	100	4	6
16	Amberlite 732	DMSO	100	4	37
17	Amberlite 732	H_2O	25	4	23
18	Amberlite 732	H_2O	40	4	25
19	Amberlite 732	H_2O	60	4	33
20	Amberlite 732	H_2O	80	4	65
21	Amberlite 732	H_2O	120	4	94
22	Amberlite 732	H_2O	100	0.5	19
20	Amberlite 732	H_2O	100	1.0	52
21	Amberlite 732	H_2O	100	2.0	68
22	Amberlite 732	H_2O	100	6.0	93
23	Amberlite 732	H_2O	100	8.0	91

[a] Reaction conditions: **1a** (0.5 mmol), indole (1.0 mmol), catalyst (10 mol%) and solvent (2.0 mL) under N_2 atmosphere at 100 ℃ for 4 h, unless otherwise noted.
[b] Isolated yields.

Table 2 Substrate scope^a





3a: R = H, 97%
3b: R = Me, 91%
3c: R = Et, 92%
3d: R = *t*-Butyl, 89%
3e: R = Br, 91%
3f: R = NO_2, 90%

3g: R = OMe, 92%
3h: R = Br, 91%
3i: R = CF_3 90%
3j: R = NO_2, 89%

3k: R = OMe, 87%
3l: R = Cl, 85%

3m, 83%　**3n**, 77%　**3o**, 86%　**3p**, 91%

3q, 96%　**3r**, 94%　**3s**, 86%　**3t**, 81%

^{a} Reaction conditions: **1** (0.5 mmol), **2** (1.0 mmol), catalyst (10 mol%) and solvent (2.0 mL) under N_2 atmosphere at 100 ℃ for 4 h, unless otherwise noted. ^{b} Isolated yields.

the steric hindrance of aldehydes. For example, 2-methoxybenzaldehyde and 2-chlorobenzaldehyde gave a slightly lower yield of the desired products than their *para*-substituted homologues (**3k**, **3l**). Similarly, 2,4-dimethylbenzaldehyde, 2,3-dimethylbenzaldehyde, and 2,6-dimethylbenzaldehyde have lower yields (**3m**～**3o**) but 3,4-dimethoxybenzaldehyde has good yield (**3p**). We next turned our attention towards substituted indoles. 1-Methyl-1*H*-indoles and 5-bromo-1*H*-indoles were subjected to the reaction with **1a**. They all gave the corresponding DIMs **3q** and **3r** in good yields. Many aliphatic aldehydes have been tested in this reaction, such formaldehyde, acetaldehyde, propionaldehyde, but only product of acetaldehyde (**3s**) was obtained with 86% yield. Surprisingly, an acetophenone can react with indole (**2a**) to produce 3,3'-(1-phenylethane-1,1-diyl)bis(1*H*-in- dole) (**3t**) in 81% yield.

The recycling of the catalytic was also investigated under the same conditions by the condensation of benzaldehyde with indoles. After completion of the reaction and adding dichloromethane (10 mL), the mixture was filtered and catalyst was recovered and reused (Figure 1). The recovered catalyst was reused six runs and resulted in a slight decrease in the catalytic activity which yield was down to 88%. Pleasingly, the yield can be recovered to 94.7% after acidification of the recovered catalyst. The recovered water was reused without any loss of yield, and the color become darker than past, but the color of water

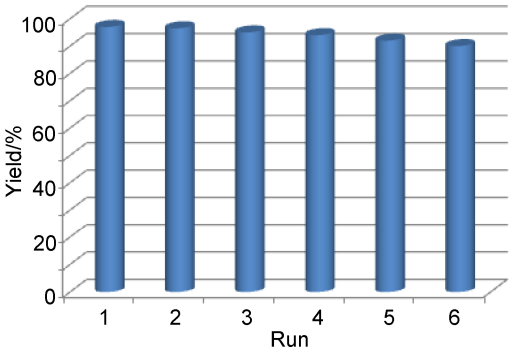
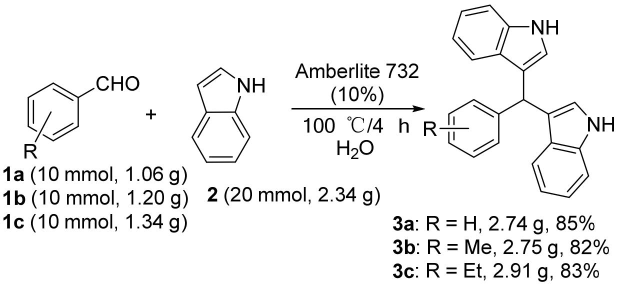


Figure 1 Recycling of the catalyst for synthesis of bis(indolyl)-methanes

can be bleached by activated carbon.

To demonstrate the synthetic utility of the condensation reactions, the gram-scale synthesis was carried out, affording products **3a**, **3b** and **3c** in 85%, 82% and 83% yields, respectively (Scheme 1). Finally, the yields of **3a** dropped to 76% and 63% when the catalyst loading was decreased to 5 and 2.5 mol% respectively in this gram-scale synthesis.



Scheme 1 Gram-scale synthesis

3 Conclusions

In summary, a simple method for conversion of aldehyde and indole into bis(indolyl)methanes derivative has been developed catalyzed by strong-acid cation exchange resin. The reaction proceeds under mild conditions and shows a broad substrate scope. It provides a convenient method to synthesize bis(indolyl)methanes. H_2O was used as solution, and recycle catalyst can be used about six times.

4 Experimental section

4.1 General information

All reactions were run under air atmosphere in Schlenk tubes. DCE, EtOH, CH_3CN, toluene and DMSO were analytical grade and not distilled before use. Commercial indoles and benzaldehydes were used without purification. ^1H NMR and ^{13}C NMR spectra were recorded using a 400 MHz spectrometer in $CDCl_3$. Melting points were determined by using a local hot-stage melting point apparatus and are uncorrected. Mass spectra were recorded using LC-MS and HRMS (ESI-TOF analyzer) equipment.

4.2 Synthesis of bis(indolyl)methanes in water catalyzed by strong-acid cation exchange resin

The amberlite 732 was wished by water for 3 times, and then soaked in 5% hydrochloric acid about 1 h. After this, the mixture was filtered off for separation of catalyst and wished by water again for pH up to 5.

Benzaldehyde (74.3 mg, 0.7 mmol), indole (117 mg, 1.0 mmol), catalyst (50 mg, 0.025 g/mL) in 2 mL water were mixed and vigorously stirred under atmosphere at 100 ℃ for 4 h. After cooling down to room temperature and adding dichloromethane (10 mL), the mixture was filtered off catalyst which was recovered and reused. The filtrate was extracted with dichloromethane (10 mL×3). Subsequently, combined of organic phase and concentrated in vacuum, the residue was purified by flash chromatography on a short silica gel to afford corresponding product.

3,3'-(Phenylmethylene)bis(1*H*-indole) (**3a**): 97% yield, reddish brown solid, m.p. 97.2～99.2 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.84 (s, 2H), 7.38 (d, J=7.9 Hz, 2H), 7.33 (dd, J=7.3, 4.5 Hz, 4H), 7.27 (t, J=7.6 Hz, 2H), 7.21 (d, J=7.1 Hz, 1H), 7.16 (t, J=7.6 Hz, 2H), 7.00 (t, J=7.5 Hz, 2H), 6.62～6.61 (m, 2H), 5.88 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 143.97, 136.64, 128.70, 128.19, 127.04, 126.11, 123.57, 121.89, 119.91, 119.66, 119.19, 111.01, 40.18. HRMS (ESI^+) calcd for $C_{23}H_{19}N_2$ $[M+H]^+$ 323.1543, found 323.1544.

3,3'-(*p*-Tolylmethylene)bis(1*H*-indole) (**3b**): 91% yield, reddish brown solid, m.p. 138～140 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.82 (s, 2H), 7.40 (dd, J=7.9 Hz, 2H), 7.33 (dt, J=8.2, 0.8 Hz, 2H), 7.25～7.22 (m, 2H), 7.16 (ddd, J=8.2, 7.1, 1.1 Hz, 2H), 7.08 (d, J=7.8 Hz, 2H), 7.00 (ddd, J=8.0, 7.1, 1.0 Hz, 2H), 6.63～6.62 (m, 2H), 5.85 (s, 1H), 2.32 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 143.97, 136.64, 128.70, 128.19, 127.04, 123.57, 121.89, 119.91, 119.66, 119.19, 111.01, 109.99, 40.18. HRMS (ESI^+) calcd for $C_{24}H_{21}N_2$ $[M+H]^+$ 337.1699, found 337.1698.

3,3'-((4-Ethylphenyl)methylene)bis(1*H*-indole) (**3c**): 92% yield, reddish brown solid, m.p. 82～84 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.72 (s, 2H), 7.44 (d, J=7.9 Hz, 2H), 7.29 (t, J=7.6 Hz, 4H), 7.21～7.17 (m, 2H), 7.14 (d, J=8.1 Hz, 2H), 7.07～7.00 (m, 2H), 6.58～6.57 (m, 2H), 5.88 (s, 1H), 2.67 (q, J=7.6 Hz, 2H), 1.27 (t, J=7.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 141.99, 141.40, 136.79, 128.74, 127.82, 127.24, 123.77, 121.96, 120.09, 119.93, 119.27, 111.24, 39.90, 28.59, 15.67. HRMS (ESI^+) calcd for $C_{25}H_{23}N_2$ $[M+H]^+$ 351.1856, found 356.1854.

3,3'-((4-(*Tert*-butyl)phenyl)methylene)bis(1*H*-indole) (**3d**): 89% yield, reddish brown solid, m.p. 97.1～99.1 ℃; ^1H NMR (400 MHz,$CDCl_3$) δ: 7.88 (s, 2H), 7.40 (d, J=8.0 Hz, 2H), 7.34 (dt, J = 8.2, 0.8 Hz, 2H), 7.26 (m, 4H),7.17～7.13 (m, 2H), 6.99 (ddd, J=8.0, 7.0, 1.0 Hz, 2H), 6.69～6.68 (m, 2H), 5.85 (s, 1H), 1.29 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) ^{13}C NMR δ: 148.79, 140.88, 136.77, 128.30, 127.24, 125.11, 123.60, 121.93, 120.10, 119.21, 111.04, 100.00, 39.72, 34.44, 31.53. HRMS (ESI^+) calcd for $C_{27}H_{27}N_2$ $[M+H]^+$ 379.2169, found 379.2171.

3,3'-((4-Bromophenyl)methylene)bis(1*H*-indole) (**3e**): 91% yield, reddish brown solid, m.p. 84.2～86.2 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.70 (s, 2H), 7.43 (dd, J=7.8, 4.3 Hz, 4H), 7.31 (d, J=8.1 Hz, 2H), 7.27～7.20 (m, 4H), 7.12～7.03 (m, 2H), 6.55～6.48 (m, 2H), 5.88 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 143.32, 136.81, 131.51, 130.69, 127.02, 123.90, 122.25, 120.10, 119.97, 119.54, 119.07, 111.46, 39.84. HRMS (ESI^+) calcd for $C_{23}H_{18}BrN_2$ $[M+H]^+$ 401.0648, found 401.0650.

3,3'-((4-Nitrophenyl)methylene)bis(1*H*-indole) (**3f**): 90% yield, orange solid, m.p. 239～241 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.13 (d, J=8.8 Hz, 2H), 8.00 (s, 2H), 7.50 (d, J=8.4 Hz, 2H), 7.38 (d, J=8.2 Hz, 2H), 7.33 (d, J=7.8 Hz, 2H), 7.19 (ddd, J=8.2, 7.1, 1.2 Hz, 2H), 7.02 (ddd, J=8.0, 7.1, 0.9 Hz, 2H), 6.68～6.67 (m, 2H), 5.98

(s, 1H); ^{13}C NMR (101 MHz, CDCl$_3$) δ: 151.91, 136.77, 129.61, 126.73, 123.71, 123.70, 122.44, 119.70, 119.64, 118.23, 111.34, 100.00, 40.29. HRMS (ESI$^+$) calcd for $C_{23}H_{18}N_3O_2$ $[M+H]^+$ 368.1394, found 368.1393.

3,3'-((3-Methoxyphenyl)methylene)bis(1*H*-indole) (**3g**): 92% yield, reddish brown solid; m.p. 175～179 ℃; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.88 (s, 2H), 7.40 (d, *J*=7.7 Hz, 2H), 7.33 (d, *J*=8.1 Hz, 2H), 7.21～7.14 (m, 3H), 7.02～6.98 (m, 2H), 6.94 (d, *J*=7.6 Hz, 1H), 6.75 (ddd, *J*=8.2, 2.6, 0.8 Hz, 1H), 6.92～6.91 (m, 1H), 6.65～6.64 (m, 2H), 5.85 (s, 1H), 3.72 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ: 159.64, 145.83, 136.76, 129.19, 127.17, 123.66, 121.98, 121.38, 119.98, 119.63, 119.30, 114.83, 111.34, 111.09, 55.19, 40.31. HRMS (ESI$^+$) calcd for $C_{24}H_{21}N_2O$ $[M+H]^+$ 353.1649, found 353.1651.

3,3'-((3-Bromophenyl)methylene)bis(1*H*-indole) (**3h**): 91% yield, reddish brown solid, m.p. 85～87 ℃; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.62 (s, 2H), 7.59 (t, *J*=1.5 Hz, 1H), 7.47 (d, *J*=7.9 Hz, 2H), 7.43 (d, *J*=7.9 Hz, 1H), 7.32～7.24 (m, 5H), 7.16 (d, *J*=7.8 Hz, 1H), 7.14～7.10 (m, 2H), 6.52～6.47 (m, 2H), 5.91 (s, 1H); ^{13}C NMR (101 MHz, CDCl$_3$) δ: 146.80, 136.82, 131.88, 130.15, 129.61, 127.63, 127.03, 124.01, 122.65, 122.30, 119.95, 119.60, 118.90, 111.54, 40.13. HRMS (ESI$^+$) calcd for $C_{23}H_{18}BrN_2$ $[M+H]^+$ 401.0648, found 401.0646.

3,3'-((3-(Trifluoromethyl)phenyl)methylene)bis(1*H*-indole) (**3i**): 90% yield, reddish brown solid, m.p. 135～137 ℃; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.76 (s, 2H), 7.71 (s, 1H), 7.53 (d, *J*=7.8 Hz, 2H), 7.42 (d, *J*=7.9 Hz, 2H), 7.38 (t, *J*=7.8 Hz, 1H), 7.34 (d, *J*=8.2 Hz, 2H), 7.26～7.22 (m, 2H), 7.08 (td, *J*=7.6, 0.8 Hz, 2H), 6.58～6.52 (m, 2H), 5.99 (s, 1H); ^{13}C NMR (101 MHz, CDCl$_3$) δ: 145.20, 136.83, 132.19, 130.79, 130.47, 128.86, 126.95, 125.62, 125.58, 123.87, 122.29, 119.83, 119.56, 118.88, 111.39, 40.22. HRMS (ESI$^+$) calcd for $C_{24}H_{18}F_3N_2$ $[M+H]^+$ 391.1417, found 391.1415.

3,3'-((3-Nitrophenyl)methylene)bis(1*H*-indole) (**3j**): 89% yield, reddish brown solid, m.p. 163～165 ℃; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 8.21 (m, 1H), 8.07 (ddd, *J*=8.2, 2.3, 1.1 Hz, 1H), 7.96 (s, 2H), 7.68 (d, *J*=7.6 Hz, 1H), 7.43 (t, *J*=7.9 Hz, 1H), 7.38～7.34 (m, 4H), 7.22～7.15 (m,2H), 7.06～6.96 (m, 2H), 6.65～6.65 (m, 2H), 5.99 (s, 1H); ^{13}C NMR (101 MHz, CDCl$_3$) δ: 148.57, 146.46, 136.82, 134.97, 129.22, 126.72, 123.77, 123.70, 122.41, 121.59, 119.65, 119.63, 118.37, 111.37, 40.10. HRMS (ESI$^+$) calcd for $C_{23}H_{18}N_3O_2$ $[M+H]^+$ 368.1394; found 368.1392.

3,3'-((2-Methoxyphenyl)methylene)bis(1*H*-indole) (**3k**): 87% yield, reddish brown solid, m.p. 96～98 ℃; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.80 (s, 2H), 7.40 (d, *J*=7.8 Hz, 2H), 7.31 (d, *J*=8.1 Hz, 2H), 7.18 (s, 1H), 7.14 (t, *J*=7.2 Hz, 3H), 6.98 (t, *J*=7.5 Hz, 2H), 6.92 (d, *J*=8.2 Hz, 1H), 6.80 (t, *J*=7.5 Hz, 1H), 6.61 (s, 2H), 6.34 (s, 1H), 3.80 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ: 156.86, 136.67, 132.32, 129.69, 127.22, 123.49, 123.45, 121.72, 120.36, 120.00, 119.56, 118.99, 110.90, 110.57, 31.97, 28.24. HRMS (ESI$^+$) calcd for $C_{24}H_{21}N_2O$ $[M+H]^+$ 353.1649, found 353.1651.

3,3'-((2-Chlorophenyl)methylene)bis(1*H*-indole) (**3l**): 85% yield, reddish brown solid, m.p. 95～97 ℃; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 8.01 (d, *J*=8.0 Hz, 1H), 7.86 (s, 2H), 7.48 (t, *J*=7.7 Hz, 1H),7.43～7.36 (m,3H), 7.33 (d, *J*=8.2 Hz, 2H), 7.19 (d, *J*=5.7 Hz, 1H), 7.15 (d, *J*=8.0 Hz, 2H), 7.08 (t, *J*=7.4 Hz, 1H), 7.01 (t, *J*=7.5 Hz, 2H), 6.59 (s, 1H), 6.33 (s, 1H); ^{13}C NMR (101 MHz, CDCl$_3$) δ: 170.08, 141.26, 136.67, 132.42, 127.48, 126.95, 126.61, 123.77, 123.73, 121.99, 119.82, 119.28, 118.31, 111.04, 36.57. HRMS (ESI$^+$) calcd for $C_{23}H_{18}ClN_2$ $[M+H]^+$ 357.1153, found 357.1151.

3,3'-((2,4-Dimethylphenyl)methylene)bis(1*H*-indole) (**3m**): 83% yield, reddish brown solid, m.p. 180～182 ℃; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.81 (s, 2H), 7.38～7.32 (m, 4H), 7.19～7.14 (m, 2H), 7.04～6.96 (m, 4H), 6.84 (d, *J*=7.3 Hz, 1H), 6.56～6.53 (m, 2H), 5.98 (s, 1H), 2.35 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ: 139.12, 136.82, 135.87, 135.43, 131.11, 128.43, 127.30, 126.56, 123.89, 121.94, 119.91, 119.45, 119.24, 111.09, 35.96, 21.07, 19.55. HRMS (ESI$^+$) calcd for $C_{25}H_{23}N_2$ $[M+H]^+$ 351.1856, found 351.1858.

3,3'-((2,6-Dimethylphenyl)methylene)bis(1*H*-indole) (**3n**): 77% yield, reddish brown solid, m.p. 172～174 ℃; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.82 (s, 2H), 7.35 (t, *J*=7.8 Hz, 4H), 7.18～7.14 (m, 2H), 7.05～6.98 (m, 3H), 6.96～6.90 (m, 2H), 6.54～6.54 (m, 2H), 6.08 (s, 1H), 2.33 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ 141.99, 136.80, 136.54, 134.67, 127.97, 127.29, 126.45, 125.17, 124.03, 121.94, 119.91, 119.61, 119.26, 111.09, 36.61, 21.04, 15.09. HRMS (ESI$^+$) calcd for $C_{25}H_{23}N_2$ $[M+H]^+$ 351.1856, found 351.1858.

3,3'-((2,3-Dimethylphenyl)methylene)bis(1*H*-indole) (**3o**): 86% yield, reddish brown solid, m.p. 248～250 ℃; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.86 (s, 2H), 7.36 (dt, *J*=8.1, 0.8 Hz, 2H), 7.29～7.26 (m, 2H), 7.17 (ddd, *J*=8.2, 7.1, 1.1 Hz, 2H), 7.11～7.07 (m, 1H), 7.02～6.97 (m, 4H), 6.64 (dd, *J*=2.4, 1.3 Hz, 2H), 6.26 (t, *J*=1.2 Hz, 1H), 2.18 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ: 141.99, 136.80, 136.54, 134.67, 127.97, 127.29, 126.45, 125.17, 124.03, 121.94, 119.91, 119.61, 119.26, 111.09, 36.61, 21.04, 15.09. HRMS (ESI$^+$) calcd for $C_{25}H_{23}N_2$ $[M+H]^+$ 351.1856, found 351.1858.

3,3'-((3,4-Dimethoxyphenyl)methylene)bis(1*H*-indole) (**3p**): 91% yield, reddish brown solid, m.p. 186～188 ℃; ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.90 (s, 2H), 7.39 (d, *J*=8.0 Hz, 2H), 7.34 (d, *J*=8.2 Hz, 2H), 7.18～7.14 (m, 2H), 7.00 (ddd, *J*=8.0, 7.1, 0.9 Hz, 2H), 6.92 (m, 1H), 6.83 (dd, *J*=8.2, 1.9 Hz, 1H), 6.76 (d, *J*=8.3 Hz, 1H), 6.63 (m, 2H), 5.83 (s, 1H), 3.84 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (101 MHz, CDCl$_3$) δ: 148.77, 147.39, 136.82, 136.79, 127.16, 123.63, 122.00, 120.67, 120.04, 119.98, 119.97, 119.29, 112.32, 111.12, 110.99, 55.92, 39.89. HRMS (ESI$^+$) calcd for $C_{25}H_{23}N_2O_2$ $[M+H]^+$ 383.1754, found 383.1752.

3,3'-(Phenylmethylene)bis(2-methyl-1*H*-indole) (**3q**): 96% yield, reddish brown solid, m.p. 234～236 ℃; ^{1}H

NMR (400 MHz, $CDCl_3$) δ: 7.73 (s, 2H), 7.24 (d, J=10.5 Hz, 7H), 7.03 (t, J=7.5 Hz, 2H), 6.97 (d, J=7.9 Hz, 2H), 6.85 (t, J=7.5 Hz, 2H), 6.00 (s, 1H), 2.06 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 135.00, 131.75, 129.05, 128.95, 128.06, 128.03, 120.57, 119.30, 119.03, 117.99, 113.38, 109.90, 39.22, 12.42. HRMS (ESI^+) calcd for $C_{25}H_{23}N_2$ $[M+H]^+$ 351.1856, found 351.1854.

3,3'-(Phenylmethylene)bis(5-bromo-1*H*-indole) (**3r**): 94% yield, reddish brown solid, m.p. 235～237 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.97 (s, 2H), 7.45 (s, 2H), 7.34～7.17 (m, 9H), 6.63 (s, 2H), 5.73 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 143.01, 135.30, 128.64, 128.51, 128.41, 126.51, 124.95, 122.26, 119.05, 117.99, 112.66, 112.55, 39.87. HRMS (ESI^+) calcd for $C_{23}H_{17}Br_2N_2$ $[M+H]^+$ 478.9753, found 478.9755.

3,3'-(Ethane-1,1-diyl)bis(1*H*-indole) (**3s**): 91% yield, light brown solid, m.p. 87～89 ℃; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.71 (s, 1H), 7.37 (d, J=7.4 Hz, 1H), 7.29 (t, J=7.7 Hz, 2H), 7.22 (dd, J=6.3, 4.4 Hz, 1H), 7.17 (d, J=7.0 Hz, 1H), 7.11 (t, J=7.6 Hz, 1H), 6.91 (t, J=8.0 Hz, 1H), 6.53 (d, J=2.3 Hz, 1H), 2.33 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 136.66, 126.93, 121.80, 121.68, 121.25, 119.76, 119.04, 111.11, 28.20, 21.77. HRMS (ESI^+) calcd for $C_{18}H_{17}N_2$ $[M+H]^+$ 261.1373, found 261.1371.

3,3'-(1-Phenylethane-1,1-diyl)bis(1*H*-indole) (**3s**): 86% yield, light blue solid, m.p. 94～96 ℃; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.71 (s, 1H), 7.37 (d, J=7.4 Hz, 1H), 7.29 (t, J=7.7 Hz, 2H), 7.24～7.20 (m, 1H), 7.17 (d, J=7.0 Hz, 1H), 7.11 (t, J=7.6 Hz, 1H), 6.91 (t, J=8.0 Hz, 1H), 6.53 (d, J=2.3 Hz, 1H), 2.33 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 148.04, 137.10, 128.10, 127.82, 126.47, 125.84, 124.71, 123.42, 122.11, 121.55, 118.94, 111.20, 43.76, 28.79. HRMS (ESI^+) calcd for $C_{24}H_{21}N_2$ $[M+H]^+$ 336.1673, found 336.1677.

Supporting Information Detailed experimental procedures and hydrogen and carbon spectrum data. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn/.

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