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Reductive Alkylation of α-Keto Imines Catalyzed by PTSA/$FeCl_3$: Synthesis of Indoles and 2,3′-Biindoles

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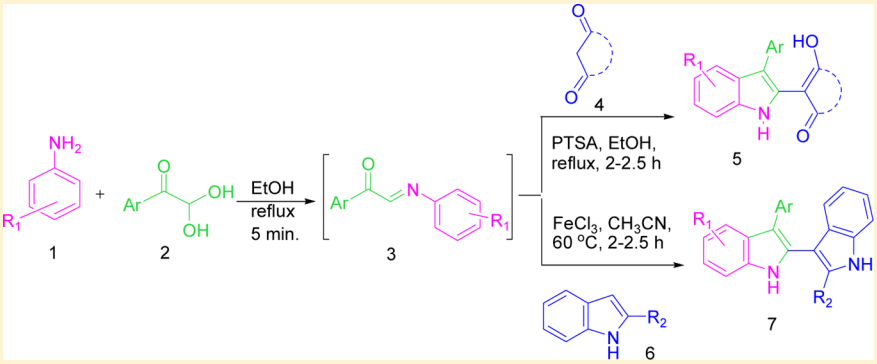
Supporting Information



ABSTRACT: A simple and efficient method for the synthesis of highly functionalized indoles and biindoles was developed. In the reaction protocol, three components were used in one pot and products were obtained in high yield in an easy workup procedure. The reaction occurred via initial reductive alkylation of α-keto imines, followed by a cyclization process in the presence of PTSA/$FeCl_3$ as catalyst.

INTRODUCTION

Indole is the most familiar molecular unit present in diverse biologically significant naturally occurring compounds and pharmaceuticals.[1] Compounds with this ring structure are considerably focused as a target pharmacophore for the development of therapeutic agents.[2] Therefore, much attention has been diverted toward the synthesis and functionalization of this molecule.[3] The long-established methods for the synthesis of indoles are based on condensation and cyclization reaction protocols.[4] However, currently, transition-metal-catalyzed C−C and C−N bond formation reactions are emerging as an alternative toward the synthesis of this versatile molecule.[5] A number of reviews on the synthesis of indoles are available in the literature.[6] However, there is an enormous need in the development of methods for the synthesis of indole and its annelated derivatives.

Biindoles, which are usually linked through 2,3′- or 3,3′-positions, constitute the basic molecular scaffold of many naturally occurring bioactive molecules, pharmaceuticals, and functional materials.[7] These molecules have also been used as key intermediates for the total synthesis of a number of other indole alkaloids possessing 2,3′- and 3,3′-biindole skeletons.[8] Consequently, substantial attention has been diverted toward the synthesis and molecular exploitation of biindoles, which include both chemical and enzymatic processes.[9] While dimerization of indoles in acidic conditions, followed by dehydrogenation, is the typical method for the preparation of biindoles,[10] transition-metal-catalyzed coupling of indolyl halides with indolylmetals has emerged as an alternative tool for the synthesis of these molecules.[11] There are also some other methods developed for the synthesis of these fascinating molecules.[12]

Utilization of imines, directly or by *in situ* generation, in the synthesis of indoles is well documented. Barluenga et al. utilized imines with *o*-dihaloarenes catalyzed by palladium under basic conditions for the synthesis of indoles.[13] The reaction was further developed, which involves an imine α-arylation, followed by an intramolecular C−N bond forming reaction in the presence of palladium catalyst.[14] An operationally simple palladium-catalyzed cyclization of *N*-aryl imines using molecular oxygen as oxidizing agent leading to indoles and their annulated derivatives was also reported.[15] Very recently, Glorius et al. reported an efficient method for the synthesis of polyfunctionalized indoles via palladium-catalyzed aerobic oxidative cyclization reaction of *N*-aryl imines.[16]

RESULTS AND DISCUSSION

In continuation to our work on indoles,[17] we report in this communication, an efficient method for the synthesis of highly functionalized indoles and biindoles involving PTSA/$FeCl_3$-catalyzed reductive alkylation of α-keto imines, followed by a cyclization process (Schemes 1 and 3). Three chemical components, anilines, arylglyoxal monohydrates, and cyclic diketones/indoles, were used in the one-pot reaction, and

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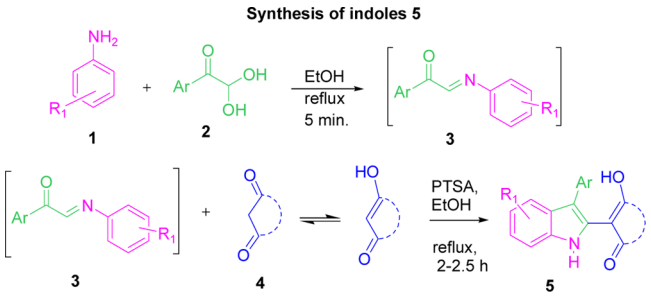
hence, a large number of compounds could be synthesized employing this methodology. The reaction procedure is simple and moderate, and most of the products were obtained in solid form during the reaction, which makes the process more versatile.

The study was initiated with the preparation of the key α-keto imine intermediate **3** (R^1 = H, Ar = Ph) from the reaction of aniline **1** (R^1 = H) and phenylglyoxal monohydrate **2**[18] (Ar = Ph), following the existing reaction protocol (Scheme 1).[19] The

Scheme 1



compound **3**, which forms (monitored with thin-layer chromatography) instantly on refluxing **1** (R^1 = H) and **2** (Ar = Ph) in ethanol, was not isolated and used directly with chroman-2,4-dione (4-hydroxy coumarin) **4** in the presence of various acid catalysts under refluxed conditions. Among all the catalysts under study, *p*-toluene sulfonic acid (PTSA) was found to be the most suitable, which afforded the product **5** (R^1 = H, Ar = Ph) in maximum yield (74%, Table 1) in 2.5 h. The

Table 1. Screening of Catalysts and Solvents

entry	solvent	catalyst	catalyst load	yield
1	EtOH		5 mol %	20
2	EtOH	I_2	5 mol %	40
3	EtOH	$Sc(OTf)_3$	5 mol %	50
4	EtOH	$In(OTf)_3$	5 mol %	55
5	EtOH	$Yb(OTf)_3$	5 mol %	50
6	EtOH	I_2	5 mol %	40
7	EtOH	PTSA	5 mol %	74
8	EtOH	PTSA	8 mol %	62
9	EtOH	PTSA	3 mol %	58
10	EtOH	$FeCl_3$	5 mol %	60
11	toluene	PTSA	5 mol %	NR
12	CH_3CN	PTSA	5 mol %	40
13	DMF	PTSA	5 mol %	30
14			5 mol %	NR

structure of the compound was ascertained from the spectroscopic data and elemental analysis. An increase or decrease in the load of the catalyst did not improve the yield of the product (entries 8 and 9, Table 1). The use of $FeCl_3$ as catalyst was also equally effective and gave the product in comparable yield (entry 10, Table 1). Aprotic as well as nonpolar solvents were not found to be suitable for the reaction (entries 11−13, Table 1). The reaction did not occur in the absence of solvent and catalyst (entry 14).

The generalization of the reaction was set up by synthesizing the compounds **5a−v** by utilizing various imines **3**, prepared from anilines **1** and arylglyoxal monohydrates **2**, with cyclic dicarbonyl compounds **4**, and characterizing them (Table 2). However, acyclic dicarbonyl compounds *viz* acetylacetone and ethyl acetoacetate did not react under identical conditions to give the expected indoles.

It was observed that the reactions were smoother in the presence of electron-withdrawing groups than the electron-donating groups at the phenyl ring of arylglyoxal monohydrates as well as in anilines, but products were obtained in comparable yields (Table 2). Among the cyclic dicarbonyl compounds **4**, 4-hydroxy coumarin was highly reactive. Products were also obtained in high yields and solid form during the reaction processes, which were purified by crystallization from ethanol. In the case of 4-hydroxy napthoquinones, some products were obtained in solid form during the reaction processes, but some others required purification by column chromatography to obtain in solid form.

A mechanism for the reaction is outlined in Scheme 2, taking the formation of **5a** as an example. First, the imine **3**, formed from the reaction of aniline **1** and phenylglyoxal monohydrate **2**, reacted with chroman-2,4-dione (4-hydroxy coumarin) **4** in the presence of PTSA to afford the intermediate [**A**]. Then, the intermediate [**A**], in the presence of acid catalyst afforded the compound **5a** as shown in Scheme 2. The bulky chroman-2,4-dione might have suitably directed the benzoyl group for the cyclization process. The mechanism was further established by performing the reaction stepwise and isolating the intermediate [**A**] and the product **5a**. Hence, when imine **3** was reacted with chroman-2,4-dione (4-hydroxy coumarin) **4** at room temperature in the presence of PTSA in ethanol, a solid compound was produced, which was filtered and purified by recrystallization from ethanol and was identified as the intermediate [**A**] from the spectroscopic data. The intermediate [**A**] was then treated in ethanol under refluxed conditions using PTSA as catalyst, which afforded the product **5a**. The structure of the compound was ascertained from the spectroscopic data and elemental analysis and found to be comparable in all respects with the product obtained from the one-pot reaction.

In order to expand the scope of the reaction, we utilized the reaction process for the synthesis of biindoles. First, it was observed that the imine **3** also forms when acetonitrile is used as solvent instead of ethanol (Scheme 3). Then, to synthesize biindoles, initially, we utilized the imine **3** (R^1 = Me, Ar = Ph) with indole (R^2 = Me) **6** in the presence of PTSA as catalyst in ethanol in refluxing conditions. The reaction occurred smoothly to afford the desired compound **7a** (R^1 = Me, Ar = Ph, R^2 = Me) in good yield (Scheme 3). The structure of the compound was ascertained from the spectroscopic data and elemental analysis. The use of I_2, $Sc(OTf)_3$, $In(OTf)_3$, and $Yb(OTf)_3$ as catalyst was not fruitful in both the solvents. Interestingly, when $FeCl_3$ was used as catalyst instead of PTSA using acetonitrile as solvent, the reaction occurred very smoothly and the products were formed in high yield on heating just at 60 °C. The reaction was also studied in various solvents, and EtOH with PTSA or CH_3CN with $FeCl_3$ was found to be suitable for the reaction. However, $FeCl_3$ in CH_3CN was considered as the best combination all in terms of easy workup and high yield of products (Scheme 3). The generalization of the reaction was set up by synthesizing a large number of compounds **7a−v** from the reaction of various imines **3** with indoles **6** and characterizing them (Table 3).

The effect of substituent in indoles, anilines, and arylglyoxals was also studied properly. In the case of 2-methylindole, the reactions were very smooth and the intermediates could be isolated in the solid form by performing the reactions at room

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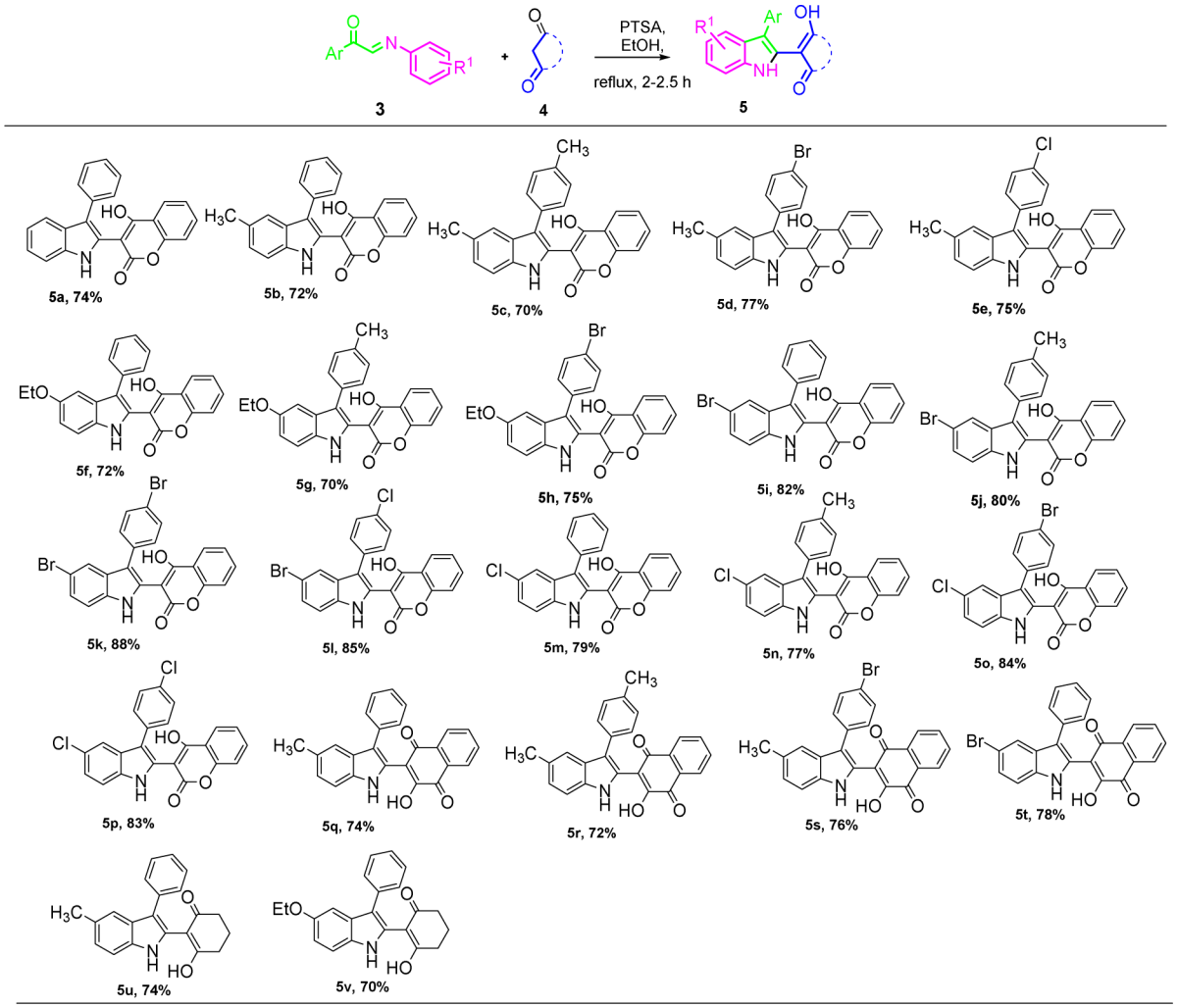
Table 2. Synthesis of Indoles 5 from the Reaction of Imines 3 and Cyclic Dicarbonyl Compounds 4



temperature. Again, the products were obtained in solid form and high yields on heating the intermediates at moderate temperature. However, in the case of 2-phenyl indole, the reactions took more time and the yields of the products were comparatively lower. Again, arylglyoxals and anilines with electron-withdrawing groups present at the aromatic ring were more reactive in comparison to their electron-donating substituents, but products were obtained in comparable yields. However, in all the cases, the desired cyclized compounds were purified by column chromatography.

The mechanism of the reaction is similar to the formation of indoles **5**. The electrophilic attack of the imine **3** occurred at the 3-position of the indole **6** to give the intermediate [**B**] (Scheme 3). Then, the intermediate [**B**] goes through a cyclization process in the presence of acid catalyst to afford the product **7**. The formation of the product was further established by isolating the intermediate [**B**] (Ar = Ph, R^1 = Me, R^2 = CH_3) obtained by performing the reaction of **3** (R^1 = CH_3) and **6** (R^2 = CH_3) at room temperature, which, on refluxing in ethanol in the presence of PTSA, or in acetonitrile in the presence of $FeCl_3$ as catalyst, afforded the compound **7a** (R^1 = Me, Ar = Ph, R^2 = Me) (Scheme 3).

We also performed the reaction by utilizing anilines **1**, arylglyoxals **2**, and cyclic diketones **4** in one pot at a time, in the presence of PTSA in ethanol under reflux conditions, which afforded the product **5** in good yield (Scheme 4). However, under identical conditions, the reaction of anilines **1**, arylglyoxals **2**, and indoles **6** produced bis-indolyl methane derivatives **8** instead of biindoles without involving aniline in the reaction process. Formation of such bis-indolyl methanes is well documented.[20] Again, the use of $FeCl_3$ as catalyst in CH_3CN under identical conditions produced the desired compounds **5** and **7** in good yield.

CONCLUSION

In conclusion, we have developed a very simple and efficient method which is applicable for the synthesis of both highly functionalized indoles and biindoles. The reaction proceeds via initial reductive alkylation of α-keto imines, followed by a cyclization process in the presence of PTSA/$FeCl_3$ as catalyst. In the reaction, three components were used in one pot, conditions were moderate, the workup procedure was simple, and most of the products were obtained in solid form during the reaction. Hence, a large number of compounds could be synthesized in a short period of time. Furthermore, the reaction has the potentiality for utilization in the synthesis of many other heterocyclic compounds of biological significance.

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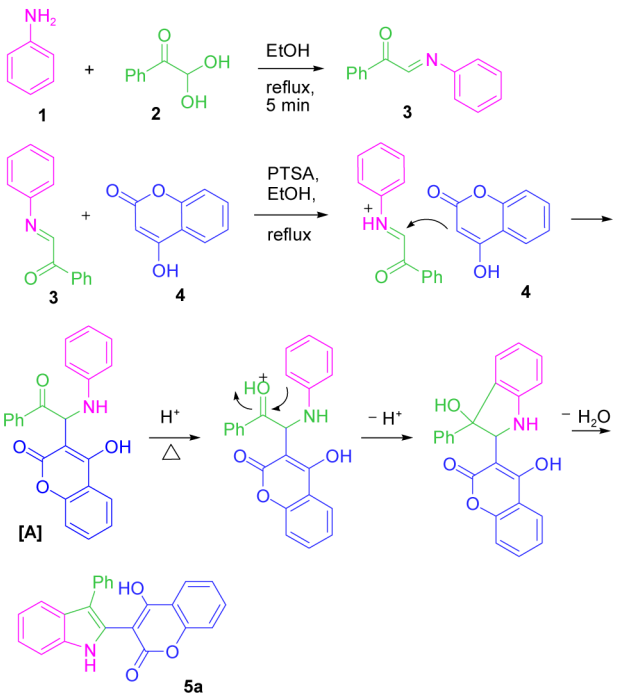
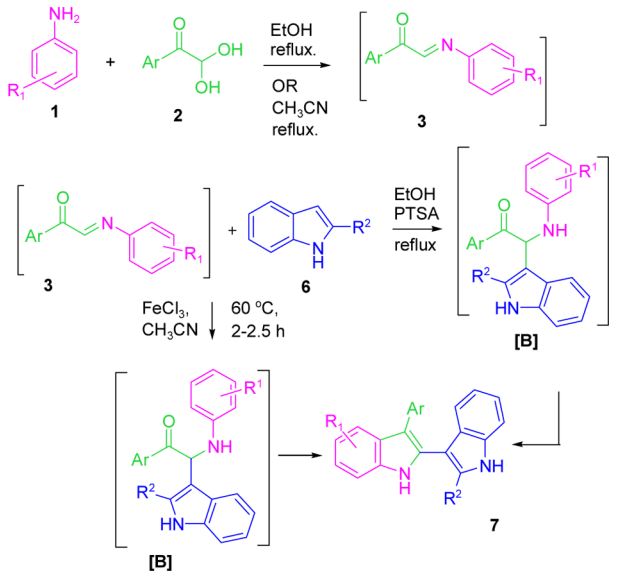
Scheme 2

Mechanism for the formation of indoles **5**



Scheme 3



EXPERIMENTAL SECTION

Melting points were recorded on a melting point apparatus and are uncorrected. IR spectra were recorded on an FTIR. ^{1}H NMR and ^{13}C NMR spectra were recorded on 300 and 75 MHz FT NMR in DMSO-d_6 using TMS as an internal standard. Chemical shifts (δ units) are given from TMS (0 ppm), and coupling constants are expressed in hertz (Hz). Chemical shifts for DMSO-d_6 were reported at 3.36, 2.50 ppm, respectively (δ units). Mass spectra were recorded on a mass spectrometer. All experiments were monitored by thin-layer chromatography (TLC). TLC was performed on precoated silica gel plates.

Experimental Procedure for the Synthesis of 5a−v. Equimolar amounts of aniline **1** (93 mg, 1 mmol) and phenylglyoxal monohydrate **2** (152 mg, 1 mmol) in 5 mL of EtOH were taken in a round-bottom flask. The reaction mixture was refluxed for 5 min and cooled to room temperature. 2-Hydroxy coumarin **4** (162 mg, 1 mmol) and PTSA (5 mol %) were added to the reaction mixture and refluxed for 2.5 h. After completion (monitored by TLC) of the reaction, the solvent was evaporated under reduced pressure and the compound was purified by column chromatography using hexane and ethyl acetate (8:2 ratio) as eluent, which gave pure compound **5a** in 74% (261 mg) yield.

Similarly, compounds **5b−v** were synthesized and characterized.

*4-Hydroxy-3-(3-phenyl-1H-indol-2-yl)-2H-chromen-2-one (**5a**).* Yield: (261 mg) 74%; mp: 176.4−177.2 °C; Reaction time: 2.5 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.19−7.98 (m, 13H), 10.96 (s, 1H, OH), 11.74 (s, 1H, NH); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ 99.1, 102.3, 113.3, 113.6, 116.6, 116.7, 121.8, 124.2, 124.4, 124.7, 127.2 (2C), 128.2, 129.1 (2C), 129.9, 132.5, 132.8, 136.5, 138.9, 153.4, 162.3, 162.8; IR (KBr) ν_{max}: 3542.0, 3287.9, 2945.2, 1671.3 cm^{-1}; MS (ESI): 354.1(M + H)$^+$; Anal. Calcd for $C_{23}H_{15}NO_3$: C, 78.18; H, 4.28; N, 3.96%. Found: C, 78.27; H, 4.22; N, 4.03%.

*4-Hydroxy-3-(5-methyl-3-phenyl-1H-indol-2-yl)-2H-chromen-2-one (**5b**).* Yield: (264 mg) 72%; mp: 198.3−199.7 °C; Reaction time: 2.5 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.39 (s, 3H), 6.97−8.06 (m, 12H), 11.02 (s, 1H, OH), 11.50 (s, 1H, NH); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ 21.5, 99.6, 103.7, 111.7, 116.3, 116.7, 119.1, 119.8, 121.1, 124.1, 124.3, 124.5, 128.3, 128.9, 129.6 (2C), 132.2, 132.6 (2C), 135.3, 136.2, 153.3, 162.1, 162.4; IR (KBr) ν_{max}: 3558.1, 3269.9, 2991.6, 1676.8 cm^{-1}; MS (ESI): 368.21 (M + H)$^+$; Anal. Calcd for $C_{24}H_{17}NO_3$: C, 78.46; H, 4.66; N, 3.81%. Found: C, 78.52; H, 4.62; N, 3.90%.

*4-Hydroxy-3-(5-methyl-3-(p-tolyl)-1H-indol-2-yl)-2H-chromen-2-one (**5c**).* Yield: (266 mg) 70%; mp: 202.8−203.9 °C; Reaction time: 2.5 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.28 (s, 3H), 2.34 (s, 3H), 6.96−8.88 (m, 11H), 10.91 (s, 1H, OH), 11.46 (s, 1H, NH); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ 21.2, 21.6, 99.9, 101.6, 111.4, 116.6, 118.1, 118.8, 123.5, 124.1, 124.4, 126.9, 128.0 (2C), 129.6, 129.9, 130.6 (2C), 132.6, 135.1, 137.1, 137.4, 153.1, 162.2, 163.8; IR (KBr) ν_{max}: 3579.9, 3433.5, 2966.8, 1659.2 cm^{-1}; MS (ESI): 382.31 (M + H)$^+$; Anal. Calcd for $C_{25}H_{19}NO_3$: C, 78.72; H, 5.02; N, 3.67%. Found: C, 78.80; H, 4.97; N, 3.70%.

*3-(3-(4-Bromophenyl)-5-methyl-1H-indol-2-yl)-4-hydroxy-2H-chromen-2-one (**5d**).* Yield: (343 mg) 77%; mp: 249.7−251.1 °C; Reaction time: 2 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.34 (s, 3H), 6.99−7.94 (m, 11H), 11.10 (s, 1H, OH), 11.59 (s, 1H, NH); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ 21.6, 99.6, 102.7, 111.6, 116.7, 116.7, 119.1, 119.8, 121.0, 124.08, 124.1, 124.4, 128.3, 129.0, 129.7 (2C), 132.0, 132.7 (2C), 135.3, 136.1, 153.2, 162.2, 162.5; IR (KBr) ν_{max}: 3568.2, 3435.7, 2876.8, 1672.8 cm^{-1}; MS (ESI): 447.01 (M + H)$^+$; Anal. Calcd for $C_{24}H_{16}BrNO_3$: C, 64.59; H, 3.61; N, 3.14%. Found: C, 64.55; H, 3.57; N, 3.19%.

*3-(3-(4-Chlorophenyl)-5-methyl-1H-indol-2-yl)-4-hydroxy-2H-chromen-2-one (**5e**).* Yield: (300 mg) 75%; mp: 240.5−242.7 °C; Reaction time: 2 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.34 (s, 3H), 6.55−7.94 (m, 11H), 11.20 (s, 1H, OH), 11.93 (s, 1H, NH); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ 21.6, 99.5, 103.2, 111.6, 115.2, 116.7, 116.7, 119.1, 124.0, 124.1, 124.4, 128.3, 128.7 (2C), 129.1 (2C), 129.7, 132.3, 132.6, 135.3, 136.0, 153.2, 162.2, 162.6; IR (KBr) ν_{max}: 3438.3, 3269.1, 2976.3, 1658.4 cm^{-1}; MS (ESI): 402.05 (M + H)$^+$; Anal. Calcd for $C_{24}H_{16}ClNO_3$: C, 71.73; H, 4.01; N, 3.49%. Found: C, 71.68; H, 4.05; N, 3.51%.

*3-(5-Ethoxy-3-phenyl-1H-indol-2-yl)-4-hydroxy-2H-chromen-2-one (**5f**).* Yield: (285 mg) 72%; mp: 200.8−201.6 °C; Reaction time: 2.5 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.30 (t, J = 18 Hz, 2H), 3.89 (q, 3H), 6.77−7.91 (m, 12H), 10.64 (s, 1H, OH), 11.47 (s, 1H, NH); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ 15.3, 63.9, 99.8, 102.1, 102.4, 108.8, 112.4, 112.8, 116.7, 124.1, 124.4, 127.0 (2C), 127.8, 129.0 (2C), 130.1, 131.9, 132.6, 133.4, 137.7, 153.1, 153.2, 162.4, 166.6; IR (KBr) ν_{max}: 3427.4, 3324.8, 2929.1, 1694.1 cm^{-1}; MS (ESI): 398.23 (M + H)$^+$; Anal. Calcd for $C_{25}H_{19}NO_4$: C, 75.55; H, 4.82; N, 3.52%. Found: C, 75.50; H, 4.88; N, 3.47%.

*3-(5-Ethoxy-3-(p-tolyl)-1H-indol-2-yl)-4-hydroxy-2H-chromen-2-one (**5g**).* Yield: (287 mg) 70%; mp: 213.8−215.3 °C; Reaction time:

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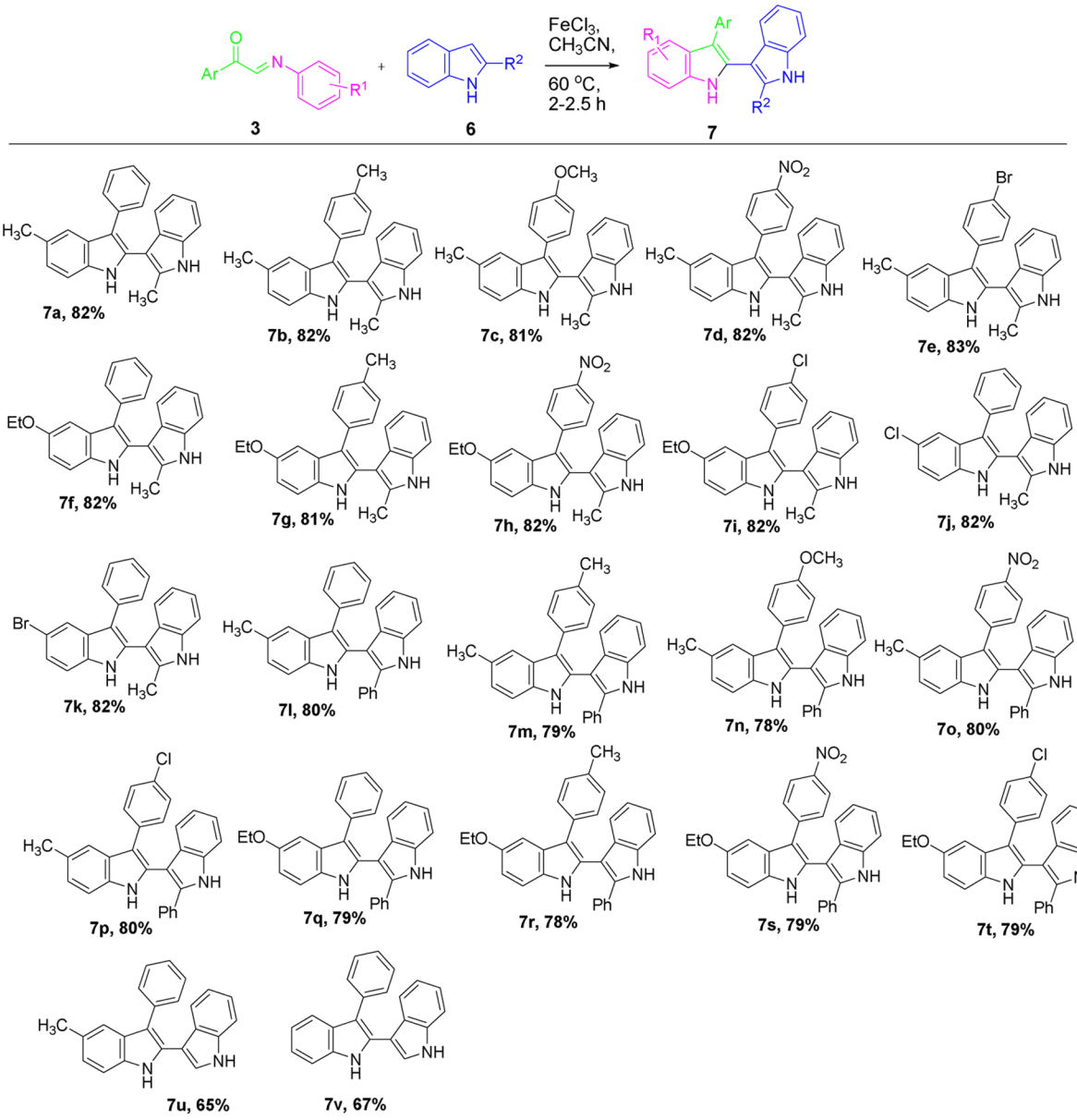
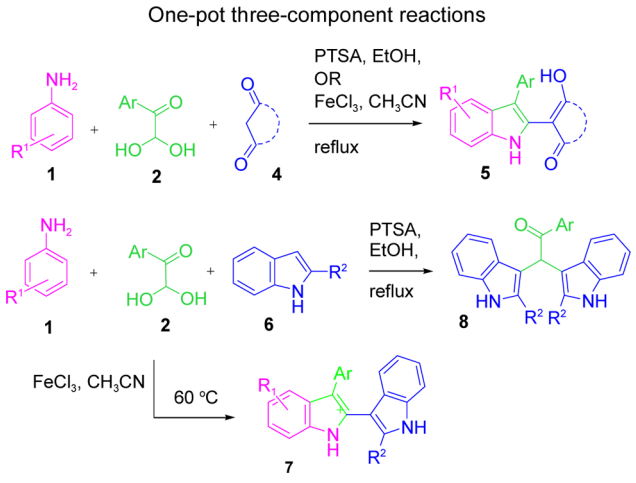
Table 3. Synthesis of Biindoles 7 from the Reaction of Imines 3 and Indoles 6



Scheme 4



2.5 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.26 (t, J = 6.00 Hz, 2H), 2.34 (s, 3H), 3.89 (q, 3H), 6.59–7.92 (m, 11H), 10.04 (s, 1H, OH), 11.41 (s, 1H, NH); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ 15.3, 21.2, 63.9, 99.9, 102.0, 102.2, 112.3, 112.5, 116.6, 116.8, 124.1, 124.3, 126.9 (2C), 129.6, 130.2 (2C), 130.7, 131.9, 132.49, 137.1, 137.9, 153.1, 153.2, 162.3, 162.3; IR (KBr) ν_{max}: 3562.3, 3437.7, 2981.3, 1664.9 cm^{-1}; MS (ESI): 412.34 (M + H)$^+$; Anal. Calcd for $C_{26}H_{21}NO_4$: C, 75.90; H, 5.14; N, 3.40%. Found: C, 75.96; H, 5.10; N, 3.37%.

*3-(3-(4-Bromophenyl)-5-ethoxy-1H-indol-2-yl)-4-hydroxy-2H-chromen-2-one (**5h**).* Yield: (356 mg) 75%; mp: 251.9–253.2 °C; Reaction time: 2.5 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.24 (t, J = 27 Hz, 2H), 3.77 (q, 3H), 6.73–7.91 (m, 11H), 10.79 (s, 1H, OH), 11.48 (s, 1H, NH); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ 15.3, 63.8, 99.4, 102.2, 103.2, 112.5, 113.2, 115.7, 116.7, 116.9, 120.9, 124.2 (2C), 124.3, 128.9, 130.0 (2C), 132.0, 132.5, 132.7, 136.5, 153.2, 153.3, 162.6, 166.5; IR (KBr) ν_{max}: 3578.4, 3467.4, 2982.3, 1674.8 cm^{-1}; MS (ESI): 477.41 (M + H)$^+$; Anal. Calcd for $C_{25}H_{18}BrNO_4$: C, 63.04; H, 3.81; N, 2.94%. Found: C, 63.12; H, 3.76; N, 2.99%.

*3-(5-Bromo-3-phenyl-1H-indol-2-yl)-4-hydroxy-2H-chromen-2-one (**5i**).* Yield: (353 mg) 82%; mp: 242.7–243.4 °C; Reaction time: 2.5 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.26–7.98 (m, 12H), 10.86

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(s, 1H, OH), 11.87 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 99.1, 102.4, 112.3, 113.8, 116.6, 116.7, 121.6, 124.1, 124.4, 124.5, 127.3 (2C), 128.3, 129.1 (2C), 131.5, 132.7, 132.8, 135.5, 138.7, 153.2, 162.3, 162.7; IR (KBr) ν_{max}: 3436.9, 3269.7, 2989.5, 1698.2 cm^{-1}; MS (ESI): 433.25 $(M + H)^+$; Anal. Calcd for $C_{23}H_{14}BrNO_3$: C, 63.91; H, 3.26; N, 3.24%. Found: C, 63.82; H, 3.31; N, 3.20%.

*3-(5-Bromo-3-(p-tolyl)-1H-indol-2-yl)-4-hydroxy-2H-chromen-2-one (**5j**).* Yield: (356 mg) 80%; mp: >300 °C; Reaction time: 2 h; ^1H NMR (300 MHz, DMSO-d_6): δ 2.28 (s, 3H), 7.19−7.92 (m, 11H), 11.09 (s, 1H, OH), 11.79 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 21.2, 99.1, 101.9, 112.2, 113.6, 116.6, 116.7, 121.5, 124.1, 124.3, 124.4, 127.1 (2C), 129.7 (2C), 129.9, 131.6, 132.7, 135.4, 137.8, 138.9, 153.2, 162.3, 162.6; IR (KBr) ν_{max}: 3542.8, 3436.3, 2982.5, 1699.5 cm^{-1}; MS (ESI): 446.43 $(M + H)^+$; Anal. Calcd for $C_{24}H_{16}BrNO_3$: C, 64.59; H, 3.61; N, 3.14%. Found: C, 64.55; H, 3.56; N, 3.20%.

*3-(5-Bromo-3-(4-bromophenyl)-1H-indol-2-yl)-4-hydroxy-2H-chromen-2-one (**5k**).* Yield: (447 mg) 88%; mp: >300 °C; Reaction time: 2.5 h; ^1H NMR (300 MHz, DMSO-d_6): δ 7.27−7.94 (m, 11H), 11.20 (s, 1H, OH), 11.93 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 98.8, 103.1, 112.4, 113.8, 116.7, 116.7, 121.6, 121.8, 124.2, 124.4, 124.9, 129.2 (2C), 131.3, 132.0, 132.1, 132.8 (2C), 135.6, 137.6, 153.3, 162.2, 162.8; IR (KBr) ν_{max}: 3575.6, 3286.7, 2964.9, 1694.6 cm^{-1}; MS (ESI): 509.32 $(M + H)^+$; Anal. Calcd for $C_{23}H_{13}Br_2NO_3$: C, 54.04; H, 2.56; N, 2.74%. Found: C, 54.09; H, 2.59; N, 2.69%.

*3-(5-Bromo-3-(4-chlorophenyl)-1H-indol-2-yl)-4-hydroxy-2H-chromen-2-one (**5l**).* Yield: (396 mg) 85%; mp: >300 °C; Reaction time: 2 h; ^1H NMR (300 MHz, DMSO-d_6): δ 7.16−8.17 (m, 11H), 11.03 (s, 1H, OH), 11.92 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 98.8, 112.4, 113.8, 116.7, 116.7, 121.8, 124.2, 124.4, 124.8, 128.9 (2C), 129.2 (2C), 131.4, 131.6, 131.7, 132.7, 133.0, 135.6, 137.5, 153.3, 162.2, 162.8; IR (KBr) ν_{max}: 3571.2, 3463.9, 2992.8, 1668.3 cm^{-1}; MS (ESI): 467.20 $(M + H)^+$; Anal. Calcd for $C_{23}H_{13}BrClNO_3$: C, 59.19; H, 2.81; N, 3.00%. Found: C, 59.23; H, 2.85; N, 2.94%.

*3-(5-Chloro-3-phenyl-1H-indol-2-yl)-4-hydroxy-2H-chromen-2-one (**5m**).* Yield: (305 mg) 79%; mp: 192.8−294.6 °C; Reaction time: 2 h; ^1H NMR (300 MHz, DMSO-d_6): δ 7.14−9.24 (m, 12H), 10.63 (s, 1H, OH), 11.85 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 99.1, 102.5, 113.3, 116.6, 116.7, 118.6, 122.0, 124.1, 124.3, 124.4, 127.2, 128.3 (2C), 129.1 (2C), 130.8, 132.7, 132.8, 135.3, 138.9, 153.2, 162.3, 162.7; IR (KBr) ν_{max}: 3571.9, 3435.7, 2962.4, 1650.9 cm^{-1}; MS (ESI): 388.32 $(M + H)^+$; Anal. Calcd for $C_{23}H_{14}ClNO_3$: C, 71.23; H, 3.64; N, 3.61%. Found: C, 71.19; H, 3.60; N, 3.66%.

*3-(5-Chloro-3-(p-tolyl)-1H-indol-2-yl)-4-hydroxy-2H-chromen-2-one (**5n**).* Yield: (308 mg) 77%; mp: 217.5−218.5 °C; Reaction time: 2.5 h; ^1H NMR (300 MHz, DMSO-d_6): δ 2.29 (s, 3H), 7.14−7.95 (m, 11H), 11.02 (s, 1H, OH), 11.80 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 21.2, 99.2, 102.1, 113.2, 116.6, 116.7, 118.5, 121.8, 124.1, 124.3, 124.3, 127.2 (2C), 129.7, 130.0, 130.9 (2C), 132.6, 135.2, 137.8, 139.1, 153.2, 162.3, 162.6; IR (KBr) ν_{max}: 3562.9, 3477.6, 2985.7, 1660.8 cm^{-1}; MS (ESI): 402.20 $(M + H)^+$; Anal. Calcd for $C_{24}H_{16}ClNO_3$: C, 71.73; H, 4.01; N, 3.49%. Found: C, 71.78; H, 3.99; N, 3.46%.

*3-(3-(4-Bromophenyl)-5-chloro-1H-indol-2-yl)-4-hydroxy-2H-chromen-2-one (**5o**).* Yield: (391 mg) 84%; mp: >300 °C; Reaction time: 2 h; ^1H NMR (300 MHz, DMSO-d_6): δ 7.17−7.96 (m, 11H), 11.21 (s, 1H, OH), 11.96 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 98.8, 103.2, 113.4, 116.7, 116.7, 118.8, 121.6, 122.3, 124.2, 124.4, 124.5, 129.2 (2C), 130.7, 132.1, 132.1, 132.7 (2C), 135.4, 137.8, 153.3, 162.2, 162.8; IR (KBr) ν_{max}: 3572.1, 3270.3, 2978.7, 1699.5 cm^{-1}; MS (ESI): 467.01 $(M + H)^+$; Anal. Calcd for $C_{23}H_{13}BrClNO_3$: C, 59.19; H, 2.81; N, 3.00%. Found: C, 59.24; H, 2.83; N, 2.95%.

*3-(5-Chloro-3-(4-chlorophenyl)-1H-indol-2-yl)-4-hydroxy-2H-chromen-2-one (**5p**).* Yield: (350 mg) 83%; mp: 269.8−270.8 °C; Reaction time: 2 h; ^1H NMR (300 MHz, DMSO-d_6): δ 7.16−9.21 (m, 11H), 10.50 (s, 1H, OH), 11.92 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 98.8, 102.5, 113.4, 116.7, 116.7, 118.8, 122.3, 124.2, 124.4, 124.5, 128.9 (2C), 129.2 (2C), 130.7, 131.7, 132.7, 133.0, 135.3, 137.7, 153.3, 162.2, 162.8; IR (KBr) ν_{max}: 3526.5, 3324.3, 2928.7, 1684.5 cm^{-1}; MS (ESI): 423.05 $(M + H)^+$; Anal. Calcd for $C_{23}H_{13}Cl_2NO_3$: C, 65.42; H, 3.10; N, 3.32%. Found: C, 65.36; H, 3.18; N, 3.30%.

*2-Hydroxy-3-(5-methyl-3-phenyl-1H-indol-2-yl)naphthalene-1,4-dione (**5q**).* Yield: (280 mg) 74%; mp: 279.9−280.2 °C; Reaction time: 2.5 h; ^1H NMR (300 MHz, DMSO-d_6): δ 2.34 (s, 3H), 6.84−8.11 (m, 12H), 10.60 (s, 1H, OH), 11.53 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 21.7, 103.2, 111.4, 119.2, 119.9, 123.7, 126.2, 126.6, 127.1, 127.7, 128.0, 129.0 (2C), 129.3, 130.9, 132.9 (2C), 133.7, 133.9, 135.7, 136.3, 136.8, 156.9, 181.4, 183.8; IR (KBr) ν_{max}: 3412.3, 3226.3, 2928.7, 1684.5 cm^{-1}; MS (ESI): 380.30 $(M + H)^+$; Anal. Calcd for $C_{25}H_{17}NO_3$: C, 79.14; H, 4.52; N, 3.69%. Found: C, 79.17; H, 4.50; N, 3.64%.

*2-Hydroxy-3-(5-methyl-3-(p-tolyl)-1H-indol-2-yl)naphthalene-1,4-dione (**5r**).* Yield: (282 mg) 72%; mp: 281.4−283.4 °C; Reaction time: 2.5 h; ^1H NMR (300 MHz, DMSO-d_6): δ 2.27 (s, 3H), 2.32 (s, 3H), 6.93−8.12 (m, 11H), 10.44 (s, 1H, OH), 11.46 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 21.2, 21.7, 102.7, 111.3, 118.3, 119.1, 119.8, 123.4, 126.2, 126.6, 127.0, 127.9, 129.3 (2C), 129.6, 132.0, 132.6 (2C), 132.8, 133.9, 134.9, 135.1, 135.5, 156.8, 181.3, 183.9; IR (KBr) ν_{max}: 3569.9, 3423.4, 2961.2, 1672.8 cm^{-1}; MS (ESI): 394.25 $(M + H)^+$; Anal. Calcd for $C_{26}H_{19}NO_3$: C, 79.37; H, 4.87; N, 3.56%. Found: C, 79.29; H, 4.90; N, 3.60%.

*2-(3-(4-Bromophenyl)-5-methyl-1H-indol-2-yl)-3-hydroxynaphthalene-1,4-dione (**5s**).* Yield: (348 mg) 76%; mp: 289.1−290.8 °C; Reaction time: 2.5 h; ^1H NMR (300 MHz, DMSO-d_6): δ 2.33 (s, 3H), 6.97−8.12 (m, 11H), 10.93 (s, 1H, OH), 11.60 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ, 21.7, 103.8, 111.5, 118.7, 120.1, 120.8, 124.0, 126.2, 126.6, 128.2, 129.1, 129.2 (2C), 130.9, 132.0, 132.9 (2C), 132.9, 133.7, 134.9, 135.1, 135.5, 156.3, 181.4, 183.8; IR (KBr) ν_{max}: 3584.2, 3464.8, 2973.1, 1674.8 cm^{-1}; MS (ESI): 459.01 $(M + H)^+$; Anal. Calcd for $C_{25}H_{16}BrNO_3$: C, 65.52; H, 3.52; N, 3.06%. Found: C, 65.56; H, 3.49; N, 3.11%.

*2-(5-Bromo-3-phenyl-1H-indol-2-yl)-3-hydroxynaphthalene-1,4-dione (**5t**).* Yield: (346 mg) 78%; mp: 284.9−285.6 °C; Reaction time: 2 h; ^1H NMR (300 MHz, DMSO-d_6): δ 6.23−8.12 (m, 12H), 10.87 (s, 1H, OH), 11.65 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 103.3, 112.2, 113.6, 117.9, 122.7, 124.5, 126.2, 126.5, 127.3, 128.2 (2C), 129.1 (2C), 130.8, 131.0, 132.9, 133.0, 133.6, 134.9, 135.3, 138.1, 157.2, 181.4, 183.7 ; IR (KBr) ν_{max}: 3416.0, 3329.7, 2930.5, 1661.1 cm^{-1}; MS (ESI): 445.12 $(M + H)^+$; Anal. Calcd for $C_{24}H_{14}BrNO_3$: C, 64.88; H, 3.18; N, 3.15%. Found: C, 64.92; H, 3.20; N, 3.10%.

*3-Hydroxy-2-(5-methyl-3-phenyl-1H-indol-2-yl)cyclohex-2-en-1-one (**5u**).* Yield: (234 mg) 74%; mp: 194.2−195.6 °C; Reaction time: 2 h; ^1H NMR (300 MHz, DMSO-d_6): δ 1.99−2.07 (m, 2H), 2.34 (s, 3H), 2.51−2.55 (t, J = 6 Hz, 2H), 3.39−3.47 (t, J = 12 Hz, 2H), 6.85−6.93 (q, 2H), 7.22−7.26 (m, 2H), 7.33−7.41 (m, 2H), 7.55−7.63 (m, 2H), 10.09 (s, 1H, OH), 11.13 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ, 21.1, 21.6, 29.9, 31.0, 105.2, 110.3, 110.9, 119.2, 123.1, 126.5 (2C), 126.9, 127.0, 128.6 (2C), 130.2, 134.0, 134.9, 135.1, 174.2, 196.9; IR (KBr) ν_{max}: 3539.1, 3276.9, 2942.6, 1664.2 cm^{-1}; MS (ESI): 318.36 $(M + H)^+$; Anal. Calcd for $C_{21}H_{19}NO_2$: C, 79.47; H, 6.03; N, 4.41%. Found: C, 79.41; H, 6.09; N, 4.35%.

*2-(5-Ethoxy-3-phenyl-1H-indol-2-yl)-3-hydroxycyclohex-2-en-1-one (**5v**).* Yield: (242 mg) 70%; mp: 257.2−259.9 °C; Reaction time: 2 h; ^1H NMR (300 MHz, DMSO-d_6): δ 1.32−1.34 (t, J = 2.8 Hz, 3H), 2.00−2.09 (m, 2H), 2.60−2.62 (t, J = 3.6 Hz, 2H), 3.40−3.47 (t, J = 8.7 Hz, 2H), 4.01−4.04 (q, 2H), 7.84−7.95 (q, 2H), 8.24−8.28 (m, 2H), 8.32−8.42 (m, 2H), 8.52−8.63 (m, 2H), 11.01 (s, 1H, OH), 12.12 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 15.3, 21.0, 30.1, 36.4, 63.8, 105.4, 110.2, 111.7, 111.8, 126.5 (2C), 127.0, 127.1, 128.6 (2C), 130.4, 131.8, 134.0, 135.8, 152.6, 173.1, 197.3; IR (KBr) ν_{max}: 3573.8, 3462.1, 2985.4, 1671.7 cm^{-1}; MS (ESI): 348.42 $(M + H)^+$; Anal. Calcd for $C_{22}H_{21}NO_3$: C, 76.06; H, 6.09; N, 4.03%. Found: C, 76.12; H, 6.15; N, 4.00%.

Experimental Procedure for the Synthesis of Intermediate [A]. Equimolar amounts of aniline **1** (93 mg, 1 mmol), phenylglyoxal

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monohydrate **2** (152 mg, 1 mmol), and 4-hydroxy coumarin **4** (162 mg, 1 mmol) were taken in a round-bottom flask containing 5 mL of EtOH. Then, 5 mol % PTSA was added to the reaction mixture, and the resulting mixture was stirred at room temperature for 1 h. The solid compound obtained was filtered and further purified by recrystallization from ethanol, which gave the compound [**A**] in (259 mg) 70% yield. The structure of the compound was determined as intermediate [**A**] from the spectroscopic analysis.

Intermediate [A]. Yield: (259 mg) 70%; ^{1}H NMR (300 MHz, DMSO-d_6): δ 4.05 (s, 1H), 6.51 (s, NH), 6.83−7.86 (m, 14H); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ 56.4, 102.6, 103.6, 116.6, 117.4 (2C), 118.4, 118.6 (2C), 119.7, 123.4 (2C), 127.8, 130.5 (2C), 131.8 (2C), 132.2 (2C), 132.6, 136.6, 153.0, 168.0.

Synthesis of 5a from Intermediate [A]. The intermediate [**A**] (371 mg, 1 mmol) was treated in ethanol (5 mL) under refluxed conditions using PTSA (5 mol %) as catalyst for 2 h. After completion of the reaction as monitored by thin-layer chromatography, solvent was evaporated under reduced pressure. The solid compound obtained was filtered and purified by recrystallization from ethanol. The structure of the compound was identified by spectroscopic data and found to be comparable in all respects with the compound **5a** prepared previously.

*Compound **5a**.* Yield: (247 mg) 70%; mp: 175.2−176.2 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.18−7.95 (m, 13H), 10.95 (s, 1H, OH), 11.72 (s, 1H, NH); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ 99.1, 102.3, 113.2, 113.6, 116.6, 116.7, 121.8, 124.3, 124.4, 124.7, 127.2 (2C), 128.2, 129.1 (2C), 129.9, 132.5, 132.8, 136.5, 138.9, 153.4, 162.3, 162.7; IR (KBr) ν_{max}: 3541.2, 3286.5, 2942.3, 1670.2 cm^{-1}; MS (ESI): 354.2(M + H)$^+$; Anal. Calcd for $C_{23}H_{15}NO_3$: C, 78.18; H, 4.28; N, 3.96%. Found: C, 78.27; H, 4.22; N, 4.03%.

Experimental Procedure for the Synthesis of Compounds 7a−v. Equimolar amounts of toluidine **1b** (107 mg, 1 mmol) and phenylglyoxal monohydrate **2** (152 mg, 1 mmol) in acetonitrile (5 mL) were taken in a round-bottom flask and refluxed for 5 min. The reaction mixture was cooled to room temperature. 2-Methy indole **6a** (131 mg, 1 mmol) and a catalytic amount of $FeCl_3$ (5 mol %) were added to the reaction mixture and stirred at 60 °C for 2.5 h. After completion of the reaction (monitored by TLC), the solvent was evaporated under reduced pressure and the compound was purified by column chromatography using hexane and ethyl acetate (8:2 ratio) as eluent, which gave the pure compound **7a** in (275 mg) 82% yield.

Similarly, compounds **7b−v** were synthesized and characterized.

*2′,5-Dimethyl-3-phenyl-1H,1′H-2,3′-biindole (**7a**).* Yield: (275 mg) 82%; mp: 155.8−156.3 °C; Reaction time: 2.5 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.05 (s, 3H), 2.30 (s, 3H), 6.50−7.98 (m, 12H), 11.06 (s, 1H, NH), 11.40 (s, 1H, NH); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ, 12.7, 21.6, 105.5, 106.2, 111.1, 111.4, 118.8, 119.0, 119.5, 120.5, 123.5, 126.7 (2C), 127.7, 128.9, 129.4 (2C), 130.4, 131.1, 133.2, 134.8, 134.9, 136.2, 136.3; IR (KBr) ν_{max}: 3411.3, 3063.8, 1660.5, 1598.6 cm^{-1}; MS (ESI): 337.41 (M + H)$^+$; Anal. Calcd for $C_{24}H_{20}N_2$: C, 85.68; H, 5.99; N, 8.33%. Found: C, 85.56; H, 6.06; N, 8.36%.

*2′,5-Dimethyl-3-(p-tolyl)-1H,1′H-2,3′-biindole (**7b**).* Yield: (287 mg) 82%; mp: 157.3−159.2 °C; Reaction time: 2.5 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.03 (s, 3H), 2.24 (s, 3H), 2.29 (s, 3H), 6.81−7.84 (m, 11H), 11.01 (s, 1H, NH), 11.30 (s, 1H, NH); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ 12.7, 21.2, 21.7, 105.5, 106.2, 111.0, 111.4, 118.8, 119.0, 119.4, 120.5, 123.5, 126.8 (2C), 127.7, 128.9, 129.4 (2C), 130.4, 131.1, 133.2, 134.8, 135.0, 136.2, 136.4; IR (KBr) ν_{max}: 3410.2, 3061.5, 1662.4, 1599.3 cm^{-1}; MS (ESI): 351.4 (M + H)$^+$; Anal. Calcd for $C_{25}H_{22}N_2$: C, 85.68; H, 6.33; N, 7.99%. Found: C, 85.73; H, 6.29; N, 8.02%.

*3-(4-Methoxyphenyl)-2′,5-dimethyl-1H,1′H-2,3′-biindole (**7c**).* Yield: (296 mg) 81%; mp: 158.2−159.4 °C; Reaction time: 2.5 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.04 (s, 3H), 2.29 (s, 3H), 3.71 (s, 3H), 6.82−7.94 (m, 11H), 11.02 (s, 1H, NH), 11.26 (s, 1H, NH); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ 12.7, 21.7, 55.4, 104.9, 106.3, 111.0, 111.3, 114.3 (2C), 118.8, 119.0, 119.3, 120.5, 123.26, 126.4, 127.6 (2C), 128.2, 129.0, 130.5, 133.2, 134.8, 134.9, 136.2, 158.5; IR (KBr) ν_{max}: 3413.5, 3065.3, 1665.1, 1595.2 cm^{-1}; MS (ESI): 367.2 (M + H)$^+$; Anal. Calcd for $C_{25}H_{22}N_2O$: C, 81.94; H, 6.05; N, 7.64%. Found: C, 81.97; H, 6.15; N, 7.58%.

*2′,5-Dimethyl-3-(4-nitrophenyl)-1H,1′H-2,3′-biindole (**7d**).* Yield: (312 mg) 82%; mp: 261.2−262.3 °C; Reaction time: 2 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.09 (s, 3H), 2.30 (s, 3H), 6.46−8.35 (m, 11H), 11.20 (s, 1H, NH), 11.72 (s, 1H, NH); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ 12.6, 21.2, 105.6, 106.2, 111.1, 111.5, 118.8, 119.1, 119.5, 120.5, 123.5, 126.7 (2C), 127.7, 128.9, 129.4 (2C), 130.4, 131.1, 133.2, 134.9, 135.0, 136.1, 136.4; IR (KBr) ν_{max}: 3412.1, 3062.4, 1667.2, 1596.3 cm^{-1}; MS (ESI): 382.2 (M + H)$^+$; Anal. Calcd for $C_{24}H_{19}N_3O_2$: C, 75.57; H, 5.02; N, 11.02%. Found: C, 75.60; H, 5.05; N, 10.97%.

*3-(4-Bromophenyl)-2′,5-dimethyl-1H,1′H-2,3′-biindole (**7e**).* Yield: (343 mg) 83%; mp: 258.5−260.3 °C; Reaction time: 2 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.06 (s, 3H), 2.29 (s, 3H), 6.82−7.90 (m, 11H), 11.09 (s, 1H, NH), 11.46 (s, 1H, NH); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ 12.7, 21.7, 105.8, 106.7, 111.1, 111.6, 118.9, 119.7, 120.2 (2C), 120.6, 124.1, 128.0, 128.6 (2C), 128.8, 130.2, 131.8 (2C), 133.1, 133.3, 133.4, 135.2, 136.2; IR (KBr) ν_{max}: 3411.3, 3067.2, 1669.4, 1591.2 cm^{-1}; MS (ESI): 416.1 (M + H)$^+$; Anal. Calcd for $C_{24}H_{19}BrN_2$: C, 69.41; H, 4.61; N, 6.74%. Found: C, 69.35; H, 4.65; N, 6.77%.

*5-Ethoxy-2′-methyl-3-phenyl-1H,1′H-2,3′-biindole (**7f**).* Yield: (300 mg) 82%; mp: 160.2−161.2 °C; Reaction time: 2.5 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.14 (t, J = 7.14 Hz, 3H), 2.08 (s, 3H), 3.83 (q, 2H), 6.56−7.90 (m, 12H), 11.11 (s, 1H, NH), 11.44 (s, 1H, NH); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ 12.7, 15.1, 63.5, 102.3, 105.3, 109.8, 111.4, 113.1, 114.7, 119.0, 119.1, 122.5, 124.3 (2C), 127.2 (2C), 128.1, 129.4, 130.2, 132.6, 133.6, 136.3, 140.5, 145.6, 153.4; IR (KBr) ν_{max}: 3419.2, 3062.8, 1661.7, 1590.2 cm-1; MS (ESI): 367.8 (M + H)$^+$; Anal. Calcd for $C_{25}H_{22}N_2O$: C, 81.94; H, 6.05; N, 7.64%. Found: C, 81.98; H, 6.08; N, 7.59%.

*5-Ethoxy-2′-methyl-3-(p-tolyl)-1H,1′H-2,3′-biindole (**7g**).* Yield: (307 mg) 81%; mp: 162.3−163.1 °C; Reaction time: 2.5 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.08 (t, J = 11.52 Hz, 3H), 2.07 (s, 3H), 2.22 (s, 3H), 3.83 (q, 2H), 6.83−8.40 (m, 12H), 11.20 (s, 1H, NH), 11.88 (s, 1H, NH); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ 12.8, 15.2, 21.8, 63.6, 102.5, 105.3, 109.9, 111.3, 113.1, 114.8, 118.9, 119.1, 122.6, 124.2 (2C), 127.1 (2C), 128.3, 129.5, 130.2, 132.6, 133.4, 136.3, 140.5, 145.7, 153.2; IR (KBr) ν_{max}: 3422.5, 3063.4, 1665.9, 1587.3 cm^{-1}; MS (ESI): 381.2 (M + H)$^+$; Anal. Calcd for $C_{26}H_{24}N_2O$: C, 82.07; H, 6.36; N, 7.36%. Found: C, 82.12; H, 6.32; N, 7.31%.

*5-Ethoxy-2′-methyl-3-(4-nitrophenyl)-1H,1′H-2,3′-biindole (**7h**).* Yield: (337 mg) 82%; mp: 165.3−166.4 °C; Reaction time: 2 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.08 (t, J = 10.78 Hz, 3H), 2.12 (s, 3H), 3.97 (q, 2H), 6.64−8.37 (m, 11H), 11.21 (s, 1H, NH), 11.70 (s, 1H, NH); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ 12.7, 15.1, 63.6, 102.4, 105.4, 109.9, 111.3, 113.1, 114.8, 118.9, 119.1, 122.5, 124.2 (2C), 127.2 (2C), 128.2, 129.5, 130.1, 132.6, 133.5, 136.4, 140.5, 145.6, 153.3; IR (KBr) ν_{max}: 3417.1, 3060.3, 1661.2, 1593.5 cm^{-1}; MS (ESI): 412.2 (M + H)$^+$; Anal. Calcd for $C_{25}H_{21}N_3O_3$: C, 72.98; H, 5.14; N, 10.21%. Found: C, 72.92; H, 5.18; N, 10.24%.

*3-(4-Chlorophenyl)-5-ethoxy-2′-methyl-1H,1′H-2,3′-biindole (**7i**).* Yield: (328 mg) 82%; mp: 198.3−199.2 °C; Reaction time: 2.5 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.14 (t, J = 13.48 Hz, 3H), 2.10 (s, 3H), 3.83 (q, 2H), 6.62−8.01 (m, 11H), 11.11 (s, 1H, NH), 11.45 (s, 1H, NH); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ 12.7, 15.1, 63.6, 102.4, 105.4, 109.8, 111.2, 113.1, 114.8, 118.9, 119.1, 122.5, 124.2 (2C), 127.2 (2C), 128.2, 129.5, 130.1, 132.6, 133.5, 136.3, 140.5, 145.6, 153.3; IR (KBr) ν_{max}: 3411.2, 3063.3, 1669.4, 1590.2 cm^{-1}; MS (ESI): 401.4 (M + H)$^+$; Anal. Calcd for $C_{25}H_{21}ClN_2O$: C, 74.90; H, 5.28; N, 6.99%. Found: C, 74.86; H, 5.32; N, 6.97%.

*5-Chloro-2′-methyl-3-phenyl-1H,1′H-2,3′-biindole (**7j**).* Yield: (291 mg) 82%; mp: 195.3−197.1 °C; Reaction time: 2 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.02 (s, 3H), 6.85−8.32 (m, 12H), 11.10 (s, 1H, NH), 11.67 (s, 1H, NH); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ 12.7, 102.3, 105.7, 107.0, 111.2, 112.6, 113.3, 114.7, 118.9, 119.0, 120.3, 120.7, 122.6, 128.9, 130.2, 131.8, 131.9, 132.4, 133.2, 133.2, 133.9, 134.6, 136.3; IR (KBr) ν_{max}: 3421.3, 3066.9, 1657.2, 1590.2

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cm^{-1}; MS (ESI): 357.4 $(M + H)^+$; Anal. Calcd for $C_{23}H_{17}ClN_2$: C, 77.41; H, 4.80; N, 7.85%. Found: C, 77.45; H, 4.77; N, 7.87%.

*5-Bromo-2′-methyl-3-phenyl-1H,1′H-2,3′-biindole (**7k**).* Yield: (328 mg) 82%; mp: 195.3−196.3 °C; Reaction time: 2 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.08 (s, 3H), 6.59−7.89 (m, 12H), 11.10 (s, 1H, NH), 11.44 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 12.7, 102.3, 105.7, 107.0, 111.2, 112.6, 113.3, 114.7, 118.9, 119.0, 120.2, 120.7, 122.5, 128.8, 130.1, 131.8, 132.0, 132.3, 133.1, 133.2, 133.9, 134.6, 136.3; IR (KBr) ν_{max}: 3425.4, 3067.2, 1667.0, 1592.3 cm^{-1}; MS (ESI): 402.4 $(M + H)^+$; Anal. Calcd for $C_{23}H_{17}BrN_2$: C, 68.84; H, 4.27; N, 6.98%. Found: C, 68.87; H, 4.36; N, 6.91%.

*5-Methyl-2′,3-diphenyl-1H,1′H-2,3′-biindole (**7l**).* Yield: (318 mg) 80%; mp: 161.6−162.4 °C; Reaction time: 2.5 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.19 (s, 3H), 6.53−7.93 (m, 17H), 11.55 (s, 1H, NH), 11.99 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 21.6, 106.3, 107.0, 111.6, 111.8, 119.2, 119.6, 119.7, 122.3, 123.9, 126.6, 126.6, 127.2, 127.3 (2C), 128.0, 128.8 (2C), 129.8, 130.0, 130.3, 133.4, 133.5, 135.0, 135.1, 135.3, 136.9; IR (KBr) ν_{max}: 3419.2, 3065.5, 1669.2, 1595.4 cm^{-1}; MS (ESI): 399.2 $(M + H)^+$; Anal. Calcd for $C_{29}H_{22}N_2$: C, 87.41; H, 5.56; N, 7.03%. Found: C, 87.48; H, 5.52; N, 7.06%.

*5-Methyl-2′-phenyl-3-(p-tolyl)-1H,1′H-2,3′-biindole (**7m**).* Yield: (325 mg) 79%; mp: 161.7−162.9 °C; Reaction time: 2.5 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.18 (s, 6H), 6.18−7.20 (m, 16H), 11.38 (s, 1H, NH), 11.56 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 21.6 (2C), 106.3, 107.0, 119.5, 119.7, 122.2, 123.9, 126.6, 126.7, 127.2, 127.3, 128.0 (2C), 128.8 (2C), 128.9, 130.1, 130.3, 133.4 (2C), 133.5, 135.0, 135.1, 135.3, 136.9(2C) ; IR (KBr) ν_{max}: 3429.3, 3059.2, 1655.4, 1595.5 cm^{-1}; MS (ESI): 413.2 $(M + H)^+$; Anal. Calcd for $C_{30}H_{24}N_2$: C, 87.35; H, 5.86; N, 6.79%. Found: C, 87.29; H, 5.92; N, 6.76%.

*3-(4-Methoxyphenyl)-5-methyl-2′-phenyl-1H,1′H-2,3′-biindole (**7n**).* Yield: (333 mg) 78%; mp: 165.3−166.2 °C; Reaction time: 2.5 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.05 (s, 3H), 3.72 (s, 3H), 6.80−7.89 (m, 16H), 11.32 (s, 1H, NH), 11.57 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 21.6, 55.8, 106.9, 111.4, 119.7, 122.3, 123.9, 126.6 (2C), 126.7(2C), 127.3, 127.3 (2C), 127.9 (2C), 128.8 (2C), 128.9, 130.1 (2C), 130.2, 133.4 (2C), 133.5, 135.0, 135.2, 135.2, 136.9, 158.6; IR (KBr) ν_{max}: 3427.9, 3058.5, 1679.1, 1595.7 cm^{-1}; MS (ESI): 429.2 $(M + H)^+$; Anal. Calcd for $C_{30}H_{24}N_2O$: C, 84.08; H, 5.65; N, 6.54%. Found: C, 84.11; H, 5.67; N, 6.51%.

*5-Methyl-3-(4-nitrophenyl)-2′-phenyl-1H,1′H-2,3′-biindole (**7o**).* Yield: (354 mg) 80%; mp: 170.1−172.3 °C; Reaction time: 2.5 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.20 (s, 3H), 6.41−8.38 (m, 16H), 11.68 (s, 1H, NH), 11.75 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 21.6, 106.0, 109.9, 112.0, 119.5, 119.8, 122.5, 124.0, 124.1, 125.5 (2C), 126.9, 127.0, 127.5, 128.7 (2C), 128.8, 129.1, 129.4 (2C), 129.6, 129.9, 132.6, 133.1, 135.3, 136.1, 137.0, 140.0, 145.7; IR (KBr) ν_{max}: 3439.4, 3060.5, 1659.2, 1595.7 cm^{-1}; MS (ESI): 444.2 $(M + H)^+$; Anal. Calcd for $C_{29}H_{21}N_3O_2$: C, 78.54; H, 4.77; N, 9.47%. Found: C, 78.50; H, 4.80; N, 9.49%.

*3-(4-Chlorophenyl)-5-methyl-2′-phenyl-1H,1′H-2,3′-biindole (**7p**).* Yield: (345 mg) 80%; mp: 172.2−173.1 °C; Reaction time: 2.5 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.18 (s, 3H), 6.49−8.39 (m, 16H), 11.66 (s, 1H, NH), 11.74 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 21.5, 105.9, 109.9, 112.0, 119.5, 119.9, 122.5, 123.9, 124.1, 125.6 (2C), 126.8, 127.0, 127.6, 128.7 (2C), 128.8, 129.0, 129.4 (2C), 129.6, 129.9, 132.6, 133.2, 135.4, 136.1, 137.1, 139.9, 145.7; IR (KBr) ν_{max}: 3429.2, 3058.5, 1669.3, 1595.5 cm^{-1}; MS (ESI): 433.2 $(M + H)^+$; Anal. Calcd for $C_{29}H_{21}ClN_2$: C, 80.45; H, 4.89; N, 6.47%. Found: C, 80.50; H, 4.82; N, 6.50%.

*5-Ethoxy-2′,3-diphenyl-1H,1′H-2,3′-biindole (**7q**).* Yield: (338 mg) 79%; mp: 163.3−164.9 °C; Reaction time: 2.5 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.11 (t, J = 5.80 Hz, 3H), 3.83 (q, 2H), 7.00−8.32 (m, 17H), 11.58 (s, 1H, NH), 11.64 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 15.3, 56.8, 63.7, 107.0, 111.9, 114.1 (2C), 115.7 (2C), 119.9, 120.3, 122.1, 127.0, 128.0 (2C), 128.8, 128.9 (2C), 129.5 (2C), 132.4 (2C), 133.4, 135.9, 136.5, 137.6 (2C), 142.1 (2C), 150.7; IR (KBr) ν_{max}: 3429.7, 3063.5, 1654.5, 1590.4 cm^{-1}; MS (ESI): 429.2 $(M + H)^+$; Anal. Calcd for $C_{30}H_{24}N_2O$: C, 84.08; H, 5.65; N, 6.54%. Found: C, 84.02; H, 5.69; N, 6.56%.

*5-Ethoxy-2′-phenyl-3-(p-tolyl)-1H,1′H-2,3′-biindole (**7r**).* Yield: (344 mg) 78%; mp: 164.2−165.7 °C; Reaction time: 2.5 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.13 (t, J = 4.33 Hz, 3H), 2.18 (s, 3H), 3.84 (q, 2H), 7.01−8.22 (m, 16H), 11.57 (s, 1H, NH), 11.68 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 15.3, 21.6, 56.8, 63.7, 106.9, 111.9, 114.1 (2C), 115.7 (2C), 119.9, 120.3, 122.1, 126.9, 128.0 (2C), 128.8, 128.9 (2C), 129.6 (2C), 132.5 (2C), 133.4, 135.9, 136.5, 137.7 (2C), 142.2 (2C), 150.7; IR (KBr) ν_{max}: 3427.2, 3052.7, 1652.1, 1595.2 cm^{-1}; MS (ESI): 443.5 $(M + H)^+$; Anal. Calcd for $C_{31}H_{26}N_2O$: C, 84.13; H, 5.92; N, 6.33%. Found: C, 84.17; H, 5.95; N, 6.31%.

*5-Ethoxy-3-(4-nitrophenyl)-2′-phenyl-1H,1′H-2,3′-biindole (**7s**).* Yield: (373 mg) 79%; mp: 179.3−180.2 °C; Reaction time: 2 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.10 (t, J = 5.26 Hz, 3H), 3.83 (q, 2H), 7.05−8.32 (m, 16H), 11.59 (s, 1H, NH), 11.69 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 15.4, 56.8, 63.7, 106.8, 111.9, 114.2 (2C), 115.7 (2C), 119.9, 120.3, 122.2, 126.9, 128.1 (2C), 128.8, 128.9 (2C), 129.7 (2C), 132.5 (2C), 133.4, 135.8, 136.6, 137.6 (2C), 142.2 (2C), 150.7; IR (KBr) ν_{max}: 3436.2, 3059.5, 1658.2, 1597.5 cm^{-1}; MS (ESI): 474.1 $(M + H)^+$; Anal. Calcd for $C_{30}H_{23}N_3O_3$: C, 76.09; H, 4.90; N, 8.87%. Found: C, 76.15; H, 4.79; N, 8.90%.

*3-(4-Chlorophenyl)-5-ethoxy-2′-phenyl-1H,1′H-2,3′-biindole (**7t**).* Yield: (364 mg) 79%; mp: 180.1−182.3 °C; Reaction time: 2.5 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.11 (t, J = 6.06 Hz, 3H), 3.83 (q, 2H), 7.10−8.35 (m, 16H), 11.55 (s, 1H, NH), 11.68 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 15.5, 56.6, 63.8, 106.6, 111.8, 114.2 (2C), 115.8 (2C), 120.0, 120.3, 122.2, 126.9, 128.1 (2C), 128.8, 128.9 (2C), 129.6 (2C), 132.4 (2C), 133.5, 135.8, 136.6, 137.7 (2C), 142.2 (2C), 150.7; IR (KBr) ν_{max}: 3437.5, 3077.3, 1688.2, 1589.2 cm^{-1}; MS (ESI): 463.7 $(M + H)^+$; Anal. Calcd for $C_{30}H_{23}ClN_2O$: C, 77.83; H, 5.01; N, 6.05%. Found: C, 77.80; H, 5.05; N, 6.08%.

*5-Methyl-3-phenyl-1H,1′H-2,3′-biindole (**7u**).* Yield: (209 mg) 65%; mp: 205.5−207.3 °C; Reaction time: 2.5 h; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.32 (s, 3H), 6.80−7.57 (m, 13H), 11.20 (s, 1H, NH), 11.34 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 21.6, 106.4, 109.0, 111.3, 111.9, 118.8, 119.2, 119.9, 121.3, 123.7, 124.5, 127.1, 127.4 (2C), 127.8, 128.6 (2C), 130.2, 133.6, 134.3, 134.9, 136.1, 136.7; IR (KBr) ν_{max}: 3423.3, 3073.2, 1668.4, 1590.2 cm^{-1}; MS (ESI): 323.1 $(M + H)^+$; Anal. Calcd for $C_{23}H_{18}N_2$: C, 85.68; H, 5.63; N, 8.69%. Found: C, 85.74; H, 5.56; N, 8.78%.

*3-Phenyl-1H,1′H-2,3′-biindole (**7v**).* Yield: (206 mg) 67%; mp: 187.3−189.1 °C; Reaction time: 2.5 h; ^{1}H NMR (300 MHz, DMSO-d_6): 7.16−7.24 (m, 2H), 7.25−8.03(m, 12H), 11.01 (s, 1H, NH), 11.29 (s, 1H, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 105.8, 108.8, 111.0, 114.6, 115.3 (2C), 118.5, 119.3 (2C), 120.7, 125.6, 126.9, 129.0 (2C), 130.2 (2C), 134.9, 135.0, 135.5, 138.1, 141.7, 142.9; IR (KBr) ν_{max}: 3419.6, 3080.4, 1666.7, 1594.2 cm^{-1}; MS (ESI): 309.1 $(M + H)^+$; Anal. Calcd for $C_{22}H_{16}N_2$: C, 85.69; H, 5.23; N, 9.08%. Found: C, 85.62; H, 5.58; N, 9.13%.

Experimental Procedure for the Synthesis of Intermediate [B]. Equimolar amounts of toludine **1** (107 mg, 1 mmol), phenylglyoxal monohydrate **2** (152 mg, 1 mmol), and 2-methylindole **6** (131 mg, 1 mmol) were taken in a round-bottom flask containing acetonitrile (5 mL). Then, 5 mol % $FeCl_3$ was added to the reaction mixture, and the resulting mixture was stirred at room temperature for 1 h. The solid compound obtained was filtered and further purified by column chromatography using hexane and ethyl acetate (8:2 ratio) as eluent, which gave the compound [**B**] in (254 mg) 72% yield. The structure of the compound was determined from the spectroscopic data.

Intermediate [B]. Yield: (254 mg) 72%; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.28 (s, 3H), 2.34 (s, 3H), 5.68 (s, 1H), 6.39 (s, NH), 6.65−7.95 (m, 13H), 11.00 (s, NH); $^{13}C\{^1H\}$ NMR (75 MHz, DMSO-d_6): δ 15.2, 21.3, 65.7, 106.9, 111.9, 114.1, 115.7, 119.8, 120.3, 122.1, 126.9, 128.0, 128.8, 128.9 (2C), 129.5, 132.4, 133.4, 135.9, 136.5, 137.5, 142.1, 150.6, 197.2.

Synthesis of 7a from [B]. The intermediate [**B**] (354 mg, 1 mmol) in acetonitrile (5 mL) was stirred at 60 °C in the presence of

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$FeCl_3$ (5 mol %) as catalyst for 2 h. After completion of the reaction, monitored by thin-layer chromatography, the solvent was evaporated under reduced pressure and the compound was purified by column chromatography using hexane and ethyl acetate (8:2 ratio) as eluent. The structure of the compound was identified by spectroscopic data and found to be comparable in all respects with the compound **7a** prepared previously.

Compound ***7(a)***. Yield: (268 mg) 80%; mp: 155.8−156.3 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.03 (s, 3H), 2.31 (s, 3H), 6.51−7.97 (m, 12H), 11.05 (s, 1H, NH), 11.42 (s, 1H, NH); ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6): δ, 12.6, 21.6, 105.4, 106.2, 111.1, 111.4, 118.8, 119.1, 119.4, 120.5, 123.5, 126.7 (2C), 127.7, 128.9, 129.4 (2C), 130.4, 131.1, 133.2, 134.8, 134.8, 136.2, 136.3; IR (KBr) ν_{max}: 3410.3, 3062.7, 1663.4, 1597.6 cm^{-1}; MS (ESI): 337.41 $(M + H)^+$; Anal. Calcd for $C_{24}H_{20}N_2$: C, 85.68; H, 5.99; N, 8.33%. Found: C, 85.56; H, 6.06; N, 8.36%.

Experimental Procedure for the Synthesis of 5 Using Three Components at a Time. Equimolar amounts of aniline **1** (93 mg, 1 mmol), phenylglyoxal monohydrate **2** (152 mg, 1 mmol), and 4-hydroxy coumarin **4** (162 mg, 1 mmol) in the presence of (5 mL) 5 mol % PTSA in ethanol (5 mL) or 5 mol % $FeCl_3$ in acetonitile were taken in a round-bottom flask. The reaction mixture was refluxed for 2.5 h. After completion of the reaction (monitored by TLC), solvent was evaporated under reduced pressure and the compound was purified by column chromatography using hexane and ethyl acetate (8:2 ratio) as eluent. The structure of the compound was ascertained as **5a** from the spectroscopic data and by comparing with the authentic sample prepared previously.

Experimental Procedure for the Synthesis of 7 Using Three Components at a Time. Equimolar amounts of toludine **1** (107 mg, 1 mmol), phenylglyoxal monohydrate **2** (152 mg, 1 mmol), and 2-methylindole **6** (131 mg, 1 mmol) in the presence of 5 mol % $FeCl_3$ in acetonitile (5 mL) were taken in a round-bottom flask. The reaction mixture was stirred at 60 °C for 2.5 h. After completion of the reaction (monitored by TLC), solvent was evaporated under reduced pressure and the compound was purified by column chromatography using hexane and ethyl acetate (8:2 ratio) as eluent. The structure of the compound was ascertained as **7a** from the spectroscopic data and by comparing with the authentic sample prepared previously.

When equimolar amounts of toludine **1**(107 mg, 1 mmol), phenylglyoxal monohydrate **2** (152 mg, 1 mmol), and 2-methylindole **6** (131 mg, 1 mmol) in the presence of 5 mol % PTSA in ethanol (5 mL) were refluxed, diindolyl methane derivative **8** was produced.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H, ^{13}C NMR spectra of new compounds. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00533.

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Notes

The authors declare no competing financial interest.

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