Tetrahedron xxx (2013) 1–7

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

I_2-promoted direct one-pot synthesis of 2,2-bisindolyl-1-arylethanones from multiform substrates arylethenes, 2-hydroxy-aromatic ketones, and carbinols

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ARTICLE INFO

Article history:
Received 29 March 2013
Received in revised form 5 June 2013
Accepted 13 June 2013
Available online xxx

Keywords:
I_2-promoted
One-pot
Friedel–Crafts alkylation
Bisindoles

ABSTRACT

An I_2-promoted domino protocol was developed to construct 2,2-bisindolyl-1-arylethanones from multiform substrates arylethenes, 2-hydroxy-aromatic ketones, and carbinols via three distinct pathways. Through a logical coupled oxidation/Friedel–Crafts alkylation domino process, a variety of 2,2-bisindolyl-1-arylethanones were synthesized in one-pot.

1. Introduction

Indole is a fundamental subunit of many bioactive compounds and natural products.[1] Among the indole derivatives, bis(indolyl) methanes (BIMs), which were widely isolated from various terrestrial and marine natural sources,[2] are well known to possess various biological activities, pharmacological activities, such as antimicrobial and antifungal,[3a] antibacterial,[3b] analgesic and anti-inflammatory activities.[3c] Notably, cancer chemotherapy with BIMs has recently been reviewed.[4] For instance, bis(5-methoxyindol-3-yl) methane was found to considerably inhibit the growth of cancer cell lines (Fig. 1).[5]

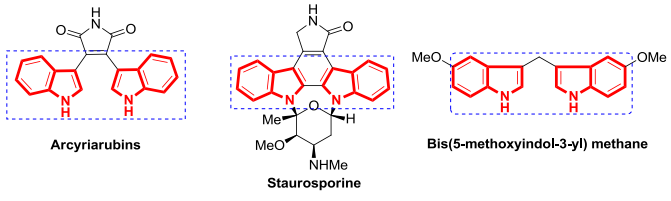

Fig. 1. Chemical structures of bioactive bisindole derivatives.

Due to the diverse activities of BIMs, many synthetic approaches have been reported for the synthesis of bis(indolyl)methanes. The most common methods involve Friedel–Crafts alkylation of indoles with aldehydes/ketones, and many kinds of catalysts was adopted to promote these reactions, such as Lewis acid,[6] protoic acid,[7a] ionic liguid,[7b,c] and other catalysts.[7d] In addition, alcohols, amines, imines, alkynes, alkenes,[8] and other substrates[9] were also regarded as effective modules to construct bis(indolyl)methanes block. Recently, Wang and co-workers proposed a graceful Rhenium-catalyzed site-switchable addition of indoles to terminal alkynes for the synthesis of bisindolylalkane derivatives.[10] Lee's group developed an excellent Au(I)-catalyzed synthetic method to construct diverse bisindoles from 3,3-disubstituted cyclopropenes.[11] Our group also presented a new method for direct synthesis of 2,2-bisindolyl-1-arylethanones from aryl methyl ketones and indoles via sp^3 C–H diarylation.[12] In this protocol, α-ketoaldehyde proved to be a key intermediate. On the basis of previous reports, we found that a wide range of terminal aryl alkenes could easily be transformed to α-iodo acetophenone in the presence of I_2/IBX in DMSO,[13] and α-iodo acetophenone was easily converted to α-ketoaldehyde in the media of DMSO via Kornblum oxidation.[14] Herein, we attempt to directly construct various 2,2-bisindolyl-1-arylethanones from arylethenes and indoles via the cascade integration of iodination/oxidation/Friedel–Crafts alkylation (Scheme 1).

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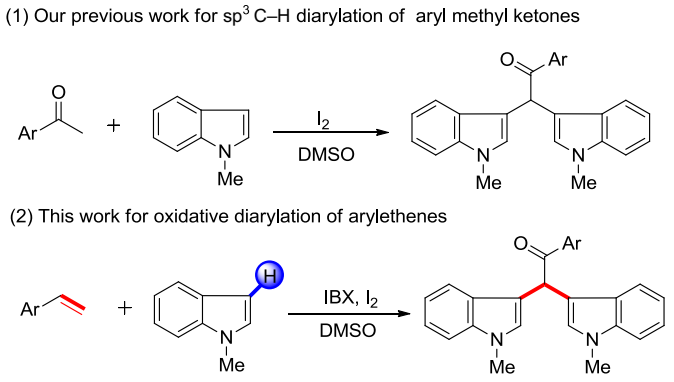
http://dx.doi.org/10.1016/j.tet.2013.06.054



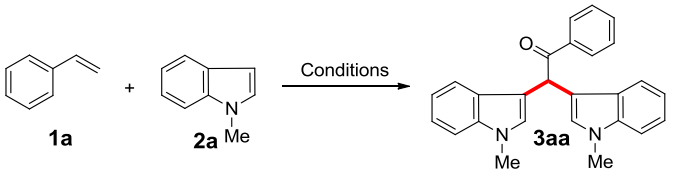
Scheme 1. Protocols for synthesis of 2,2-biaryl-1-arylethanones.

2. Results and discussion

Initially, the reaction of styrene (**1a**) with *N*-methylindole (**2a**) was chosen as a model reaction for optimization of the conditions. First, we screened a series of oxidants for the reaction, such as TBHP, DMP, BTI, *m*-CPBA, HTIB, DDQ, $PhI(OAc)_2$, and H_2O_2. Unfortunately, these oxidants failed to obtain the desired product **3aa** (Table 1, entries 1–8). To our delight, the reaction led to the desired product (**3aa**) in a very low yield of 6% using IBX as oxidant (Table 1, entry 9). Moreover, several different additives (NIS, KI, and TBAI) was not found to promote the reaction (Table 1, entries 10–12). In addition, the reaction could not perform without I_2 (Table 1, entry 13). Elevation or decrease of the reaction temperature could not improve the reaction yields (Table 1, entries 14–16). After several experimental optimizations toward the dosage of I_2 (Table 1, entries 17–19), we finally found that **1a** (0.5 mmol) reacted with I_2/IBX (0.75 mmol/0.5 mmol) in DMSO at 80 °C for 3 h, which was followed by the addition of **2a** (1.0 mmol) at room temperature for another 5 h, the desired product (**3aa**) was afforded in 66% yield (Table 1, entry 18).

With the optimal conditions in hand, the scope of the transformation was investigated in the media of I_2/IBX, and the results were summarized in Table 2. As illustrated in Table 2, arylethenes bearing electron-donating or -withdrawing groups, such as Me, OMe, *t*-Bu, F, Cl, Br, and CN, could perform smoothly with *N*-methylindole **2a** to afford the desired products **3aa**–**3ma** in moderate to good yields (54–75%). Furthermore, 2-naphthyl ethene (**1n**) and biphenyl ethane (**1o**) also reacted with *N*-methylindole **2a** to obtain the desired products **3na** and **3oa** in 61% and 68% yields, respectively. The results demonstrated that neither the electronic nature nor steric hindrance of the arylethenes had considerable influence on the reaction efficiency. Furthermore, the target compound **3fa** was determined by X-ray crystallographic analysis (Fig. 2).

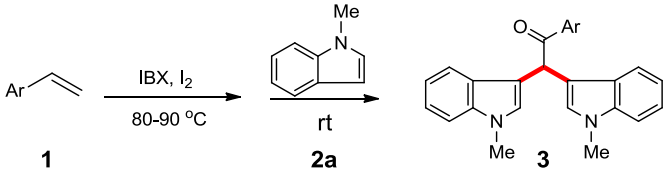
Table 1
Optimization of the reaction conditions



Entry	Additive (equiv)	Oxidant (equiv)	Temp (°C)	Yield[c] (%)
1[a]	I_2 (1.0)	TBHP (1.0)	80	nr
2[a]	I_2 (1.0)	DMP (1.0)	80	nr
3[a]	I_2 (1.0)	BTI (1.0)	80	nr
4[a]	I_2 (1.0)	*m*-CPBA (1.0)	80	nr
5[a]	I_2 (1.0)	HTIB (1.0)	80	nr
6[a]	I_2 (1.0)	DDQ (1.0)	80	nr
7[a]	I_2 (1.0)	$PhI(OAc)_2$ (1.0)	80	nr
8[a]	I_2 (1.0)	H_2O_2 (1.0)	80	nr
9[a]	I_2 (1.0)	IBX (1.0)	80	6
10[a]	NIS (1.0)	IBX (1.0)	80	nr
11[a]	KI (1.0)	IBX (1.0)	80	nr
12[a]	TBAI (1.0)	IBX (1.0)	80	nr
13[a]	—	IBX (1.0)	80	nr
14[b]	I_2 (1.0)	IBX (1.0)	80	62
15[b]	I_2 (1.0)	IBX (1.0)	60	42
16[b]	I_2 (1.0)	IBX (1.0)	100	58
17[b]	I_2 (2.0)	IBX (1.0)	80	64
18[b]	**I_2 (1.5)**	**IBX (1.0)**	**80**	**66**
19[b]	I_2 (0.5)	IBX (1.0)	80	45

[a] Reaction conditions: **1a** (0.5 mmol), **2a** (1.0 mmol), additive (0.5 mmol), oxidant (0.5 mmol) were heated at 80 °C in 3 mL DMSO for 3 h.
[b] Reaction conditions: **1a** (0.5 mmol), I_2, and oxidant (0.5 mmol) were heated at 80 °C for 3 h and then **2a** (1.0 mmol) was added at room temperature for another 5 h.
[c] Isolated yield. IBX=*o*-iodoxy-benzoic acid, TBHP=*tert*-butyl hydroperoxide, DMP=1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1*H*)-one, BTI=[bis-(trifluoroacetoxy)iodo]benzene, *m*-CPBA=3-chloroperbenzoic acid, HTIB=[hydro(-tosyloxy)iodo]benzene, DDQ=2,3-dichloro-5,6-dicyano-1,4-benzoquinone. nr=no reaction.

Table 2
Reaction scope of arylethenes[a]



Entry	**1** (Ar)	**3**	Yields[b] (%)
1	**1a** (C_6H_5)	**3aa**	66
2	**1b** (3-Me–C_6H_4)	**3ba**	62
3	**1c** (4-Me–C_6H_4)	**3ca**	61
4	**1d** (2,4-Me_2–C_6H_3)	**3da**	64
5	**1e** (2,4,6-Me_3–C_6H_2)	**3ea**	54
6	**1f** (4-*t*-Bu–C_6H_4)	**3fa**	67
7	**1g** (4-MeO–C_6H_4)	**3ga**	58
8	**1h** (3-F–C_6H_4)	**3ha**	63
9	**1i** (4-F–C_6H_4)	**3ia**	62
10	**1j** (4-Cl–C_6H_4)	**3ja**	70
11	**1k** (3-Br–C_6H_4)	**3ka**	74
12	**1l** (4-Br–C_6H_4)	**3la**	75
13	**1m** (4-CN–C_6H_4)	**3ma**	70
14	**1n** (2-Naphthyl)	**3na**	61
15	**1o** (4-Ph–C_6H_4)	**3oa**	68

[a] Reaction conditions: **1** (0.5 mmol), I_2 (0.75 mmol), and IBX (0.5 mmol) were heated in 3 mL DMSO at 80 °C for 2–4 h, and then **2a** (1.0 mmol) was added for another 5–8 h.
[b] Isolated yields.

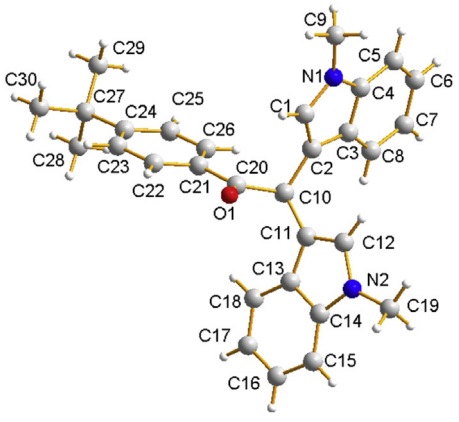
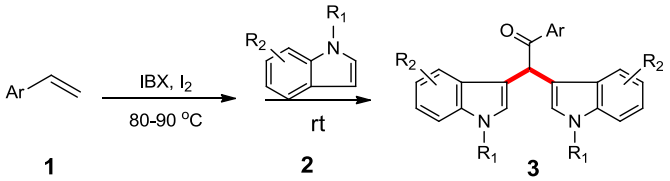


Fig. 2. X-ray crystal structure of compound **3fa**.

Subsequently, a series of indole derivatives and arylethenes were examined. The electronic and steric nature of arylethenes had little influence on the reaction efficiency, and all the corresponding products were obtained in 55%–72% yields (Table 3, entries 1–6). Then we turned our attention to the indole derivatives (**2c**–**2h**). The substrates (**2c** and **2d**) bearing electron-rich substituents could perform smoothly to give the corresponding products in generally good yields (Table 3, **3ac** and **3ad**). However, the electron-withdrawing groups, such as 6-Br and 6-NO_2, were shown to largely decrease the reactivity, affording the desired products **3ae** and **3af** in relatively low yields (Table 3). Meanwhile, the *N*-allylindole **2g** and *N*-benzylindole **2h** also gave their corresponding products **3ag** and **3ah** in 26% and 37% yields, respectively.

Table 3
Reaction scope of arylethenes and indole derivatives[a]

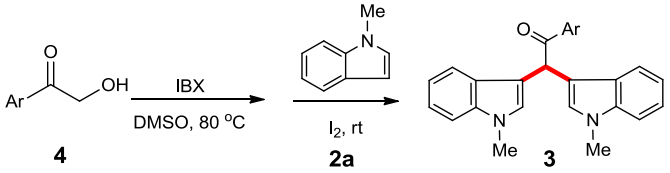


Entry	**1** (Ar)	**2**	**3**	Yields[b] (%)
1	**1a** (C_6H_5)	**2b** (R_1=H, R_2=H)	**3ab**	60
2	**1g** (4-MeO–C_6H_5)		**3gb**	55
3	**1k** (3-Br–C_6H_4)		**3kb**	62
4	**1m** (4-CN–C_6H_4)		**3mb**	72
5	**1n** (2-Naphthyl)		**3nb**	60
6	**1o** (4-Ph–C_4H_4)		**3ob**	70
7	**1a** (C_6H_5)	**2c** (R_1=H, R_2=6-Me)	**3ac**	71
8		**2d** (R_1=H, R_2=2-Me)	**3ad**	75
9		**2e** (R_1=H, R_2=6-Br)	**3ae**	45
10		**2f** (R_1=H, R_2=6-NO_2)	**3af**	Trace
11		**2g** (R_1=allyl, R_2=H)	**3ag**	26
12		**2h** (R_1=benzyl, R_2=H)	**3ah**	37

[a] Reaction conditions: **1** (0.5 mmol), I_2(0.75 mmol), and IBX (0.5 mmol) were heated in 3 mL DMSO at 80–90 °C for 2–4 h, and then **2** (1.0 mmol) was added for another 5–10 h.
[b] Isolated yields.

To further expand the scope of the substrates, 2-hydroxyaromatic ketones, such as **4a**–**4d** were also investigated. To our delight, 2-hydroxy-aromatic ketones could easily be transformed to arylglyoxals in the presence of IBX in DMSO, which then reacted with *N*-methylindole (**2a**) in the presence of I_2 to afford the corresponding products in one-pot. The desired products were afforded in moderate to good yields (55–72%, Table 4, entries 1–4).

Table 4
Scope of 2-hydroxy-aromatic ketones[a]

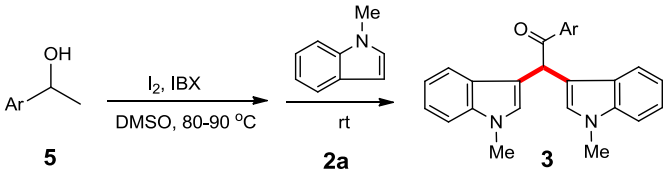


Entry	**4** (Ar)	**3**	Yields[b] (%)
1	**4a** (C_6H_5)	**3aa**	60
2	**4b** (4-Me–C_6H_4)	**3ca**	55
3	**4c** (4-F–C_6H_4)	**3ia**	62
4	**4d** (4-Br–C_6H_4)	**3la**	72

[a] Reaction conditions: **4** (0.5 mmol) and IBX (0.5 mmol) were heated in 3 mL DMSO at 80 °C for 3–5 h, and then **2a** (1 mmol) and I_2 (0.75 mmol) were added at room temperature for another 5–10 h.
[b] Isolated yields.

To our delight, 1-arylethanols **5** were also found compatible for the transformation in the presence of IBX and I_2 in DMSO. The results are summarized in Table 5. Here, 1-arylethanols **5** were treated with IBX (1.0 equiv) and I_2 (1.5 equiv) in DMSO at 80–90 °C, and then 2.0 equiv of *N*-methylindole **2a** was added to the mixture at room temperature. 1-Phenylethanol and 1-(4-bromophenyl) ethanol (**5a** and **5c**) could smoothly afford the expected products in 76% and 78% yields (Table 5, **3aa** and **3la**), respectively. However, when the substrates **5b** and **5d** were used, the desired products (**3pa** and **3qa**) were only obtained in relatively low yields, possibly due to the strong steric hindrance involved.

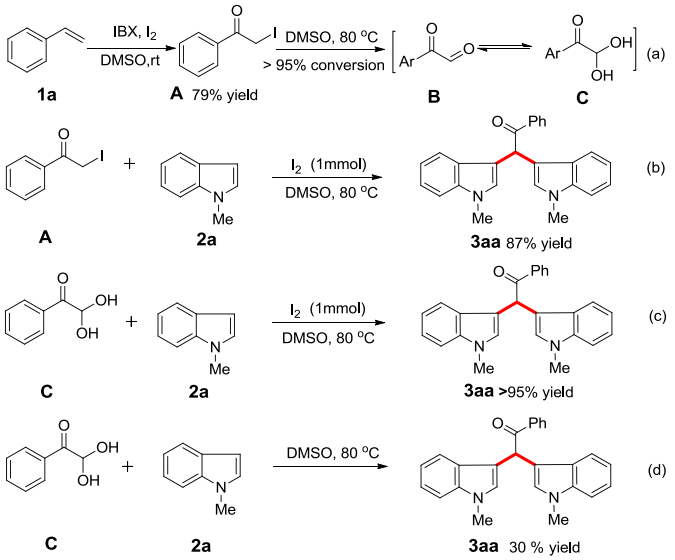
Table 5
Scope of 1-arylethanols[a]



Entry	**5** (Ar)	**3**	Yields[b] (%)
1	**5a** (C_6H_5)	**3aa**	76
2	**5b** (2-MeO–C_6H_4)	**3pa**	45
3	**5c** (4-Br–C_6H_4)	**3la**	78
4	**5d** (6-MeO–naphthyl)	**3qa**	42

[a] Reaction conditions: **5** (0.5 mmol), IBX (0.5 mmol), and I_2 (0.75 mmol) were heated in 3 mL DMSO at 80–90 °C for 3–5 h, and then **2a** (1.0 mmol) was added at room temperature for another 5–10 h.
[b] Isolated yields.

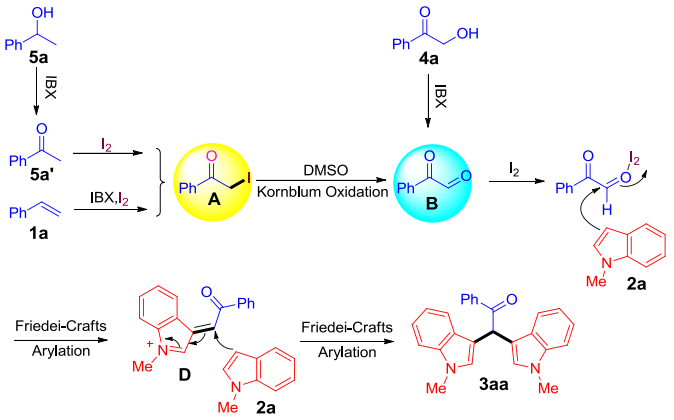
To gain insight into the mechanism, a series of control experiments were also performed (Scheme 2). Styrene (**1a**) was converted into α-iodo acetophenone (**A**) in 79% yield using the I_2/IBX system (Scheme 2a).[13] Furthermore, phenacyl iodine (**A**) could be converted into phenylglyoxal (**B**) or hydrated hemiacetal (**C**) in a quantitative conversion in DMSO at 80 °C (Scheme 2a).[14] In addition, phenacyl iodine (**A**) could react with *N*-methylindole **2a** and I_2 to obtain the product (**3aa**) in 87% yield (Scheme 2b). The reaction of hydrated hemiacetal (**C**) with **2a** also proceeded smoothly in excellent yield (>95%) (Scheme 2c). These results clearly demonstrated that phenacyl iodine (**A**) and phenylglyoxal (**B**) may be key intermediates in the transformation. However, when hydrated hemiacetal (**C**) was tested in the absence of I_2, **3aa** was obtained in only 30% yield after 10 h (Scheme 2d). This results indicated that



Scheme 2. Controlled experiment to prove the mechanism.

iodine also played an important role in the Friedel–Crafts alkylation process.

On the basis of the results described above and previous reports,[12,15] a possible mechanism of the present reaction was proposed using styrene (**1a**) and *N*-methylindole (**2a**) as an example (Scheme 3). Initially, the substrate **1a** was converted into the intermediate α-iodo acetophenone (**A**) in the presence of I_2. Subsequently, intermediate **A** was conveniently converted to phenylglyoxal (**B**) in the media of DMSO via Kornblum oxidation.[14] Carbinol **5a** was oxidized by IBX to afford acetophenone **5a′**, which was followed by iodination and Kornblum oxidation to give phenylglyoxal (**B**). In addition, 2-hydroxy-1-phenylethanone **4a** was easily oxidized to phenylglyoxal (**B**) by oxidant IBX.[16] Then, the aldehyde group of phenylglyoxal (**B**) was activated by excess or regenerated Lewis acid I_2.[7a,17] *N*-Methy-lindole **2a** could attack the activated aldehyde group of phenylglyoxal (**B**) to give the 3-alkylidene-3*H*-indolium cation **D**. Finally, another *N*-methylindole **2a** could further trap the cation **D** to give the desired product **3aa**.



Scheme 3. The plausible mechanism of the present reaction.

3. Conclusion

In summary, we have developed an efficient I_2-promoted domino oxidative dual-(het)arylation process to construct 2,2-bisindolyl-1-arylethanones from multiform substrates arylethenes, 2-hydroxy-aryl ketones, and 1-arylethanols. In the transformation, two mechanism-different reactions (oxidation and subsequent Friedel–Crafts alkylation) were assembled in a single reactor. Applications of this methodology for the construction of other heterocycles are currently being investigated in our laboratory.

4. Experimental

4.1. General

All substrates and reagents were commercially available and used without further purification. TLC analysis was performed using pre-coated glass plates. Column chromatography was performed using silica gel (200–300 mesh). IR spectra were recorded on a Perkin–Elmer PE-983 infrared spectrometer as KBr pellets with absorption in cm^{-1}. ^1H spectra were recorded in $CDCl_3$ or DMSO on 400/600 MHz NMR spectrometers and resonances (δ) are given in parts per million relative to tetramethylsilane. Data are reported as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, m=multiplet), coupling constants (Hertz) and integration. ^{13}C spectra were recorded in $CDCl_3$ or DMSO on 100/150 MHz NMR spectrometers and resonances (δ) are given in ppm. HRMS were obtained on a 7.0 TFTMS equipped with ESI. The X-ray crystal structure determinations of **3fa** was obtained on a Bruker SMART APEX CCD system. Melting points were determined using XT-4 apparatus and not corrected.

4.2. General procedure for synthesis of 3 (3aa as an example)

A sealed tube was charged with styrene (**1a**) (52 mg, 0.5 mmol), IBX (140 mg, 0.5 mmol), and iodine (189.5 mg, 0.75 mmol) at room temperature, and dried solvent DMSO (3 mL) was then added. The resulting mixture was stirred at 80–85 °C for 2 h, after disappearance of the reactant (monitored by TLC), then added *N*-methylindole **2a** (134 mg, 1.0 mmol) at room temperature for another 5 h. After the reaction completed, then added 50 mL water to the mixture, extracted with EtOAc three times (3×50 mL). The extract was washed with 10% $Na_2S_2O_3$ solution, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc=10:1) to afford the desired product **3aa** as a brown solid (66% yield).

4.3. Characterization data

*4.3.1. 2,2-Bis(1-methyl-1H-indol-3-yl)-1-phenylethanone (**3aa**).*[12] Yield 66%; brown solid, mp 79–81 °C; IR (KBr): 1684, 1614, 1595, 1540, 1471, 1371, 1330, 1198, 1013 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm)=8.10 (d, *J*=7.2 Hz, 2H), 7.56 (d, *J*=7.8 Hz, 2H), 7.49 (t, *J*=7.2 Hz, 1H), 7.39 (t, *J*=7.6 Hz, 2H), 7.28 (s, 1H), 7.21 (s, 1H), 7.20 (d, *J*=7.8 Hz, 2H), 7.07 (t, *J*=7.2 Hz, 2H), 6.87 (s, 2H), 6.52 (s, 1H), 3.66 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm)=198.6, 137.2, 137.0, 132.8, 128.7, 128.5, 127.0, 121.7, 119.1, 119.0, 112.8, 109.3, 41.7, 32.7; HRMS (ESI): *m*/*z* $[M+Na]^+$ calcd for $C_{26}H_{22}N_2ONa$: 401.1624; found: 401.1624.

*4.3.2. 2,2-Bis(1-methyl-1H-indol-3-yl)-1-(m-tolyl)ethanone (**3ba**).* Yield 62%; yellow solid, mp 178–181 °C; IR (KBr): 1687, 1613, 1584, 1471, 1266, 1174, 1155, 1131, 1118, 1013 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm)=8.05 (t, *J*=8.4 Hz, 2H), 7.70 (d, *J*=7.8 Hz, 2H), 7.41 (d, *J*=7.2 Hz, 1H), 7.37 (d, *J*=7.8 Hz, 3H), 7.32 (t, *J*=7.2 Hz, 2H), 7.19 (t, *J*=7.2 Hz, 2H), 6.99 (s, 2H), 6.66 (s, 1H), 3.73 (s, 6H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)=198.8, 138.3, 137.1, 136.8, 133.6, 129.1, 128.5, 128.4, 126.9, 125.9, 121.6, 119.0, 118.9, 112.7, 109.3, 41.5, 32.7, 21.4; HRMS (ESI): *m*/*z* $[M+Na]^+$ calcd for $C_{27}H_{24}N_2ONa$: 415.1781; found: 415.1780.

*4.3.3. 2,2-Bis(1-methyl-1H-indol-3-yl)-1-p-tolylethanone (**3ca**).*[12] Yield 61%; brown solid; mp 137–139 °C; IR (KBr): 1675, 1605, 1547, 1471, 1371, 1330, 1181, 1012, 975, 740, 689 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm)=8.05 (d, *J*=7.6 Hz, 2H), 7.58 (d, *J*=8.0 Hz, 2H), 7.29 (d, *J*=8.0 Hz, 2H), 7.22 (t, *J*=7.6 Hz, 4H), 7.09 (t, *J*=7.6 Hz, 2H), 6.88 (s, 2H), 6.53 (s, 1H), 3.66 (s, 6H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)=198.2, 143.6, 137.1, 134.2, 129.2, 128.9, 128.5, 126.9, 121.6, 119.0, 118.9, 112.8, 109.3, 41.4, 32.7, 21.6; HRMS (ESI): *m*/*z* $[M+Na]^+$ calcd for $C_{27}H_{24}N_2ONa$: 415.1781; found: 415.1782.

*4.3.4. 1-(2,4-Dimethylphenyl)-2,2-bis(1-methyl-1H-indol-3-yl)ethanone (**3da**).* Yield 64%; red solid; mp 63–66 °C; IR (KBr): 1682, 1611, 1470, 1401, 1329, 1197, 1153, 1132, 1012 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm)=7.80 (d, *J*=7.2 Hz, 1H), 7.53 (d, *J*=7.2 Hz, 2H), 7.27 (d, *J*=7.2 Hz, 1H), 7.20 (s, 3H), 7.06 (t, *J*=6.0 Hz, 2H), 7.03 (s, 1H), 6.97 (d, *J*=6.6 Hz, 1H), 6.91 (s, 2H), 6.36 (s, 1H), 3.67(s, 6H), 2.42 (s, 3H), 2.30 (s,3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)=202.0, 141.7, 139.2, 137.1, 135.1, 132.8, 129.1, 128.4, 127.0, 126.2, 121.6, 119.0, 113.1, 109.3,

44.2, 32.7, 21.4, 21.3; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{28}H_{26}N_2ONa$: 429.1937; found: 429.1945.

*4.3.5. 1-Mesityl-2,2-bis(1-methyl-1H-indol-3-yl)ethanone (**3ea**).* Yield 54%; yellow solid; mp 94–97 °C; IR (KBr): 1696, 1611, 1469, 1400, 1329, 1150, 1132, 1014, cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm)=7.33 (d, *J*=7.2 Hz, 4H), 7.24 (s, 1H), 7.22 (s, 1H), 7.15 (t, *J*=7.2 Hz, 2H), 6.95 (t, *J*=7.8 Hz, 2H), 6.75 (s, 2H), 5.97 (s, 1H), 3.73 (s, 6H), 2.26 (s, 3H), 1.87 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)= 207.4, 139.7, 138.6, 136.8, 134.1, 128.5, 128.4, 127.2, 121.4, 119.2, 118.8, 111.8, 109.1, 47.4, 32.8, 21.1, 19.4; HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{29}H_{29}N_2O$: 421.2274; found: 421.2275.

*4.3.6. 1-(4-(tert-Butyl)phenyl)-2,2-bis(1-methyl-1H-indol-3-yl)ethanone (**3fa**).* Yield 67%; red solid; mp 247–250 °C; IR (KBr): 1684, 1602, 1472, 1365, 1346, 1270, 1231, 1189, 1110, 1010 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm)=8.06 (d, *J*=8.4 Hz, 2H), 7.57 (d, *J*=7.8 Hz, 2H), 7.41 (d, *J*=8.4 Hz, 2H), 7.27 (d, *J*=7.8 Hz, 2H), 7.22–7.19 (m, 2H), 7.07 (t, *J*=7.8 Hz, 2H), 6.87 (s, 2H), 6.52 (s, 1H), 3.67 (s, 6H), 1.30 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)=198.1, 156.4, 137.2, 134.3, 128.7, 128.5, 127.1, 125.5, 121.6, 119.1, 119.0, 113.0, 109.3, 41.5, 35.0, 32.7, 31.0; HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{30}H_{31}N_2O$: 435.2431; found: 435.2433.

*4.3.7. 1-(4-Methoxyphenyl)-2,2-bis(1-methyl-1H-indol-3-yl)ethanone (**3ga**).*[12] Yield 58%; brown solid; mp 137–139 °C; IR (KBr): 1669, 1600, 1574, 1465, 1329, 1262, 1225, 1174, 1013, 978, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm)=8.13 (d, *J*=8.8 Hz, 2H), 7.58 (d, *J*=7.6 Hz, 2H), 7.30 (d, *J*=8.4 Hz, 2H), 7.22 (d, *J*=7.6 Hz, 2H), 7.09 (t, *J*=8.4 Hz, 2H), 6.91 (s, 1H), 6.89 (s, 3H), 6.51 (s, 1H), 3.82 (s, 3H), 3.68 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)=197.2, 163.2, 137.1, 131.0, 129.6, 128.4, 127.0, 121.6, 119.0, 118.9, 113.7, 112.9, 109.3, 55.3, 41.2, 32.7; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{27}H_{24}N_2O_2Na$: 431.1730; found: 431.1732.

*4.3.8. 1-(3-Fluorophenyl)-2,2-bis(1-methyl-1H-indol-3-yl)ethanone (**3ha**).* Yield 63%; red solid; mp 150–153 °C; IR (KBr): 1683, 1608, 1477, 1448, 1426, 1373, 1330, 1269, 1210, 1196, 1131, 1013 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm)=7.84 (s, 1H), 7.59 (d, *J*=7.8 Hz, 2H), 7.39 (d, *J*=4.8 Hz, 1H), 7.25 (d, *J*=7.8 Hz, 2H), 7.19 (d, *J*=7.8 Hz, 2H), 7.11 (d, *J*=7.8 Hz, 1H), 7.06 (d, *J*=7.2 Hz, 3H), 6.90 (s, 2H), 6.43 (s, 1H), 3.65 (s, 6H); ^{13}C NMR (100 MHz, CDCl3): δ (ppm)=197.2, 159.9, 137.2, 134.0, 133.9, 131.4, 128.5, 127.2, 124.4, 121.6, 119.2, 119.1, 116.7, 116.5, 112.1, 109.3, 45.7, 32.7; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{26}H_{21}FN_2ONa$: 419.1530; found: 419.1532.

*4.3.9. 1-(4-Fluorophenyl)-2,2-bis(1-methyl-1H-indol-3-yl)ethanone (**3ia**).* Yield 62%; red solid; mp 184–186 °C; IR (KBr): 1679, 1596, 1505, 1483, 1465, 1372, 1330, 1224, 1197, 1157, 1031, 1012 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm)=8.12 (t, *J*=6.6 Hz, 2H), 7.54 (d, *J*=7.8 Hz, 2H), 7.28 (d, *J*=7.8 Hz, 2H), 7.21 (t, *J*=7.2 Hz, 2H), 7.09–7.04 (m, 4H), 6.86 (s, 2H), 6.46 (s, 1H), 3.67 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)=197.0, 166.7, 137.2, 133.4, 131.4, 131.3, 128.4, 126.9, 121.7, 119.2, 118.8, 115.7, 112.5, 109.4, 41.7, 32.8; HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{26}H_{22}FN_2O$: 397.1711; found: 397.1713.

*4.3.10. 1-(4-Chlorophenyl)-2,2-bis(1-methyl-1H-indol-3-yl)ethanone (**3ja**).*[12] Yield 70%; white solid; mp 150–153 °C; IR (KBr): 1680, 1588, 1545, 1466, 1423, 1400, 1371, 1329, 1265, 1232, 1198, 1089, 1011, 981, 811, 746 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm)=8.06 (d, *J*=8.4 Hz, 2H), 7.56 (d, *J*=8.0 Hz, 2H), 7.39 (d, *J*=8.4 Hz, 2H), 7.32 (d, *J*=8.4 Hz, 2H), 7.24 (d, *J*=7.6 Hz, 2H), 7.11 (t, *J*=14.8 Hz, 2H), 6.87 (s, 2H), 6.46 (s, 1H), 3.70 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)=197.3, 139.2, 137.2, 135.1, 130.2, 128.9, 128.5, 126.8, 121.8, 119.2, 118.8, 112.3, 109.4, 41.8, 32.8; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{26}H_{21}ClN_2ONa$: 435.1235; found: 435.1232.

*4.3.11. 1-(3-Bromophenyl)-2,2-bis(1-methyl-1H-indol-3-yl)ethanone (**3ka**).* Yield 74%; brown solid; mp 200–203 °C; IR (KBr): 1688, 1473, 1425, 1373, 1330, 1226, 1209, 1196, 1012 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm)=8.24 (s, 1H), 8.00 (d, *J*=7.8 Hz, 1H), 7.59 (d, *J*=7.8 Hz, 1H), 7.54 (d, *J*=7.8 Hz, 2H), 7.27 (d, *J*=8.4 Hz, 2H), 7.28–7.20 (m, 3H), 7.08 (t, *J*=7.8 Hz, 2H), 6.85 (s, 2H), 6.43(s, 1H), 3.66 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)=197.1, 138.6, 137.2, 135.6, 131.6, 130.1, 128.5, 127.3, 126.8, 122.9, 121.8, 119.2, 118.9, 112.2, 109.4, 41.9, 32.8; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{26}H_{21}BrN_2ONa$: 479.0730; found: 479.0732.

*4.3.12. 1-(4-Bromophenyl)-2,2-bis(1-methyl-1H-indol-3-yl)ethanone (**3la**).*[12] Yield 75%; brown solid; mp 168–170 °C; IR (KBr): 1681, 1583, 1535, 1474, 1423, 1372, 1330, 1196, 1176, 1070, 1009 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm)=7.95 (d, *J*=8.4 Hz, 2H), 7.52 (t, *J*=8.4 Hz, 4H), 7.29 (d, *J*=8.4 Hz, 2H), 7.22 (t, *J*=8.0 Hz, 2H), 7.08 (t, *J*=7.6 Hz, 2H), 6.85 (s, 2H), 6.43 (s, 1H), 3.67 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)=197.5, 137.2, 135.5, 131.8, 130.3, 128.5, 127.9, 126.8, 121.8, 119.2, 118.8, 112.3, 109.4, 41.8, 32.8; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{26}H_{21}BrN_2ONa$: 479.0729; found: 479.0727.

*4.3.13. 4-(2,2-Bis(1-methyl-1H-indol-3-yl)acetyl)benzonitrile (**3ma**).* Yield 70%; yellow solid; mp 225–228 °C; IR (KBr): 2229, 1685, 1473, 1373, 1330, 1230, 1198, 1013 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm)=8.12 (d, *J*=7.2 Hz, 2H), 7.63 (d, *J*=7.8 Hz, 2H), 7.52 (d, *J*=7.8 Hz, 2H), 7.29 (d, *J*=7.8 Hz, 2H), 7.23 (t, *J*=7.8 Hz, 2H), 7.09 (t, 7.2 Hz, 2H), 6.85 (s, 2H), 6.43 (s, 1H), 3.67 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)=196.9, 139.9, 137.2, 132.3, 129.0, 126.7, 121.9, 119.3, 118.7, 118.0, 115.7, 111.7, 109.5, 42.3, 32.7; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{27}H_{21}N_3ONa$: 426.1577; found: 426.1580.

*4.3.14. 2,2-Bis(1-methyl-1H-indol-3-yl)-1-(naphthalen-2-yl)ethanone (**3na**).*[12] Yield 61%; brown solid; mp 107–110 °C; IR (KBr): 1674, 1624, 1593, 1536, 1470, 1424, 1372, 1330, 1214, 1180, 1155, 1127, 1067, 1013 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm)=8.69 (s, 1H), 8.14 (d, *J*=7.2 Hz, 1H), 7.88 (d, *J*=8.0 Hz, 1H), 7.82 (d, *J*=8.8 Hz, 2H), 7.61 (d, *J*=8.0 Hz, 2H), 7.53 (t, *J*=7.2 Hz, 1H), 7.47 (t, *J*=7.2 Hz, 1H), 7.28 (d, *J*=8.4 Hz, 2H), 7.21 (t, *J*=8.8 Hz, 2H), 7.08 (t, *J*=7.2 Hz, 2H), 6.91 (s, 2H), 6.69 (s, 1H), 3.66 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)=198.6, 137.2, 135.4, 134.2, 132.5, 130.2, 129.7, 128.5, 128.4, 128.3, 127.6, 127.0, 126.6, 124.7, 121.7, 119.1, 119.0, 112.8, 109.4, 41.8, 32.8; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{30}H_{24}N_2ONa$: 451.1781; found: 451.1779.

*4.3.15. 1-(Biphenyl-4-yl)-2,2-bis(1-methyl-1H-indol-3-yl)ethanone (**3oa**).*[12] Yield 68%; brown solid; mp 191–193 °C; IR (KBr): 1680, 1602, 1556, 1537, 1473, 1423, 1371, 1330, 1221, 1183, 1156, 1131, 1118, 1009 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm)=8.19 (d, *J*=8.4 Hz, 2H), 7.62 (d, *J*=8.8 Hz, 3H), 7.57 (d, *J*=7.2 Hz, 3H), 7.43 (t, *J*=7.6 Hz, 2H), 7.36 (t, *J*=7.2 Hz, 1H), 7.29 (d, *J*=8.0 Hz, 2H), 7.22 (d, *J*=7.6 Hz, 2H), 7.09 (t, *J*=7.6 Hz, 2H), 6.89 (s, 2H), 6.56 (s, 1H), 3.69 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)=198.1, 145.4, 139.9, 137.2, 135.5, 129.4, 128.9, 128.5, 128.1, 127.2, 127.0, 121.7, 119.1, 119.0, 112.7, 109.4, 41.7, 32.8; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{32}H_{26}N_2ONa$: 477.1937; found: 477.1941.

*4.3.16. 2,2-Di(1H-indol-3-yl)-1-phenylethanone (**3ab**).*[12] Yield 60%; brown solid; mp 135–138 °C; IR (KBr): 3397, 3381, 3057, 1736, 1679, 1618, 1595, 1458, 1419, 1340, 1220, 1201, 1091, 1002 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6): δ (ppm)=10.94 (s, 1H), 8.18 (d, *J*=7.2 Hz, 2H), 7.58 (d, *J*=7.8 Hz, 2H), 7.55 (d, *J*=7.2 Hz, 2H), 7.47 (t, *J*=7.2 Hz, 2H), 7.36 (t, *J*=8.4 Hz, 2H), 7.20 (s, 2H), 7.07 (t, *J*=7.2 Hz, 2H), 6.965 (t, *J*=7.2 Hz, 2H), 6.67 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6): δ (ppm)= 198.0, 136.6, 136.2, 132.9, 128.7, 128.6, 126.5, 124.3, 121.1, 119.0, 118.6, 112.9, 111.5, 41.6; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{24}H_{18}N_2ONa$: 373.1311; found: 373.1321.

*4.3.17. 2,2-Di(1H-indol-3-yl)-1-(4-methoxyphenyl)ethanone (**3gb**).*[12] Yield 55%; brown solid; mp 220–222 °C; IR (KBr): 3408,

Please cite this article in press as: Jia, F.-C.; et al., Tetrahedron (2013), http://dx.doi.org/10.1016/j.tet.2013.06.054

3376, 3044, 2965, 2929, 1665, 1595, 1507, 1456, 1417, 1338, 1264, 1226, 1163, 1118, 1091, 1004 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ (ppm)= 10.91 (s, 2H), 8.17 (d, J=8.8 Hz, 2H), 7.57 (d, J=8.0 Hz, 2H), 7.35 (d, J=8.0 Hz, 2H), 7.17 (t, J=7.6 Hz, 2H), 7.05 (t, J=7.6 Hz, 2H), 7.00–6.92 (m, 4H), 6.61 (s, 1H), 3.79 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm)=196.4, 162.9, 136.3, 130.9, 129.3, 126.5, 124.3, 120.9, 119.0, 118.4, 113.9, 113.3, 111.5, 55.4, 41.2; HRMS (ESI): m/z $[M+Na]^+$ calcd for $C_{25}H_{20}N_2O_2Na$: 403.1417; found: 403.1401.

*4.3.18. 1-(3-Bromophenyl)-2,2-di(1H-indol-3-yl)ethanone (**3kb**).* Yield 62%; white solid; mp 255–258 °C; IR (KBr): 3404, 3375, 3061, 2858, 1685, 1561, 1458, 1414, 1340, 1269, 1218, 1197, 1090, 1013 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ (ppm)=10.94 (s, 2H), 8.26 (s, 1H), 8.17 (d, J=8.0 Hz, 1H), 7.75 (d, J=7.6 Hz, 1H), 7.57 (d, J=7.6 Hz, 2H), 7.43 (t, J=8.0 Hz, 1H), 7.34 (d, J=8.0 Hz, 2H), 7.12 (s, 2H), 7.06 (t, J=7.6 Hz, 2H), 6.95 (t, J=7.4 Hz, 2H), 6.66 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm)=196.7, 138.6, 136.3, 135.6, 131.0, 130.9, 127.6, 126.5, 124.6, 122.2, 121.1, 119.1, 118.6, 112.5, 111.6, 41.8; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{24}H_{18}BrN_2O$: 429.0597; found: 429.0591.

*4.3.19. 4-(2,2-Di(1H-indol-3-yl)acetyl)benzonitrile (**3mb**).* Yield 72%; yellow solid; mp 119–123 °C; IR (KBr): 3401, 3124, 2361, 2339, 2231, 1728, 1686, 1457, 1402, 1339, 1244, 1214, 1097, 1045 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm)=8.02 (d, 8.4 Hz, 2H), 7.99 (s, 2H), 7.49 (d, J=7.2 Hz, 2H), 7.45 (d, J=7.8 Hz, 2H), 7.17 (d, J=7.8 Hz, 2H), 7.11 (t, J=7.4 Hz, 2H), 7.03 (t, J=7.4 Hz, 2H), 6.60 (s, 2H), 6.34 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)=197.6, 139.5, 136.3, 132.3, 128.9, 126.1, 124.2, 122.2, 119.7, 118.5, 117.9, 115.6, 112.6, 111.6, 42.6; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{25}H_{18}N_3O$: 376.1444; found: 376.1444.

*4.3.20. 2,2-Di(1H-indol-3-yl)-1-(naphthalen-2-yl)ethanone (**3nb**).*[12] Yield 60%; brown solid; mp 205–208 °C; IR (KBr): 3505, 3408, 3397, 3054, 2963, 2868, 1672, 1621, 1591, 1454, 1416, 1355, 1336, 1306, 1263, 1216, 1170, 1092, 1025, 1010 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ (ppm)=10.94 (s, 2H), 9.00 (s, 1H), 8.13 (d, J=8.8 Hz, 1H), 8.10 (d, J=8.0 Hz, 1H), 7.96 (d, J=8.0 Hz, 1H), 7.93 (s, 1H), 7.65–7.59 (m, 4H), 7.34 (d, J=8.0 Hz, 2H), 7.25 (s, 2H), 7.05 (t, J=7.6 Hz, 2H), 6.95 (t, J=7.6 Hz, 2H), 6.86 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm)=197.9, 136.3, 134.8, 133.8, 132.2, 130.0, 129.6, 128.5, 128.2, 127.5, 126.8, 126.5, 124.5, 124.4, 121.0, 119.0, 118.5, 113.0, 111.5, 40.1; HRMS (ESI): m/z $[M+Na]^+$ calcd for $C_{28}H_{20}N_2ONa$: 423.1468; found: 423.1476.

*4.3.21. 1-([1,1′-Biphenyl]-4-yl)-2,2-di(1H-indol-3-yl)ethanone (**3ob**).* Yield 70%; red solid; mp 116–119 °C; IR (KBr): 3407, 3054, 1673, 1557, 1456, 1339, 1217, 1186, 1096 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm)=8.13 (d, J=8.4 Hz, 2H), 7.96 (s, 2H), 7.55 (s, 1H), 7.54 (s, 1H), 7.53 (s, 2H), 7.52 (s, 2H), 7.41 (t, J=7.2 Hz, 2H), 7.36 (d, J=7.2 Hz, 1H), 7.18 (d, J=7.8 Hz, 2H), 7.11 (t, J=7.2 Hz, 2H), 7.04 (t, J=7.2 Hz, 2H), 6.61 (s, 2H), 6.47 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)=198.6, 145.5, 139.7, 136.4, 135.3, 129.4, 128.9, 128.1, 127.2, 126.5, 124.2, 122.0, 119.5, 118.8, 113.7, 111.5, 42.1; HRMS (ESI): m/z $[M+Na]^+$ calcd for $C_{30}H_{22}N_2ONa$: 449.1624; found: 449.1622.

*4.3.22. 2,2-Bis(6-methyl-1H-indol-3-yl)-1-phenylethanone (**3ac**).*[12] Yield 71%; brown solid; mp 207–210 °C; IR (KBr): 3430, 3396, 3397, 1667, 1628, 1595, 1454, 1338, 1340, 1247, 1218, 1101 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm)=7.95 (d, J=8.0 Hz, 2H), 7.80 (s, 2H), 7.25 (s, 2H), 7.07 (q, J=7.6 Hz, 4H), 6.97 (s, 2H), 6.81 (s, 2H), 6.59 (d, J=8.0 Hz, 2H), 2.28 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)=198.6, 138.3, 136.9, 131.6, 131.2, 130.5, 127.4, 125.1, 123.6, 121.3, 120.9, 118.3, 110.9, 55.9, 21.5; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{26}H_{21}N_2O$: 377.1648; found: 377.1643.

*4.3.23. 2,2-Bis(2-methyl-1H-indol-3-yl)-1-phenylethanone (**3ad**).*[12] Yield 75%; brown solid; mp 202–204 °C; IR (KBr): 3406, 3376, 1674, 1579, 1459, 1427, 1300, 1221, 1008 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ (ppm)=10.84 (s, 2H), 8.04 (d, J=7.6 Hz, 2H), 7.51 (t, J=7.2 Hz, 1H), 7.41 (t, J=7.6 Hz, 2H), 7.22 (d, J=8.0 Hz, 2H), 7.16 (d, J=8.0 Hz, 2H), 6.92 (t, J=7.2 Hz, 2H), 6.78 (t, J=7.6 Hz, 2H), 6.44 (s, 1H), 2.13 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm)= 198.6, 137.0, 135.0, 132.8, 132.7, 128.6, 128.2, 119.7, 118.2, 118.1, 110.4, 107.7, 42.1, 11.9; HRMS (ESI): m/z $[M+Na]^+$ calcd for $C_{26}H_{22}N_2ONa$: 401.1624; found: 401.1620.

*4.3.24. 2,2-Bis(6-bromo-1H-indol-3-yl)-1-phenylethanone (**3ae**).*[12] Yield 45%; brown solid; mp 68–70 °C; IR (KBr): 3339, 2954, 2925, 2856, 1714, 1676, 1612, 1595, 1450, 1401, 1332, 1286, 1213, 1047, 1023 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ (ppm)= 11.13 (s, 2H), 8.18 (t, J=7.2 Hz, 2H), 7.47–7.58 (m, 7H), 7.25 (d, J=8.0 Hz, 2H), 7.12 (d, J=7.6 Hz, 2H), 7.70 (d, J=11.2 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm)=197.6, 137.2, 136.3, 133.0, 128.6, 128.5, 125.5, 121.4, 120.8, 114.1, 113.9, 113.1, 79.1, 41.3; HRMS (ESI): m/z $[M+Na]^+$ calcd for $C_{24}H_{16}Br_2N_2ONa$: 528.9522; found: 530.9509.

*4.3.25. 2,2-Bis(1-allyl-1H-indol-3-yl)-1-phenylethanone (**3ag**).*[12] Yield 26%; brown solid; mp 163–165 °C; IR (KBr): 1686, 1467, 1443, 1334, 1216, 1188 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm)=8.09 (d, J=8.0 Hz, 2H), 7.57 (d, J=8.0 Hz, 2H), 7.49 (t, J=7.2 Hz, 1H), 7.39 (t, J=7.6 Hz, 2H), 7.28 (d, J=8.0 Hz, 2H), 7.22 (s, 1H), 7.20 (s, 1H), 7.17 (d, J=8.4 Hz, 1H), 7.06 (t, J=7.2 Hz, 2H), 6.93 (s, 1H), 6.51 (s, 1H), 5.96–5.88 (m, 2H), 5.11 (d, J=10.0 Hz, 2H), 5.03 (s, 1H), 4.99 (s, 1H), 4.62 (d, J=5.2 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)=198.5, 137.0, 136.7, 133.4, 132.7, 128.7, 128.5, 127.6, 127.3, 121.7, 119.3, 119.1, 117.1, 113.1, 109.8, 48.8, 41.9; HRMS (ESI): m/z $[M+Na]^+$ calcd for $C_{30}H_{26}N_2ONa$: 453.1937; found: 453.1942.

*4.3.26. 2,2-Bis(1-benzyl-1H-indol-3-yl)-1-phenylethanone (**3ah**).*[12] Yield 37%; brown solid; mp 188–190 °C; IR (KBr): 1685, 1607, 1493, 1466, 1448, 1374, 1359, 1335, 1197, 1172 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm)=8.09 (d, J=7.6 Hz, 2H), 7.59 (d, J=8.0 Hz, 2H), 7.46 (t, J=7.6 Hz, 1H), 7.36 (t, J=7.6 Hz, 2H), 7.19–7.16 (m, 7H), 7.11 (t, J=7.2 Hz, 3H), 7.04 (d, J=7.2 Hz, 3H), 6.98 (s, 2H), 6.96 (t, J=7.2 Hz, 3H), 6.53 (s, 1H), 5.16 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)=198.3, 137.5, 137.0, 136.9, 132.7, 128.7, 128.6, 128.5, 128.1, 127.4, 127.36, 126.5, 121.9, 119.4, 119.3, 113.3, 109.9, 49.9, 42.2; HRMS (ESI): m/z $[M+Na]^+$ calcd for $C_{38}H_{30}N_2ONa$: 553.2250; found: 553.2292.

*4.3.27. 1-(2-Methoxyphenyl)-2,2-bis(1-methyl-1H-indol-3-yl)ethanone (**3pa**).* Yield 45%; red solid; mp 173–176 °C; IR (KBr): 1677, 1594, 1482, 1431, 1331, 1283, 1239, 1192, 1159, 1015 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm)=7.59 (d, J=7.8 Hz, 3H), 7.35 (t, J=7.2 Hz, 1H), 7.24 (d, J=7.8 Hz, 2H), 7.18 (t, J=7.8 Hz, 2H), 7.05 (t, J=7.2 Hz, 2H), 6.88 (s, 4H), 6.62 (s, 1H), 3.80 (s, 3H), 3.64 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)=201.5, 157.9, 137.1, 132.8, 131.0, 128.9, 128.3, 127.4, 121.3, 120.5, 119.3, 118.8, 113.1, 111.4, 109.1, 55.5, 45.4, 32.6; HRMS (ESI): m/z $[M+Na]^+$ calcd for $C_{27}H_{24}N_2O_2Na$: 431.1730; found: 431.1733.

*4.3.28. 1-(6-Methoxynaphthalen-2-yl)-2,2-bis(1-methyl-1H-indol-3-yl)ethanone (**3qa**).* Yield 42%; brown solid; mp 239–243 °C; IR (KBr): 1679, 1616, 1473, 1349, 1331, 1273, 1252, 1230, 1175, 1154, 1061 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm)=8.57 (s, 1H), 8.17 (d, J=9.0 Hz, 1H), 8.11 (d, J=9.0 Hz, 1H), 7.85 (d, J=9.0 Hz, 1H), 7.60 (d, J=7.8 Hz, 2H), 7.29 (d, J=8.4 Hz, 2H), 7.23 (s, 1H), 7.21 (d, J=7.8 Hz, 2H), 7.16 (d, J=9.0 Hz, 1H), 7.09 (t, J=7.2 Hz, 2H), 6.90 (s, 2H), 6.65 (s, 1H), 3.99 (s, 3H), 3.68 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm)= 197.9, 158.4, 137.9, 137.2, 132.6, 132.3, 131.6, 130.5, 128.7, 128.5, 127.0, 126.9, 121.7, 119.2, 119.0, 113.0, 112.7, 109.4, 87.0, 57.0, 41.8, 32.8;

Please cite this article in press as: Jia, F.-C.; et al., Tetrahedron (2013), http://dx.doi.org/10.1016/j.tet.2013.06.054

HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{31}H_{27}N_2O_2$: 459.2067; found: 459.2071.

Acknowledgements

We thank the National Natural Science Foundation of China (Grant 21032001 and 21272085). We also thank Dr. Chuanqi Zhou, Hebei University, for analytical support.

Supplementary data

^1H NMR, ^{13}C NMR, and HRMS spectra for all compounds, X-ray crystal structures of compounds **3fa** is available. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.06.054.

References and notes

1. (a) Sundberg, R. J. *The Chemistry of Indoles*; Academic: New York, NY113; (b) Lounasmaa, M.; Tolvanen, A. *Nat. Prod. Rep.* **2000**, *17*, 175; (c) Hibino, S.; Chozi, T. *Nat. Prod. Rep.* **2001**, *18*, 66; (d) Zaimoku, H.; Taniguchi, T.; Ishibashi, H. *Org. Lett.* **2012**, *14*, 1656.
2. (a) Bifulco, G.; Bruno, I.; Riccio, R.; Bifulco, G.; Bruno, I.; Riccio, R.; Lavayre, J.; Bourdy, G. *J. Nat. Prod.* **1995**, *58*, 1254; (b) Garbe, T. R.; Kobayashi, M.; Shimizu, N.; Kobayashi, M.; Shimizu, N.; Takesue, N.; Ozawa, M.; Yukawa, H. *J. Nat. Prod.* **2000**, *63*, 596.
3. (a) Kobayashi, M.; Aoki, S.; Gato, K.; Matsunami, K.; Kurosu, M.; Kitagawa, I. *Chem. Pharm. Bull.* **1994**, *42*, 2449; (b) Chakrabarty, M.; Basak, R.; Harigaya, Y. *Heterocycles* **2001**, *55*, 2431; (c) Sujatha, K.; Perumal, P. T.; Muralidharan, D.; Rajendra, M. *Indian J. Chem.* **2009**, *48B*, 267.
4. (a) Safe, S.; Papineni, S.; Chintharlapalli, S. *Cancer Lett.* **2008**, *269*, 326; (b) Inamoto, T.; Papineni, S.; Chintharlapalli, S.; Cho, S. D.; Safe, S.; Kamat, A. M. *Mol. Cancer Ther.* **2008**, *7*, 3825; (c) McDougal, A.; Gupta, M. S.; Morrow, D.; Ramamoorthy, K.; Lee, J. E.; Safe, S. H. *Breast Cancer Res. Treat.* **2001**, *66*, 147; (d) Wang, T. T.; Milner, M. J.; Milner, J. A.; Kim, Y. S. *J. Nutr. Biochem.* **2006**, *17*, 659.
5. (a) Maciejewska, D.; Szpakowska, I.; Wolska, I.; Niemyjska, M.; Mascini, M.; Maj-Zurawska, M. *Bioelectrochemistry* **2006**, *69*, 1; (b) Maciejewska, D.; Niemyjska, M.; Wolska, I.; Waostowski, M.; Rasztawicka, M. *Z. Naturforsch., B: Chem. Sci.* **2004**, *59*, 1137.
6. (a) Chen, D.; Yu, L.; Wang, P. G. *Tetrahedron Lett.* **1996**, *37*, 4467; (b) Nair, V.; Abhilash, K. G.; Vidya, N. *Org. Lett.* **2005**, *7*, 5857; (c) Ko, S.; Lin, C.; Tu, Z.; Wang, Y. F.; Wang, C. C.; Yao, C. F. *Tetrahedron Lett.* **2006**, *47*, 487; (d) Cui, S. C.; Li, Q. J. *Tetrahedron* **2004**, *60*, 6679; (e) Soueidan, M.; Collin, J.; Gil, R. *Tetrahedron Lett.* **2006**, *47*, 5467.
7. (a) Bandgar, B. P.; Shaikh, K. A. *Tetrahedron Lett.* **2003**, *44*, 1959; (b) Ji, S. J.; Zhou, M. F.; Gu, D. G.; Jiang, Z. Q. *Eur. J. Org. Chem.* **2004**, *7*, 1584; (c) Mi, X.; Luo, S.; He, J.; Cheng, J. P. *Tetrahedron Lett.* **2004**, *45*, 4567; (d) Sharma, G. V. M.; Reddy, J. J.; Lakshmi, P. S.; Krishna, P. R. *Tetrahedron Lett.* **2004**, *45*, 7729.
8. Shiri, M.; Zolfigol, M. A.; Kruger, H. G.; Tanbakouchian, Z. *Chem. Rev.* **2010**, *110*, 2250.
9. (a) Dong, H. M.; Lu, H. H.; Lu, L. Q.; Chen, C. B.; Xiao, W. J. *Adv. Synth. Catal.* **2007**, *349*, 1597; (b) Guo, X. W.; Pan, S. P.; Liu, J. H.; Li, Z. P. *J. Org. Chem.* **2009**, *74*, 8848.
10. Xia, D. X.; Wang, Y.; Du, Z. T.; Zheng, Q. Y.; Wang, C. Y. *Org. Lett.* **2012**, *14*, 588.
11. Young, P. C.; Hadfield, M. S.; Arrowsmith, L.; Macleod, K. M.; Mudd, R. J.; Jordan-Hore, J. A.; Lee, A. L. *Org. Lett.* **2012**, *14*, 898.
12. Zhu, Y. P.; Liu, M. C.; Jia, F. C.; Yuan, J. J.; Gao, Q. H.; Lian, M.; Wu, A. X. *Org. Lett.* **2012**, *14*, 3392.
13. (a) Yadav, J. S.; Subba Reddy, B. V.; Singh, A. P.; Basak, A. K. *Tetrahedron Lett.* **2008**, *49*, 5880; (b) Moorthy, J. N.; Senapati, K.; Singhal, N. *Tetrahedron Lett.* **2009**, *50*, 2493; (c) Donohoe, T. J.; Kabeshov, M. A.; Rathi, A. H.; Smith, I. E. D. *Org. Biomol. Chem.* **2012**, *10*, 1093.
14. Kornblum, N.; Powers, J. W.; Anderson, G. J.; Jones, W. J.; Larson, H. O.; Levand, O.; Weaver, W. M. *J. Am. Chem. Soc.* **1957**, *79*, 6562.
15. Jiang, H. F.; Huang, H. W.; Cao, H.; Qi, C. R. *Org. Lett.* **2010**, *12*, 5561.
16. (a) Nicolou, K. C.; Montagnon, T.; Baran, P. S.; Zhong, Y. L. *J. Am. Chem. Soc.* **2002**, *124*, 2245; (b) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2008**, *108*, 5299; (c) Zhdankin, V. V. *J. Org. Chem.* **2011**, *76*, 1185.
17. (a) Jaratjaroonphong, J.; Sathalalai, S.; Techasauvapak, P.; Reutrakul, V. *Tetrahedron Lett.* **2009**, *50*, 6012; (b) Zhang, J. T.; Zhu, D. P.; Yu, C. M.; Wan, C. F.; Wang, Z. Y. *Org. Lett.* **2010**, *12*, 2841.