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$RuCl_3/SnCl_2$ mediated synthesis of pyrrolo[2,3-*c*]carbazoles and consequent preparation of indolo[2,3-*c*]carbazoles

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ABSTRACT

A simple method for the synthesis of pyrrolo[2,3-*c*]carbazoles from *N*-alkylated-3-aminocarbazole derivatives and ethylene glycol has been developed via heteroannulation reaction using $RuCl_3/SnCl_2$ system. Moreover indolo[2,3-*c*]carbazoles were prepared from various pyrrolo[2,3-*c*]carbazoles in good yields.

1. Introduction

Aryl- and heteroaryl-annulated carbazoles, such as pyridocarbazoles, indolocarbazoles, and pyrrolocarbazoles have attracted growing attention since they are distributed in numerous natural products with diverse useful bioactivities.[1] Among them, many efforts have been devoted to the design and synthesis of pyrrolocarbazoles,[2] which seem to be the most intriguing, and thus have proven to be very important in medicinal chemistry. For example, the pyrrolo[2,3-*a*] and [3,4-*c*]carbazoles have great importance due to their inhibiting properties toward pim kinase inhibitors[3] and Chk1 inhibitors,[4] respectively. Having a common core of pyrrolo[2,3-*c*]carbazole, dictyodendrins A–E (Fig. 1) were isolated from *dictyodendrilla verongiformis*, the first marine natural products with telomerase inhibitory properties showing 100% inhibition at 50 μg/mL.[5]

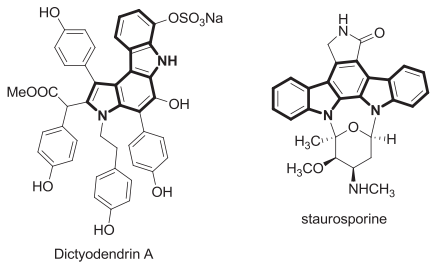

Fig. 1. Pyrrolo[2,3-*c*]carbazole and indolo[2,3-*a*]carbazole alkaloids.

Indolocarbazole, the benzene analog of pyrrolocarbazole, represents one of the most important classes of heterocycles. The syntheses of indolocarbazoles[6] have received great attention because of their existence in many natural products with potent biological activities.[1] Over the past few decades, transition metal-catalyzed reactions have been recognized as a useful synthetic tool for the construction of wide range of compounds in organic synthesis.[7] In recent years ruthenium has been emerged as one of the most useful transition metal catalyst in organic synthesis.[8] As a result, various useful ruthenium catalyzed reactions have been explored.

In this paper, we describe a regioselective and good yielding procedure for the preparation of pyrrolo[2,3-*c*]carbazoles from heteroannulation of *N*-alkylated-3-aminocarbazoles with ethylene glycol, mediated by $RuCl_3/SnCl_2$ system in the presence of 1,2-bis(diphenylphosphino)ethane (dppe) as a ligand. This method provides a route for the construction of a variety of substituted pyrrolo[2,3-*c*]carbazole derivatives as shown in Scheme 1. Moreover, we wish to report an annulation of this pyrrolo[2,3-*c*]carbazoles extend into indolo[2,3-*c*]carbazoles by reacting with acetonylacetone using *p*-TSA as catalyst.

2. Results and discussion

3-Aminocarbazole derivatives can be easily prepared based on literature procedure.[9] An initial experiment 9-ethyl-3-

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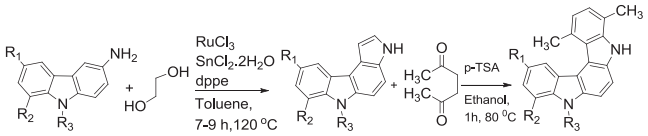
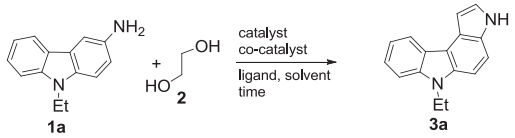


Scheme 1. The schematic representation of present work.

aminocarbazole **1a** was reacted with ethylene glycol **2** in the presence of $RuCl_3$, $SnCl_2{\cdot}2H_2O$, and dppe in acetonitrile. The desired heteroannulated product **3a** was isolated in low yield. Encouraged by this result **1a** and **2** were taken as model substrates, and the representative results are summarized in Tables 1 and 2. With the preliminary result in hand, we investigated various reaction parameters. On the basis of the aforementioned line of reasoning, an array of solvents was undertaken, such as toluene, $CHCl_3$, THF, acetonitrile, DMA, acetone, and dioxane. Interestingly, $CHCl_3$, DMA, dioxane/H_2O, and acetonitrile gave the desired product in lower yields, whereas no product was detected when using THF and acetone as shown in Table 1. The best yields were obtained when the reactions were carried out in toluene.

Table 1
Optimization condition for the conversion of **1a** to **3a**[a]



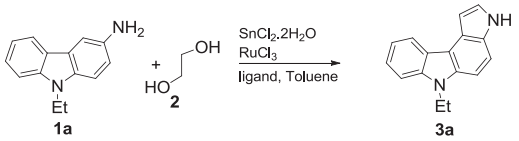
1a **2** **3a**

S.No	Catalyst	Co-catalyst	Solvent	Temp/°C, time/h	Yield[e]
1[b]	$PdCl_2(PPh_3)_2$	$SnCl_2{\cdot}2H_2O$	Toluene	120, 12	—
2[b]	$RuCl_3$	$SnCl_2{\cdot}2H_2O$	Toluene	120, 12	30
3[b]	$RhCl(PPh_3)_3$	$SnCl_2{\cdot}2H_2O$	Toluene	120, 12	16
4	$RuCl_3$	$InCl_3$	Toluene	120, 12	—
5	$RuCl_3$	$SbCl_3$	Toluene	120, 12	12
6	$RuCl_3$	$CeCl_3{\cdot}7H_2O$	Toluene	120, 12	30
7	$RuCl_3$	$AlCl_3$	Toluene	120, 12	25
8	$RuCl_3$	$ZnCl_2$	Toluene	120, 12	28
9	$RuCl_3$	$Bi(NO_2)_3{\cdot}5H_2O$	Toluene	120, 12	—
10	$RuCl_3$	$FeCl_3{\cdot}6H_2O$	Toluene	120, 12	—
11[c]	$RuCl_3$	$SnCl_2{\cdot}2H_2O$	Dioxane/H_2O	120, 12	35
12	$RuCl_3$	$SnCl_2{\cdot}2H_2O$	Toluene	120, 4	42
13	**$RuCl_3$**	**$SnCl_2{\cdot}2H_2O$**	**Toluene**	**120, 12**	**73**
14[d]	$RuCl_3$	$SnCl_2{\cdot}2H_2O$	Toluene	140, 12	73
15	$RuCl_3$	$SnCl_2{\cdot}2H_2O$	THF	120, 12	—
16	$RuCl_3$	$SnCl_2{\cdot}2H_2O$	$CHCl_3$	120, 12	18
17	$RuCl_3$	$SnCl_2{\cdot}2H_2O$	DMA	140, 12	15
18	$RuCl_3$	$SnCl_2{\cdot}2H_2O$	Acetone	120, 12	—
19	$RuCl_3$	$SnCl_2{\cdot}2H_2O$	Acetonitrile	120, 12	26
20	$RuCl_3$	—	Toluene	140, 12	—

The bold letter indicates the optimized condition of this reaction.
[a] Unless otherwise stated, all the reactions were carried out in a pressure tube using 5.0 mL solvent, 18 mol % catalyst, 15 mol % of dppe, 1.0 equiv 9-ethyl-3-aminocarbazole, 2.0 equiv ethylene glycol, 3.0 equiv co-catalyst.
[b] Catalyst (6 mol %), 5 mol % dppe, and 3.0 equiv co-catalyst were used.
[c] Dioxane/H_2O in the ratio 9:1.
[d] Catalyst (24 mol %) and 20 mol % dppe were used.
[e] Isolated yields.

When **1a** and **2** were treated with $RuCl_3$ (6 mol %) and dppe (5 mol %) in the presence of $SnCl_2$ (3.0 equiv) for 12 h at 120 °C, compound **3a** was obtained in 30% yield (Table 1, entry 2). It is intriguing to note that without the addition of $SnCl_2$ heteroannulation reaction could not be promoted (Table 1, entry 20), while in the presence of $SnCl_2$ (3.0 equiv), compound **3a** was obtained in 73% yield. We screened other co-catalysts, such as $SbCl_3$, $CeCl_3{\cdot}7H_2O$, $AlCl_3$, $ZnCl_2$, which took longer reaction times (12 h) and gave lower yields of **3a** (Table 1, entries 5–8). No product was formed by using $InCl_3$, $Bi(NO_2)_3{\cdot}5H_2O$, $FeCl_3{\cdot}6H_2O$ (Table 1, entries 4, 9, and 10).

Table 2
Ligand effect on heteroannulation of **1a**[a]



1a **2** **3a**

Entry	Ligand	Temp/°C, time (h)	Yield[b]
1	dppe	120, 4	42
2	dppe	120, 8	73
3	—	140, 24	14
4	$P(OEt)_3$	140, 12	36
5	PCy_3	140, 12	35
6	BINAP	140, 12	21
7	PPh_3	140, 12	42
8	dppp	140, 24	21
9	dppf	140, 24	28

[a] All the reactions were carried out in a pressure tube using 5.0 mL toluene, 18 mol % $RuCl_3$, 15 mol % ligand, 1.0 equiv 9-ethyl-3-aminocarbazole, 2.0 equiv ethylene glycol, 3.0 equiv $SnCl_2{\cdot}2H_2O$.
[b] Isolated yields.

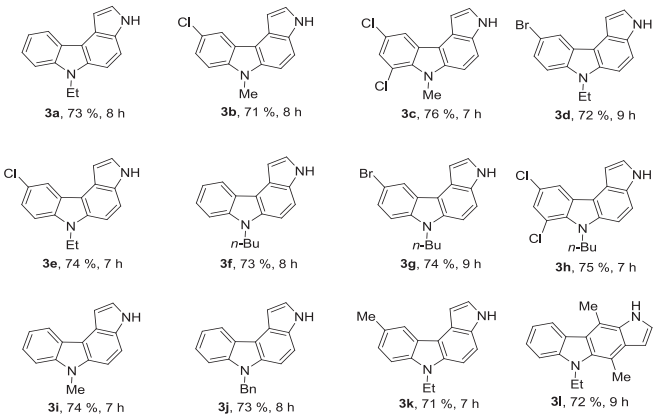
$RuCl_3$ was found to be an efficient catalyst in this reaction compared with other catalysts, such as $PdCl_2(PPh_3)_2$ and $RhCl(PPh_3)_3$. The best result was achieved by using 18 mol % $RuCl_3$, 15 mol % dppe, and 3.0 equiv of $SnCl_2$ in 5 mL of toluene at 120 °C for 8 h. Further increase in temperature did not show any significant improvement in yield (Table 1, entry14). Attempts to reduce the catalyst loading were only partly successful as lesser amount of pyrrolo[2,3-*c*]carbazole **3a** was formed, when 6 mol % catalyst was employed. On the other hand, using 18 mol % catalyst loading gave good conversion, and identical yields were obtained with 24 mol % catalyst loading, although the reaction time was slightly prolonged as shown in Table 1.

Subsequently, the effect of ligands were further investigated under the above optimized solvent, catalyst, and co-catalyst, it indicated that ligands played an important role in this heteroannulation reaction. All the results are listed in Table 2. When heteroannulation of **1a** was carried out in the absence of ligand, the corresponding product **3a** was obtained in 16% yield (Table 2, entry 3). While in the presence of ligand the product **3a** was obtained with improved yield, which confirms the key role of ligand in this heteroannulation reaction. We were delighted to find that dppe was the most effective ligand for this reaction. In the presence of dppe the cyclization of **1a** afforded **3a** in 73% yield under the optimized condition (Table 2, entry 2).

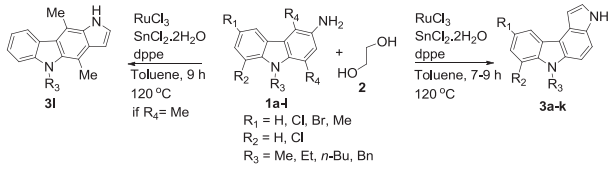
With optimized conditions in our hand, we explored the scope of this method with respect to an array of *N*-alkylated-3-aminocarbazoles **1a**–**k** as summarized in Table 3. Various derivatives of **1a**–**k** smoothly underwent heteroannulation reaction to afford the desired pyrrolo[3,2-*c*]carbazole **3a**–**k** in good yields (Scheme 2). When R_4 was substituted with methyl group pyrrolo[3,2-*b*]carbazole **3l** was obtained in good yield. The structure of product **3c** was also confirmed by single-crystal X-ray analysis[10] (Fig. 2).

Carbazole is obtained by the reaction of acetonylacetone with indole in the presence of Lewis acid.[9e] We wish to apply this methodology for pyrrolo[2,3-*c*]carbazole into indolo[2,3-*c*]carbazoles (Scheme 3). The desired indolo[2,3-*c*]carbazoles were successfully synthesized in good yields by reacting acetonylacetone (1.0 equiv) with various pyrrolo[2,3-*c*]carbazoles (1.0 equiv) and using *p*-toluenesulfonic acid (*p*-TSA, 0.5 equiv) as a catalyst. The yield of the product was slightly lower when toluene was used as solvent instead of ethanol. Reaction of pyrrolocarbazoles (**3j**, **3k**, and **3l**) with acetonylacetone works well however the products are not identifiable from the spectroscopic data (Table 4).

Table 3
$RuCl_3/SnCl_2$ catalyzed heteroannulation of various *N*-alkylated-3-aminocarbazoles[a]



[a] All the reactions were carried out in a pressure tube using 5.0 mL toluene, 1.0 equiv 3-aminocarbazoles, 2.0 equiv ethylene glycol, 3.0 equiv $SnCl_2 \cdot 2H_2O$, 18 mol % $RuCl_3$, 15 mol % dppe, 120 °C.



Scheme 2. Synthesis of various pyrrolo[2,3-*c*]carbazole derivatives.

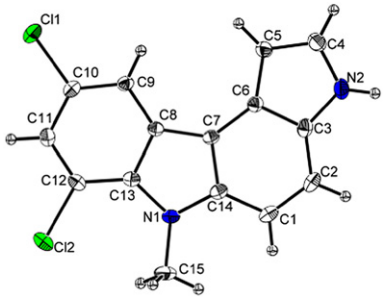
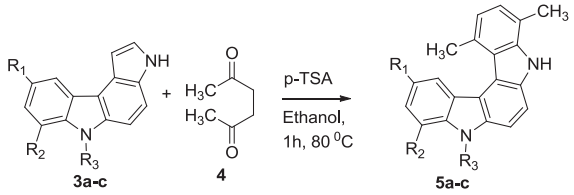


Fig. 2. ORTEP diagram of **3c**.



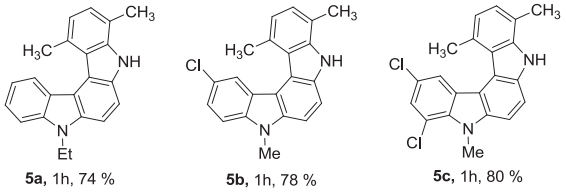
Scheme 3. Synthesis of indolo[2,3-*c*]carbazoles.

Based on the mechanism proposed for the synthesis of indole from aniline,[11] the possible reaction pathways for the synthesis of pyrrolocarbazole are shown in Scheme 4 with path *a* and path *b*. In the first step $RuCl_3$ oxidized the ethylene glycol (**2**) forming the imine intermediate, and then $SnCl_2$ reduces this imine into **IA**, this **IA** is again oxidized by $RuCl_3$ and gives rise to **IIA**.

Then in path *a*, after formation of **IIA** followed by the proton exchange producing the **IIIA**. Elimination of water molecule gives rise to the final product **3a**.

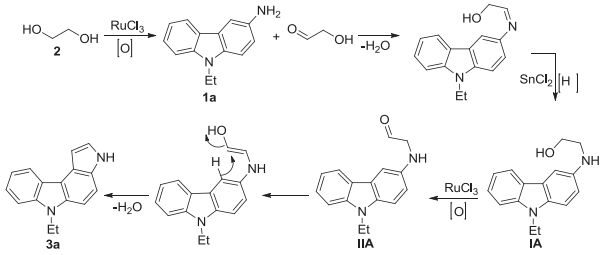
In path *b*, after the formation of **IIA**, one more 3-aminocarbazole molecule (**1a**) reacts with **IIA** and gives rise to the **IIIA**, in the final step removal of **1a** produced the desired product **3a**.

Table 4
Preparation of indolo[2,3-*c*]carbazoles form pyrrolo[2,3-*c*]carbazoles[a]

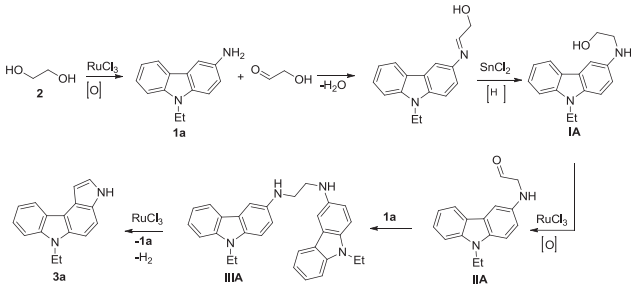


[a] All the reactions were carried out in a pressure tube using 5.0 mL ethanol, 1.0 equiv pyrrolocarbazole, 1.0 equiv acetonylacetone, 0.5 equiv *p*-TSA stirred at 80 °C for 1 h.

Path *a*:



Path *b*:



Scheme 4. Possible mechanism for synthesis of **3a**.

3. Conclusions

In summary, we have developed a unique and direct approach for constructing pyrrolo[2,3-*c*]carbazole and pyrrolo[3,2-*b*]carbazole in good yields using $RuCl_3/SnCl_2$ mediated system. The synthesized pyrrolo[2,3-*c*]carbazoles easily converted into indolo [2,3-*c*]carbazoles on reaction with acetonylacetone in good yields.

4. Experimental section

4.1. General information

All ^1H, ^{13}C NMR spectra were recorded on AV-400 spectrometer operating at 400 and 100 MHz, respectively. Chemical shifts for ^1H NMR are expressed in parts per million (ppm) relative to tetramethylsilane (δ 0.00 ppm). Chemical shifts for ^{13}C NMR are expressed in parts per million relative to $CDCl_3$ (δ 77.0 ppm). Multiplicities were indicated as follows s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, and coupling constants (Hz). Chemical shifts of common trace ^1H NMR impurities ($CDCl_3$, ppm): H_2O, 1.56; EtOAc, 1.26, 2.05, 4.12; CH_2Cl_2, 5.30; $CDCl_3$, 7.26. IR spectra were recorded on FT/IR-5300 spectrometer; absorptions are reported in cm^{-1}. Mass spectra were recorded on either using EI technique or LCMS-2010A mass spectrometer. Elemental analyses

(C, H, and N) were recorded on EA 1112 analyzer in School of Chemistry, University of Hyderabad. Routine monitoring of the reactions was performed by TLC silica gel plates 60 F_{254} were used. Compounds were visualized with a UV light at 254 nm. Further visualization was achieved by staining with iodine. Column chromatography was carried out employing neutral alumina. Commercially available reagents and solvents were used without further purification and were purchased. Melting points were measured in open capillary tubes and are uncorrected.

4.2. General procedure for the preparation of pyrrolo[2,3-*c*] carbazole (3a–l)

An oven dried 25 mL Ace pressure tube was charged with $RuCl_3$ (18 mol %), dppe (15 mol %), and toluene (5 mL) along with *N*-alkylated-3-aminocarbazole **1a**–**l** (1.0 equiv), $SnCl_2$ (3.0 equiv), and ethylene glycol **2** (2.0 equiv), and then capped with a Teflon screw cap and the mixture was heated to 120 °C and stirred for 8 h. After completion of the reaction, followed by thin layer chromatography (TLC), the mixture was cooled to room temperature, the solvent was evaporated, and dissolved in EtOAc. The resulting solution was directly filtered through a pad of Celite and washed with EtOAc. The combined organic layers were washed with water, dried over anhydrous Na_2SO_4, and then concentrated under reduced pressure to give a crude product. The crude product was purified by column chromatography on neutral alumina using EtOAc/hexane as the eluent. The solvent was evaporated to dryness to get the pure product **3a**–**l**.

4.3. General procedure for the preparation of indolo[2,3-*c*] carbazole (5a–c)

An oven dried 25 mL Ace pressure tube was charged with pyrrolocarbazole **3a**–**c** (1.0 equiv), acetonylacetone **4** (1.0 equiv), and *p*-toluenesulfonic acid (*p*-TSA) (0.5 equiv) along with 5 mL of ethanol then capped with a Teflon screw cap and the mixture was stirred at 80 °C for 1 h. After completion of the reaction, followed by thin layer chromatography (TLC), the mixture was cooled to room temperature, the solvent was evaporated and dissolved in EtOAc. The resulting organic layer was washed with water, dried over anhydrous Na_2SO_4, and then concentrated under reduced pressure to give a crude product. The crude product was purified by column chromatography on neutral alumina using EtOAc/hexane as the eluent. The solvent was evaporated to dryness to get the pure product **5a**–**c**.

*4.3.1. 6-Ethyl-3,6-dihydropyrrolo[2,3-c]carbazole (**3a**).* Brown colored viscous liquid; yield: 73%; IR (KBr): 3408, 3051, 2968, 2928, 2858, 1707, 1587, 1477, 1450, 1375, 1331, 1228, 1180, 1151, 1087, 1020, 889, 781, 748 cm^{-1}; EtOAc/hexanes (3:7); R_f=0.57; ^1H NMR (400 MHz, TMS, $CDCl_3$): δ 8.35–8.33 (m, 2H), 7.52–7.50 (m, 3H), 7.34–7.32 (m, 3H), 7.13 (s, 1H), 4.46 (q, 2H, J=5.76 Hz), 1.46 (t, 3H, J=6.64 Hz); ^{13}C NMR (100 MHz, TMS, $CDCl_3$): δ 139.0, 134.9, 130.5, 124.2, 123.8, 123.1, 121.4, 121.3, 118.3, 113.6, 109.9, 108.3, 104.2, 100.8, 37.7, 14.3; LC–MS: m/z=235 $(M+H)^+$, positive mode; Anal. Calcd for molecular formula $C_{16}H_{14}N_2$; C, 82.02; H, 6.02; N, 11.98%; found: C, 82.15; H, 6.38; N, 11.86%.

*4.3.2. 9-Chloro-6-methyl-3,6-dihydropyrrolo[2,3-c]carbazole (**3b**).* White colored solid; yield: 71%, mp: 116 °C; IR (KBr): 3427, 2924, 2854, 1714, 1456, 1361, 1290, 1062, 1014, 868, 788 cm^{-1}; EtOAc/hexanes (3:7); R_f=0.42; ^1H NMR (400 MHz, TMS, $CDCl_3$): δ 8.32 (s, 1H), 8.21–8.20 (m, 1H), 7.53–7.51 (m, 1H), 7.39–7.31 (m, 3H), 7.26–7.24 (m, 1H), 7.05 (s, 1H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, TMS, $CDCl_3$): δ 138.4, 136.7, 130.6, 124.5, 123.95, 123.91, 123.8, 121.2, 120.6, 112.7, 110.6, 109.2, 104.3, 100.8, 29.5; LC–MS: m/z=256 $(M+H)^+$, 257 (M+1) positive mode; Anal. Calcd for molecular formula $C_{15}H_{11}N_2Cl$; C, 70.73; H, 4.35; N, 11.00%; found: C, 70.81; H, 4.26; N, 10.85%.

*4.3.3. 7,9-Dichloro-6-methyl-3,6-dihydropyrrolo[2,3-c]carbazole (**3c**).* White colored solid; yield: 76%, mp: 142 °C; IR (KBr): 3441, 3406, 2922, 1657, 1550, 1456, 1367, 1284, 1107, 844, 775, 731, 706 cm^{-1}; EtOAc/hexanes (3:7); R_f=0.54; ^1H NMR (400 MHz, TMS, $CDCl_3$): δ 8.40 (s, 1H), 8.066–8.061 (m, 1H), 7.54–7.52 (m, 1H), 7.37–7.36 (m, 1H), 7.33–7.32 (m, 1H), 7.24–7.22 (m, 1H), 7.00–6.99 (m, 1H), 4.21 (s, 3H); ^{13}C NMR (100 MHz, TMS, $CDCl_3$): δ 137.7, 133.8, 130.8, 126.5, 125.2, 124.7, 123.5, 120.8, 119.3, 116.1, 112.6, 111.4, 104.5, 100.8, 32.3; LC–MS: m/z=287 $(M-H)^-$, 289 (M+2) negative mode; Anal. Calcd for molecular formula $C_{15}H_{10}N_2Cl_2$; C, 62.03; H, 3.49; N, 9.69%; found; C, 64.76; H, 5.38; N, 8.54%.

*4.3.4. 9-Bromo-6-ethyl-3,6-dihydropyrrolo[2,3-c]carbazole (**3d**).* Brown colored viscous liquid; yield: 72%, IR (KBr): 3414, 2959, 2926, 2856, 2058, 1996, 1712, 1616, 1462, 1367, 1302, 1091, 794, 742 cm^{-1}; EtOAc/hexanes (3:7); R_f=0.60; ^1H NMR (400 MHz, TMS, $CDCl_3$): δ 8.45 (s, 1H), 8.375–8.370 (m, 1H), 7.57–7.48 (m, 2H), 7.40 (s, 1H), 7.37–7.28 (m, 2H), 7.07 (s, 1H), 4.43 (q, 2H, J=7.28 Hz), 1.43 (t, 3H, J=7.24 Hz); ^{13}C NMR (100 MHz, TMS, $CDCl_3$): δ 137.6, 135.4, 130.6, 126.4, 124.7, 124.4, 123.7, 121.3, 112.8, 111.1, 110.6, 109.7, 104.3, 100.9, 37.9, 14.0; LC–MS: m/z=315 $(M+H)^+$, 317 (M+2), positive mode; Anal. Calcd for molecular formula $C_{16}H_{13}N_2Br$; C, 61.36; H, 4.18; N, 8.94%; found: C, 61.28; H, 4.21; N, 8.86%.

*4.3.5. 9-Chloro-6-ethyl-3,6-dihydropyrrolo[2,3-c]carbazole (**3e**).* Brown colored viscous liquid; yield: 74%, IR (KBr): 3393, 2924, 2858, 1736, 1622, 1462, 1302, 1259, 1099, 794 cm^{-1}; EtOAc/hexanes (3:7); R_f=0.51; ^1H NMR (400 MHz, TMS, $CDCl_3$): δ 8.40 (s, 1H), 8.23 (s, 1H), 7.57–7.55 (m, 1H), 7.40–7.38 (m, 3H), 7.31–7.29 (m, 1H), 7.08 (s, 1H), 4.43 (q, 2H, J=7.2 Hz), 1.44 (t, 3H, J=7.2 Hz); ^{13}C NMR (100 MHz, TMS, $CDCl_3$): δ 137.3, 135.5, 131.8, 131.1, 130.5, 128.8, 124.4, 123.8, 121.3, 120.7, 110.6, 109.2, 104.3, 100.8, 37.9, 14.0; LC–MS: m/z=269 $(M+H)^+$, 270 (M+1) positive mode; Anal. Calcd for molecular formula $C_{16}H_{13}N_2Cl$; C, 71.51; H, 4.88; N, 10.42%; found: C, 71.65; H, 4.79; N, 10.36%.

*4.3.6. 6-Butyl-3,6-dihydropyrrolo[2,3-c]carbazole (**3f**).* Brown colored viscous liquid; yield: 73%, IR (KBr): 3402, 3051, 2959, 2928, 2872, 1689, 1583, 1481, 1456, 1367, 1329, 1151, 1084, 1020, 881, 781, 748 cm^{-1}. EtOAc/hexanes (3:7); R_f=0.68; ^1H NMR (400 MHz, TMS, $CDCl_3$): δ 8.35 (s, 1H), 8.31 (d, 1H, J=7.64 Hz), 7.54–7.43 (m, 3H), 7.39–7.37 (m, 1H), 7.34–7.29 (m, 2H), 7.13 (s, 1H), 4.40 (t, 2H, J=7.08 Hz), 1.93–1.88 (m, 2H), 1.47–1.39 (m, 2H), 0.95 (t, 3H, J=7.28 Hz); ^{13}C NMR (100 MHz, TMS, $CDCl_3$): δ 139.5, 135.4, 130.5, 124.1, 123.8, 123.7, 122.9, 121.4, 121.2, 118.2, 109.7, 108.5, 104.6, 101.0, 43.1, 31.4, 20.6, 13.9; LC–MS: m/z=263 $(M+H)^+$, positive mode; Anal. Calcd for molecular formula $C_{18}H_{18}N_2$; C, 82.41; H, 6.92; N, 10.68%; found: C, 82.55; H, 6.81; N, 10.56%.

*4.3.7. 9-Bromo-6-butyl-3,6-dihydropyrrolo[2,3-c]carbazole (**3g**).* Greenish colored viscous liquid; yield: 74%, IR (KBr): 3400, 2957, 2926, 2856, 1720, 1606, 1454, 1375, 1329, 1099, 1016, 794 cm^{-1}. EtOAc/hexanes (3:7); R_f=0.63; ^1H NMR (400 MHz, TMS, $CDCl_3$): δ 8.74 (s, 1H), 8.22–8.18 (m, 2H), 7.52–7.49 (m, 3H), 7.45–7.43 (m, 1H), 7.31–7.27 (m, 1H), 4.36 (t, 2H, J=7.12 Hz), 1.98–1.89 (m, 2H), 1.47–1.41 (m, 2H), 0.97 (t, 3H, J=7.32 Hz); ^{13}C NMR (100 MHz, TMS, $CDCl_3$): δ 138.1, 135.8, 130.5, 126.4, 124.5, 124.4, 123.6, 121.2, 112.6, 110.9, 110.5, 109.9, 104.5, 100.8, 43.2, 31.3, 20.5, 13.8; LC–MS: m/z=341 $(M+H)^+$, 343 (M+2), positive mode; Anal. Calcd for molecular formula $C_{18}H_{17}N_2Br$; C, 63.35; H, 5.02; N, 8.21%; found: C, 63.48; H, 4.91; N, 8.15%.

*4.3.8. 6-Butyl-7,9-dichloro-3,6-dihydropyrrolo[2,3-c]carbazole (**3h**).* White colored solid; yield: 75%, mp: 138 °C; IR (KBr): 3389,

2961, 2926, 2856, 1620, 1554, 1469, 1371, 1296, 1109, 777, 734 cm^{-1}; EtOAc/hexanes (3:7); R_f=0.66; ^1H NMR (400 MHz, TMS, $CDCl_3$): δ 8.45 (s, 1H), 8.129–8.125 (m, 1H), 7.56 (d, 1H, J=8.84 Hz), 7.39–7.38 (m, 2H), 7.30–7.26 (m, 1H), 7.04 (s, 1H), 4.73 (t, 2H, J=7.52 Hz), 1.91–1.83 (m, 2H), 1.47–1.40 (m, 2H), 0.96 (t, 3H, J=7.32 Hz); ^{13}C NMR (100 MHz, TMS, $CDCl_3$): δ 137.1, 133.1, 130.7, 126.8, 125.3, 124.7, 123.5, 120.9, 119.3, 115.9, 112.7, 111.4, 104.8, 100.8, 44.6, 33.0, 20.1, 13.9; LC–MS: m/z=331 $(M+H)^+$, 333 (M+2), positive mode; Anal. Calcd for molecular formula $C_{18}H_{16}N_2Cl_2$; C, 65.27; H, 4.87; N, 8.46%; found: C, 62.43; H, 3.55; N, 9.61%.

*4.3.9. 6-Methyl-3,6-dihydropyrrolo[2,3-c]carbazole (**3i**).* Pale black colored viscous liquid; yield: 74%, IR (KBr): 3393, 2920, 2851, 1699, 1647, 1539, 1450, 1242, 1018, 966 cm^{-1}; EtOAc/hexanes (3:7); R_f=0.65; ^1H NMR (400 MHz, TMS, $CDCl_3$): δ 8.32 (s, 1H), 8.28 (d, 1H, J=7.72 Hz), 7.50–7.48 (m, 1H), 7.45–7.44 (m, 2H), 7.34 (s, 1H), 7.29–7.27 (m, 2H), 7.09 (s, 1H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, TMS, $CDCl_3$): δ 140.1, 136.0, 130.6, 124.2, 123.9, 122.9, 121.4, 121.2, 118.4, 113.5, 109.8, 108.3, 104.3, 100.9, 29.4; LC–MS: m/z=221 $(M+H)^+$, positive mode; Anal. Calcd for molecular formula $C_{15}H_{12}N_2$; C, 81.79; H, 5.49; N, 12.72%; found: C, 81.68; H, 5.56; N, 12.65%.

*4.3.10. 6-Benzyl-3,6-dihydropyrrolo[2,3-c]carbazole (**3j**).* Black colored viscous liquid; yield: 73%, IR (KBr): 3354, 3061, 2916, 2858, 1959, 1907, 1819, 1685, 1614, 1579, 1494, 1448, 1359, 1263, 1205, 1165, 1120, 1076, 1018, 908, 823, 752, 700 cm^{-1}; EtOAc/hexanes (3:7); R_f=0.60; ^1H NMR (400 MHz, TMS, $CDCl_3$): δ 8.37 (s, 1H), 8.34 (d, 1H, J=7.72 Hz), 7.48–7.46 (m, 1H), 7.44–7.43 (m, 2H), 7.40–7.39 (m, 1H), 7.26 (s, 1H), 7.24–7.22 (m, 3H), 7.15–7.12 (m, 4H), 5.62 (s, 2H); ^{13}C NMR (100 MHz, TMS, $CDCl_3$): δ 139.8, 137.7, 135.6, 130.7, 128.79, 128.70, 127.2, 126.3, 124.3, 124.2, 123.2, 121.4, 121.3, 118.8, 110.0, 108.7, 104.7, 101.0, 46.7; LC–MS: m/z=297 $(M+H)^+$, positive mode; Anal. Calcd for molecular formula $C_{21}H_{16}N_2$; C, 85.11; H, 5.44; N, 9.45%; found; C, 85.06; H, 5.48; N, 9.56%.

*4.3.11. 6-Ethyl-9-methyl-3,6-dihydropyrrolo[2,3-c]carbazole (**3k**).* Pale white colored solid; yield: 71%, mp: 48 °C; IR (KBr): 3443, 2924, 2856, 1651, 1456, 1371, 1294, 1244, 1143, 1018 cm^{-1}. EtOAc/hexanes (3:7); R_f=0.60; ^1H NMR (400 MHz, TMS, $CDCl_3$): δ 8.24 (s, 1H), 8.06 (s, 1H), 7.45–7.42 (m, 1H), 7.35–7.33 (m, 1H), 7.30–7.24 (m, 3H), 7.09–7.08 (m, 1H), 4.39 (q, 2H, J=7.2 Hz), 2.59 (s, 3H), 1.39 (t, 3H, J=7.2 Hz); ^{13}C NMR (100 MHz, TMS, $CDCl_3$): δ 137.4, 135.1, 130.4, 127.5, 125.3, 124.0, 123.3, 121.5, 121.3, 113.4, 109.6, 108.0, 104.3, 100.9, 37.8, 21.5, 14.1; LC–MS: m/z=247 $(M-H)^-$, negative mode; Anal. Calcd for molecular formula $C_{17}H_{16}N_2$; C, 82.22; H, 6.49; N, 11.28%; found: C, 82.13; H, 6.51; N, 11.36%.

*4.3.12. 5-Ethyl-4,10-dimethyl-1,5-dihydropyrrolo[3,2-b]carbazole (**3l**).* Pale black colored viscous liquid; yield: 72%, IR (KBr): 3400, 2922, 2852, 2368, 1712, 1647, 1458, 1093, 1016 cm^{-1}; EtOAc/hexanes (3:7); R_f=0.70; ^1H NMR (400 MHz, TMS, $CDCl_3$): δ 8.24 (d, 1H, J=7.8 Hz), 8.12 (s, 1H), 7.44–7.42 (m, 1H), 7.39–7.37 (m, 1H), 7.34 (t, 1H, J=2.64 Hz), 7.21–7.17 (m, 1H), 6.719–6.715 (m, 1H), 4.63 (q, 2H, J=7.12 Hz), 2.98 (s, 3H), 2.97 (s, 3H), 1.42 (t, 3H, J=7 Hz); ^{13}C NMR (100 MHz, TMS, $CDCl_3$): δ 142.5, 134.9, 131.1, 128.6, 124.8, 124.58, 124.50, 122.2, 120.1, 117.8, 111.3, 107.8, 106.0, 100.9, 39.6, 15.2, 15.0, 14.5; LC–MS: m/z=263 $(M+H)^+$, positive mode; Anal. Calcd for molecular formula $C_{18}H_{18}N_2$; C, 82.41; H, 6.92; N, 10.68%; found: C, 82.31; H, 6.81; N, 10.75%.

*4.3.13. 8-Ethyl-1,4-dimethyl-5,8-dihydroindolo[2,3-c]carbazole (**5a**).* Yellow colored solid; yield 74%, mp: 78 °C; IR Neat: 3416, 2926, 2849, 1651, 1275, 1103, 1022, 750 cm^{-1}; EtOAc/hexanes (3:7); R_f=0.63; ^1H NMR (400 MHz, TMS, $CDCl_3$): δ 8.45 (d, 1H, J=8.04 Hz), 8.14 (s, 1H), 7.62–7.60 (m, 1H), 7.56–7.54 (m, 1H), 7.51–7.45 (m, 2H), 7.25–7.21 (m, 2H), 7.04 (d, 1H, J=6.9 Hz), 4.51 (q, 2H, J=6.4 Hz), 3.00 (s, 3H), 2.61 (s, 3H), 1.51 (t, 3H, J=7.2 Hz); ^{13}C NMR (100 MHz, TMS, $CDCl_3$): δ 139.6, 139.5, 135.9, 135.0, 131.0, 125.7, 125.0, 124.4, 123.4, 123.2, 121.5, 117.1, 116.5, 116.1, 116.0, 109.3, 108.0, 107.3, 37.8, 23.4, 16.6, 13.9; LC–MS: m/z=313 $(M+H)^+$, positive mode; Anal. Calcd for molecular formula $C_{22}H_{20}N_2$; C, 84.58; H, 6.45; N, 8.97%; found: C, 84.46; H, 6.41; N, 9.07%.

*4.3.14. 11-Chloro-1,4,8-trimethyl-5,8-dihydroindolo[2,3-c]carbazole (**5b**).* Yellow colored solid; yield 78%, mp: 98 °C; IR Neat: 3402, 2926, 2852, 1728, 1668, 1454, 1317, 1257, 1149, 1089, 1022, 794 cm^{-1}; EtOAc/hexanes (3:7); R_f=0.64; ^1H NMR (400 MHz, TMS, $CDCl_3$): δ 8.38 (d, 1H, J=1.72 Hz), 8.16 (s, 1H), 7.63–7.61 (m, 1H), 7.51–7.49 (m, 1H), 7.42–7.36 (m, 2H), 7.23 (d, 1H, J=7.28 Hz), 7.11–7.09 (m, 1H), 3.93 (s, 3H), 2.98 (s, 3H), 2.60 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 139.9, 138.9, 137.4, 135.9, 129.2, 126.0, 124.3, 123.7, 123.0, 122.1, 121.9, 121.3, 117.3, 114.6, 113.9, 111.8, 110.8, 108.7, 29.9, 23.4, 17.1; LC–MS: m/z=333 $(M+H)^+$, 335 (M+2) positive mode; Anal. Calcd for molecular formula $C_{21}H_{17}N_2Cl$; C, 75.78; H, 5.15; N, 8.42%; found: C, 75.86; H, 5.09; N, 8.37%.

*4.3.15. 9,11-Dichloro-1,4,8-trimethyl-5,8-dihydroindolo[2,3-c]carbazole (**5c**).* Yellow colored solid; yield 80%, mp: 132 °C; IR Neat: 3433, 2924, 2854, 1722, 1651, 1456, 1315, 1261, 1105, 1074, 1028 cm^{-1}; EtOAc/hexanes (3:7); R_f=0.70; ^1H NMR (400 MHz, TMS, $CDCl_3$): δ 8.24 (s, 1H), 8.20 (s, 1H), 7.67–7.65 (m, 1H), 7.54–7.52 (m, 1H), 7.38 (s, 1H), 7.23 (s, 1H), 7.10 (d, 1H, J=7.4 Hz), 4.34 (s, 3H), 2.88 (s, 3H), 2.60 (s, 3H); ^{13}C NMR (100 MHz, TMS, $CDCl_3$): δ 139.6, 138.5, 135.3, 134.4, 130.5, 126.8, 126.2, 125.8, 122.8, 122.7, 122.3, 122.0, 116.3, 115.8, 115.7, 115.0, 110.9, 107.7, 32.5, 23.4, 16.6; LC–MS: m/z=365 $(M-H)^-$, 367 (M+2) negative mode; Anal. Calcd for molecular formula $C_{21}H_{16}N_2Cl_2$; C, 68.68; H, 4.39; N, 7.63%; found: C, 68.56; H, 4.45; N, 7.58%.

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Supplementary data

Spectroscopic data, LC–MS, and elemental analysis for all new compounds. Supplementary data related to this article can be found online at doi:10.1016/j.tet.2012.01.070.

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10. The CCDC deposition number for compound **3c** is 841557; molecular formula: $C_{15}H_{10}C_{l2}N_2$. chemical formula weight is 289.15; monoclinic; unit cell parameters: a=9.274(2) Å, b=5.6445(9) Å, c=24.572(4) Å, α=90°, β=95.794(17)°, γ=90°. Space group $P21/n$.
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