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Phosphine-free thiopseudourea-Pd(II) complex catalyzed Larock heteroannulation of 2-haloamines with internal alkynes

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ABSTRACT

We examined the Pd-catalyzed heteroannulation of 2-haloamines with internal alkynes under phosphine-free conditions. The thiopseudourea palladium(II) complex (**5**) found to be an efficient catalyst for the Pd induced heteroannulation. Achieved high turnover number for the heteroannulation reactions of internal alkynes with 2-iodoaniline. A variety of 2-bromoanilines and *N*-tosyl substituted 2-bromoanilines effectively reacted with different substituted internal alkynes to give the corresponding indoles in good to high yields (1:1 ratio of regioisomers).

1. Introduction

The phosphine-free palladium catalyzed heteroannulation of internal alkynes with 2-haloamines is an important synthetic method for 2,3-disubstituted indole formation [1–3]. The indole nucleus is an important compound, found in numerous natural products and biological active materials [4,5]. Widespread use of indole nucleus in pharmaceutical studies [6,7], aimed to develop efficient synthetic methods. Compared to many reported methods for the indole synthesis [8–14], the palladium-catalyzed indolization is emerged as a powerful synthetic method (Larock indole synthesis) (Scheme 1) [1]. This reaction is normally performed with 5 mol% of $Pd(OAc)_2$ for 2-iodoanilines and the same is not possible for 2-bromo or 2-chloroanilines. A number of heterogeneous [15–20] and homogeneous [21–25] Pd catalysts were reported for Larock indolization. Among them *N*-phenylurea [21] and 1,1′-bis(di-*tert*-butylphosphino)ferrocene [22] ligands based high loading Pd catalysts have shown better results. Few reports are available for the synthesis of 2,3-diphenyl-1-tosyl indole from *N*-tosyl-2-haloanilines with diphenylacetylene [1,19].

Herein, we report heteroannulation of 2-haloamines with internal alkynes using an efficient thiopseudourea Pd(II) complex (**5**) (Fig. 1). Recently, we have reported the synthesis (**1**) and its application for Suzuki–Miyaura, Sonogashira, Heck and Hiyama cross coupling reaction [26].

2. Results and discussion

Initially, we studied the catalytic activity of thiopseudourea Pd(II) complex (**5**) for the heteroannulation reaction between 2-iodoaniline and diphenylacetylene using 0.01 mol% of catalyst with various bases in DMF (*N*,*N*-dimethylformamide) at 130 °C (Table 1). Among the studied bases, $LiOH\cdot H_2O$ found to be the best (entry 4). Furthermore, the reaction efficiently proceeded with 4.0 equiv of $LiOH\cdot H_2O$ (with respect to 2-iodoaniline) to afford 2,3-diphenylindole in an excellent yield (entry 4). With the optimized base (4.0 equiv of $LiOH\cdot H_2O$), apart from DMF, the role of various solvents was studied (entries 8–10). The best results achieved with DMF solvent. Under the similar experimental conditions with 0.01 mol% $Pd(OAc)_2$ very low yield was observed (entry 11). In order to study the effect of temperature, we have conducted the experiment at 100 °C for 48 h and observed very low yield (entry 12). Further, the activity of different phosphine-free ligands **1a–c** (Fig. 2) with $Pd(OAc)_2$ was studied under the same reaction conditions that resulted in moderate to good yields (entries 13–15). We confirm that thiopseudourea-Pd(II) complex is an efficient catalyst for heteroannulation of 2-haloamine with diphenylacetylene.

From the above optimized reaction conditions (0.01 mol% of **5**, DMF 2 mL, $LiOH\cdot H_2O$ 4 equiv at 130 °C), reactions of 2-iodoaniline

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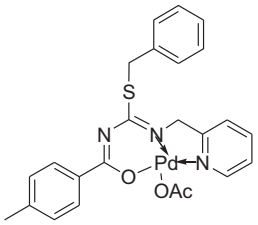


Fig. 1. Thiopseudourea Pd(II) complex (**5**).

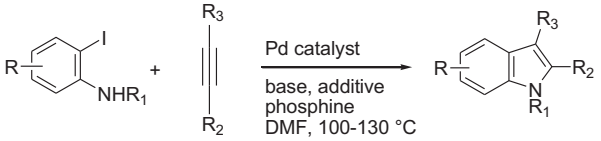
(1.0 mmol) with various alkynes (1.5 mmol) were investigated (Table 2). Substituent on the diphenylacetylene has modest effect on the reaction time and yield. Unsymmetrical meta and para-substituted diphenylacetylenes also resulted in high yields without any regioselectivity and the isolated indole products contain both regioisomers in 1:1 ratio (entries 4–6). The complete deprotection of the acetyl group was observed, when *N*-acetyl substituted 2-iodoaniline was used as the substrate, leading to the formation of corresponding non-*N*-substituted indole (entry 7). We tried the indolization of 2-iodoaniline with 1-phenylacetylene and but-2-yne-1,4-diol without any success.

Further, decrease in catalyst loading to 0.001 mol%, the reaction also proceeds well with high conversion (entry 2). However, higher turnover number (TON) (6.3×10^5) was obtained while using comparatively lower catalyst concentration (0.0001 mol%) with prolonged reaction time (entry 3).

Encouraged by these results, we investigated the indolization of various 2-bromoanilines which are expected less reactive compared to 2-iodoaniline (Table 3). In our case, reactions of all the 2-bromoanilines with diphenylacetylene afforded the desired products (entries 1–5). Higher yields (80–90%) were obtained with 0.1 mol% of catalyst loading compared to 0.01 mol% (74% yield, entry 2). When unsymmetrical alkynes reacted with 2-bromoaniline, the corresponding 2,3-diphenylindole regioisomers in 1:1 ratio were formed and the same in case of 2-iodoaniline (entries 6–8).

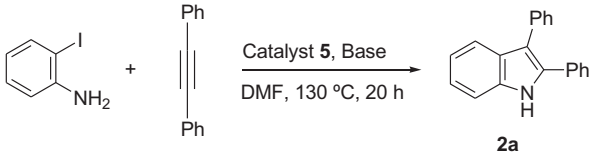
Further, we have studied the scope of our catalyst system to *N*-tosyl substituted 2-bromoaniline with diphenylacetylenes (Table 4). In all the studied *N*-tosyl substituted 2-bromoanilines, the products are corresponding *N*-tosyl substituted 2,3-diphenylindoles (entries 1–5) with high yields. Our catalyst system could not work well in case of 2-chloroaniline and *N*-tosyl substituted 2-chloroaniline with diphenylacetylene (Table 3, entry 9 and Table 4, entry 6).

We propose the mechanism (Scheme 2) of Pd(II) complex (**5**) catalyzed indolization based on previous reports. The means of this transformation proceed through the following steps: (a) at high temperatures, the palladium(II) complex (**5**) converts to Pd(0), (b) oxidative addition of 2-haloamine (C–X bond) to Pd(0) producing a Pd(II)–aryl complex [27,28]; (c) insertion of the alkyne into the Pd–C bond of aryl-Pd(II) complex [29,30], (d) C–N coupling to give the indole and regeneration of Pd(0) catalyst [30]. The alternative Pd(II)/Pd(IV) catalytic cycle seems to be very unlikely at higher temperatures [31,32].



Scheme 1. Larock indole synthesis.

Table 1
Thiopseudourea Pd(II) complex (**5**) catalyzed heteroannulation of 2-iodoaniline with diphenylacetylene.[a]



2a

Entry	Base (equiv)	Solvent	Yield (%)[b]
1	NaOAc (4)	DMF	5
2	Na_2CO_3 (4)	DMF	23
3	K_3PO_4 (4)	DMF	20
4	LiOH·H_2O (4)	DMF	97
5	LiOH·H_2O (3)	DMF	96
6	LiOH·H_2O (2)	DMF	56
7	LiOH·H_2O (1)	DMF	37
8	LiOH·H_2O (3)	DMSO	12
9	LiOH·H_2O (3)	DMA	64
10	LiOH·H_2O (3)	NMP	34
11[c]	LiOH·H_2O (3)	DMF	20
12[d]	LiOH·H_2O (3)	DMF	33
13[e]	LiOH·H_2O (3)	DMF	64
14[e]	LiOH·H_2O (3)	DMF	82
15[e]	LiOH·H_2O (3)	DMF	80

[a] Reaction conditions: 2-iodoaniline 1 mmol, diphenylacetylene 1.5 mmol, base 4.0 mmol, catalyst 0.01 mol%, solvent 2 mL, reaction temperature 130 °C.
[b] Isolated yield.
[c] 0.1 mol% of the $Pd(OAc)_2$.
[d] Reaction temperature 100 °C and reaction time 48 h.
[e] 0.05 mol% of $Pd(OAc)_2$/0.01 mol% of ligand (**1a** or **1b** or **1c**).

3. Conclusions

In conclusion, we proved that the phosphine-free thiopseudourea Pd(II) complex is an efficient catalyst for heteroannulation of internal alkynes with 2-haloamines and *N*-tosyl substituted 2-bromoanilines. The heteroannulation of 2-bromoanilines and *N*-tosyl substituted 2-bromoanilines proceeded well to afford the corresponding products in good to high yields under a low catalyst loading of 0.1 mol%. Work is in progress in our laboratory to develop a new catalyst with high regioselectivity for Larock indole synthesis.

4. Experimental section

4.1. General procedure for the synthesis of picolyl sulphonamide ligand (*1a*)

Picolyl amine (5 mmol) was added drop wise to solution of tosyl chloride (15 mmol) in dry dichloromethane (30 mL) at 0 °C and allows stirring for 3 h. After that the mixture was warmed to room temperature and stirred for another 12 h. After filtration, the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate) to afford the compound as a white solid (80–85% yield).

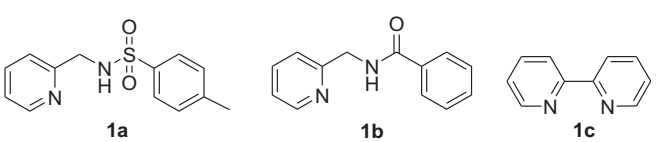
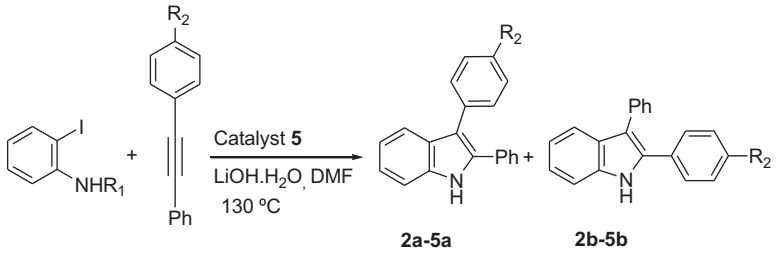


Fig. 2. Nitrogen ligands **1a**–**c**.

Table 2
Thiopseudourea Pd(II) complex (**5**) catalyzed heteroannulation of 2-iodoanilines with alkynes.[a]



Entry	R_1	R_2	Catalyst (mol%)	Product	Ratio	Time/h	Yield (%)[b]
1	H	H	0.01	**2a**	na	20	98
2	H	H	0.001	**2a**	na	24	92
3	H	H	0.0001	**2a**	na	30	63
4	H	4-Me	0.01	**3a**/**3b**	1/1	20	92
5	H	F	0.01	**4a**/**4b**	1/1	24	87
6	H	3-Me	0.01	**5a**/**5b**	1/1	20	86
7	Ac	H	0.01	**2a**	na	20	90

[a] Reaction conditions: 2-iodoaniline 1 mmol, alkyne 1.5 mmol, LiOH·H_2O 4.0 mmol, catalyst **5**, DMF 2 mL, reaction temperature 130 °C.
[b] Isolated yield.

*4.1.1. (Pyridin-2-yl)-N-tosylmethanamine (**1a**)*

^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 8.44 (d, J = 4.34 Hz, 2H), 7.72 (d, J = 8.12 Hz, 2H), 7.62 (t, J = 8.49 Hz, 1H), 7.34 (d, J = 7.74 Hz, 1H), 7.27 (d, J = 7.93 Hz, 2H), 7.16 (t, J = 6.98 Hz, 1H), 4.16 (d, J = 6.04 Hz, 2H), 3.0 (s, 1H), 2.40 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.9, 148.8, 143.2, 136.7, 136.5, 129.5, 127.0, 122.5, 121.9, 47.4, 21.3; ESI-MS (m/z) $(M + H)^+$ = 263; HRMS: calcd for $C_{13}H_{15}O_2N_2S$ $(M + H)^+$ = 263.08463, found: 263.08487.

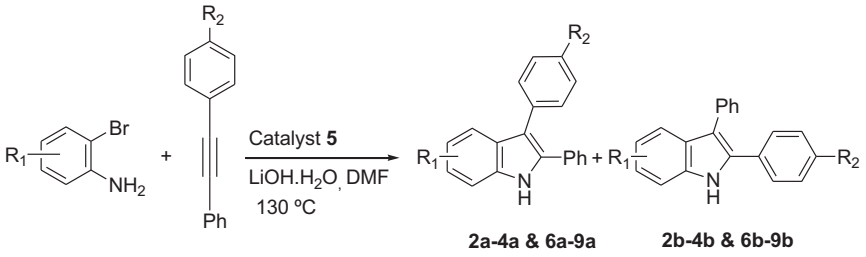
*4.2. General procedure for the synthesis of N-((pyridin-2-yl)methyl) benzamide (**1b**)*

Picolyl amine (5 mmol) was added drop wise to solution of benzoyl chloride (7.5 mmol) in dry dichloromethane (30 mL) at 0 °C and allows stirring for 30 min. After that triethylamine (15 mmol) was added drop wise over 15 min. After the addition, mixture was warmed to room temperature and stirred for another 12 h. After filtration, the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (eluent: hexane/ethyl acetate) to afford the compound as a white solid (90% yield).

*4.2.1. N-((Pyridin-2-yl)methyl)benzamide (**1b**)*

^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 8.56 (d, J = 3.99 Hz, 1H), 7.88 (d, J = 7.99 Hz, 2H), 7.67–7.70 (m, 2H), 7.50 (t, J = 7.99 Hz, 2H), 7.44 (t, J = 7.99 Hz, 2H), 7.21 (t, J = 7.99 Hz, 1H), 4.76 (d, J = 4.99 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.3, 156.1, 148.8, 136.8, 134.2, 131.4, 128.4, 127.0, 122.4, 122.3, 44.6; ESI-MS (m/z) $(M + H)^+$ = 213;

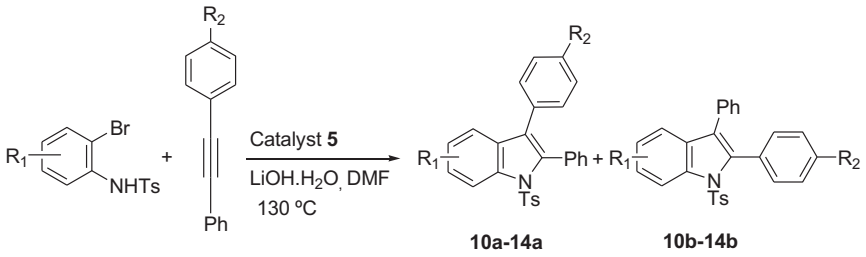
Table 3
Thiopseudourea Pd(II) complex (**5**) catalyzed heteroannulation of 2-bromoanilines with alkynes.[a]



Entry	R_1	R_2	Catalyst (mol%)	Product	Ratio	Time/h	Yield (%)[b]
1	H	H	0.1	**2a**	na	20	90
2	H	H	0.01	**2a**	na	30	74
3	4-F	H	0.1	**6a**	na	20	90
4	4-Me	H	0.1	**7a**	na	20	94
5	4,6-Me	H	0.1	**8a**	na	20	80
6	H	4-Me	0.1	**3a**/**3b**	1/1	20	86
7	H	4-F	0.1	**4a**/**4b**	1/1	20	80
8	H	4-Cl	0.1	**9a**/**9b**	1/1	20	82
9	H	H	1.0	**2a**	na	30	19[c]

[a] Reaction conditions: 2-bromoaniline 1 mmol, alkyne 1.5 mmol, LiOH·H_2O 4.0 mmol, catalyst **5**, DMF 2 mL, reaction temperature 130 °C.
[b] Isolated yield.
[c] Reaction for 2-chlooroaniline.

Table 4
Thiopseudourea Pd(II) complex catalyzed heteroannulation of *N*-tosyl-2-bromoanilines with alkynes.[a]



Entry	R_1	R_2	Catalyst (mol%)	Product	Ratio	Time/h	Yield (%)[b]
1	H	H	0.1	**10a**	na	24	90
2	4-Me	H	0.1	**11a**	na	24	92
3	4-F	H	0.1	**12a**	na	24	83
4	H	4-F	0.1	**13a**/**13b**	1/1	24	92
5	H	3-Me	0.1	**14a**/**14b**	1/1	24	87
6	H	H	1.0	**10a**	na	30	15[c]

[a] Reaction conditions: *N*-tosyl-2-bromoaniline 1 mmol, alkyne 1.5 mmol, $LiOH \cdot H_2O$ 4.0 mmol, catalyst **5**, DMF 2 mL, reaction temperature 130 °C.
[b] Isolated yield.
[c] Reaction for *N*-tosyl-2-chloroaniline.

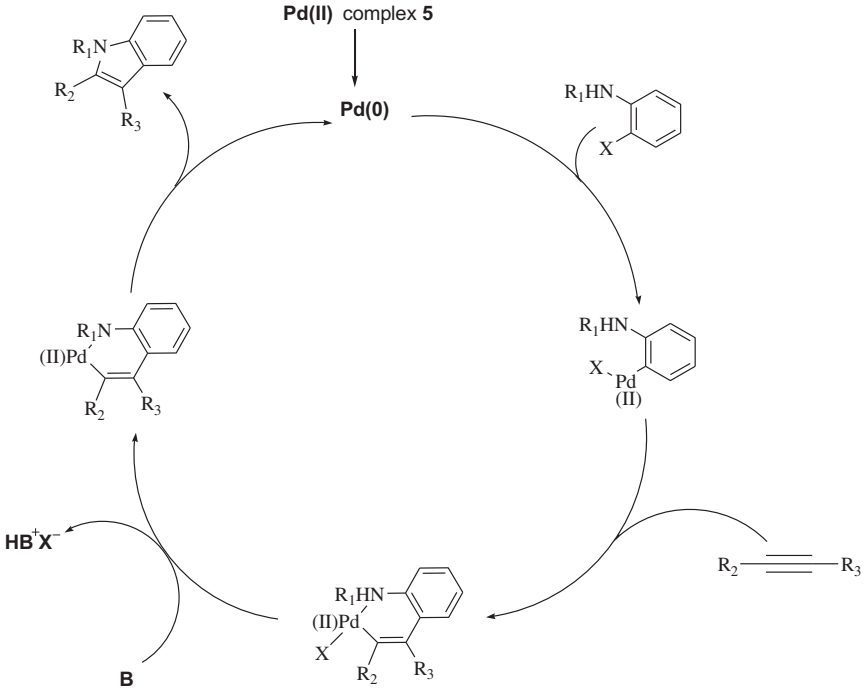
HRMS: calcd for $C_{13}H_{13}ON_2$ $(M + H)^+ = 213.10204$, found: 213.10224.

4.3. General procedure for the Larock indolization of 2-iodoaniline and 2-bromoanilines

The 25 mL RB-flask was charged with 2-haloamines (1 mmol), diphenylacetylene (1.5 mmol), $LiOH \cdot H_2O$ (4 mmol) and catalyst (0.001 mol% of **5** in 2 mL *N*,*N*-dimethylformamide). The reaction mixture was stirred at 130 °C for 20 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate (20 mL) and washed with brine water. The combined organic phase was dried over anhydrous Na_2SO_4. After removal of the solvent, the residue was subjected to column chromatography on silica gel using ethyl acetate and hexane to afford the indole product in high purity. In case of 2-bromoanilines, 0.1 mol% of catalyst **5** was applied.

4.3.1. 2,3-Diphenyl-1H-indole (***2a***)

^1H NMR (300 MHz, $CDCl_3$, TMS): δ 8.11 (s, 1H), 7.62 (d, $J = 8.30$ Hz, 1H), 7.14–7.41 (m, 12H), 7.08 (t, $J = 7.55$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.8, 135.0, 134.0, 132.6, 130.1, 128.6, 128.4, 128.1, 127.6, 126.1, 122.6, 120.3, 119.6, 115.0, 110.8; ESI-MS (m/z) $(M + H)^+ = 270$.



Scheme 2. Possible catalytic cycle of Pd(II) complex (**5**) catalyzed indolization of 2-haloamine with an internal alkyne.

*4.3.2. 2-p-Tolyl-3-phenyl-1H-indole (**3a**) and 3-p-tolyl-2-phenyl-1H-indole (**3b**)*

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 8.07 (s, 2H), 7.60 (d, J = 7.55 Hz, 2H), 7.04–7.40 (m, 24H), 2.38 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.5, 135.8, 135.7 (d), 135.2 (d), 134.2, 133.8, 132.8, 131.9, 130.1, 129.9, 129.7, 129.3, 129.2, 128.8 (d), 128.6, 128.4, 128.0, 127.9, 127.5, 126.1, 122.6, 122.4, 120.3 (d), 119.7, 119.5, 110.8, 110.7, 21.2; ESI-MS (m/z) $(M + H)^+ = 284$.

*4.3.3. 2-(4-Fluorophenyl)-3-phenyl-1H-indole (**4a**) and 3-(4-fluorophenyl)-2-phenyl-1H-indole (**4b**)*

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 8.13 (s, 1H), 8.07 (s, 1H), 7.61 (d, J = 7.55 Hz, 1H), 7.57 (d, J = 7.55 Hz, 1H), 7.23–7.38 (m, 16H), 7.18 (t, J = 8.30 Hz, 2H), 6.96–7.11 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.9, 163.2, 135.8, 135.7, 134.8, 134.1, 133.1, 132.4, 131.6, 131.5, 130.0, 129.9, 129.8, 128.7, 128.5, 128.0, 127.7, 126.2, 122.7, 120.4, 119.6, 119.3, 115.8, 115.6, 115.3, 110.9, 110.8; EI-MS (m/z) $(M)^+ = 287$.

*4.3.4. 2-m-Tolyl-3-phenyl-1H-indole (**5a**) and 3-m-tolyl-2-phenyl-1H-indole (**5b**)*

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 8.08 (s, 2H), 7.63 (d, J = 7.36 Hz, 2H), 7.04–7.41 (m, 24H), 2.32 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.1, 137.8, 135.7, 135.0, 134.8, 134.1, 133.8, 132.5, 132.4, 130.6, 130.0, 128.4, 128.3, 128.0, 127.4, 127.1, 126.9, 126.0, 125.4, 122.4, 120.2, 119.6, 119.5, 110.8, 21.4, 21.3; ESI-MS (m/z) $(M + H)^+ = 284$; HRMS: calcd for $C_{21}H_{18}N$ $(M + H)^+ = 284.1450$, found: 284.1439.

*4.3.5. 5-Fluoro-2,3-diphenyl-1H-indole (**6a**)*

^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 8.09 (s, 1H), 6.89–7.36 (m, 13H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.8, 135.8, 134.5, 132.3, 130.4, 130.2, 129.8, 129.1, 128.7, 128.6, 128.0, 127.9, 126.4, 111.6, 111.4, 111.1, 110.7; EI-MS (m/z) $(M)^+ = 287$.

*4.3.6. 5-Methyl-2,3-diphenyl-1H-indole (**7a**)*

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 8.12 (s, 1H), 7.22–7.44 (m, 12H), 7.05 (t, J = 7.93 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.2, 134.1, 132.7, 130.1, 129.6, 128.9, 128.5, 128.4, 128.0, 127.5, 126.1, 124.2, 119.1, 114.6, 110.5, 21.5; ESI-MS (m/z) $(M + H)^+ = 284$.

*4.3.7. 5,7-Dimethyl-2,3-diphenyl-1H-indole (**8a**)*

^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 7.87 (s, 1H), 7.36–7.39 (m, 4H), 7.32 (t, J = 8.54 Hz, 2H), 7.27 (t, J = 7.32 Hz, 2H), 7.21–7.23 (m, 3H), 6.81 (s, 1H), 2.49 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.3, 133.9, 133.7, 132.9, 130.1, 129.9, 128.5, 128.4, 128.1, 127.4, 126.1, 124.9, 119.6, 116.8, 21.4, 16.5; ESI-MS (m/z) $(M + H)^+ = 298$; HRMS: calcd for $C_{22}H_{20}N$ $(M + H)^+ = 298.1600$, found: 298.1595.

*4.3.8. 2-(4-Chlorophenyl)-3-phenyl-1H-indole (**9a**) and 3-(4-chlorophenyl)-2-phenyl-1H-indole (**9b**)*

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 8.16 (s, 1H), 8.11 (s, 1H), 7.62 (d, J = 7.55 Hz, 1H), 7.57 (d, J = 5.28 Hz, 1H), 7.04–7.37 (m, 24H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.9, 135.8, 134.6, 134.3, 133.5, 133.4, 132.7, 132.6, 132.3, 131.9, 131.3, 131.1, 130.0, 129.3, 128.8, 128.7 (d), 128.6, 128.1, 127.8, 126.4, 126.1, 122.9, 122.8, 120.5, 119.7, 119.3, 110.9 (d); EI-MS (m/z) $(M)^+ = 303$.

4.4. General procedure for the Larock indolization of N-tosyl substituted 2-bromoanilines

The 25 mL RB-flask was charged with *N*-tosyl substituted 2-bromoanilines (1 mmol), diphenylacetylene (2 mmol), $LiOH\cdot H_2O$ (4 mmol) and 0.1 mol% of catalyst **5** in 2 mL DMF. The reaction mixture was stirred at 130 °C for 24 h. Then, the reaction mixture was cooled to room temperature, diluted with ethyl acetate (20 mL) and washed with brine water. The combined organic phase was dried over anhydrous Na_2SO_4. After removal of the solvent, the residue was subjected to column chromatography on silica gel using ethyl acetate and hexane to afford the indole product in high purity.

*4.4.1. 2,3-Diphenyl-1-tosyl-indole (**10a**)*

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 8.38 (d, J = 8.30 Hz, 1H), 7.45 (d, J = 7.55 Hz, 1H), 7.37 (t, J = 8.30 Hz, 1H), 7.14–7.30 (m, 11H), 7.05 (d, J = 8.30 Hz, 4H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.5, 137.1, 136.7, 135.2, 132.5, 132.0, 130.8, 130.3, 129.7, 129.2, 128.4, 128.1, 127.2, 126.8, 125.1, 124.7, 124.1, 119.9, 116.1, 21.5; ESI-MS (m/z) $(M + H)^+ = 424$; HRMS: calcd for $C_{27}H_{22}NO_2S$ $(M + H)^+ = 424.1373$, found: 424.1371.

*4.4.2. 5-Methyl-2,3-diphenyl-1-tosyl-indole (**11a**)*

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 8.27 (d, J = 8.49 Hz, 1H), 7.20–7.45 (m, 13H), 7.05–7.07 (m, 3H), 2.39 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.3, 136.9, 135.4, 135.2, 133.8, 132.7, 132.0, 131.5, 130.9, 130.7, 130.1, 129.8, 129.2, 128.5, 128.3, 128.1, 127.5, 127.2, 126.8, 126.5, 119.7, 115.9, 110.5, 21.5, 21.3; ESI-MS (m/z) $(M)^+ = 437$.

*4.4.3. 5-Fluoro-2,3-diphenyl-1-tosyl-indole (**12a**)*

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 8.35 (dd, J = 4.53 Hz, 1H), 7.20–7.40 (m, 12H), 7.09–7.15 (m, 2H), 7.02–7.06 (m, 2H), 2.31 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.8, 144.7, 138.5, 134.9, 133.4, 132.1, 131.9, 131.6, 130.5, 129.8, 129.5, 129.3, 128.6, 128.5, 128.2, 128.1, 127.8, 127.2, 127.1, 126.8, 117.5, 113.0, 112.7, 21.5; ESI-MS (m/z) $(M + H)^+ = 442$; HRMS: calcd for $C_{27}H_{21}NO_2FS$ $(M + H)^+ = 442.1258$, found: 442.1277.

*4.4.4. 2-(4-Fluorophenyl)-3-phenyl-1-tosyl-indole (**13a**) and 3-(4-fluorophenyl)-2-phenyl-1-tosyl-indole (**13b**)*

^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 8.37 (d, J = 8.90 Hz, 2H), 7.16–7.45 (m, 21H), 6.87–7.07 (m, 11H), 2.31 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.3, 144.6, 144.5, 137.2, 137.1, 136.8, 135.6, 135.3, 133.9, 133.7, 132.4, 132.0, 131.4, 131.3, 130.7, 130.2 (d), 129.7, 129.3 (d), 128.5, 128.2, 127.3, 127.0, 126.9, 126.8, 125.2 (d), 125.0, 124.2, 124.1, 123.6, 122.7, 120.4, 119.9, 119.6, 116.1, 115.3, 115.0, 114.5, 114.3, 21.5; ESI-MS (m/z) $(M + H)^+ = 442$; HRMS: calcd for HRMS: calcd for $C_{27}H_{20}NO_2FNaS$ $(M + Na)^+ = 464.1096$, found: 464.1107.

*4.4.5. 2-m-Tolyl-3-phenyl-1-tosyl-indole (**14a**) and 3-m-tolyl-2-phenyl-1-tosyl-indole (**14b**)*

^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 8.38 (d, J = 8.30 Hz, 2H), 7.46 (d, J = 7.74 Hz, 2H), 7.18–7.40 (m, 17H), 6.90–7.11 (m, 12H), 6.82 (d, J = 7.55 Hz, 1H), 2.31 (s, 6H), 2.28 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.4, 144.1, 137.6, 137.2, 136.9, 136.6, 135.8, 135.7, 135.5, 135.3, 132.7, 132.0, 130.9, 130.6, 130.4, 130.1, 129.7, 129.6, 129.2, 129.0, 128.7, 128.5, 128.3, 128.0, 127.9, 127.6, 127.1, 127.0, 126.9 (d), 125.4, 125.2, 125.0 (d), 124.0, 120.6, 120.4, 120.0, 119.9, 110.8, 110.3, 21.5, 21.3; ESI-MS (m/z) $(M)^+ = 437$.

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Appendix A. Supplementary material

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jorganchem.2013.05.049.

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