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Three-component reaction involving metal-free heteroannulation of *N*-Boc-3-amido indole, aryl aldehydes, and aromatic alkynes under microwave conditions: synthesis of highly diversified δ-carbolines ☆

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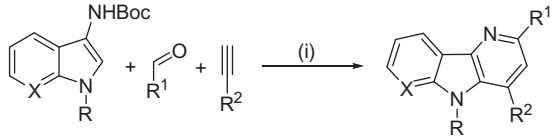
ABSTRACT

An efficient synthesis toward highly diversified δ-carbolines via one-pot multicomponent reaction using *N*-Boc-3-amido indoles, aryl aldehydes, and aromatic terminal alkynes under microwave conditions has been described.

Search for one-pot multicomponent reactions (MCRs)[1] that allow multi-bond formation in a single step to furnish products comprising portions of all the components has become one of the major challenges for the organic chemists. Over the years several important multicomponent reactions, such as, Biginelli,[2] Passerini,[3] Ugi,[4] and Mannich-type[5] have been extensively used for rapid transformations of mixtures of relatively simple 3 or 4 starting materials into the complex heterocyclic structures for pharmaceutical development. As part of our continuing effort on the development of new routes for the synthesis of indole-based natural products[6] as well as polyheterocycles[7], we embarked with a search for MCR involving amino functionalized indoles as one of the components. In recent years MCRs with alkynes as one of the components[8] have, although, received much attention and achieved great progress, indoles, in general, despite being a privileged[9] pharmaceutical template have remained relatively under explored.[10] We envisaged that owing to the activated nature of the indole ring, thus being prone to electrophilic attack, and use of either 2 or 3-amino substituted indoles as one of the components in a MCR with an aldehyde and a terminal aromatic alkyne as other components may facilitate heteroannulation via 6-*endo* cyclization either at C-3 or C-2 nucleophilic carbon of the indole. In the first instance, due to relatively poor stability and limited synthetic accessibility of the 2-amino indoles,[11] we proceeded to explore MCR with 3-amino indoles and report our findings in this letter. The methodology allows direct access to the synthesis of highly substituted δ-carbolines.

We commenced our studies by assessing the compatibility of N-protected 3-amidoindoles to MCR due to the poor shelf life of free amines.[12] We argued that protecting amino function with an acid/heat[13] labile protecting group such as Boc, may allow the resulting *N*-Boc-3-amido indole derivative amicable to MCR by allowing the generation of free amine in situ which in turn would immediately get trapped in the presence of aldehydes to form Schiff base. Initial attempts to carry out MCR involving *N*-Boc-3-



1a X = C; R = H **2** **3** **4-6**
1b X = C; R = CH_3
1c X = N; R = H

Scheme 1. Reagents and optimal conditions: (i) 30%, TFA in CH_3CN 90 °C, μW, 1.5 h.

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Table 1
Optimization of reaction conditions for the conversion of **1a–4a**

Entry	Reaction conditions	Temp (°C)	Time (h)	Yield of **4a**
1	10% CuI/10% $Yb(OTf)_3$ in CH_3CN	90	16	0
2	10% CuI/10% $Yb(OTf)_3$ in CH_3CN	130/μW	1.5	0
3	CH_3CN	130/μW	1.5	0
4	10% CuI/10% TFA/$Yb(OTf)_3$ in CH_3CN	90	1.5	28
5	10% CuI/10% TFA in CH_3CN	90	1.5	35
6	10% CuI/30% TFA in CH_3CN	90	1.5	48
7	10% TFA in CH_3CN	90	1.5	50
8	30% TFA in CH_3CN	90	16	62
9	30% TFA in CH_3CN	90/μW	1.5	73
10	30% TFA in CH_3CN	rt	0.5	—
		90/μW	1.0	68
11	30% TFA in H_2O	90/μW	1.5	0
12	30% TFA in toluene	90/μW	1.5	54
13	*p*-TsOH in CH_3CN	90/μW	1.5	34
14	10% $FeCl_3$ in toluene	110	24	0
15	10% $FeCl_3$/30% TFA in toluene	110	24	47

amido indoles[14] (**1a**), phenylacetylene, and 4-chlorobenzaldehyde (Scheme 1) utilizing a reaction condition similar to those used for MCR involving aryl amine, terminal aromatic alkyne, and aryl aldehyde by Nagarajan and co-workers (10% CuI/10% $Yb(OTf)_3$ in acetonitrile under reflux at 80 °C),[15] failed to furnish any adducts or products through additions/annulations. Since TLC of the crude product exhibited the presence of protected *N*-Boc-3-amido indoles under this condition, further reaction in microwave conditions at 130 °C, to facilitate the deprotection of the Boc group at elevated temperatures[13] still failed to yield the desired product despite complete disappearance of *N*-Boc-3-amido indoles. Indeed, it was unclear as to whether free 3-aminoindole was liberated in situ from *N*-Boc-3-amido indoles or the latter underwent degradation at elevated temperature. This led us to carry out a series of reactions both under metal-free as well as under acidic conditions by applying either conventional or microwave heating. In general, heating the reaction mixture in the absence of acidic conditions failed to produce any annulated product.

A careful examination of the reaction products under 10% TFA in CH_3CN revealed the presence of the unreacted *N*-Boc-3-amido indoles thereby furnishing δ-carboline in low yield. This prompted us to increase the concentration of TFA from 10% to 30%, which then afforded the desired δ-carbolines in 62% yield (Table 1; entry **8**) after heating for 16 h. To further improve the yield and reduce the reaction timings, the reaction was carried out under microwave conditions at 90 °C and we were pleased to obtain the desired product **4a**[16] in 73% isolated yield (Table 1; entry **9**). Conducting the reaction in the presence of $FeCl_3$ or replacing TFA with *p*-TsOH or solvents (toluene, water) offered no improvements in the yield. Similarly, attempt to allow Schiff base formation at room temperature followed by heating in microwave had no influence on the yield of δ-carbolines.

The 5*H*-pyrido[3,2-*b*]indoles are useful building blocks as well as important skeletons of biologically active alkaloids such as, cryptolepine,[17] quindoline,[18] and glycozoline.[19] The roots of these species are used for the treatment of malaria and other infectious and noninfectious diseases such as antimuscarinic, antibacterial, antiviral, antiplasmodial,[20] and antihyperglycemic.[21] Thus, due to their various and important biological activities, a MCR reaction would be a new entry to the synthesis of highly diversified δ-carbolines.

A careful survey of the literature revealed few reports[22] dealing with the synthesis of δ-carbolines. Papamical et al.[22a] have described the synthesis of less diverse δ-carbolines via the reaction of 3-acylaminoindoles and 1,3-dicarbonyl compounds. Recently Jeanty et al.[23] reported the synthesis of natural glycozoline δ-carboline using Aza-Fischer indole cyclization; whereas other methods reported prefer Pd-catalyzed intramolecular arylation[24] reactions. To the best of our knowledge, MCR for the synthesis of δ-carbolines has not yet been reported and this led us to investigate the scope and limitation of our three component reaction for the synthesis of δ-carbolines.

The *N*-Boc-3-amido indole **1a** was treated with a range of aryl aldehydes and aromatic alkynes using the optimized conditions to synthesize small array δ-carbolines **4a–g**. In the subsequent studies 1-methyl-*N*-Boc-3-amido indole **1b** was subjected to MCR furnishing δ-carbolines **5a–d** in 68–75% yield. Next, we applied our methodology to yet another indole derivative. *N*-Boc-3-amido-7-azaindole[25] **1c** and treated it with a series of aldehydes and aryl alkynes to furnish δ-carbolines based on **6a–n**. The crude products were purified by column chromatography and characterized using NMR and mass. Yields and structure of compounds are summarized in Table 2 and as evident in most cases of aryl aldehydes

Table 2
Synthesis of δ-carbolines **4–6**

Entry	Amine	R^1	R^2	Product	Yield (%)
1	**1a**	4-Cl–C_6H_4	C_6H_5	**4a**	73
2	**1a**	4-Br–C_6H_4	C_6H_5	**4b**	64
3	**1a**	4-C_2H_5O–C_6H_4	C_6H_5	**4c**	71
4	**1a**	4-CH_3–C_6H_4	C_6H_5	**4d**	52
5	**1a**	4-OH–C_6H_4	C_6H_5	**4e**	66
6	**1a**	3,4-Di-OCH_3–C_6H_4	C_6H_5	**4f**	70
7	**1a**	4-Cl–C_6H_4	4-CH_3–C_6H_4	**4g**	71
8	**1b**	4-Cl–C_6H_4	4-CH_3–C_6H_4	**5a**	75
9	**1b**	4-Cl–C_6H_4	4-*t*-$C(CH_3)_3$–C_6H_4	**5b**	70
10	**1b**	4-Br–C_6H_4	4-CH_3–C_6H_4	**5c**	68
11	**1b**	4-Br–C_6H_4	4-*t*-$C(CH_3)_3$–C_6H_4	**5d**	72
12	**1c**	4-Cl–C_6H_4	C_6H_5	**6a**	67
13	**1c**	4-Br–C_6H_4	C_6H_5	**6b**	69
14	**1c**	4-F–C_6H_4	C_6H_5	**6c**	62
15	**1c**	4-C_2H_5O–C_6H_4	C_6H_5	**6d**	68
16	**1c**	3,4-Di-Cl–C_6H_4	C_6H_5	**6e**	59
17	**1c**	4-CH_3–C_6H_4	C_6H_5	**6f**	64
18	**1c**	3,4-Di-OCH_3–C_6H_4	C_6H_5	**6g**	66
19	**1c**	4-OH–C_6H_4	C_6H_5	**6h**	63
20	**1c**	4-Cl–C_6H_4	4-OCH_3–C_6H_4	**6i**	58
21	**1c**	4-C_2H_5O–C_6H_4	4-CH_3–C_6H_4	**6j**	67
22	**1c**	4-$N(CH_3)_2$–C_6H_4	4-CH_3–C_6H_4	**6k**	71
23	**1c**	3,4-Di-OCH_3–C_6H_3	4-CH_3–C_6H_4	**6l**	68
24	**1c**	4-Cl–C_6H_4	4-*t*-$C(CH_3)_3$–C_6H_4	**6m**	69
25	**1c**	4-OH–C_6H_4	4-*t*-$C(CH_3)_3$–C_6H_4	**6n**	62

and aromatic alkynes, the three-component reaction proceeded smoothly under the optimized condition and the corresponding products were obtained in moderate to good yields (52–75%). The electronic effect appeared to have negligible effect on the reaction since either electron withdrawing or the electron donating groups on the different aromatic rings offered products with minimal variation in yields. Similarly, introduction of methyl group at *N*-1 in the indole ring had no effect on the yields of annulated products. An attempt to employ aliphatic aldehydes or alkynes failed to furnish title compounds that indicates limitations of our MCR strategy.

In summary, we have developed an efficient method for the synthesis of highly substituted δ-carboline derivatives under metal catalyst-free conditions. In general the strategy involves one-pot multicomponent synthesis of highly diversified δ-carbolines by irradiating a mixture of *N*-Boc-3-amido indoles, aromatic terminal alkynes, and aryl aldehydes under acidic conditions.

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References and notes

1. (a) Ganem, B. *Acc. Chem. Res.* **2009**, *42*, 463–472; (b) Zhu, J.; Bienayme, H. In *Multicomponent Reactions*; Wiley-VCH: Weinheim, 2005; (c) Bienayme, H.; Hulme, C.; Oddon, G.; Schmitt, P. *Chem. Eur. J.* **2000**, *6*, 3321–3329; (d) Domling, A.; Ugi, I. *Angew. Chem., Int. Ed.* **2000**, *39*, 3168–3210; (e) Zhu, J. *Eur. J. Org. Chem.* **2003**, *7*, 1133–1144; (f) Ramon, D. J.; Yus, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 1602–1634; (g) Ulaczyk-Lesanko, A.; Hall, D. G. *Curr. Opin. Chem. Biol.* **2005**, *9*, 266–276; (h) Biggs-Houck, J. E.; Younai, A.; Shaw, J. T. *Curr. Opin. Chem. Biol.* **2010**, *14*, 371–382.
2. (a) Biginelli, P. *Chem. Ber.* **1891**, *24*, 1317–1319; (b) Sweet, F.; Fissekis, J. D. *J. Am. Chem. Soc.* **1973**, *95*, 7841–8749; (c) Kappe, C. O. *J. Org. Chem.* **1997**, *62*, 7201–7204.
3. (a) Passerini, M.; Simone, L. *Gazz. Chim. Ital.* **1921**, *51*, 126–129; (b) Bossio, R.; Marcaccini, S.; Pepino, R.; Torroba, T. *Synthesis* **1993**, 783–785; (c) Denmark, S. E.; Fan, Y. *J. Org. Chem.* **2005**, *70*, 9667–9676.
4. (a) Ugi, I.; Meyr, R.; Fetzer, U.; Steinbrückner, C. *Angew. Chem.* **1959**, *71*, 386–388; (b) Ugi, I.; Lohberger, S.; Karl, R. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed., Pergamon: Oxford, 1991; Vol. 2, pp 1083–1109; (c) Keating, T. A.; Armstrong, R. W. *J. Am. Chem. Soc.* **1995**, *117*, 7842–7843; (d) Ross, G. F.; Herdtweck, E.; Ugi, I. *Tetrahedron* **2002**, *58*, 6127–6133.
5. (a) Mannich, C.; Krösche, W. *Arch. Pharm.* **1912**, *250*, 647–667; (b) Tramontini, M. *Synthesis* **1973**, 703–775; (c) Arend, M.; Westermann, B.; Risch, N. *Angew. Chem., Int. Ed.* **1998**, *37*, 1044–1070; (d) Wei, C.; Li, Z.; Li, C.-J. *Org. Lett.* **2003**, *5*, 4473–4475; (e) Wei, C.; Li, C. J. *J. Am. Chem. Soc.* **2003**, *125*, 9584–9585.
6. (a) Agarwal, P. K.; Sawant, D.; Sharma, S.; Kundu, B. *Eur. J. Org. Chem.* **2009**, *2*, 292–303; (b) Sharma, S.; Kundu, B. *Tetrahedron Lett.* **2008**, *49*, 7062–7065.
7. (a) Sharma, S. K.; Sharma, S.; Agarwal, P. K.; Kundu, B. *Eur. J. Org. Chem.* **2009**, *9*, 1309–1312; (b) Saha, B.; Sharma, S.; Sawant, D.; Kundu, B. *Tetrahedron Lett.* **2007**, *48*, 1379–1383; (c) Saha, B.; Kumar, R.; Maulik, P. R.; Kundu, B. *Tetrahedron Lett.* **2006**, *47*, 2765–2769; (d) Sawant, D.; Kumar, R.; Maulik, P. R.; Kundu, B. *Org. Lett.* **2006**, *8*, 1525–1528.
8. (a) Wei, C.; Zhang, L.; Li, C. J. *Synlett* **2004**, 1472–1483; (b) Guchhait, S. K.; Jadeja, K.; Madaan, C. *Tetrahedron Lett.* **2009**, *50*, 6861–6865; (c) Kikuchi, S.; Iwai, M.; Fukuzawa, S. *Synlett* **2007**, 2639–2642; (d) Baudelle, R.; Melnyk, P.; Deprez, B.; Tartar, A. *Tetrahedron* **1998**, *54*, 4125–4140; (e) Cao, K.; Zhang, F.; Tu, Y.-Q.; Zhuo, X.-T.; Fan, C.-A. *Chem. Eur. J.* **2009**, *15*, 6332–6334; (f) Bortolotti, B.; Leardini, R.; Nanni, D.; Zanardi, G. *Tetrahedron* **1993**, *49*, 10157–10174; (g) Appendino, G.; Cicione, L.; Minassi, A. *Tetrahedron Lett.* **2009**, *50*, 5559–5561.
9. (a) Bennasar, M. L.; Vidal, B.; Bosch, J. *J. Org. Chem.* **1997**, *62*, 3597–3609; (b) Zhang, H. C.; Ye, H.; Moretto, A. F.; Brumeld, K. K.; Maryano, B. E. *Org. Lett.* **2000**, *2*, 89–92; (c) Marugan, J. J.; Manthey, C.; Anaclerio, B.; Lafrance, L.; Lu, T.; Markotan, T.; Leonard, K. A.; Crysler, C.; Eisennagel, S.; Dasgupta, M.; Tomczuk, B. *J. Med. Chem.* **2005**, *48*, 926–934; (d) Faul, M. M.; Winneroski, L. L.; Krumrich, C. A. *J. Org. Chem.* **1998**, *63*, 6053–6058.
10. For review see: Sapi, J.; Laronze, J. Y. *Arkivoc* **2004**, 208–222. and references cited therein.
11. (a) Hino, T.; Nakagawa, M.; Hashizume, T.; Yamaji, N.; Miwa, Y. *Tetrahedron Lett.* **1970**, *11*, 2205–2208; (b) Nakagawa, M.; Yamaguchi, H.; Hino, T. *Tetrahedron Lett.* **1970**, *11*, 4035–4038. and references cited therein; (c) Roy, S.; Gribble, G. W. *Tetrahedron Lett.* **2007**, *48*, 1003–1005; (d) Witulski, B.; Alayrac, C.; Tevzadze-Saeftel, L. *Angew. Chem., Int. Ed.* **2003**, *42*, 4257–4260.
12. (a) Roy, S.; Gribble, G. W. *Tetrahedron Lett.* **2008**, *49*, 1531–1533; (b) Robinson, M. M.; Robinson, B. L.; Butler, F. P. *J. Am. Chem. Soc.* **1958**, *81*, 743–747.
13. Wasserman, H. H.; Berger, G. D.; Cho, K. R. *Tetrahedron Lett.* **1982**, *23*, 465–468.
14. To a stirred solution of 3-nitro indole (1 mmol) in methanol was added saturated solution of ammonium chloride solution (4 mL). Zn dust was added to the reaction mixture (10 mmol) portion wise over 15 min while maintaining the temperature at 0 °C. After 10 min, $(Boc)_2O$ (1.2 mmol) was added and the reaction mixture was allowed to warm to room temperature. After completion of the reaction, the reaction mixture was filtered through Celite, the methanol was distilled off under vacuo and the aqueous residue was extracted with DCM (3×15 mL) .The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated. The crude product was purified by column chromatography to afford **1a–c**.
tert-Butyl 1H-pyrrolo[2,3-b]pyridin-3-ylcarbamate (**1c**)*:* Yield = 0.857 g (60%), light yellow solid, mp 184–186 °C, R_f = 0.42 (2:8 EtOAc/hexane) IR (KBr) ν_{max} 3340, 2955, 1685, 1588, 1462, 1366, 1162 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ = 9.80 (1H, s, NH), 8.31 (1H, dd, J = 4.8, 1.4 Hz ArH), 7.90–7.86 (1H, m, ArH), 7.55 (1H, s, CONH), 7.11–7.05 (1H, m, ArH), 6.49 (1H, s, ArH), 1.51 (9H, s, $3 \times CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 146.5, 143.3, 126.2, 115.5, 114.5, 113.8, 80.6, 28.5 ppm. Mass (ES^+) m/z 234.2 (M^++1). Anal. Calcd for $C_{12}H_{15}N_3O_2$: C, 61.79; H, 6.48; N, 18.01. Found: C, 61.75; H, 6.49; N, 18.04.
15. Gaddam, V.; Ramesh, S.; Nagarajan, R. *Tetrahedron* **2010**, *66*, 4218–4222.
16. A mixture of *N*-Boc-3-amido indoles **1a–c** (1.0 mmol), aldehydes **2** (1.0 mmol), and alkynes **3** (1.5 mmol) was treated with 30% solution of trifluoroacetic acid in MeCN (5 mL), placed in a 10 mL microwave vial containing a stirring bar. The reaction mixture was heated at 90 °C for 1.5 h in microwave (Biotage). The reaction mixture was cooled to ambient temperature, washed with aq $NaHCO_3$ (20 mL), and extracted with DCM (2×30 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed in vacuo. The crude product was purified on a silica gel column using ethyl acetate/hexane (v/v 1:4) as eluent to afford **4a–g**, **5a–d**, and **6a–n**.
2-(4-Chlorophenyl)-4-phenyl-5H-pyrido[3,2-b]indole (**4a**)*:*Yield = 0.222 g (73%), brown solid, mp >250 °C, R_f = 0.52 (2:8 EtOAc/hexane). IR (KBr) ν_{max} 3071, 2367, 1589, 1461, 1380 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$ + DMSO-d_6) δ = 11.15 (1H, s, NH), 8.34 (1H, d, J = 7.5 Hz, ArH), 8.20 (2H, d, J = 7.8 Hz, ArH), 7.85 (1H, d, J = 8.4 Hz, ArH), 7.62–7.45 (9H, m, ArH), 7.27 (1H, t, J = 7.3 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 147.7, 142.3, 141.7, 138.6, 136.4, 132.9, 131.9, 129.9, 129.1, 128.5, 128.1, 127.5, 121.8, 120.3, 119.5, 116.3, 112.2 ppm. Mass (ES^+) m/z 355.1 (M^++1). Anal. Calcd for $C_{23}H_{15}ClN_2$: C, 77.85; H, 4.26; N, 7.89. Found: C, 77.88; H, 4.25; N, 7.87.
17. (a) Clinquart, E. *Bull. Acad. R. Med. Belg.* **1929**, *9*, 627–635; (b) Tackie, A. N.; Sharaf, M. H. M.; Schiff, P. L., Jr.; Boye, G. L.; Crouch, R. C.; Martin, G. E. *J. Heterocycl. Chem.* **1991**, *28*, 1429–1435.
18. Dwuma-Badu, D.; Ayin, J. S. K.; Fiagbe, N. I. Y.; Knapp, J. E.; Shiff, P. L., Jr.; Slatkin, D. J. J. *Pharm. Sci.* **1978**, *67*, 433–434.
19. (a) Chakraborty, D. P. *Tetrahedron Lett.* **1966**, *7*, 661–664; (b) Chakraborty, D. P. *Phytochemistry* **1969**, *8*, 762–769.
20. Wright, C. W.; Addae-Kyereme, J.; Breen, A. G.; Brown, J. E.; Cox, M. F., et al *J. Med. Chem.* **2001**, *44*, 3187–3194.
21. (a) Bierer, D. E.; Dubenko, L. G.; Zhang, P.; Lu, Q.; Imbach, P. A.; Garofalo, A. W.; Phuan, P. W.; Fort, D. M.; Litvak, J.; Gerber, R. E.; Sloan, B.; Luo, J.; Cooper, R.; Reaven, G. M. *J. Med. Chem.* **1998**, *41*, 2754–2764; (b) Yang, S. W.; Abdel-Kader, M.; Marga, S. M.; Werkhoven, C. M.; Wisse, J. H.; Bursuker, I.; Neddermann, K.; Fairchild, C.; Suarez, C. R.; Menendez, A. T.; Lane, K.; Kingston, D. G. I. *J. Nat. Prod.* **1999**, *62*, 976–983.
22. (a) Papamicael, C.; Queguiner, G.; Bourguignon, J.; Dupas, G. *Tetrahedron Lett.* **2001**, *57*, 5385–5391; (b) Desarbre, E.; Merour, J. Y. *Synthesis* **1997**, 73–78; (c) Merour, J.-Y.; Meour, A. *Synthesis* **1994**, 767–769; (d) Spaeth, E. *Chem. Ber.* **1940**, *73*, 719–721; (e) Rocca, P.; Cochennec, C.; Marsais, F.; Thomas-dit-Dumont, L.; Mallet, M.; Godard, A.; Queguner, G. *J. Org. Chem.* **1993**, *58*, 7832–7838.
23. Jeanty, M.; Blu, J.; Suzenet, F.; Guillaumet, G. *Org. Lett.* **2009**, *11*, 5142–5145.
24. (a) Philippe, F.; Steven, H.; Beata, D. H.; Agnes, P. B.; Katrien, M.; Peter, M.; Bert, U. W. M. *Tetrahedron* **2008**, *64*, 6030–6037; (b) Takehiko, I.; Akito, Y.; Takao, S. *J. Chem. Soc., Perkin Trans. 1., Org. Bioorg. Chem.* **1999**, *11*, 1505–1510; (c) Rocca, P.; Cochennec, C.; Marsais, F.; Thomas-dit-Dumont, L.; Mallet, M. *J. Org. Chem.* **1993**, *58*, 7832–7838; (d) Erwan, A.; Patrick, R.; Francis, M.; Alain, G.; Guy, Q. *J. Heterocycl. Chem.* **1997**, *34*, 1205–1210; (e) Leroy, G. M.; Pingchen, C. F.; Seth, Y. A.; Alison, N.; Alice, M. C. *Med. Chem. Res.* **1999**, *9*, 118–132.
25. *2-(4-Chlorophenyl)-4-phenyl-5H-pyrido[2′,3′:4,5]pyrrolo[2,3-b]pyridine* (**6a**)*:* Yield = 0.204 g (67%), light brown solid, mp >250 °C, R_f = 0.48 (2:8 EtOAc/hexane). IR (KBr) ν_{max} 3071, 2375, 1599, 1462, 1366, 1162 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ = 12.12 (1H, s, NH), 8.67–8.58 (2H, m, ArH), 8.31 (2H, d, J = 8.4 Hz, ArH), 8.05 (1H, s, ArH), 7.91 (2H, d, J = 7.0 Hz, ArH), 7.63–7.55 (5H, m, ArH), 7.35 (1H, t, J = 5.8 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.5, 148.7, 140.3, 138.3, 135.8, 133.1, 133.0, 129.6, 129.2, 129.0, 128.9, 128.7, 128.4, 117.8, 116.4, 114.6 ppm. Mass (ES^+) m/z 356.1 (M^++1). Anal. Calcd for $C_{22}H_{14}ClN_3$: C, 74.26; H, 3.97; N, 11.81. Found: C, 74.22; H, 3.98; N, 11.84.