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SYNTHESIS OF PYRIDOPYRROLO[2,1-*a*]ISOINDOLES BY PALLADIUM-CATALYZED ANNULATION

Song Su Kang, Eul Kgun Yum*, and Nack-Do Sung[a]

Department of Chemistry, Chungnam National University, Yusung, Daejon 305-764, Korea

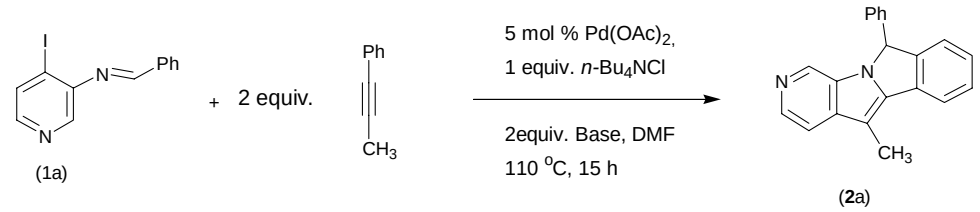
[a]Division of Applied Biology and Chemistry, Chungnam National University, Yusung, Daejon 305-764, Korea

Abstract – Diverse pyridopyrrolo[2,1-*a*]isoindoles were prepared by palladium -catalyzed annulation of benzylidene(4-iodopyridin-3-yl)amines and aromatic substituted internal alkynes under $Pd(OAc)_2$, *n*-Bu_4NCl, and Et_3N at 110 ^oC.

The condensed indole nucleus has attracted considerable attention in recent years since it is the structural framework of several natural products.[1-3] Specifically, olivacine and elliptine derivatives have been used in clinical trials as anti-cancer agents.[4] More recently, an indoloquinoline alkaloid isolated from the West African plant *Crypolepis sanguinolenta* was reported to have a strong antiplasmodial activity.[5] Although the aza analogues of ellipticine and indoloquinoline have strong antibacterial, antimycotic, and antitumor activities, few methods of synthesizing condensed azaindole analogues have been reported in the literature.[1,6] Recently, Larock and our group have reported effective annulation methods[7] using internal alkynes to prepare a variety of condensed heterocycles, such as indoles,[8] isoindolo[2,1-*a*]indoles,[9] carbolines,[10] azaindoles,[11] and pyrroloquinolines.[12] Our continued interest is in condensed azaindole derivatives as prospective biologically active substances. Therefore, we applied palladium-catalyzed annulation to pyridopyrrolo[2,1-*a*]isoindoles, for which has been no practical synthetic method to date. Here, we a report a facile synthesis of various pyridopyrrolo[2,1-*a*]isoindoles by palladium-catalyzed annulation of internal alkynes with benzylidine(*o*-iodopyridinyl)amines.

The benzylidene(4-iodopyridin-3-yl)amines (**1a**-**1c**) were prepared from 4-iodo-3-aminopyridine[13] and the corresponding aldehyde by azeotrophic condensation as the starting material for palladium-catalyzed annulation. Initially, we chose the palladium-catalyzed reaction of benzylidene(4-iodopyridin-3-yl)amine (**1a**) with 1-phenylpropyne under various palladium species and bases to optimize the reaction conditions. The results are summarized in Table 1.

Table1. Optimization of pyridopyrrolo[2,1-*a*]isoindoles by palladium-catalyzed annulation.

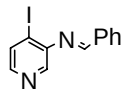
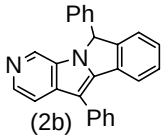
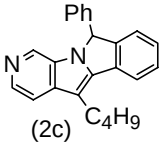
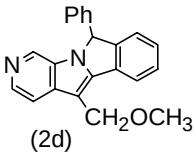
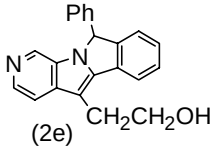
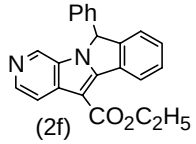
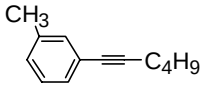
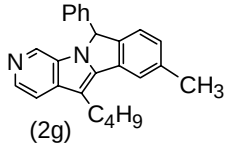
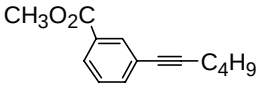
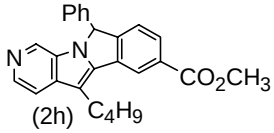
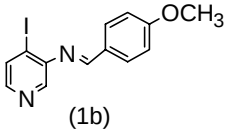
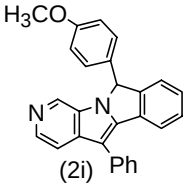
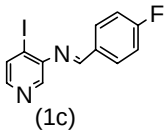
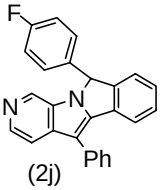


Entry[a]	Pd source	Base	Cl source	Yield (%)
1	$Pd(OAc)_2$	*i*-Pr_2NEt	LiCl	57
2	"	Et_3N	"	<5
3	"	*i*-Pr_2NEt	*n*-Bu_4NCl	60
4	"	Et_3N	"	65
5	"	Na_2CO_3	"	<5
6	"	$CsCO_3$	"	6
7	$Pd(PPh_3)_4$	Et_3N	"	<5
8	"	*i*-Pr_2NEt	"	7
9	"	*i*-Pr_2NEt	LiCl	<5
10	$Pd(dba)_2$	Et_3N	*n*-Bu_4NCl	53
11	"	*i*-Pr_2NEt	"	30
12	"	"	LiCl	34
13	$Pd(PPh_3)_2Cl_2$	"	LiCl	<5
14	"	Et_3N	*n*-Bu_4NCl	50
15	"	*i*-Pr_2NEt	"	47

[a] All reactions were run on a 0.5 mmol scale with 10 mL of DMF.

First, we examined the effect of different bases with $Pd(OAc)_2$ as the palladium source using 1 equiv. of LiCl or *n*-Bu_4NCl (Entries 1-6). The reactions using Et_3N or *i*-Pr_2NEt as the base had higher yields of the desired product as compared with other inorganic bases (Entries 1, 3, and 4). We also examined the effects of palladium species with different organic bases. The reaction using $Pd(OAc)_2$ gave a higher yield of the desired product than did the reactions using other palladium species. From these results, the maximum yield of the desired product was obtained with 5 mol% $Pd(OAc)_2$, 1 equiv. *n*-Bu_4NCl, 2 equiv. Et_3N, and 2 equiv. alkyne in DMF at 110 °C. We examined the diversification of pyridopyrrolo[2,1-*a*]isoindoles using benzylidene(4-iodopyridin-3-yl)amine (**1a**-**1c**) and aryl substituted internal alkynes under optimized reaction conditions. The results are summarized in Table 2.

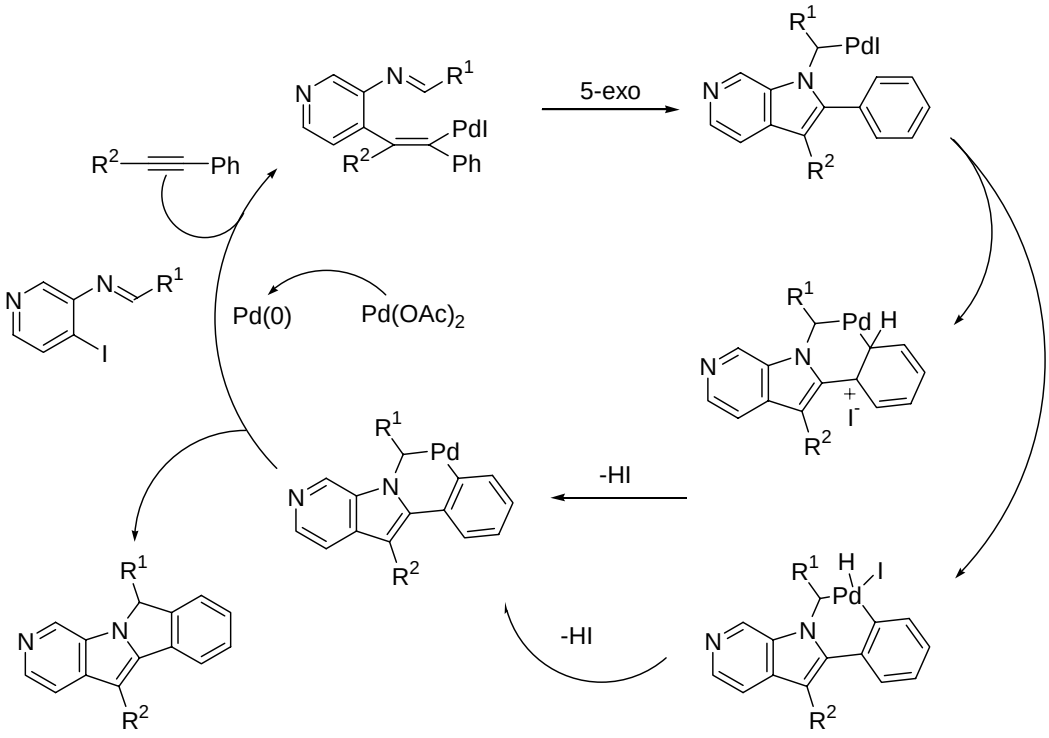
Table 2. Synthesis of pyridopyrrolo[2,1-*a*]isoindoles by palladium-catalyzed internal alkynes.

Entry[a]	Imine	Alkyne	Product	Reaction time (h)	Yields (%)
1	 (1a)	Ph—≡—Ph	 (2b)	11	67
2		Ph—≡—C_4H_9	 (2c)	44	58
3		Ph—≡—CH_2OCH_3	 (2d)	30	48
4		Ph—≡—CH_2CH_2OH	 (2e)	24	55
5		Ph—≡—$CO_2C_2H_5$	 (2f)	3	62
6			 (2g)	34	51
7			 (2h)	7	43
8	 (1b)	Ph—≡—Ph	 (2i)	15	65
9	 (1c)	Ph—≡—Ph	 (2j)	16	65

[a] All reactions were run on a 0.5 mmol scale with 10 mL of DMF at 110^{o}C.

The reactions of imine (**1a**) with various functionalized internal alkynes provided reasonable yields of pyridopyrrolo[2,1-*a*]isoindoles. However, the final reaction times were quite dependent on the substituent of the

internal alkyne (Entries 1-5). We also examined the regiochemistry of the closure of the phenyl ring with *meta*-substituted phenyl internal alkynes (Entries 6 and 7). Single regioisomeric products were obtained and identified by ^{1}H-NMR spectral analysis. Finally, the annulation of functionalized imines (**1b** and **1c**) with diphenylacetylene also afforded 65% yields of pyridopyrrolo[2,1-*a*]isoindoles in short reaction times (Entries 8-9). The pyridopyrrolo[2,1-*a*]isoindoles were formed *via* the same mechanism as previously suggested for Larock's isoindolo[2,1-*a*]indole synthesis (Scheme 1) .[9b]



Scheme 1

In summary, the palladium-catalyzed annulation of benzylidene(4-iodopyridin-3-yl)amines with phenyl substituted internal alkynes provided pyridopyrrolo[2,1-*a*]isoindoles in moderate yields with high regioselectivity. In the synthetic procedure, variation of the imines and internal alkynes could be used to synthesize diverse pyridopyrrolo[2,1-*a*]isoindoles.

EXPERIMENTAL

IR spectra were obtained using a JASCO FT-IR 410 spectrometer. All the ^{1}H- and ^{13}C-NMR spectra were recorded on a Varian 400-MHz spectrometer. Chemical shifts are given as values relative to tetramethylsilane (TMS) as an internal standard. The GC/MS spectra were obtained on a Shimadzu QP 1000. Melting points were determined on a Mut-TEM apparatus and are uncorrected. Microanalyses were performed at Chungnam National University with a CE Instrument EA 1110. The products were purified by flash chromatography on 230- to 400-mesh ASTM 60 silica gel. All the bases, *n*-Bu_4NCl, and palladium species were purchased from Aldrich Chemical Co. The other chemicals were used as obtained from commercial sources, unless otherwise noted.

General procedure for the synthesis of the aryl alkynes[9b]

To a solution of an iodo- or bromoarene (10.0 mmol) and a terminal alkyne (12, 0 mmol) in Et_3N (40 mL) was added $PdCl_2(PPh_3)_2$ (140 mg, 2 mol%) in Et_3N (40 mL). The mixture was then stirred for 5 min, and CuI (200 mg, 1 mmol) was added. The resulting mixture was heated under a nitrogen atmosphere at 50 ºC. The reaction mixture was allowed to cool to rt, and the ammonium salt was removed by filtration. The solvent was removed under reduced pressure, and then the residue was removed under reduced pressure. The residue was purified by column chromatography on silica gel to afford the pure alkynes.

Preparation of benzylidene(4-iodo-pyridin-3-yl)amine (**1a**)

A mixture of 3-amino-4-iodopyridine (1.2 g, 5.5 mmol), benzaldehyde (0.58 g, 5.5 mmol), and a molecular sieve (1g) in benzene (40 mL) was refluxed for 24 h using the Dean-Stark apparatus to remove the water produced. The reaction mixture was monitored by TLC to establish completion. The reaction mixture was then cooled to rt, and the solvent was removed under reduced pressure. The oily residue was dissolved in a minimal amount of ethanol and cooled. The resulting solid was collected to afford 1.23 g (73%) of the imine (**1a**) as a yellow solid. mp 82-83°C; IR (KBr, cm^{-1}) 1623; ^{1}H-NMR ($CDCl_3$) δ 8.32 (s 1H, -N=CH-), 8.14 (s, 1H Ar-H), 8.03 (d, *J* = 5.2 Hz, 1H, Ar-H), 7.97 (dd, *J* = 6, 1.6, 1H, Ar-H), 7.54-7.48 (m, 4H, Ar-H); ^{13}C-NMR ($CDCl_3$) δ 162.03, 149.75, 146.69, 138.49, 135.22, 133.55, 132.16, 129.24, 128.83, 105.14; MS (EI) (*m/z*) 309 (M^++1, 11), 308 (M^+, 100), 204 (11), 127 (15), 89 (15), 77 (230); Anal. Calcd for $C_{12}H_9N_2I$: C, 46.78; H, 2.94; N, 9.09. Found: C, 46.76; H, 2.89; N, 9.11.

4-Methoxybenzylidene(4-iodo-pyridin-3-yl)amine (**1b**)

The compound (**1b**) was prepared by condensation of 3-amino-4-iodopyridine (1.2 g, 5.5 mmol) with 4-methoxybenzaldehyde (0.82 g, 5.5 mmol). The product was 1.29 g (70%) of a yellow solid obtained by column chromatography with hexane-ethyl acetate (3:1). mp 109-110 ºC; IR (KBr, cm^{-1}) 1619; ^{1}H-NMR ($CDCl_3$) δ 8.14(s, 1H, -N=CH-), 8.03 (s, 1H, Ar-H), 7.91 (d, *J* = 5.2 Hz, 1H, Ar-H), 7.81 (d, *J* = 8.8 Hz 2H, Ar-H), 7.71 (d, *J* = 5.6 Hz, 1H, Ar-H), 6.90 (d, *J* = 8.8 Hz, 2H, Ar-H), 3.77 (s, 3H, OCH_3); ^{13}C-NMR ($CDCl_3$) δ 162.78, 161.10, 149.92, 146.26, 138.58, 133.46, 131.03, 128.26, 114.22, 105.32, 55.36; MS (EI) (*m/z*) 339 (M^++1, 12), 338 (M^+, 100), 337 (M^+-1, 58), 168 (20), 105 (17), 77 (21), 51 (29), 50 (23); Anal. Calcd for $C_{13}H_{11}N_2OI$: C, 46.18; H, 3.28; N, 8.28. Found: C, 46.15; H, 3.27; N, 8.25.

4-Fluorobenzylidene(4-iodo-pyridin-3-yl)amine (**1c**)

The compound (**1c**) was prepared by the condensation of 3-amino-4-iodopyridine (1.2 g, 5.5 mmol) with 4-fluorobenzaldehyde (0.75 g, 5.5 mmol). The product was 1.42 g (80%) of a yellow solid obtained by column chromatography with hexane-ethyl acetate (10:1). mp 90-91°C; IR (KBr, cm^{-1}) 1629; ^{1}H-NMR ($CDCl_3$) δ 8.30 (s, 1H, Ar-H), 8.14 (s, 1H, -N=CH-), 8.04 (d, *J* = 8.8 Hz, 1H, Ar-H), 8.00-7.96 (m. 2H, Ar-H), 7.83 (d, *J* = 5.2 Hz, 1H,

Ar-H), 7.21-7.17 (m, 2H, Ar-H); ^{13}C-NMR ($CDCl_3$) δ 165.15 (d, $^1J_{C\text{-}F}$ = 252 Hz), 160.49, 149.59, 146.80, 138.46, 133.63, 131.37 (d, $^3J_{C\text{-}F}$ = 8.6 Hz), 116.13 (d, $^2J_{C\text{-}F}$ = 21.8 Hz), 105.21, 94.36; MS (EI) (*m/z*) 327 (M^++1, 9), 326 (M^+, 47), 325 (M^+-1, 26), 204 (17), 177 (11), 145 (11), 125 (9), 107 (19), 86 (15), 70 (14), 57 (16), 43 (100); Anal. Calcd for $C_{12}H_8N_2FI$: C, 44.20; H, 2.47; N, 8.59. Found: C, 44.17; H, 2.44; N, 8.63.

General procedure for the palladium-catalyzed formation of pyridopyrrolo[2,3-*a*]isoindoles

Palladium acetate (6 mg, 0.025 mmol), *n*-Bu_4NCl (139 mg, 0.5 mmol), Et_3N (101 mg, 1.0 mmol), benzylidene(4-iodo-pyridin-3-yl)amine (154 mg, 0.5 mmol), diphenylacetylene (178 mg, 1.0 mmol), and DMF (10 mL) were added to a pressure tube equipped with a stirring bar. After heating the reaction mixture for 11 h at 110 ºC, the resulting solution was diluted with ethyl acetate and washed with saturated aqueous ammonium chloride. The organic layer was dried over $MgSO_4$, filtered, and concentrated. The residue was purified by column chromatography using hexane-ethyl acetate (1:1). 5,10-Diphenyl-10*H*-pyrido[4',3':4,5]pyrrolo[2,1-*a*]isoindole (**2b**) (120 mg, 67%) was obtained as a yellow solid. mp 140-141 ℃; IR (KBr) 3028, 1603, 1447, cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 8.34 (d, *J* = 0.8 Hz, 1H, Ar-H), 8.20 (d, *J* = 5.6 Hz, 1H, Ar-H), 7.91 (dd, *J* = 4.4, 2.2 Hz, 1H, Ar-H), 7.77-7.74 (m, 2H, Ar-H), 7.65 (dd, *J* = 4.4, 2.2 Hz, 1H, Ar-H), 7.56 (t, *J* = 7.6 Hz, 2H, Ar-H), 7.43-7.23 (m, 7H, Ar-H), 7.21-7.19 (m, 2H, Ar-H), 6.26 (s, 1H, ArCH); ^{13}C-NMR ($CDCl_3$) δ 147.72, 142.56, 139.37, 137.93, 136.52, 133.64, 133.03, 130.78, 130.33, 129.30, 129.07, 128.90, 128.83, 128.76, 128.43, 127.15, 126.83, 124.06, 121.74, 114.56, 108.90, 64.73; MS (EI) (*m/z*) 358 (M^+, 100), 281 (4); Anal. Calcd for $C_{26}H_{18}N_2$: C, 87.12; H, 5.06; N, 7.82. Found: C, 87.13; H, 5.08; N, 7.79.

The following compounds were obtained using the above general procedure.

5-Methyl-10-phenyl-10*H*-pyrido[4',3':4,5]pyrrolo[2,1-*a*]isoindole (**2a**)

The compound (**2a**) was obtained as a yellow solid in 65% yield from benzylidene(4-iodo-3-pyridinyl)amine (**1a**) and 1-phenyl-1-propyne with a 15-h reaction. mp 162-163℃; IR (KBr, cm^{-1}) 2916, 1449; ^{1}H-NMR ($CDCl_3$) δ 8.26 (s, 1H, Ar-H), 8.18 (d, *J* = 5.6 Hz, 1H, Ar-H), 7.84 (d, *J* = 7.6 Hz, 1H, Ar-H), 7.48-7.43 (m, 2H, Ar-H), 7.33-7.26 (m, 5H, Ar-H), 7.14-7.12 (m, 2H, Ar-H), 6.15 (s, 1H, ArCH), 2.58 (s, 3H, $-CH_3$); ^{13}C-NMR ($CDCl_3$) δ 147.34, 143.01, 138.41, 138.25, 138.17, 132.56, 131.43, 130.13, 129.18, 128.65, 128.50, 128.00, 127.02, 124.10, 121.52, 113.94, 101.71, 64.56, 8.76; MS (EI) (*m/z*) 297 (M^++1, 12), 296 (M^+,100), 219 (39), 146 (14); Anal. Calcd for $C_{21}H_{16}N_2$: C, 85.11; H, 5.44; N, 9.45. Found: C, 85.07; H, 5.46; N, 9.47

5-*n*-Butyl-10-phenyl-10*H*-pyrido[4',3':4,5]pyrrolo[2,1-*a*]isoindole (**2c**)

The compound (**2c**) was obtained as a yellow solid in 58% yield from benzylidene-(4-iodo-3-pyridinyl)amine (**1a**) and 1-phenyl-1-hexyne with a 44-h reaction. mp 144-145℃; IR (KBr, cm^{-1}) 2927, 1610, 1451; ^{1}H-NMR ($CDCl_3$) δ 8.26 (s, 1H, Ar-H), 8.16 (d, *J* = 5.6 Hz, 1H, Ar-H), 7.81 (d, *J* = 8.0, Ar-H), 7.49 (dd, *J* = 4.4, 1.2 Hz, 1H, Ar-H), 7.43-7.39 (m, 1H, Ar-H), 7.32-7.21 (m, 4H, Ar-H), 7.12-7.10 (m, 2H, Ar-H), 6.12 (s, 1H, ArC<u>H</u>), 3.03 (t, *J* = 7.2

Hz, 2H, -C<u>H</u>$_2$CH$_2$CH$_2$CH$_3$), 1.77 (quintet, *J* = 7.6 Hz, 2H, CH$_2$C<u>H</u>$_2$CH$_2$CH$_3$), 1.47 (sextet, *J* = 7.6 Hz, 2H, CH$_2$CH$_2$C<u>H</u>$_2$CH$_3$), 0.97 (t, *J* = 7.2 Hz, 3H, CH$_3$); ^{13}C-NMR (CDCl$_3$) δ 147.34, 142.73, 138.36, 138.25, 137.60, 132.70, 131.33, 130.14, 129.12, 128.56, 128.46, 127.90, 126.96, 124.04, 121.49, 114.13, 107.46, 64.45, 33.05, 23.97, 22.57, 13.99; MS (EI) (*m/z*) 338 (M$^+$, 8), 294 (100), 218 (21), 146 (16), 77 (13), 41 (22); Anal. Calcd for C$_{24}$H$_{22}$N$_2$: C, 85.17; H, 6.55; N, 8.28. Found: C, 85.17; H, 6.54; N, 8.29.

5-Methoxymethyl-10-phenyl-10*H*-pyrido[4',3':4,5]pyrrolo[2,1-*a*]isoindole (**2d**)

The compound (**2d**) was obtained as a yellow solid in 48% yield from benzylidene(4-iodo-3-pyridinyl)amine (**1a**) and 1-phenyl-1-hexyne with a 30-h reaction. mp 133-134℃; IR (KBr, cm^{-1}) 2930, 1454; ^{1}H-NMR (CDCl$_3$) δ 8.23 (s, 1H, Ar-H), 8.18 (d, *J* = 6 Hz, 1H, Ar-H), 7.93 (d, *J* = 8 Hz, 1H, Ar-H), 7.56 (dd, *J* = 4.8, 0.8, 1H, Ar-H) 7.43 (t, *J* = 7.2 Hz, Ar-H), 7.31-7.28 (m, 5H, Ar-H), 7.23-7.1 (m, 2H, Ar-H), 6.14 (s, 1H, ArCH), 4.91 (s, 2H, -CH$_2$O), 3.48 (s, 3H, OCH$_3$); ^{13}C-NMR (CDCl$_3$) δ 147.56, 144.94, 138.94, 137.78, 137.36, 132.78, 130.58, 130.01, 129.16, 128.71, 128.61, 128.59, 126.99, 123.94, 122.49, 114.07, 103.10, 64.81, 64.75, 57.68; MS (EI) (*m/z*) 326 (M$^+$, 19), 295 (100), 218 (45), 147 (48), 77 (39), 51 (27); Anal. Calcd for C$_{22}$H$_{18}$N$_2$O: C, 80.96; H, 5.56; N, 8.58. Found: C, 80.93; H, 5.53; N, 8.58.

5-(2-Hydroxyethyl)-10-phenyl-10*H*-pyrido[4',3':4,5]pyrrolo[2,1-*a*]isoindole (**2e**)

The compound (**2e**) was obtained as a yellow solid in 55% yield from benzylidene(4-iodo-3-pyridinyl)amine (**1a**) and 4-phenyl-4-butyn-1-ol with a 24-h reaction. mp 149-150 ºC; IR (KBr, cm^{-1}) 3397, 2924, 2854; ^{1}H-NMR (CDCl$_3$) δ 8.22 (s, 1H, Ar-H), 8.09 (d, *J* = 5.2 Hz, 1H, Ar-H), 8.01 (d, *J* = 7.6 Hz, 1H, Ar-H), 7.61 (d, *J* = 5.2 1H, Ar-H) 7.49 (t, *J* = 7.2 Hz, Ar-H), 7.38-7.30 (m, 5H, Ar-H), 7.15 (dd, *J* = 6.0, 2.0 , 2H, Ar-H), 5.67 (s, 1H, ArCH), 4.85 (br, 1H, -OH), 3.76 (t, *J* =7.2 2H, -C<u>H</u>$_2$CH$_2$OH), 3.21 (t, *J* = 6.8, 2H, CH$_2$C<u>H</u>$_2$OH); ^{13}C-NMR (CDCl$_3$) δ 147.52, 143.08, 138.91, 137.86, 137.17, 132.37, 130.63, 129.66, 129.04, 128.55, 128.35, 128.28, 126.93, 124.17, 121.79, 114.30, 103.61, 63.50, 61.57, 27.86; MS (EI) (*m/z*) 326 (M$^+$, 26), 295 (100), 218 (8), 147 (8); Anal. Calcd for C$_{22}$H$_{18}$N$_2$O: C, 80.96; H, 5.56; N, 8.58. Found: C, 80.93; H, 5.55; N, 8.57.

Ethyl 10-Phenyl-10*H*-pyrido[4',3':4,5]pyrrolo[2,1-*a*]isoindole-5-carboxylate (**2f**)

The compound (**2f**) was obtained as a yellow solid in 62% yield from benzylidene(4-iodo-3-pyridinyl)amine (**1a**) and ethyl phenylpropiolate with a 3-h reaction.; mp 153-154℃; IR (KBr, cm^{-1}) 1684; ^{1}H-NMR (CDCl$_3$) δ 8.80 (d, *J* = 7.2 Hz, 1H, Ar-H), 8.32 (d, *J* = 5.6 Hz, 1H Ar-H), 8.23 (s, 1H, Ar-H), 8.01 (d, *J* = 5.6 Hz, 1H, Ar-H), 7.50 (t, *J* = 7.2 Hz, 1H, Ar-H), 7.40 (t, *J* = 7.2 Hz, 1H, Ar-H), 7.33-7.31 (m, 3H, Ar-H), 7.25 (d, *J* = 8 Hz, 1H, Ar-H), 7.11 -7.08 (m, 2H, Ar-H), 6.13 (s, 1H, ArCH), 4.50 (q, *J* = 7.2 Hz, 2H, -COOCH$_2$), 1.53 (t, *J* = 7.2 Hz, 3H, -COOCH$_2$C<u>H</u>$_3$); ^{13}C-NMR (CDCl$_3$) δ 164.79, 150.91, 148.37, 141.08, 136.49, 136.24, 133.02, 130.14, 129.81, 129.68, 129.34, 129.06, 128.84, 127.05, 126.15, 123.42, 116.79, 99.44, 65.24, 60.12, 14.57; MS (EI) (*m/z*) 355 (M$^+$+1, 34), 354 (M$^+$, 100), 325 (58), 309 (29), 282 (38), 281 (46), 140 (23), 126 (20); Anal. Calcd for C$_{28}$H$_{18}$N$_2$O$_2$:

C, 77.95; H, 5.12; N, 7.90. Found: C, 77.97; H, 5.10; N, 7.90.

5-*n*-Butyl-7-methyl-10-phenyl-10*H*-pyrido[4',3':4,5]pyrrolo[2,1-*a*]isoindole (**2g**)

The compound (**2g**) was obtained as a yellow solid in 51% yield from benzylidene(4-iodo-3-pyridinyl)amine (**1a**) and 1-(3-methyl-phenyl)-1-hexyne in a 34-h reaction; mp 178-179℃; IR (KBr, cm^{-1}) 2952, 1607, 1455; ^{1}H-NMR ($CDCl_3$) δ 8.23 (s, 1H, Ar-H), 8.17 (d, *J* = 5.6 Hz, 1H, Ar-H), 7.62 (s, 1H, Ar-H), 7.49 (d, *J* = 6.0 Hz, 1H, Ar-H), 7.31-7.30 (m, 3H, Ar-H), 7.13-7.10 (m, 4H, Ar-H), 6.12 (s, 1H, $ArCH_2$), 3.09 (t, *J* = 7.6 Hz, 2H, -$C\underline{H}_2CH_2CH_2CH_3$), 2.45 (s, 3H, Ar-$CH_3$), 1.79 (quintet, *J* = 7.6 Hz, 2H, $CH_2C\underline{H}_2CH_2CH_3$), 1.48 (sextet, *J* = 7.6 Hz, 2H, $CH_2CH_2C\underline{H}_2CH_3$), 0.99 (t, *J* = 7.2 Hz, 3H, $CH_2CH_2CH_2C\underline{H}_3$); ^{13}C-NMR ($CDCl_3$) δ 144.77, 138.65, 138.43, 138.17, 137.68, 132.63, 131.51, 130.22, 129.15, 129.06, 128.87, 128.54, 126.96, 123.76, 122.09, 114.16, 107.33, 64.34, 33.10, 24.02, 22.60, 21.53, 14.04; MS (EI) (*m/z*) 353 (M^++1, 12), 352 (M^+, 35), 309 (100), 294 (24), 146 (16); Anal. Calcd for $C_{25}H_{24}N_2$: C, 85.19; H, 6.86; N, 7.95. Found: C, 85.18; H, 6.87; N, 7.95.

Methyl 5-Butyl-10-phenyl-10*H*-pyrido[4',3':4,5]pyrrolo[2,1-*a*]isoindole-9-carboxylate (**2h**)

The compound (**2h**) was obtained as a yellow oil in 43% yield from benzylidene(4-iodo-3-pyridinyl)amine (**1b**) and methyl-2-(1-hexynyl)benzoate in a 7-h reaction. IR (Neat, cm^{-1}) 1689; ^{1}H-NMR ($CDCl_3$) δ 8.45 (s, 1H, Ar-H), 8.15 (s, 1H, Ar-H), 8.04 (d, *J* = 5.6 Hz, 1H, Ar-H), 7.96 (dd, *J* = 6.8, 1.2 Hz, 1H, Ar-H), 7.48 (d, *J* = 5.6 Hz, 1H, Ar-H), 7.33-7.27 (m, 4H, Ar-H), 7.10-7.08 (m, 2H, Ar-H), 6.18 (s, 1H, ArCH), 3.96 (s, 3H, $COOCH_3$), 3.08 (t, *J* = 7.2 Hz, 2H, -$C\underline{H}_2CH_2CH_2CH_3$), 1.80 (quintet, *J*= 7.6 Hz, 2H, $CH_2C\underline{H}_2CH_2CH_3$), 1.48 (sextet, *J* = 7.6 Hz, 2H, $CH_2CH_2C\underline{H}_2CH_3$), 0.99 (t, *J* = 7.6 Hz, 3H, $CH_2CH_2CH_2C\underline{H}_3$); ^{13}C-NMR (CDCl3) δ 166.38, 151.65, 141.75, 137.92, 137.62, 137.53, 132.39, 131.71, 130.74, 130.05, 129.34, 129.27, 128.87, 126.91, 124.02,122.51, 114.39, 108.38, 64.50, 52.31, 32.94, 23.90, 22.46, 13.93; MS (EI) (*m/z*) 396 (M^+, 32), 353 (100), 146 (10), 294 (24), 146 (15), 105 (11), 91 (7), 51 (3); Anal. Calcd for $C_{26}H_{24}N_2O_2$: C, 78.76; H, 6.10; N, 7.07. Found: C, 78.75; H, 6.09; N, 7.10.

10-(4-Methoxyphenyl)-5-phenyl-10*H*-pyrido[4',3':4,5]pyrrolo[2,1-*a*]isoindole (**2i**)

The compound (**2i**) was obtained as a yellow solid in 65% yield from 4-methoxybenzylidene-(4-iodo-3-pyridinyl)amine (**1b**) and diphenylacetylene in a 15-h reaction. mp 195-196℃; IR (KBr, cm^{-1}) 3029, 1609, 1512, 1250; ^{1}H-NMR ($CDCl_3$) δ 8.37 (s, 1H, Ar-H), 8.21 (d, *J* = 5.6 Hz, 1H, Ar-H), 7.87 (d, *J* = 6.8, Hz, 1H, Ar-H), 7.71 (d, *J* = 7.2 Hz, 2H, Ar-H), 7.62 (d, *J* = 5.6 Hz, 1H, Ar-H), 7.52 (t, *J* = 7.6 Hz, 2H, Ar-H), 7.37 (t, *J* = 7.6 Hz, 1H, Ar-H), 7.30-7.18 (m, 3H, Ar-H), 7.08 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.84 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.10 (s, 1H, ArCH), 3.72 (s, 3H, OCH_3); ^{13}C-NMR ($CDCl_3$) δ 159.80, 147.89, 142.28, 139.14, 136.31, 133.52, 132.87 ,130.62, 130.18, 129.66, 128.89, 128.76, 128.61, 128.41, 128.20, 126.66, 123.90, 121.53, 114.52, 114.40, 108.62, 64.12, 60.19, 55.09; MS (EI) (*m/z*, relative mass) 388 (M^+, 100), 281 (50), 194 (31), 172 (29), 77 (14), 51 (7); Anal. Calcd for $C_{27}H_{20}N_2O$: C, 83.48; H, 5.19; N, 7.21. Found: C, 83.44; H, 5.24; N, 7.23.

10-(4-Fluorophenyl)-5-phenyl-10*H*-pyrido[4',3':4,5]pyrrolo[2,1-*a*]isoindole (**2j**)

The compound (**2j**) was obtained as a yellow solid in 65% yield from 4-fluoro- benzylidene(4-iodo-3-pyridinyl)-amine (**1c**) and diphenylacetylene in a 16-h reaction. mp 135-136°C; IR (KBr, cm^{-1}) 3029, 1604, 1467; ^{1}H-NMR ($CDCl_3$) δ 8.29 (s, 1H, Ar-H), 8.18 (d, *J* = 5.6 Hz, 1H, Ar-H), 7.88 (d, *J* = 7.6 Hz, 1H, Ar-H), 7.71 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.62 (d, *J* = 5.6 Hz, 1H, Ar-H), 7.53 (t, *J* = 7.6 Hz, 2H, Ar-H), 7.38 (t, *J* = 7.6 Hz, 1H, Ar-H),7.32-7.24 (m, 2H, Ar-H), 7.20-7.12 (m, 3H, Ar-H), 7.01 (t, *J* = 8.4 Hz, 2H, Ar-H), 6.14 (s, 1H, $ArCH_2$); ^{13}C-NMR ($CDCl_3$) δ 162.76 (d, $^1J_{C\text{-}F}$ = 247.7 Hz), 147.42, 142.40, 139.12, 136.51, 133.67, 133.64, 133.31, 132.51, 130.53, 130.09, 128.92, 128.83, 128.77, 128.48, 126.83, 123.89, 121.69, 116.23 (d, $^2J_{C\text{-}F}$ = 21.8 Hz), 114.56, 108.95, 63.79; MS (EI) (*m/z)* 376(M^+, 100), 299 (22), 281 (53), 188 (33), 95 (22), 75 (21), 51(12); Anal. Calcd for $C_{26}H_{17}N_2F$: C, 82.96; H, 4.55; N, 7.44; F, 5.05. Found: C, 82.91; H, 4.50; N, 7.40; F, 5.03.

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