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Article

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Regio- and Stereoselective Domino Synthesis of Oxazolo fused Pyridoindoles and Benzofurooxazolo Pyridines from *ortho*-Alkynylarylaldehydes

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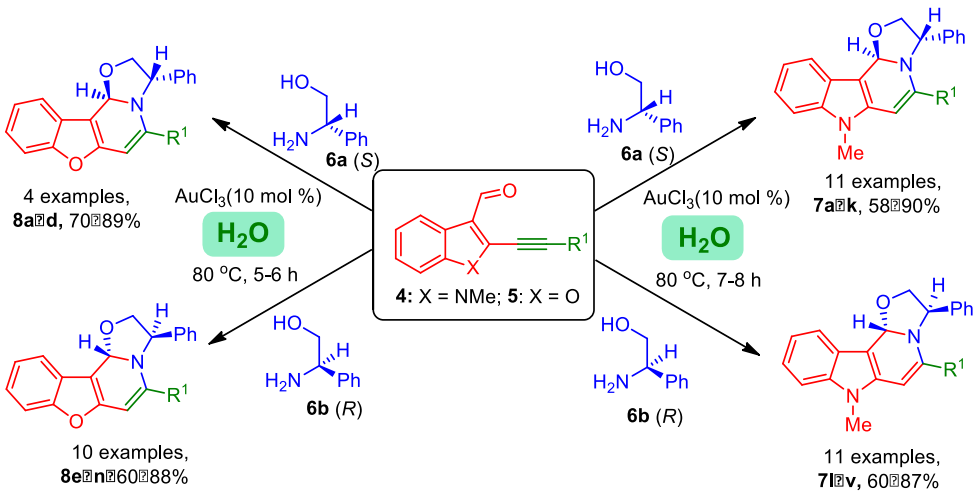


ABSTRACT: An environmentally benign Au(III)-catalyzed regio- and stereoselective domino synthesis of oxazolo fused pyridoindoles **7a**–**v** and benzofurooxazolo pyridines **8a**–**n** by the reaction of *o*-alkynylaldehydes **4a**–**t** and **5a**–**k** with (*S*)-phenylglycinol **6a** and (*R*)-phenylglycinol **6b** under mild reaction condition using water as reaction medium is reported. The reaction proceeded *via* selective C–N bond formation on the more electrophilic alkynyl

carbon through 6-*endo-dig* cyclization. The reaction tolerates a wide variety of functional groups. The developed chemistry has been successfully extended for the synthesis of diverse class of γ-carbolines and benzofuro[3,2-*c*]pyridines using corresponding ester hydrochlorides of serine, threonine and cystine as a nitrogen source.

INTRODUCTION

N-heterocycles and their derivatives are privileged scaffolds for the synthesis of bioactive molecules as they offer improved solubility, bioavailability and have wide spread applications in pharmaceutical industry.[1] Domino reactions[2–4] are very familiar to generate complex structure by forming many bond and functionality at once without changing the reaction condition. Formation of C–C and C–N bond through transition-metal-catalysts have been extensively studied and attracts the interest of many organic chemists.[5] An easily accessible synthetic methodologies to produce analogues of natural product-like compounds under mild reaction conditions are in high demand. In this context, catalytic cyclization of heteroatom-functionalized alkynes is one of the fundamental approaches. Among the transition metals, gold has unique properties like alkynophilicity,[6] soft Lewis acidity[7–8] which makes it versatile and intriguing catalyst for various C-C bond forming reactions for the synthesis of heterocycles.

Literature reports revealed that pyridoindoles and benzofuropyridines have vast biological importance[9–11] and are also used as pharmaceutically active[12–14] compounds. Pyridoindoles possesses potent anti-BVDV activity,[15] *in-vitro* cytotoxic activity[16] against different human cancer cell lines and present in various antitumor agents. γ-Carbolines which are analogues of pyridoindoles are found in various natural products, and demonstrated as an anti-alzheimer, (Figure 1, A)[17] antimalarial (Figure 1, B)[18a-b] and antiplasmodial agent.[18c] Benzofuropyridines and its derivatives are known to involved in the central nervous system

activity (Figure 1, C).[19] Similarly, oxazolo fused derivatives are extensively studied for their antitumor, antimicrobial activities and present in anti-inflammatory drug like Flunoxaprofen (Figure 1, D).[20] Pyridine substituted benzoxazoles and quinoline fused oxazoles have been disclosed as a cryptosporidium parvum inosine 5'-monophosphate dehydrogenase (CpIMPDH) inhibitor (Figure 1, E).[21]

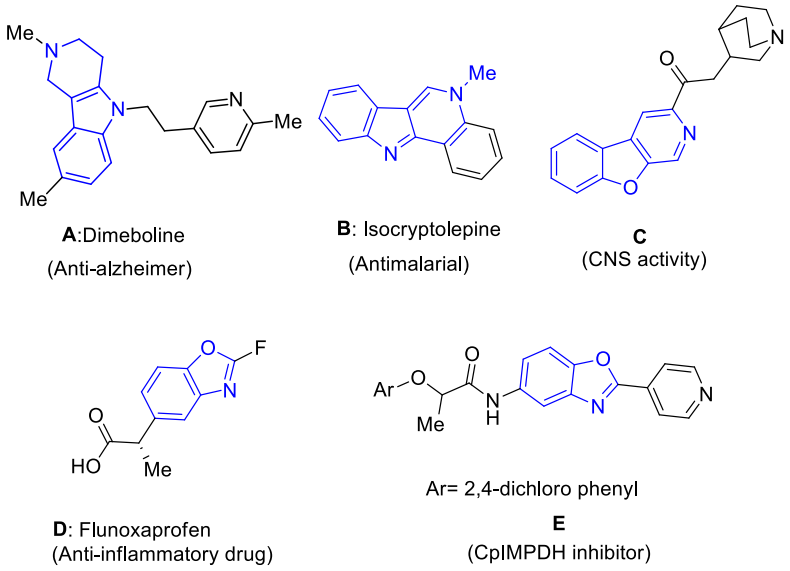


Figure 1. Examples of biologically active: Pyridoindoles, Benzofuropyridines and Fused oxazoles.

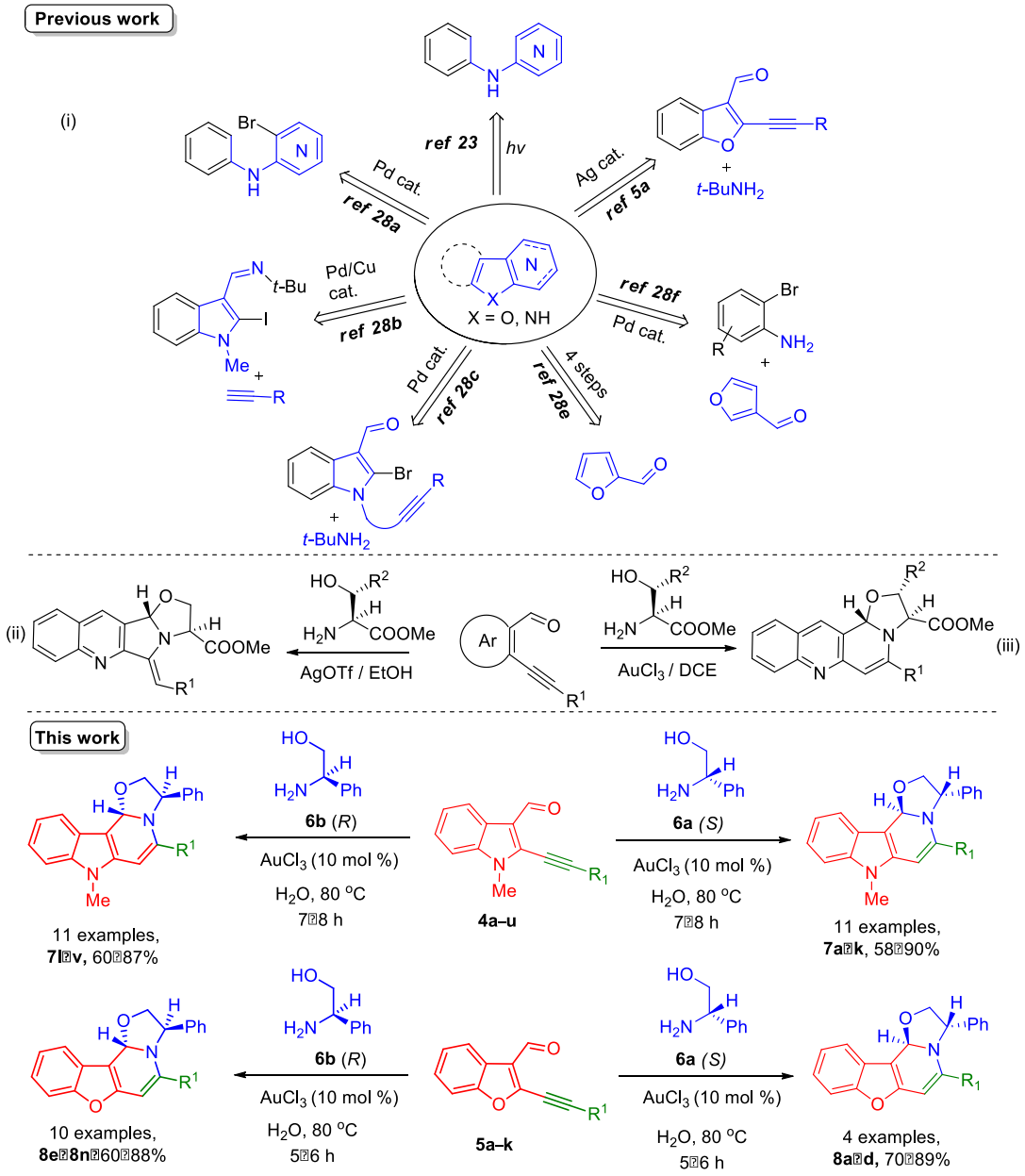
Previously, Robinson and Thornley[22] reported the multistep synthesis of pyridoindoles from 4-chloropyridine and *o*-phenylene diamine. Clark *et.al* synthesized carbolines *via* photocyclization of anilino-pyridines.[23] Later, pyridoindoles were obtained by using Fischer reaction,[24] Graebe Ullmann method[25,26] and by using transition-metal-catalyzed coupling reactions.[27] In 1999, Sakamoto explained palladium-catalyzed amination and arylation reaction to generate carbolines.[28a] Larock and co-workers reported the synthesis of β and γ-Carbolines using alkynes substrate by the palladium/copper-catalyzed electrophilic cyclization.[28b-c] In 2012,

Nagarajan *et.al*. reported the synthesis pyrido[2,3-*b*]indoles via Pd-catalyzed amidation followed by cyclization.[28d]

Correspondingly, several methods are available in literature for the synthesis of furopyridines (Scheme 1i). In 2007, Miyazaki designed a template for the synthesis of furo[3,2-*c*]pyridines from furan-2-carbaldehyde in four steps.[28e] Later, Doucet *et. al.* reported one-pot methodology for the synthesis of furoquinolines through sequential amination and intramolecular palladium-catalyzed direct arylation.[28f] Very recently, our group have noted a silver-catalyzed tandem strategy for the synthesis benzofuropyridines by the reaction of *o*-alkynylaldehyde with *tert*-butylamine.[5a] Despite the numerous findings, development of eco-friendly protocols which offers low environment impact remains elusive. Thus aqueous reaction which makes aqueous suspension, feasible and prominent with high efficiency protocols are challenging.[29] Water as a solvent fulfill many criteria such as nontoxic, nonflammable, inexpensive, readily availability. Organic compounds show hydrophobic interaction with water which imparts a significant effect on rate and selectivity, hence reduce the unwanted side products.

Stereoselective syntheses of heterocyclic cores have emerging significance due to the difference in biological activity of each isomer. The significant importance of chiral heterocycles justifies the development of new synthetic methodologies. Literature survey revealed that in the past ten year a wide range of heterocyclic scaffolds have been synthesized from *o*-alkynyldehydes; however, the stereoselective synthesis of heterocycles has not been much explored. Recently for the first time we have reported the stereoselective synthesis of thiazolo and oxazolo fused naphthyridines, thienopyridines, isoquinolines and pyrroloquinolines from *o*-alkynyldehydes (Scheme 1ii and iii).[28g-h]

Scheme 1. Designed Domino Approach for the Regio- and Stereoselective Synthesis of Oxazolo fused Pyridoindoles and Benzofurooxazolo Pyridines



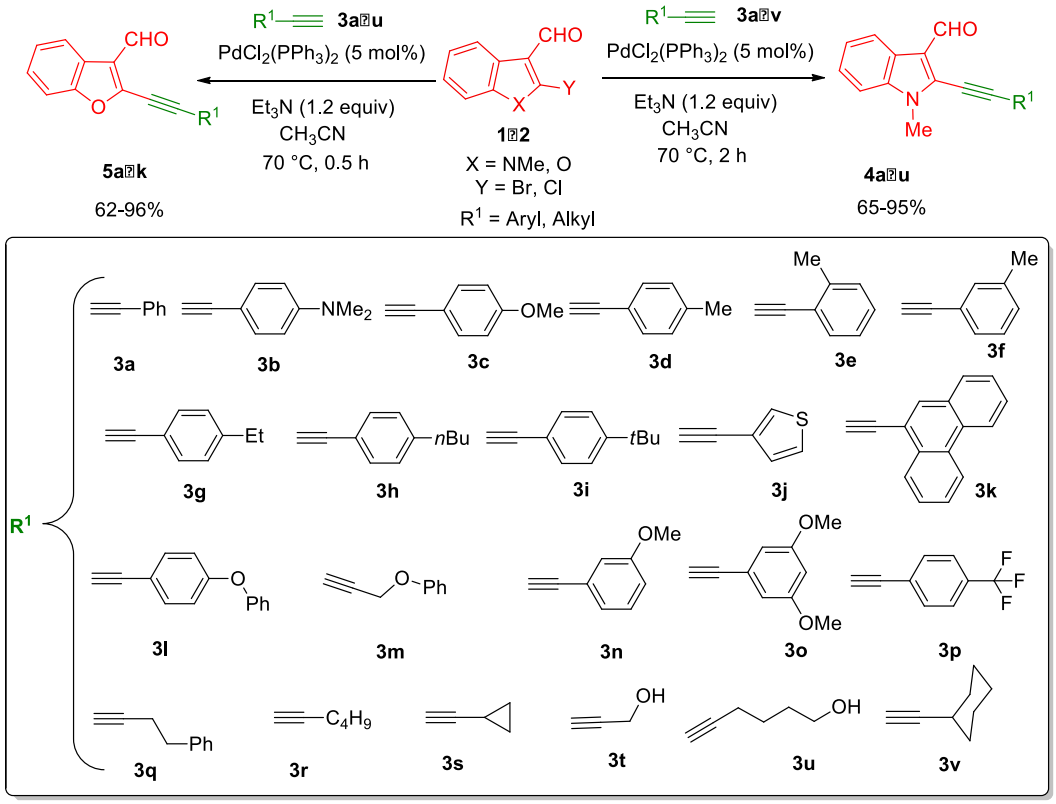
In continuation of our ongoing efforts on the domino and tandem synthesis of heterocycles from *o*-alkynyaldehydes,[4b,5a-c,30] we envisioned that the reaction of indolo- and benzofurano *o*-alkynyldehydes with chiral (*S*)-phenylglycinol and (*R*)-phenylglycinol might offer an opportunity for the regio- and stereoselective synthesis of oxazolo fused pyridoindoles and

benzofurooxazolo pyridines under mild reaction condition. This domino synthesis would minimize the required chemical quantity, unwanted side products and processing time in step economical. Optically active heterocyclic core moiety having *N*-atom are used in asymmetric fusion working as chiral templates[31] or ligands.[32]

RESULTS AND DISCUSSION

Preparation of *ortho*-Alkynylaldehydes. To probe the viability of the designed domino strategy, *ortho*-alkynylaldehydes **4a–t** and **5a–k** were readily prepared by standard Sonogashira cross-coupling reaction of commercially available and readily accessible *ortho*-haloaldehydes **1** and **2** with terminal alkynes **3a–v** (Scheme 2).[33] This coupling procedure has readily accommodated a large variety of functional groups and provided the coupling products **4a–t** and **5a–k** in good to excellent yields.

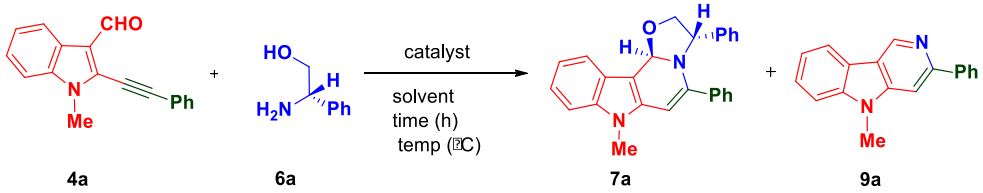
Scheme 2. Preparation of *ortho*-Alkynylaldehydes



In order to find the optimal reaction condition, we selected (phenylethynyl)*N*-methylindole (**4a**) and (*S*)-2-phenylglycinol (**6a**) as a model substrates for the reaction (Table 1). Various transition-metal-catalysts along with different solvents were examined. Reaction of alkyne **4a** (0.5 mmol) with **6a** (0.55 mmol) using 5 mol % of $AgNO_3$ in 2.0 mL of CH_2Cl_2 at 25 °C for 12 h; the desired product oxazolo fused pyridoindole **7a** was not observed (Table 1, entry 1). When reaction was performed using DCE as a solvent at 60 °C for 24 h; product **7a** was observed in 5% yield along with γ–carboline **9a** in 10% yield (entry 2). Increase in the temperature from 60 to 80 °C and catalyst loading from 5 to 10 mol %, product **7a** was obtained in 15% and **9a** in 20% yield (entry 3). Further increase in the reaction temperature and change the solvent provided the product **9a** in 30% yield; however the yield of the desired product **7a** remained same (entry 4). When reaction was carried out using EtOH as solvent at 80 °C, desired product **7a** was obtained in 25% yield and **9a** in 35% yield (entry 5). Interestingly when we performed the reaction in water, product **7a** was formed exclusively in 40% yield without the formation of product **9a** (entry 6). Employing other silver catalysts with different counteranions, such as AgOAc, AgOTf and AgI resulted in 25–35% yield of the product **7a** (entries 7–9). Transition-metal-catalysts other than silver, such as $PdCl_2$, $Pd(OAc)_2$ and $Cu(OTf)_2$ provided the product **7a** in 10–20% yield (entries 10–12). Impressive results were obtained with $AuCl_3$ in H_2O at 80 °C for 8 h, afforded **7a** in 80% yield as a sole product (entry 13). Reaction time increases by decreasing the amount of catalyst from 10 to 5 mol % afforded lower yield of **7a** (entry14). Increasing the amount of $AuCl_3$ from 10 to 15 mol % in H_2O afforded the product **7a** in 70% (entry 15). No significant effect in the yield of product **7a** was observed by using other gold catalysts like $HAuCl_4$ and AuCl (entries 16 and 17). Trace amount of product **7a** was obtained after 24 h by using other lewis acid like $AlCl_3$ (entry 18). However, in the absence of catalyst, the

reactant remained almost unchanged even after 30 h (entry 19). After analysis it was observed that the 10 mol % $AuCl_3$ in water at 80 °C was efficient reaction condition for the synthesis of product **7a.**

Table 1. Optimization of Reaction Conditions[a]



4a 6a 7a 9a

entry	catalyst (mol %)	conditions			yield (%)	
		solvent	temp (^oC)	time (h)	**7a**	**9a**
1.	$AgNO_3$ (5)	CH_2Cl_2	25	12	NR	NR
2.	$AgNO_3$ (5)	DCE	60	24	5	10
3.	$AgNO_3$ (10)	DCE	80	24	15	20
4.	$AgNO_3$ (10)	DMF	110	24	15	30
5.	$AgNO_3$ (10)	EtOH	80	24	25	35
6.	$AgNO_3$ (10)	H_2O	80	24	40	00
7.	AgOAc (10)	H_2O	80	24	30	00
8.	AgOTf (10)	H_2O	80	24	35	00
9.	AgI (10)	H_2O	80	24	25	00
10.	$PdCl_2$ (10)	H_2O	80	24	15	00
11.	$Pd(OAc)_2$ (10)	H_2O	80	24	20	00
12.	$Cu(OTf)_2$ (10)	H_2O	80	24	10	00
13.	**$AuCl_3$ (10)**	**H_2O**	**80**	**8**	**80**	**00**
14.	$AuCl_3$ (5)	H_2O	80	18	45	00

15.	$AuCl_3$ (15)	H_2O	80	8	70	00
16.	$HAuCl_4$ (10)	H_2O	80	8	45	15
17.	AuCl (10)	H_2O	80	8	50	10
18.	$AlCl_3$ (10)	H_2O	70	24	10	00
19.	-	H_2O	80	30	-	-

[a]The reactions were performed using 0.5 mmol of *o*-alkynylaldehyde **4a**, 0.55 mmol of amine **6a** in 2.0 mL of solvent. DCE = 1,2-Dichloroethane. DMF = *N*,*N*-Dimethylformamide. NR = no reaction.

The formation of regioselective 6-*endo-dig* cyclized product **7a** was characterized by ^{1}H NMR, ^{13}C NMR, mass and 2D spectroscopic data. Appearence of peaks at 6.04 ppm as a multiplet, 4.98 and 4.12 ppm as diastereotopic protons in ^{1}H NMR of **7a** and disappearance of the two characteristic peaks of alkynyl carbons in ^{13}C NMR spectrum suggested the formation of the desired cyclized product **7a**. No distinct NOE effect was observed between H_b and H_a in compounds **7h**, **7n**, **8e** and **8m** (Figure 2). These results suggested that H_a and H_b are located in the trans orientation (see supporting information).

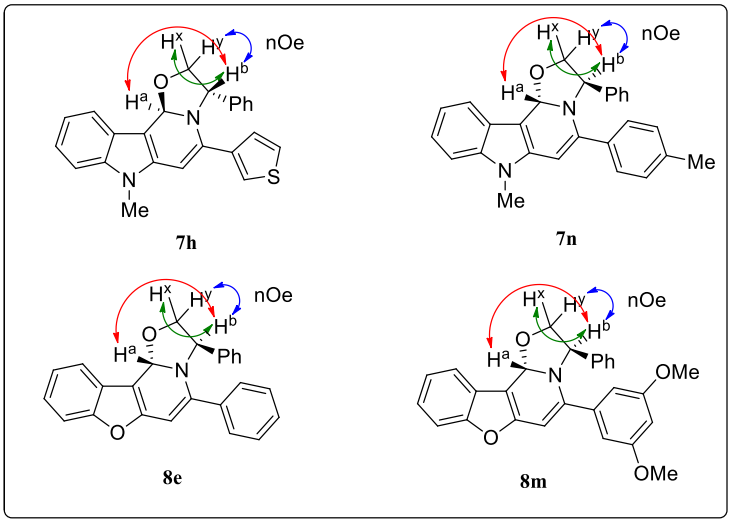
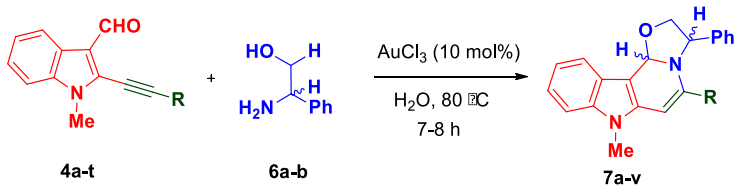


Figure 2. NOESY interactions of **7h**, **7n**, **8e** and **8m**.

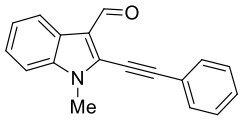
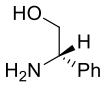
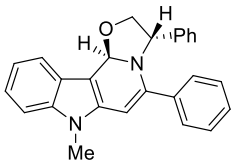
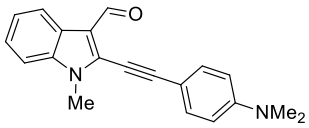
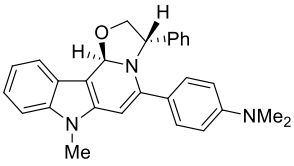
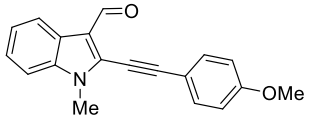
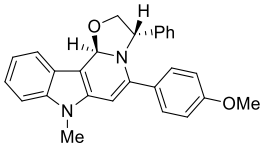
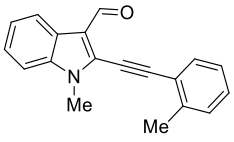
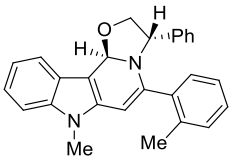
Synthesis of oxazolo fused pyridoindoles (**7a–v**). Subsequently, we checked the scope and generality of this domino strategy. As shown in table 2, the reaction is feasible towards a variety of *o*-alkenylaldehydes (**4a–t**) containing different alkynyl substituents. We commenced our strategy by reacting *o*-alkenylaldehydes **4** with (*S*)-2-phenylglycinol (**6a**) which is an amine source (Table 2). The observation shows that use of amino alcohols **6a** and **6b** gave good yield and have equal reactivity towards the substrate **4**. When electronically neutral and donating groups such as Ph (**4a**), 4–N(Me_2)–C_6H_4 (**4b**), 4–OMe–C_6H_4 (**4c**), 2–Me–C_6H_4 (**4d**), 4–Et–C_6H_4 (**4e**), 4–*n*Bu–C_6H_4 (**4f**), and 4–*t*Bu–C_6H_4 (**4g**) were used, the reaction proceeded well and afforded the products **7a–g** in 82–90% yields (Table 2, entries 1–7). While diastereomeric mixture of compound **7d** and **7d'** was obtained when *ortho*-tolyl substituted alkyne was used (entry 4), which may be due to the steric hindrance of methyl group present at *ortho* position. Product **7h** was obtained in 90% yield with thienyl substituted alkyne (entry 8). With aliphatic alkynes such as –CH_2–OPh and –CH_2OH, the reaction provided the desired products **7i** and **7j** in 60 and 58% yields, respectively (entries 9 and 10). Alkyne **4k**, bearing two methoxy groups at *meta* positions on the phenyl ring, afforded the cyclized product **7k** in 65% yield (entry 11), which may be due to the reduced electrophilicity at the proximal end of the alkyne thereby reduced the efficiency of the desired transformation. Encouraged by the above results, we further extended the same protocol with (*R*)-2-phenylglycinol (**6b**). Reaction of substrate **4c**, **4l**, **4m**, **4f** and **4n** with (*R*)-2-phenylglycinol (**6b**) afforded the desired product **7l–p** in 81–87% yields (entries 12–16). When **4o** alkyne was used, diastereomeric mixture of product **7q** and **7q'** was observed (entry 17), which may be due to the steric hindrance of phenanthrene ring. During the course of our study, we observed that the diastereomeric mixtures of **7d** and **7q** were not affected by the H_2O. The reaction was well tolerated with alkynes **4p-r**, bearing a cyclopropyl,

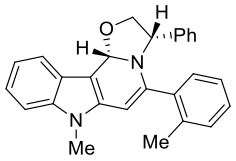
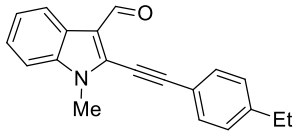
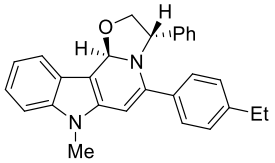
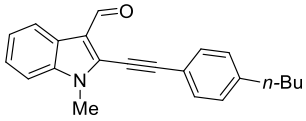
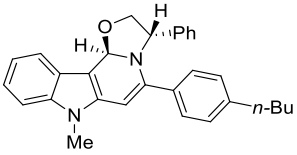
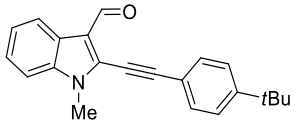
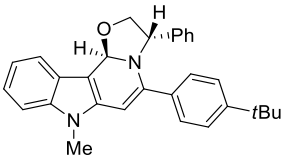
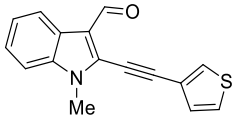
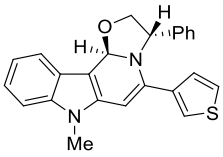
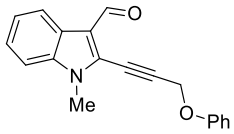
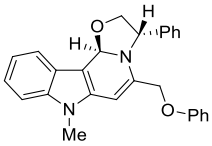
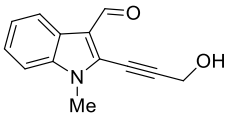
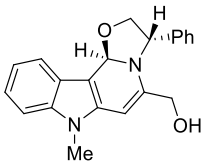
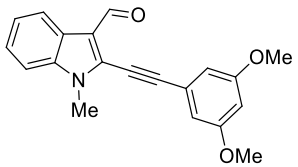
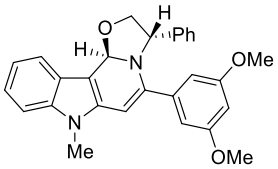
cyclohexyl and *n*-butyl group gave the desired products **7r–t** in 62–70% yields (entries 18–20). Reaction of *o*-alkynylaldehydes **4s** and **4t** bearing electron withdrawing groups such as 3–OMe and 4–CF_3 groups, provided the corresponding products **7u–v** in 68% and 60% yields respectively.

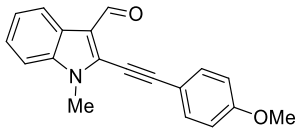
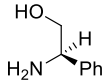
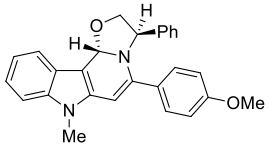
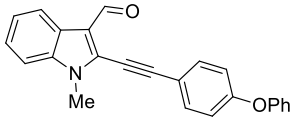
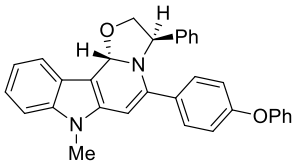
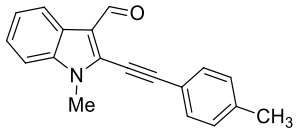
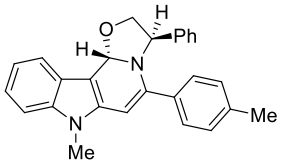
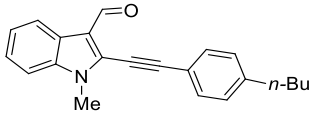
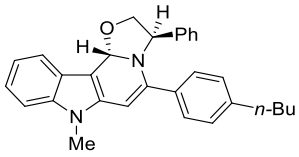
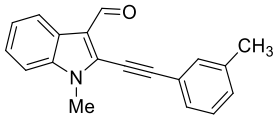
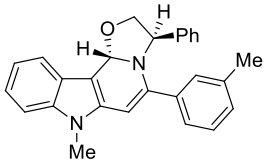
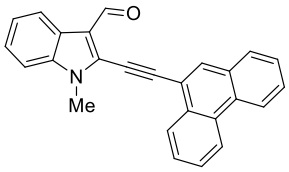
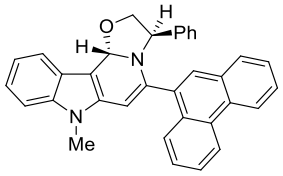
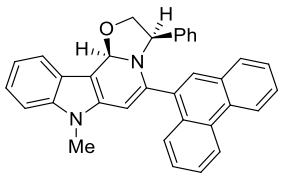
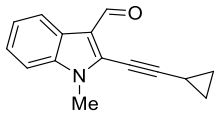
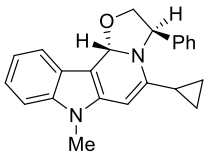
Table 2. Domino Synthesis of Oxazolo Fused Pyridoindoles[a]

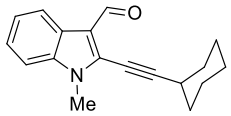
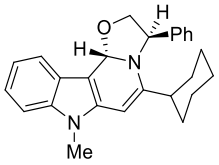
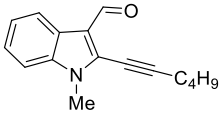
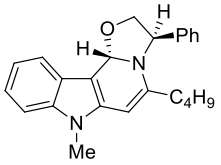
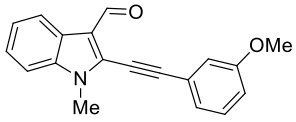
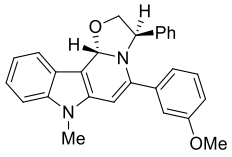
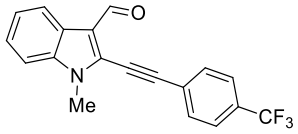
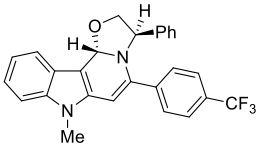


4a-t 6a-b 7a-v

entry	Substrate		amine	Product		yield (%)
1		**4a**	 (*S*) **6a**		**7a**	80
2		**4b**	**6a**		**7b**	90
3		**4c**	**6a**		**7c**	88
4		**4d**	**6a**		**7d**	87 (55:45)

						**7d'**	
5		**4e**	**6a**		**7e**	87
6		**4f**	**6a**		**7f**	86
7		**4g**	**6a**		**7g**	82
8		**4h**	**6a**		**7h**	90
9		**4i**	**6a**		7**i**	60
10		**4j**	**6a**		**7j**	58
11		**4k**	**6a**		**7k**	65

12		**4c**	 (*R*) **6b**		**7l**	87
13		**4l**	**6a**		**7m**	86
14		**4m**	**6b**		**7n**	84
15		**4f**	**6b**		**7o**	82
16		**4n**	**6b**		**7p**	81
17		**4o**	**6a**		**7q**	78 (54:46)
					**7q'**	
18		**4p**	**6a**		**7r**	70[b]

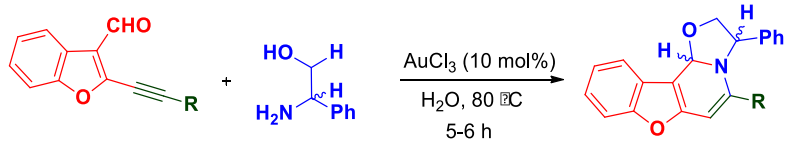
19		**4q**	**6a**		**7s**	65[b]
20		**4r**	**6b**		**7t**	62[b]
21		**4s**	**6b**		**7u**	68
22		**4t**	**6b**		**7v**	60

[a]Reactions were performed using *o*-alkynylaldehyde **4** (0.5 mmol), amine **6a**–**b** (0.55 mmol), 10 mol % of $AuCl_3$ in 2.0 mL of H_2O at 80 °C for 7 h. [b] Reaction time= 8 h.

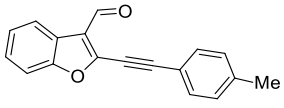
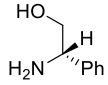
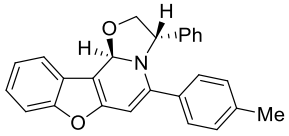
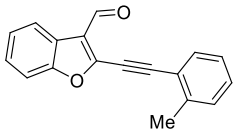
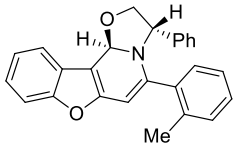
Synthesis of benzofurooxazolo pyridine (8a–n). Benzofuropyridine nucleus has a wide range of biological and pharmaceutical properties.[34] To gain further insight into successful transformation of a variety of tetrahydrooxazolo[3ˈ,2ˈ:1,2]pyrido[4,3-*b*]indoles, we continued our investigation by examining various fused furan substrates **5a–k** with phenylglycinol **6a** and **6b**. The reaction afforded the benzofuro fused oxazolopyridine **8a–n** in good to excellent yields and required less reaction time (8 *vs* 6 h) (Table 3). Reaction of alkynes **5a** and **5b**, bearing electron-donating substituent such as 4–Me and 2–Me to the triple bond of the phenyl ring showed the capability to trigger the *6-endo-dig* cyclization and provided the respective products **8a–b** in 86 and 82% yields respectively (Table 3, entries 1 and 2). However, product **8b** and **8b'**was observed as a diastereomeric mixture. Substrate **5c** bearing an electron-rich heterocycle

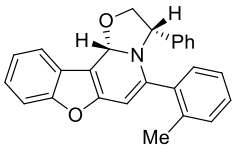
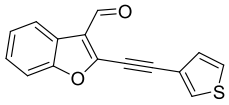
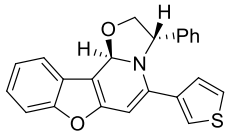
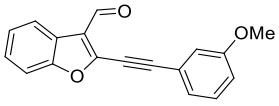
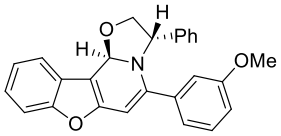
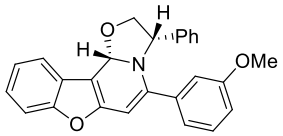
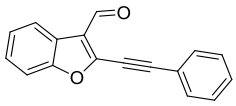
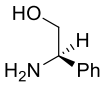
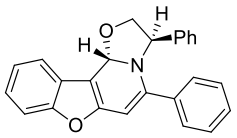
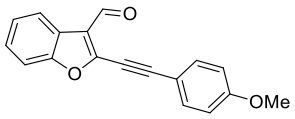
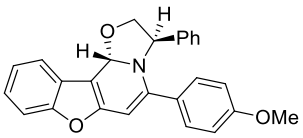
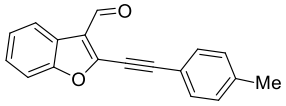
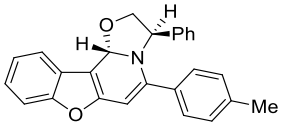
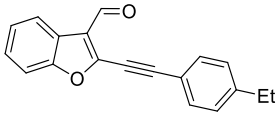
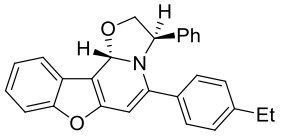
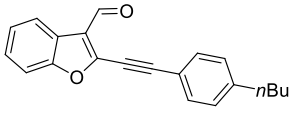
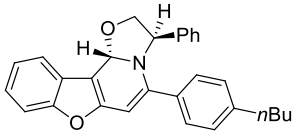
thiophene on reaction with amine **6a** proved to be favorable for the reaction and afforded the desired product **8c** in 89% yield. The product **8d** and **8d'**was obtained as diastereomeric mixture in 70% yield when substrate having 3–OMe at the phenyl ring was used. Next, we extended our strategy with (*R*)-2-phenylglycinol (**6b**). Reaction of **5a, 5b** and **5e–h** bearing electron-neutral and releasing groups afforded the desired product **8e–j** comparatively in satisfactory yields (entries 5–10). When 2-methyl substituted phenyl ring was used, product **8j** and **8j'** was observed as a diastereomeric mixture. Substrate **5c** with a thienyl group successfully provided the product **8k** in 88% yield; however, cyclohexyl-substituted as a *o*-alkynylaldehydes **5i** gave the product **8l** in 69% yield (entry 12). When an electron–withdrawing group (3,5 di–Methoxy and 4–CF_3) on the phenyl ring was reacted, subsequent products **8m** and **8n** were obtained in good yields (entries 13 and 14).

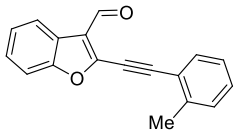
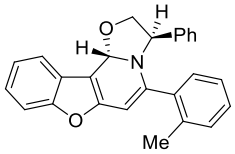
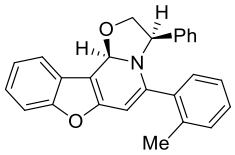
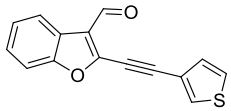
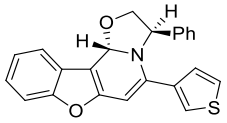
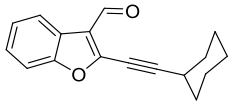
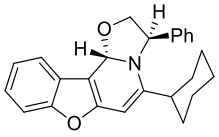
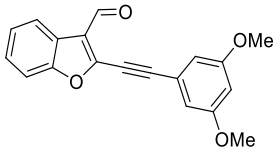
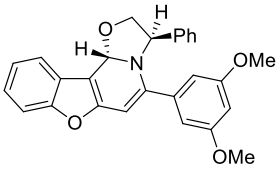
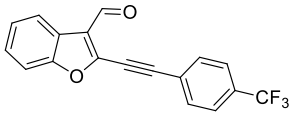
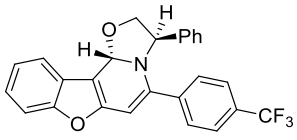
Table 3. Domino Synthesis of Benzofuro Fused Oxazolopyridine[a]



5a-k **6a-b** **8a-n**

entry	substrate		amine	product		yield (%)
1.		**5a**	 (*S*) **6a**		**8a**	86
2.		**5b**	**6a**		**8b**	82 (55:45)
					8b'	

						
3.		**5c**	**6a**		**8c**	89
4.		**5d**	**6a**		**8d**	70 (53:47)
					**8d'**	
5.		**5e**	 (*R*) **6b**		**8e**	74
6.		**5f**	**6b**		**8f**	86
7.		**5a**	**6b**		**8g**	85
8.		**5g**	**6b**		**8h**	82
9.		**5h**	**6b**		**8i**	81

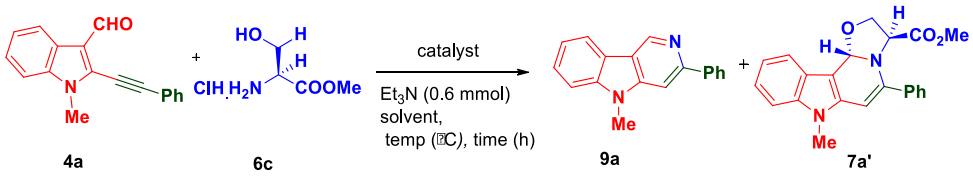
10.		**5b**	**6b**		**8j**	80 (55:45)
					**8j'**	
11.		**5c**	**6b**		**8k**	88
12.		**5i**	**6b**		**8l**	69[b]
13.		**5j**	**6b**		**8m**	62
14.		**5k**	**6b**		**8n**	60

[a]The reactions were performed using *o*-alkynylaldehyde **5** (0.5 mmol), amine **6a**–**b** (0.55 mmol), 10 mol % of $AuCl_3$ in 2.0 mL of H_2O at 80 °C for 5 h. [b] Reaction time = 6 h.

With above successful results, we further extended our investigation for the synthesis of γ-carbolines (Scheme 3) and benzofuropyridines (Scheme 4). During the course of our study, we thought that if amine would attack first onto the alkyne then it generate quartery ammonium ion which leads to the formation of γ-carbolines, if electron-withdrawing group was introduced at alpha carbon of the amine (see Scheme 5, Path **B**). For this, we selected amino esters, serine **6c**, threonine **6d** and cysteine **6e** as an amine source. We initiated to optimize the reaction by using **4a** and **6c** as a model substrate (Table 4). Reaction of **4a** (0.5 mmol) with **6c** (0.55 mmol) using

10 mol % of $AgNO_3$ in 2.0 mL of DCE at 60 °C afforded the product **9a** in 8% yield after 24 h (Table 4, entry 1). Increasing the temperature from 60 to 80 °C, slightly increased the product yield **9a** (entry 2). When DMF was used as a solvent at 110 °C, **9a** was formed in 25% yield after 24 h (entry 3). When EtOH was used as a solvent, a significant improvement in the yield of the product **9a** was observed (entry 4). Water was ineffective for this reaction (entry 5). Interestingly, using 5 mol % of $AuCl_3$ in DCE at 70 °C afforded the product **9a** in 60% yield even after 7 h. Increasing the catalyst loading from 5 to 10 mol % afforded the product **9a** in 82% yield after 6 h. We also tried this reaction using threonine **6d** and cysteine **6e** as an amine source and found that **9a** was formed in lower yields (entries 9 and 10). 10 mol % of $AuCl_3$ in DMF at 110 °C after 5h afforded **9a** in 65% yield (entry 11).

Table 4. Optimization of the Reaction Conditions[a]

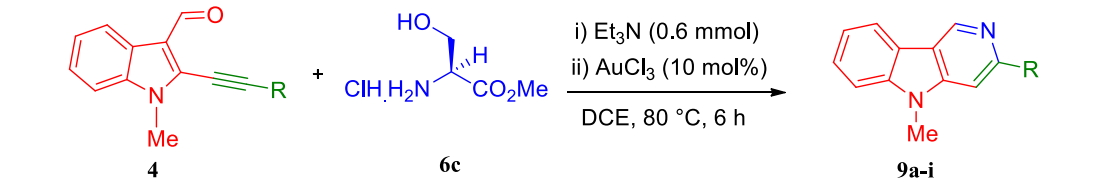


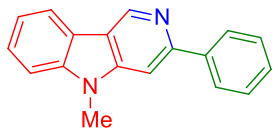
entry	catalyst (mol %)	conditions			yield (%)	
		solvent	temp (°C)	time (h)	**7a'**	**9a**
1.	$AgNO_3$ (10)	DCE	60	24	0	8
2.	$AgNO_3$ (10)	DCE	80	24	0	10
3.	$AgNO_3$ (10)	DMF	110	24	0	25
4.	$AgNO_3$ (10)	EtOH	80	24	0	35
5.	$AgNO_3$ (10)	H_2O	80	24	0	0
6.	$AuCl_3$(5)	H_2O	80	24	0	0

7.	$AuCl_3$(5)	DCE	80	7	0	60
8.	$AuCl_3$(10)	DCE	80	6	0	82
9.	$AuCl_3$(10)[b]	DCE	80	6	0	76
10.	$AuCl_3$(10)[c]	DCE	80	6	0	72
11.	$AuCl_3$(10)	DMF	120	5	0	65

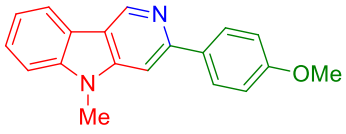
[a]The reactions were performed using 0.5 mmol of *o*-alkynylaldehyde **4a**, 0.55 mmol of amine **6c**, 0.6mmol of Et_3N in 2.0 mL of solvent. [b]Threonine **6d** was used. [c]Cysteine **6e** was used. DCE = 1,2-Dichloroethane. DMF = *N*,*N*-dimethylformamide.

Scheme 3. Domino Synthesis of γ-Carbolines[a]

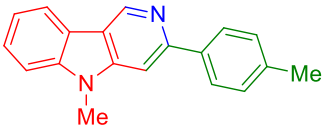




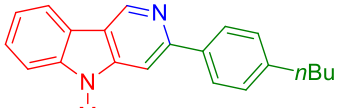
9a, 83%, 76%.[b] 72%[c]



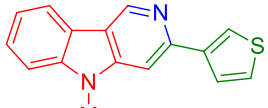
9b, 87%, 82%,[b] 76%[c]



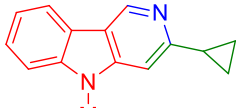
9c, 85%, 78%[b]



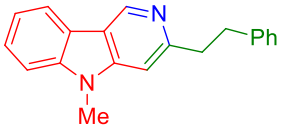
9d, 84%



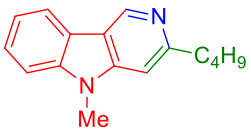
9e, 88%



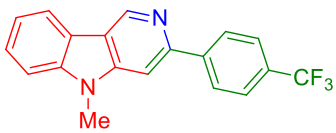
9f, 75%, 72%[b]



9g, 72%



9h, 70%

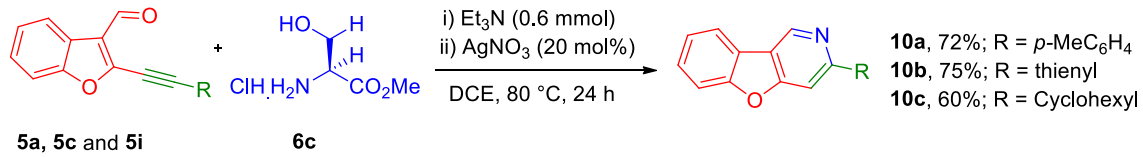


9i, 65%, 61%,[b] 54%[c]

[a]The reactions were performed using *o*-alkynylaldehyde **4** (0.5 mmol), L-Serine methyl ester hydrochloride **6c** (0.55 mmol), Et_3N (0.6 mmol), 10 mol % of $AuCl_3$ in 2.0 mL of DCE at 80 °C for 6 h. [b]L-Threonine methyl ester hydrochloride **6d** was used. [c]L-Cysteine methyl ester hydrochloride **6e** was used.

Synthesis of Substituted γ-Carbolines (9a–i). The scope and generality of the reaction was examined by employing *o*-alkynyl-1*H*-indole-3-carbaldehydes **4a**, **4c, 4m, 4f, 4h, 4p, 4u, 4r** and **4t** with L-Serine methyl ester hydrochloride **6c** for the synthesis of a diversely substituted pyrido[4,3-*b*]indole **9a–i** (Scheme 3). The substrates **4a** having phenyl group gave **9a** in 83% yield; whereas, **4c, 4m** and **4f** bearing an electron-donating substituents such as *p*-OMe, *p*-Me, *p*-*n*Bu, provided the corresponding products **9b**, **9c** and **9d** in slightly better yields as 87%, 85% and 84% respectively as compare to **9a.** Using thienyl group as an alkyne source afforded the product **9e** in 88% yield. Aliphatic alkynes such as cyclopropyl, -CH_2-CH_2-Ph and *n*-hexyl were also feasible in providing the desired product **9f**, **9g** and **9h** in 75%, 72% and 70% yields respectively. However, electron withdrawing group such as *p*-CF_3 lowered the yield of product **9i.**

Scheme 4. Domino Synthesis of Benzofuro[3,2-*c*]pyridines[a]

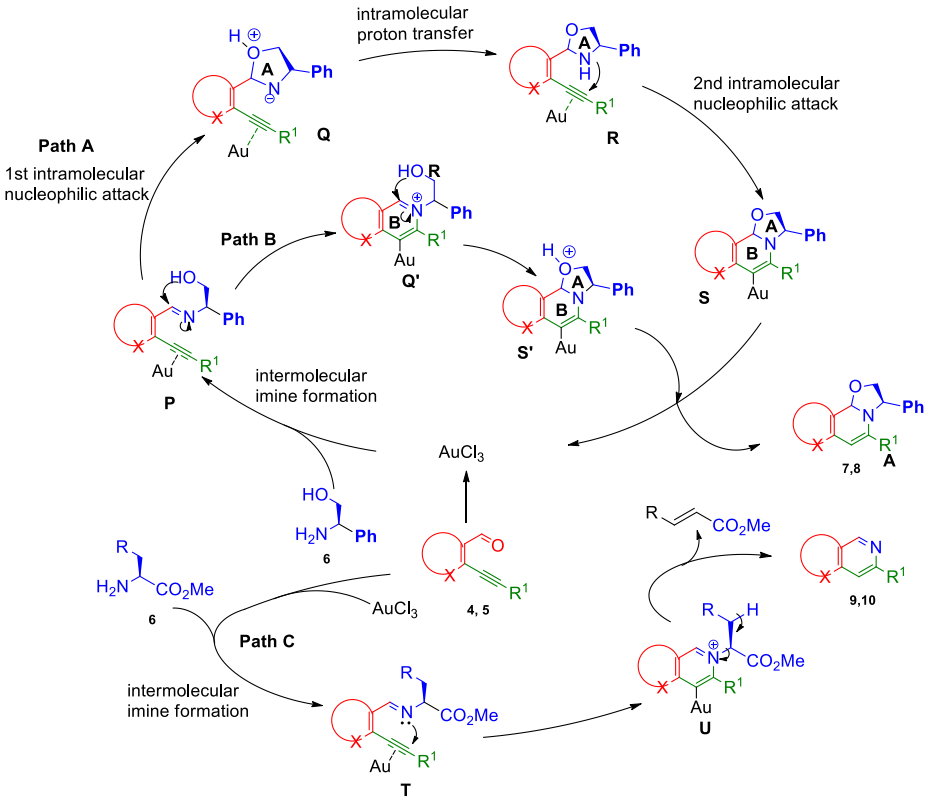


Synthesis of Substituted Benzofuro[3,2-*c*]pyridines. Inspired by the above results, we explored the reaction with the *o*-alkynylbenzofuran-3-carbaldehydes **5d**, **5g** and **5j** with L-Serine methyl ester hydrochloride **6c**. Nevertheless it gave better results with $AgNO_3$ instead of $AuCl_3$ catalyst and furnished differently substituted benzofuro[3,2-*c*]pyridines **10a–c** in 60–75% yields after 24 h (Scheme 4).

In the light of these above preliminary results, a catalytic cycle for this domino transformation was proposed as shown in Scheme 5. Initially reaction of *o*-alkynyl aldehyde **4** and **5** with nucleophilic amine **6** produced condensation species **P**. After this, two possibilities

exist for the formation of compound **7**, **8** i.e. either ring A forms first than ring B or vice versa. Ring A could be formed prior as **P** on activation by $AuCl_3$ would undergo first intramolecular nucleophilic attack of OH group onto imine carbon to afford **Q**. Intramolecuar proton transfer would then produce **R** which upon π-activation by $AuCl_3$ would undergo second intramolecular nucleophic attack of -NH onto the triple bond to afford **S** to give desired compound **7** and **8**. Alternatively, ring B could be formed initially by the activation of triple bond by $AuCl_3$ to give **Q'** followed by second intramolecular nucleophilic attack to furnish **S'** which after subsequent deprotonation would give compound **7** and **8.** Subsequently Path C shows the product formation of Pyrido[4,3-*b*]indole and Benzofuro[3,2-c]pyridines which favours that path B is more enthusiastic over path A.

Scheme 5. **Probable Mechanism**



CONCLUSIONS

In summary, we have developed Au(III)-catalyzed domino protocol in water which allowed a facile access to a vast variety of pyridoindole/benzofuropyridine fused oxazole using readily available starting materials in good yields with high regioselectivity under mild reaction conditions. The reaction proceeded with high 6-*endo*-*dig* regioselectivity. This methodology appeared to be very general and compatible with differently substituted starting materials having different electronic properties thus, increasing its applicability to various functional groups. From a synthetic point of view, the net transformation involves a one-step conversion of simple, inexpensive and readily available starting materials into an interesting class of fused heterocyclic scaffolds. It is likely that the efficiency of this environment friendly method combined with its operational simplicity will make it attractive for the construction of variety of heterocyclic compounds.

EXPERIMENTAL SECTION

General Information. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded in $CDCl_3$ and DMSO-d_6. Chemical shifts for protons are reported in ppm from tetramethylsilane with the residual $CHCl_3$ and DMSO resonance as internal reference. Chemical shifts for carbons are reported in ppm from tetramethylsilane and are referenced to the carbon resonance of the solvent. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz, and integration. High-resolution mass spectra were recorded on QqTOF mass analyzer. TLC analysis was performed on commercially prepared 60 F_{254} silica gel plates and visualized by either UV irradiation or by staining with I_2. Chemical yields are referred to the pure isolated substances Chromatographic purification of the label compounds was accomplished by column chromatography using 100–

200 mesh size silica gel. Anhydrous forms of all reagents such as diethyl ether, hexanes, ethyl acetate, DCE, DMF, Et_3N, $AuCl_3$, AuCl, Silver nitrate, palladium salts and copper salts were used directly as obtained commercially unless otherwise noted.

Procedure for the Synthesis of Starting materials 4 and 5. The starting materials **4** and **5** were prepared by the Sonogashira coupling reaction[36,6a] of corresponding haloaldehyde with terminal alkynes using the reported procedure and confirmed by comparison of its physical and spectral data (^{1}H NMR, ^{13}C NMR, and HRMS). The structure and purity of the known starting materials **4a**,[33] **4q,**[28b] **4r**[33] and **5a–j**[5a] were confirmed by comparison of their physical and spectral data (^{1}H NMR and ^{13}C NMR) with those reported in literature.

*2-((4-(Dimethylamino)phenyl)ethynyl)-1-methyl-1H-indole-3-carbaldehyde (**4b**).* The product was obtained as brown semi-solid (142.1 mg, 94%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.15 (s, 1H), 8.22 (d, J = 6.8 Hz, 1H), 7.38 (d, J = 8.3 Hz, 2H), 7.27–7.19 (m, 3H), 6.57 (d, J = 9.2 Hz, 2H), 3.77 (s, 3H), 2.93 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 185.0, 150.9, 137.4, 133.8, 133.1, 124.54, 124.48, 123.2, 121.9, 118.7, 111.6, 109.5, 107.1, 103.6, 75.9, 40.0, 31.0; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{20}H_{18}N_2O]$ 303.1497, found 303.1495.

*2-((4-Methoxyphenyl)ethynyl)-1-methyl-1H-indole-3-carbaldehyde (**4c**).* The product was obtained as brown needles (133.1 mg, 92%): mp 162–166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.16 (s, 1H), 8.23 (d J = 6.88 Hz, 1H), 7.46 (d, J = 8.4 Hz, 2H), 7.29–7.17 (m, 3H), 6.85–6.83 (m, 2H), 3.79–3.76 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 185.2, 160.8, 137.4, 133.5, 132.7, 124.8, 124.5, 123.5, 122.0, 119.4, 114.3, 113.1, 109.6, 101.6, 76.4, 55.4, 31.1; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{19}H_{15}NO_2]$ 290.1181, found 290.1198.

*1-Methyl-2-(o-tolylethynyl)-1H-indole-3-carbaldehyde (**4d**).* The product was obtained as brown needles (123.0 mg, 90%): mp 158–162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.19 (s, 1H), 8.25 (d J = 9.6 Hz, 1H), 7.44 (d, J = 8.28 Hz, 2H), 7.32–7.23 (m, 3H), 7.16 (d, J = 8.2 Hz, 2H), 3.84 (s, 3H), 2.22 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 185.2, 140.3, 137.5, 131.7, 129.5, 124.9, 124.4, 123.5, 122.2, 119.7, 118.1, 109.6, 101.6, 70.1, 31.2, 21.7; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{19}H_{15}NO]$ 274.1232, found 274.1251.

*2-((4-Ethylphenyl)ethynyl)-1-methyl-1H-indole-3-carbaldehyde (**4e**).* The product was obtained as brown needles (127.9 mg, 89%): mp 148–152 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.19 (s, 1H), 8.25 (d J = 8.4 Hz, 1H), 7.46 (d, J = 7.6 Hz, 2H), 7.31–7.23 (m, 4H), 7.18–7.16 (m, 1H), 3.82 (s, 3H), 2.62 (q, J = 7.64, 15.28 Hz, 2H), 1.19 (t, J = 7.24 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 185.3, 146.6, 137.2, 131.8, 128.2, 126.4, 125.0, 124.9, 124.0, 123.4,123.3, 122.0, 121.0, 119.5, 115.1, 109.6, 76.8, 31.7, 28.9, 15.3; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{20}H_{17}NO]$ 288.1388, found 288.1405.

*2-((4-Butylphenyl)ethynyl)-1-methyl-1H-indole-3-carbaldehyde (**4f**).* The product was obtained as pale yellow needles (138.8 mg, 88%): mp 154–158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.16 (s, 1H), 8.23 (d, J = 7.3 Hz, 1H), 7.42 (d, J = 7.9 Hz, 2H), 7.27–7.18 (m, 3H), 7.13 (d, J = 7.9 Hz, 2H), 3.76 (s, 3H), 2.56 (t, J = 7.6 Hz, 2H), 1.54–1.51 (m, 2H), 1.30-1.23 (m, 2H), 0.88–0.85 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 185.2, 139.7, 137.0, 132.7, 128.53, 128.45, 126.7, 124.6, 124.2, 123.3, 122.0, 119.5, 109.5, 102.3, 70.1, 34.3, 32.4, 30.8, 21.8, 14.1; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{22}H_{21}NO]$ 316.1701, found 316.1721.

*2-((4-(tert-Butyl)phenyl)ethynyl)-1-methyl-1H-indole-3-carbaldehyde (**4g**).* The product was obtained as brown needles (134.0 mg, 85%): mp 139–143 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ

10.27 (s, 1H), 8.33 (d, J = 8.4 Hz, 1H), 7.56 (d, J = 8.4 Hz, 2H), 7.45 (d, J = 7.64 Hz, 2H), 7.38–7.33 (m, 3H), 3.92 (s, 3H), 1.35 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 185.3, 153.2, 131.6, 125.8, 124.9, 124.5, 123.5, 122.1, 119.6, 118.2, 109.6, 101.6, 76.8, 34.8, 31.2, 31.1; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{22}H_{21}NO]$ 316.1701, found 316.1721.

*1-Methyl-2-(thiophen-3-ylethynyl)-1H-indole-3-carbaldehyde (**4h**).* The product was obtained as pale yellow needles (126.0 mg, 95%): mp 146–150 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 10.19 (s, 1H), 8.28 (d, J = 7.6 Hz, 1H), 7.68–7.67 (m,1H), 7.36–7.33 (m, 2H), 7.32–7.30 (m, 1H), 7.28–7.26 (m, 1H), 7.25–7.24 (m, 1H), 3.82 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 185.1, 137.4, 132.1, 130.9, 129.6, 126.2, 124.9, 124.3, 123.4, 122.0, 120.2, 119.7, 109.6, 96.3, 31.1; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{16}H_{11}NOS]$ 266.0640, found 266.0661.

*1-Methyl-2-(3-phenoxyprop-1-yn-1-yl)-1H-indole-3-carbaldehyde (**4i**).* The product was obtained as brown oily (107.1 mg, 74%): ^1H NMR (400 MHz, $CDCl_3$) δ 10.13 (s, 1H), 8.02–8.00 (m, 1H), 7.28–7.21 (m, 4H), 6.94 (t, J = 6.8 Hz, 1H), 6.84 (d, J = 8.4 Hz, 2H), 4.45 (s, 2H), 3.60 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 184.5, 157.3, 137.1, 129.8, 123.5, 122.9, 122.0, 114.4, 110.0, 72.6, 36.3, 30.1; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{19}H_{15}NO_2]$ 290.1181, found 290.1198.

*2-(3-Hydroxyprop-1-yn-1-yl)-1-methyl-1H-indole-3-carbaldehyde (**4j**).* The product was obtained as brown semi-solid (75.7 mg, 71%): mp 132–136 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 10.03 (s, 1H), 8.23 (d, J = 3.8 Hz, 1H), 7.33–7.26 (m, 3H), 4.62 (s, 2H), 3.54 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 185.6, 137.0, 125.0, 123.54, 123.51, 122.9, 121.8, 119.6, 109.7, 73.2, 51.2, 30.9; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{13}H_{11}NO_2]$ 214.0868, found 214.0838.

*2-((3,5-Dimethoxyphenyl)ethynyl)-1-methyl-1H-indole-3-carbaldehyde (**4k**).* The product was obtained as brown needles (111.8 mg, 70%): mp 153–157 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.27 (s, 1H), 8.33 (d J = 7.64 Hz, 1H), 7.39–7.23 (m, 3H), 6.77–7.76 (m, 2H), 6.57 (s, 1H), 3.89 (s, 3H), 3.86–3.85 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 185.1, 160.7, 137.4, 131.9, 125.0, 123.5, 122.1, 119.8, 109.7, 109.5, 106.2, 103.0, 101.2, 76.8, 60.4, 55.5, 31.2; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{20}H_{17}NO_3]$ 320.1287, found 320.1310.

*1-Methyl-2-((4-phenoxyphenyl)ethynyl)-1H-indole-3-carbaldehyde (**4l**).* The product was obtained as dark brown needles (158.1 mg, 90%): mp 165–169 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.16 (s, 1H), 8.17–8.11 (m, 1H), 7.76 (d, J = 9.16 Hz, 1H), 7.61–7.56 (m, 1H), 7.49–7.43 (m, 2H), 7.38 (t, J = 8.4 Hz, 1H), 7.32–7.20 (m, 3H), 7.15–7.10 (m, 3H), 7.06 (d, J = 9.1 Hz, 1H), 3.92 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 184.1, 158.6, 155.3, 134.1, 130.4, 130.3, 124.9, 124.5, 120.8, 120.0, 119.7, 118.6, 118.2, 114.8, 111.0, 77.9, 76.9, 31.2; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{24}H_{17}NO_2]$ 352.1338, found 352.1332.

*1-Methyl-2-(p-tolylethynyl)-1H-indole-3-carbaldehyde (**4m**).* The product was obtained as pale brown needles (121.6 mg, 89%): mp 158–162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.19 (s, 1H), 8.25 (d, J = 9.6 Hz, 1H), 7.44 (d, J = 8.3 Hz, 2H), 7.32–7.23 (m, 3H), 7.16 (d, J = 8.2 Hz 2H), 3.84 (s, 3H), 2.34 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 185.2, 140.3, 137.5, 131.7, 129.4, 124.9, 124.5, 123.5, 122.2, 119.7, 118.1, 109.6, 101.6, 69.6, 31.2, 21.7; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{19}H_{15}NO]$ 274.1232, found 274.1251.

*1-Methyl-2-(m-tolylethynyl)-1H-indole-3-carbaldehyde (**4n**).* The product was obtained as brown needles (123.0 mg, 90%): mp 156–160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.19 (s, 1H), 8.25 (d J = 9.6 Hz, 1H), 7.44 (d, J = 8.28 Hz, 2H), 7.32–7.23 (m, 3H), 7.16 (d, J = 8.2 Hz, 2H), 3.84 (s,

3H), 2.37 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 185.4, 140.4, 137.4, 131.7, 129.4, 124.9, 124.5, 123.4, 122.1, 119.6, 118.1, 109.6, 101.6, 31.0, 21.6; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{19}H_{15}NO]$ 274.1232, found 274.1251.

*1-Methyl-2-(phenanthren-9-ylethynyl)-1H-indole-3-carbaldehyde (**4o**).* The product was obtained as brown needles (156.3 mg, 87%): mp 145–149 °C; ^{1}H NMR (400 MHz, DMSO) δ 10.35 (s, 1H), 8.92 (d, J= 8.4 Hz, 1H), 8.86 (d, J = 8.4 Hz, 1H), 8.53 (s, 1H), 8.47 (d, J = 7.6 Hz, 1H), 8.17 (d, J = 8.4 Hz, 1H), 8.08 (d, J = 8.4 Hz, 1H), 7.89–7.76 (m, 3H), 7.73–7.66 (m, 2H), 7.43 (t, J = 6.84 Hz, 1H), 7.34 (t, J = 7.6 Hz, 1H), 4.07 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 184.0, 137.3, 133.9, 130.9, 130.5, 130.3, 129.7, 129.5, 129.0, 128.8, 128.0, 127.9, 127.8, 126.0, 125.1, 123.9, 123.6, 123.5, 123.1, 120.8, 119.1, 117.0, 111.2, 99.3, 81.9, 79.2, 31.7; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{26}H_{17}NO]$ 360.1388, found 360.1352.

*2-(Cyclopropylethynyl)-1-methyl-1H-indole-3-carbaldehyde (**4p**).* The product was obtained as red oily (89.3 mg, 80%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.27 (s, 1H), 8.17–8.15 (m, 1H), 7.34–7.30 (m, 3H), 3.68 (s, 3H) 2.13–2.07 (m, 1H), 1.12–1.08 (m, 2H), 0.97–0.92 (m, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 184.0, 137.1, 123.2, 122.7, 119.4, 114.0, 109.8, 30.1, 17.7, 9.4; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{15}H_{13}NO]$ 224.1075, found 224.1077.

*2-((3-Methoxyphenyl)ethynyl)-1-methyl-1H-indole-3-carbaldehyde (**4s**).* The product was obtained as yellow needles (108.5 mg, 75%): mp 162–166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.17 (s, 1H), 8.23 (d, J = 6.9 Hz, 1H), 7.47 (d, J = 8.4 Hz, 2H), 7.29–7.21 (m, 3H), 6.84 (t, J = 8.4 Hz, 2H), 3.80 (s, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 185.1, 160.9, 137.5, 133.4, 132.7, 124.9, 124.52, 123.45, 122.1, 119.5, 114.4, 113.2, 109.6, 101.6, 55.3, 31.0; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{19}H_{15}NO_2]$ 290.1181, found 290.1198.

*1-Methyl-2-((4-(trifluoromethyl)phenyl)ethynyl)-1H-indole-3-carbaldehyde (**4t**).* The product was obtained as pale yellow needles (139.1 mg, 85%): mp 158–162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.17 (s, 1H), 8.23 (d J = 8.4 Hz, 1H), 7.69–7.58 (m, 4H), 7.32–7.23 (m, 3H), 3.8 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 184.9, 137.6, 132.0, 130.8, 128.9, 125.8 (q, $J_{C\text{-}F}$ = 3.8 Hz, 1C), 125.61, 125.57, 125.3, 125.0, 124.3, 123.7, 123.4, 122.8, 122.2, 120.3, 109.9, 99.3, 79.6, 31.2; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{19}H_{12}F_3NO]$ 328.0949, found 328.0965.

*1-Methyl-2-(4-phenylbut-1-yn-1-yl)-1H-indole-3-carbaldehyde (**4u**).* The product was obtained as brown solid (112.0 mg, 78%): mp 132–136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.03 (s, 1H), 8.29–8.27 (m, 1H), 7.36–7.32 (m, 3H), 7.31–7.28 (m, 3H), 7.26–7.23 (m, 2H), 3.64 (s, 3H), 3.02–2.98 (m, 2H), 2.93–2.89 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 185.2, 139.7, 137.0, 132.7, 128.53, 128.45, 126.7, 124.6, 124.2, 123.3, 122.0, 119.5, 109.5, 102.3, 70.1, 34.3, 30.8, 21.8; HRMS (ESI) $[M]^+$ calcd for $[C_{20}H_{17}NO]$ 287.1310, found 287.1309.

*2-((4-(Trifluoromethyl)phenyl)ethynyl)benzofuran-3-carbaldehyde (**5k**).* The product was obtained as yellow needles (113.1 mg, 72%): mp 146–150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.35 (s, 1H), 8.18 (d, J = 6.88 Hz, 1H), 7.70 (q, J = 8.4, 22.16 Hz, 4H), 7.52–7.38 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 185.2, 154.8, 146.9, 132.3, 127.5, 125.7 (q, $J_{C\text{-}F}$ = 1.2 Hz, 1C), 125.6, 124.5, 123.2, 122.6, 111.3, 98.9, 79.0; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{18}H_9F_3O_2]$ 315.0633, found 315.0648.

Procedure for the Synthesis of Compound 7 and 8. To a solution of 0.5 mmol of *o*-alkynyl aldehyde **4** and **5** in 2.0 mL H_2O, was added 0.55 mmol of amine **6a**–**b** followed by the addition of 10 mol % of $AuCl_3$. The reaction mixture was allowed to stir at 80 °C for 5–8 h. The disappearance of the starting material was determined by TLC. The reaction mixture was then

washed with brine solution and was extracted with ethyl acetate (2 x 10 mL). The combined organic fractions were dried over anhydrous Na_2SO_4 and concentrated under vacuum to yield the crude product. The crude product was purified by column chromatography on neutral alumina/silica gel using chloroform/methnol as the eluent.

(3S,11cR)-7-Methyl-3,5-diphenyl-2,3,7,11c-tetrahydrooxazolo[3',2':1,2]pyrido[4,3-b]indole ***(7a).*** The product was obtained as pale yellow needles (151.4 mg, 80%): mp 110–114 °C; $[\alpha]_D^{31}$ = -115.0 (c 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.09 (s, 1H), 8.58 (d, *J* = 7.3 Hz, 1H), 7.55–7.50 (m, 2H), 7.40–7.30 (m, 5H), 7.26–7.22 (m, 3H), 6.99–6.92 (m, 3H), 6.07–6.04 (m, 1H), 4.98 (t, *J* = 11 Hz, 1H), 4.16–4.11 (m, 1H), 3.78 (s, 3H); ^{13}C{^{1}H} NMR (400 MHz, $CDCl_3$) δ 150.4, 145.2, 142.3, 136.7, 135.6, 133.1, 130.5, 129.4, 129.1, 129.0, 127.1, 123.6, 123.4, 120.3, 120.1, 110.1, 108.3, 70.1, 61.8, 30.4; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{26}H_{22}N_2O$ 379.1810, found 379.1804.

*N,N-Dimethyl-4-((3S,11cR)-7-methyl-3-phenyl-2,3,7,11c-tetrahydrooxazolo[3',2':1,2]pyrido [4,3-b]indol-5-yl)aniline (**7b**).* The product was obtained as pale brown needles (189.7 mg, 90%): mp 129–133 °C; $[\alpha]_D^{31}$ = –80.0 (c 0.05, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.91 (s, 1H), 8.56 (d, *J* = 8.4 Hz, 1H), 7.49–7.47 (m, 1H), 7.40 (s, 1H), 7.35–7.31 (m, 3H), 7.19–7.16 (m, 4H), 6.95–6.91 (m, 2H), 6.64–6.62 (m, 2H), 6.21–6.18 (m, 1H), 4.96–4.91 (m, 1H), 4.24–4.16 (m, 1H), 3.80 (s, 3H), 2.92 (s, 6H); ^{13}C{^{1}H} NMR (400 MHz, $CDCl_3$) δ 152.3, 151.3, 145.8, 142.4, 136.8, 136.3, 130.9, 129.5, 129.1, 128.9, 127.1, 123.7, 123.5, 120.7, 120.0, 119.8, 111.7, 110.0, 108.3, 69.3, 61.6, 40.0, 29.6; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{28}H_{27}N_3O$ 422.2232, found 422.2224.

*(3S,11cR)-5-(4-Methoxyphenyl)-7-methyl-3-phenyl-2,3,7,11c-tetrahydrooxazolo[3',2':1,2]pyrido [4,3-b]indole (**7c**).* The product was obtained as pale yellow crystals (179.3 mg, 88%): mp 132–134 °C; $[\alpha]_D^{31}$ = -118.7 (c 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.08 (s, 1H), 8.64 (d, J = 7.32 Hz, 1H), 7.47–7.20 (m, 10H), 6.94 (s, 3H), 6.16–6.12 (m, 1H), 5.02-4.93 (m, 1H), 4.25–4.14 (m, 1H), 3.82 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.1, 150.7, 145.5, 142.5, 136.7, 135.9, 129.5, 129.1, 129.0, 128.5, 127.7, 127.1, 126.8, 125.2, 123.6, 123.5, 120.4, 120.2, 114.4, 110.1, 108.5, 69.9, 61.8, 55.5, 30.4; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{27}H_{24}N_2O_2]$ 409.1916, found 409.1908.

7-Methyl-3-phenyl-5-(o-tolyl)-2,3,7,11c-tetrahydrooxazolo[3',2':1,2]pyrido[4,3-b]indole (dr = 55:45) ***(7d + 7d').*** The product was obtained as a yellow needles (170.7 mg, 87%): mp 156–159 °C; $[\alpha]_D^{31}$ = -77.6 (c 0.05, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.56 (s, 1H, major), 10.28 (s, 1H, major), 8.93 (d, J = 7.6 Hz, 1H, major), 8.70 (d, J = 8.4 Hz, 1H, minor), 7.60 (d, J = 6.9 Hz, 1H, major), 7.55–7.27 [m, 13H, including 6H (major) + 7H (minor)], 7.17–7.06 [m, 6H, including 3H (major) + 3H (minor)], 7.01 (t, J = 8.4 Hz, 1H, major), 6.77 [d, J = 7.6 Hz, 2H, including 1H (major) + 1H (minor)], 6.63 [d, J = 7.6 Hz, 2H, including 1H (major) + 1H (minor)], 6.49 [d, J = 6.9 Hz, 2H, including 1H (major) + 1H (minor)], 5.91–5.88 (m, 1H, minor), 5.50–5.46 (m, 1H, major), 4.99–4.86 [m, 2H, including 1H (major) + 1H (minor)], 4.02–3.81 [m, 8H, including 4H (major) + 4H (minor)], 2.16 [s, 3H, including 3H (major) + 3H (minor)]; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 150.2 (major), 149.7 (minor), 145.7 (major), 145.3 (minor), 142.5 (major), 142.4 (minor), 137.5 (minor), 137.2 (major), 137.1 (minor), 136.6 (major), 135.2 (major), 134.6 (minor), 132.3 (major), 132.2 (minor), 130.91 (major), 130.85 (minor), 130.79 (minor), 130.76 (major), 130.1 (major), 129.8 (major), 129.7 (minor), 129.6 (minor), 129.1 (major), 129.0 (major + minor), 128.9 (major + minor), 127.5 (major + minor),

126.6 (major + minor), 125.8 (major), 124.7 (minor), 124.0 (minor), 123.8 (major), 123.6 (minor), 120.8 (major), 120.6 (minor), 120.5 (major), 120.3 (minor), 110.10 (minor), 110.08 (major), 108.4 (minor), 108.0 (major), 71.5 (major), 70.7 (minor), 61.8 (minor), 61.6 (major), 30.41 (major), 30.38 (minor), 19.9 (major), 19.1 (minor); HRMS (ESI) $[M+H]^+$ Calcd for $[C_{27}H_{24}N_2O]$ 393.1967, found 393.1968.

*(3S,11cR)-5-(4-Ethylphenyl)-7-methyl-3-phenyl-2,3,7,11c-tetrahydrooxazolo[3',2':1,2]pyrido [4,3-b]indole (**7e**).* The product was obtained as brown needles (176.8 mg, 87%): mp 93–96 °C; $[\alpha]_D^{31}$ = -100.1 (c 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.01 (s, 1H), 8.54–8.50 (m, 1H), 7.35–7.09 (m, 10H), 6.96–6.91 (m, 3H), 6.06 (dd, J = 9.16, 3.68 Hz, 1H), 4.95 (m, 1H), 4.13 (dd, J = 12.84, 3.68 1H), 3.74 (s, 3H), 2.67 (q, J = 14.6, 7.3 Hz, 2H), 1.23 (t, J = 7.36 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 150.7, 147.1, 145.3, 142.3, 136.6, 135.8, 130.4, 129.4, 129.1, 129.0, 128.6, 127.1, 127.0, 123.6, 123.4, 120.3, 120.0, 110.1, 108.2, 69.9, 61.8, 30.3, 29.6, 15.3; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{28}H_{26}N_2O]$ 407.2123, found 407.2131.

*(3S,11cR)-5-(4-Butylphenyl)-7-methyl-3-phenyl-2,3,7,11c-tetrahydrooxazolo[3',2':1,2]pyrido [4,3-b]indole (**7f**).* The product was obtained as brown needles (186.9 mg, 86%): mp 78–72 °C; $[\alpha]_D^{31}$ = –77.0 (c 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.10 (s, 1H), 8.62 (d, J = 7.8 Hz, 1H), 7.45–7.41 (m, 1H), 7.35–7.27 (m, 4H), 7.24–7.11 (m, 5H), 6.93–6.92 (m, 3H), 6.10 (dd, J = 9.6, 4.1 Hz, 1H), 5.02–4.96 (m, 1H), 4.16 (dd, J = 13.2, 4.1 Hz, 1H), 3.80 (s, 3H), 2.67 (t, J = 7.1 Hz, 2H), 1.63 (q, J = 15.1, 7.3 Hz, 2H), 1.38 (sext, J = 7.3 Hz, 2H), 0.94 (t, J = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 150.8, 145.8, 145.4, 142.4, 136.9, 135.8, 130.4, 129.5, 129.1, 129.0, 128.6, 127.1, 127.0, 123.8, 123.5, 120.4, 120.2, 110.1, 108.2, 70.0, 61.8, 35.4, 33.3, 30.3, 22.2, 13.9; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{30}H_{30}N_2O]$ 435.2437, found 435.2439.

*(3S,11cR)-5-(4-(tert-Butyl)phenyl)-7-methyl-3-phenyl-2,3,7,11c-tetrahydrooxazolo[3',2':1,2] pyrido[4,3-b]indole (**7g**).* The product was obtained as brown needles (178.2 mg, 82%): mp 110–114 °C; $[\alpha]_D^{31}$ = –74.7 (c 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.00 (s,1H), 8.50 (d, J = 7.64 Hz, 1H), 7.43–7.36 (m, 3H), 7.29–7.28 (m, 2H), 7.24–7.18 (m, 5H), 7.11–7.09 (d, J = 7.64 Hz, 1H), 6.94–6.92 (m, 2H), 6.12–6.08 (m, 1H), 4.98 (t, J = 12.2 Hz, 1H), 4.19–4.15 (m, 1H), 3.74 (s, 3H), 1.35 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 154.0, 150.7, 145.2, 142.2, 136.6, 135.8, 130.2, 129.4, 129.04, 128.97, 128.6, 127.1, 126.9, 123.4, 123.3, 120.2, 120.1, 110.1, 108.2, 69.8, 61.8, 34.9, 31.5, 30.3; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{30}H_{30}N_2O]$ 435.2437, found 435.2426.

*(3S,11cR)-7-Methyl-3-phenyl-5-(thiophen-3-yl)-2,3,7,11c-tetrahydrooxazolo[3',2':1,2]pyrido [4,3-b]indole (**7h**).* The product was obtained as brown needles (173.0 mg, 90%): mp 155–159 °C; $[\alpha]_D^{31}$ = –154.8 (c 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.95 (s, 1H), 8.46 (d, J = 7.8, Hz, 1H), 7.69 (s, 1H), 7.46–7.36 (m, 3H), 7.31–7.19 (m, 6H), 6.95–6.93 (m, 2H), 6.23–6.19 (m, 1H), 4.94 (t, J = 13.72 Hz, 1H), 4.26–4.22 (m, 1H), 3.75 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 146.0, 145.2, 142.3, 136.5, 135.8, 132.8, 129.5, 129.3, 129.2, 129.0, 128.7, 128.6, 127.6, 126.9, 123.4, 123.3, 120.1, 120.0, 110.2, 108.7, 70.0, 61.9, 30.4; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{24}H_{20}N_2OS]$ 385.1375, found 385.1391.

*(3S,11cR)-7-Methyl-5-(phenoxymethyl)-3-phenyl-2,3,7,11c-tetrahydrooxazolo[3',2':1,2]pyrido [4,3-b]indole (**7i**).* The product was obtained as brown needles (122.5 mg, 60%): mp 84–88 °C; $[\alpha]_D^{31}$ = –65.3 (c 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.59 (s, 1H), 8.25 (s, 1H), 7.98 (s, 1H), 7.38–7.15 (m, 5H), 6.92–6.87 (m,3H), 6.37 (s, 1H), 5.65–5.53 (m, 1H), 4.76–4.67 (m, 2H), 4.36–4.31 (m, 2H), 3.68 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 156.9, 146.2, 145.9, 145.8, 142.3, 136.9, 135.1, 129.8, 129.7, 129.4, 129.3, 128.6, 127.3, 123.5, 122.9, 122.3, 120.1, 119.9,

114.9, 110.3, 107.6, 69.0, 66.4, 62.9, 30.4; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{27}H_{24}N_2O_2]$ 409.1916, found 409.1935.

*((3S,11cR)-7-Methyl-3-phenyl-2,3,7,11c-tetrahydrooxazolo[3',2':1,2]pyrido[4,3-b]indol-5-yl)methanol (**7j**).* The product was obtained as red oily (96.4 mg, 58%); $[\alpha]_D^{31}$ = -90.1 (c 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.55 (s, 1H), 8.46 (d, J = 8.4 Hz, 1H), 7.95 (s, 1H), 7.50 (t, J = 7.64 Hz, 1H), 7.37–7.23 (m, 3H), 7.13–7.12 (d, J = 7.6 Hz, 1H), 6.99–6.97 (m, 2H), 6.29–6.26 (m, 1H), 5.11–5.07 (m, 1H), 4.67–4.54 (m, 3H), 4.27–4.23 (m, 1H), 3.73 (s,1H), 3.54 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 151.5, 146.4, 142.6, 136.7, 135.9, 129.5, 129.0, 128.8, 128.2, 127.5, 122.9, 122.6, 120.1, 119.2, 111.4, 106.0, 67.4, 62.4, 59.9, 30.1; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{21}H_{20}N_2O_2]$ 333.1603, found 333.1612.

*(3S,11cR)-5-(3,5-Dimethoxyphenyl)-7-methyl-3-phenyl-2,3,7,11c-tetrahydrooxazolo[3',2':1,2]pyrido[4,3-b]indole (**7k**).* The product was obtained as brown needles (142.5 mg, 65%): mp 123–127 °C; $[\alpha]_D^{31}$ = -92.1 (c 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.03 (s, 1H), 8.60 (d J = 7.8 Hz, 1H), 7.47 (t, J = 7.6 Hz, 1H), 7.41 (s, 1H), 7.36–7.29 (m, 3H), 7.20 (brs, 3H), 7.01–6.99 (m, 2H), 6.53 (s, 1H), 6.08–6.06 (s, 2H), 4.96–4.90 (m, 1H), 4.20–4.15 (m, 1H), 3.82 (s, 6H), 3.57 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.1, 160.6, 150.3, 145.4, 142.5, 136.9, 136.1, 134.6, 129.6, 129.1, 129.0, 127.1, 123.8, 123.6, 120.5, 120.3, 110.2, 108.0, 107.6, 102.6, 70.1, 61.9, 56.0, 55.4, 30.4; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{28}H_{26}N_2O_3]$ 439.2022, found 439.2045.

*(3R,11cS)-5-(4-Methoxyphenyl)-7-methyl-3-phenyl-2,3,7,11c-tetrahydrooxazolo[3',2':1,2]pyrido[4,3-b]indole (**7l**).* The product was obtained as pale yellow needles (177.7 mg, 87%): mp 87–91 °C; $[\alpha]_D^{31}$ = +124.9 (c 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.01 (s, 1H), 8.57 (d, J = 7.6 Hz, 1H), 7.41–7.35 (m, 2H), 7.29–7.24 (m, 3H), 7.20–7.17 (m, 4H), 6.91–6.90 (m, 4H), 6.11–

6.09 (m, 1H), 4.94 (t, J = 10.7 Hz, 1H), 4.17–4.12 (m, 1H), 3.79–3.77 (m, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 161.1, 150.7, 145.5, 142.3, 136.9, 136.0, 129.5, 129.1, 129.0, 127.0, 125.2, 123.8, 123.5, 120.8, 120.0, 114.5, 110.1, 108.5, 69.9, 61.8, 55.5, 30.4; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{27}H_{24}N_2O_2]$ 409.1916, found 409.1908.

*(3R,11cS)-7-Methyl-5-(4-phenoxyphenyl)-3-phenyl-2,3,7,11c-tetrahydrooxazolo[3',2':1,2]pyrido [4,3-b]indole (**7m**).* The product was obtained as brown needles (202.3 mg, 86%): mp 130–134 °C; $[\alpha]_D^{31}$ = +130.4 (c 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.04 (s, 1H), 8.57–8.56 (m,1H), 7.37–7.33 (m, 4H), 7.28–7.20 (m, 2H), 7.18–7.09 (m, 4H), 7.04–7.03 (d, J = 8.4 Hz, 3H), 6.96–6.93 (m, 4H), 6.11–6.08 (m, 1H), 4.96 (t, J = 13 Hz, 1H), 4.17–4.13 (m, 1H), 3.77 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 159.6, 155.5, 150.1, 145.3, 142.3, 136.9, 135.8, 130.1, 129.4, 129.2, 129.0, 127.2, 127.1, 124.6, 123.7, 123.4, 120.3, 120.1, 119.9, 110.1, 108.5, 70.1, 61.9, 30.4; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{32}H_{26}N_2O_2]$ 471.2073, found 471.2095.

*(3R,11cS)-7-Methyl-3-phenyl-5-(p-tolyl)-2,3,7,11c-tetrahydrooxazolo[3',2':1,2]pyrido[4,3-b]indole (**7n**).* The product was obtained as brown needles (164.8 mg, 84%): mp 113–117 °C; $[\alpha]_D^{31}$ = +217.8 (c 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 8.52 (d, J = 7.8 Hz, 1H), 7.51–7.38 (m, 2H), 7.35 (s, 1H), 7.31–7.09 (m, 7H), 6.93–6.91 (m, 3H), 6.07–6.05 (dd, J = 10.6, 3.2 Hz, 1H), 4.94 (t, J = 9.6 Hz, 1H), 4.15 (dd, J = 12.5, 3.7 Hz, 1H), 3.75 (s, 3H), 2.37 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 150.7, 145.3, 142.3, 140.8, 136.5, 135.8, 130.2, 129.6, 129.4, 129.1, 129.0, 127.1, 126.9, 123.5, 123.4, 120.3, 120.1, 110.1, 108.3, 69.8, 61.8, 30.3, 21.4; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{27}H_{24}N_2O]$ 393.1967, found 393.1953.

*(3R,11cS)-5-(4-Butylphenyl)-7-methyl-3-phenyl-2,3,7,11c-tetrahydrooxazolo[3',2':1,2] pyrido[4,3-b]indole. (**7o**).* The product was obtained as brown needles (178.2 mg, 82%): mp 84–

87 °C; $[\alpha]_D^{31}$ = +78.2 (c 0.1, $CHCl_3$): ^1H NMR (400 MHz, $CDCl_3$) δ 9.97 (s, 1H), 8.51 (d, J = 7.6 Hz, 1H), 7.40–7.36 (m, 2H), 7.30–7.27 (m, 3H), 7.24–7.06 (m, 6H), 6.90–6.89 (m, 2H), 6.05 (dd, J = 9.92, 3.80 Hz, 1H), 4.92 (t, J = 12.2 Hz, 1H), 4.12 (dd, J = 13.72, 4.56 Hz, 1H), 3.73 (s, 3H), 2.62 (t, J = 7.6 Hz, 2H), 1.59 (m, 2H), 1.34 (sext, J = 7.6 Hz, 2H), 0.90 (t, J = 7.3 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.7, 151.0, 145.9, 145.5, 142.5, 139.5, 136.3, 135.8, 130.3, 129.6, 129.1, 129.0, 128.2, 127.1, 126.7, 123.6, 123.4, 120.4, 120.2, 110.2, 108.3, 69.9, 61.9, 35.4, 33.3, 30.2, 22.3, 13.9; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{30}H_{30}N_2O]$ 435.2437, found 435.2439.

*(3R,11cS)-7-Methyl-3-phenyl-5-(m-tolyl)-2,3,7,11c-tetrahydrooxazolo[3',2':1,2]pyrido[4,3-b]indole (**7p**).* The product was obtained as brown needles (158.9 mg, 81%): mp 118–122 °C; $[\alpha]_D^{31}$ = +92.33 (c 0.1, $CHCl_3$): ^1H NMR (400 MHz, $CDCl_3$) δ 10.12 (s, 1H), 8.67 (d, J = 5.2 Hz, 1H), 7.60–7.52 (m, 2H), 7.42–7.35 (m, 2H), 7.31–7.30 (m, 2H), 7.24–7.21 (m, 2H), 7.91 (brs, 2H), 6.77–6.68 (m, 1H), 6.02 (s, 1H), 4.96–4.90 (m, 1H), 4.15–4.11 (m, 1H), 3.84 (s, 3H), 2.13 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 150.8, 145.5, 142.5, 137.0, 129.7, 129.1, 129.0, 128.6, 127.0, 126.5, 123.9, 123.7, 120.6, 120.3, 110.1, 108.2, 70.2, 61.8, 30.3, 21.4; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{27}H_{24}N_2O]$ 393.1967, found 393.1963.

7-Methyl-5-(phenanthren-9-yl)-3-phenyl-2,3,7,11c-tetrahydrooxazolo[3',2':1,2]pyrido[4,3-b]indole (dr=54:46) *(**7q** + **7q'**).* The product was obtained as a brown needles (186.6 mg, 78%): mp 165–169 °C; $[\alpha]_D^{31}$ = +75.6 (c 0.05, $CHCl_3$): ^1H NMR (400 MHz, $CDCl_3$) δ 10.70–10.69 (m, 1H, minor), 9.94 (s, 1H, major), 9.07–9.05 (m, 1H, major), 8.70–8.66 [m, 4H, including 2H (major) + 2H (minor)], 8.56–8.55 (m, 1H, minor), 8.40 (s, 1H, major), 8.03–8.01 (m, 1H, minor), 7.73–7.37 [m, 18H, including 9H (major) + 9H (minor)], 7.23–7.19 (m, 1H, major), 7.13–6.99 [m, 7H, including 3H (major) + 4H (minor)], 6.90–6.83 [m, 2H, including 1H (major) + 1H

(minor)], 6.56–6.54 [m, 2H, including 1H (major) + 1H (minor)], 5.85–5.83 (m, 1H, minor), 5.53–5.51 (m, 1H, major), 4.93–4.88 (m, 1H, major), 4.70–4.65 (m, 1H, minor), 4.10–4.04 (m, 1H, major), 3.84–3.76 [m, 7H, including 3H (major) + 4H (minor)]; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 149.2 (minor), 148.8 (major), 145.8 (major), 145.7 (minor), 142.7 (minor), 142.6 (major), 138.3 (minor), 137.5 (major), 136.0 (major), 135.2 (minor), 131.6 (major), 131.3 (minor), 130.9 (minor), 130.8 (major), 130.3 (major), 130.2 (minor), 130.1 (major), 129.9 (major), 129.80 (major), 129.77 (minor), 129.20 (minor), 129.15 (major), 129.0 (minor), 128.9 (major), 128.8 (major + minor), 128.72 (minor), 128.67 (major), 128.4 (major + minor), 128.3 (minor), 128.2 (major), 128.1 (major + minor), 127.7 (minor), 127.5 (major), 127.4 (major), 127.0 (minor), 126.6 (major + minor), 125.5 (major), 125.3 (minor), 124.1 (minor), 123.7 (major), 123.6 (major + minor), 123.2 (major + minor), 122.8 (major), 122.5 (minor), 121.1 (minor), 120.9 (major), 120.7 (minor), 120.5 (major), 110.4 (minor), 110.1 (major), 109.4 (major + minor), 109.33 (major), 109.29 (minor), 70.5 (major), 70.2 (minor), 61.9 (minor), 61.5 (major), 30.4 (major + minor); HRMS (ESI) $[M+H]^+$ Calcd for $[C_{34}H_{26}N_2O]$ 479.2123, found 479.2121.

*(3R,11cS)-5-Cyclopropyl-7-methyl-3-phenyl-2,3,7,11c-tetrahydrooxazolo[3',2':1,2]pyrido[4,3-b]indole (**7r**).* The product was obtained as a yellow semi-solid (119.9 mg, 70%); $[\alpha]_D^{31}$ = +110.6 (c 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.71 (s, 1H), 8.37 (d, J = 7.6 Hz, 1H), 7.49 (s, 1H), 7.42 (t, J = 7.6 Hz, 1H), 7.35–7.13 (m, 7H), 6.82–6.78 (m, 1H), 4.78 (t, J = 12.2 Hz, 1H), 4.45–4.41 (m, 1H), 3.78 (s, 3H), 1.34–1.16 (m, 5H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 152.6, 146.2, 142.3, 136.6, 135.6, 129.4, 129.0, 126.8, 123.3, 123.0, 120.0, 119.0, 110.0, 106.0, 68.9, 62.9, 30.3, 14.9, 8.8, 8.3; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{23}H_{22}N_2O]$ 343.1810, found 343.1814.

*(3R,11cS)-5-Cyclohexyl-7-methyl-3-phenyl-2,3,7,11c-tetrahydrooxazolo[3',2':1,2]pyrido[4,3-b]indole (**7s**).* The product was obtained as a yellow semi-solid (125.0 mg, 65%); $[\alpha]_D^{31}$ = +114.9 (c 0.1, $CHCl_3$): ^1H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H), 8.36 (d, J = 7.6 Hz, 1H), 7.49–7.45 (m, 2H), 7.33 (d, J = 7.6 Hz, 1H), 7.29–7.23 (m, 4H), 7.04–7.02 (m, 2H), 6.33–6.29 (m, 1H), 4.75–4.71 (m, 1H), 4.40–4.36 (m, 1H), 3.82 (m, 3H), 2.25–2.18 (m, 1H), 1.86–1.80 (m, 2H), 1.70–1.68 (m, 3H), 1.54–1.37 (m, 5H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 157.6, 146.3, 142.4, 136.0, 129.53, 129.46, 129.3, 129.13, 129.07, 128.9, 126.4, 125.0, 123.5, 123.1, 120.4, 119.3, 110.0, 104.5, 70.6, 62.9, 40.6, 34.1, 30.1, 26.4, 26.3, 25.4; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{26}H_{28}N_2O]$ 385.2280, found 385.2271.

*(3R,11cS)-5-Butyl-7-methyl-3-phenyl-2,3,7,11c-tetrahydrooxazolo[3',2':1,2]pyrido[4,3-b]indole (**7t**).* The product was obtained as a red oily (111.1 mg, 62%); $[\alpha]_D^{31}$ = +140.6 (c 0.1, $CHCl_3$): ^1H NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1H), 8.41–8.39 (m, 1H), 7.51 (s, 1H), 7.45 (t, J = 6.9 Hz, 1H), 7.31–7.24 (m, 5H), 7.09–7.07 (m, 2H), 6.28–6.26 (m, 1H), 4.77–4.71 (m, 1H), 4.39–4.36 (m, 1H), 3.77 (s, 3H), 1.80–1.75 (m, 1H), 1.59–1.53 (m, 1H), 1.40 (sext, J = 7.6 Hz, 2H), 1.22–1.16 (m, 2H), 0.87 (t, J = 6.9 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 152.8, 146.1, 142.3, 136.4, 135.5, 129.4, 129.0, 128.6, 128.5, 128.4, 126.9, 126.6, 123.3, 123.1, 120.2, 119.3, 110.1, 106.5, 68.8, 62.8, 33.1, 31.0, 30.3, 22.4, 13.6; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{24}H_{26}N_2O]$ 359.2123, found 359.2142.

*(3R,11cS)-5-(3-Methoxyphenyl)-7-methyl-3-phenyl-2,3,7,11c-tetrahydrooxazolo[3',2':1,2]pyrido[4,3-b]indole (**7u**).* The product was obtained as a brown needles (138.9 mg, 68%);%): mp 154–159 °C $[\alpha]_D^{31}$ = +109.1 (c 0.1, $CHCl_3$): ^1H NMR (400 MHz, $CDCl_3$) δ 10.12–9.97 (m, 1H), 8.62–8.52 (m, 1H), 7.52–7.46 (m, 3H), 7.40–7.38 (m, 2H), 7.33 (t, J = 7.6 Hz, 2H), 7.26–7.24 (m, 3H), 7.09–7.03 (m, 2H), 6.94 (s. 1H), 6.07 (s, 1H), 4.96 (t, J = 9.9 Hz, 1H), 4.21–4.14 (m, 1H),

3.85 (s, 3H), 3.63 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 161.1, 150.7, 145.5, 142.5, 136.9, 135.9, 129.5, 129.1, 129.0, 127.0, 125.2, 123.8, 123.5, 120.5, 120.1, 114.4, 110.1, 108.5, 69.9, 61.8, 55.5, 30.4; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{27}H_{24}N_2O_2]$ 409.1916, found 409.1908.

*(3R,11cS)-7-Methyl-3-phenyl-5-(4-(trifluoromethyl)phenyl)-2,3,7,11c-tetrahydrooxazolo [3',2':1,2]pyrido[4,3-b]indole (**7v**).* The product was obtained as off-white needles (133.9 mg, 60%); %): mp 152–156 °C $[\alpha]_D^{31}$ = +123.1 (c 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.10 (s, 1H), 8.62 (d, J = 8.4 Hz, 1H), 8.27–8.12 (m, 1H), 7.84–7.60 (m, 2H), 7.54–7.50 (m, 2H), 7.40–7.32 (m, 2H), 7.24–7.17 (m, 4H), 6.94–6.92 (m, 2H), 5.97 (dd, J = 9.9, 3.8 Hz, 1H), 4.92 (t, J = 9.9 Hz, 1H), 4.14 (dd, J = 13.8, 4.6 Hz, 1H), 3.85 (3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 154.0, 150.7, 145.2, 142.2, 136.6, 135.8, 130.2, 129.4, 129.04, 128.97, 128.6, 127.1, 126.9, 125.9 (q, $J_{C\text{-}F}$ = 2.8 Hz, 1C), 123.4, 123.3, 120.2, 120.1, 110.1, 108.2, 69.8, 61.8, 30.3; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{27}H_{21}F_3N_2O]$ 447.1684, found 447.1674.

*(3S,11cR)-3-Phenyl-5-(p-tolyl)-3,11c-dihydro-2H-benzofuro[3,2-c]oxazolo[3,2-a]pyridine (**8a**).* The product was obtained as pale yellow needles (163.2 mg, 86%): mp 110–114 °C; $[\alpha]_D^{31}$ = -315.0 (c 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.43 (s, 1H), 8.63 (d, J = 7.6 Hz, 1H), 7.71 (s, 1H), 7.59–7.57 (m, 2H), 7.49–7.45 (m, 2H), 7.28–7.23 (m, 5H), 7.03–6.93 (m, 3H), 6.14 (dd, J = 3.8, 9.1 Hz, 1H), 5.06 (t, J = 11.7 Hz, 1H), 4.13 (dd, J = 3.8, 12.9 Hz, 1H), 2.42 (s, 3H); $^{13}C\{^{1}H\}$ NMR (400 MHz, $CDCl_3$) δ 162.7, 157.9, 154.9, 141.7, 140.1, 134.9, 131.4, 129.5, 129.43, 129.35, 127.3, 126.2, 125.0, 124.6, 119.6, 112.5, 112.0, 71.7, 61.9, 21.5; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{26}H_{21}NO_2$ 380.1651, found 380.1673.

3-Phenyl-5-(o-tolyl)-3,11c-dihydro-2H-benzofuro[3,2-c]oxazolo[3,2-a]pyridine (dr = 55:45) ***(8b + 8b').*** The product was obtained as a yellow needles (155.6 mg, 82%): mp 156–159 °C; $[\alpha]_D^{31}$ =

-310.6 (c 0.05, $CHCl_3$): ^1H NMR (400 MHz, $CDCl_3$) δ 11.01 (s, 1H, major), 10.9 (s, 1H, minor), 8.96–8.94 (m, 1H, major), 8.83–8.81 (m, 1H, minor), 7.68–7.64 [m, 2H, including 1H (major) + 1H (minor)], 7.60–7.56 [m, 2H, including 1H (major) + 1H (minor)], 7.48–7.36 [m, 6H, including 3H (major) + 3H (minor)], 7.21–7.06 [m, 10H, including 5H (major) + 5H (minor)], 6.88–6.77 [m, 5H, including 2H (major) + 3H (minor)], 6.52–6.52 (m, 1H, major), 6.04–6.00 (m, 1H, major), 5.61–5.57 (m, 1H, minor), 5.13–5.04 (m, 2H, including 1H (major) + 1H (minor)], 4.03–3.90 [m, 2H, including 1H (major) + 1H (minor)], 2.18 [s, 6H, including 3H (major)+ 3H (minor)]; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.9 (major), 162.5 (minor), 157.9 (major), 157.8 (minor), 154.2 (major), 153.8 (minor), 140.7 (minor), 140.6 (major), 136.7 (minor), 136.4 (major), 133.9 (major, 133.5 (minor), 131.44 (minor), 131.35 (major), 131.31 (major), 131.28 (minor), 131.24 (major), 131.20 (minor), 131.1 (major), 130.9 (minor), 129.8 (major), 129.5 (minor), 129.4 (major), 129.3 (minor), 129.11 (major), 129.06 (minor), 127.7 (minor), 126.9 (major), 126.8 (major), 126.2 (minor), 126.0 (major), 125.9 (minor), 125.8 (major), 125.4 (minor), 124.7 (minor), 124.6 (major), 119.7 (major), 119.6 (minor), 112.7 (minor), 112.4 (major), 111.9 (major + minor), 73.3 (major), 72.6 (minor), 61.9 (minor), 61.7 (major), 19.8 (major), 19.1 (minor); HRMS (ESI) $[M+H]^+$ Calcd for $[C_{26}H_{21}NO_2]$ 380.1651, found 380.1673.

*(3S,11cR)-3-Phenyl-5-(thiophen-3-yl)-3,11c-dihydro-2H-benzofuro[3,2-c]oxazolo[3,2-a]pyridine (**8c**).* The product was obtained as pale yellow needles (165.3 mg, 89%): mp 107–111 °C; $[\alpha]_D^{31}$ = -330.2 (c 0.1, $CHCl_3$): ^1H NMR (400 MHz, $CDCl_3$) δ 10.56 (s, 1H), 8.66 (d J = 6.8 Hz, 1H), 7.79–7.76 (m, 2H), 7.59–7.54 (m, 3H), 7.43–7.39 (m, 1H), 7.35–7.34 (m, 1H), 7.26–7.24 (m, 3H), 7.07–7.05 (m, 2H), 6.31–6.28 (m, 1H), 5.11 (t, J = 11.44 Hz, 1H), 4.23–4.19 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.5, 157.8, 150.2, 140.5, 134.8, 131.9, 131.3, 129.9,

129.5, 129.4, 128.4, 128.2, 127.2, 126.0, 125.1, 124.5, 119.5, 112.6, 111.9, 72.0, 62.1; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{23}H_{17}NO_2S]$ 372.1058, found 372.1071.

5-(3-Methoxyphenyl)-3-phenyl-3,11c-dihydro-2H-benzofuro[3,2-c]oxazolo[3,2-a]pyridine (dr = 53:47) ***(8d + 8d')***. The product was obtained as a yellow needles (138.4 mg, 70%): mp 97–101 °C; $[\alpha]_D^{31}$ = -310.1 (c 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.68 (s, 1H, minor), 10.51 (s, 1H, major), 8.66 (d, J = 7.6 Hz, 1H), 7.71 [s, 2H, including 1H (major) + 1H (minor)], 7.56–7.29 [m, 10H, including 5H (major) + 5H (minor)], 7.22–7.15 [m, 6H, including 3H (major) + 3H (minor)], 7.10–7.00 [m, 6H, including 3H (major) + 3H (minor)], 6.63 (d, J = 6.9 Hz, 1H, minor), 6.41 [s, 1H, major), 6.14 (s, 2H, including 1H (major) + 1H (minor)], 5.09 [t, J = 11.4 Hz, 2H, including 1H (major) + 1H (minor)], 4.13 [t, J = 12.2 Hz, 2H, including 1H (major) + 1H (minor)], 3.86 (s, 3H, major), 3.60 (s, 3H, minor); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.6 (major + minor), 160.0 (minor), 157.8 (major + minor), 154.3 (major), 140.5 (minor), 140.2 (major), 134.9 (major + minor), 131.3 (major + minor), 130.1 (major), 129.5 (minor), 129.4 (major + minor), 127.44 (major), 127.35 (major + minor), 127.2 (minor), 126.04 (minor), 125.98 (major), 125.4 (minor), 125.1 (major), 124.7 (major + minor), 122.0 (minor), 121.0 (major), 119.6 (major + minor), 118.0 (major), 116.6 (minor), 114.8 (major + minor), 112.4 (minor), 112.3 (major), 111.9 (major + minor), 72.2 (major), 71.8 (minor), 62.0 (major + minor), 55.9 (major), 55.3 (minor), 31.6 (minor), 31.3 (major); HRMS (ESI) $[M+H]^+$ Calcd for $[C_{26}H_{21}NO_3]$ 396.1600, found 396.1601.

(3R,11cS)-3,5-Diphenyl-3,11c-dihydro-2H-benzofuro[3,2-c]oxazolo[3,2-a]pyridine ***(8e).*** The product was obtained as pale yellow crystals (135.2 mg, 74%): mp 112–116 °C; $[\alpha]_D^{31}$ = +280.9 (c 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.66 (s, 1H), 8.77 (d, J = 12.4 Hz, 1H), 7.91 (s, 1H), 7.71 (s, 1H), 7.60–7.54 (m, 4H), 7.47–7.39 (m, 2H), 7.22–7.16 (m, 3H), 6.99–6.97 (m, 3H),

6.13 (dd, *J* = 9.92, 3.84 Hz 1H), 5.13–5.07 (m, 1H), 4.10 (dd, *J* = 13.76, 4.6 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 162.7, 157.9, 154.5, 140.5, 134.8, 132.2, 131.3, 131.1, 129.5, 129.4, 129.0, 127.3, 126.0, 125.4, 124.7, 119.7, 112.5, 112.0, 72.1, 62.0; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{25}H_{19}NO_2]$ 366.1494, found 366.1510.

(3R,11cS)-5-(4-Methoxyphenyl)-3-phenyl-3,11c-dihydro-2H-benzofuro[3,2-c]oxazolo[3,2-a]pyridine ***(8f).*** The product was obtained as pale yellow needles (170.0 mg, 86%): mp 98–102 °C; $[\alpha]_D^{31}$ = +340.5 (c 0.1, $CHCl_3$): ^1H NMR (400 MHz, $CDCl_3$) δ 10.55 (s, 1H), 8.70 (d, *J* = 8.40 Hz, 1H), 7.69 (s, 1H), 7.59–7.54 (m, 2H), 7.46–7.42 (m, 1H), 7.23–7.20 (m, 5H), 7.01–6.99 (m, 4H), 6.20 (dd, *J* = 9.9, 3.8 Hz 1H), 5.11–5.06 (m, 1H), 4.14 (dd, *J* = 13.7, 4.6 Hz, 1H), 3.84 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 162.7, 161.6, 157.9, 154.8, 140.3, 135.0, 131.2, 129.5, 129.4, 127.3, 126.0, 125.2, 124.4, 124.2, 119.7, 114.7, 112.6, 111.9, 71.8, 61.9, 55.6; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{26}H_{21}NO_3]$ 396.1600, found 396.1620.

(3R,11cS)-3-Phenyl-5-(p-tolyl)-3,11c-dihydro-2H-benzofuro[3,2-c]oxazolo[3,2-a]pyridine ***(8g).*** The product was obtained as brown needles (161.3 mg, 85%): mp 123–127 °C; $[\alpha]_D^{31}$ = +320.3 (c 0.1, $CHCl_3$):^1H NMR (400 MHz, $CDCl_3$) δ 10.66 (s, 1H), 8.78 (d, *J* = 7.6 Hz, 1H), 7.70 (s, 1H), 7.59–7.58 (m, 2H), 7.49–7.44 (m, 2H), 7.25–7.20 (m, 5H), 7.06–7.04 (m, 3H), 6.18 (dd, *J* = 9.2, 3.8 Hz 1H), 5.16–5.11 (m, 1H), 4.14 (dd, *J* = 13.7, 4.6 Hz, 1H), 2.44 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 162.6, 157.8, 154.8, 141.6, 140.4, 140.4, 134.9, 131.2, 129.44, 129.39, 129.3, 127.3, 126.0, 125.4, 124.5, 119.7, 112.5, 111.9, 71.9, 61.9, 21.4; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{26}H_{21}NO_2]$ 380.1651, found 380.1675.

(3R,11cS)-5-(4-Ethylphenyl)-3-phenyl-3,11c-dihydro-2H-benzofuro[3,2-c]oxazolo[3,2-a]pyridine ***(8h)****.* The product was obtained as brown needles (161.3 mg, 82%): mp 138–142 °C;

$[\alpha]_D^{31}$ = +317.2 (c 0.1, $CHCl_3$):^{1}H NMR (400 MHz, $CDCl_3$) δ 10.66 (s, 1H), 8.79 (d, J = 12.4 Hz, 1H), 7.73 (s, 1H), 7.63–7.58 (m, 2H), 7.51–7.46 (m, 2H), 7.27–7.24 (m, 5H), 7.07–7.05 (m, 3H), 6.22 (dd, J = 9.92, 3.8 Hz 1H), 5.19–5.13 (m, 1H), 4.17 (dd, J = 9.92, 3.8 Hz, 1H), 2.76 (q, J = 7.6 Hz, 2H), 1.30 (t J = 9.9 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.6, 157.8, 154.9, 147.8, 140.3, 134.9, 131.2, 129.5, 129.4, 129.3, 128.9, 127.3, 126.0, 125.3, 124.5, 119.7, 112.4, 111.9, 71.9, 61.9, 28.7, 15.2; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{27}H_{23}NO_2]$ 394.1807, found 394.1821.

*(3R,11cS)-5-(4-Butylphenyl)-3-phenyl-3,11c-dihydro-2H-benzofuro[3,2-c]oxazolo[3,2-a]pyridine (**8i**)*. The product was obtained as brown needles (170.7 mg, 81%): mp 145–149 °C; $[\alpha]_D^{31}$ = +308.6 (c 0.1, $CHCl_3$):^{1}H NMR (400 MHz, $CDCl_3$) δ 10.62 (s, 1H), 8.74 (d, J = 7.64 Hz, 1H), 7.68 (s, 1H), 7.58–7.53 (m, 2H), 7.44–7.40 (m, 2H), 7.20–7.12 (m, 6H), 6.98–6.97 (m, 2H), 6.17 (dd, J = 10.0, 3.8 Hz 1H), 5.09 (t, J = 13.0 Hz 1H), 4.11 (dd, J = 13.7, 3.8 Hz, 1H), 2.65 (t, J = 7.6 Hz, 2H), 1.60 (quin, J = 7.6 Hz, 2H), 1.35 (sixet, J = 7.6 Hz, 2H), 0.90 (t, J = 7.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.6, 157.8, 154.9, 146.5, 140.3, 134.9, 131.2, 129.5, 129.4, 129.3, 128.2, 127.3, 126.6, 126.0, 125.3, 124.5, 119.7, 112.5, 111.9, 71.9, 61.9, 35.4, 33.3, 22.2, 13.9; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{29}H_{27}NO_2]$ 422.2120, found 422.2142.

3-Phenyl-5-(o-tolyl)-3,11c-dihydro-2H-benzofuro[3,2-c]oxazolo[3,2-a]pyridine (dr=55:45) ***(8j + 8j').*** The product was obtained as a yellow needles (151.8 mg, 80%): mp 155–159 °C; $[\alpha]_D^{31}$ = +312.6 (c 0.05, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.87 (s, 1H, minor), 10.82 (s, 1H, major), 8.83–8.77 [m, 2H, including 1H (major) + 1H (minor)], 8.57–8.51 [m, 2H, including 1H (major) + 1H (minor)], 7.97–7.93 [t, J = 8.7 Hz, 2H, including 1H (major) + 1H (minor)], 7.80–7.75 [m, 2H, including 1H (major) + 1H (minor)], 7.67–7.61 [m, 2H, including 1H (major) + 1H (minor)], 7.57–7.47 [m, 2H, including 1H (major) + 1H (minor)], 7.35–7.21 [m, 8H, including

4H (major) + 4H (minor)], 7.14–7.12 (m, 1H, major), 7.08–7.06 (m, 1H, minor), 6.96–6.94 (m, 1H, major), 6.83 (d, J = 7.8 Hz, minor), 6.21 (t, J = 5.0 Hz, 1H, minor), 6.14 (t, J = 5.0 Hz, 1H, major), 5.96–5.92 (m, 1H, major), 5.60–5.57 (m, 1H, minor), 4.76–4.67 [m, 2H, including 1H (major) + 1H (minor)], 4.13–4.08 [m, 2H, including 1H (major) + 1H (minor)], 2.46 (s, 3H, minor), 2.24 (m, 3H, major); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 163.0 (major), 162.6 (minor), 158.0 (major), 157.9 (minor), 154.2 (major), 153.8 (minor), 141.1 (minor), 140.9 (major), 136.8 (minor), 136.4 (major), 134.0 (minor), 133.6 (major), 131.50 (minor), 131.47 (major), 131.4 (major), 131.3 (minor), 131.1 (minor), 131.0 (major), 129.8 (major), 129.6 (minor), 129.42 (major), 129.38 (minor), 129.2 (minor), 129.1 (major), 127.7 (major + minor), 126.9 (minor), 126.8 (major), 126.3 (minor), 126.11 (major), 126.06 (minor), 126.0 (minor), 125.6 (major + minor), 124.8 (minor), 124.6 (major), 119.8 (major), 119.7 (minor), 112.8 (major), 112.4 (minor), 111.92 (minor), 111.90 (major), 73.4 (major), 72.7 (minor), 61.8 (major), 61.7 (minor), 19.9 (major), 19.1 (minor); HRMS (ESI) $[M+H]^+$ Calcd for $[C_{26}H_{21}NO_2]$ 380.1651, found 380.1673.

*(3R,11cS)-3-Phenyl-5-(thiophen-3-yl)-3,11c-dihydro-2H-benzofuro[3,2-c]oxazolo[3,2-a]pyridine (**8k**).* The product was obtained as yellow needles (163.4 mg, 88%): mp 105–109 °C; $[\alpha]_D^{31}$ = +328.5 (c 0.1, $CHCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.56 (s, 1H), 8.68 (d, J = 7.6 Hz, 1H), 7.79–7.74 (m, 2H), 7.59–7.46 (m, 3H), 7.42–7.39 (m, 1H), 7.35–7.29 (m, 2H), 7.25–7.16 (m, 1H), 7.04–7.03 (m, 2H), 6.83 (s, 1H), 6.30 (dd, J = 10.0, 3.8 Hz 1H), 5.14–5.08 (m, 1H), 4.22 (dd, J = 13.0, 3.8 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 162.5, 157.8, 150.1, 140.4, 134.8, 131.8, 131.4, 130.0, 129.5, 129.4, 129.0, 128.4, 128.2, 127.1, 126.0, 125.1, 124.5, 119.5, 112.7, 112.0, 72.0, 62.0; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{23}H_{17}NO_2S]$ 372.1058, found 372.1071.

(3R,11cS)-5-Cyclohexyl-3-phenyl-3,11c-dihydro-2H-benzofuro[3,2-c]oxazolo[3,2-a]pyridine ***(8l).*** The product was obtained as red oily (128.2 mg, 69%): $[\alpha]_D^{31}$ = +278.1 (c 0.1, $CHCl_3$): ^1H NMR (400 MHz, $CDCl_3$) δ 10.38 (s, 1H), 8.65 (s, 1H), 7.75 (s, 1H), 7.57–7.52 (m, 2H), 7.42–7.38 (m, 1H), 7.30–7.26 (m, 3H), 7.14–7.12 (m, 2H), 6.49 (s, 1H), 4.93–4.88 (m, 1H), 4.40–4.32 (m,1H), 2.36–2.26 (m, 1H), 1.97–1.86 (m, 2H), 1.73–1.66 (m, 2H), 1.54–1.47 (m, 4H), 1.37–1.32 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.6, 162.1, 157.6, 135.0, 130.1, 129.6, 129.4, 126.6, 126.0, 123.1, 119.6, 111.8, 109.0, 70.5, 62.7, 41.0, 33.8, 33.4, 26.2, 26.0, 25.3; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{25}H_{25}NO_2]$ 372.1964, found 372.1973.

*(3R,11cS)-5-(3,5-Dimethoxyphenyl)-3-phenyl-3,11c-dihydro-2H-benzofuro[3,2-c]oxazolo[3,2-a]pyridine (****8m****).* The product was obtained as yellow needles (131.9 mg, 62%): mp 102–106 °C; $[\alpha]_D^{31}$ = +317.0 (c 0.1, $CHCl_3$): ^1H NMR (400 MHz, $CDCl_3$) δ 10.59 (s, 1H), 8.72 (d, J = 7.6 Hz, 1H), 7.72 (s, 1H), 7.58–7.56 (m, 2H), 7.44–7.41 (m, 1H), 7.28–7.22 (m, 3H), 7.15–7.07 (m, 4H), 6.58 (s, 1H), 6.16 (dd, J = 9.9, 3.8 Hz 1H), 6.10 (s, 1H), 5.10 (t, J = 13.0 Hz, 1H), 4.15 (dd, J = 13.0, 3.8 Hz, 1H), 3.84 (s, 3H), 3.60 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.5, 161.3, 160.7, 157.8, 154.3, 140.4, 135.1, 133.6, 131.2, 129.4, 129.3, 127.4, 126.0, 125.3, 124.6, 119.6, 112.2, 111.9, 107.9, 107.3, 103.0, 72.0, 62.0, 56.1, 55.4; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{27}H_{23}NO_4]$ 426.1705, found 426.1715.

*(3R,11cS)-3-Phenyl-5-(4-(trifluoromethyl)phenyl)-3,11c-dihydro-2H-benzofuro[3,2-c]oxazolo[3,2-a]pyridine (****8n****).* The product was obtained as yellow needles (130.0 mg, 60%): mp 122–126 °C; $[\alpha]_D^{31}$ = +335.1 (c 0.1, $CHCl_3$): ^1H NMR (400 MHz, $CDCl_3$) δ 10.70 (s, 1H), 8.74 (d, J = 7.6 Hz, 1H), 8.25 (s, 1H), 7.86 (s, 1H), 7.70 (s, 1H), 7.65–7.63 (m, 1H), 7.57–7.52 (m, 2H), 7.41–7.37 (m, 1H), 7.23–7.16 (m, 4H), 7.04–7.03 (m, 2H), 6.98 (dd, J = 10.0, 3.8 Hz, 1H), 5.08–5.02 (m, 1H), 4.04 (dd, J = 13.0, 3.8 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ

162.6, 157.9, 152.7, 140.8, 135.7, 134.5, 133.2, 133.0, 131.5, 131.4, 129.7, 129.5, 127.4, 126.5 (q, $J_{C\text{-}F}$ = 4.7 Hz, 1C), 126.0, 125.7, 125.4, 125.1, 124.6, 121.9, 119.5, 112.5, 112.0, 72.6, 62.4; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{26}H_{18}F_3NO_2]$ 434.1368, found 434.1381.

Procedure for the Synthesis of Compound 9 and 10. To a solution of 0.5 mmol of *o*-alkynyl aldehyde **4** and **5** in 2.0 mL DCE, was added 0.55 mmol of amine **6a**–**b** and 0.6 mmol of Et_3N followed by the addition of 10 mol % of $AuCl_3$. The reaction mixture was allowed to stir at 80 °C for 6 h (for compound **9**) and 24 h (for compound **10**). The disappearance of the starting material was determined by TLC. The reaction mixture was then washed with brine solution and was extracted with ethyl acetate (2 x 10 mL). The combined organic fractions were dried over anhydrous Na_2SO_4 and concentrated under vacuum to yield the crude product. The crude product was purified by column chromatography on neutral alumina/silica gel using ethylacetate/hexane as the eluent. The structure and purity of the known compounds**9a**[31a] and **10a-c**[6a] were confirmed by comparison of their physical and spectral data (^{1}H NMR and ^{13}C NMR) with those reported in literature.

5-Methyl-3-phenyl-5H-pyrido[4,3-b]indole (**9a**). This compound was obtained as a yellow crystals (107.2 mg, 83%), mp 95–99 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.25 (s, 1H), 8.06 (d, J = 7.3 Hz, 1H), 8.02–8.00 (m, 2H), 7.57 (s, 1H), 7.46–7.39 (m, 3H), 7.34–7.31 (m, 2H), 7.26–7.22 (m, 1H), 3.76 (s, 3H).

*3-(4-Methoxyphenyl)-5-methyl-5H-pyrido[4,3-b]indole (**9b**)*. This compound was obtained as a yellow solid (125.3 mg, 87%), mp 115–119 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.27 (s, 1H), 8.10 (d, J = 7.9 Hz, 1H), 8.02 (d, J = 8.6 Hz, 2H), 7.54 (s, 1H), 7.49 (t, J = 7.9 Hz, 1H), 7.37 (d, J = 8.6 Hz, 1H), 7.29 (t, J = 8.0 Hz, 1H), 7.01–6.98 (m, 2H), 3.84 (s, 3H), 3.80 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 160.0, 153.1, 146.1, 141.96, 141.3, 133.0, 128.3, 126.4, 121.3,

120.45, 120.43, 118.1, 114.0, 108.7, 99.6, 55.3, 28.9; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{19}H_{16}N_2O]$: 289.1341, found 289.1363.

*5-Methyl-3-(p-tolyl)-5H-pyrido[4,3-b]indole (**9c**)* The product was obtained as brown solid (115.7 mg, 85%): mp 116–118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.29 (s, 1H), 8.11 (d, J = 7.9 Hz, 1H), 7.97 (d, J = 7.9 Hz, 2H), 7.58 (s, 1H), 7.49 (t, J= 7.4 Hz, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.31–7.27 (m, 3H), 3.79 (s, 3H), 2.41 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 153.5, 146.1, 142.1, 141.4, 138.2, 137.7, 129.4, 127.0, 126.5, 121.3, 120.5, 120.4, 118.4, 108.8, 100.1, 29.0, 21.2; HRMS (ESI) $[M]^+$calcd for $[C_{19}H_{16}N_2]$ 272.1313, found 272.1313.

*3-(4-Butylphenyl)-5-methyl-5H-pyrido[4,3-b]indole. (**9d**)* The product was obtained as brown solid (132.0 mg, 84%): mp 116–118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.21 (s, 1H), 8.02–8.01 (m, 1H), 7.91–7.89 (m, 2H), 7.50 (s, 1H), 7.43–7.39 (m, 1H), 7.29–7.27 (m, 1H), 7.22–7.16 (m, 3H), 3.71 (s, 3H), 2.58 (t, J = 7.9 Hz, 2H), 1.60–1.52 (m, 2H), 1.35–1.25 (m, 2H), 0.86 (t, J = 7.3 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 153.4, 146.1, 143.4, 141.9, 141.4, 137.6, 128.8, 127.0, 126.6, 121.2, 120.5, 118.4, 108.8, 100.2, 35.3, 33.5, 29.0, 22.3; HRMS (ESI) $[M]^+$ calcd for $[C_{22}H_{22}N_2]$ 314.1783, found $[M]^+$ 314.1783.

*5-Methyl-3-(thiophen-3-yl)-5H-pyrido[4,3-b]indole (**9e**).* This compound was obtained as a brown needles (116.3 mg, 88 %), mp 130–134 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.24 (s, 1H), 8.11 (d, J = 7.9 Hz, 1H), 7.96 (d, J = 2.4 Hz, 1H), 7.74–7.72 (m, 1H), 7.53–7.48 (m, 2H), 7.41–7.38 (m, 2H), 7.30 (t, J = 7.3 Hz, 1H), 3.82 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 149.2, 146.0, 141.9, 141.5, 126.7, 126.3, 126.2, 123.0, 121.3, 120.7, 120.6, 118.4, 108.9, 100.2, 29.1; HRMS (ESI) :$[M]^+$ Calcd for $[C_{16}H_{12}N_2S]$ 264.0721, found 264.0721.

*3-Cyclopropyl-5-methyl-5H-pyrido[4,3-b]indole (**9f**):* This compound was obtained as a yellow solid (83.4 mg, 75 %), mp 122–126 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.01 (s, 1H), 7.97 (d, J = 7.9 Hz, 1H), 7.40–7.36 (m, 1H), 7.27 (d, J = 8.6 Hz, 1H), 7.20–7.17 (m, 1H), 6.98 (s, 1H), 3.6 (s, 3H), 2.14–2.07 (m, 1H), 1.05–1.01 (m, 2H), 0.97–0.92 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 158.4, 145.9, 141.7, 141.1, 126.2, 121.5, 120.3, 120.2, 117.8, 108.9, 100.4, 28.9, 17.8, 9.7; HRMS (ESI) :$[M+H]^+$ Calcd for $[C_{15}H_{14}N_2]$ 223.1235, found : 223.1235.

*5-Methyl-3-phenethyl-5H-pyrido[4,3-b]indole (**9g**)*. The product was obtained as brownish yellow solid (103.1 mg, 72%): mp 112–116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.17 (s, 1H), 8.03 (d, J = 7.3 Hz, 1H), 7.45–7.41 (m, 1H), 7.32 (d, J = 8.0 Hz, 1H), 7.23 (d, J = 7.3 Hz, 1H), 3.68 (s, 3H), 3.21–3.17 (m, 2H), 3.10–3.06 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 156.4, 145.9, 141.7, 141.4, 141.1, 128.5, 128.3, 126.5, 125.9, 121.3, 120.53, 120.47, 108.8, 102.6, 40.6, 36.6, 29.0; HRMS (ESI) $[M+H]^+$ calcd for $[C_{20}H_{18}N_2]$ 287.1548, found 287.1524

*3-Butyl-5-methyl-5H-pyrido[4,3-b]indole (**9h**)*. This compound was obtained as a yellow solid (83.4 mg, 70%), mp 115–119 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.11 (s, 1H), 8.01 (d, J = 7.92 Hz, 1H), 7.41 (t, J = 8.0 Hz, 1H), 7.31 (d, J = 7.9 Hz, 1H), 7.23–7.18 (m, 1H), 7.04 (s, 1H), 3.72 (s, 3H), 2.88 (t, J = 7.6 Hz, 2H), 1.75–1.68 (m, 2H), 1.38–1.33 (m, 2H), 0.89 (t, J = 7.32 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 158.1, 146.0, 141.7, 141.1, 126.2, 121.4, 120.4, 120.3, 117.7, 108.7, 102.1, 38.7, 32.6, 28.9, 22.6, 14.0; HRMS (ESI) $[M+H]^+$ Calcd for $[C_{16}H_{18}N_2]$ 239.1548, found 239.1537.

*5-Methyl-3-(4-(trifluoromethyl)phenyl)-5H-pyrido[4,3-b]indole (**9i**)*. This compound was obtained as a brown needles (117.5 mg, 65 %), mp 124–128 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.33 (s, 1H), 8.20–8.14 (m, 3H), 7.72 (d, J = 8.0 Hz, 2H), 7.67 (s, 1H), 7.56–7.52 (m, 1H), 7.43

(d, J = 8.0 Hz, 1H), 7.33 (t, J = 6.7 Hz, 1H), 3.8 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 151.8, 145.9, 143.8, 142.4, 141.6, 127.4, 127.0, 125.6 (q, J_{C-F} = 3.8 Hz, 1C), 121.1, 120.8, 119.2, 109.0, 101.0, 29.2; HRMS (ESI) :$[M]^+$ Calcd for $[C_{19}H_{13}F_3N_2]$ 326.1031, found 326.1030.

3-(p-Tolyl)benzofuro[3,2-c]pyridine (**10a**). The product was obtained as a yellow needles (93.3 mg, 72%): mp 144–148 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.28 (s, 1H), 8.02 (d, J = 7.6 Hz, 1H), 7.97–7.95 (m, 2H), 7.87 (s, 1H), 7.61–7.59 (m, 1H), 7.55–7.49 (m, 1H), 7.43–7.39 (m, 1H), 7.31 (d, J = 7.6 Hz, 2H), 2.42 (s, 3H).

3-(Thiophen-3-yl)benzofuro[3,2-c]pyridine (**10b**). The product was obtained as a yellow needles (94.2 mg, 75%): mp 133–137 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.1 (s, 1H), 7.95–7.92 (m, 2H), 7.72 (s, 1H), 7.65 (d, J = 5.3 Hz 1H), 7.54–7.53 (m, 1H), 7.44 (t, J = 7.6 Hz, 1H), 7.37–7.34 (m, 2H).

3-Cyclohexylbenzofuro[3,2-c]pyridine (**10c**). The product was obtained as a yellow oil (82.9 mg, 66%); ^1H NMR (400 MHz, $CDCl_3$) δ 9.07 (s, 1H), 7.91 (d, J = 7.6 Hz, 1H), 7.52–7.50 (m, 1H), 7.45– 7.39 (m, 1H), 7.33–7.29 (m, 2H), 2.84–2.78 (m, 1H), 1.99–1.95 (m, 2H), 1.84–1.80 (m, 2H), 1.72–1.69 (m, 1H), 1.56–1.43 (m, 2H), 1.41–1.34 (m, 2H), 1.29–1.17 (m, 1H).

ASSOCIATED CONTENT

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Notes

The authors declare no competing financial interest.

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Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.-

^{1}H NMR, ^{13}C NMR and HRMS spectra (PDF)

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