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On Water: Silver-Catalyzed Domino Approach for the Synthesis of Benzoxazine/Oxazine Fused Isoquinolines and Naphthyridines from *ortho*-Alkynylaldehydes

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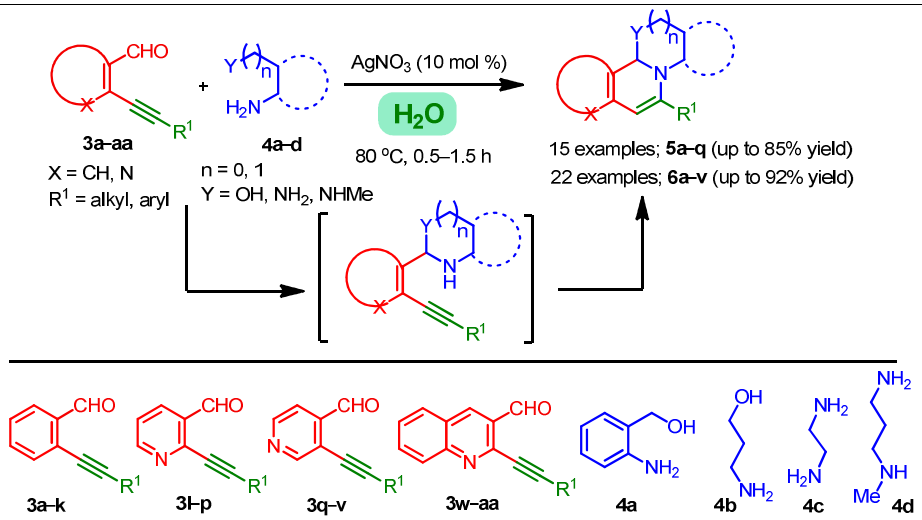


ABSTRACT: An operationally simple domino approach for the silver-catalyzed synthesis of oxazine/benzoxazine fused isoquinolines **5a–q** and naphthyridines **6a–v** by the reaction of *ortho*-alkynylaldehydes **3a–aa** with amines having embedded nucleophiles **4a–d** under mild reaction condition in water is described. The reaction showed selective C-N bond formation on more electrophilic alkynyl carbon resulting in the formation of *6-endo-dig* cyclised

product. The competitive experiments showed the viability of intramolecular nucleophilic attack over intermolecular attack of external nucleophile. This methodology accommodates wide functional group variation which proves to be useful for structural and biological assessment.

INTRODUCTION

The increasing significance of synthetic organic chemistry in pharmaceutical sciences demands the development of new strategies to synthesize a collection of natural product-like compounds.[1] For several decades; a large effort has been devoted for the development of new, efficient catalytic transformations to achieve high molecular complexity from simple starting materials. Domino reactions are one of such attractive processes that enhance the synthetic efficiency by using more than two reactants to create complex products with an optimal number of new bonds and functionalities.[1a,2a] Among various catalysts used, transition metal-catalyzed domino processes have shown to affect the efficient conversion using simple starting materials to complex molecules in a stepwise manner.[2b-f] Particularly silver-catalyzed cyclizations have acquired tremendous success due to their cost and capability to activate alkyne, alkene and allene functionalities at low-catalyst loading under mild reaction condition.[3]

As a privileged fragment, 1,2-dihydroisoquinoline skeleton is an important substructure occur in both natural products and therapeutic agents having wide applications in pharmaceutical research.[4] Functionalized benzoxazines have attracted considerable attention due to their prominent biological activities. They are known to act as antidepressant, anti-inflammatory, antitumor[5a-d] and antimalarial agents[6] (Figure 1, **A**). They also act as phosphatidylinositol-3-kinase (PI3K) inhibitor,[7] neuroprotective antioxidants,[8] 5-HT1A/B/D receptor antagonists,[9] antiarrhythmics against ischemia-reperfusion injury[10] and act as

intermediate for the synthesis of various natural product such as glyantrypine, fumiquinazoline F, fumiquinazoline G, and fiscalin B.[11] Their analogues exhibit high selectivity as competitive antagonist for the M4 receptor and parkinsonism.[12] Their derivatives have shown thrombin inhibitory and glycoprotein IIb/IIIa receptor antagonistic activity[13] and were evaluated as progesterone receptor (PR) antagonists[14] (Figure 1, **B**).

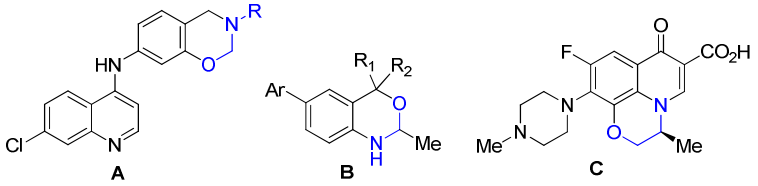


Figure 1. Significant examples of biologically active benzoxazine core

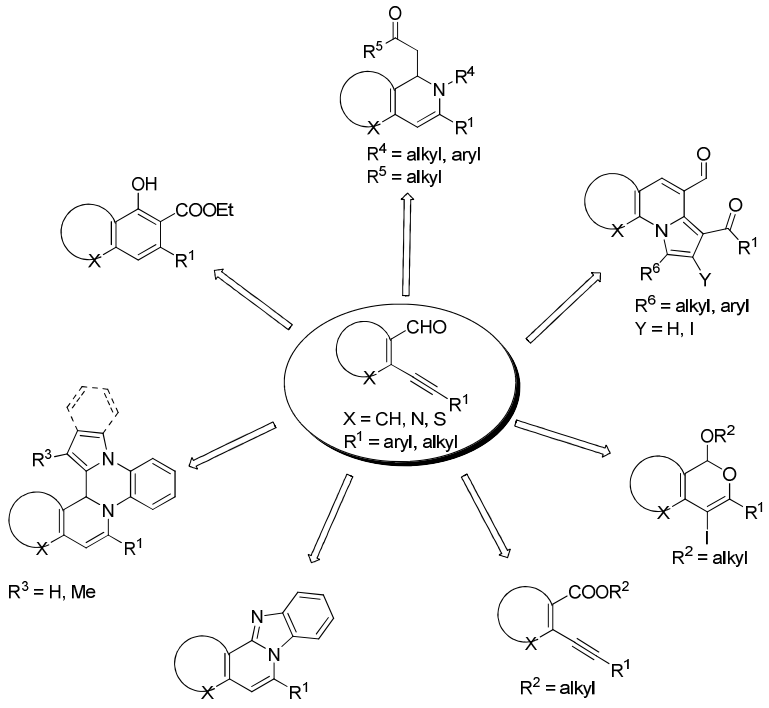
Substituted benzoxazines such as levofloxacin are known to act as antibacterial agent (Figure 1, **C**).[15] 1,3-Benzoxazines have been used as herbicides and agricultural microbiocides as well as bactericide and fungicide.[5a-d,16a] Further, *N*-haloacetyl derivatives of benzoxazines inhibit methane production in ruminants.[16b] As a privileged fragment, oxazine core is also found in many natural products exhibiting remarkable biological activities[17a-f] and also acts as synthetic intermediates in synthesis as well.[18] Because of such enriched biological profile, significant efforts are being continued and are still required for the development of efficient eco-friendly methods for their construction.

Using cascade addition of nucleophiles[19a] and cyclization,[19b-l] various reports are present in the literature showing the syntheses of fused 1,2-dihydroisoquinolines[20-22]/ isoquinolines,[23] naphthyridines[23g-h,24] in the presence of various transition-metal catalysts or even in their absence.[25] Moreover, 1,3-benzoxazines were synthesized using 2-(allyloxy)benzylamines with syngas in the presence of rhodium(I) catalyst.[26a-b] Their synthesis have been reported using metal catalysts such as Au,[26c] $Cu(OTf)_2$[26d] and also in the absence of metal.[26e-f] Along this, some polymeric 1,3-benzoxazines were also synthesized

without using catalyst.[26g-h] Similarly, synthesis of substituted 1,3-oxazine have been reported by both metal[26e-f] and non-metal catalyst.[26j]

Development of new and efficient synthetic strategies is as important as offering its reduced environmental impacts. Therefore, many reactions are being carried out in eco-friendly condition. Thus, reactions of water insoluble organic compounds taking place in aqueous suspension are becoming prominent, proceeding with high efficiency and possess feasible synthetic protocol.[27] Water is an ideal solvent since it fulfils many criteria; it is nontoxic, non-flammable, and abundantly available and inexpensive.[27] Use of water imparts often a significant effect on the both rate and selectivity of organic reactions through hydrophobic interactions and enrichment of organic substrates in local hydrophobic environment.[28]

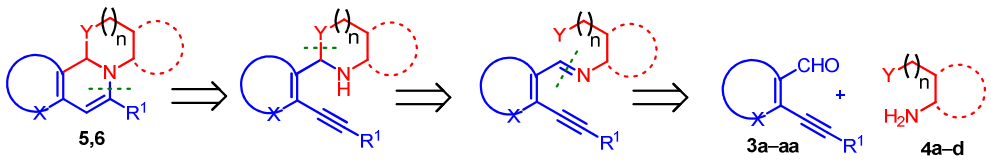
Scheme 1. **Heterocycles Synthesized in our Laboratory Using *o*-Alkynylaldehydes**



Motivated by importance of biological activity and as a part of our ongoing efforts to synthesize *N*-heterocycles by activation of alkyne (Scheme 1),[29] and also on the basis of our recent preliminary reports regarding the synthesis of fused polyheterocyclic quinoxalines and

benzimidazoles,[23g-h] we thought that *o*-alkynylaldehydes could further be used to synthesize fused isoquinolines/naphthyridines with new heterocyclic frame. We thereby envisaged that reactions of *ortho*-alkynylaldehyde **3a–aa** and amines having embedded nucleophiles **4a–d** through intermolecular condensation would provide the corresponding imines, which in the presence of appropriate alkyne activators would afford fused isoquinolines/naphthyridines in an apparently simple way. Designed retrosynthetic pathway is shown in Scheme 2. This cascade strategy would involve the formation of two new C–N bonds and one new C–Y bond thereby leading to the formation of two heterocyclic rings in one-pot. This has prompted us to explore and develop a convergent domino strategy for the divergent preparation of fused array of isoquinolines, keeping in mind the environmental considerations. Herein, we present our recent efforts for the silver-catalyzed regioselective domino synthesis of benzoxazine/oxazine fused isoquinolines and naphthyridines in water.

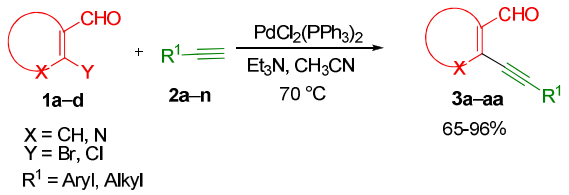
Scheme 2. Designed Reterosythetic Pathway for the Synthesis of Oxazine/Benzoxazine Fused Isoquinolines and Naphthyridines



RESULTS AND DISCUSSION

Preparation of *ortho*-alkynylaldehydes. To probe the viability of the designed domino strategy, *ortho*-alkynylaldehydes **3a–aa** were readily prepared by standard Sonogashira cross-coupling reaction of commercially available and readily accessible *ortho*-haloaldehydes **1a–d** with terminal alkynes **2a–n** (Scheme 3).[29b] This coupling procedure has readily accommodated a large variety of functional groups and provided the coupling products **3a–aa** in good to excellent yields.

Scheme 3. Preparation of *ortho*-Alkynylaldehydes



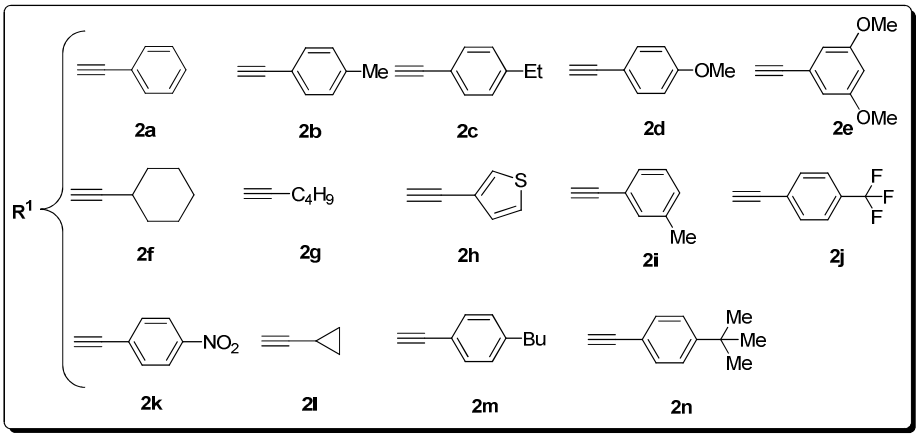
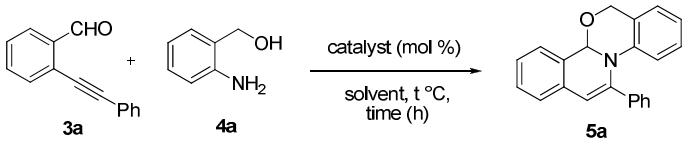


Table 1. Optimization of Reaction Conditions[a]



entry	catalyst (mol %)	conditions			yield (%)
		solvent	*t* °C	time (h)	
1	$AgNO_3$ (5)	CH_2Cl_2	25	4	38
2	$AgNO_3$ (10)	CH_2Cl_2	25	4	60
3	$AgNO_3$ (10)	THF	50	1	62
4	$AgNO_3$ (10)	EDC	70	1	73
5	$AgNO_3$ (10)	DMF	110	1	70
6	$AgNO_3$ (10)	Toulene	70	1	40
7	$AgNO_3$ (10)	EtOH	70	1	64

8	**$AgNO_3$ (10)**	**H_2O**	**80**	**1**	**81**
9	AgOAc (10)	H_2O	80	1	71
10	AgOTf (10)	H_2O	80	1	76
11	AgI (10)	H_2O	80	1	74
12	-	H_2O	80	1	-
13	$PdCl_2$ (10)	H_2O	80	2	55
14	$Pd(OAc)_2$ (10)	H_2O	80	2	55
15	CuI (10)	H_2O	80	3	70
16	$AlCl_3$ (10)	H_2O	80	6	trace

[a]The reactions were performed using 0.5 mmol of *o*-alkynylaldehyde **3a**, 1.1 equiv of amine **4a** in 2.0 mL of solvent.

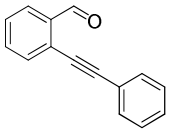
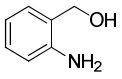
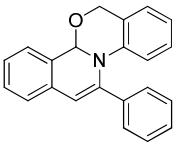
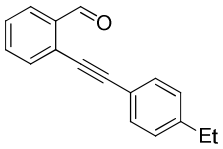
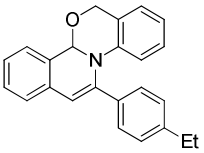
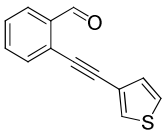
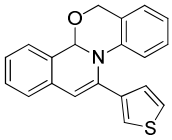
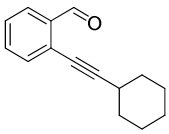
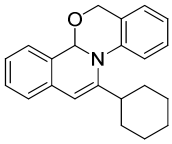
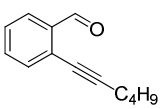
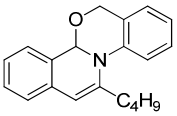
In order to find an optimal reaction condition, we selected 2-phenylethynyl benzaldehyde (**3a**) and (2-aminophenyl)methanol (**4a**) as model substrates (Table 1). Reaction of alkyne **3a** (0.5 mmol) with amine **4a** (1.1 equiv.) using 5 mol % of $AgNO_3$ in 2.0 mL of CH_2Cl_2 at 25 °C for 4 h afforded the formation of desired product **5a** in 38% yield (Table 1, entry 1). Increasing the amount of $AgNO_3$ from 5 to 10 mol % in CH_2Cl_2 afforded the product **5a** in 60% yield (entry 2). Different solvents such as THF, EDC, DMF, toluene, ethanol were examined at elevated temperatures, it was observed that the respective reaction did not attain the desired levels of reactivity and provided the formation of product **5a** in 40–73% yield (entries 3–7). When water was employed as a solvent, reaction proceeded to completion and it provided the formation of desired product **5a** in 81% yield in 1 h at 80 °C (entry 8). Other silver catalysts with different counter anions like AgOAc, AgOTf, AgI resulted in 71–76% yield of the desired product **5a** (entries 9–11). However, in the absence of catalyst, reactants remained almost unchanged during the course of reaction (entry 12). Transition-metal-catalysts other than silver like $PdCl_2$, $Pd(OAc)_2$ and CuI afforded the formation of desired product **5a** in

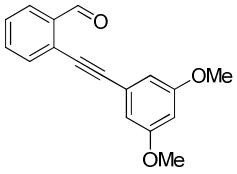
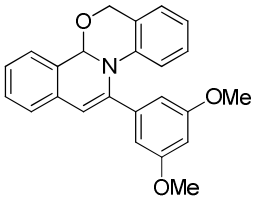
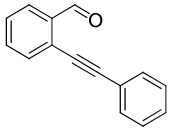
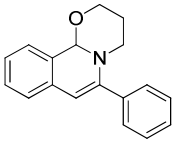
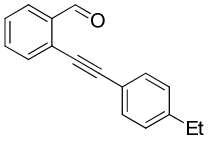
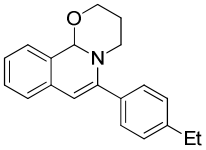
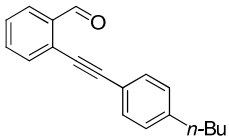
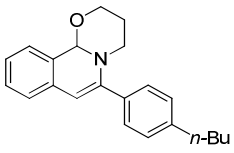
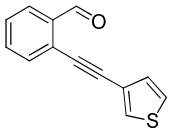
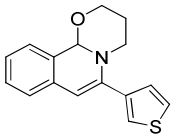
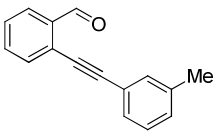
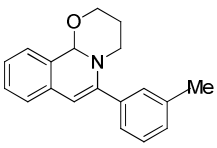
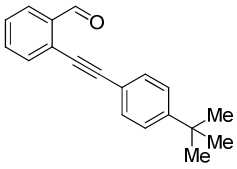
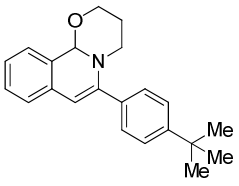
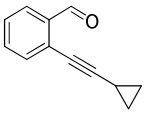
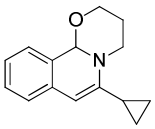
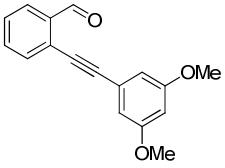
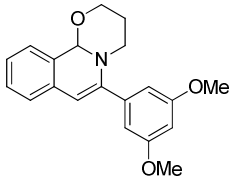
lower yields (entries 13–15). Reaction with Lewis acid $AlCl_3$ fails to afford the desired product (entry 16). The formation of regioselective *6-endo-dig* cyclized product **5a** was characterized by ^1H, ^{13}C NMR and mass spectroscopic data. Appearence of peaks at 5.95 ppm as a singlet & 5.26, 5.09 ppm as a diastereotopic doublets in ^1H NMR of **5a** and disappearance of the two peaks of alkynyl carbons in its characteristic region in ^{13}C NMR spectrum suggested the formation of desired cyclized product **5a**. X-ray crystallographic analysis of **5a** confirmed the formation of *6-endo-dig* cyclized product (see supporting information).

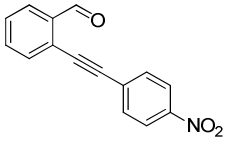
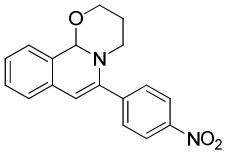
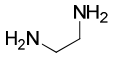
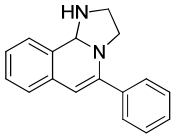
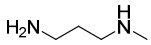
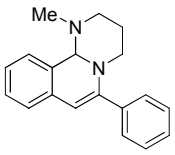
Synthesis of benzoxazine/oxazine fused isoquinolines. Having demonstrated the viability of this domino strategy, we then investigated the generality and scope of the transformation under the optimized condition (Table 2). As shown in Table 2, the reaction is tolerant towards a variety of *o*-alkynylaldehydes **3** bearing different alkynyl substituents. We commenced our study by the reaction of amines having embedded nucleophiles **4a–d** with substrate **3**. The results of this study are summarized in table 2 showing that use of amine **4a** gave better yield of respective product than the use of **4b, 4c, 4d** and also reaction was a bit faster in the case of former amine. When electronically neutral, moderately donating groups such as Ph, 4-Et-C_6H_4 **3a**–**b** were used, reaction preceded well and afforded products **5a**–**b** in 81 and 83% yields respectively (Table 2, entries 1–2). When strong donating group such as thienyl was used, reaction proceeded well and afforded the product **5c** in 85% yield (entry 3). With aliphatic groups such as cyclohexyl and *n*-butyl, the reaction provided the respective desired products **5d–e** in 77 and 75% yields respectively (entries 4–5). Alkynes **3f** bearing two methoxy group at meta position of the phenyl ring afforded the cyclized products **5f** in comparatively lower yield (entry 6), which may be the result of the reduced electrophilicity at the proximal end of alkyne which thereby reduced the efficiency of the desired transformation. Encouraged by above results, we further extended the same protocol with 3-

aminopropan-1-ol **4b**. Reaction of substrates **3a**–**c**, **3g**–**i** with 3-aminopropan-1-ol proceeded well and afforded the desired products **5g**–**l** in 75–82% yields (Table 2, entries 7–12). Alkynes **3j**, bearing a cyclopropyl group provided the desired products **5m** in 71% yields, (entry 13). Reaction of amine **4b** with 2-((4-nitrophenyl)ethynyl)-quinoline-3-carbaldehyde (**3m**) bearing an electron-withdrawing nitro group at para position of the phenyl ring fails to afford the desired product **5o** (entry 15). Reaction of **3a** with ethane-1,2-diamine (**4c**) afforded the desired product **5p** in 68% yield (entry 16); however an inseparable complex mixture was obtained when N-methylpropane-1,3-diamine (**4d)** was reacted with **3a** (entry 17).

Table 2. Domino Synthesis of Benzoxazine/Oxazine Fused Isoquinolines[a]

entry	substrate		amine	product		yield (%)
1		**3a**	 **4a**		**5a**	81
2		**3b**	**4a**		**5b**	83
3		**3c**	**4a**		**5c**	85
4		**3d**	**4a**		**5d**	77
5		**3e**	**4a**		**5e**	75

6		**3f**	**4a**		**5f**	70
7		**3a**	 **4b**		**5g**	75
8		**3b**	**4b**		**5h**	79
9		**3g**	**4b**		**5i**	78
10		**3c**	**4b**		**5j**	82
11		**3h**	**4b**		**5k**	77
12		**3i**	**4b**		**5l**	76
13		**3j**	**4b**		**5m**	71
14		**3f**	**4b**		**5n**	67

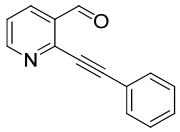
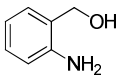
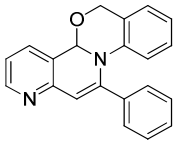
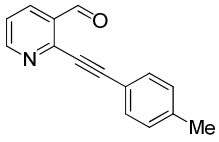
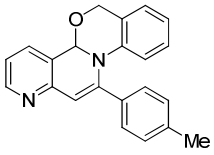
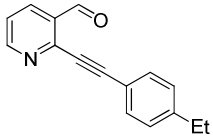
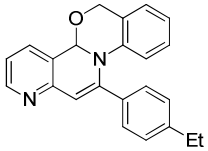
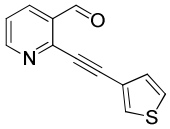
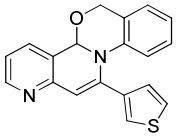
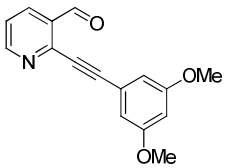
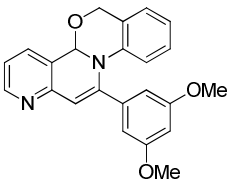
15		**3k**	**4b**		**5o**	– [b]
16		**3a**	 **4c**		**5p**	68
17		**3a**	 **4d**		**5q**	– [b]

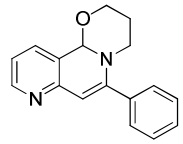
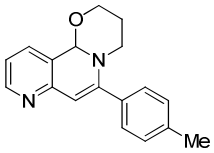
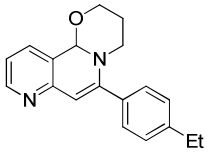
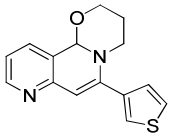
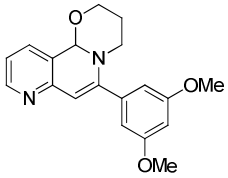
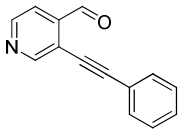
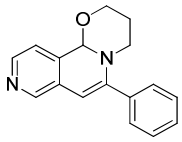
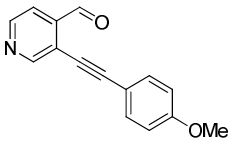
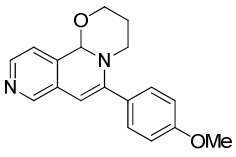
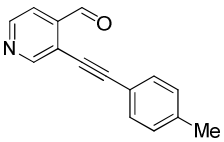
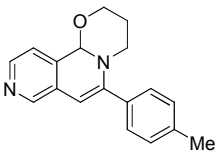
[a]The reactions were performed using *o*-alkynylaldehyde **3** (0.5 mmol), amine **4a**–**d** (1.1 equiv), 10 mol % of $AgNO_3$ in 2.0 mL of H_2O at 80 °C for 1–1.5 h. [b]An inseparable mixture of products.

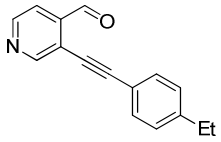
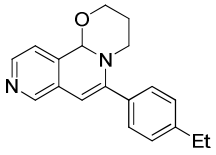
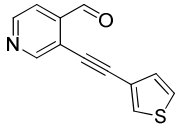
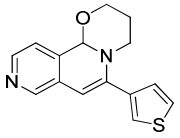
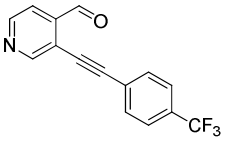
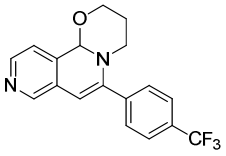
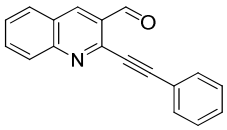
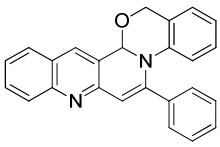
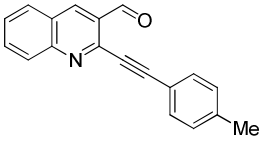
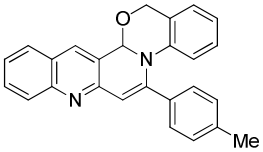
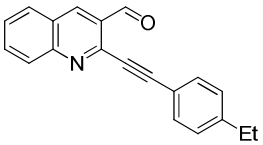
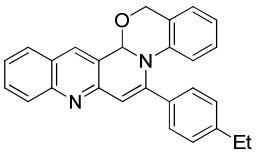
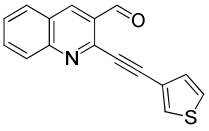
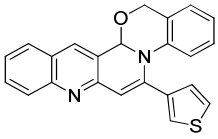
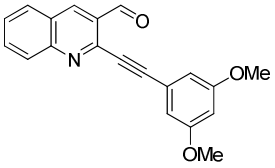
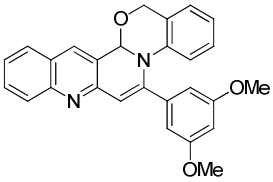
Synthesis of benzoxazine/oxazine fused naphthyridines. To gain further insight into the reaction, we continued our study by examining various nitrogen containing substrates **3l**–**aa** furnished differently substituted benzoxazino/oxazino-naphthyridines **6a**–**v** (Table 3) and a similar kind of observation can be inferred. Alkynes **3l**–**o** with electron-donating groups provided the respective desired products **6a**–**d** in 88–92% yields (entries 1–4) whereas alkyne **3p** bearing methoxy groups at meta position of the phenyl ring afforded the product **6e** in 75% yield (entry 5). Switching from aromatic amine (2-aminophenyl)methanol (**4a**) to aliphatic amine 3-aminopropan-1-ol (**4b**), the reaction proceeded with comparatively lower levels of reactivity (entries 6–16). We have also explored the reaction of 3-(substitutedethynyl)isonicotinaldehydes **3q**–**v** with amines **4a**–**b** (entries 11–16). The desired products **6k**–**o** was obtained in good yields (entries 11–15). Presence of electron-withdrawing $–CF_3$ group at *para* position retarded the reaction and product was obtained in 62% yield (entries 16).

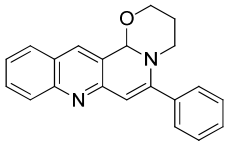
We further switched our strategy to two ring system in order to explore more diversity and complexity. So we reacted 2-(substituted)quinoline-3-carbaldehydes **3w**–**aa** with amines **4a** and **4b**. We observed that reaction was slightly sluggish than in the case of substituted pyridine alkynylaldehydes **3l**–**v**. The substituted benzoxazino fused naphthyridines **6q**–**u** were obtained in 72–87% yields (entries 17–21). Reaction of alkyne **3w** with 3-aminopropan-1-ol proceeded well and provided the oxazino-naphthyridine **6v** in 81% yield (entry 22). All the synthesized products were fully characterized by the ^{1}H NMR, ^{13}C-NMR, HRMS and X-ray crystallographic analysis (Figure 2). Products were obtained as racemic mixtures as no optical rotation was observed.

Table 3. Domino Synthesis of Fused Benzoxazino/Oxazino-Naphthyridines[a]

entry	substrate		amine	product		yield (%)
1		**3l**	 **4a**		**6a**	88
2		**3m**	**4a**		**6b**	90
3		**3n**	**4a**		**6c**	89
4		**3o**	**4a**		**6d**	92
5		**3p**	**4a**		**6e**	75

6		**3l**	**4b**		**6f**	82
7		**3m**	**4b**		**6g**	86
8		**3n**	**4b**		**6h**	84
9		**3o**	**4b**		**6i**	88
10		**3p**	**4b**		**6j**	69
11		**3q**	**4b**		**6k**	80
12		**3r**	**4b**		**6l**	86
13		**3s**	**4b**		**6m**	82

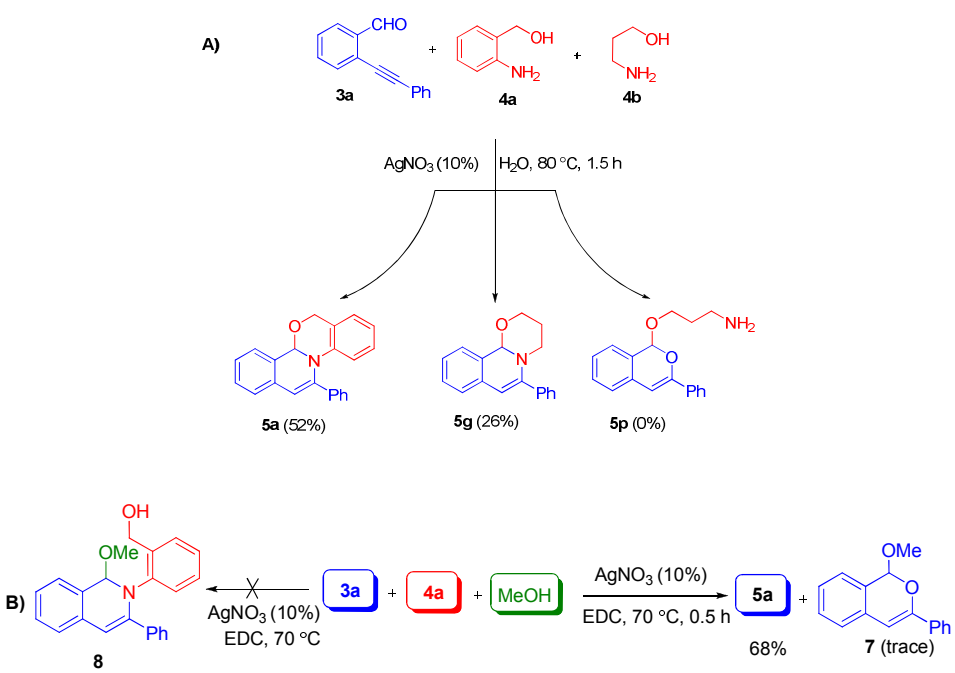
14		**3t**	**4b**		**6n**	81
15		**3u**	**4b**		**6o**	86
16		**3v**	**4b**		**6p**	62
17		**3w**	**4a**		**6q**	83
18		**3x**	**4a**		**6r**	87
19		**3y**	**4a**		**6s**	85
20		**3z**	**4a**		**6t**	87
21		**3aa**	**4a**		**6u**	72

22	**3w**	**4b**		**6v**	81

[a]The reactions were performed using *o*-alkynylaldehyde **3** (0.5 mmol), amine **4a**–**b** (1.1 equiv), 10 mol % of $AgNO_3$ in 2.0 mL of H_2O at 80 °C for 0.5–1 h.

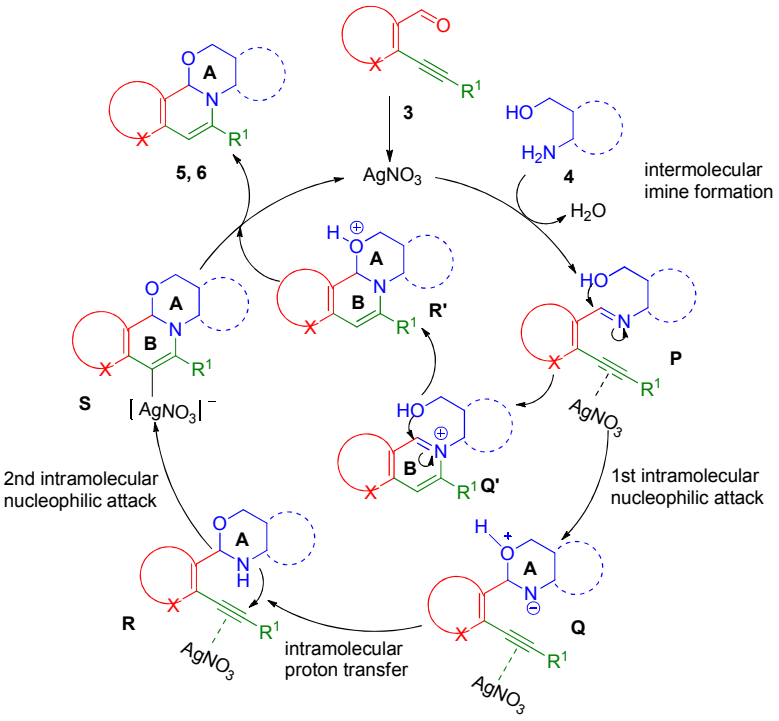
Competitive study. In order to see the comparative studies of different nucleophiles such as (2-aminophenyl)methanol (**4a**), 3-aminopropan-1-ol (**4b**) and methanol, we carried out different sets of reactions (Scheme 4). Firstly, we studied the relative reactivity between aromatic and aliphatic nucleophiles by choosing 2-(phenylethynyl)benzaldehyde **3a**, amines **4a** and **4b** (1.1 equiv) in H_2O using 10 mol % $AgNO_3$ as a catalyst (Scheme 4, A). We observed the product **5a** was obtained in 52% yield and product **5g** in 26% yield. The reason can be attributed that the second intramolecular attack in case of amine **4a** is more favourable due to rigid and optimum conformation imparted by aryl ring for faster trapping of imine formed than in case of amine **4b**. Formation of compound **5p** was not at all observed.

Scheme 4. **Competitive Study**



We also studied the comparison of the reactivity between an intramolecular and an intermolecular reaction. We carried out the reaction of alkynylaldehyde **3a**, amine **4a** and MeOH (1.1 equiv) in EDC using 10 mol% $AgNO_3$ (Scheme 4, **B**). It was found that fused benzoxazine **5a** was formed as a major product in 68% yield whereas 1-methoxy-1*H*-isochromene **7**[23g] was formed in trace amount. Formation of 2-(2-(1*H*-pyrrol-1-yl)phenyl)-1-methoxy-3-phenyl-1,2-dihydroisoquinoline **8** was not at all observed. This clearly shows that intramolecular reaction is favoured over intermolecular reaction as amine **4a** with attached nucleophile is in close proximity to attack onto imine carbon as compared to distal methanol molecules.

Scheme 5. **Probable Mechanism**



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 **3** with nucleophilic amine **4** produced condensation species **P**. After this, two possibilities exit for the formation of compound **5**, **6** i.e. either ring A forms first than ring B or vice versa. Ring A

could be formed prior as **P** on activation by silver 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 $AgNO_3$ would undergo second intramolecular nucleophic attack of NH onto the triple bond to afford **S** to give desired compound **5**, **6**. Alternatively, ring B could be formed initially by the activation of triple bond by silver to give **Q'** followed by second intramolecular nucleophilic attack to furnish **R'** which after subsequent deprotonation would give compound **5**, **6**.

CONCLUSIONS

In summary, we have developed Ag(I)-catalyzed domino protocol in water which allowed a facile access to an impressive variety of benzoxazines/oxazines fused isoquinolines and naphthyridines using readily available starting materials in good yields with high regioselectivity under mild reaction conditions. The reaction proceeded with high *6-endo-dig* regioselectivity and confirmed by X-ray crystallographic studies. The competitive experiments demonstrated the practicality of intramolecular nucleophilic attack over intermolecular attack. The product formation was also found to be higher in case of aromatic amine over aliphatic amine. The method appeared to be very general and compatible with differently substituted starting materials having different electronic properties 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 $CDCl_3$. Chemical shifts for protons are reported in ppm from tetramethylsilane with the residual $CHCl_3$ 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. Anhydrous forms of all reagents such as diethyl ether, hexanes, ethyl acetate, EDC, Et_3N, 2-bromobenzaldehyde, 3-bromoisonicotinaldehyde, 2-bromonicotinaldehyde, 2-chloroquinoline -3-carbaldehyde, 3-bromobenzo[*b*]thiophene-2-carbaldehyde, Silver nitrate, palladium salts and copper salts were used directly as obtained commercially unless otherwise noted.

Procedure for the Synthesis of Compound 5 and 6. To a solution of 0.5 mmol of *o*-alkynyl aldehyde **3** in 2.0 mL H_2O, was added 1.1 equiv of amine **4** followed by the addition of 10 mol % of $AgNO_3$. The reaction mixture was allowed to stir at 80 °C for 0.5–1.5 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 using hexane/ethyl acetate as the eluent.

The structure and purity of the known starting materials **3a**, **3c**, **3o–q,** [23g] **3d**, **3l**, **3aa,** [29c] **3m**, **3r**, **3w–z**,[24b] **3f**, **3h**, **3k**,[30a] **3e**, **3j**,[30b] **3s**,[29e] **3i**,[23h] **3g**[30c] were confirmed by comparison of their physical and spectral data (^{1}H NMR and ^{13}C NMR) with those reported in literature.

2-((4-ethylphenyl)ethynyl)benzaldehyde (3b). The product was obtained as orange semi solid (90.2 mg, 77%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.67 (s, 1H), 7.96 (dd, J = 7.8, 0.92 Hz, 1H), 7.65–7.63 (m, 1H), 7.59 (td, J = 7.3, 1.8 Hz, 1H), 7.50 (d, J = 8.3 Hz, 2H), 7.44 (t, J = 7.3 Hz, 1H), 7.23 (d, J = 8.2 Hz, 2H), 2.69 (q, J = 7.8 Hz, 2H), 1.27 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.7, 145.6, 135.7, 133.7, 133.1, 131.6, 128.3, 128.0, 127.9, 127.1, 119.4, 96.6, 84.2, 28.8, 15.2; HRMS (ESI) $[M]^+$ Calcd for $[C_{17}H_{14}O]$ 234.1045, found 234.1046.

3-((4-Ethylphenyl)ethynyl)isonicotinaldehyde (3t). The product was obtained as pale yellow needle crystals (92.9 mg, 79%): mp 72–76 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.62 (s, 1H), 8.95 (s, 1H), 8.71 (d, J = 5.1 Hz, 1H), 7.71 (d, J = 5.1 Hz, 1H), 7.48 (d, J = 8.1 Hz, 2H),7.22 (d, J = 8.0 Hz, 2H), 2.61 (q, J = 7.3 Hz, 2H), 1.17 (t, J = 7.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.8, 154.5,149.0, 140.2, 140.0, 131.7, 129.3, 121.6, 119.1, 118.5, 99.4, 81.3, 32.8, 19.1; HRMS (ESI) $[M]^+$ Calcd for $[C_{16}H_{13}NO]$ 235.0997, found 235.0998.

3-(Thiophen-3-ylethynyl)isonicotinaldehyde (3u). The product was obtained as orange needle crystals (89.6 mg, 84%): mp 66–70 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.50 (s, 1H),8.86 (s, 1H), 8.63 (d, J = 5.2 Hz, 1H), 7.63 (d, J = 5.1 Hz, 1H), 7.58 (d, J = 2.2 Hz, 1H),7.30–7.28 (m, 1H), 7.17 (d, J = 3.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.6, 154.3,149.0, 140.3, 130.5, 129.6, 126.0, 121.4, 120.6, 119.2, 94.3, 81.5; HRMS (ESI) $[M]^+$ Calcd for $[C_{12}H_7NOS]$ 213.0248, found 213.0248.

3-((4-(Trifluoromethyl)phenyl)ethynyl)isonicotinaldehyde (3v). The product was obtained as yellow crystals (96.3 mg, 70%): mp 80–86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.53 (s, 1H), 8.93 (s, 1H), 8.72 (d, J = 5.1 Hz, 1H), 7.70 (d, J = 5.1 Hz, 1H), 7.62 (q, J = 8.0 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.3, 154.6, 149.9, 140.6, 132.1, 125.6 (q, J = 3.8 Hz),

125.4, 125.0, 120.4, 119.6, 97.1, 84.1; HRMS (ESI) $[M]^+$ Calcd for $[C_{15}H_8F_3NO]$ 275.0558, found 275.0558.

12-Phenyl-4b,6-dihydrobenzo[4,5][1,3]oxazino[2,3-*a*]isoquinoline (5a). The product was obtained as pale yellow crystals (126.1 mg, 81%): mp 176–180 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 7.3 Hz, 1H), 7.34–7.30 (m, 1H), 7.25–7.23 (m, 6H), 7.18 (d, J = 8.1 Hz, 1H), 7.05 (d, J = 7.4 Hz, 1H), 6.91 (t, J = 8.0 Hz, 1H), 6.78 (t, J = 8.1 Hz, 1H), 6.22 (d, J = 8.1 Hz, 1H), 6.09 (s, 1H), 5.95 (s, 1H), 5.26 (d, J = 18.1 Hz, 1H), 5.09 (d, J = 14.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.8, 139.8, 136.9, 132.3, 129.0, 128.6, 128.4, 128.0, 127.8, 126.8, 126.0, 125.8, 124.7, 124.3, 123.8, 122.5, 105.7, 85.0, 68.0; HRMS (ESI) $[M]^+$ Calcd for $[C_{22}H_{17}NO]$ 311.1310, found 311.1309.

Compound **5a** was crystallized in the triclinic crystal system with space group P 21. The single-crystal X-ray data were collected using graphite monochromated Mo Kα radiation (λ= 0.71073 Å). The structures were solved using SIR-92 and refined by the full matrix least-squares technique on F2 using the SHELXL-97 program within the WinGX v1.80.05 software package. Crystal data for **5a**: $C_{22}H_{17}NO$, M= 311.37, Monoclinic, space group P 21, a= 11.3784(19) Å, b= 5.7382(8) Å, c= 13.148(3) Å, α = 90, β = 114.27(2), γ = 90, V = 782.6(2) Å^3, Z= 2, T= 296 K, D calcd= 1.321 Mg/m3, R(int) = 0.0203, R1 = 0.0503, wR2 = 0.1050 [I > 2σ(I)], R1 = 0.0664, wR2 = 0.1157 (all data), GOF = 1.058. Crystallographic data for **5a** have been deposited with the Cambridge Crystallographic Data Centre. CCDC 932014, contain all crystallographic details of this publication and is available free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html. For further details on the crystal structure of compound **5a**, see the CIF file (Supporting Information).

12-(4-Ethylphenyl)-4b,6-dihydrobenzo[4,5][1,3]oxazino[2,3-*a*]isoquinoline (5b). The product was obtained as a pale yellow semi-solid (140.9 mg, 83%): ^{1}H NMR (400 MHz,

$CDCl_3$) δ 7.39 (d, J = 8.2 Hz, 1H), 7.31–7.27 (m, 1H), 7.21–7.18 (m, 1H), 7.16–7.10 (m, 3H), 7.05–7.02 (m, 3H), 6.91–6.87 (m, 1H), 6.77 (t, J = 7.8 Hz, 1H), 6.22 (d, J = 8.7 Hz, 1H), 6.06 (s, 1H), 5.93 (s, 1H), 5.23 (d, J = 14.2 Hz, 1H), 5.07 (d, J = 15.1 Hz, 1H), 2.60 (q, J = 7.4 Hz, 2H), 1.21–1.17 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.0, 140.8, 139.9, 134.2, 132.5, 128.9, 128.5, 128.3, 127.4, 126.6, 125.9, 125.8, 124.6, 124.2, 123.7, 122.3, 105.4, 85.0, 68.0, 26.9, 15.4; HRMS (ESI) $[M]^+$ Calcd for $[C_{24}H_{21}NO]$ 339.1623, found 339.1623

12-(Thiophen-3-yl)-4b,6-dihydrobenzo[4,5][1,3]oxazino[2,3-*a*]isoquinoline (5c). The product was obtained as brown needles (134.9 mg, 85%): mp 104–108 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 8.1 Hz, 1H), 7.18–7.17 (m, 1H), 7.06–7.04 (m, 1H), 7.02–6.97 (m, 3H), 6.92 (t, J = 7.3 Hz, 2H), 6.80 (t, J = 7.3 Hz, 1H), 6.63–6.61 (m, 1H), 6.29 (d, J = 8.8 Hz, 1H), 6.15 (s, 1H), 5.96 (s, 1H), 5.13 (d, J = 14.6 Hz, 1H), 4.99 (d, J = 14.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.0, 150.2, 140.4, 139.1, 137.1, 134.4, 128.4, 127.6, 125.9, 125.1, 124.8, 124.71, 124.68, 123.6, 123.4, 121.9, 120.4, 105.6, 84.5, 67.9; HRMS (ESI) $[M]^+$ Calcd for $[C_{20}H_{15}NOS]$ 317.0874, found 317.0875.

12-Cyclohexyl-4b,6-dihydrobenzo[4,5][1,3]oxazino[2,3-*a*]isoquinoline (5d). The product was obtained as a pale yellow semi-solid (122.2 mg, 77%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23–7.17 (m, 2H), 7.16–7.09 (m, 2H), 7.07–7.00 (m, 4H), 5.71–5.69 (m, 2H), 5.09 (d, J = 15.1 Hz, 1H), 4.88 (d, J = 15.1 Hz, 1H), 2.58–2.51 (m, 1H), 1.98–1.95 (m, 1H) 1.78–1.75 (m, 1H), 1.57–1.47 (m, 4H), 1.45–1.36 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.5, 140.7, 132.4, 131.0, 129.1, 127.4, 125.8, 125.4, 124.93, 124.89, 124.7, 124.6, 123.8, 98.1, 84.8, 67.7, 38.4, 26.7, 26.5, 26.1; HRMS (ESI) $[M]^+$ Calcd for $[C_{22}H_{23}NO]$ 317.1780, found 317.1781.

12-Butyl-4b,6-dihydrobenzo[4,5][1,3]oxazino[2,3-*a*]isoquinoline (5e). The product was obtained as a brown oil (109.3 mg, 75%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.29 (m, 2H),

7.24–7.18 (m, 3H), 7.17–7.12 (m, 2H), 7.08 (d, J = 7.4 Hz, 1H), 5.81 (s, 1H), 5.74 (s, 1H), 5.20 (d, J = 15.1 Hz, 1H), 4.98 (d, J = 15.1 Hz, 1H), 1.47–1.43 (m, 2H), 0.93–0.87 (m, 4H), 0.80 (t, J = 9.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.4, 140.8, 132.4, 130.8, 129.1, 127.6, 125.8, 125.2, 125.0, 124.9, 124.8, 124.7, 123.5, 100.3, 84.8, 67.6, 32.5, 29.6, 22.1, 13.7; HRMS (ESI) $[M]^+$ Calcd for $[C_{20}H_{21}NO]$ 291.1623, found 291.1623.

12-(3,5-Dimethoxyphenyl)-4b,6-dihydrobenzo[4,5][1,3]oxazino[2,3-*a*]isoquinoline (5f). The product was obtained as a yellow semi-solid (130.0 mg, 70%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 6.9 Hz, 1H), 7.33–7.29 (m, 1H), 7.24–7.16 (m, 3H), 7.02 (d, J = 7.4 Hz, 1H), 6.92 (t, J = 8.2 Hz, 1H), 6.83 (t, J = 7.8 Hz, 1H), 6.34–6.31 (m, 3H), 6.07 (s, 1H), 5.95 (s, 1H), 5.24 (d, J = 14.6 Hz, 1H), 5.07 (d, J = 14.7 Hz,1H), 3.62 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2, 140.7, 139.9, 138.8, 132.1, 129.0, 126.9, 126.0, 125.9, 124.6, 124.4, 123.7, 122.7, 106.8, 105.2, 100.2, 96.4, 84.9, 68.0, 55.3; HRMS (ESI) $[M]^+$ Calcd for $[C_{24}H_{21}NO_3]$ 371.1521, found 371.1520.

6-Phenyl-2,3,4,11b-tetrahydro-[1,3]oxazino[2,3-*a*]isoquinoline (5g). The product was obtained as a brown semi-solid (98.8 mg, 75%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.30 (m, 5H), 7.23–7.18 (m, 2H), 7.08 (t, J = 8.1 Hz, 1H), 6.96 (d, J = 8.1 Hz, 1H), 5.97 (s, 1H), 5.51 (s, 1H), 4.07–4.01 (m, 2H), 3.74–3.70 (m, 1H), 3.30–3.22 (m, 1H), 2.03–1.93 (m, 1H), 1.88–1.77 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1, 137.6, 132.7, 129.1, 128.3, 128.2, 127.9, 127.4, 125.0, 124.8, 123.7, 101.8, 88.7, 68.1, 47.7, 26.8; HRMS (ESI) $[M]^+$ Calcd for $[C_{18}H_{17}NO]$ 263.1310, found 263.1310.

6-(4-Ethylphenyl)-2,3,4,11b-tetrahydro-[1,3]oxazino[2,3-*a*]isoquinoline (5h). The product was obtained as a brown semi-solid (115.1 mg, 79%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (t, J = 8.0 Hz, 3H), 7.24 (t, J = 10.2 Hz, 3H), 7.14 (t, J = 9.1 Hz, 1H), 7.05 (d, J = 7.3 Hz, 1H), 6.04 (s, 1H), 5.58 (s, 1H), 4.15–4.05 (m, 2H), 3.84–3.81 (m, 1H), 3.36–3.29 (m, 1H), 2.70–

2.68 (m, 2H), 2.05–1.88 (m, 2H), 1.37–1.26 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 143.9, 139.2, 134.9, 132.1, 129.4, 128.2, 127.6, 124.9, 123.5, 114.0, 101.6, 87.7, 68.0, 47.6, 26.8, 22.6, 14.1; HRMS (ESI) $[M]^+$ Calcd for $[C_{20}H_{21}NO]$ 291.1623, found 291.1624.

6-(4-Butylphenyl)-2,3,4,11b-tetrahydro-[1,3]oxazino[2,3-*a*]isoquinoline (5i). The product was obtained as a red oil (124.6 mg, 78%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.23 (m, 4H), 7.23–7.19 (m, 2H), 7.14 (t, J = 6.8, 1H), 7.05 (d, J = 10.1 Hz, 1H), 6.04 (s, 1H), 5.57 (s, 1H), 4.15–4.05 (m, 2H), 2.60–2.57 (m, 4H), 1.73–1.59 (m, 4H), 1.42–1.34 (m, 2H), 0.95 (t, J = 8.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1, 142.5, 134.7, 132.7, 128.9, 128.1, 127.3, 124.8, 124.7, 101.6, 88.7, 68.0, 47.6, 35.3, 33.4, 26.8, 22.3, 13.9; HRMS (ESI) $[M]^+$ Calcd for $[C_{22}H_{25}NO]$ 319.1936, found 319.1937.

6-(Thiophen-3-yl)-2,3,4,11b-tetrahydro-[1,3]oxazino[2,3-*a*]isoquinoline (5j). The product was obtained as a red semi-solid (113.1 mg, 84%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.33 (m, 2H), 7.28–7.23 (m, 2H), 7.15–7.12 (m, 1H), 7.09–7.08 (m, 1H), 7.04 (d, J = 8.8 Hz, 1H), 6.00 (s, 1H), 5.66 (s, 1H), 4.16–4.05 (m, 2H), 3.85–3.80 (m, 1H), 3.33 (t, J=13.0 Hz, 1H), 2.07–1.93 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.1, 137.8, 132.4, 129.1, 127.9, 127.4, 125.4, 125.1, 124.9, 123.6, 123.5, 102.0, 88.6, 68.1, 47.7, 26.8; HRMS (ESI) $[M]^+$ Calcd for $[C_{16}H_{15}NOS]$ 269.0874, found 269.0874.

2,3,4,11b-Tetrahydro-6-*m*-tolyl-[1,3]oxazino[2,3-*a*]isoquinoline (5k). The product was obtained as a dark yellow semi-solid (112.6 mg, 77%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22–7.16 (m, 3H), 7.13–7.04 (m, 4H), 6.97 (d, J = 7.3 Hz, 1H), 5.96 (s, 1H), 5.49 (s, 1H), 4.08–3.97 (m, 2H), 3.76–3.71 (m, 1H), 3.28–3.20 (m, 1H), 2.31 (s, 3H), 1.98–1.76 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 137.9,137.5, 132.7, 129.1, 129.0, 128.6, 128.0, 127.4, 125.4, 124.9, 124.8, 123.6, 101.6, 88.7, 68.0, 47.7, 26.9, 21.4; HRMS (ESI) $[M]^+$ Calcd for $[C_{19}H_{19}NO]$ 277.1467, found 277.1467.

6-(4-(*tert*-Butyl)phenyl)-2,3,4,11b-tetrahydro-[1,3]oxazino[2,3-*a*]isoquinoline (5l). The product was obtained as orange crystals (121.4 mg, 76%): mp 96–100°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.30 (m, 2H), 7.24–7.21 (m, 2H), 7.19–7.14 (m, 2H), 7.04 (t, J = 8.8 Hz, 1H), 6.95 (d, J = 8.0 Hz, 1H), 5.95 (s, 1H), 5.48 (s, 1H), 4.07–3.96 (m, 2H), 3.85–3.72 (m, 2H), 1.97–1.92 (m, 1H), 1.87–1.74 (m, 1H), 1.25 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.8, 145.2, 134.6, 132.7, 129.0, 127.9, 127.4, 125.1, 124.8, 124.7, 123.5, 101.6, 88.7, 68.0, 47.6, 34.6, 31.3, 26.9; HRMS (ESI) $[M]^+$ Calcd for $[C_{22}H_{25}NO]$ 319.1936, found 319.1935.

6-Cyclopropyl-2,3,4,11b-tetrahydro-[1,3]oxazino[2,3-*a*]isoquinoline (5m). The product was obtained as a red yellow semi-solid(80.7 mg, 71%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19–7.16 (m, 2H), 7.06–7.02 (m, 1H), 6.96–6.94 (m, 1H), 5.91 (s, 1H), 5.45 (s, 1H), 4.15–4.03 (m, 2H), 3.40–3.35 (m, 2H), 1.59–1.45 (m, 2H), 0.92–0.77 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 133.0, 128.8, 127.4, 124.4, 123.1, 114.0, 97.3, 88.9, 68.7, 46.4, 27.1, 13.1, 5.6, 5.5; HRMS (ESI) $[M]^+$ Calcd for $[C_{15}H_{17}NO]$ 227.1310, found 227.1310.

6-(3,5-Dimethoxyphenyl)-2,3,4,11b-tetrahydro-[1,3]oxazino[2,3-*a*]isoquinoline (5n). The product was obtained as a pale yellow semi-solid (108.3 mg, 67%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29–7.24 (m, 2H), 7.15–7.11 (m, 1H), 7.06–7.02 (m, 1H), 6.54 (s, 2H), 6.45–6.44 (m, 1H), 6.01 (s, 1H), 5.61 (s, 1H), 4.12–4.02 (m, 2H), 3.79 (s, 6H), 3.35–3.28 (m, 2H), 2.07–1.89 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 145.1, 139.5, 132.5, 129.1, 127.4, 125.1, 124.8, 123.7, 106.5, 101.5, 100.1, 88.7, 68.1, 55.4, 47.7, 27.1; HRMS (ESI) $[M]^+$ Calcd for $[C_{20}H_{21}NO_3]$ 323.1521, found 323.1520.

5-Phenyl-1,2,3,10b-tetrahydroimidazo[2,1-*a*]isoquinoline (5p). The product was obtained as a brown semi-solid (84.4 mg, 68%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (t, J = 8.1 Hz, 1H), 7.47–7.41 (m, 4H), 7.40–7.38 (m, 1H), 7.28–7.27 (m, 1H), 7.03–7.00 (m, 1H), 6.70 (d, J = 8.0 Hz, 1H), 6.19 (s, 1H), 5.00 (s, 1H), 4.08–4.03 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ

158.1, 141.6, 136.5, 132.6, 129.3, 128.7, 128.2, 127.3, 127.0, 126.1, 123.3, 119.9, 114.0, 113.1, 106.3, 49.8, 49.7; HRMS (ESI) $[M]^+$ Calcd for $[C_{17}H_{16}N_2]$ 248.1313, found 248.1313.

12-Phenyl-4b,6-dihydrobenzo[4,5][1,3]oxazino[2,3-*f*][1,6]naphthyridine (6a). The product was obtained as yellow needles (137.4 mg, 88%): mp 154–158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43–8.41 (m, 1H), 7.55 (d, J = 7.3 Hz, 1H), 7.19–7.15 (m, 5H), 7.02–6.98 (m, 1H), 6.95 (d, J = 7.3 Hz, 1H), 6.84 (t, J = 7.3 Hz, 1H), 6.69 (t, J = 8.1 Hz, 1H), 6.12 (d, J = 8.1 Hz, 1H), 6.08 (s, 1H), 5.98 (s, 1H), 5.13 (d, J = 16.8 Hz, 1H), 4.99 (d, J = 14.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.1, 150.1, 145.0, 139.1, 136.2, 134.4, 128.5, 128.3, 128.1, 125.9, 124.7, 123.7, 123.0, 122.0, 120.4, 106.2, 84.7, 68.0; HRMS (ESI) $[M]^+$ Calcd for $[C_{21}H_{16}N_2O]$ 312.1263, found 312.1263.

12-(*p*-Tolyl)-4b,6-dihydrobenzo[4,5][1,3]oxazino[2,3-*f*][1,6]naphthyridine (6b). The product was obtained as yellow crystals (146.9 mg, 90%): mp 166–170 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44–8.43 (m, 1H), 7.57 (d, J = 7.4 Hz, 1H), 7.08–7.06 (m, 2H), 7.03–6.97 (m, 4H), 6.87 (t, J = 14.6 Hz, 1H), 6.74 (t, J = 7.3 Hz, 1H), 6.18 (d, J = 13.3 Hz, 1H), 6.09 (s, 1H), 6.00 (s, 1H), 5.15 (d, J = 14.6 Hz, 1H), 5.01 (d, J = 14.6 Hz, 1H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.3, 150.2, 145.2, 139.2, 138.4, 134.3, 133.3, 128.8, 128.4, 128.3, 126.0, 124.7, 123.8, 122.9, 122.2, 120.4, 106.2, 84.8, 68.0, 21.3; HRMS (ESI) $[M]^+$ Calcd for $[C_{22}H_{18}N_2O]$ 326.1419, found 326.1420.

12-(4-Ethylphenyl)-4b,6-dihydrobenzo[4,5][1,3]oxazino[2,3-*f*][1,6]naphthyridine (6c). The product was obtained as yellow crystals (151.5 mg, 89%): mp 162–166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45–8.44 (m, 1H), 7.59 (d, J = 7.3 Hz, 1H), 7.11–7.09 (m, 2H), 7.06–6.98 (m, 3H), 6.96–6.93 (m, 2H), 6.78–6.73 (m, 2H), 6.18 (d, J = 8.0 Hz, 1H), 6.11 (s, 1H), 6.02 (s, 1H), 5.17 (d, J = 13.9 Hz, 1H), 5.02 (d, J = 13.9 Hz, 1H), 2.56 (q, J = 7.3 Hz, 2H), 1.08 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.3, 150.0, 145.3, 139.2, 138.5,

134.3, 133.4, 128.7, 128.5, 126.0, 124.7, 123.8, 122.9, 122.0, 120.4, 106.1, 84.8, 68.0, 28.6, 15.3; HRMS (ESI) $[M]^+$ Calcd for $[C_{23}H_{20}N_2O]$ 340.1576, found 340.1576.

12-(Thiophen-3-yl)-4b,6-dihydrobenzo[4,5][1,3]oxazino[2,3-*f*][1,6]naphthyridine (6d). The product was obtained as brown needles (146.5 mg, 92%): mp 100–104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43–8.42 (m, 1H), 7.55 (d, J = 8.1 Hz, 1H), 7.18–7.17 (m, 1H), 7.06–7.04 (m, 1H), 7.02–6.97 (m, 2H), 6.92 (t, J = 7.3 Hz, 1H), 6.80 (t, J = 7.3 Hz, 1H), 6.63–6.61 (m, 1H), 6.29 (d, J = 8.8 Hz, 1H), 6.15 (s, 1H), 5.96 (s, 1H), 5.13 (d, J = 14.6 Hz, 1H), 4.99 (d, J = 14.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.0, 150.2, 140.4, 139.1, 137.1, 134.4, 128.4, 127.6, 125.9, 125.1, 124.8, 124.7, 123.6, 123.4, 121.9, 120.4, 105.6, 84.5, 67.9; HRMS (ESI) $[M]^+$ Calcd for $[C_{19}H_{14}N_2OS]$ 318.0827, found 318.0828.

12-(3,5-Dimethoxyphenyl)-4b,6-dihydrobenzo[4,5][1,3]oxazino[2,3-*f*][1,6]naphthyridine (6e). The product was obtained as pale yellow needles (139.6 mg, 75%): mp 80–86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47–8.45 (m, 1H), 7.60 (d, J = 7.3 Hz, 1H), 7.06 (m, 1H), 6.99 (d, J = 7.4 Hz, 1H), 6.92–6.88 (m, 1H), 6.80 (t, J = 8.1 Hz, 1H), 6.32 (s, 2H), 6.28 (d, J = 8.0 Hz, 1H), 6.22–6.20 (m, 1H), 6.14 (s, 1H), 6.03 (s, 1H), 5.18 (d, J = 13.9 Hz, 1H), 5.02 (d, J = 13.9 Hz, 1H), 3.58 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 151.0, 150.1,145.1, 139.2, 138.0, 134.6, 128.1, 126.1, 124.7, 123.7, 123.2, 122.2, 120.6, 107.1, 106.7, 105.9, 101.0, 84.7, 68.1, 55.3; HRMS (ESI) $[M]^+$ Calcd for $[C_{23}H_{20}N_2O_3]$ 372.1474, found 372.1474.

6-Phenyl-2,3,4,11b-tetrahydro-[1,3]oxazino[2,3-*f*][1,6]naphthyridine (6f). The product was obtained as a brown oil (108.4 mg, 82%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36–8.35 (m, 1H), 7.47–7.45 (m, 1H), 7.32–7.27 (m, 5H), 6.94–6.91 (m, 1H), 6.01 (s, 1H), 5.66 (s, 1H), 4.09–3.95 (m, 2H), 3.72–3.67 (m, 1H), 3.37–3.19 (m, 2H), 1.88–1.82 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.7, 150.7, 150.2, 137.1, 135.5, 129.2, 128.7, 128.4, 120.4, 119.9,

102.1, 88.9, 68.5, 47.9, 27.6; HRMS (ESI) $[M]^+$ Calcd for $[C_{17}H_{16}N_2O]$ 264.1263, found 264.1263.

6-(*p*-Tolyl)-2,3,4,11b-tetrahydro-[1,3]oxazino[2,3-*f*][1,6]naphthyridine (6g). The product was obtained as brown crystals (119.7 mg, 86%): mp 110–114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39–8.38 (m, 1H), 7.47 (d, J = 6.6 Hz, 1H), 7.22–7.14 (m, 4H), 6.96–6.93 (m, 1H), 6.03 (s, 1H), 5.66 (s, 1H), 4.08–4.01 (m, 2H), 3.77–3.73 (m, 1H), 3.27–3.20 (m, 1H), 2.32 (s, 3H), 2.09–1.84 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.4, 150.3, 149.9, 138.2, 135.2, 133.9, 129.0, 128.0, 120.0, 119.5, 101.7, 88.6, 68.2, 47.6, 27.2, 21.3; HRMS (ESI) $[M]^+$ Calcd for $[C_{18}H_{18}N_2O]$ 278.1419, found 278.1419.

6-(4-Ethylphenyl)-2,3,4,11b-tetrahydro-[1,3]oxazino[2,3-*f*][1,6]naphthyridine (6h). The product was obtained as a brown oil (122.8 mg, 84%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39–8.38 (m, 1H), 7.48–7.46 (m, 1H), 7.23 (d, J = 9.5 Hz, 2H), 7.19–7.16 (m, 2H), 6.95–6.92 (m, 1H), 6.03 (s, 1H), 5.66 (s, 1H), 4.11–4.04 (m, 1H), 4.01–3.98 (m,1H), 3.37–3.73 (m, 1H), 3.27–3.20 (m, 1H), 2.61 (q, J = 8.0 Hz, 2H), 1.91–1.83 (m, 2H), 1.21 (t, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.6, 150.5, 149.8, 144.4, 135.0, 134.1, 128.1, 127.8, 120.0, 119.4, 101.9, 88.7, 68.2, 47.6, 28.6, 27.2, 15.3; HRMS (ESI) $[M]^+$ Calcd for $[C_{19}H_{20}N_2O]$ 292.1576, found 292.1576.

6-(Thiophen-3-yl)-2,3,4,11b-tetrahydro-[1,3]oxazino[2,3-*f*][1,6]naphthyridine (6i). The product was obtained as a brown oil (118.9 mg, 88%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (dd, J = 5.1, 1.4 Hz, 1H), 7.45 (dd, J = 7.3, 1.4 Hz, 1H), 7.31–7.27 (m, 2H), 7.02–7.00 (m, 1H), 6.95–6.92 (m, 1H), 5.99 (s, 1H), 5.74 (s, 1H), 4.11–4.04 (m, 1H), 4.01-3.98 (m, 1H) 3.81–3.76 (m, 1H), 3.28–3.21 (m, 1H), 1.95–1.85 (m, 1H), 1.30–1.27 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.1, 152.0, 151.1, 145.5, 137.8, 135.8, 128.3, 126.5, 124.9, 120.8,

120.4, 102.9, 89.2, 69.0, 48.3, 27.9; HRMS (ESI) $[M]^+$ Calcd for $[C_{15}H_{14}N_2OS]$ 270.0827, found 270.0827.

6-(3,5-Dimethoxyphenyl)-2,3,4,11b-tetrahydro-[1,3]oxazino[2,3-*f*][1,6]naphthyridine (6j). The product was obtained as a pale yellow semi-solid (111.9 mg, 69%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45–8.44 (m, 1H), 7.52 (d, J = 7.3 Hz, 1H), 7.02–6.99 (m, 1H), 6.52 (s, 2H), 6.47–6.46 (m, 1H), 6.07 (s, 1H), 5.76 (s, 1H), 4.14–4.13 (m, 1H), 4.06 (td, J = 12.8, 3.2 Hz, 1H), 3.88–3.81 (m, 2H), 3.79 (s, 6H), 3.29 (td, J = 13.8, 2.8 Hz, 1H), 2.03–1.92 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 151.4, 150.5, 149.7, 139.3, 138.6, 135.1, 119.6, 106.3, 101.6, 100.5, 88.7, 68.3, 55.5, 47.6, 27.4; HRMS (ESI) $[M]^+$ Calcd for $[C_{19}H_{20}N_2O_3]$ 324.1474, found 324.1475.

6-Phenyl-2,3,4,11b-tetrahydro-[1,3]oxazino[2,3-*a*][2,6]naphthyridine (6k). The product was obtained as a brown oil (105.7 mg, 80%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 2H), 7.43– 7.41 (m, 5H), 7.23 (d, J = 5.1 Hz, 1H), 6.10 (s, 1H), 5.57 (s, 1H), 4.22–4.08 (m, 2H), 3.83–3.79 (m, 1H), 3.36–3.29 (m, 1H), 2.01–1.91 (m, 1H), 1.46–1.45 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 145.4, 142.0, 137.2, 130.9, 128.3, 127.7, 125.9, 124.0, 121.5, 97.7, 87.2, 68.5, 47.6, 27.0; HRMS (ESI) $[M]^+$ Calcd for $[C_{17}H_{16}N_2O]$ 264.1263, found 264.1263.

6-(4-Methoxyphenyl)-2,3,4,11b-tetrahydro-[1,3]oxazino[2,3-*a*][2,6]naphthyridine (6l). The product was obtained as a brown semi-solid (126.6 mg, 86%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 2H), 7.27 (d, J = 8.8 Hz, 2H), 7.14 (d, J = 5.1 Hz, 1H), 6.91 (d, J = 8.8 Hz, 2H), 6.03 (s, 1H), 5.50 (s, 1H), 4.16–4.03 (m, 2H), 3.82–3.80 (m, 3H), 3.77–3.76 (m, 1H) 3.30–3.23 (m, 1H), 1.30–1.22 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 146.8, 145.5, 145.3, 130.7, 129.4, 129.2, 128.6, 121.5, 113.7, 97.2, 87.3, 68.4, 55.3, 47.4, 27.0; HRMS (ESI) $[M]^+$ Calcd for $[C_{18}H_{18}N_2O_2]$ 294.1368, found 294.1367.

6-(*p*-Tolyl)-2,3,4,11b-tetrahydro-[1,3]oxazino[2,3-*a*][2,6]naphthyridine (6m). The product was obtained as brown crystals (114.1 mg, 82%): mp 95–98 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 2H), 7.27–7.17 (m, 5H), 6.06 (s, 1H), 5.53 (s, 1H), 4.19–4.15 (m, 1H), 4.08 (td, J = 11.7, 2.2 Hz, 1H), 3.83–3.79 (m, 1H), 3.33–3.25 (m, 1H), 2.40 (s, 3H), 1.98–1.84 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.1, 145.5, 145.3, 138.2, 134.0, 130.8, 129.0, 128.1, 121.5, 97.2, 87.3, 68.4, 47.5, 27.0, 21.3; HRMS (ESI) $[M]^+$ Calcd for $[C_{18}H_{18}N_2O]$ 278.1419, found: 278.1420.

6-(4-Ethylphenyl)-2,3,4,11b-tetrahydro-[1,3]oxazino[2,3-*a*][2,6]naphthyridine (6n). The product was obtained as a brown semi-solid (118.4 mg, 81%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 2H), 7.24–7.16 (m, 4H), 7.10 (d, J = 5.1 Hz, 1H), 5.99 (s, 1H), 5.46 (s, 1H), 4.12–4.08 (m, 1H), 4.04–3.98 (m, 1H), 3.77–3.73 (m, 1H), 3.22 (td, J = 14.6, 2.2 Hz, 1H), 2.62 (q, J = 8.0 Hz, 2H), 2.54 (d, J = 1.4 Hz, 1H), 1.88–1.82 (m, 1H), 1.23–1.18 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.2, 145.5, 145.3, 144.4, 134.1, 130.7, 128.6, 128.1, 127.8, 121.5, 97.1, 87.2, 68.4, 47.4, 28.6, 27.0, 15.4; HRMS (ESI) $[M]^+$ Calcd for $[C_{19}H_{20}N_2O]$ 292.1576, found 292.1575.

6-(Thiophen-3-yl)-2,3,4,11b-tetrahydro-[1,3]oxazino[2,3-*a*][2,6]naphthyridine (6o). The product was obtained as yellow brown needles (116.2 mg, 86%): mp 100–104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30–8.29 (m, 2H), 7.30 (d, J = 2.7 Hz, 2H), 7.09 (d, J = 5.0 Hz, 1H), 7.02–7.00 (m, 1H), 5.97 (s, 1H), 5.56 (s, 1H), 4.13–4.08 (m, 1H), 4.01 (td, J = 11.9, 2.3 Hz, 1H), 3.79–3.75 (m, 1H), 3.28–3.21 (m, 1H), 1.96–1.86 (m, 1H), 1.30–1.18 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 145.4, 142.0, 137.2, 130.9, 128.3, 127.6, 125.9, 124.0, 121.5, 97.7, 87.2, 68.5, 47.6, 27.0; HRMS (ESI) $[M]^+$ Calcd for $[C_{15}H_{14}N_2OS]$ 270.0827, found 270.0827.

6-(4-(Trifluoromethyl)phenyl)-2,3,4,11b-tetrahydro-[1,3]oxazino[2,3-*a*][2,6] naphthyridine (6p). The product was obtained as off white crystals (103.0 mg, 62%): mp 150–154 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38–8.35 (m, 2H), 7.66 (d, J = 8.2 Hz, 2H), 7.49 (d, J = 7.8 Hz, 2H), 7.17 (d, J = 4.6 Hz, 1H), 6.03 (s, 1H), 5.54 (s, 1H), 4.18–4.04 (m, 2H), 3.71–3.66 (m, 1H), 3.36–3.29 (m, 1H), 1.94–1.84 (m, 1H), 1.33 (d, J = 13.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.2, 145.5, 140.6, 131.1, 128.6, 128.0, 125.4 (q, J = 3.8 Hz), 121.5, 98.4, 87.1, 68.3, 47.6, 27.0; HRMS (ESI) $[M]^+$ Calcd for $[C_{18}H_{15}F_3N_2O]$ 332.1136, found 332.1137.

6-Phenyl-13b,15-dihydrobenzo[*b*]benzo[4,5][1,3]oxazino[2,3-*f*][1,6]naphthyridine (6q). The product was obtained as yellow needle crystals (150.4 mg, 83%): mp 138–142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.95 (d, J = 8.8 Hz, 1H), 7.68 (d, J = 8.8 Hz, 1H), 7.58 (t, J = 7.3 Hz, 1H), 7.35–7.29 (m, 3H), 7.23–7.21 (m, 3H), 7.09–7.07 (m, 1H), 7.02 (d, J = 7.3 Hz, 1H), 6.80 (m, 1H), 6.73 (t, J = 8.1 Hz, 1H), 6.44 (s, 1H), 6.15 (s, 1H), 5.14 (d, J = 13.9 Hz, 1H), 5.04 (d, J = 13.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 148.4, 146.8, 138.4, 136.0, 133.2, 130.0, 129.5, 128.8, 128.7, 128.3, 128.0, 127.9, 127.5, 127.1, 126.7, 125.2, 124.8, 124.1, 122.6, 108.8, 85.0, 67.9; HRMS (ESI) $[M]^+$ Calcd for $[C_{25}H_{18}N_2O]$ 362.1419, found 362.1420.

6-(*p*-Tolyl)-13b,15-dihydrobenzo[*b*]benzo[4,5][1,3]oxazino[2,3-*f*][1,6]naphthyridine (6r). The product was obtained as pale yellow needles (163.7 mg, 87%): mp 146–150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 7.3 Hz, 1H), 7.61–7.56 (m, 1H), 7.34 (t, J = 8.1 Hz, 1H), 7.25 (d, J = 8.0 Hz, 2H), 7.07–7.02 (m, 3H), 6.82 (t, J = 7.3 Hz, 1H), 6.76 (t, J = 8.1 Hz, 1H), 6.47 (s, 1H), 6.17–6.16 (m, 2H), 5.13 (d, J = 13.1 Hz, 1H), 5.04 (d, J = 13.9 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 148.5, 146.7, 145.2, 138.5, 133.3, 132.7, 129.9, 128.4, 128.2, 127.9, 127.8, 127.4, 127.1,

126.8, 125.1, 124.7, 124.3, 122.4, 121.9, 109.0, 85.1, 67.8, 21.3; HRMS (ESI) $[M]^+$ Calcd for $[C_{26}H_{20}N_2O]$ 376.1576, found 376.1577.

6-(4-Ethylphenyl)-13b,15-dihydrobenzo[b]benzo[4,5][1,3]oxazino[2,3-*f*][1,6]naphthyridine (6s). The product was obtained as pale yellow crystals (165.9 mg, 85%): mp 158–162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s,1H), 7.95 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 7.3 Hz, 1H), 7.58 (td, J = 8.8, 1.5 Hz 1H), 7.34 (t, J = 8.1 Hz, 1H), 7.25 (d, J = 8.0 Hz, 2H), 7.07–7.02 (m, 3H), 6.82 (t, J = 7.3 Hz, 1H), 6.76 (t, J = 8.1 Hz, 1H), 6.47 (s, 1H), 6.17–6.16 (m, 2H), 5.13 (d, J = 13.2 Hz, 1H), 5.04 (d, J = 13.9 Hz, 1H), 2.58 (q, J = 7.3 Hz, 2H), 1.18–1.15 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 148.5, 146.7, 145.2, 138.5, 133.3, 132.7, 129.9, 128.7, 128.4, 128.2, 127.9, 127.8, 127.5, 127.4, 127.1, 126.8, 125.1, 124.7, 124.3, 122.4, 121.9, 109.0, 67.8, 28.6, 15.2; HRMS (ESI) $[M]^+$ Calcd for $[C_{27}H_{22}N_2O]$ 390.1732, found 390.1733.

6-(Thiophen-3-yl)-13b,15-dihydrobenzo[b]benzo[4,5][1,3]oxazino[2,3-*f*][1,6]naphthyridine (6t). The product was obtained as a dark red semi-solid(160.3 mg, 87%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.93 (d, J = 8.2 Hz, 1H), 7.68 (d, J = 8.2 Hz, 1H), 7.59 (td, J = 9.6, 2.8 Hz, 1H), 7.33 (td, J = 7.8, 2.8 Hz, 1H), 7.30–7.29 (m, 1H), 7.14–7.12 (m, 1H), 7.04 (d, J = 7.3 Hz, 1H), 6.90–6.80 (m, 3H), 6.94 (s, 1H), 6.29 (d, J = 8.2 Hz, 1H), 6.13 (s, 1H), 5.13 (d, J = 13.2 Hz, 1H), 5.03 (d, J = 14.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.6, 148.6, 141.9, 138.6, 137.3, 133.1, 130.0, 128.4, 127.9, 127.7, 127.4, 127.1, 126.8, 125.5, 125.2, 125.1, 124.8, 124.0, 122.47, 122.44, 108.2, 67.8; HRMS (ESI) $[M]^+$ Calcd for $[C_{23}H_{16}N_2OS]$ 368.0983, found 368.0983.

6-(3,5-Dimethoxyphenyl)-13b,15-dihydrobenzo[*b*]benzo[4,5][1,3]oxazino[2,3-*f*][1,6]naphthyridine (6u). The product was obtained as yellow needles (152.1 mg, 72%): mp 86–90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 8.01 (d, J = 8.1 Hz, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.64 (td, J = 5.8, 1.4 Hz, 1H), 7.39 (t, J = 7.3 Hz, 1H), 7.07 (d, J = 6.6 Hz, 1H),

6.91–6.83 (m, 2H), 6.54–6.52 (m, 3H), 6.42–6.41 (m, 1H), 6.31 (d, J = 7.3 Hz, 1H), 6.20 (s, 1H), 5.18 (d, J = 13.9 Hz, 1H), 5.08 (d, J =13.9 Hz, 1H), 3.66 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 151.5, 148.5, 146.5, 138.5, 137.9, 133.1, 129.9, 128.4, 127.9, 127.2, 127.1, 126.8, 125.2, 124.6, 124.1, 122.3, 122.2, 108.9, 106.3, 101.4, 85.0, 67.8, 55.3; HRMS(ESI) $[M]^+$ Calcd for $[C_{27}H_{22}N_2O_3]$ 422.1630, found 422.1631.

6-Phenyl-2,3,4,13b-tetrahydrobenzo[*b*][1,3]oxazino[2,3-*f*][1,6]naphthyridine (6v). The product was obtained as a brown oil (127.3 mg, 81%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.86 (d, J = 8.8 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.54 (t, J = 8.0 Hz, 1H), 7.43–7.42 (m, 1H), 7.39–7.32 (m, 4H), 7.28 (t, J = 7.3 Hz, 1H), 6.09 (s, 1H), 5.82 (s, 1H), 4.15–4.01 (m, 2H), 3.78–3.73 (m, 1H), 3.41–3.39 (m, 1H), 3.28–3.25 (t, J = 10.3 Hz, 1H), 1.96–1.83 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 151.3, 148.9, 138.9, 132.6, 130.0, 129.4, 128.8, 128.6, 128.4, 127.9, 127.8, 126.5, 124.4, 121.7, 102.2, 84.4, 68.4, 47.7, 26.9; HRMS (ESI) $[M]^+$ Calcd for $[C_{21}H_{18}N_2O]$ 314.1419, found 314.1420.

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Supporting Information: Supplementary data (^{1}H NMR, ^{13}C NMR spectra and HRMS), CIF for compound **5a** (CCDC 932014) associated with this article is available free of charge via the Internet at http://pubs.acs.org.

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