Tetrahedron 70 (2014) 5863–5871

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

A palladium-catalyzed facile and general method for the stereoselective synthesis of (*E*)-3-arylidene-3,4-dihydro-2*H*-1,4-benzoxazines and their naphthoxazine analogues

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ARTICLE INFO

Article history:
Received 27 January 2014
Received in revised form 24 May 2014
Accepted 10 June 2014
Available online 19 June 2014

Keywords:
1,4-Benzoxazine
1,4-Naphthoxazine
Palladium catalyst
Stereoselective
Cyclization

ABSTRACT

Palladium-catalyzed cyclocondensation of an aryl iodide with *N*-tosyl-2-(prop-2′-ynyloxy)aniline at room temperature is shown to constitute a convenient general method for the synthesis of (*E*)-3-arylidene-3,4-dihydro-2*H*-1,4-benzoxazines in moderate to very good yields. The method could also be extended to the synthesis of (*E*)-3-arylidene-2*H*-naphth[1,2-*b*][1,4]oxazines. The regio- and stereo-selectivity of the process, short reaction time, operational simplicity, and use of inexpensive starting materials represent its attractive features.

1. Introduction

Heterocycles having heteroatoms at 1,4-positions and fused to a benzene ring are considered as important targets in medicinal chemistry due to their wide range of biological and therapeutic potentials. Among them, 2*H*-1,4-benzoxazines have been an integral part of many naturally occurring and bioactive agents.[1] In particular, 3-substituted-3,4-dihydro-2*H*-1,4-benzoxazine has attracted considerable attention in recent times as it constitutes the structural motif of potent drugs,[2a,b] and bioactive natural[2c] and synthetic[2d,e] compounds, and acts as a valuable building block in the synthesis of compounds of therapeutic interest.[2f,g] Besides, 2- and 3-ylidene-1,4-benzoxazine derivatives have been shown to be important pharmaceutical agents. For example, compound **1** (Fig. 1) has proved to be a potential agent for treating infections caused by *Mycobacterium* species,[3a] while naturally occurring compound **2**, isolated from a fermentation broth of *Streptomyces* sp., is identified as an inhibitor of glutathione *S*-transferase, an enzyme implicated in drug resistance in cancer chemotherapy.[3b] Besides, compound **3** possesses significant CNS depressing activity.[3c] Recently, Rh-catalyzed asymmetric hydrogenation of the exocyclic double bond of (*Z*)-3-(arylidene)-1,4-benzoxazines (**4**, R=aryl group) has been shown to provide an easy access to the corresponding saturated chiral products[4] (upto 98.6% ee), implying that 3-(or 2-)-ylidene-1,4-benzoxazines **4** could be profitably used in the synthesis of biologically active scaffolds by functional group manipulation around the exocyclic double bond.[5]

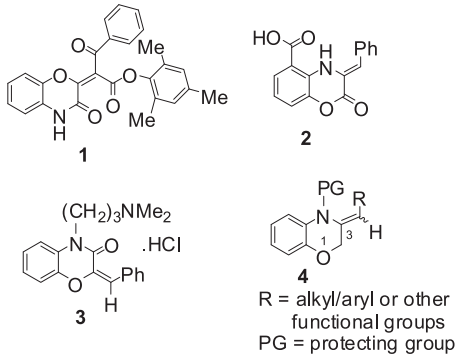

Fig. 1. Some biologically important 1,4-benzoxazine derivatives.

Emergence of such promising results has stimulated new investigations into the synthesis of 3-substituted-1,4-benzoxazines. As a consequence, a number of both conventional[6] and modern synthetic methods[7] have been developed for the synthesis of 3-substituted-3,4-dihydro-2*H*-1,4-benzoxazines. But methods for the synthesis of 3-ylidene-3,4-dihydro-1,4-benzoxazine **4** and its 2-oxo derivatives have been limited in number.[8,9] In particular, the

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http://dx.doi.org/10.1016/j.tet.2014.06.036
0040-4020/

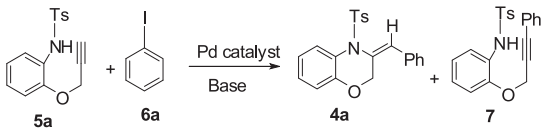
report[9] based on palladium-catalyzed reaction describes the synthesis of the (*Z*)-isomers of compound **4** (R=Aryl group) utilizing a multi-step reaction sequence. On the other hand, syntheses of (*Z*)-2-(arylidene)-1,4-benzoxazine, a regioisomer of **4**, are accomplished using palladium[10a] and copper catalyst,[10b] though employment of gold catalysis[10c] affords such compound as a mixture of (*E*)- and (*Z*)-stereoisomers. Surprisingly, a stereoselective method for the general synthesis of the (*E*)-isomers of both 2- and 3-arylidene-3,4-dihydro-1,4-benzoxazines is not known,[11] which prevents the exploration of their potential in industrial and academic research. Thus, development of a facile and general method for stereoselective synthesis of these compounds remains an important challenge in organic synthesis.

With our recent success in palladium-catalyzed heteroannulations[12] of suitably designed substrates leading to the synthesis of various heterocycles including 1,2,3-triazolo-1,4-benzoxazines,[12f] we became interested in the synthesis of the *E*-isomers of **4** via one-pot palladium-catalyzed reactions. We envisioned that a straightforward and stereoselective synthesis of (*E*)-3-arylidene-1,4-benzoxazines **4** (R=aryl, PG=Ts) could be achieved by performing the reaction between *N*-tosyl-2-(prop-2′-ynyloxy)aniline **5a** and aryl iodide **6** under appropriate catalyzed conditions. The goal was indeed realized as described in this paper.[13]

2. Results and discussion

The starting substrates *N*-tosyl-2-(prop-2′-ynyloxy)aniline **5a** and its naphthyl analogue **5b** could easily be prepared using few reaction steps starting from commercially available 2-nitrophenol and 2-nitro-1-naphthol, respectively (see Supplementary data). In view of the immense success of the '*Sonogashira catalyst*' in various heteroannulations, we were initially keen to employ $Pd(PPh_3)_2Cl_2$/CuI for the reaction between **5a** and **6a**; however, carrying out this reaction at rt in the presence of K_2CO_3 as base furnished the desired (*E*)-3-benzylidene-3,4-dihydro-1,4-benzoxazine (**4a**) with low yield (14%) along with the *C*-phenylated internal alkyne **7** (35%). This result prompted us to optimize the reaction conditions by screening different reaction parameters such as catalyst, co-catalyst, base, solvent, etc. and selected results are presented in Table 1. To find out the best palladium catalyst, we then employed $Pd(OAc)_2/PPh_3$ in place of $Pd(PPh_3)_2Cl_2$, but this exclusively furnished the alkyne **7**, which could not be cyclized to **4a** even after heating the reaction at 90 °C for several hours (Table 1, entry 2). Realizing that the formation of **4a** is not occurring through the acyclic intermediate **7** formed via Sonogashira's pathway, we decided to eliminate CuI from this reaction. Indeed, removal of CuI along with the use of Et_3N considerably suppressed the formation of **7**, but product **4a** was still isolated with poor yield (Table 1, entry 3). Gratifyingly, replacing the base Et_3N by a stronger one, viz. K_2CO_3 led to the exclusive formation of **4a** with 69% yield (Table 1, entry 4). Next, we performed this reaction without PPh_3, but the yield of **4a** (Table 1, entry 5) dropped significantly suggesting the necessity of PPh_3 in this reaction. In the subsequent experiments, we screened few more palladium catalysts (Table 1, entries 6–8) to improve the yield further, but none of them appeared to be superior to $Pd(OAc)_2/PPh_3$. Among the solvents screened, DMF was found to be the best. Thus, the reaction conditions of entry 4 of Table 1 were considered to be optimal. However, when tosyl group of **5a** was replaced by H/Me/BOC and the resulting substrates were allowed to react separately with phenyl iodide (**6a**) under the optimized reaction conditions, these reactions did not furnish the corresponding desired products even after extending the reaction time to 24 h. In these cases, only *C*-phenylated products (at terminal acetylene moiety) of the substrates were isolated in moderate yields (20–40%) along with recovery of the starting material (10–30%). Therefore, the *N*-tosylated acetylenic substrate like **5a** was found to be necessary for this reaction.

Table 1
Optimization of the reaction conditions for the synthesis of **4a**[a,b]



5a **6a** **4a** **7**

Entry	Catalyst	Co-catalyst	Base	Time (h)	Yield (%)	
					4a	**7**
1	$Pd(PPh_3)_2Cl_2$	CuI	K_2CO_3	8	14	35
2	$Pd(OAc)_2/PPh_3$	CuI	K_2CO_3	2	0	56
3	$Pd(OAc)_2/PPh_3$	—	Et_3N	16	15	30
4	*$Pd(OAc)_2/PPh_3$*	*—*	*K_2CO_3*	*2*	*69*	*0*
5	$Pd(OAc)_2$	—	K_2CO_3	4	22	0
6	$Pd(PPh_3)_4$	—	K_2CO_3	3	50	0
7[c]	$PdCl_2/PPh_3$	—	K_2CO_3	5	61	0
8[c]	Pd/C, PPh_3	—	K_2CO_3	5	14	0

[a] *N*-Tosyl-2-(prop-2′-ynyloxy)aniline **5a** (1.0 equiv), phenyl iodide **6a** (1.15 equiv), palladium catalyst (0.05 equiv), PPh_3 (0.2 equiv), CuI (0.1 equiv, only for entries 1 and 2), Bu_4NBr (0.1 equiv), base (4.0 equiv) in anhydrous DMF at room temp (except entries 7 and 8).

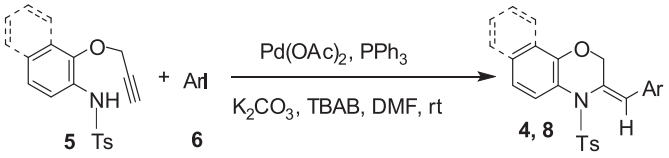
[b] Room temp implies temperature between 35 °C and 40 °C.

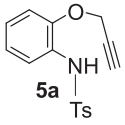
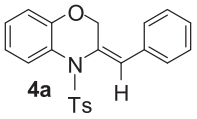
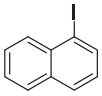
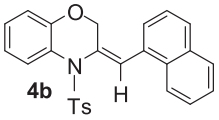
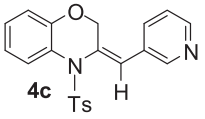
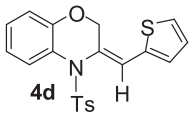
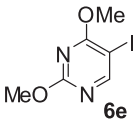
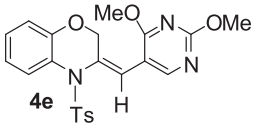
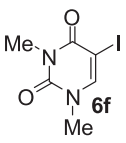
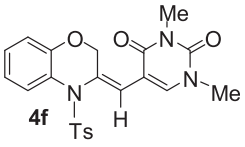
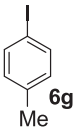
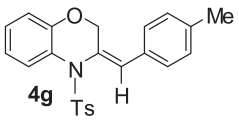
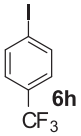
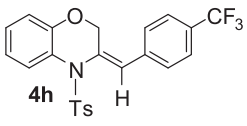
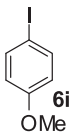
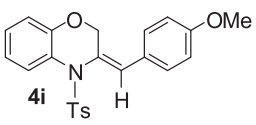
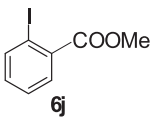
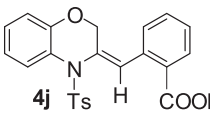
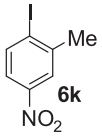
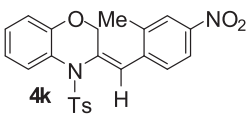
[c] Reaction mixture was heated to 80 °C as no reaction took place at room temperature.

In order to study the scope and generality of this transformation, we performed the reaction of **5a** with various iodides **6a**–**k** (Table 2, entries 2–11) under optimized reaction conditions. A range of functional groups both electron donating (e.g., OMe, Me) and withdrawing (e.g., CO_2Me, CF_3, NO_2) were found to be tolerated under these reaction conditions. As can be seen from Table 2, aromatic iodides **6a**,**b** without any functional group afforded the desired products with very good yields (Table 2, entries 1 and 2). Heteroaryl iodides **6c**–**f** were also found to be equally able to furnish the desired products (Table 2, entries 3–6). To our disappointment, however, when *p*-iodotoluene **6g** was employed as the coupling partner, the corresponding product **4g** was obtained in moderate yield (Table 2, entry 7). Nevertheless, replacing methyl group of **6g** by trifluoromethyl resulted in the improvement of the corresponding product (Table 2, entry 8). Iodides **6i** and **6j** having *para*-methoxy and carbomethoxy groups furnished the corresponding products **4i** (58%) and **4j** (74%), respectively (Table 2, entries 9 and 10). However, presence of both methyl and nitro groups in the aryl iodide as in **6k** afforded the product in moderate yield (Table 2, entry 11). All the reactions were found to be very clean in nature. Besides, no formation of any isomer of product **4** with (*Z*)-stereochemistry or of seven-membered ring product formed via 7-*endo*-*dig* cyclization was observed in any case.

Next, we became interested to employ **5b** as an acetylenic substrate in this reaction in order to obtain the naphtho analogue of product **4**. To our gratification, **5b** reacted successfully with phenyl iodide (**6a**) under the optimized reaction conditions to yield the targeted (*E*)-3-benzylidene-2*H*-naphth[1,2-*b*][1,4]oxazine **8a** in 74% yield (Table 2, entry 12). 3-Iodopyridine (**6c**) was also found to be equally effective to produce the corresponding product **8b** (Table 2, entry 13). We then examined the effects of both electron donating and withdrawing groups (EDGs and EWGs) on aryl iodides in this reaction. Accordingly, when iodides containing EDG such as *p*-methyl- and *p*-bromoiodobenzene (**6g** and **6l**) were allowed to react individually with acetylene **5b**, moderate yields (54–57%) of the corresponding products **8c** and **8d** were observed (Table 2, entries 14 and 15). On the other hand, with the electron-withdrawing nitro group at the *para*-position of the aryl iodide, **6j** provided the excellent yield (83%) of the expected product **8e** (Table 2, entry 16). To the best of our knowledge, 3-arylidene-2*H*-naphth[1,2-*b*][1,4]benzoxazines **8** are hitherto unknown heterocycles. It is worth mentioning

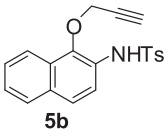
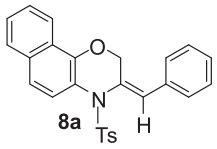
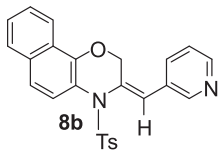
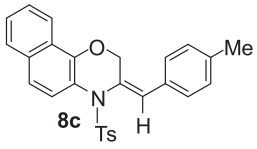
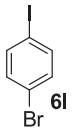
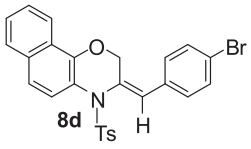
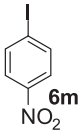
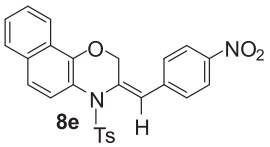
Table 2
Synthesis of (*E*)-3-arylidine-3,4-dihydro-2*H*-1,4-benzoxazines (**4**) and their naphtho analogues **8**[a]



Entry	Acetylene **5**	Aryl iodide **6**	Time[b] (h)	Product	Yield[c] (%)
1			2.0		69
2	**5a**		3.0		71
3	**5a**		2.5		70
4	**5a**		2.0		78
5	**5a**		5.5		68
6	**5a**		3.0		79
7	**5a**		2.5		38
8	**5a**		5.0		51
9	**5a**		5.0		58
10	**5a**		3.5		74
11	**5a**		2.5		55

(*continued on next page*)

Table 2 (*continued*)

Entry	Acetylene **5**	Aryl iodide **6**	Time[b] (h)	Product	Yield[c] (%)
12[d]	 **5b**	**6a**	4.0	 **8a**	74
13[d]	**5b**	**6c**	4.0	 **8b**	79
14[d]	**5b**	**6g**	7.0	 **8c**	54
15[d]	**5b**	 **6l**	5.0	 **8d**	57
16[d]	**5b**	 **6m**	5.5	 **8e**	83

[a] Acetylene **5a**/**5b** (0.5 mmol), iodide **6** (0.57 mmol), $Pd(OAc)_2$ (0.025 mmol), PPh_3 (0.1 mmol), K_2CO_3 (2.0 mmol), and *n*-Bu_4NBr (0.05 mmol), in DMF (4 mL), at room temperature.
[b] Time indicating the completion of reaction as monitored through TLC.
[c] Yields were calculated based on **5a**/**5b**.
[d] In contrast to entries 1–11, iodide **6** was applied in slight excess (1.5 equiv with respect to acetylene) to compensate for partial deiodination of **6** observed during the reaction.

that (+)-4-propyl-9-hydroxynaphthoxazine (PHNO), a new dopaminomimetic with selective D_2 agonist properties, has been reported to be useful in the treatment of Parkinson's disease.[14]

The structures of the synthesized compounds, 3-arylidene derivatives of 3,4-dihydro-2*H*-1,4-benzoxazines and naphth[1,2-*b*][1,4]oxazines (**4** and **8**) were unambiguously deduced by spectroscopic (^1H, ^{13}C and DEPT NMR experiments, IR, mass) and analytical evidences. Notably, the chemical shifts of the olefinic proton in the (*Z*)-isomers of 3-arylidene-1,4-benzoxazines **4** have been reported[9] to lie in the range between 6 and 7 ppm. However, the olefinic proton signals of our products (**4**, **8**) appeared downfield (δ_H>7 ppm), attributed to the deshielding effect of the tosyl group in proximity, indicating the *E*-stereochemistry of the exocyclic double bond. Besides, NOE experiments and $^3J_{CH}$ coupling constant values between olefinic proton and methylenic carbon (OCH_2) of the 1,4-oxazine ring of the products provided additional support in favor of *E*-stereochemistry. In literature,[8a,9,15] $^3J_{CH}$ values more than 7 Hz were attributed to (*E*)-stereoisomers and less than 5 Hz to (*Z*)-isomers. In the present case, $^3J_{CH}$ values of the products **4** and **8** were between 7 and 9 Hz suggesting (*E*)-stereochemistry (see ^{13}C NMR data of **4a**, **4d**, **4i**, **8a**, **8c** in experimental). Finally, single crystal X-ray diffraction analysis of two representative products **4d** and **8a** confirmed the stereochemistry and structure simultaneously (Fig. 2).

Based on known palladium chemistry and control experiments, a plausible reaction mechanism is proposed (Scheme 1). Oxidative addition of aryl iodide **6** to Pd(0), formed in situ[16a] from $Pd(OAc)_2$ and PPh_3, produces the species ArPd(II)I (**A**). This subsequently

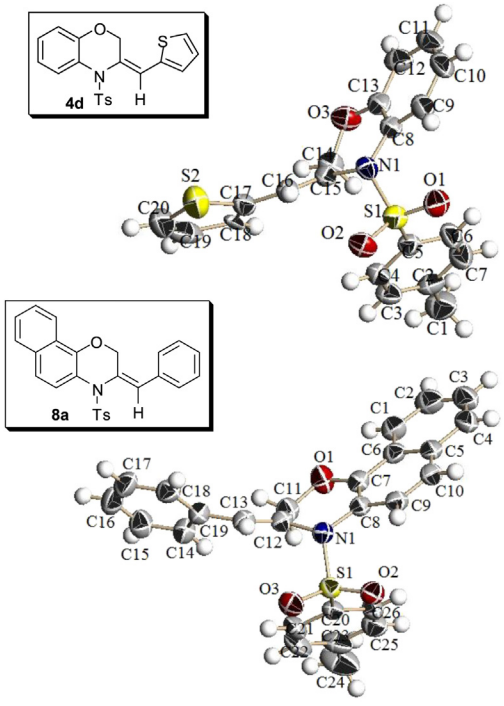
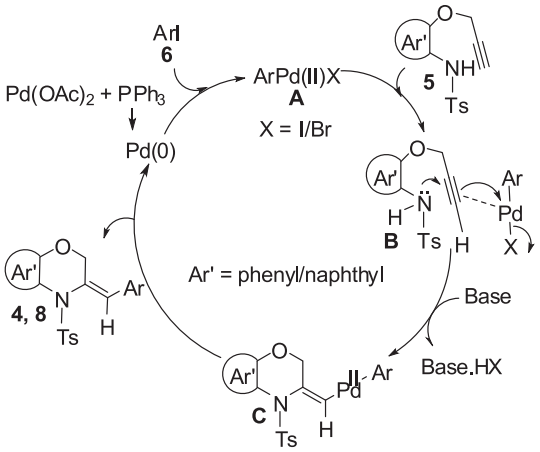
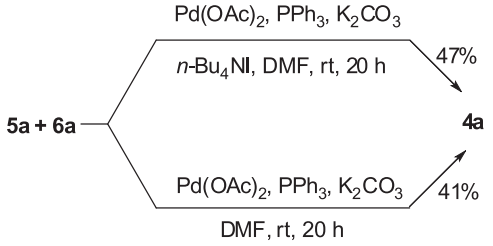


Fig. 2. ORTEP representations of products **4d** and **8a**.



Scheme 1. Possible reaction mechanism.

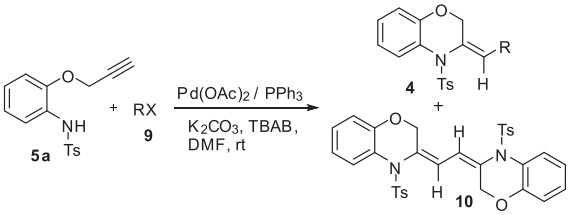
activates the triple bond of the acetylenic moiety to undergo intramolecular nucleophilic attack[16b,c] by the neighboring nitrogen atom (*N*-Ts) to generate the vinylic palladium intermediate species **C** via *trans*-aminopalladation.[16d,e] Finally, reductive elimination[16f] from intermediate **C** might result in the formation of the product (**4**/**8**) ensuring *E*-stereochemistry and regeneration of Pd(0) to make the catalytic cycle active. Possibly, tetrabutylammonium bromide (Bu_4NBr) is participating in halogen exchange reaction[17] with intermediate species **A** leading to the formation of the more reactive species RPd(II)Br for expediting the process, while also performing the role of phase-transfer catalyst in order to facilitate the reaction by increasing the amount of base in the reaction system. This hypothesis was tested by performing control experiments. Accordingly, in two separate experiments (Scheme 2), acetylene **5a** was allowed to react with phenyl iodide **6a** in DMF at room temperature for 20 h in the presence of $Pd(OAc)_2$ (5 mol %), PPh_3 (20 mol %), and K_2CO_3; either Bu_4NI was used in place of Bu_4NBr or no ammonium salt used. Surprisingly, both the reactions were found to be incomplete. However, the reaction involving Bu_4NI led to the isolation of the cyclized product **4a** with 47% yield along with the recovery of acetylenic substrate **5a** (24%). In the other reaction, the product **4a** was isolated with 41% yield while the acetylenic substrate **5a** remained unreacted to the extent of 26%. These experiments pointed out the importance of Bu_4NBr in this reaction.[18]

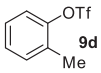
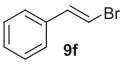
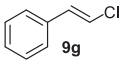
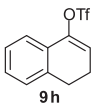


Scheme 2. Control experiments to establish the role of Bu_4NBr.

After successful demonstration of the reaction of **5a** with various aryl iodides **6**, we planned to extend the scope of this reaction further by employing internal alkynes or aryl bromide/chloride/triflate (or corresponding vinyl analogue). Our initial attempts to employ the internal alkyne **7** as substrate in the reactions with different aryl iodides turned out to be unfruitful, suggesting possible steric hindrance induced by substitution on the alkyne moiety (see mechanism of Scheme 1). Thereafter, we studied the reactions of **5a** with other halides/triflates in place of aryl iodide **6** as described in Table 3. We initially studied the reaction of phenyl

Table 3
Reactions of **5a** with aryl and vinyl bromide/chloride/triflate **9**[a]



Entry	RX (**9**)	Time (h)	Product **4** (% yield)[b]	Product **10** (% yield)[b]
1	 **9a**	6	**4a** (0%)	**10** (40%)
2	 **9b**	12	**4a** (0%)	**10** (42%)
3	 **9c**	5	**4a** (0%)	**10** (55%)
4	 **9d**	12	**4l** (0%)	**10** (37%)
5	 **9e**	6	**4m** (32%)	**10** (20%)
6	 **9f**	12	**4n** (50%)	**10** (27%)
7	 **9g**	11	**4n** (0%)	**10** (25%)
8	 **9h**	12	**4o** (73%)	**10** (0%)

[a] Reaction conditions: **5a** (0.5 mmol), substrate **9** (0.57 mmol), $Pd(OAc)_2$ (0.028 mmol), PPh_3 (0.11 mmol), K_2CO_3 (2.0 mmol), and *n*-Bu_4NBr (0.057 mmol), in DMF (4 mL) at room temperature.
[b] Yields were calculated based on **5a**.

bromide with **5a** under the optimized reaction conditions. Surprisingly, there was no sign of the formation of the expected product **4a** in TLC; instead a slower moving spot was found to be developed during the course of the reaction. The spectral analysis of this purified product (40% yield) indicated the formation of the bis-heteroannulated product **10** (Table 3, entry 1). This structural conclusion was further confirmed by X-ray diffraction analysis (for ORTEP diagram, see Fig. 3). Formation of the product **10** can be attributed to the synthesis of the dimer of the acetylenic substrate

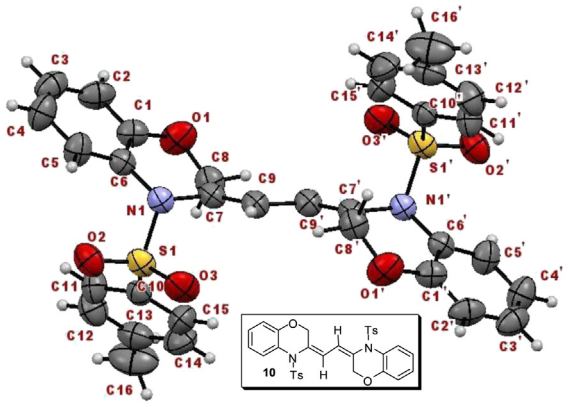
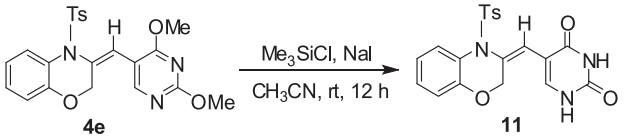


Fig. 3. ORTEP representation of product **10**.

5a followed by intramolecular cyclization. However, the subsequent employment of the phenyl chloride (**9b**) and triflates (**9c** and **9d**) in this reaction led to the observations of the same product **10** in moderate yields (Table 3, entries 2–4). We then focused our attention on the reactivity of vinyl iodide/bromide/chloride/triflate (entries 5–8 of Table 3). On the other hand, employment of vinyl iodide (**9e**) resulted in a mixture of expected product **4m** (32%) and the side product **10** (20%) (Table 3, entry 5). Next, though the use of β-bromostyrene (**9f**) in this reaction increased the yield of the desired product **4n** to the extent of 50%, the reaction was found to be somewhat slower (Table 3, entry 6); in contrast, β-chlorostyrene (**9g**) did not afford any targeted product **4** except the side product **10** in low yield (25%). Pleasingly, vinyl triflate **9h** furnished the desired product **4o** (73%) exclusively with complete suppression of the side product **10**.

In recent reports,[19] 2,3-dihydro-1,4-benzodioxepins linked with uracil or its 5-fluoro derivative showed good antiproliferative activity against human breast cancer cell lines (MCF-7). With our interest on uracil derivatives,[20] we decided to apply this methodology for the preparation of novel uracil derivatives with possible biological activities. Indeed, the synthesis of novel 5-substituted *N*,*N*-dimethyluracil derivative **4f** could easily be accomplished adopting our reaction protocol (Table 2, entry 6). In addition, one of the synthesized products **4e** (Table 2, entry 5), a 2,4-dimethoxy pyrimidine derivative, could easily be demethylated by treating with trimethylsilyl chloride and sodium iodide at rt leading to the formation of a novel uracil derivative **11** (Scheme 3). The cytotoxicity assays of the synthesized compounds including uracil derivatives **4f** and **11** in various cancer cell lines are under investigation.



Scheme 3. Synthesis of 5-substituted uracil derivative **11**.

Since *N*-unsubstituted 1,4-benzoxazines are biologically important,[2e,3a,b,21] we also attempted N-deprotection reactions of **4a** at different temperature (−78 °C to −30 °C) using the known reagent sodium naphthalenide.[12d] Unfortunately, the desired product was not obtained despite repeated attempts. Instead, 1,4-benzoxazine-3-one (**12**) was isolated with up to 50% yield. Efforts are currently underway to establish the appropriate protocol for deprotection.

3. Conclusions

In conclusion, we have developed a palladium-catalyzed efficient and general method for the stereoselective synthesis of (*E*)-3-arylidene-3,4-dihydro-2*H*-1,4-benzoxazines (**4**) and their naphthoxazine derivatives **8**. The reaction provides moderate to very good yield of the products at room temperature within few hours and tolerates various functional groups. The use of the inexpensive starting materials, short reaction time period, regio- and stereoselectivity, and operational simplicity make the process attractive. The scope and limitation of this reaction protocol have been examined by employing aryl bromide/chloride/triflate and their corresponding vinyl analogues. The method can also be applied to the synthesis of uracil derivatives of biological interest. Besides, the (*E*)-stereochemistry of the exocyclic double bond in the products (**4**, **8**, and **10**) was firmly established by spectroscopic data and X-ray diffraction analysis.[22] The synthetic utility of the exocyclic double bond[4,5,8b] is likely to be explored further for the generation of scaffolds based on diversity oriented synthesis. The work in this direction is currently under progress.

4. Experimental section

4.1. General

Reagents were purchased from commercial sources and used without further purifications. Reactions were performed under argon atmosphere. Thin layer chromatography (TLC) was performed on silica gel 60 F_{254} aluminum sheets [Merck, Germany] and visualization of the developed chromatogram was achieved by UV absorbance. Column chromatography was carried out on Merck silica gel (100–200 mesh). Solvents were purified using standard means. ^{1}H and ^{13}C NMR spectra were recorded with Bruker-300 or 600 MHz NMR spectrometers. IR spectra were recorded with a JASCO FT/IR-4200 infrared spectrometer either neat or as KBr plates; only major peaks were reported in cm^{-1}. Melting points were determined on a microscopic apparatus and were uncorrected. Mass spectra were recorded by JEOL MS 700 mass spectrometer or Q-TOF-Micro mass spectrometer operating in electron spray ionization (ESI) or fast atom bombardment (FAB) mode. Elemental analyses were performed on an automated carbon, hydrogen, nitrogen, and sulfur analyzer at IICB, Kolkata. Crystallographic data were obtained with a Bruker Kappa Apex 2 instrument.

4.2. General procedure for the synthesis of (*E*)-3-arylidene-4-tosyl-3,4-dihydro-2*H*-1,4-benzoxazines (4) and -naphth[1,2-*b*][1,4]oxazines (8)

A mixture of $Pd(OAc)_2$ (4 mg, 5 mol %) and PPh_3 (20 mg, 20 mol %) in dry DMF (2 mL) was stirred for 10 min under argon atmosphere. Aryl iodide **6** (0.382 mmol, 1.15 equiv with respect to acetylene **5a**), K_2CO_3 (183 mg, 1.33 mmol), and *n*-Bu_4NBr (11 mg, 0.033 mmol) were added to it successively. The resulting reaction mixture was allowed to stir for another 10 min. A solution of acetylenic substrate **5a** (0.332 mmol) in dry DMF (2 mL) was added drop wise to the reaction mixture. The whole reaction mixture was then allowed to stir at room temperature under argon atmosphere. After completion of the reaction (monitored by TLC), the solvent was removed under reduced pressure and the crude mixture was poured into water (20 mL). The aqueous layer was extracted with ethyl acetate (20 mL×3). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. The resulting crude residue was purified through column chromatography over silica gel (100–200 mesh) using ethyl acetate/petroleum ether as eluent to obtain the product **4**.

The same procedure was adopted for the synthesis of the naphtho analogues **8** using **5b** as acetylenic substrate. Here, the only difference was that aryl iodide (**6**) was used in slight excess (1.5 equiv with respect to acetylene **5b** instead of 1.15 equiv) as partial deiodination was observed during the course of reaction.

The reaction procedure for the synthesis of the products reported in Table 3 was similar to that of acetylenic substrate **5a** and aryl iodide **6** as described above. The only difference was that aryl bromide/chloride/triflate or corresponding vinyl analogue was used in place of aryl iodide (**6**).

4.3. Spectral data of (*E*)-3-arylidene-4-tosyl-3,4-dihydro-2*H*-1,4-benzoxazines (4) and naphth[1,2-*b*][1,4]oxazines (8)

*4.3.1. (E)-3-Benzylidene-4-tosyl-3,4-dihydro-2H-1,4-benzoxazine (**4a**).* Yield: 69%; yellowish white solid, R_f (30% EtOAc/petroleum ether) 0.65, mp 128–130 °C; IR (KBr): 3026, 1590, 1361, 1169 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H 2.42 (s, 3H), 4.19 (s, 2H), 6.75 (d, J=8.1 Hz, 1H), 7.01 (t, J=7.2 Hz, 1H), 7.08–7.15 (m, 3H), 7.23–7.26 (m, 3H), 7.32–7.39 (m, 3H), 7.50 (d, J=7.5 Hz, 2H), 7.85 (d, J=7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C 21.6, 61.7 ($^3J_{CH}$=8.1 Hz), 116.9, 121.1, 125.0, 126.1, 126.8, 127.8, 128.2, 128.6, 128.9, 129.7, 132.2, 134.2,

134.6, 144.5, 147.2; HRMS (EI^+): calcd for $C_{22}H_{19}NO_3S$ ($[M]^+$) 377.1085, found 377.1088.

*4.3.2. (E)-3-[(Naphthalen-1-yl)methylidene]-4-tosyl-3,4-dihydro-2H-1,4-benzoxazine (**4b**).* Yield: 71%; white solid, R_f (30% EtOAc/petroleum ether) 0.42, mp 154–156 °C; IR (KBr): 3056, 1591, 1360, 1165 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ_H 2.39 (s, 3H), 4.05 (s, 2H), 6.78 (d, J=8.1 Hz, 1H), 7.04 (t, J=7.5 Hz, 1H), 7.13 (t, J=7.5 Hz, 1H), 7.18–7.26 (m, 3H), 7.45 (t, J=7.5 Hz, 1H), 7.53–7.61 (m, 4H), 7.75 (s, 1H), 7.86 (t, J=9.1 Hz, 2H), 7.96 (d, J=7.8 Hz, 1H), 8.10 (d, J=7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C 21.6, 62.0, 117.1, 121.2, 124.93, 124.99, 125.2, 125.9, 126.36, 126.44, 126.72, 126.75, 127.7, 128.4, 128.8, 129.8, 130.0, 130.6, 131.4, 131.8, 133.4, 134.5, 144.6, 147.3; HRMS (ESI^+): calcd for $C_{26}H_{21}NNaO_3S$ ($[M+Na]^+$) 450.1139, found 450.1175.

*4.3.3. (E)-3-[(Pyridin-3-yl)methylidene]-4-tosyl-3,4-dihydro-2H-1,4-benzoxazine (**4c**).* Yield: 70%; yellow solid, R_f (60% EtOAc/petroleum ether) 0.42, mp 124–125 °C; IR (KBr): 1597, 1362, 1168 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ_H 2.42 (s, 3H), 4.16 (s, 2H), 6.77 (d, J=7.8 Hz, 1H), 7.03 (t, J=7.5 Hz, 1H), 7.12 (t, J=7.5 Hz, 1H), 7.21–7.27 (m, 2H), 7.33 (t, J=6.1 Hz, 1H), 7.48–7.50 (m, 4H), 7.86 (d, J=8.1 Hz, 1H), 8.39 (s, 1H), 8.55–8.57 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C 21.6, 61.5, 116.9, 121.3, 123.5, 124.8, 126.0, 126.9, 127.6, 129.8, 130.3, 130.8, 134.2, 136.2, 144.8, 147.0, 148.9, 149.2; HRMS (EI^+): calcd for $C_{21}H_{18}N_2O_3S$ ($[M]^+$) 378.1038, found 378.1036.

*4.3.4. (E)-3-[(Thiophen-2-yl)methylidene]-4-tosyl-3,4-dihydro-2H-1,4-benzoxazine (**4d**).* Yield: 78%; yellow solid, R_f (30% EtOAc/petroleum ether) 0.41, mp 110–112 °C; IR (KBr): 3064, 1584, 1360, 1164 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ_H 2.40 (s, 3H), 4.44 (s, 2H), 6.77 (d, J=8.1 Hz, 1H), 6.99–7.15 (m, 4H), 7.20 (d, J=7.8 Hz, 2H), 7.26–7.28 (m, 1H), 7.37 (d, J=4.5 Hz, 1H), 7.43 (d, J=8.1 Hz, 2H), 7.76 (d, J=8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C 21.6, 63.7 ($^3J_{CH}$=8.4 Hz), 116.9, 121.4, 123.3, 125.8, 126.6, 127.2, 127.3, 127.58, 127.62, 129.60, 129.64, 134.5, 136.3, 144.5, 148.2; HRMS (EI^+): calcd for $C_{20}H_{17}NO_3S_2$ ($[M]^+$) 383.0649, found 383.0650.

*4.3.5. (E)-3-[(2,4-Dimethoxypyrimidin-5-yl)methylidene]-4-tosyl-3,4-dihydro-2H-1,4-benzoxazine (**4e**).* Yield: 68%; brown solid, R_f (40% EtOAc/petroleum ether) 0.37, mp 142–143 °C; IR (KBr): 2955, 1596, 1392, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ_H 2.42 (s, 3H), 4.02 (s, 6H), 4.04 (s, 2H), 6.75 (dd, J=1.1, 8.0 Hz, 1H), 6.98–7.03 (m, 2H), 7.10 (td, J=1.2, 7.7 Hz, 1H), 7.24–7.27 (m, 2H), 7.49 (d, J=8.1 Hz, 2H), 7.83–7.86 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C 21.6, 54.3, 55.0, 61.3, 109.7, 116.9, 121.1, 122.6, 124.7, 125.98, 126.8, 127.8, 129.3, 129.7, 134.4, 144.7, 146.8, 157.4, 165.1, 168.5; HRMS (ESI^+): calcd for $C_{22}H_{21}N_3NaO_5S$ ($[M+Na]^+$) 462.1099, found 462.1119.

*4.3.6. (E)-3-[(N,N′-Dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)methylidene]-4-tosyl-3,4-dihydro-2H-1,4-benzoxazine (**4f**).* Yield: 79%; light yellow solid, R_f (40% EtOAc/petroleum ether) 0.15, mp 143–145 °C; IR (KBr): 3046, 1710, 1657, 1592, 1353, 1169 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ_H 2.40 (s, 3H), 3.38 (s, 3H), 3.44 (s, 3H), 4.14 (s, 2H), 6.72–6.74 (m, 2H), 6.98 (t, J=7.4 Hz, 1H), 7.08–7.11 (m, 2H), 7.23–7.26 (m, 2H), 7.53 (d, J=7.8 Hz, 2H), 7.81 (d, J=7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C 21.6, 28.3, 37.3, 62.7, 107.9, 116.9, 121.0, 122.2, 124.8, 125.6, 126.8, 127.8, 129.7, 130.0, 134.3, 142.5, 144.6, 147.1, 151.0, 161.4; HRMS (ESI^+): calcd for $C_{22}H_{21}N_3NaO_5S$ ($[M+Na]^+$) 462.1099, found 462.1079.

*4.3.7. (E)-3-(4-Methylbenzylidene)-4-tosyl-3,4-dihydro-2H-1,4-benzoxazine (**4g**).* Yield: 38%; white solid, R_f (30% EtOAc/petroleum ether) 0.56, mp 132–134 °C; IR (KBr): 3031, 1590, 1358, 1163 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ_H 2.36 (s, 3H), 2.42 (s, 3H), 4.19 (s, 2H), 6.75 (d, J=7.8 Hz, 1H), 6.98–7.12 (m, 4H), 7.17–7.26 (m, 5H), 7.49 (d, J=8.1 Hz, 2H), 7.84 (d, J=7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C 21.3, 21.6, 61.7, 116.9, 121.0, 125.1, 126.1, 126.8, 127.8, 127.9, 128.9, 129.3, 129.7, 131.3, 132.3, 134.6, 138.2, 144.5, 147.2; ESI-MS: m/z 414.23 $[M+Na]^+$. Anal. Calcd for $C_{23}H_{21}NO_3S$: C, 70.56; H, 5.41; N, 3.58. Found: C, 70.60; H, 5.45; N, 3.53.

*4.3.8. (E)-3-(4-Trifluoromethylbenzylidene)-4-tosyl-3,4-dihydro-2H-1,4-benzoxazine (**4h**).* Yield: 51%; white solid, R_f (40% EtOAc/petroleum ether) 0.67, mp 138–140 °C; IR (KBr): 1592, 1359, 1171 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ_H 2.42 (s, 3H), 4.17 (s, 2H), 6.77 (br d, J=7.8 Hz, 1H), 7.02 (t, J=7.3 Hz, 1H), 7.12 (app t, J=7.3 Hz, 1H), 7.24–7.27 (m, 5H), 7.49 (d, J=8.1 Hz, 2H), 7.64 (d, J=7.8 Hz, 2H), 7.85 (br d, J=8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ_C 21.6, 61.9, 117.0, 121.4, 123.9 (q, J=270 Hz), 125.0, 125.6 (q, J=3.7 Hz), 126.1, 127.0, 127.7, 129.2, 129.81, 130.07, 130.08 (q, J=32.6 Hz), 130.8, 134.5, 137.9, 144.8, 147.2; HRMS (ESI^+): calcd for $C_{23}H_{18}F_3NNaO_3S$ ($[M+Na]^+$) 468.0857, found 468.0890.

*4.3.9. (E)-3-(4-Methoxybenzylidene)-4-tosyl-3,4-dihydro-2H-1,4-benzoxazine (**4i**).* Yield: 58%; white solid, R_f (30% EtOAc/petroleum ether) 0.45, mp 136–138 °C; IR (KBr): 2923, 1603, 1354, 1168 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ_H 2.41 (s, 3H), 3.82 (s, 3H), 4.19 (s, 2H), 6.74 (d, J=7.8 Hz, 1H), 6.89 (d, J=8.1 Hz, 2H), 6.99 (t, J=7.1 Hz, 1H), 7.06–7.12 (m, 3H), 7.19–7.25 (m, 3H), 7.49 (d, J=7.8 Hz, 2H), 7.83 (d, J=8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C 21.6, 55.3, 61.8 ($^3J_{CH}$=7.9 Hz), 114.1, 116.9, 121.0, 125.2, 126.1, 126.6, 126.8, 127.1, 127.8, 129.8, 130.4, 132.0, 134.7, 144.5, 147.2, 159.6; HRMS (EI^+): calcd for $C_{23}H_{21}NO_4S$ ($[M]^+$) 407.1191, found 407.1189.

*4.3.10. (E)-3-(2-Carbomethoxybenzylidene)-4-tosyl-3,4-dihydro-2H-1,4-benzoxazine (**4j**).* Yield: 74%; greenish yellow solid, R_f (30% EtOAc/petroleum ether) 0.25, mp 140–141 °C; IR (KBr): 2956, 1712, 1591, 1360, 1171 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ_H 2.41 (s, 3H), 3.92 (s, 3H), 3.96 (s, 2H), 6.71–6.76 (m, 1H), 6.98–7.12 (m, 3H), 7.24–7.26 (m, 2H), 7.42 (t, J=7.4 Hz, 1H), 7.49–7.56 (m, 3H), 7.68 (s, 1H), 7.90 (d, J=8.1 Hz, 1H), 8.04 (d, J=7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ_C 21.6, 52.4, 61.5, 116.1, 116.9, 121.0, 124.9, 126.0, 126.6, 127.8, 128.0, 128.4, 129.8, 130.6, 131.1, 132.2, 132.9, 134.8, 135.3, 144.5, 146.9, 167.0; ESI-MS: m/z 457.92 $[M+Na]^+$. Anal. Calcd for $C_{24}H_{21}NO_5S$: C, 66.19; H, 4.86; N, 3.22. Found: C, 66.16; H, 4.83; N, 3.17.

*4.3.11. (E)-3-(2-Methyl-4-nitrobenzylidene)-4-tosyl-3,4-dihydro-2H-1,4-benzoxazine (**4k**).* Yield: 55%; light yellow solid, R_f (40% EtOAc/petroleum ether) 0.64, mp 120–121 °C; IR (KBr): 3064, 1591, 1520, 1349, 1169 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ_H 2.41 (s, 3H), 2.46 (s, 3H), 4.01 (s, 2H), 6.78 (d, J=7.8 Hz, 1H), 7.04 (t, J=7.2 Hz, 1H), 7.12 (d, J=8.1 Hz, 2H), 7.24–7.26 (m, 3H), 7.48 (d, J=8.1 Hz, 2H), 7.91 (d, J=8.1 Hz, 1H), 8.05 (d, J=8.1 Hz, 1H), 8.10 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C 20.1, 21.6, 61.6, 117.1, 121.0, 121.4, 124.7, 124.9, 125.7, 126.9, 127.5, 128.8, 129.5, 129.8, 131.3, 134.3, 139.2, 140.1, 144.9, 147.0, 147.4; HRMS (EI^+): calcd for $C_{23}H_{20}N_2O_5S$ ($[M]^+$) 436.1092, found 436.1091.

*4.3.12. (E)-3-Allylidene-4-tosyl-3,4-dihydro-2H-1,4-benzoxazine (**4m**).* Yield: 32%; gum, R_f (30% EtOAc/petroleum ether) 0.57; IR (KBr): 2984, 1652, 1593, 1489, 1361, 1299, 1254, 1167 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ_H 2.39 (s, 3H), 4.12 (s, 2H), 5.35 (d, J=10.2 Hz, 1H), 5.51 (d, J=16.8 Hz, 1H), 6.33–6.45 (m, 1H), 6.69–6.77 (m, 2H), 6.95–7.01 (m, 1H), 7.09 (td, J=1.3, 7.6 Hz, 1H), 7.20 (d, J=8.1 Hz, 2H), 7.41 (d, J=8.1 Hz, 2H), 7.80 (dd, J=1.5, 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C 21.6, 61.6, 116.9, 121.2, 122.8, 126.0, 126.8, 127.0, 128.2, 129.6, 130.9, 134.5, 144.4, 147.4; HRMS (FAB^+): calcd for $C_{18}H_{18}NO_3S$ ($[M+H]^+$) 328.1007, found 328.1012.

*4.3.13. (E)-3-((E)-3-Phenylallylidene)-4-tosyl-3,4-dihydro-2H-1,4-benzoxazine (**4n**).* Yield: 50%; white solid, R_f (30% EtOAc/petroleum ether) 0.59, mp 110–112 °C; IR (KBr): 3029, 2922, 1594, 1488, 1455, 1358, 1298, 1247, 1166 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ_H 2.39 (s,

3H), 4.21 (s, 2H), 6.74–6.79 (m, 2H), 6.82 (d, J=15.0 Hz, 1H), 6.88 (d, J=10.8 Hz, 1H), 6.98–7.01 (m, 1H), 7.08–7.11 (m, 1H), 7.20 (d, J=7.8 Hz, 2H), 7.26–7.29 (m, 1H), 7.33–7.35 (m, 2H), 7.43 (br d, J=8.4 Hz, 4H), 7.84 (dd, J=1.5, 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ_C 21.6, 62.8117.0, 121.2, 121.3, 125.3, 126.0, 126.7, 126.8, 127.6, 127.7, 128.5, 128.8, 129.7, 130.9, 134.6, 136.4, 137.4, 144.5, 147.4; HRMS (EI$^+$): calcd for $C_{24}H_{21}NO_3S$ ([M]$^+$) 403.1242, found 403.1243.

*4.3.14. (E)-3-((3,4-Dihydronaphthalen-1-yl)methylene)-4-tosyl-3,4-dihydro-2H-1,4-benzoxazine (**4o**).* Yield: 73%; white solid, R_f (30% EtOAc/petroleum ether) 0.59, mp 112–114 °C; IR (KBr): 1590, 1488, 1356, 1299, 1261, 1166 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H 2.39 (br s, 5H), 2.81(t, J=7.9 Hz, 2H), 4.08 (s, 2H), 5.83 (br s, 1H), 6.75 (d, J=7.8 Hz, 1H), 7.00–7.03 (m, 2H), 7.08–7.25 (m, 7H), 7.49 (d, J=7.8 Hz, 2H), 7.89 (d, J=7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C 21.6, 23.3, 27.6, 61.8, 117.1, 121.0, 124.5, 125.0, 126.7, 126.8, 127.7, 127.8, 129.6, 129.7, 129.8, 131.0, 132.5, 133.7, 134.7, 135.7, 144.5, 147.2; HRMS (FAB$^+$): calcd for $C_{26}H_{24}NO_3S$ ([M+H]$^+$) 430.1476, found 430.1456.

*4.3.15. (E)-3-Benzylidene-4-tosyl-3,4-dihydro-2H-naphth[1,2-b][1,4]oxazine (**8a**).* Yield: 74%; brown solid, R_f (30% EtOAc/petroleum ether) 0.42, mp 152–154 °C; IR (KBr): 3050, 1595, 1357, 1171 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H 2.41 (s, 3H), 4.32 (s, 2H), 7.16–7.27 (m, 4H), 7.34–7.54 (m, 9H), 7.79 (d, J=7.8 Hz, 1H), 7.95 (d, J=7.8 Hz, 1H), 8.01 (d, J=9.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ_C 21.6, 61.5 ($^3J_{CH}$=7.8 Hz), 119.4, 120.3, 121.4, 124.5, 124.7, 125.6, 126.2, 127.4, 127.9, 128.3, 128.6, 129.0, 129.8, 132.2, 132.5, 134.1, 134.3, 141.7, 144.6; HRMS (ESI$^+$): calcd for $C_{26}H_{21}NNaO_3S$ ([M+Na]$^+$) 450.1139 found 450.1157.

*4.3.16. (E)-3-[(Pyridin-3-yl)methylidene]-4-tosyl-3,4-dihydro-2H-naphth[1,2-b][1,4]oxazine (**8b**).* Yield: 79%; brown solid, R_f (40% EtOAc/petroleum ether) 0.22, mp 119–121 °C; IR (KBr): 1594, 1465, 1406, 1359, 1273, 1168, 1095 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H 2.40 (s, 3H), 4.29 (s, 2H), 7.23–7.29 (m, 3H), 7.33–7.37 (m, 1H), 7.39–7.55 (m, 6H), 7.79 (d, J=7.8 Hz, 1H), 7.94 (d, J=7.8 Hz, 1H), 8.01 (d, J=9.0 Hz, 1H), 8.42 (br s, 1H), 8.58 (d, J=4.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C 21.6, 61.2, 119.2, 120.6, 121.3, 123.5, 124.2, 124.6, 125.7, 126.3, 127.4, 127.8, 128.2, 129.9, 130.3, 130.4, 132.2, 133.8, 136.4, 141.6, 144.8, 149.0, 149.2; ESI-MS: m/z 451.28 [M+Na]$^+$. Anal. Calcd for $C_{25}H_{20}N_2O_3S$: C, 70.07; H, 4.70; N, 6.54. Found: C, 70.04; H, 4.75; N, 6.51.

*4.3.17. (E)-3-(4-Methylbenzylidene)-4-tosyl-3,4-dihydro-2H-naphth[1,2-b][1,4]oxazine (**8c**).* Yield: 54%; white solid, R_f (30% EtOAc/petroleum ether) 0.44, mp 148–149 °C; IR (KBr): 1594, 1467, 1408, 1358, 1269, 1162, 1095, 1045, 802, 669 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H 2.38 (s, 3H), 2.39 (s, 3H), 4.32 (s, 2H), 7.06 (d, J=7.5 Hz, 2H), 7.14–7.26 (m, 4H), 7.31 (s, 1H), 7.38–7.52 (m, 5H), 7.78 (d, J=7.5 Hz, 1H), 7.93–8.02 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C 21.3, 21.6, 61.5 ($^3J_{CH}$=7.8 Hz), 119.5, 120.2, 121.4, 124.5, 124.7, 125.5, 126.1, 127.4, 127.6, 127.9, 128.9, 129.3, 129.8, 131.3, 132.2, 132.5, 134.2, 138.3, 141.8, 144.5; HRMS (ESI$^+$): calcd for $C_{27}H_{23}NNaO_3S$ ([M+Na]$^+$) 464.1296, found 464.1271.

*4.3.18. (E)-3-(4-Bromobenzylidene)-4-tosyl-3,4-dihydro-2H-naphth[1,2-b][1,4]oxazine (**8d**).* Yield: 57%; white solid, R_f (30% EtOAc/petroleum ether) 0.37, mp 182–184 °C; IR (KBr): 1587, 1355, 1162 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H 2.40 (s, 3H), 4.29 (s, 2H), 7.04 (d, J=8.1 Hz, 2H), 7.20–7.26 (m, 3H), 7.36–7.54 (m, 7H), 7.79 (d, J=7.8 Hz, 1H), 7.94 (d, J=8.1 Hz, 1H), 7.99 (d, J=9.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C 21.6, 61.5, 119.4, 120.5, 121.3, 122.5, 124.3, 124.7, 125.6, 126.2, 127.4, 127.9, 129.1, 129.8, 130.5, 131.1, 131.9, 132.2, 133.2, 134.1, 141.7, 144.7; ESI-MS: m/z 528.18, 530.18 [M+Na]$^+$ for ^{79}Br, ^{81}Br. Anal. Calcd for $C_{26}H_{20}BrNO_3S$: C, 61.66; H, 3.98; N, 2.77. Found: C, 61.59; H, 3.94; N, 2.80.

*4.3.19. (E)-3-(4-Nitrobenzylidene)-4-tosyl-3,4-dihydro-2H-naphth[1,2-b][1,4]oxazine (**8e**).* Yield: 83%; light yellow solid, R_f (30% EtOAc/petroleum ether) 0.59, mp 156–157 °C; IR (KBr): 2924, 1597, 1349, 1167 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H 2.40 (s, 3H), 4.33 (s, 2H), 7.22–7.26 (m, 2H), 7.34–7.39 (m, 3H), 7.42–7.51 (m, 5H), 7.80 (d, J=7.8 Hz, 1H), 7.93–8.02 (m, 2H), 8.27 (d, J=8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C 21.6, 61.7, 119.4, 120.8, 121.3, 123.9, 124.1, 124.6, 125.8, 126.4, 127.5, 127.8, 129.5, 129.7, 129.9, 131.6, 132.3, 133.9, 140.9, 141.8, 144.9, 147.3; ESI-MS: m/z 495.20 [M+Na]$^+$. Anal. Calcd for $C_{26}H_{20}N_2O_5S$: C, 66.09; H, 4.27; N, 5.93. Found: C, 66.04; H, 4.23; N, 5.97.

*4.3.20. (1E,2E)-1,2-Bis(4-tosyl-2H-benzo[b][1,4]oxazin-3(4H)-ylidene)ethane (**10**).* Yield: 20–55% (see Table 3 in text); colorless crystalline solid, R_f (30% EtOAc/petroleum ether) 0.58, mp 172–174 °C; IR (KBr): 1625, 1592, 1488, 1357, 1298, 1251, 1169 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H 2.40 (s, 6H), 4.27 (s, 4H), 6.70 (s, 2H), 6.79 (dd, J=1.0, 7.8 Hz, 2H), 6.99–7.04 (m, 2H), 7.10–7.16 (m, 2H), 7.21 (d, J=8.1 Hz, 4H), 7.39 (d, J=8.1 Hz, 4H), 7.78 (dd, J=1.3, 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C 21.6, 62.5, 117.1, 121.6, 121.7, 125.2, 126.1, 127.2, 127.6, 129.7, 132.1, 134.2, 144.8, 148.0; HRMS (ESI$^+$): calcd for $C_{32}H_{28}N_2NaO_6S_2$ ([M+Na]$^+$) 623.1286 found 623.1293.

4.4. Synthesis of (*E*)-3-[(2′,4′-dioxo-1′,2′,3′,4′-tetrahydropyrimidine-5-yl)methylidene]-4-tosyl-3,4-dihydro-2*H*-1,4-benzoxazine (11)

To a well-stirred solution of compound **4e** (90 mg, 0.20 mmol) in anhydrous acetonitrile were added anhydrous sodium iodide (92 mg, 0.61 mmol) and trimethylsilyl chloride (0.76 mL, 0.61 mmol) successively. The resulting solution was then allowed to stir at room temperature for 18 h under argon atmosphere. After removing the solvent under reduced pressure, the residue was poured into water (10 mL) and extracted with ethyl acetate (3×12 mL). The combined ethyl acetate extracts were washed with saturated sodium metabisulphite solution (8 mL) and water (8 mL), respectively. Solvent was dried over anhydrous sodium sulfate and concentrated in vacuo. The resulting residue was purified through silica gel (100–200 mesh) chromatography using 2% methanol in chloroform as eluent to obtain the titled compound **11** as a light yellow solid (72 mg, yield 86%); R_f (100% EtOAc) 0.50, mp>300 °C; IR (KBr): 2924, 1689, 1591, 1473, 1437, 1408, 1315, 1267 cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz): δ_H 2.37 (s, 3H), 4.23 (s, 2H), 6.62 (s, 1H), 6.77 (d, J=7.8 Hz, 1H), 7.00 (t, J=7.4 Hz, 1H), 7.12 (t, J=7.5 Hz, 1H), 7.36 (d, J=7.5 Hz, 2H), 7.45–7.49 (m, 3H), 7.66 (d, J=7.8 Hz, 1H), 11.26 (s, 1H), 11.36 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz): δ_C 21.1, 62.2, 106.4, 116.9, 120.9, 123.0, 124.6, 125.2, 127.1, 127.4, 127.7, 130.0, 133.7, 142.1, 144.7, 147.0, 150.9, 162.8; ESI-MS: m/z 433.79 [M+Na]$^+$. Anal. Calcd for $C_{20}H_{17}N_3SO_5$: C, 58.38; H, 4.16; N. 10.21. Found: C, 58.43; H, 4.13, N. 10.17.

4.5. Synthesis of 2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (12)

Sodium (73.1 mg, 3.18 mmol) was added to a solution of naphthalene (448 mg, 3.50 mmol) in dry THF (5 mL). After stirring for 2 h at room temperature, a greenish solution was appeared. To a well-stirred solution of tosylated compound **4a** (60 mg, 0.159 mmol) in dry THF (3 mL) at −65 °C was added the aforesaid greenish solution drop wise and the whole reaction mixture was allowed to stir at −65 °C for 20 min. After consumption of the starting materials (TLC), the reaction mixture was quenched with 2–3 drops of water and extracted with ethyl acetate (3×10 mL). The organic extracts were dried over anhydrous sodium sulfate and concentrated in vacuo. The resulting residue was purified through silica gel

(100–200 mesh) column chromatography using 20% ethyl acetate in petroleum ether as eluent to obtain the titled compound **12** as a light brown solid (11.8 mg, yield 50%); R_f (30% EtOAc/petroleum ether) 0.21, mp 152–154 °C (reported[23] mp 171–173 °C); ^{1}H NMR ($CDCl_3$, 300 MHz): δ_H 4.62 (s, 2H), 6.79–6.82 (m, 1H), 6.95–6.98 (m, 3H), 8.39 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C 67.3, 115.9, 116.9, 122.7, 124.3, 126.0, 143.7, 165.7; MS (EI^+): m/z 149 $[M]^+$.

Acknowledgements

K.B. and B.D. thank Council of Scientific and Industrial Research, New Delhi for their fellowship. Financial support from CSIR network project (CSC 0108) is gratefully acknowledged.

Supplementary data

X-ray crystallographic data of **4d**, **8a** and **10**, and characterization data of **5a** and **5b** are included. Copies of ^{1}H, ^{13}C NMR spectra of compounds **5a**,**b**, **4**, **8**, **10**, **11**, and **12** are also incorporated. Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2014.06.036.

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