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# Domino aziridine ring opening and Buchwald–Hartwig type coupling-cyclization by palladium catalyst

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ABSTRACT

Highly important *trans*-3,4-dihydro-2*H*-1,4-benzoxazine moieties were easily synthesized by domino aziridine ring opening with *o*-bromophenols and *o*-chlorophenols followed by the palladium catalyzed coupling-cyclization (intramolecular $C_{(aryl)}$–$N_{(amide)}$ bond formation) with good to excellent yields.



## 1. Introduction

For the past few years tremendous advances have been made in the development of cross-coupling methodology.[1] The leading application of cross-coupling chemistry, particularly C–N bond-forming reactions are important in medicinal chemistry, pharmaceutical companies and in academic laboratories. The cross-coupling reactions by utilization of less reactive, inexpensive aryl bromides and aryl chlorides are a challenging task. For the immense majority of these reactions, the scope, experimental ease and reliability of a method are much more important.

In pharmaceutical industry, compounds containing phenoxazine and 1,4-benzoxazine moieties have known to be potent drugs as ion channel activators, vasodilator agents and anti-oxidants (Fig. 1).[2] Usually, 1,4-benzoxazine compounds were synthesized by multistep processes like cyclocondensation of *o*-aminophenols with suitable dihalo derivatives,[3] reaction of *o*-aminophenols with α-halo acyl bromides then subsequent reduction of carbonyl group by $BH_3$,[4] and alkylation of *o*-nitrophenol by haloester followed by reductive cyclization to yield 1,4-benzoxazine moiety.[5]

Later on 1,4-benzoxazine moieties were synthesized by reacting epoxides with *o*-halosulfonamides followed by subsequent cyclization,[6] epoxide ring opening with *o*-aminophenols followed by cyclocondensation and reacting aryl/vinyl iodides with 1-azido-2-(prop-2-ynyloxy)benzene in the presence of palladium–copper catalyst. Using Hantzsch 1,4-dihydropyridine (HEH) and Pd/C as catalyst, 2*H*-1,4-benzoxazine derivatives were synthesized from 1,2-epoxy-3-(2-nitroaryloxy)propanes. Also, 2-[*N*-benzyl(or alkyl)-*N*-prop-2-ynyl]-aminophenyl tosylate was used to synthesize 1,4-benzoxazine skeleton using palladium catalyzed C–O bond formation reaction.[7]

Recently, we have developed copper-catalyzed oxidation chemistry,[8] and reported 1,1′-binaphthyl-2,2′-diamine (BINAM)–CuI as an efficient catalyst for the synthesis of diaryl ethers and aryl alkyl ethers through Ullmann coupling.[9] To strengthen this field, we have developed a simple, efficient and alternative method to the conventional multistep process to prepare 1,4-benzoxazine skeleton in a single step process from readily available *o*-iodophenols

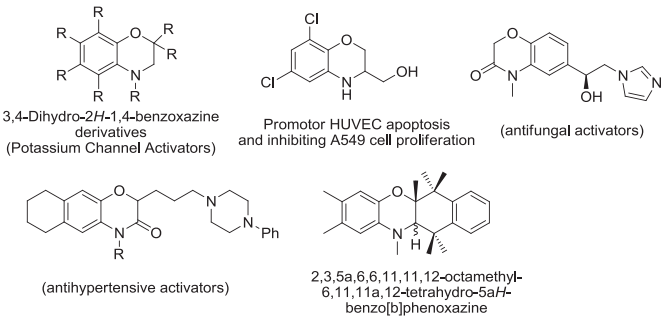


**Fig. 1.** Biologically important compounds having 1,4-benzoxazine as a core skeleton.[2]

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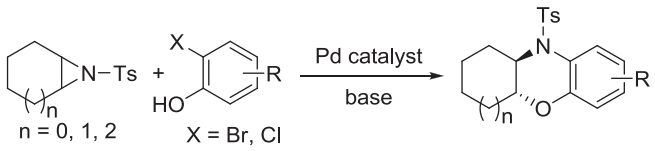
and aziridines using copper-catalyzed domino ring opening followed by Goldberg cyclization.[10] However, less reactive and inexpensive bromo and chlorophenols refused to react under the optimized reaction condition to give 1,4-benzoxazine derivatives.

To devise a more efficient and general catalyst system for the domino synthesis of *trans*-1,4-benzoxazines, we explored the use of simple and commercially available chelating ligand using palladium as metal source and readily available aziridines, inexpensive *o*-bromophenols and *o*-chlorophenols as starting materials (Scheme 1).




**Scheme 1.** Proposed scheme for palladium-catalyzed domino reaction.

## 2. Results and discussion

In the initial studies, the synthesis of a 1,4-benzoxazine moiety **3** was carried out using 5 mol% of $Pd(OAc)_2$ and 10 mol% of (±)-BINAP in toluene at 110 °C from 7-tosyl-7-azabicyclo[4.1.0] heptane **1** with *o*-bromophenol **2** and $Cs_2CO_3$ by domino aziridine ring opening followed by palladium catalyzed Buchwald–Hartwig coupling-cyclization and the reaction mixture provided **3** in 71% yield in 48 h. The trans stereochemistry of the product was deduced from the coupling constants of the methine protons in the $^1$H NMR spectrum.

We screened the domino reaction with several phosphorous-based ligands, which are shown in Fig. 2 to increase the efficiency of the reaction, and the results are summarized in Table 1. Among the phosphine ligands examined for the domino reaction, (±)-BINAP was found to be best ligand (entry 1). Then the reaction was screened with several palladium sources, although all of them catalyzed the domino reaction, the $Pd_2(dba)_3$ turned out to be the best palladium source of choice as it gave quantitative yield (entry 6).

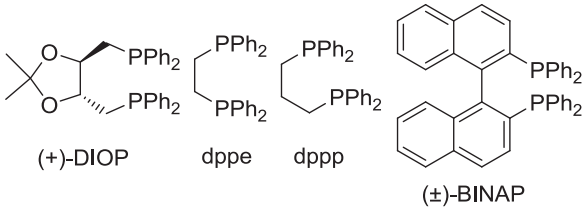
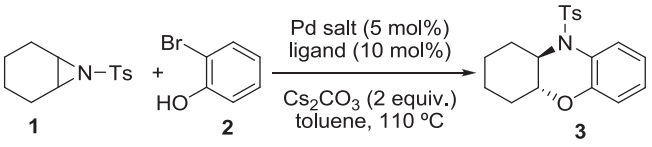



**Fig. 2.** Ligands screened for the palladium catalyzed-domino reaction.

Further, the reaction was optimized by changing the solvents and bases to increase the efficiency of the domino reaction and the results are summarized in Table 2. Toluene and $Cs_2CO_3$ continued to be choice of solvent and base for the domino reaction. When the reaction was carried out using $Pd_2(dba)_3$ without ligand (±)-BINAP, the reaction did not proceed to completion and gave only 29% yield after 3 days (Table 2, entry 11).

Using the above mentioned optimized reaction conditions, we initiated our investigation into the scope of the (±)-BINAP–$Pd_2(dba)_3$ complex catalyzed domino aziridine ring opening and Buchwald–Hartwig type coupling-cyclization. By using this methodology various types of 1,4-benzoxazine derived from several aziridines and substituted *o*-bromophenols/*o*-chlorophenols and the results are summarized in Table 3. The trans stereochemistry of the products was determined by $^1$H NMR.

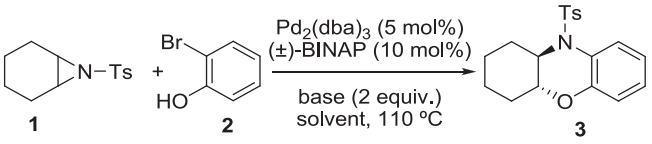
**Table 1**
Ligand and palladium source screening for the domino aziridine ring opening and coupling-cyclization for the synthesis of **3**




| Entry | Pd salts | Ligands | Time | Yield[a] (%) |
|---|---|---|---|---|
| 1 | $Pd(OAc)_2$ | BINAP | 48 | 71 |
| 2 | $Pd(OAc)_2$ | $PPh_3$ | 72 | 0[b] |
| 3 | $Pd(OAc)_2$ | dppe | 72 | 0[b] |
| 4 | $Pd(OAc)_2$ | dppp | 72 | 0[b] |
| 5 | $Pd(OAc)_2$ | DIOP | 72 | 0[b] |
| 6 | $Pd_2(dba)_3$ | BINAP | 48 | 99 |
| 7 | $PdCl_2$ | BINAP | 72 | 55 |
| 8 | $Pd(OCOCF_3)_2$ | BINAP | 48 | 84 |
| 9 | $K_2PdCl_4$ | BINAP | 72 | 60 |
| 10 | $Pd(acac)_2$ | BINAP | 72 | 43 |
| 11 | $PdCl_2$(dppf) | BINAP | 72 | 29 |

[a] Isolated yields.
[b] Only aziridine opened product was observed.

**Table 2**
Effect of solvents, bases and catalyst loading on the domino reaction



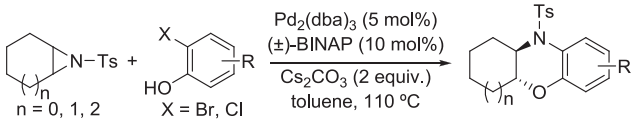

| Entry | Solvents | Bases | Time | Yield[a] (%) |
|---|---|---|---|---|
| 1 | Toluene | $Cs_2CO_3$ | 48 | 99 |
| 2 | DMF | $Cs_2CO_3$ | 72 | 71 |
| 3 | Acetonitrile | $Cs_2CO_3$ | 72 | 45 |
| 4 | THF | $Cs_2CO_3$ | 72 | 47 |
| 5 | Dioxane | $Cs_2CO_3$ | 60 | 99 |
| 6 | DMSO | $Cs_2CO_3$ | 72 | 26 |
| 7 | Toluene | $K_2CO_3$ | 72 | 31 |
| 8 | Toluene | NaOMe | 48 | 83 |
| 9 | Toluene | $K_3PO_4$ | 72 | 45 |
| 10 | Toluene | $Na_2CO_3$ | 72 | 28 |
| 11 | Toluene | $Cs_2CO_3$ | 72 | 29[b] |

[a] Isolated yields.
[b] $Pd_2(dba)_3$ (5 mol%) was used without ligand.

Several aziridines in combination with *o*-bromophenols and *o*-chlorophenols gave the corresponding 1,4-benzoxazine moieties in good to excellent yields. In case of aziridine, when the aziridine ring is fused with six-membered ring, it gave quantitative yield with simple *o*-bromophenol. When electron-withdrawing or electron-donating groups are present on the *o*-bromophenol, the yields were slightly reduced. When the aziridine ring is fused with five- or seven-membered rings, the yields were slightly reduced. In the case of *o*-chlorophenols the catalyst loading and the reaction temperature were increased to increase the yields of the corresponding 1,4-benzoxazine products (entries 11 and 12). The acyclic, simple aziridine also reacted well under the optimized reaction conditions and gave moderate to good yields and based on $^1$H NMR of crude reaction mixture it was confirmed that only one regioisomer formed (entries 13 and 14).

In previous report we have demonstrated coupling kinetic resolution for the synthesis of optically active 1,4-benzoxazines through single-step process.[11] In order to explore the asymmetric version of the reaction, further, we screened the reaction with optically active (*S*)-BINAP instead of (±)-BINAP. Only partial resolution is observed and the moderate selectivity factor ($s$=3.3)[12] was obtained (Scheme 2).

**Table 3**
The scope of the palladium catalyzed domino ring opening and coupling-cyclization



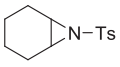
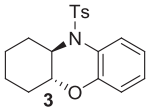
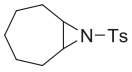
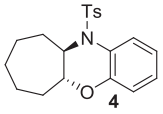
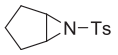
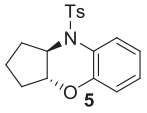
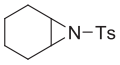
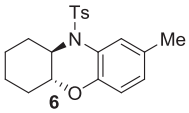
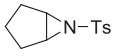
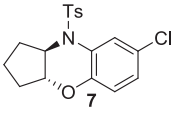
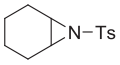
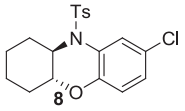
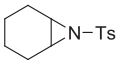
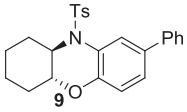
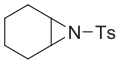
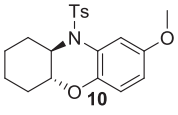
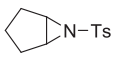
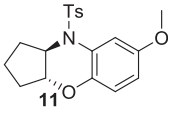
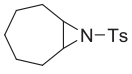
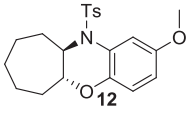
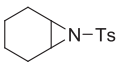
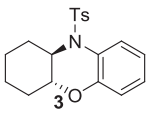
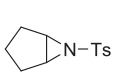
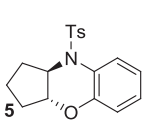
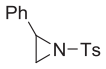
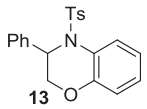
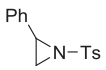
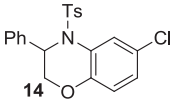
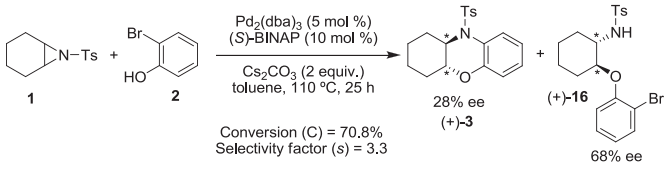

| Entry | Aziridines | Products | Time (h) | Yield[a] (%) |
|---|---|---|---|---|
| 1 |  |  **3** | 48 | 99 |
| 2 |  |  **4** | 60 | 62 |
| 3 |  |  **5** | 60 | 76 |
| 4 |  |  **6** | 48 | 61 |
| 5 |  |  **7** | 52 | 66 |
| 6 |  |  **8** | 72 | 76 |
| 7[b] |  |  **9** | 72 | 84 |
| 8 |  |  **10** | 48 | 90 |
| 9 |  |  **11** | 48 | 76 |
| 10 |  |  **12** | 48 | 67 |
| 11[c,d] |  |  **3** | 96 | 78 |
| 12[c,d] |  |  **5** | 96 | 40 |

**Table 3** (*continued*)

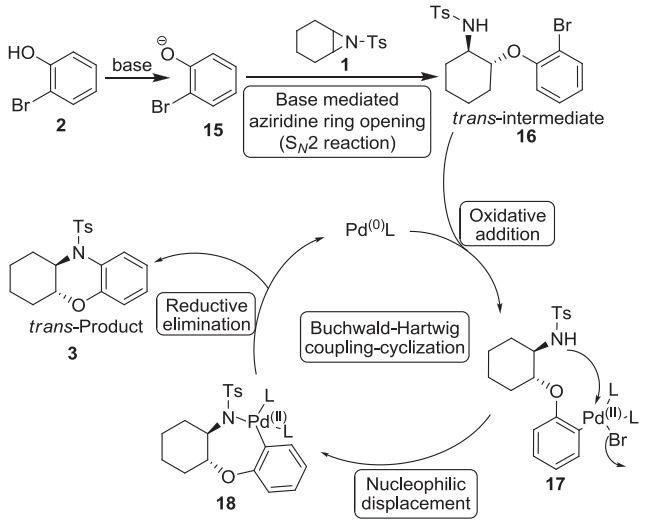
| Entry | Aziridines | Products | Time (h) | Yield[a] (%) |
|---|---|---|---|---|
| 13 |  |  **13** | 72 | 62 |
| 14 |  |  **14** | 72 | 45 |

[a] Isolated yield.
[b] Reaction was carried out at 130 °C.
[c] *o*-Chlorophenol was used instead of *o*-bromophenol.
[d] $Pd_2(dba)_3$ (10 mol%), and 20 mol % (±)-BINAP were used at 130 °C.




**Scheme 2.** Domino ring opening/coupling kinetic resolution.

The possible reaction pathway is described in Scheme 3 based on the previous literature[1a] and the observed stereochemistry of the products. Initially, $Cs_2CO_3$ abstracts the proton from *o*-bromophenol **2** to provide corresponding phenoxide ion **15**. The phenoxide **15**, on reaction with aziridine **1** provided a trans-intermediate **16**. Then the palladium(0) catalyst oxidatively added to the trans-intermediate **16** and produced another intermediate **17**. Then nucleophilic displacement took place at palladium(II) centre to produce a cyclic intermediate **18**. The cyclic intermediate **18** upon reductive elimination gave the corresponding trans-product **3** and simultaneously regenerated the palladium(0) catalyst, which will be utilized for the next catalytic cycle.




**Scheme 3.** The plausible mechanistic explanation.

## 3. Conclusions

In conclusion, for the first time we have developed a novel and practical protocol for the synthesis of the *trans*-1,4-benzoxazine moiety by domino ring opening followed by Buchwald–Hartwig type coupling-cyclization using the easily available $Pd_2(dba)_3$–(±)-BINAP complex as catalyst and $Cs_2CO_3$ as base. A variety of *trans*-1,4-

benzoxazine moieties were synthesized from corresponding aziridines with less reactive, inexpensive *o*-bromophenols and *o*-chlorophenols.

## 4. Experimental section

### 4.1. General

All reactions were carried out in reaction tubes under nitrogen atmosphere. Ligands and palladium salts, *o*-bromophenol and $Cs_2CO_3$ were purchased from Aldrich Chemical Company and used without further purification. The aziridines and substituted *o*-bromophenols were made using literature procedures.[13] Toluene was purchased from SRL chemicals, India and dried over sodium wire. Reactions were performed by using Aldrich Stirrer. Thin-layer chromatography (TLC) was performed using Merck silica gel 60 $F_{254}$ precoated plates (0.25 mm) and visualized by UV fluorescence quenching. Silica gel (particle size 100–200 mesh) purchased from SRL India was used for chromatography. $^1$H and $^{13}$C NMR spectra were recorded on a Bruker 400 MHz instrument. $^1$H NMR spectra were reported relative to $Me_4Si$ ($\delta$ 0.0 ppm) or residual $CHCl_3$ ($\delta$ 7.26 ppm). $^{13}$C NMR spectra were reported relative to $CDCl_3$ ($\delta$ 77.16 ppm). FTIR spectra were recorded on a Nicolet 6700 spectrometer and are reported in frequency of absorption ($cm^{-1}$). High-resolution mass spectra (HRMS) were recorded on Q-Tof Micro mass spectrometer.

### 4.2. Typical experimental procedure for the domino ring opening/coupling-cyclization reaction (entry 1, Table 3)

$Pd_2(dba)_3$ (22.9 mg, 0.025 mmol), (±)-BINAP (31 mg, 0.05 mmol), aziridine (125.5 mg, 0.5 mmol), *o*-bromophenol (58 μL, 0.5 mmol) and $Cs_2CO_3$ (325.8 mg, 1.0 mmol) were taken under nitrogen atmosphere in a 10 mL reaction tube equipped with a septum. To this reaction mixture, 2.2 mL toluene was added and heated at 110 °C for 48 h. After completion of the reaction (the reaction progress was monitored by TLC), the reaction mixture was allowed to cool, toluene was evaporated under rotavapor and the crude reaction mixture was purified directly using column chromatography on silica gel using ethyl acetate/hexane as eluent to afford *trans*-10-tosyl-2,3,4,4a,10,10a-hexahydro-1*H*-phenoxazine 171 mg (99%).

*4.2.1. trans-8-Methyl-10-tosyl-2,3,4,4a,10,10a-hexahydro-1H-phenoxazine (**6**, entry 4, Table 3).* White solid, mp 118–120 °C, $R_f$ (10% ethyl acetate/hexanes) 0.71; IR ($CDCl_3$): 2936, 2865, 2358, 1600, 1454, 1353, 1266, 1169, 1056, 903, 819, 729, 663 $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$1.13–1.49 (m, 4H, $CH_2CH_2$), 1.66–1.76 (2H, m, $CHCH_2$), 1.99–2.07 (1H, m, CH), 2.26 (3H, s, $CH_3$), 2.27 (3H, s, $CH_3$), 2.53–2.61 (CH, m, 1H), 3.28 (1H, ddd, *J*=10.6, 10.6 and 4.0 Hz, NCH), 3.39 (1H, ddd, *J*=10.6, 10.5 and 3.2 Hz, OCH), 6.52 (1H, d, *J*=8.4 Hz, CH), 6.77 (1H, d, *J*=8.0 Hz, CH), 7.04 (2H, d, *J*=8.0 Hz, CHCH), 7.17 (2H, d, *J*=8.0 Hz, CHCH), 7.54 (1H, s, CH); $^{13}$C NMR (100 MHz): $\delta$ 21.1, 21.7, 24.1, 32.0, 33.6, 65.5, 81.1, 116.8, 126.7, 126.8, 127.6, 127.7, 129.4, 131.7, 133.7, 143.9, 150.7; HRMS: MS (ESI, *m*/*z*): $[MNa]^+$, found 380.1284. $C_{20}H_{23}NO_3NaS$ requires 380.1296.

*4.2.2. trans-4a,10a-8-Phenyl-10-tosyl-2,3,4,4a,10,10a-hexahydro-1H-phenoxazine (**9**, entry 7, Table 3).* White solid, mp 109–111 °C, $R_f$ (10% ethyl acetate/hexanes) 0.68; IR ($CDCl_3$): 2931, 2861, 1600, 1482, 1353, 1268, 1166, 1059, 818, 703, 664 $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 1.16–1.30 (2H, m, $CH_2$), 1.30–1.45 (2H, m, $CH_2$), 1.45–1.58 (2H, m, $CH_2$), 1.69–1.79 (2H, m, $CH_2$), 2.03–2.11 (1H, m, CH), 2.26 (3H, s, $CH_3$), 2.57–2.66 (1H, m, CH), 3.36 (1H, ddd, *J*=10.8, 10.6 and 4.0 Hz, NCH), 3.46 (1H, ddd, *J*=11.0, 10.6 and 3.6 Hz, OCH), 6.69 (1H, d, *J*=8.4 Hz, CH), 7.04 (1H, d, *J*=8.0 Hz, CH), 7.21 (2H, d, *J*=8.0 Hz, CHCH), 7.26 (1H, t, *J*=7.6 Hz, CH), 7.37 (2H, t, *J*=7.6 Hz, CHCH), 7.55 (2H, d, *J*=7.6 Hz, CHCH), 8.0 (1H, d, *J*=2.0 Hz, CH); $^{13}$C NMR (100 MHz): $\delta$ 21.7, 24.1, 24.7, 32.0, 33.6, 65.4, 81.1, 117.4, 124.7, 124.9, 127.0, 127.2, 127.7, 128.1, 128.9, 129.5, 133.6, 135.3, 140.4, 144.1, 152.2; HRMS: MS (ESI, *m*/*z*): $[MH]^+$, found 420.1652. $C_{25}H_{26}NO_3S$ requires 420.1633.

*4.2.3. trans-8-Methoxy-10-tosyl-2,3,4,4a,10,10a-hexahydro-1H-phenoxazine (**10**, entry 8, Table 3).* White solid, mp 88–90 °C, $R_f$ (10% ethyl acetate/hexanes) 0.61; IR ($CDCl_3$): 2934, 2863, 1602, 1499, 1455, 1354, 1264, 1216, 1168, 1057, 815, 730, 666 $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 1.10–1.49 (4H, m, $CH_2CH_2$), 1.66–1.77 (1H, m, CH), 1.98–2.08 (1H, m, CH), 2.27 (3H, s, $CH_3$), 2.55–2.64 (1H, m, CH), 3.27 (1H, t, *J*=10.0 Hz, NCH), 3.411 (1H, t, *J*=10.8 Hz, OCH), 3.74 (3H, s, $OCH_3$), 6.49–6.58 (2H, m, CHCH), 7.05 (2H, d, *J*=7.2 Hz, CHCH), 7.21 (2H, d, *J*=8.4 Hz, CHCH), 7.33 (1H, s, CH); $^{13}$C NMR (100 MHz): δ 21.7, 24.2, 24.7, 32.0, 33.7, 56.0, 65.5, 81.3, 111.1, 112.4, 117.5, 127.6, 128.4, 129.4, 133.5, 144.0, 146.8, 154.5; HRMS: MS (ESI, *m*/*z*):$[MH]^+$, found 374.1432. $C_{20}H_{24}NO_4S$ requires 374.1426.

*4.2.4. trans-3a,9a-7-Methoxy-9-tosyl-1,2,3,3a,9,9a-hexahydrobenzo[b]cyclopenta[e][1,4]oxazine (**11**, entry 9, Table 3).* White solid, mp 103–105 °C, $R_f$ (10% ethyl acetate/hexanes) 0.64; IR ($CDCl_3$): 2924, 1608, 1496, 1356, 1267, 1215, 1168, 1097, 952, 733, 668 $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 1.49–1.61 (1H, m, CH), 1.73–1.90 (3H, m, $CHCH_2$), 1.91–2.02 (1H, m, CH), 2.29 (3H,s, $CH_3$), 2.44–2.54 (1H, m, CH), 3.21–3.31 (1H, m, NCH), 3.73 (3H, s, $OCH_3$), 3.76–3.86 (1H, m, OCH), 6.49 (1H, dd, *J*=8.8 and 2.8 Hz, CH), 6.62 (1H, d, *J*=8.8 Hz, CH), 7.11 (2H, d, *J*=8.0 Hz, CHCH), 7.41 (2H, d, *J*=8.0 Hz, CHCH), 7.61 (1H, d, *J*=2.8 Hz, CH); $^{13}$C NMR (100 MHz): $\delta$ 18.5, 21.7, 25.5, 28.6, 56.0, 63.1, 80.8, 108.1, 111.7, 118.4, 127.8, 129.7, 133.9, 143.4, 144.3, 154.3; HRMS: MS (ESI, *m*/*z*): found 360.1261. $C_{19}H_{22}NO_4S$ requires 360.1270.

*4.2.5. trans-2-Methoxy-11-tosyl-5a,6,7,8,9,10,10a,11-octahydrobenzo[b]cyclohepta[e][1,4]oxazine (**12**, entry 10, Table 3).* Gummy solid, $R_f$ (10% ethyl acetate/hexanes) 0.63; IR ($CDCl_3$): 2930, 2863, 1603, 1499, 1454, 1351, 1265, 1214, 1164, 1030, 813, 727, 666 $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 1.32–1.54 (5H, m, $CHCH_2CH_2$), 1.54–1.66 (3H, m, $CHCH_2$), 1.94–2.05 (1H, m, CH), 2.27 (3H, s, $CH_3$), 2.23–2.38 (1H, m, CH), 3.42 (1H, ddd, *J*=9.8, 9.7 and 4.0 Hz, NCH), 3.73 (3H, s, $OCH_3$), 3.96 (1H, ddd, *J*=9.8, 9.7 and 4.0 Hz, OCH), 6.56 (2H, d, *J*=1.6 Hz, CHCH), 7.05 (2H, d, *J*=8.0 Hz, CHCH), 7.18–7.21 (1H, m, CH), 7.23 (2H, d, *J*=8.4 Hz, CHCH); $^{13}$C NMR (100 MHz): $\delta$ 21.7, 23.8, 24.8, 25.1, 33.6, 34.5, 55.9, 64.8, 84.0, 112.4, 113.0, 117.4, 127.3, 128.5, 129.4, 134.7, 143.7, 147.4, 154.9; HRMS: MS (ESI, *m*/*z*): found 388.1599. $C_{21}H_{26}NO_4S$ requires 388.1583.

*4.2.6. trans-3-Phenyl-4-tosyl-3,4-dihydro-2H-benzo[b][1,4]oxazine (**13**, entry 13, Table 3).* White solid, mp 138–141 °C, $R_f$ (10% ethyl acetate/hexanes) 0.62; IR ($CDCl_3$): 2930, 1599, 1497, 1361, 1169, 906, 736, 662, 581 $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$2.41 (3H, s, $CH_3$), 3.25 (1H, dd, *J*=14.4, 10.4 Hz, NCH), 4.38 (1H, dd, *J*=14.4 Hz, 2.4, OCHaHb), 4.21 (1H, dd, *J*=10.2, 2.4 Hz, OCHaHb), 6.94 (1H, dd, *J*=8.2, 1.6 Hz, CH), 7.0 (1H, td, *J*=8.2, 1.6 Hz, CH), 7.10–7.15 (1H, m, CH), 7.21 (2H, dd, *J*=8.0, 2.0 Hz, CHCH), 7.30 (2H, d, *J*=8.0 Hz, CHCH), 7.34–7.41 (3H, m, CHCHCH), 7.58 (2H, d, *J*=8.4 Hz, CHCH), 7.93 (1H, dd, *J*=8.2, 1.6 Hz, CH); $^{13}$C NMR (100 MHz): $\delta$ 21.6, 50.4, 73.3, 117.8, 121.3, 123.6, 125.0, 126.1, 126.5, 127.5, 128.9, 130.2, 135.7, 137.2, 144.6, 147.5; HRMS: MS (ESI, *m*/*z*): found 366.1148. $C_{21}H_{20}NO_3S$ requires 366.1164.

*4.2.7. trans-6-Chloro-3-phenyl-4-tosyl-3,4-dihydro-2H-benzo[b][1,4]oxazine (**14**, entry 14, Table 3).* White solid, mp 154–156 °C, $R_f$ (10% ethyl acetate/hexanes) 0.60; IR ($CDCl_3$): 2930, 1588, 1488, 1357, 1165, 1060, 755, 701, 664 $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 2.43 (3H, s, $CH_3$), 3.21 (1H, dd, *J*=14.6, 10.6 Hz, NCH), 4.17 (1H, dd, *J*=9.2, 2.4 Hz, OCHaCHb), 4.36 (1H, dd, *J*=7.2, 2.4 Hz, OCHaCHb), 6.87 (1H, d, *J*=8.8 Hz, CH), 7.08 (1H, dd, *J*=4.4, 2.4 Hz, CH), 7.19 (2H, dd, *J*=3.8, 2.0 Hz, CHCH), 7.33 (2H, d, *J*=8.0 Hz, CHCH), 7.35–7.41 (3H, m, CHCHCH), 7.61 (2H, d, *J*=8.4 Hz, CHCH), 7.96 (1H, d, *J*=2.4 Hz, CH); $^{13}$C NMR (100 MHz): $\delta$ 21.8, 50.1, 73.5, 118.8, 124.4, 126.1, 126.4,

127.6, 129.0, 129.1, 130.3, 135.3, 136.8, 145.0, 146.1; HRMS: MS (ESI, $m/z$): found 400.0789. $C_{21}H_{19}NO_4S$ requires 400.0774.

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## Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2012.08.054.

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