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Alumina-Supported Cu(II), A Versatile and Recyclable Catalyst for Regioselective Ring Opening of Aziridines and Epoxides and Subsequent Cyclization to Functionalized 1,4-Benzoxazines and 1,4-Benzodioxanes

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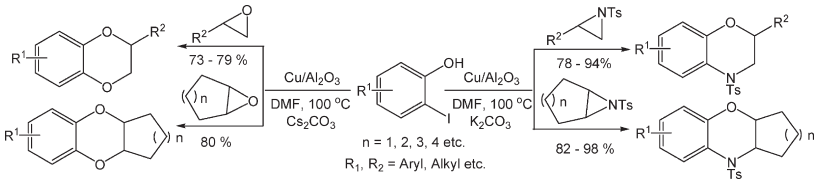

An easily accessible catalyst, alumina-supported copper(II), efficiently catalyzes the ring opening of aziridines and epoxides followed by cyclization of the corresponding intermediate to produce a variety of functionalized 1,4-benzoxazines and 1,4-benzodioxanes, respectively, in one pot without any ligand in high yields. The ring cleavages of aziridines and epoxides are highly regioselective. The catalyst is inexpensive, non-air-sensitive, environmentally friendly, and recyclable. The function of the catalyst and the reaction pathway are postulated. This protocol is successfully utilized for the formation of three carbon−heteroatom bonds, namely, C−O, C−N, and C−S, in one pot.

Introduction

The molecules containing 1,4-benzoxazines and 1,4-benzodioxanes moieties have attracted considerable interest in recent times because of their potential therapeutic properties.[1,2] Flumioxazin **1** and thidiazimin **2** (Figure 1) have been successfully used as effective herbicides with protoporphyrinogen oxidase inhibiting action in chlorophyll biosynthetic pathway.[3] 2-Arylidine-4-aminoalkyl-2*H*-1,4-benoxazin-(4*H*)-ones and related compounds were found to exhibit significant CNS (central nervous system) depression.[4] On the other hand 2-*N*,*N*-diethylaminomethyl-1,4-benzodioxane **4** and its derivatives are used as reversible and irreversible antagonists at adrenergic receptor.[5] They are also found in a variety of natural products.[6]

Thus, the synthesis of these heterocyclic units have received renewed interest. Several protocols for the synthesis of benzoxazines, such as cyclo-condensation of aminophenols with α-halogeno acyl bromides followed by carbonyl reduction using BH_3,[7] alkylation of *o*-nitrophenol with haloester and subsequent reductive cyclization,[8] and epoxide ring opening with *o*-fluorosulfonamides followed by cyclization under solid−liquid phase transfer catalysis[9] in neat, are noteworthy among others.[10] On the other hand, the most common method for the synthesis of 1,4-benzodioxanes are

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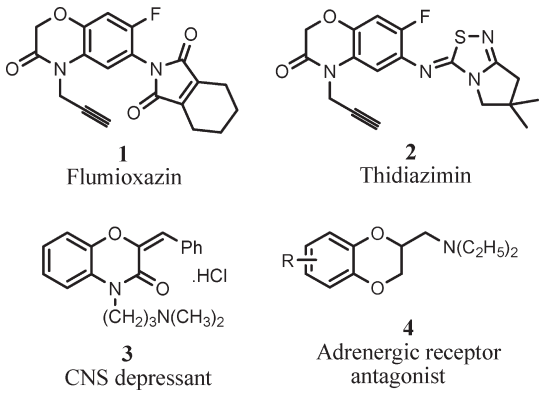


FIGURE 1. Some biologically important compounds.

based on the reaction of catechol with epoxides or α-haloalkenes or similar substrates.[11] A Pd-catalyzed intramolecular etherification of α-halo alcohols leading to 1,4-benzodioxanes is also reported.[12] However, despite the availability of these multistep procedures a more efficient one-pot process is highly desirable.

The domino reaction is a useful and attractive tool in organic synthesis as it provides a cost- and energy-effective process.[13] Recently, Sekar et al. reported a synthesis of *trans*-3,4-dihydra-2*H*-1,4-benzoxazine by CuI/ethylenediamine-catalyzed domino aziridine ring opening with *o*-iodophenol followed by cyclization.[14] However, this method employed only cycloalkane fused aziridines, and not a single reaction with noncycloalkane fused aziridine was addressed. Earlier, Bao et al. described a similar approach for the synthesis of 1,4-benzodioxanes involving ring opening of epoxides and cyclization catalyzed by Cu_2O/1,10-phenanthroline.[15] Although this method covers a wide range of epoxides, in several reactions regioselectivity of epoxide ring cleavage is not controlled. Considering the great potential of 1,4-benzoxazines and 1,4-benzodioxanes, we became interested to develop a general protocol for access to both molecules. Recently we introduced a stable alumina-supported Cu(II) catalyst for the coupling of thiols with aryl halides[16a] and electrophilic substitution by PhSeBr in organoboranes, organosilanes, and organostannanes.[16b] We report here another novel application of this unique catalyst for the ring opening of aziridines and epoxides by 2-iodophenols and simultaneous cyclization to produce the 1,4-benzoxazines and 1,4-benzodioxanes, respectively (Scheme 1)

Results and Discussion

To optimize the reaction conditions, a series of experiments were carried out with variation of different reaction

SCHEME 1. Copper-Catalyzed Ring Opening−Cyclization Using 2-Iodophenols

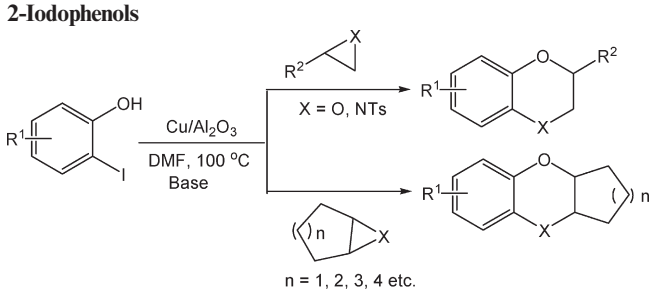
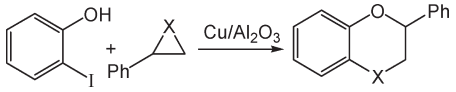


TABLE 1. Optimization of Reaction Conditions[a]



entry	X	solvent	base	temp (°C)	time (h)	yield (%)
1	NTs	THF	K_2CO_3	70	16	37
2		toluene	K_2CO_3	110	16	19
3		H_2O	K_2CO_3	100	16	0
4		DMF	K_2CO_3	100	8	93
5		DMF	K_2CO_3	100	8	0[b]
6		DMF	Cs_2CO_3	100	8	85
7		DMF	K_3PO_4	100	16	55
8		DMF	NaOH	100	16	46
9	O	THF	K_2CO_3	70	16	30
10		toluene	K_2CO_3	110	16	tr
11		H_2O	K_2CO_3	100	16	0
12		DMF	K_2CO_3	100	8	20
13		DMF	Cs_2CO_3	100	8	81
14		DMF	Cs_2CO_3	100	8	0[b]
15		DMF	K_3PO_4	100	16	35
16		DMF	NaOH	100	16	51

[a]Reactions were carried out in the presence of 4 mol % of Cu/Al_2O_3 catalyst unless otherwise stated. [b]Reactions were carried out in the absence of Cu/Al_2O_3 catalyst.

parameters such as solvent, base, temperature, etc. for a representative reaction of 2-iodophenol and 2-phenyl-*N*-tosyl aziridine/styrene oxide in the presence of Cu/Al_2O_3 catalyst. The results are summarized in Table 1. Among the various solvents investigated DMF was found to perform better at 100 °C for both the reactions. Potassium carbonate was found to give the best yields in aziridine reactions (Table 1, entry 4), whereas the reactions of epoxides needed cesium carbonate (Table 1, entry 13). The amount of catalyst was optimized to 4 mol %. Nevertheless, the reactions did not proceed at all in the absence of catalyst (Table 1, entries 5 and 14).

Thus, in a typical experimental procedure, a mixture of aziridine/epoxide and 2-iodophenol in DMF was heated at 100 °C in the presence of Cu/Al_2O_3 and a base, K_2CO_3/Cs_2CO_3, for a certain period of time (TLC). Standard work-up and purification by column chromatography provided the product.

A series of diversely functionalized 1,4-benzoxazines were synthesized by this procedure using a variety of substituted *N*-tosyl aziridines. The results are reported in Table 2. This reaction is equally effective for the participation of 2-phenyl-substituted, 2,3-dialkyl-disubstituted, and cycloalkane fused aziridines. The reactions of 2-substituted and 2,3-disubstituted aziridines were not addressed earlier.[14] However, these reactions are of much interest because of the issue of the

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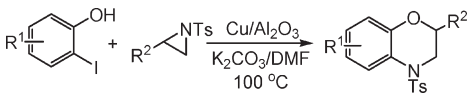
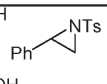
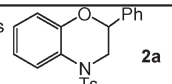
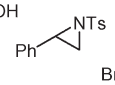
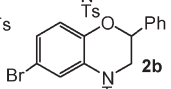
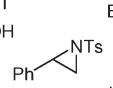
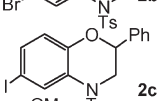
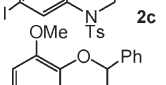
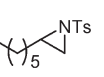
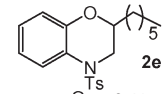
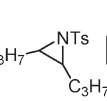
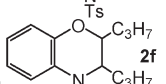
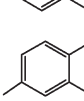
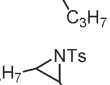
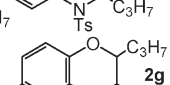
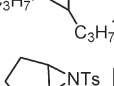
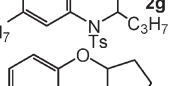
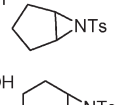
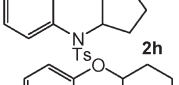
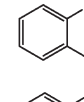
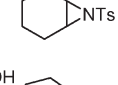
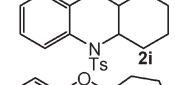
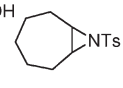
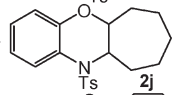
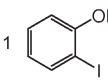
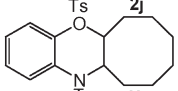
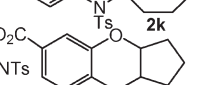
TABLE 2. Copper-Catalyzed Synthesis of 1,4-Benzoxazines



entry	iodophenol	aziridine	product	time (h)	yield (%)[a]	ref
1			 **2a**	8	93	9
2			 **2b**	9	92	
3			 **2c**	8	94	
4			 **2d**	10	88	
5			 **2e**	10	78	9
6			 **2f**	9	91	
7			 **2g**	9	90	
8			 **2h**	8	95	14
9			 **2i**	8	98	14
10			 **2j**	8.5	93	14
11			 **2k**	9	89	14
12			 **2l**	8.5	90	
13			 **2m**	8.5	93	
14			**2n**	9	89	
15			**2o**	12	82	
16			**2p**	12	83	

[a]Isolated yield of pure product.

regioselectivity in the ring opening of aziridine and hence formation of product. We have found that the ring opening of the 2-substituted aziridines and cyclization (Table 2, entries 1−4) are highly regioselective, ending up with only one regioisomer using Cu/Al_2O_3 catalyst. The identity of the product (Table 2, entry 1) was unequivocally established as 3,4-dihydro-2-phenyl-4-tosyl-(2*H*)benzo[*b*][1,4]oxazine by X-ray crystal data (Figure 2, **2a**).[17a] By analogy, the other products (Table 2, entries 2−5) were also characterized as the corresponding 2-phenyl/hexyl benzoxazine by comparison of their spectral data (IR, ^1H and ^{13}C NMR) with those of product in entry 1, Table 2. To investigate the regioselectivity of cleavage of aziridine and epoxide rings a few control experiments were carried out. The reaction of 2-phenyl-*N*-tosyl aziridine with phenol in the presence of Cu/Al_2O_3 and K_2CO_3 provided only one product by the cleavage at 2-position adjacent to the Ph ring possibly because of stabilization of carbocation by phenyl ring (Scheme 2). The same reaction with K_2CO_3 only or Al_2O_3/K_2CO_3 provided a mixture of two regioisomers together with unreacted aziridines. This indicates a decisive role of Cu/Al_2O_3 catalyst in aziridine ring cleavage leading to only one isomer (Scheme 2). Very interestingly, for comparison, when this reaction was performed with CuI/ethylenediamine,[14] no benzoxazine was obtained. Moreover, the reaction of 2-iodophenol with cyclooctane fused *N*-tosyl aziridine, which gave 48% yield in an earlier procedure,[14] furnished 89% yield by our procedure. This demonstrates the superiority of our catalyst over CuI/ethylenediamine.[14] In fact, the reaction of 2-iodophenols with all cycloalkane-fused aziridines provided high yields of corresponding benzoxazines. The ring junction stereochemistry of the products in entries 8−10 of Table 2 is found to be *trans* as determined by the ^1H NMR spectroscopic data, which are in good agreement with the values of the reported compounds.[14] The X-ray crystal structures of the products in entries 8 and 15 (Table 2) also confirmed the *trans* stereochemistry (Figure 2, **2h**, **2o**).[17b,c] The formation of one single regioisomeric product from the reaction of 2-iodophenol and indene-fused aziridine is also very noteworthy. The structure of this product was also confirmed by X-ray crystal data (Figure 2, **2p**).[17d] Thus all the reactions (aziridine cleavage + cyclization) using this Cu/Al_2O_3 catalyst are highly regio- and stereoselective. Several substituted 2-iodophenols (Table 2, entries 2, 3, 4, 7, 12, 13, and 14) participated in this reaction without any difficulty, producing highly functionalized 1,4-benzoxazines that are of much potential for pharmaceutical uses.

SCHEME 2. Cu-Catalyzed Regioselective Aziridine Ring Opening

Similarly, the reactions of 2-iodophenols with epoxides produced corresponding 1,4-benzodioxanes *via* epoxide ring

(17) (a) CCDC no. for the compound **2a**, 786009. (b) CCDC no. for the compound **2h**, 786010. (c) CCDC no. for the compound **2o**, 786008. (d) CCDC no. for the compound **2p**, 786006. (e) CCDC no. for the compound **3f**, 786007.

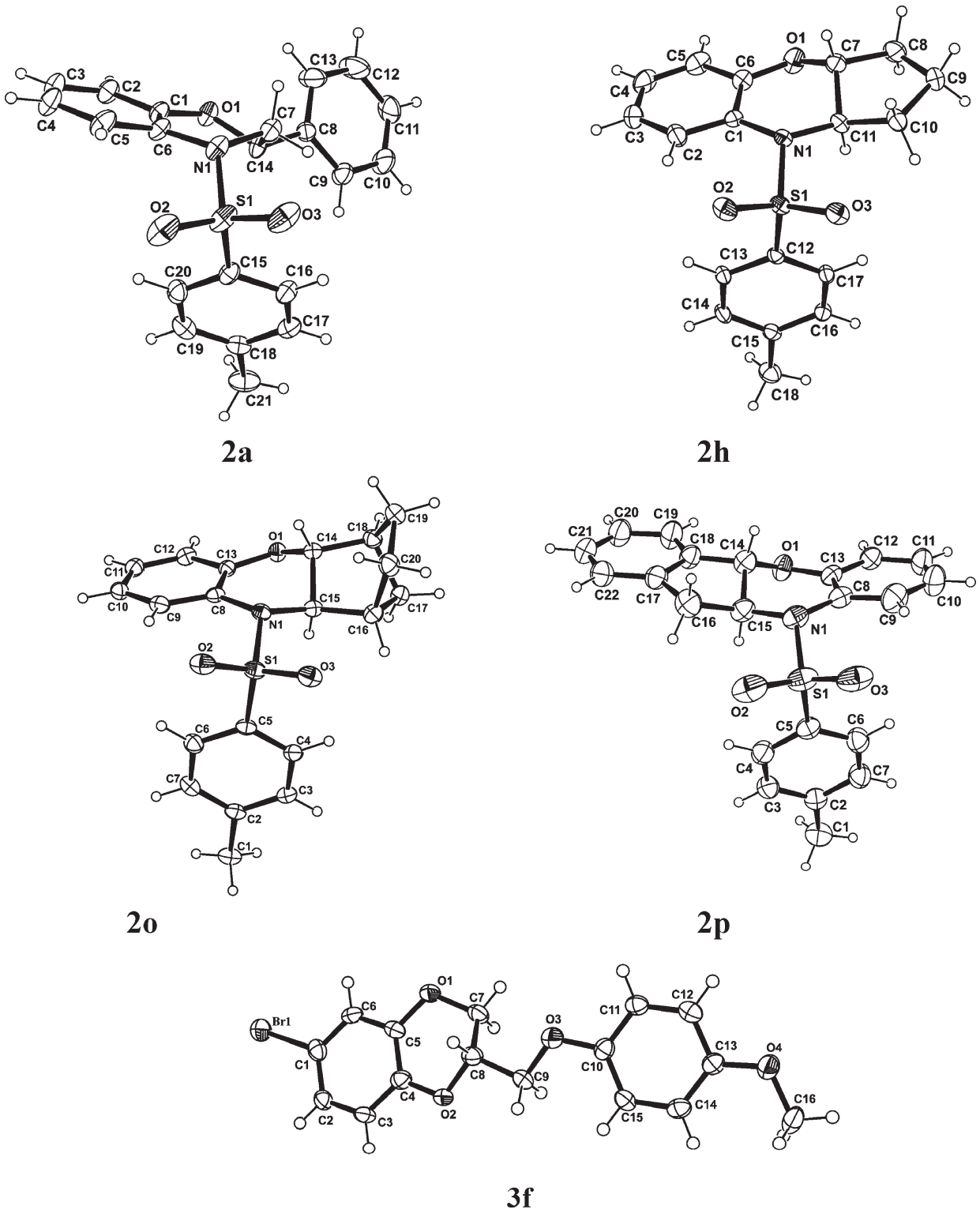
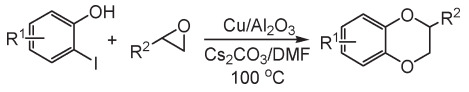


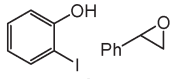
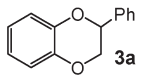
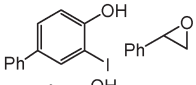
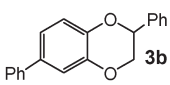
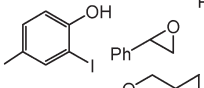
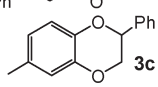
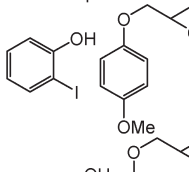
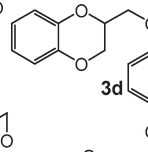
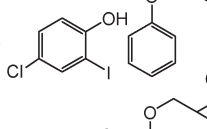
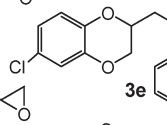
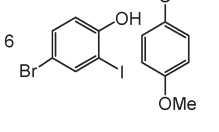
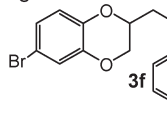
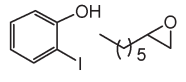
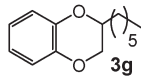
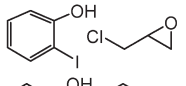
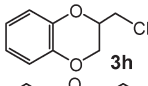
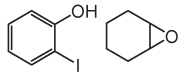
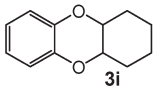
FIGURE 2. ORTEP diagram of some functionalized 1,4-benzoxazines and 1,4-benzodioxanes.

opening followed by cyclization. The results are reported in Table 3. These reactions are also highly regioselective, producing only one regioisomeric set of products in contrast to the formation of a mixture of regioisomers using Cu_2O/1,10-phenanthroline.[15] Very interestingly the minor product observed using Cu_2O/1,10-phenanthroline was obtained as the sole product in our procedure using Cu/Al_2O_3 as shown in Table 3, entries 3 and 5. The regioisomeric identities of the products are established by comparison of their spectroscopic data (^1H and ^{13}C NMR) with those reported earlier.[15] In one case (Table 3, entry 6), the structure was also confirmed by X-ray crystal data (Figure 2, **3f**).[17e]

In general, the reactions of both aziridines and epoxides are very clean and high-yielding compared to other methods. The

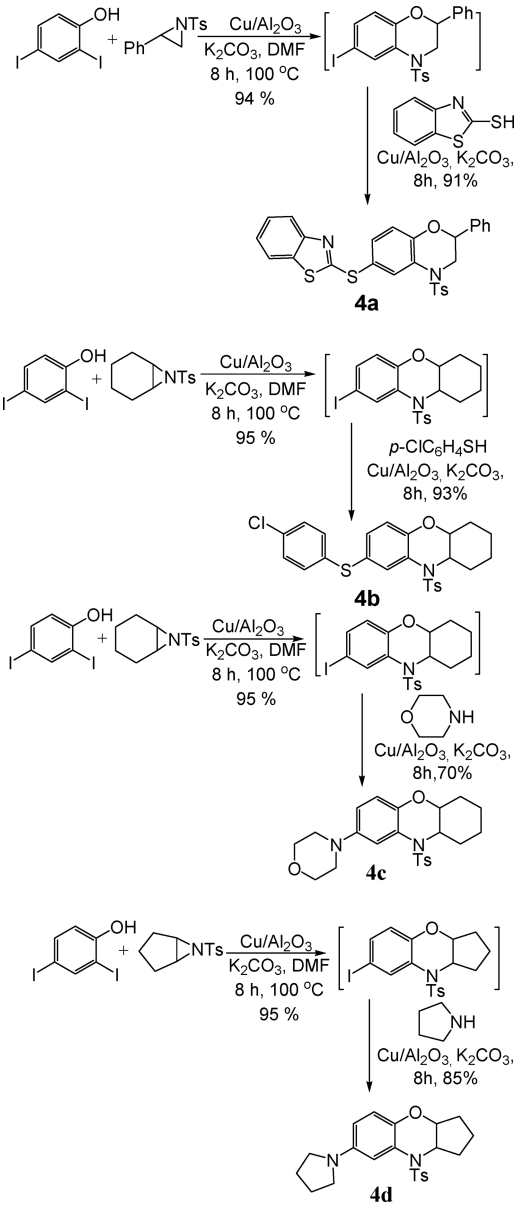
TABLE 3. Copper-Catalyzed Synthesis of 1,4-Benzodioxanes



entry	iodophenol	epoxide	product	time (h)	yield (%)[a]	ref
1			 **3a**	8	81	15
2			 **3b**	9.5	78	
3			 **3c**	9	79	15
4			 **3d**	10	81	
5			 **3e**	10	78	15
6			 **3f**	10	79	
7			 **3g**	9	79	
8			 **3h**	10	73	18
9			 **3i**	8	80	15

[a]Isolated yield of pure product.

SCHEME 3. Cu-Catalyzed One-Pot Synthesis of 1,4-Benzoxazine Thioethers and 1,4-Benzoxazine Amines



procedure is compatible with a variety of functional groups such as CHO, Cl, Br, CO_2Et, OMe, etc. present in 2-iodophenol and differently substituted aziridines and epoxides.

The Cu/Al_2O_3 catalyst was recovered and reused for 7 subsequent reactions without any appreciable loss of efficiency. No significant leaching of the catalyst in the reaction mixture was observed (0.497 mmol g^{-1} after seventh cycle compared to 0.517 mmol g^{-1} as determined by ICP-MS). A remarkable application of this protocol is demonstrated by the consecutive formation of three carbon−heteroatom bonds, namely, C−O, C−N and C−S, in one stroke leading to the synthesis of 1,4-benzoxazine thioethers and amines (Scheme 3). These compounds (**4a**, **4b**, **4c**, and **4d**) are of much importance as potential herbicides and are usually synthesized through a multistep process.[3]

To investigate the mechanism, a series of experiments were conducted. The X-ray photo electron spectroscopic (XPS) study of the fresh and used catalyst at the Cu 2p level shows the $2p_{3/2}$ lines at 934.7 and 933.7 eV, respectively, with characteristic shakeup features (Figure 3a and c).[19]

This clearly indicates that Cu is in a +2 oxidation state before and after the reaction (a slightly higher value in the binding energy of Cu^{2+} in the fresh catalyst is due to a combined contribution of $CuSO_4$ and $Cu(OH)_2$ on the surface of alumina). On the other hand, the X-band EPR spectrum of the fresh catalyst shows four well-defined hyperfine lines for a solid sample at 77 K resulting from the coupling of the unpaired electron with the nuclear spin of Cu(II) (Figure 4). The regenerated catalyst also shows a very similar EPR

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(19) (a) Chary, K.V. R.; Sagar, G. V.; Srikanth, C. S.; Rao, V. V. *J. Phys. Chem. B.* **2007**, *111*, 543–550. (b) Choudary, B. M.; Sridhar, C.; Kantam, M. L.; Venkanna, G. T.; Sreedhar, B. *J. Am. Chem. Soc.* **2005**, *127*, 9948–9949. (c) Adolphi, B.; Berger, O.; Fischer, W.-J. *Appl. Surf. Sci.* **2001**, *179*, 102–108. (d) *Handbook for X-ray Photoelectron Spectroscopy*; Chastain, J., Roger, C. K., Jr., Eds.; Physical Electronics Inc.: Eden Prairie, MN, 1995.

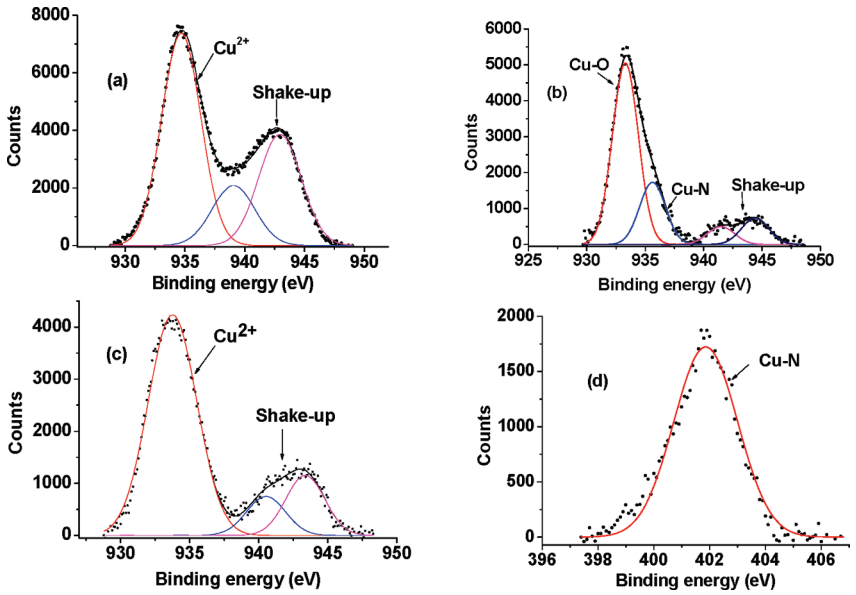


FIGURE 3. XPS of Cu $2p_{3/2}$ for (a) fresh catalyst, (b) Cu(II)-intermediate complex, and (c) used catalyst; (d) XPS of N 1s for Cu(II)-intermediate complex.

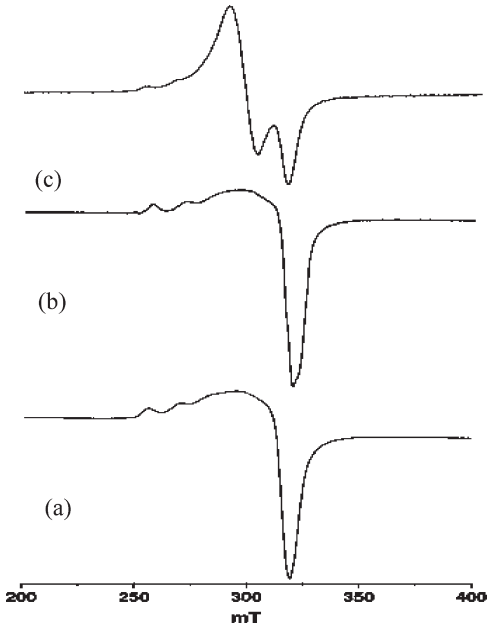
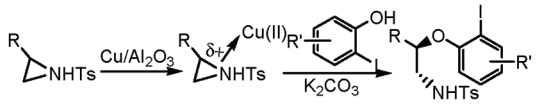


FIGURE 4. X-band EPR spectral pattern of Cu^{2+} in (a) fresh catalyst, (b) used catalyst, and (c) intermediate complex **B**.

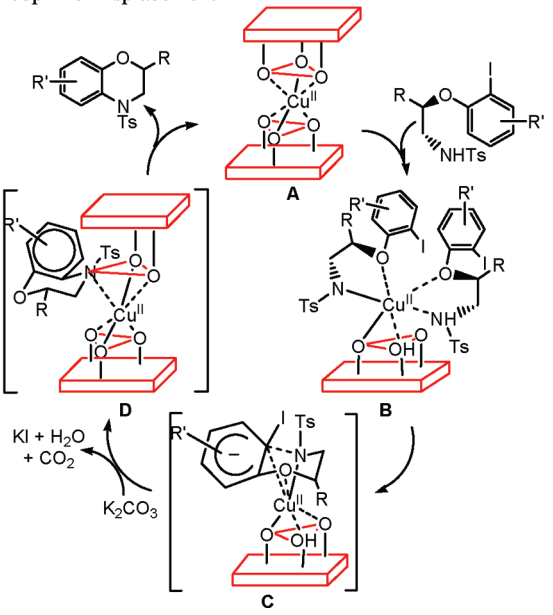
spectrum as observed in the fresh catalyst. The g values of the fresh catalyst are $g_{\|} = 2.41367$, 2.5408 and $g_{\perp} = 2.1406$, and those of the used catalyst are $g_{\|} = 2.3940$, 2.5296 and $g_{\perp} = 2.0741$, indicating a tetragonally distorted octahedral geometry for Cu(II).[20] The regioselective formation of 1,4-benzoxazine and 1,4-benzodioxane from the corresponding aziridines and epoxides indicates a Cu(II)-catalyzed regioselective ring opening[21]

SCHEME 4. Probable Mechanistic Pathway

Step 1. Copper Catalyzed Regioselective Aziridine Ring Opening



Step 2. Cyclization through C-N Bond Formation *via* Cu-Assisted Nucleophilic Displacement



followed by C−N or C−O coupling leading to the product. Thus the copper catalyst shows a dual role in ring opening as well as cross-coupling steps. To understand the cross-coupling pathway *via* C−N bond formation, cyclopentane-fused aziridine was chosen as a model substrate as the corresponding ring-opened product was easily prepared on treatment with 2-iodophenol using K_2CO_3 alone. On the other hand,

(20) (a) Matsuoka, M.; Ju, W.-S.; Takahashi, K.; Yamashita, H.; Anpo, M. *J. Phys. Chem. B* **2000**, *104*, 4911–4915. (b) Kantam, M. L.; Chakravarti, R.; Neelima, B.; Arundhati, R.; Sreedhar, B. *Appl. Catal., A* **2007**, *333*, 136–142.

(21) (a) Ghorai, M. K.; Shukla, D.; Das, K. *J. Org. Chem.* **2009**, *74*, 7013–7022. (b) Hong, D.; Lin, X.; Zhu, Y.; Lei, M.; Wang, Y. *Org. Lett.* **2009**, *11*, 5678–5681. (c) Barluenga, J.; Vázquez-villa, H.; Ballesteros, A.; González, J. M. *Org. Lett.* **2002**, *4*, 2817–2819.

a styrene aziridine provided a mixture of products on similar treatment. Thus, when the fresh catalyst was treated with the ring-opened product of cyclopentane-fused aziridine with 2-iodophenol, a dirty white complex **B** was formed. The EPR spectral pattern of this intermediate complex **B** exhibited a dramatic change from the earlier *g* values now at 2.212 with $g_{\|} = 2.41276$, 2.4840 and $g_{\perp} = 2.04$, 2.124, which is indicative of an even more distorted octahedral environment with an axial distortion at the metal center. The formation of these type of intermediate is also not unprecedented.[19b,22] The XPS of Cu $2p_{3/2}$ and N 1s lines appear at 935.6 and 401.8 eV, respectively, which is assigned for Cu−N bonds (the larger peak at 933.2 is due to Cu−O bond) (Figure 3b and d). The atom ratio of Cu:N was found to be 0.5, indicating two N-atoms are associated with each Cu(II) unit. Thus the formation of Cu(II)-intermediate complex **B** is proposed. Although we were not being able to isolate any further intermediate complex, we speculate that a Cu-assisted nucleophilic displacement of I^- of the arene[19b,23] by the N of the aziridine residue took place *via* the transients C and D. The elimination of the suitable benzoxazine or benzodioxane from the coordination sphere of Cu(II) regenerates the catalyst, which initiates the next cycle. Thus, on the basis of these results of model study with cyclopentane-fused aziridine, we suggest a possible general reaction pathway as outlined in Scheme 4.

Conclusion

In summary, we have developed a very powerful tool for the synthesis of 1,4-benzoxazines and 1,4-benzodioxanes by a sequential one-pot ring opening/cyclization of aziridines and epoxides, respectively, using a heterogeneous Al_2O_3-supported Cu(II) catalyst. This protocol has also been used for a one-pot synthesis of 1,4-benzoxazine thioethers and amines demonstrating formation of the consecutive three bonds C−O, C−N, and C−S in one stroke. These 1,4-benzoxazine thioethers and amines are of high potential as herbicides. In addition this Cu/Al_2O_3-catalyzed procedure offers significant advantages over other methods because of its high yields, excellent regioselectivity in aziridine and epoxide ring opening, generality (applicable to aziridines and epoxides), versatility (compatibility with a wide variety of substrates), and reusability of the catalyst . To the best of our knowledge, this is the first report of control of regioselectivity in Cu-catalyzed domino ring opening/cyclization mediated synthesis of 1,4-benzoxazines and 1,4-benzodioxanes. It is likely that solid alumina surface acts as a microligand and promotes creation of a stable active site that provides unique catalytic function providing better control over regio- and stereoselectivity.[24] Nevertheless, this demonstrates the potential of our alumina-supported Cu(II) catalyst for a variety of organic reactions.

Experimental Section

General. IR spectra were taken as thin films for liquid compounds and as KBr pellets for solids. NMR spectra were recorded at 300 and 500 MHz for ^{1}H NMR and at 75 and 125 MHz for ^{13}C NMR in $CDCl_3$ solutions. XPS measurements were performed with a spectrometer fitted with an EA125 hemispherical analyzer and a monochromatized Al KR (1486.6 eV) source. X-band EPR measurements were carried out at 77 K. The Cu/Al_2O_3 was prepared following our procedure reported earlier.[16a]

General Experimental Procedure for the Synthesis of 1,4-Benzoxazines. Representative Procedure for the Synthesis of 2-Phenyl-4-(toluene-4-sulfonyl)-3,4-dihydro-2*H*-benzo[1,4]oxazine (Table 2, entry 1). To a solution of 2-iodophenol (264 mg, 1.2 mmol) and 2-phenyl-1-(toluene-4-sulfonyl)-aziridine (274 mg, 1 mmol) in DMF (4 mL) were added K_2CO_3 (276 mg, 2 mmol) and Cu/Al_2O_3 catalyst (80 mg, 4 mol %), and the mixture was heated at 100 °C (oil bath) for 8 h. The reaction mixture was allowed to cool, extracted with EtOAc (3 × 20 mL), and washed with dilute NaOH solution (5%) and brine. The organic phase was dried (Na_2SO_4) and evaporated to leave the crude product, which was purified by column chromatography over silica gel (hexane/EtOAc = 90:10) to provide pure 2-phenyl-4-(toluene-4-sulfonyl)-3,4-dihydro-2*H*-benzo[1,4]oxazine as a yellow solid (340 mg, 93%) mp 146 °C; IR (KBr) 3018, 2928, 2864, 1915, 1799, 1726, 1597, 1583, 1489, 1450, 1356, 1215, 1166, 1057, 927, 754 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.42 (s, 3H), 3.26 (dd, J_1 = 10.35 Hz, J_2 = 14.4 Hz, 1H), 4.21−4.25 (m, 1H), 4.36−4.42 (m, 1H), 6.93−7.03 (m, 2H), 7.11−7.13 (m, 1H), 7.21−7.23 (m, 2H), 7.30 (d, J = 8.02 Hz, 2H), 7.35−7.39 (m, 3H), 7.59 (d, J = 8.02, 2H) 7.94 (d, J = 8.193, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.7, 50.4, 73.3, 117.8, 121.2, 123.5, 124.9, 126.0 (2C), 126.5, 127.5 (2C), 128.9 (3C), 130.1 (2C), 135.6, 137.2, 144.6, 147.5 ppm. HRMS: *m*/*z* calcd for $C_{21}H_{19}NO_3S$ [M + Na^+] 388.2833; found 388.0983.

After workup the residual catalyst was washed with water (5 × 3 mL), EtOAc (3 × 4 mL), and acetone (3 × 4 mL). The solid was then dried at 100 °C for 8 h for further use. The catalyst was recycled 7 times without appreciable loss of activity.

General Experimental Procedure for the Synthesis of 1,4-Benzodioxanes. Representative Procedure for the Synthesis of 2-Phenyl-2,3-dihydro-benzo[1,4]dioxane (Table 3, entry 1). To a solution of 2-iodophenol (264 mg, 1.2 mmol) and styrene oxide (180 mg, 1.5 mmol) in DMF (4 mL) were added Cs_2CO_3 (650 mg, 2 mmol) and Cu/Al_2O_3 catalyst (80 mg, 4 mol %), and the mixture was heated at 100 °C (oil bath) for 8 h. The reaction mixture was allowed to cool, extracted with EtOAc (3 × 20 mL), and washed with dilute NaOH solution (5%) and brine. The organic phase was dried (Na_2SO_4) and evaporated to leave the crude product, which was purified by column chromatography over silica gel (hexane/EtOAc = 90:10) to provide pure 2-phenyl-2,3-dihydro-benzo[1,4]dioxane as a colorless liquid (172 mg, 81%). The spectroscopic data (^{1}H NMR and ^{13}C NMR) of this product are in good agreement with those of an authentic sample.[15]

Preparation of Complex B. A mixture of Cu/Al_2O_3 catalyst (100 mg, 5 mol %) and the ring-opened product of cyclopentene-fused *N*-tosyl aziridine by 2-iodo phenol (458 mg, 1 mmol) in DMF (3 mL) was heated at 100 °C for 8 h. The mixture was cooled to room temperature, the supernatant liquid was filtered off, and the dirty white residue was thoroughly washed with water, ethylacetate, and acetone and dried to get the complex **B**.

Recyclability of the Catalyst. The catalyst was recycled up to a seventh run without appreciable loss of efficiency for the representative reaction of 2-phenyl-*N*-tosyl aziridine and 2-iodophenol (Figure 5). The copper loading of the catalyst after seventh cycle was found to be 0.497 mmol g^{-1} compared to 0.517 mmol g^{-1} in the fresh catalyst (as detected by ICP-MS).

Although the representative procedure is based on a 1 mmol scale reaction, it has been scaled up to 5 g scale with reproducible results. The compounds are of high purity as checked by ^{13}C NMR.

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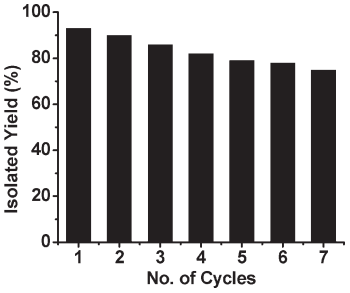

FIGURE 5. Recyclability of the Cu/Al_2O_3 catalyst.

The known compounds were identified by comparison of their spectra with those of authentic samples (see references in Tables 2 and 3). The unknown compounds were properly characterized by their spectroscopic data (IR, ^1H and ^{13}C NMR, and HRMS or elemental analysis), which are provided below in order of their entries in the respective tables.

6-Bromo-3,4-dihydro-2-phenyl-4-tosyl-2*H*-benzo[*b*][1,4]oxazine (Table 2, entry 2). Yellow solid (mp 160 °C); IR (KBr) 3107, 2922, 2852, 1919, 1595, 1481, 1357, 1246, 1167, 1062, 927, 813, 752, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.24 (s, 3H), 3.02 (dd, J_1 = 10.21 Hz, J_2 = 15.0 Hz, 1H), 3.97−4.01 (m, 1H), 4.13−4.18 (m, 1H), 6.62 (d, J = 8.736 Hz, 1H), 6.98−7.04 (m, 3H), 7.12−7.19 (m, 5H), 7.42 (d, J = 8.27 Hz, 2H), 7.90−7.91 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 49.9, 73.3, 112.9, 119.1, 124.6, 125.9 (2C), 127.0, 127.4 (2C), 128.8 (2C), 128.9, 129.1, 130.1 (2C), 135.1, 136.6, 144.8, 146.4 ppm. HRMS: m/z calcd for $C_{21}H_{18}BrNO_3S$ [M + Na^+] 466.0101; found 466.0088.

3,4-Dihydro-6-iodo-2-phenyl-4-tosyl-2*H*-benzo[*b*][1,4]oxazine (Table 2, entry 3). Yellow solid (mp 172 °C); IR (KBr) 3117, 2925, 2860, 1918, 1597, 1483, 1367, 1266, 1170, 1064, 925, 811, 748, 695 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.35 (s, 3H), 3.12 (dd, J_1 = 10.24 Hz, J_2 = 15.0 Hz, 1H), 4.09−4.13 (m, 1H), 4.24−4.29 (m, 1H), 6.62 (d, J = 8.61 Hz, 1H), 7.13−7.10 (m, 2H), 7.21−7.34 (m, 6H), 7.54 (d, J = 8.23 Hz, 2H), 8.18−8.19 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.7, 49.9, 73.4, 82.7, 119.7, 125.7, 125.9 (2C), 127.4 (2C), 128.8 (2C), 128.9, 130.1, 130.3 (2C), 133.0, 135.1, 136.6, 144.9, 147.3 ppm. HRMS: m/z calcd for $C_{21}H_{18}INO_3S$ [M + Na^+] 513.9831; found 513.995.

3,4-Dihydro-8-methoxy-2-phenyl-4-tosyl-2*H*-benzo[*b*][1,4]oxazine-5-carbaldehyde (Table 2, entry 4). Orange solid (mp 185 °C); IR (KBr) 3650, 3355, 3064, 2943, 2865, 2254, 1687, 1589, 1500, 1445, 1357, 1278, 1257, 1166, 1046, 912, 814, 732, 669 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.40 (s, 3H), 3.26 (dd, J_1 = 11.5 Hz, J_2 = 15.5 Hz, 1H), 3.89 (s, 3H), 4.25−4.28 (m, 2H), 6.95 (d, J = 8.5 Hz, 1H), 7.11−7.13 (m, 2H), 7.29−7.34 (m, 6H), 7.49 (d, J = 8.5 Hz, 1H), 7.68 (d, J = 8.5 Hz, 1H), 10.18 (s,1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.6, 49.8, 56.3, 72.9, 109.2, 121.1, 125.0, 125.8 (2C), 126.5, 128.2 (2C), 128.8 (2C), 128.9, 130.4 (2C), 134.3, 136.7, 139.0, 145.5, 152.8, 187.6 ppm. HRMS: m/z calcd for $C_{23}H_{21}NO_5S$ [M + Na^+] 446.1038; found 446.1038.

2-Hexyl-3,4-dihydro-4-tosyl-2*H*-benzo[*b*][1,4]oxazine (Table 2, entry 5). Colorless liquid; IR (neat) 2953, 2929, 2858, 1599, 1583, 1489, 1354, 1247, 1166, 1089, 813, 754, 680 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.84−0.92 (m, 3H), 1.19−1.41 (m, 7H), 1.46−1.58 (m, 3H), 2.37 (s, 3H), 3.04−3.26 (m, 1H), 3.87 (d, J = 11.1 Hz, 1H), 4.23−4.28 (m, 1H), 6.70−6.81 (m, 1H), 6.95−6.98 (m, 1H), 7.05−7.07 (m, 1H), 7.18−7.23 (m, 2H), 7.44−7.53 (m, 2H), 7.89−7.92 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 21.5, 22.6, 24.5, 25.8, 28.8, 30.1, 52.7, 64.7, 117.4, 120.9, 126.0, 126.3, 127.2 (2C), 129.8 (2C), 135.5, 144.1, 144.2, 146.3 ppm. HRMS: m/z calcd for $C_{21}H_{27}NO_3S$ [M + Na^+] 396.1604; found 396.1609.

3,4-Dihydro-2,3-dipropyl-4-tosyl-2*H*-benzo[*b*][1,4]oxazine (Table 2, entry 6). White solid (mp 119 °C); IR (KBr) 3045, 2956, 2870, 1597, 1579, 1487, 1346, 1251, 1170, 1089, 945, 896, 812, 759, 684 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.80−0.91 (m, 6H), 1.28−1.36 (m, 6H), 1.47−1.56 (m, 2H), 2.33 (s, 3H), 3.06−3.09 (m, 1H), 4.10−4.16 (m, 1H), 6.76 (d, J = 9 Hz, 1H), 6.92 (t, J = 8.4 Hz, 1H), 7.02 (t, J = 6.67 Hz, 1H), 7.18 (d, J = 8.2 Hz, 2H), 7.45 (d, J = 8.2 Hz, 2H), 7.92 (d, J = 9.0 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8 (2C), 18.5, 18.9, 21.6, 26.7, 33.8, 55.5, 73.6, 117.1, 120.9, 121.6, 126.1, 126.2, 127.3 (2C), 129.9 (2C), 135.9, 144.1, 147.4 ppm. HRMS: m/z calcd for $C_{21}H_{27}NO_3S$ [M + Na^+] 396.1607; found 396.1609.

3,4-Dihydro-6-methyl-2,3-dipropyl-4-tosyl-2*H*-benzo[*b*][1,4]oxazine (Table 2, entry 7). White solid (mp 121 °C); IR (KBr) 3031, 2956, 2934, 2874, 1596, 1499, 1467, 1349, 1237, 1170, 955, 809, 687 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.78−0.91 (m, 6H), 1.16−1.27 (m, 6H), 1.28−1.50 (m, 2H), 2.29 (s, 3H), 2.33 (s, 3H), 3.01−3.04 (m, 1H), 4.06−4.11 (m, 1H), 6.64 (d, J = 8.3 Hz, 1H), 6.83−6.86 (m, 1H), 7.17 (d, J = 8.2 Hz, 2H), 7.45 (d, J = 8.2 Hz, 2H), 7.72 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.6, 13.7, 18.4, 18.7, 20.8, 21.4, 26.6, 33.7, 55.4, 73.3, 116.5, 121.1, 126.2, 126.9, 127.2 (2C), 129.7 (2C), 130.1, 135.8, 143.9, 145.0 ppm. HRMS: m/z calcd for $C_{22}H_{29}NO_3S$ [M + Na^+] 410.1768; found 410.1766.

Ethyl-9-tosyl-[1,2,3,3a,9,9a]-hexahydrobenzo[*b*]cyclopenta[e]-[1,4]oxazine-6-carboxylate (Table 2, entry 12). White solid (mp 132 °C); IR (KBr) 3394, 3001, 2985, 2964, 1705, 1597, 1568, 1494, 1464, 1357, 1300, 1269, 1172, 1120, 881, 763, 661 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.27 (t, J = 7.1 Hz, 3H), 1.57−1.61 (m, 1H), 1.76−1.88 (m, 3H), 1.94−2.01 (m, 1H), 2.26 (s, 3H), 2.49 (m, 1H), 3.29−3.32 (m, 1H), 3.81−3.87 (m, 1H), 4.23 (q, J = 7.1 Hz, 2H), 7.09 (d, J = 8.0 Hz, 2H), 7.36−7.42 (m, 3H), 7.51 (d, J = 9.0 Hz, 1H), 8.03 (d, J = 8.79, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3, 18.3, 21.5, 25.3, 28.4, 60.9, 62.8, 80.7, 119.3, 122.1, 122.9, 127.1, 127.6 (2C), 129.7 (2C), 131.6, 133.8, 144.5, 148.6, 165.7 ppm. HRMS: m/z calcd for $C_{21}H_{23}NO_5S$ [M + H^+] 402.1370; found 402.1406.

8-Phenyl-10-tosyl-2,3,4,4a,10,10a-hexahydro-1H-phenoxazine (Table 2, entry 13). White solid (mp 121 °C); IR (KBr) 3446, 3032, 2937, 2862, 1483, 1357, 1276, 1168, 1055, 812, 759, 665, 570 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.30−1.65 (m, 4H), 1.82−1.86 (m, 2H), 2.16−2.19 (m, 1H), 2,35 (s, 3H), 2.72−2.76 (m, 1H), 3.45−3.50 (m, 1H), 3.55−3.62 (m, 1H), 6.81 (d, J = 8.3 Hz, 1H), 7.14 (d, J = 8.2 Hz, 2H),7.30−7.36 (m, 4H), 7.47 (t, J = 7.7 Hz, 2H), 7.67 (d, J = 7.1 Hz, 2H), 8.13 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 24.0, 24.6, 31.9, 33.5, 65.3, 80.9, 117.4, 124.6, 124.7, 126.6, 126.8 (2C), 127.1, 127.5 (2C), 128.8 (2C), 129.4 (2C),133.6, 135.1, 140.2, 143.9, 152.1 ppm. HRMS: m/z, calcd for $C_{25}H_{25}NO_3S$ [M + Na^+] 442.1452; found 442.1453.

2-Methyl-11-tosyl-5a,6,7,8,9,10,10a,11-octahydrobenzo[*b*]cyclohepta[e][1,4]oxazine (Table 2, entry 14). White solid (mp 129 °C); IR (KBr) 3057, 2929, 2858, 1940, 1595, 1502, 1454, 1348, 1259, 1165, 1064, 1008, 958, 819, 713, 669, 567 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.41−1.55 (m, 6H), 1.57−1.67 (m, 3H), 2.05−2.06 (m, 1H), 2.35 (s, 6H), 3.45−3.52 (m, 1H), 3.99−4.05 (m, 1H), 6.60 (d, J = 8.1 Hz, 1H), 6.85−6.88 (m,1H), 7.10 (d, J = 10.7 Hz, 2H), 7.26 (d, J = 8.1 Hz, 2H), 7.47−7.49 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.9, 21.6, 23.7, 24.7, 25.0, 33.5, 34.0, 64.7, 83.7, 116.6, 127.2 (2C), 127.4, 127.5, 127.8, 129.2 (2C), 132.1, 134.6, 143.5, 151.3 ppm. HRMS: m/z calcd for $C_{21}H_{25}NO_3S$ [M + Na^+] 394.1454; found 394.1453.

(Table 2, entry 15). White solid (mp 155 °C); IR (KBr) 3041, 2902, 2872, 2355, 1921, 1597, 1485, 1357, 1284, 1242, 1168, 1084, 1020, 945, 923, 815, 750, 665, 576 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.37−1.40 (m, 2H), 1.5−1.7 (m, 4H), 2.28 (s, 3H), 2.45 (s, 1H), 2.71−2.73 (m, 1H), 3.13 (s, 1H), 3.52−3.54 (m, 1H), 6.73−6.76 (m, 1H), 6.84−6.88 (m, 2H), 7.13 (d, J = 7.8 Hz, 2H), 7.50 (d, J = 7.8 Hz, 2H), 8.19 (d, J = 7.98 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.7, 21.6, 31.4, 37.1, 38.6, 41.8, 69.7, 86.1, 119.1, 120.9, 121.7, 125.0, 126.4, 127.7 (2C), 129.7 (2C), 133.2,

144.3, 149.0 ppm. HRMS: m/z calcd for $C_{20}H_{21}NO_3S$ [M + Na^+] 378.1146; found 378.1140.

10-Tosyl-4b,10,10a,11-tetrahydrobenzo[*b*]indeno[2,1-*e*][1,4]oxazine (Table 2, entry 16). White solid (mp 160 °C); IR (KBr) 3030, 2920, 2856, 1483, 1359, 1242, 1170, 1087, 812, 756, 665 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.33 (s, 3H), 3.37−3.42 (m, 1H), 3.59−3.69 (m, 2H), 4.98 (d, J = 8.6 Hz, 1H), 6.98−7.09 (m, 3H), 7.16 (d, J = 8.3 Hz, 2H), 7.30−7.32 (m, 3H), 7.39−7.41 (m, 1H), 7.49 (d, J = 8.3 Hz, 2H), 8.18−8.21 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 35.7, 64.8, 81.5, 118.7, 122.0, 122.6, 123.6, 125.5, 125.9, 127.3, 127.6, 127.8 (2C), 128.8, 129.8 (2C), 133.9, 137.5, 139.0, 144.4, 148.6 ppm. HRMS: m/z calcd for $C_{22}H_{19}NO_3S$ [M + Na^+] 400.0984; found 400.0983.

2,3-Dihydro-2,6-diphenylbenzo[*b*][1,4]dioxine (Table 3, entry 2). White solid (mp 118 °C); IR (KBr) 3059, 2926,, 1587, 1518, 1485, 1313, 1267, 1234, 1126, 1057, 895, 819, 752, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.09 (dd, J_1 = 8.9 Hz, J_2 = 11.4 Hz, 1H), 4.39−4.43 (m, 1H), 5.17−5.21 (m, 1H), 7.04−7.09 (m, 1H), 7.14−7.18 (m, 1H), 7.25−7.27 (m, 1H), 7.28−7.32 (m, 1H), 7.40−7.46 (m, 7H), 7.56−7.59 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 69.6, 75.4, 116.2, 117.5, 117.9, 120.4, 126.7 (2C), 126.9 (3C), 128.7 (2C), 128.8 (2C), 135.1, 136.5, 140.7, 142.7, 144.1 ppm. HRMS: m/z calcd. for $C_{20}H_{16}O_2$ [M + H^+] 289.1226; found 289.1223.

2-[(4-Methoxyphenoxy)methyl]-2,3-dihydrobenzo[*b*][1,4]dioxine (Table 3, entry 4). Colorless liquid; IR (neat) 3043, 2997, 2931, 2833, 1593, 1508, 1494, 1267, 1230, 1107, 1043, 823, 750 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.81 (s, 3H), 4.11−4.16 (m, 1H), 4.21−4.27 (m, 2H), 4.41−4.46 (m, 1H), 4.56−4.60 (m, 1H), 6.87−6.97 (m, 8H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.7, 65.4, 67.1, 71.5, 114.7 (2C), 115.7 (2C), 117.3, 117.5, 121.6, 121.8, 143.0, 143.2, 152.5, 154.3 ppm. HRMS: m/z calcd for $C_{16}H_{16}O_4$ [M + Na^+] 295.0945; found 295.0946.

2-[(4-Methoxyphenoxy)methyl]-6-bromo-2,3-dihydrobenzo-[*b*][1,4]dioxine (Table 3, entry 6). White solid (mp 90 °C); IR (KBr) 3061, 2962, 2935, 2835, 1585, 1487, 1479, 1271, 1232, 1055, 821, 800, 740 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.78 (s, 3H), 4.05−4.10 (m, 1H), 4.16−4.21 (m, 2H), 4.36−4.40 (m, 1H), 4.50−4.52 (m, 1H), 6.76−6.82 (m, 1H), 6.83−6.88 (m, 4H), 6.94−6.98 (m, 1H), 7.07−7.08 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.7, 65.3, 67.0, 71.5, 113.2, 114.8 (2C), 115.7 (2C), 118.6, 120.3, 124.4, 142.5, 143.8, 152.4, 154.5 ppm. HRMS: m/z calcd for $C_{16}H_{15}BrO_4$ [M + Na^+] = 373.0051; found 373.0051.

2-Hexyl-2,3-dihydrobenzo[*b*][1,4]dioxine (Table 3, entry 7). Colorless liquid; IR (neat) 3043, 2955, 2928, 2858, 1593, 1494, 1465, 1267, 1255, 1045, 906, 746 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.89−0.93 (m, 3H), 1.27−1.42 (m, 6H), 1.55−1.71 (m, 4H), 3.86 (dd, J_1 = 7.7 Hz, J_2 = 11.1 Hz, 1H), 4.07−4.15 (m, 1H), 4.21−4.23 (m, 1H), 6.82−6.88 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 22.7, 25.0, 29.3, 31.1, 31.8, 68.2, 73.2, 117.0, 117.4, 121.2, 121.5, 143.6, 143.4 ppm. HRMS: m/z calcd for $C_{14}H_{20}O_2$ [M + H^+] 221.1535; found 221.1536.

8-(4-Chlorophenylthio)-1,2,3,4,4a,10,10a-heptahydro-10-tosyl-10*H*-phenoxazine (Scheme 2, 4a). Yellow gummy liquid; IR (neat) 3064, 2941, 2886, 1597, 1475, 1359, 1267, 1168, 1089, 1047, 813, 754, 677 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.19−1.27 (m, 2H), 1.28−1.49 (m, 4H), 1.78−1.82 (m, 2H), 2.36 (s, 3H), 3.42−3.58 (m, 2H), 6.70 (d, J = 8.4 Hz, 1H), 7.09−7.11 (m, 3H), 7.15−7.29 (m, 6H), 7.88 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 23.9, 24.6, 31.8, 33.3, 65.0, 80.8, 118.1, 126.7, 127.5 (2C), 128.7, 129.2 (2C), 129.5 (2C), 130.4, 130.8, 130.9 (2C), 132.5, 133.8, 136.0, 144.1, 152.4 ppm. HRMS: m/z calcd for $C_{25}H_{24}ClNO_3S_2$ [M + Na^+] 508.0785; found 508.0784.

6-(Benzo[d]thiazol-2-ylthio)-3,4-dihydro-2-phenyl-4-tosyl-2*H*-benzo[*b*][1,4]oxazine (Scheme 2, 4b). Yellow solid (mp 152 °C); IR (KBr) 3103, 3034, 2922, 1595, 1479, 1454, 1346, 1244, 1161, 1003, 920, 812, 748, 677 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.41 (s, 3H), 3.27−3.29 (m, 1H), 4.34−4.45 (m, 2H), 7.05 (d, J = 8.5 Hz, 1H), 7.25 (d, J = 7 Hz, 2H), 7.29 (d, J = 8.5 Hz, 3H), 7.38−7.47 (m, 5H), 7.64−7.69 (m, 3H), 7.89 (d, J = 8.0 Hz, 1H), 8.34 (s, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7, 49.9, 73.9, 119.3, 120.8, 121.0, 121.8, 124.3, 124.7, 125.9 (2C), 126.2, 127.5 (2C), 128.9 (2C), 129.1, 130.2 (2C), 131.8, 133.5, 135.1, 135.4, 136.4, 144.9, 149.3, 153.9, 170.8 ppm. HRMS: m/z calcd for $C_{28}H_{22}N_2O_3S_3$ [M + H^+] 531.0864; found 531.0865.

1,2,3,4,4a,10,10a-Heptahydro-8-morpholino-10-tosyl-10*H*-phenoxazine (Scheme 2, 4c). Brown gummy liquid; IR (neat) 2941, 2864, 1494, 1357, 1273, 1168, 1051, 813, 754, 665 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.37−1.39 (m, 2H), 1.39−1.43 (m, 3H), 1.51−1.53 (m, 1H), 1.77−1.78 (m, 3H), 2.07−2.10 (m, 1H), 2.33 (s, 3H), 3.07−3.15 (m, 3H), 3.33−3.36 (m, 1H), 3.44−3.49 (m, 1H), 3.85−3.87 (m, 3H), 6.62 (s, 2H), 7.11 (d, J = 8 Hz, 3H), 7.25 (d, J = 8.5 Hz, 1H), 7.93 (s, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7, 24.1, 24.7, 32.0, 33.7, 50.6 (2C), 65.5, 67.0 (2C), 81.2, 114.2, 114.6, 117.2, 127.6 (2C), 128.3, 129.4(2C), 133.6, 143.9, 146.7, 146.8 ppm. HRMS: m/z calcd for $C_{23}H_{28}N_2O_4S$ [M + H^+] 429.1842; found 429.1875.

7-(Pyrrolidin-1-yl)-9-tosyl-1,2,3,3a,9,9a-hexahydrobenzo[e]cyclopenta[*b*][1,4]oxazine (Scheme 2, 4d). Brown gummy liquid; IR (neat) 2958, 2924, 2883, 1739, 1492, 1359, 1168, 1087, 813, 754, 665 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.04−1.05 (m, 1H), 1.41−1.43 (m, 2H), 1.60−1.68 (m, 3H), 1.71−1.82 (m, 4H), 2.12 (s, 3H), 2.32−2.35 (m, 1H), 3.04−3.15 (m, 4H), 3.61−3.65 (m, 1H); 6.07 (d, J = 7.4 Hz, 1H), 6.45 (d, J = 8.8 Hz, 1H), 6.96 (d, J = 8.3 Hz, 2H), 7.13−7.22 (m, 1H), 7.28 (d, J = 8.3 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.3, 21.5, 25.3, 25.4, 28.2, 28.5, 48.4 (2C), 63.2, 80.3, 106.5, 109.2, 118.0, 127.8 (2C), 129.5 (2C), 131.2, 133.6, 133.8, 143.2, 143.9 ppm. HRMS: m/z calcd. for $C_{22}H_{26}N_2O_3S$ [M + H^+] 399.1736; found 399.1719.

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Supporting Information Available: Copies of ^1H and ^{13}C NMR spectra of all products listed in Tables 2 and 3 and Scheme 3 and crystallographic data of compounds **2a**, **2h**, **2o**, and **2p** in Table 2 and **3f** in Table 3. This material is available free of charge *via* the Internet at http://pubs.acs.org.