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Synthesis of Oxazolidines and Dihydroxazines via Cyclization of α-Aminated Ketones

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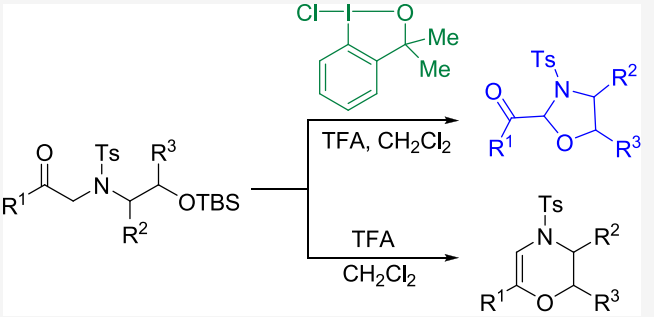
ABSTRACT: A new approach to oxazolidines and dihydroxazines was developed by regioselective cyclization of α-aminated ketones under transition metal-free conditions. Oxazolidine derivatives were generated in the presence of chloro benziodoxole and TFA, while dihydroxazines were formed without a hypervalent iodine reagent. The reaction was performed under room temperature and gave the products in good to excellent yields.



INTRODUCTION

Oxazolidine and dihydroxazine derivatives are widely distributed in many valuable drug candidates and other biologically active compounds.[1,2] They also have been used as versatile building blocks in synthetic chemistry. Consequently, a number of methods for the construction of oxazolidine and dihydroxazine have been developed in the past several decades. Condensation of 1,2-aminol alcohols with aldehydes, ketones, or alkenes is a convenient method to form an oxazolidine ring.[3] Oxazolidines could also be prepared by [3 + 2] cycloaddition of aziridines with aldehydes or epoxides with imines.[4] 1,1-Difunctionalization of alkenes is another efficient method to synthesize oxazolidines.[5] Dihydroxazine could be prepared via the reaction between protected amino acids and carbonyl compounds.[6] The synthesis also could be achieved through a hydroamination of alkynes[7] or a reaction between triazoles and halohydrins.[8]

Recent decades have witnessed prosperous development of hypervalent iodine reagents and their applications in modern organic synthesis.[9] Hypervalent iodine reagents possess very attractive characteristics, including the ready availability, mild reaction conditions, and environmental benignity.[10] Novel hypervalent iodine reagents have not only been used in oxidative reactions but also play an essential role in many other synthetic transformations. For example, Rehbein et al. disclosed the regiodivergent synthesis of indoles and tryptophans mediated by hypervalent iodine reagent **1** through *C,H*-amination (Scheme 1a).[11] The fluorocyclization of allylaminoethanol could be realized by a hypervalent fluoroiodine reagent (Scheme 1b).[12] The chiral hypervalent iodine reagents have also been developed for the enantioselective dearomatization of phenols (Scheme 1c).[13]

In the past several years, our group have been engaged in the hypervalent iodine reagent-mediated transformation of alkenes to construct functionalized heterocycles.[12,14] Herein, we reported the synthesis of oxazolidines from α-aminated ketones in the presence of TFA and chloro benziodoxole **2**. Dihydroxazines were obtained without the addition of hypervalent iodine reagent (Scheme 1d).

RESULTS AND DISCUSSION

Initially, we performed the reaction by using *N*-(2-((*tert*-butyldimethylsilyl)oxy)ethyl)-4-methyl-*N*-(2-oxo-2-phenylethyl) benzenesulfonamide **4a** as substrate in the presence of TFA and $PhI(OAc)_2$ in dichloromethane at room temperature for 4 h. The product oxazolidine **5a** was obtained in 32% yield (Table 1, entry 1). We then examined the hypervalent iodine reagents for this transformation (entries 2−5). The yield of product could be improved to 79% when bis(trifluoroacetic acid)iodobenzene (PIFA) was employed. The reaction proceeded smoothly when benziodoxole **1**−**3** were used; especially the use of benziodoxole **2** afforded the product in quantitative yield. We also performed the reaction in other solvents; no product was obtained with acetone, DMF, MeCN, THF, or Et_2O, and moderated yield was obtained in toluene (entries 6−12). The reaction in chloroform gave the same result as in dichloromethane (entry 8). When hypervalent

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Scheme 1. Applications of Hypervalent Iodine Reagents

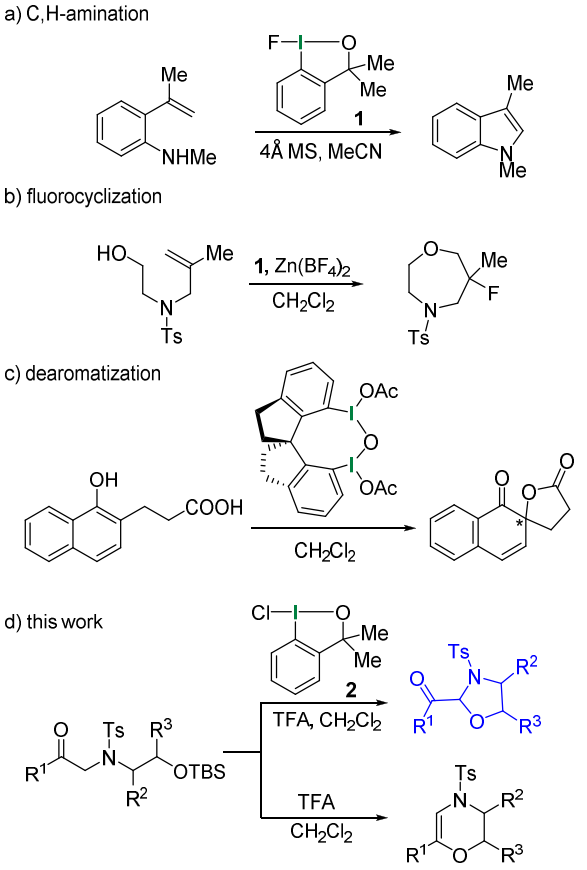
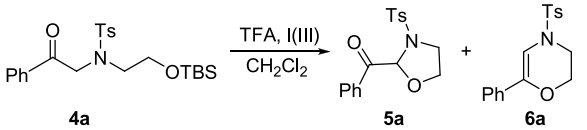


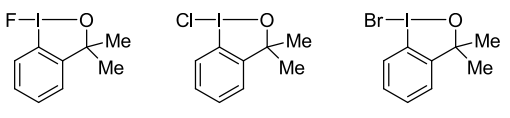
Table 1. Optimization of the Reaction Conditions[a,b]



4a 5a 6a

entry	I(III) reagent	solvent	product	yield (%)
1	PIDA	CH_2Cl_2	**5a**	32
2	PIFA	CH_2Cl_2	**5a**	79
3	**1**	CH_2Cl_2	**5a**	60
4	**2**	CH_2Cl_2	**5a**	99
5	**3**	CH_2Cl_2	**5a**	76
6	**2**	acetone	**5a**	n.d.
7	**2**	DMF	**5a**	n.d.
8	**2**	$CHCl_3$	**5a**	99
9	**2**	CH_3CN	**5a**	n.d.
10	**2**	THF	**5a**	n.d.
11	**2**	Et_2O	**5a**	n.d.
12	**2**	toluene	**5a**	49
13		CH_2Cl_2	**6a**	99

[a]The reactions were carried out using **4a** (0.2 mmol, 1 equiv), TFA (2 equiv), and hypervalent iodine (1.2 equiv) in solvent (0.05 M). n.d. = not determined. [b]

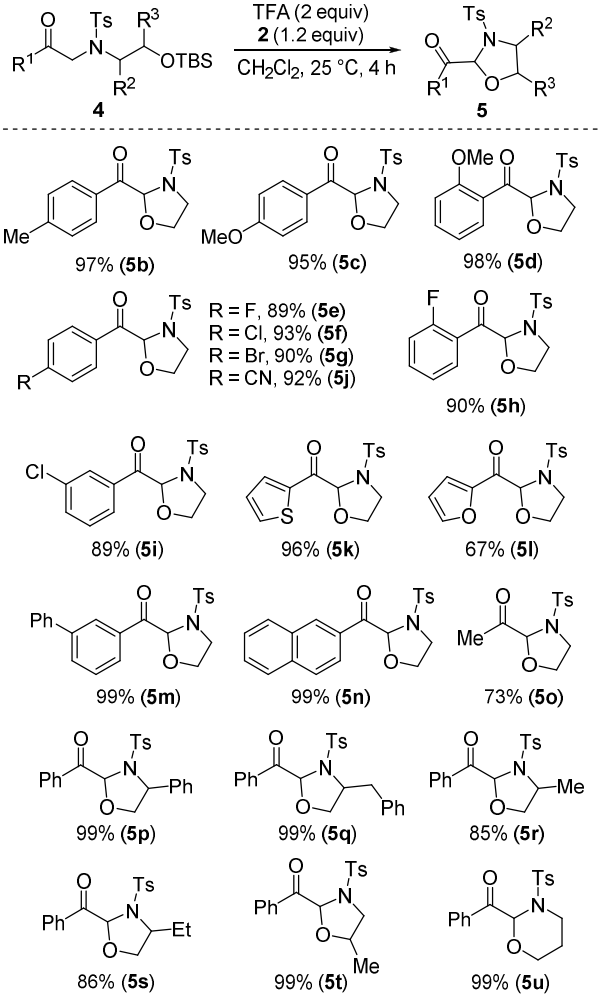


1 2 3

iodine reagent was omitted, the reaction provided dihydroxazine product **6a** instead of **5a** (entry 13).

With the optimized reaction conditions in hand, we then examined the scope of α-aminated ketones with different substituents (Scheme 2). First, we explored the substrates in

Scheme 2. Formation of Oxazolidines 5[a]



[a]The reactions were carried out using **4** (0.3 mmol, 1 equiv), TFA (2 equiv), and chloroiodane **2** (1.2 equiv) in CH_2Cl_2 (0.05 M).

which R^1 is a substituted phenyl group, and R^2 and R^3 are hydrogen-substituted compounds. The substrates with electron-donating groups at the 4- and 2-positions of the benzene ring, such as methyl and methoxy, underwent the reaction smoothly to generate the products **5b**–**5d** in great yields of 95–98%. Halogen substituents such as fluoro, chloro, and bromo could be tolerated under the reaction conditions. The substrates with substituents at the 2-, 3-, or 4-position of benzene ring participated in this reaction and gave the desired products **5e**–**5i** in 89–93% yields. In addition, the substrate with the *p*-cyanophenyl group provided the oxazolidine product in 92% yield (**5j**). Substrates with 2-thienyl and 2-furyl groups underwent the reaction and furnished the products **5k** and **5l** in 96 and 67% yields, respectively. The reactivity was the same as model reaction when R^1 is a biphenyl or 2-naphthyl substituent (**5m** and **5n**). When R^1 was a methyl group, the reactivity of the substrate significantly reduced, affording the product **5o** in 73% yield. Next, we investigated the substrates in which R^1 was a phenyl group. The substrates exhibited excellent reactivity when R^2 was a

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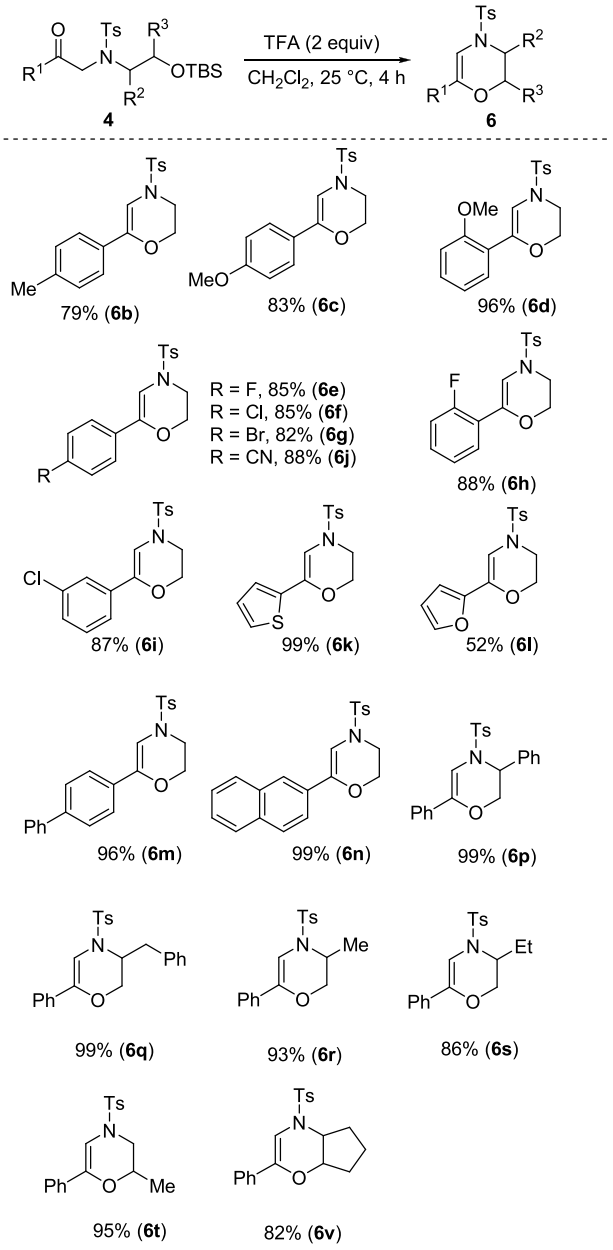
phenyl or benzyl group (**5p** and **5q**). However, product formation was slightly inhibited when R^2 was an alkyl group (**5r** and **5s**). However, when R^3 was a methyl group, the desired product could be obtained in almost quantitative yield (**5t**). We tried to increase the carbon number of amino alcohol and found that a six-membered ring product could be obtained in 99% yield (**5u**). No seven-membered ring product was observed by further increasing the carbon number of the substrate.

When the substrate **4a** subjected to the reaction conditions without hypervalent iodine reagent, no oxazolidine product was observed, and dihydroxazine **6a** was obtained in quantitative yield. We further examined the substrate scope of substituted α-aminated ketone **4a** under the reaction conditions to form dihydroxazine derivatives (Scheme 3).

Scheme 3. Formation of Dihydroxazines 6[a]

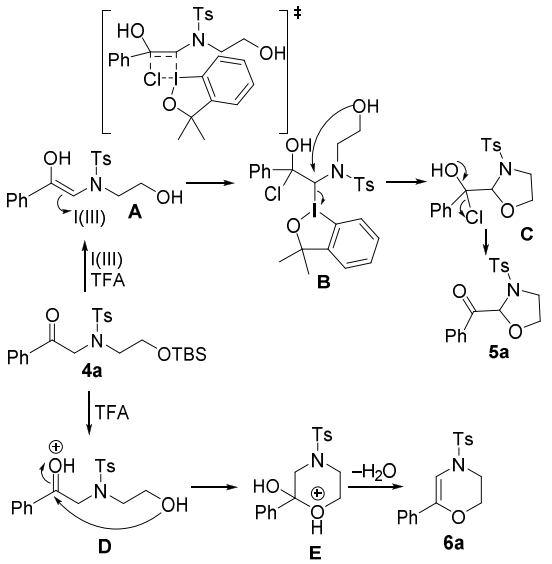


[a]The reactions were carried out using **4** (0.3 mmol, 1 equiv) and TFA (2 equiv) in CH_2Cl_2 (0.05 M).

The electron-donating groups such as methyl and methoxyl tolerated well under the reaction conditions and afforded the desired products in good yields (**6b** and **6c**). With the substituents at the *ortho*- or *meta*-position, the reaction proceeded well and gave the dihydroxazine products in good to excellent yields (**6d**, **6h**, and **6i**). The substrates with a halogen atom underwent the reaction smoothly to provide dihydroxazines in ca. 80% yields (**6e**−**6g**). When the functional group cyano was introduced to the substrate, the reaction proceeded and gave the corresponding product in 88% yield (**6j**). The reactivity of the substrate bearing a biphenyl group was similar to model reaction (**6m**). The substrate with a 2-naphthyl or 2-thienyl substituent underwent the reaction efficiently, and the products were obtained in excellent yields (**6n** and **6k**). The reaction became sluggish when a furan group was introduced to the substrate (**6l**). The R^2 group of the substrate, which was phenyl or benzyl, exhibited good reactivity and afforded the corresponding products in quantitative yields (**6p** and **6q**). When R^2 or R^3 was the alkyl substituent, the reaction occurred and provided dihydroxazine derivatives in 82−95% yields (**6r**−**6v**). The extension of the carbon chain inhibited the formation of the dihydroxazine product.

Based on the results and our previous work[14] of hypervalent iodine reagents, we proposed the reaction pathway for the synthesis of oxazolidines and dihydroxazines (Scheme 4). The

Scheme 4. Proposed Reaction Pathways



substrate **4a** undergoes deprotection to generate intermediate **A** in the presence of TFA. The C−C double bond of the enol attacks chloro benziodoxole **2** to form intermediate **B** through the four-membered-ring transition state. The cyclization occurs with the elimination of aryl iodine to give intermediate **C**. Finally, formation of ketone **5a** occurs by leaving the chloride ion. If the reaction takes place without a hypervalent iodine reagent, after deprotection of the substrate with TFA, a nucleophilic attack of the hydroxyl group to the carbonyl group occurs to form ketal **E**. Then, dehydration of intermediate **E** happens to generate product **6a**.

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CONCLUSIONS

In summary, we have developed a new method for the synthesis of oxazolidines and dihydroxazines from α-aminated ketones under mild reaction conditions. The formation of oxazolidine or dihydroxazine products is determined by the addition of a hypervalent iodine reagent or not. A variety of functional groups could be tolerated in the reaction conditions. This transformation presents a practical procedure to deliver multi-substituted oxazolidine and dihydroxazine products.

EXPERIMENTAL SECTION

General Methods. Unless otherwise noted, all commercially available reagents and solvents were used without further purification. Column chromatography was generally performed on silica gel (200−300 mesh), and reactions were monitored by thin-layer chromatography (TLC) using silica gel GF254 plates with UV light to visualize the course of reaction. Melting points were determined on a ShenGuang WRS-2 melting point apparatus. The ^{1}H NMR and ^{13}C{^{1}H} NMR spectra were recorded in $CDCl_3$ (internal standard: 7.26 ppm, ^{1}H; 77.0 ppm, ^{13}C) using a Bruker AV-300 (300 MHz) or AV-400 (400 MHz) NMR spectrometer. The chemical shifts (δ) are reported in ppm and coupling constants (J) in Hz. High-resolution mass data (HRMS) were obtained using the ESI technique. The hypervalent iodine reagent **2**[15] and substrates **4**[16] were prepared according to literature procedures with some modification.

Procedure for the Synthesis of 4a. *N*-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-4-methylbenzenesulfonamide (989 mg, 3 mmol), 2-bromo-1-phenylethan-1-one (594 mg, 3 mmol), K_2CO_3 (828 mg, 6 mmol), and CuI (57 mg, 0.3 mmol) were added to 15 mL of DMF in order. The mixture was stirred at room temperature for 16 h. After completion of the reaction, the resulting mixture was diluted with 30 mL 10% NH_4Cl solution and extracted with ethyl acetate. The organic layer was concentrated and purified by column chromatography to give the corresponding product. Other derivatives were obtained by the same procedure.

General Procedure for the Synthesis of Oxazolidine 5a. Chloroiodine reagent **2** (71 mg, 0.24 mmol, 1.2 equiv) and **4a** (89 mg, 0.2 mmol, 1.0 equiv) were dissolved in DCM (4 mL) in an oven-dried Schlenk tube, and then TFA (31 μL, 0.4 mmol, 2.0 equiv) was added. The reaction mixture was stirred at room temperature for 4 h. After completion of the reaction, the resulting mixture was concentrated and purified by column chromatography to give the corresponding product.

General Procedure for the Synthesis of Dihydroxazine 6a. Compound **4a** (89 mg, 0.2 mmol, 1.0 equiv) was dissolved in DCM (4 mL) in an oven-dried Schlenk tube, and then TFA (31 μL, 0.4 mmol, 2.0 equiv) was added. The reaction mixture was stirred at room temperature for 4 h. After completion of the reaction, the resulting mixture was concentrated and purified by column chromatography to give the corresponding product.

General Procedure for the Synthesis of 5a in Gram Scale. Chloroiodine reagent **2** (1.07 g, 3.6 mmol, 1.2 equiv) and **4a** (1.32 g, 3 mmol, 1.0 equiv) were dissolved in DCM (60 mL) in an oven-dried round-bottom flask, and then TFA (0.5 mL, 6 mmol, 2.0 equiv) was added. The reaction mixture was stirred at room temperature for 8 h. After completion of the reaction, the resulting mixture was concentrated and purified by column chromatography (petroleum ether/ethyl acetate = 8:1) to give product **5a** (0.89 g, 90%).

General Procedure for the Synthesis of 6a in Gram Scale. Compound **4a** (1.32 g, 3 mmol, 1.0 equiv) was dissolved in DCM (60 mL) in an oven-dried round-bottom flask, and then TFA (0.5 mL, 6 mmol, 2.0 equiv) was added. The reaction mixture was stirred at room temperature for 4 h. After completion of the reaction, the resulting mixture was concentrated and purified by column chromatography (petroleum ether/ethyl acetate = 15:1) to give product **6a** (0.86 g, 91%).

*Phenyl(3-tosyloxazolidin-2-yl)methanone (**5a**).* Yield: 99% (66 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 8:1) and obtained as a white solid. m.p.:105−107 °C. ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.18 (dt, J = 7.2, 1.4 Hz, 2H), 7.86−7.76 (m, 2H), 7.68−7.56 (m, 1H), 7.56−7.44 (m, 2H), 7.36 (s, 2H), 6.61 (s, 1H), 4.16−3.99 (m, 1H), 3.78−3.66 (m, 1H), 3.50−3.34 (m, 2H), 2.45 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, chloroform-*d*) δ 192.3, 144.8, 134.6, 134.1, 133.7, 130.1, 129.4, 128.9, 128.1, 87.9, 66.3, 45.8, 21.7. HRMS (ESI) m/z: [M + Na]$^+$ calcd for $C_{17}H_{17}NO_4SNa$, 354.0771. Found, 354.0768.

*p-Tolyl(3-tosyloxazolidin-2-yl)methanone (**5b**).* Yield: 97% (67 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 8:1) and obtained as a white solid. m.p.:104−106 °C. ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.15−8.05 (m, 2H), 7.89−7.72 (m, 2H), 7.41−7.29 (m, 4H), 6.61 (s, 1H), 4.16−4.01 (m, 1H), 3.83−3.65 (m, 1H), 3.53−3.36 (m, 2H), 2.47 (s, 3H), 2.45 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, chloroform-*d*) δ 191.9, 145.1, 144.7, 134.6, 131.1, 130.0, 129.5, 129.5, 128.0, 87.8, 66.2, 45.7, 21.9, 21.7. HRMS (ESI) m/z: [M + Na]$^+$ calcd for $C_{18}H_{19}NO_4SNa$, 368.0927. Found, 368.0923.

*(4-Methoxyphenyl)(3-tosyloxazolidin-2-yl)methanone (**5c**).* Yield: 95% (69 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 8:1) and obtained as a white solid. m.p.:153−154 °C. ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.28−8.16 (m, 2H), 7.92−7.80 (m, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.07−6.97 (m, 2H), 6.63 (s, 1H), 4.22−4.07 (m, 1H), 3.92 (s, 3H), 3.84−3.70 (m, 1H), 3.53−3.42 (m, 2H), 2.49 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, chloroform-*d*) δ 190.8, 164.3, 144.8, 134.6, 131.9, 130.0, 128.1, 126.6, 114.1, 87.8, 66.2, 55.6, 45.7, 21.7. HRMS (ESI) m/z: [M + Na]$^+$ calcd for $C_{18}H_{19}NO_5SNa$, 384.0876. Found, 384.0872.

*(2-Methoxyphenyl)(3-tosyloxazolidin-2-yl)methanone (**5d**).* Yield: 98% (71 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 8:1) and obtained as a colorless oil. ^{1}H NMR (300 MHz, chloroform-*d*) δ 7.45−7.38 (m, 2H), 7.33 (dd, J = 7.6, 1.8 Hz, 1H), 7.24−7.16 (m, 1H), 6.99 (d, J = 8.0 Hz, 2H), 6.76−6.60 (m, 2H), 6.39 (s, 1H), 3.73−3.66 (m, 1H), 3.64 (s, 3H), 3.39 (ddd, J = 10.5, 7.4, 4.9 Hz, 1H), 3.34−3.24 (m, 1H), 3.14 (ddd, J = 10.5, 7.8, 6.1 Hz, 1H), 2.12 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, chloroform-*d*) δ 195.5, 158.5, 144.0, 134.6, 134.3, 130.8, 129.5, 127.5, 124.7, 120.6, 111.4, 89.5, 65.9, 55.5, 45.6, 21.3. HRMS (ESI) m/z: [M + Na]$^+$ calcd for $C_{18}H_{19}NO_5SNa$, 384.0876. Found, 384.0874.

*(4-Fluorophenyl)(3-tosyloxazolidin-2-yl)methanone (**5e**).* Yield: 89% (62 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 8:1) and obtained as a white solid. m.p.:138−140 °C. ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.24 (dd, J = 8.7, 5.5 Hz, 2H), 7.82 (d, J = 8.0 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 7.18 (t, J = 8.6 Hz, 2H), 6.57 (s, 1H), 4.16−3.99 (m, 1H), 3.83−3.68 (m, 1H), 3.52−3.33 (m, 2H), 2.46 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, chloroform-*d*) δ 190.8, 166.2 (d, $^1J_{C\text{-}F}$ = 255.0 Hz), 144.9, 134.3, 132.2 (d, $^3J_{C\text{-}F}$ = 9.8 Hz), 130.0, 130.0, 128.0, 116.0 (d, $^2J_{C\text{-}F}$ = 21.8 Hz), 87.9, 66.3, 45.7, 21.7. HRMS (ESI) m/z: [M + Na]$^+$ calcd for $C_{17}H_{16}FNO_4SNa$, 372.0676. Found, 372.0671.

*(4-Chlorophenyl)(3-tosyloxazolidin-2-yl)methanone (**5f**).* Yield: 93% (68 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 8:1) and obtained as a white solid. m.p.:145−147 °C. ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.24−8.14 (m, 2H), 7.92−7.80 (m, 2H), 7.58−7.48 (m, 2H), 7.40 (d, J = 8.0 Hz, 2H), 6.60 (s, 1H), 4.25−4.06 (m, 1H), 3.88−3.70 (m, 1H), 3.54−3.43 (m, 2H), 2.50 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, chloroform-*d*) δ 191.3, 145.0, 140.7, 134.3, 131.9, 130.9, 130.1, 129.2, 128.1, 88.0, 66.4, 45.7, 21.8. HRMS (ESI) m/z: [M + Na]$^+$ calcd for $C_{17}H_{16}ClNO_4SNa$, 388.0381. Found, 388.0372.

*(4-Bromophenyl)(3-tosyloxazolidin-2-yl)methanone (**5g**).* Yield: 90% (74 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 8:1) and obtained as a white solid. m.p.:147−149 °C. ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.16−8.05 (m, 2H), 7.91−7.82 (m, 2H), 7.75−7.64 (m, 2H), 7.39 (d, J = 8.0 Hz, 2H), 6.57 (s, 1H), 4.23−4.01 (m, 1H), 3.83−3.69 (m, 1H), 3.54−3.38 (m, 2H), 2.50 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, chloroform-*d*) δ 191.5, 145.0, 134.2, 132.2, 130.9, 130.1, 129.8, 129.6, 128.0, 87.9, 66.3, 45.7, 21.8. HRMS

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(ESI) m/z: $[M + Na]^+$ calcd for $C_{17}H_{16}BrNO_4SNa$, 431.9876. Found, 431.9871.

(2-Fluorophenyl)(3-tosyloxazolidin-2-yl)methanone (**5h**). Yield: 90% (63 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 8:1) and obtained as a white solid. m.p.:74−75 °C. ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.04 (t, J = 7.3 Hz, 1H), 7.95 (d, J = 7.7 Hz, 2H), 7.79−7.67 (m, 1H), 7.50 (d, J = 7.7 Hz, 2H), 7.33 (dd, J = 11.0, 8.2 Hz, 1H), 6.55 (d, J = 7.8 Hz, 1H), 4.14 (dp, J = 9.0, 3.6, 2.7 Hz, 1H), 3.91−3.74 (m, 2H), 3.70−3.59 (m, 1H), 2.59 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-*d*) δ 191.9 (d, $^3J_{C\text{-}F}$ = 4.6 Hz), 161.9 (d, $^1J_{C\text{-}F}$ = 254.4 Hz), 144.7, 135.7 (d, $^3J_{C\text{-}F}$ = 9.0 Hz), 134.8, 131.5 (d, $^4J_{C\text{-}F}$ = 2.6 Hz), 130.2, 128.0, 124.9 (d, $^3J_{C\text{-}F}$ = 3.5 Hz), 123.1 (d, $^2J_{C\text{-}F}$ = 13.2 Hz), 116.9 (d, $^2J_{C\text{-}F}$ = 23.0 Hz), 89.9 (d, $^4J_{C\text{-}F}$ = 7.5 Hz), 66.6, 46.2, 21.8. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{17}H_{16}FNO_4SNa$, 372.0676. Found, 372.0673.

(3-Chlorophenyl)(3-tosyloxazolidin-2-yl)methanone (**5i**). Yield: 89% (65 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 8:1) and obtained as a white solid. m.p.:106−108 °C. ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.09 (dt, J = 6.3, 1.6 Hz, 2H), 7.86−7.74 (m, 2H), 7.61−7.55 (m, 1H), 7.50−7.41 (m, 1H), 7.35 (d, J = 8.0 Hz, 2H), 6.50 (s, 1H), 4.06 (td, J = 7.2, 6.7, 4.3 Hz, 1H), 3.73 (ddd, J = 11.4, 6.5, 4.3 Hz, 1H), 3.54−3.33 (m, 2H), 2.45 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-*d*) δ 191.2, 144.9, 135.1, 134.4, 134.0, 130.2, 130.1, 129.3, 128.0, 127.6, 88.0, 66.4, 45.7, 21.7. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{17}H_{16}ClNO_4SNa$, 388.0381. Found, 388.0375.

4-(3-Tosyloxazolidine-2-carbonyl)benzonitrile (**5j**). Yield: 92% (66 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 8:1) and obtained as a white solid. m.p.:129−130 °C. ^{1}H NMR (400 MHz, chloroform-*d*) δ 8.35−8.25 (m, 2H), 7.89−7.77 (m, 4H), 7.38 (d, J = 8.0 Hz, 2H), 6.52 (s, 1H), 4.16−4.03 (m, 1H), 3.75 (ddd, J = 11.5, 6.7, 4.2 Hz, 1H), 3.54−3.37 (m, 2H), 2.48 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-*d*) δ 191.3, 145.1, 136.6, 134.2, 132.6, 130.1, 129.8, 128.0, 117.1, 88.1, 66.5, 45.7, 21.7. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{18}H_{16}N_2O_4SNa$, 379.0723. Found, 379.0717.

Thiophen-2-yl(3-tosyloxazolidin-2-yl)methanone (**5k**). Yield: 96% (65 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 8:1) and obtained as a white solid. m.p.:112−113 °C. ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.26 (dd, J = 3.9, 1.1 Hz, 1H), 7.89−7.81 (m, 2H), 7.79 (dd, J = 5.0, 1.1 Hz, 1H), 7.39 (d, J = 8.0 Hz, 2H), 7.24 (dd, J = 5.0, 3.8 Hz, 1H), 6.45 (s, 1H), 4.18−4.11 (m, 1H), 3.83−3.72 (m, 1H), 3.56−3.41 (m, 2H), 2.49 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-*d*) δ 185.8, 144.9, 140.0, 135.6, 135.1, 134.4, 130.1, 128.8, 128.0, 88.5, 66.4, 45.7, 21.7. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{15}H_{15}NO_4S_2Na$, 360.0335. Found, 360.0329.

Furan-2-yl(3-tosyloxazolidin-2-yl)methanone (**5l**). Yield: 67% (43 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 8:1) and obtained as a pale yellow solid. m.p.:116−118 °C. ^{1}H NMR (300 MHz, chloroform-*d*) δ 7.84−7.75 (m, 2H), 7.66 (dd, J = 14.0, 2.7 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 6.59 (dd, J = 3.7, 1.7 Hz, 1H), 6.31 (s, 1H), 4.18−4.03 (m, 1H), 3.80−3.61 (m, 1H), 3.56−3.34 (m, 2H), 2.43 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-*d*) δ 181.2, 149.4, 148.1, 144.8, 134.2, 130.0, 127.9, 121.4, 112.7, 87.5, 66.4, 45.7, 21.7. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{15}H_{15}NO_5SNa$, 344.0563. Found, 344.0560.

[1,1′-Biphenyl]-4-yl(3-tosyloxazolidin-2-yl)methanone (**5m**). Yield: 99% (81 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 8:1) and obtained as a white solid. m.p.:167−168 °C. ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.29 (d, J = 8.0 Hz, 2H), 7.86 (d, J = 7.9 Hz, 2H), 7.76 (d, J = 8.0 Hz, 2H), 7.67 (d, J = 6.7 Hz, 2H), 7.49 (dt, J = 14.3, 7.2 Hz, 3H), 7.38 (d, J = 7.9 Hz, 2H), 6.68 (s, 1H), 4.13 (q, J = 5.2, 4.2 Hz, 1H), 3.89−3.70 (m, 1H), 3.46 (dp, J = 7.7, 5.5, 3.5 Hz, 2H), 2.48 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-*d*) δ 191.9, 146.7, 144.9, 139.8, 134.6, 132.3, 130.1, 130.06, 129.1, 128.5, 128.1, 127.5, 127.4, 88.0, 66.4, 45.8, 21.8. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{23}H_{21}NO_4SNa$, 430.1084. Found, 430.1080.

Naphthalen-2-yl(3-tosyloxazolidin-2-yl)methanone (**5n**). Yield: 99% (76 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 8:1) and obtained as a white solid. m.p.:143−145 °C. ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.84 (d, J = 1.8 Hz, 1H), 8.12 (dd, J = 8.6, 1.8 Hz, 1H), 8.06−8.00 (m, 1H), 7.94−7.82 (m, 4H), 7.60 (dddd, J = 18.8, 8.1, 6.9, 1.4 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 6.77 (s, 1H), 4.18−4.06 (m, 1H), 3.83−3.70 (m, 1H), 3.55−3.42 (m, 2H), 2.44 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-*d*) δ 192.3, 144.9, 135.9, 134.5, 132.5, 132.0, 130.8, 130.1, 129.2, 128.7, 128.1, 127.9, 127.0, 124.3, 88.1, 66.4, 45.8, 21.8. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{21}H_{19}NO_4SNa$, 404.0927. Found, 404.0915.

1-(3-Tosyloxazolidin-2-yl)ethan-1-one (**5o**). Yield: 73% (39 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 8:1) and obtained as a colorless oil. ^{1}H NMR (300 MHz, chloroform-*d*) δ 7.94−7.76 (m, 2H), 7.41 (d, J = 8.0 Hz, 2H), 5.46 (s, 1H), 4.04 (td, J = 7.0, 4.7 Hz, 1H), 3.70−3.38 (m, 3H), 2.50 (s, 3H), 2.39 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-*d*) δ 202.4, 145.0, 133.6, 130.3, 128.0, 90.5, 77.4, 66.7, 46.1, 25.3, 21.8. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{12}H_{15}NO_4SNa$, 292.0614. Found, 292.0611.

Phenyl(4-phenyl-3-tosyloxazolidin-2-yl)methanone (**5p**). Yield: 99% (81 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 8:1) and obtained as a white solid. m.p.:147−148 °C. ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.18 (dt, J = 7.2, 1.4 Hz, 2H), 7.75−7.65 (m, 1H), 7.65−7.55 (m, 2H), 7.32 (d, J = 1.6 Hz, 2H), 7.26−7.18 (m, 5H), 7.06 (d, J = 8.0 Hz, 2H), 6.63 (s, 1H), 5.16 (dd, J = 7.2, 2.2 Hz, 1H), 4.54 (dd, J = 8.7, 7.1 Hz, 1H), 4.12 (dd, J = 8.7, 2.2 Hz, 1H), 2.39 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-*d*) δ 192.1, 142.7, 138.4, 137.0, 133.9. 133.5, 128.7, 128.6, 128.5, 128.1, 127.6, 127.1, 126.8, 88.2, 75.6, 61.0, 21.1. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{23}H_{21}NO_4SNa$, 430.1083. Found, 430.1074.

(4-Benzyl-3-tosyloxazolidin-2-yl)(phenyl)methanone (**5q**). Yield: 99% (84 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 8:1) and obtained as a colorless oil. ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.05 (dt, J = 7.1, 1.4 Hz, 2H), 7.89−7.82 (m, 2H), 7.71−7.60 (m, 1H), 7.53 (dd, J = 8.3, 6.8 Hz, 2H), 7.41−7.27 (m, 5H), 7.24−7.17 (m, 2H), 6.50 (s, 1H), 4.23−4.07 (m, 1H), 3.97−3.89 (m, 2H), 3.41 (dd, J = 13.5, 3.4 Hz, 1H), 2.77 (dd, J = 13.5, 10.7 Hz, 1H), 2.48 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-*d*) δ 192.3, 143.9, 137.1, 137.1, 134.2, 133.8, 129.5, 129.2, 128.9, 128.7, 128.7, 127.7, 126.8, 87.9, 70.9, 59.0, 38.9, 21.6. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{24}H_{23}NO_4SNa$, 444.1240. Found, 444.1232.

(4-Methyl-3-tosyloxazolidin-2-yl)(phenyl)methanone (**5r**). Yield: 85% (59 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 8:1) and obtained as a white solid. m.p.:101−102 °C. ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.08 (dt, J = 7.1, 1.4 Hz, 2H), 7.83−7.78 (m, 2H), 7.69−7.61 (m, 1H), 7.54 (dd, J = 8.3, 6.8 Hz, 2H), 7.35 (d, J = 8.1 Hz, 2H), 6.53 (s, 1H), 4.19 (dd, J = 8.2, 6.4 Hz, 1H), 4.09 (qd, J = 6.4, 2.8 Hz, 1H), 3.78 (dd, J = 8.2, 2.9 Hz, 1H), 2.48 (s, 3H), 1.39 (d, J = 6.3 Hz, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-*d*) δ 192.5, 143.7, 137.5, 134.2, 133.9, 129.5, 129.0, 128.8, 127.7, 87.9, 74.4, 53.9, 21.6, 19.2. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{18}H_{19}NO_4SNa$, 368.0927. Found, 368.0921.

(4-Ethyl-3-tosyloxazolidin-2-yl)(phenyl)methanone (**5s**). Yield: 86% (62 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 8:1) and obtained as a white solid. m.p.:95−97 °C. ^{1}H NMR (300 MHz, chloroform-*d*) δ 8.12−8.04 (m, 2H), 7.84−7.75 (m, 2H), 7.65 (td, J = 6.2, 2.6 Hz, 1H), 7.59−7.51 (m, 2H), 7.34 (d, J = 8.1 Hz, 2H), 6.49 (s, 1H), 4.13 (td, J = 7.1, 3.1 Hz, 1H), 4.00−3.89 (m, 2H), 2.47 (s, 3H), 1.87 (ddt, J = 14.9, 7.4, 3.8 Hz, 1H), 1.77−1.68 (m, 1H), 0.90 (d, J = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-*d*) δ 192.7, 143.7, 137.4, 134.4, 133.9, 129.5, 129.0, 128.8, 127.7, 88.1, 71.7, 59.1, 25.6, 21.7, 9.4. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{19}H_{21}NO_4SNa$, 382.1084. Found, 382.1080.

(5-Methyl-3-tosyloxazolidin-2-yl)(phenyl)methanone (**5t**). Yield: 99% (69 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 8:1) and obtained as a white solid. m.p.:94−95 °C. ^{1}H NMR (400 MHz, chloroform-*d*) δ 8.21−8.12 (m, 2H), 7.87−7.79 (m, 2H), 7.69−7.58 (m, 1H), 7.51 (dd, J = 8.5, 7.1 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 6.49 (s, 1H), 3.86 (dd, J = 12.2, 5.9 Hz, 1H), 3.70

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(dp, J = 9.6, 6.0 Hz, 1H), 3.03 (dd, J = 12.2, 9.5 Hz, 1H), 2.46 (s, 3H), 1.27 (d, J = 6.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, chloroform-d) δ 192.5, 144.7, 135.0, 133.9, 133.9, 130.0, 129.4, 128.7, 127.9, 88.1, 75.1, 52.6, 21.6, 18.4. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{18}H_{19}NO_4SNa$, 368.0927. Found, 368.0921.

Phenyl(3-tosyl-1,3-oxazinan-2-yl)methanone (**5u**). Yield: 99% (69 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 8:1) and obtained as a white solid. m.p.:136−138 °C. ^1H NMR (300 MHz, chloroform-d) δ 8.25−8.07 (m, 2H), 7.86 (d, J = 8.0 Hz, 2H), 7.65 (t, J = 7.4 Hz, 1H), 7.53 (t, J = 7.6 Hz, 2H), 7.37 (d, J = 8.0 Hz, 2H), 6.64 (s, 1H), 3.88−3.62 (m, 4H), 2.49 (s, 3H), 1.64 (ddq, J = 23.4, 11.7, 6.2 Hz, 1H), 1.36−1.29 (m, 1H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-d) δ 194.2, 143.9, 137.2, 134.3, 134.0, 129.8, 129.4, 128.7, 127.7, 83.2, 63.0, 40.9, 23.3, 21.7. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{18}H_{19}NO_4SNa$, 368.0927. Found, 368.0924.

6-Phenyl-4-tosyl-3,4-dihydro-2H-1,4-oxazine (**6a**).[17] Yield: 99% (63 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 15:1) and obtained as a white solid. m.p.:102−104 °C. ^1H NMR (300 MHz, chloroform-d) δ 7.78−7.64 (m, 2H), 7.58−7.43 (m, 2H), 7.41−7.26 (m, 5H), 6.74 (s, 1H), 3.81 (dd, J = 5.0, 3.6 Hz, 2H), 3.68−3.56 (m, 2H), 2.44 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-d) δ 144.2, 140.7, 133.8, 133.7, 130.0, 128.4, 128.0, 127.4, 123.7, 101.8, 63.3, 43.4, 21.6. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{17}H_{17}NO_3SNa$, 338.0821. Found, 338.0819.

6-(p-Tolyl)-4-tosyl-3,4-dihydro-2H-1,4-oxazine (**6b**). Yield: 79% (52 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 15:1) and obtained as a colorless oil. ^1H NMR (300 MHz, chloroform-d) δ 7.75−7.67 (m, 2H), 7.43−7.32 (m, 4H), 7.21−7.13 (m, 2H), 6.69 (s, 1H), 3.79 (dd, J = 5.1, 3.6 Hz, 2H), 3.61 (dd, J = 5.0, 3.5 Hz, 2H), 2.44 (s, 3H), 2.37 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-d) δ 144.1, 141.0, 138.0, 133.7, 130.9, 129.9, 129.1, 127.4, 123.7, 101.1, 63.3, 43.4, 21.6, 21.2. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{18}H_{19}NO_3SNa$, 352.0978. Found, 352.0977.

6-(4-Methoxyphenyl)-4-tosyl-3,4-dihydro-2H-1,4-oxazine (**6c**). Yield: 83% (57 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 15:1) and obtained as a viscous solid. ^1H NMR (300 MHz, chloroform-d) δ 7.76−7.66 (m, 2H), 7.46−7.37 (m, 2H), 7.37−7.29 (m, 2H), 6.93−6.82 (m, 2H), 6.59 (s, 1H), 3.82 (s, 3H), 3.77 (dd, J = 5.0, 3.5 Hz, 2H), 3.63−3.55 (m, 2H), 2.43 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-d) δ 159.7, 144.2, 141.1, 133.8, 130.0, 127.5, 126.5, 125.3, 113.9, 100.4, 63.4, 55.5, 43.5, 21.7. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{18}H_{19}NO_4SNa$, 368.0927. Found, 368.0924.

6-(2-Methoxyphenyl)-4-tosyl-3,4-dihydro-2H-1,4-oxazine (**6d**). Yield: 96% (66 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 15:1) and obtained as a pale yellow solid. m.p.:86−87 °C. ^1H NMR (300 MHz, chloroform-d) δ 7.58−7.47 (m, 2H), 7.27 (dd, J = 7.7, 1.7 Hz, 1H), 7.09 (d, J = 8.0 Hz, 2H), 7.06−6.97 (m, 1H), 6.93 (s, 1H), 6.74−6.65 (m, 2H), 3.70 (s, 3H), 3.64 (t, J = 4.3 Hz, 2H), 3.35 (t, J = 4.3 Hz, 2H), 2.19 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-d) δ 155.8, 143.8, 136.6, 133.5, 129.6, 128.3, 127.1, 126.8, 122.1, 120.2, 110.8, 106.8, 63.0, 55.3, 43.2, 21.4. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{18}H_{19}NO_4SNa$, 368.0927. Found, 368.0919.

6-(4-Fluorophenyl)-4-tosyl-3,4-dihydro-2H-1,4-oxazine (**6e**). Yield: 85% (57 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 15:1) and obtained as a white solid. m.p.:85−88 °C. ^1H NMR (300 MHz, chloroform-d) δ 7.73−7.65 (m, 2H), 7.46−7.39 (m, 2H), 7.32 (d, J = 8.0 Hz, 2H), 7.05−6.94 (m, 2H), 6.63 (s, 1H), 3.78 (dd, J = 5.0, 3.6 Hz, 2H), 3.63−3.54 (m, 2H), 2.42 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-d) δ 162.6 (d, $^1J_{C\text{-}F}$ = 245.9 Hz), 144.2, 140.0, 133.7, 130.0, 129.9 (d, $^4J_{C\text{-}F}$ = 3.3 Hz), 127.4, 125.6 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 115.3 (d, $^2J_{C\text{-}F}$ = 21.6 Hz), 101.5 (d, $^5J_{C\text{-}F}$ = 1.7 Hz), 63.4, 43.3, 21.6. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{17}H_{16}FNO_3SNa$, 356.0727. Found, 356.0721.

6-(4-Chlorophenyl)-4-tosyl-3,4-dihydro-2H-1,4-oxazine (**6f**). Yield: 85% (59 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 15:1) and obtained as a white solid. m.p.:85−86 °C. ^1H NMR (300 MHz, chloroform-d) δ 7.78−7.70 (m, 2H), 7.50−7.42 (m, 2H), 7.42−7.33 (m, 4H), 6.76 (s, 1H), 3.85 (dd, J = 5.1, 3.5 Hz, 2H), 3.71−3.56 (m, 2H), 2.48 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-d) δ 144.3, 139.7, 133.7, 133.6, 132.2, 130.0, 128.5, 127.3, 124.9, 102.2, 63.4, 43.3, 21.6. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{17}H_{16}ClNO_3SNa$, 372.0432. Found, 372.0429.

6-(4-Bromophenyl)-4-tosyl-3,4-dihydro-2H-1,4-oxazine (**6g**). Yield: 82% (64 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 15:1) and obtained as a white solid. m.p.:116−117 °C. ^1H NMR (300 MHz, chloroform-d) δ 7.69 (d, J = 7.9 Hz, 2H), 7.46 (d, J = 8.3 Hz, 2H), 7.41−7.31 (m, 4H), 6.73 (s, 1H), 3.80 (t, J = 4.2 Hz, 2H), 3.60 (t, J = 4.2 Hz, 2H), 2.44 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-d) δ 144.3, 133.6, 132.7, 131.5, 130.1, 127.4, 125.2, 121.8, 102.2, 77.3, 63.4, 43.3, 21.7. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{17}H_{16}BrNO_3SNa$, 415.9927. Found, 415.9925.

6-(2-Fluorophenyl)-4-tosyl-3,4-dihydro-2H-1,4-oxazine (**6h**). Yield: 88% (59 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 15:1) and obtained as a colorless oil. ^1H NMR (300 MHz, chloroform-d) δ 7.89 (d, J = 8.1 Hz, 2H), 7.67 (t, J = 8.1 Hz, 1H), 7.50 (d, J = 7.8 Hz, 2H), 7.41−7.34 (m, 1H), 7.33−7.17 (m, 2H), 7.11 (d, J = 7.0 Hz, 1H), 4.06 (q, J = 5.2, 4.7 Hz, 2H), 3.75 (q, J = 5.4, 4.8 Hz, 2H), 2.58 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-d) δ 159.1 (d, $^1J_{C\text{-}F}$ = 249.0 Hz), 144.3, 135.2 (d, $^3J_{C\text{-}F}$ = 4.5 Hz), 133.7, 130.1, 128.9 (d, $^3J_{C\text{-}F}$ = 8.3 Hz), 127.5, 127.2 (d, $^3J_{C\text{-}F}$ = 3.0 Hz), 124.2 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 121.8 (d, $^2J_{C\text{-}F}$ = 10.5 Hz), 116.1 (d, $^2J_{C\text{-}F}$ = 23.3 Hz), 107.3 (d, $^4J_{C\text{-}F}$ = 16.5 Hz), 63.6, 43.5, 21.8. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{17}H_{16}FNO_3SNa$, 356.0727. Found, 356.0720.

6-(3-Chlorophenyl)-4-tosyl-3,4-dihydro-2H-1,4-oxazine (**6i**). Yield: 87% (61 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 15:1) and obtained as a white solid. m.p.:89−91 °C. ^1H NMR (300 MHz, chloroform-d) δ 7.72 (d, J = 7.9 Hz, 2H), 7.51−7.47 (m, 1H), 7.37 (td, J = 5.5, 3.1 Hz, 3H), 7.30−7.25 (m, 2H), 6.77 (s, 1H), 3.83 (t, J = 4.2 Hz, 2H), 3.66−3.60 (m, 2H), 2.46 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-d) δ 144.3, 139.3, 135.5, 134.5, 133.6, 130.1, 129.6, 127.9, 127.4, 123.8, 121.6, 102.8, 63.4, 43.3, 21.7. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{17}H_{16}ClNO_3SNa$, 372.0432. Found, 372.0436.

4-(4-Tosyl-3,4-dihydro-2H-1,4-oxazin-6-yl)benzonitrile (**6j**). Yield: 88% (60 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 15:1) and obtained as a white solid. m.p.:110−111 °C. ^1H NMR (300 MHz, chloroform-d) δ 7.77−7.68 (m, 2H), 7.68−7.55 (m, 4H), 7.37 (d, J = 8.0 Hz, 2H), 6.92 (s, 1H), 3.89 (t, J = 4.1 Hz, 2H), 3.69−3.61 (m, 2H), 2.47 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-d) δ 144.6, 138.4, 138.1, 133.6, 132.2, 130.2, 127.3, 123.7, 118.9, 110.8, 104.8, 63.5, 43.3, 21.7. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{18}H_{16}N_2O_3SNa$, 363.0774. Found, 363.0769.

6-(Thiophen-2-yl)-4-tosyl-3,4-dihydro-2H-1,4-oxazine (**6k**). Yield: 99% (64 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 15:1) and obtained as a pale yellow solid. m.p.:96−97 °C. ^1H NMR (300 MHz, chloroform-d) δ 7.78−7.70 (m, 2H), 7.39 (d, J = 8.0 Hz, 2H), 7.26 (dd, J = 5.0, 1.3 Hz, 1H), 7.17 (dd, J = 3.7, 1.3 Hz, 1H), 7.04 (dd, J = 5.1, 3.6 Hz, 1H), 6.71 (s, 1H), 3.82 (dd, J = 5.0, 3.5 Hz, 2H), 3.70−3.60 (m, 2H), 2.49 (s, 3H).$^{13}C\{^1H\}$ NMR (75 MHz, chloroform-d) δ 144.3, 137.4, 137.3, 133.7, 130.1, 127.5, 127.4, 124.4, 122.4, 101.2, 63.6, 43.5, 21.7. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{15}H_{15}NO_3S_2Na$, 344.0386. Found, 344.0382.

6-(Furan-2-yl)-4-tosyl-3,4-dihydro-2H-1,4-oxazine (**6l**). Yield: 52% (32 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 15:1) and obtained as a yellow oil. ^1H NMR (300 MHz, chloroform-d) δ 7.79−7.68 (m, 2H), 7.38−7.34 (m, 2H), 7.33 (s, 1H), 6.72 (s, 1H), 6.40 (dd, J = 3.3, 1.8 Hz, 1H), 6.36−6.26 (m, 1H), 3.80 (dd, J = 5.1, 3.5 Hz, 2H), 3.64−3.45 (m, 2H), 2.44 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-d) δ 148.3, 144.2, 141.8, 134.0, 133.7, 130.0, 127.4, 111.2, 105.6, 101.9, 63.4, 43.5, 21.6. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{15}H_{15}NO_4SNa$, 328.0614. Found, 328.0610.

6-([1,1′-Biphenyl]-4-yl)-4-tosyl-3,4-dihydro-2H-1,4-oxazine (**6m**). Yield: 96% (75 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 15:1) and obtained as a white solid. m.p.:160−162 °C. ^1H NMR (300 MHz, chloroform-d) δ 7.76−7.69 (m, 2H),

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7.65−7.55 (m, 6H), 7.51−7.42 (m, 2H), 7.36 (dd, J = 11.4, 7.6 Hz, 3H), 6.79 (s, 1H), 3.83 (dd, J = 5.0, 3.6 Hz, 2H), 3.63 (t, J = 4.3 Hz, 2H), 2.44 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-d) δ 144.3, 140.9, 140.6, 140.6, 134.0, 132.8, 130.1, 129.0, 127.6, 127.6, 127.2, 127.1, 124.2, 102.1, 63.5, 43.6, 21.8. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{23}H_{21}NO_3SNa$, 414.1134. Found, 414.1130.

*6-(Naphthalen-2-yl)-4-tosyl-3,4-dihydro-2H-1,4-oxazine (**6n**).* Yield: 99% (73 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 15:1) and obtained as a white solid. m.p.:165−166 °C. ^1H NMR (300 MHz, chloroform-d) δ 7.96 (d, J = 1.8 Hz, 1H), 7.86−7.79 (m, 3H), 7.78−7.72 (m, 2H), 7.60 (dd, J = 8.7, 1.8 Hz, 1H), 7.52−7.45 (m, 2H), 7.34 (d, J = 8.0 Hz, 2H), 6.90 (s, 1H), 3.89 (dd, J = 5.0, 3.6 Hz, 2H), 3.66 (dd, J = 5.0, 3.6 Hz, 2H), 2.43 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-d) δ 144.1, 140.5, 133.6, 133.2, 132.9, 130.8, 129.9, 128.0, 128.1 , 127.6, 127.3, 126.4, 126.0, 122.5, 121.4, 102.4, 63.3, 43.3, 21.6. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{21}H_{19}NO_3SNa$, 388.0978. Found, 388.0973.

*3,6-Diphenyl-4-tosyl-3,4-dihydro-2H-1,4-oxazine (**6p**).* Yield: 99% (77 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 15:1) and obtained as a white solid. m.p.:168−170 °C. ^1H NMR (300 MHz, chloroform-d) δ 7.67 (d, J = 7.7 Hz, 2H), 7.49 (d, J = 7.5 Hz, 2H), 7.37−7.23 (m, 10H), 6.90 (d, J = 4.4 Hz, 1H), 5.03 (s, 1H), 4.40 (dd, J = 11.2, 4.3 Hz, 1H), 3.34−3.30 (m, 1H), 2.41 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-d) δ 143.7, 140.3, 137.1, 133.8, 133.1, 129.5, 128.2, 128.0, 127.6, 127.4, 127.0, 126.3, 123.3, 101.1, 66.5, 55.1, 21.2. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{23}H_{21}NO_3SNa$, 414.1134. Found, 414.1126.

*3-Benzyl-6-phenyl-4-tosyl-3,4-dihydro-2H-1,4-oxazine (**6q**).* Yield: 99% (80 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 15:1) and obtained as a white solid. m.p.:94−97 °C. ^1H NMR (300 MHz, chloroform-d) δ 7.75−7.64 (m, 2H), 7.64−7.53 (m, 2H), 7.43−7.28 (m, 10H), 6.80 (d, J = 1.4 Hz, 1H), 4.03 (dd, J = 10.7, 5.2 Hz, 1H), 3.93 (d, J = 10.9 Hz, 1H), 3.07−2.86 (m, 2H), 2.80 (dd, J = 11.0, 2.2 Hz, 1H), 2.42 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-d) δ 144.1, 140.4, 137.2, 134.0, 133.7, 130.1, 129.9, 128.8, 128.6, 128.2, 127.4, 127.0, 123.9, 100.4, 63.2, 54.3, 36.9, 21.7. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{24}H_{23}NO_3SNa$, 428.1291. Found, 428.1281.

*3-Methyl-6-phenyl-4-tosyl-3,4-dihydro-2H-1,4-oxazine (**6r**).* Yield: 93% (61 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 15:1) and obtained as a colorless oil. ^1H NMR (300 MHz, chloroform-d) δ 7.76−7.66 (m, 2H), 7.58−7.51 (m, 2H), 7.42−7.32 (m, 5H), 6.75 (d, J = 1.4 Hz, 1H), 4.15−4.04 (m, 1H), 3.94 (dd, J = 10.7, 1.4 Hz, 1H), 2.99 (dd, J = 10.8, 2.3 Hz, 1H), 2.45 (s, 3H), 1.33 (d, J = 6.8 Hz, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-d) δ 144.0, 139.8, 134.0, 133.7, 130.0, 128.4, 128.0, 127.4, 123.7, 100.2, 67.0, 48.5, 21.6, 17.0. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{18}H_{19}NO_3SNa$, 352.0978. Found, 352.0970.

*3-Ethyl-6-phenyl-4-tosyl-3,4-dihydro-2H-1,4-oxazine (**6s**).* Yield: 86% (59 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 15:1) and obtained as a colorless oil. ^1H NMR (300 MHz, chloroform-d) δ 7.66 (d, J = 8.3 Hz, 2H), 7.53−7.46 (m, 2H), 7.38−7.27 (m, 5H), 6.67 (d, J = 1.5 Hz, 1H), 4.00 (dd, J = 10.8, 1.4 Hz, 1H), 3.76 (t, J = 7.5 Hz, 1H), 2.83 (dd, J = 10.8, 2.4 Hz, 1H), 2.41 (s, 3H), 1.70 (dd, J = 14.3, 7.4 Hz, 1H), 1.55 (dq, J = 14.0, 7.1 Hz, 1H), 1.05 (t, J = 7.5 Hz, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-d) δ 144.0, 140.4, 134.0, 133.7, 130.0, 128.4, 128.1, 127.5, 123.8, 100.2, 65.0, 54.2, 23.4, 21.7, 10.5. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{19}H_{21}NO_3SNa$, 366.1134. Found, 366.1129.

*2-Methyl-6-phenyl-4-tosyl-3,4-dihydro-2H-1,4-oxazine (**6t**).* Yield: 95% (63 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 15:1) and obtained as a white solid. m.p.:102−104 °C. ^1H NMR (300 MHz, chloroform-d) δ 7.71 (dd, J = 8.2, 1.5 Hz, 2H), 7.51 (dt, J = 8.1, 1.4 Hz, 2H), 7.43−7.29 (m, 5H), 6.74 (d, J = 1.4 Hz, 1H), 3.84 (dq, J = 13.0, 1.4 Hz, 1H), 3.62−3.52 (m, 1H), 2.96 (ddd, J = 13.0, 8.8, 1.3 Hz, 1H), 2.44 (s, 3H), 1.31 (dd, J = 6.3, 1.3 Hz, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-d) δ 144.1, 140.4, 133.9, 133.8, 130.0, 128.4, 128.0, 127.3, 123.8, 101.3, 68.9, 48.7, 21.7, 18.1. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{18}H_{19}NO_3SNa$, 352.0978. Found, 352.0976.

*2-Phenyl-4-tosyl-4,4a,5,6,7,7a-hexahydrocyclopenta[b][1,4]-oxazine (**6v**).* Yield: 82% (58 mg). Purified by column chromatography (petroleum ether/ethyl acetate = 15:1) and obtained as a white solid. m.p.:195−197 °C. ^1H NMR (300 MHz, chloroform-d) δ 7.76−7.69 (m, 2H), 7.56−7.46 (m, 2H), 7.38−7.29 (m, 5H), 6.72 (s, 1H), 4.13 (dt, J = 10.8, 7.9 Hz, 1H), 2.70−2.57 (m, 1H), 2.44 (s, 3H), 2.42−2.33 (m, 1H), 2.19 (dtd, J = 12.1, 7.5, 4.7 Hz, 1H), 1.91 (dddd, J = 14.9, 13.3, 11.5, 6.2 Hz, 3H), 1.74−1.61 (m, 1H). $^{13}C\{^1H\}$ NMR (75 MHz, chloroform-d) δ 144.2, 141.2, 133.8, 133.1, 129.9, 128.4, 128.0, 127.4, 124.0, 104.5, 81.0, 58.8, 27.0, 25.7, 21.6, 18.2. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{20}H_{21}NO_3SNa$, 378.1134. Found, 378.1138.

■ ASSOCIATED CONTENT

Data Availability Statement

The data underlying this study are available in the published article and its Supporting Information.

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.3c00690.

^1H NMR and $^{13}C\{^1H\}$ NMR of the synthesized compounds (PDF)

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Notes

The authors declare no competing financial interest.

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