PAPER

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Synthesis of sulfur-containing benzo[b]pyrrolo[2,1-c][1,4]oxazine-3,9-diones: blue light promoted radical cyclization process†

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The selective and controllable construction of spio-tricyclic skeletons through visible light promoted radical cyclization still remains challenging. Herein, a general and convenient protocol for the blue light-promoted radical-mediated cascade spiro-cyclization/Michael addition of N-arylpropiolamides with thiophenols under metal-free conditions was developed. In this protocol, commercially available hydrochloric acid was employed as the cheap promoter and air as the sustainable oxidant. In addition, many functional groups tolerate the reaction conditions and produce a series of sulfur-containing benzo[b]pyrrolo[2,1-c] [1,4]oxazine-3,9-diones.
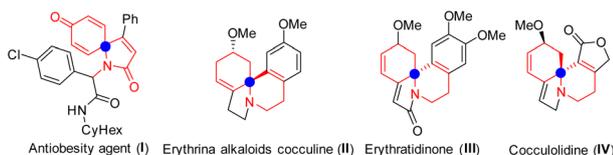
Introduction

It is well known that spirocyclic compounds can be used in photochromism,[1] organic optoelectronics,[2] and medicinal chemistry,[3] and have also played an important role in organic synthesis.[4] Antiobesity agent (I) is a selective histamine-3 receptor (H3R) modulator[5] (Scheme 1). Among the spirocyclic compounds, N-containing spiro-products show important bioactivity as anticancer, antimicrobial and anti-inflammatory agents.[6] In recent years, the Erythrina alkaloid cocculine II has attracted considerable attention because of its wide range of biological properties.[7] Furthermore, some biologically active

Scheme 1 Biologically active spirocycles.

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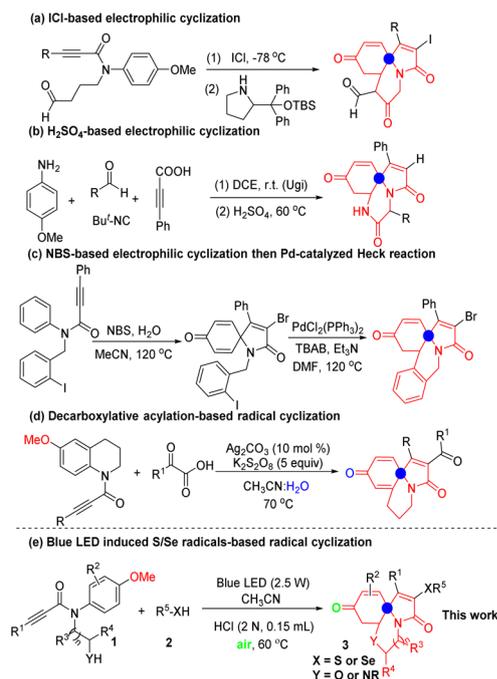
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spirocycles with hypnotic, hypotensive, and CNS activity are found in numerous active molecules, such as the erythrina, aspidosperma, and strychnos families.[8]

Because of its unique properties, tremendous efforts have been made to construct the spirotricyclic derivatives in the past ten years.[9] Among them, the dearomatization of arenes is an effective method for the synthesis of spiro compounds. In 2011, a catalytic enantioselective method for synthesizing fused spiro-tricyclic compounds has been developed. In this reaction, Gaunt and co-workers[10] developed ICl-based electrophilic dearomatization of anisidine derivatives (Scheme 2a). In 2016, Srivastava and the co-workers reported a diastereo- and regio-selective Ugi/ipso-cyclization/aza-michael cascade reaction to the synthesis of alkaloid-mimicking tricyclic skeletons[11] (Scheme 2b). In the reaction, the use of H_2SO_4 played an important role in the dearomative cyclization.

On the other hand, transition metal promoted dearomatization has become one of the most popular reaction models with great achievements. In 2012, Li developed a general method for the synthesis of spiro[4,5]trienones by the intramolecular ipso-halocyclization of 4-(p-unsubstituted-aryl)-1-alkynes[12] (Scheme 2c). Subsequently, the azaquaternary tricyclic skeletons could be obtained via Pd-catalyzed intramolecular Heck reaction. In 2020, Reddy and the co-workers reported a Ag-catalyzed oxidative ipso-cyclization via decarboxylative acylation/alkylation to construct pyrrolo-[2,1-j]-quinolone[13] (Scheme 2d), which was a challenging framework found in tricyclic marine alkaloids.[14]

It is worth noting that Qiu and co-workers have paid more attention to the green and mild construction of spio-tricyclic skeletons over the past years.[15] Considering that our group's main research interest is the controllable synthesis of nitrogen-containing heterocycles based on the selective functionalization

Scheme 2 Methods for the synthesis of spirotricyclic derivatives.

of alkynes.[16] So, in this paper, we would like to share a blue light-promoted[17] radical-mediated spiro-tricyclization of *N*-arylpropiolamides with thio(sele)phenols under metal-free conditions (Scheme 2e).

Results and discussion

At the initial stage of the investigations, the synthesized *N*-(2-hydroxyethyl)-*N*-(4-methoxyphenyl)-3-phenylpropiolamide **1a** and the purchased 4-methylbenzenethiol **2a** were chosen as model substrates to optimize the reaction conditions using blue LED as the light source (Table 1). Firstly, the influence of the blue LED power on the reaction is explored and 2.5 W was the most effective light power among the tested 1.5 W, 2.5 W, and 3.5 W (entries 1–3). To our delight, when the reaction temperature was raised to 50 °C, the expected product 1-phenyl-2-(*p*-tolylthio)-5,6,7a,8-tetrahydro-3*H*,9*H*-benzo[*b*]pyrrolo[2,1-*c*][1,4]oxazine-3,9-dione **3a** was obtained in 47% yield (entry 4, Table 1).

Further, the reaction temperature was increased to 60 °C and 70 °C, and it was found that the optimum temperature of this reaction was 60 °C with the desired product **3a** obtained in 56% yield (entries 4–6). In order to further optimize the reaction results, the effect of the amount of **2a** on the reaction was evaluated. As shown in entries 7–9, a better result was obtained by using 1.5 equiv of **2a**, giving the desired product **3a** in 62% yield. Changing the reaction solvent to MeOH, DMF, THF, or toluene has no good effect on the reaction (entries 11–14). When adding 0.15 mL 1.1 N HCl to this reaction, a 68% yield was achieved (entry 15, Table 1). Encouraged by this result, the effect of the additive HCl to this reaction was further explored. Replacing 1.1 N HCl to 2.0 N HCl or 3.0 N HCl, 2.0 N HCl was the

**Table 1** Optimization of the reaction conditions[a]

Entry	Blue LDE (x (W))	Solvent	Additive (y mL)	T (°C)	Yield **3a**[b] (%)
1	1.5	MeCN	—	r.t.	33
2	2.5	MeCN	—	r.t.	36
3	3.5	MeCN	—	r.t.	31
4	2.5	MeCN	—	50	47
5	2.5	MeCN	—	60	56
6	2.5	MeCN	—	70	49
7[c]	2.5	MeCN	—	60	62
8[d]	2.5	MeCN	—	60	40
9[e]	2.5	MeCN	—	60	43
11[c]	2.5	MeOH	—	60	16
12[c]	2.5	DMF	—	60	12
13[c]	2.5	THF	—	60	47
14[c]	2.5	Toluene	—	60	51
15[c]	2.5	MeCN	1.1 N HCl (0.15)	60	68
16[c]	2.5	MeCN	2.0 N HCl (0.15)	60	76
17[c]	2.5	MeCN	3.0 N HCl (0.15)	60	60
18[c]	2.5	MeCN	2.0 N HCl (0.10)	60	65
19[c]	2.5	MeCN	2.0 N HCl (0.20)	60	67
20[c]	2.5	MeCN	2.0 N HCl (0.25)	60	70
21[c]	2.5	MeCN	NaCl (1.0 equiv)	60	35
22[c]	2.5	MeCN	2.0 N HCl (0.15)	r.t.	47

[a] Standard conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), air, in 2 mL of CH₃CN were stirred under blue LED, 12 h. [b] Isolated yield based on **1a**. [c] **2a** (1.5 equiv) was used. [d] **2a** (2.5 equiv) was used. [e] **2a** (1.0 equiv) was used.

optimal choice, leading to the desired product **3a** in 76% yield (entries 15–17, Table 1). In addition, increasing or decreasing the amount of 2.0 N HCl led to a decrease in the **3a** yield (entries 18–20, Table 1). When NaCl was used as the chlorine radical source, there was no significant increase in the yield of product **3a** (entry 21). Next, with the addition of 0.15 mL of 2.0 N HCl, the reaction temperature was lowered to room temperature and the yield was found only 45% (entry 22). Finally, the standard reaction conditions were established as follows: a mixture of **1a** (0.2 mmol), **2a** (0.3 mmol), and 0.15 mL 2.0 N HCl in 2 mL MeCN were stirred under 2.5 W blue LED at 60 °C in air.

With the optimal conditions established, the general utilization of the photomediated spiro-tricyclization of *N*-hydroxylethyl-*N*-arylpropiolamides with thio(sele)phenols was probed. As shown in Table 2, diverse *N*-arylpropionamides with different substituents in the alkynyl moiety were all tolerated, and the yields of the corresponding products **3a–d** were satisfactory (64–82% yields). In addition, the 1.0 mmol experiment of **1a** was carried out under standard conditions to obtain the desired product **3a** in 72% yield. Furthermore, the substituent R^1 could be replaced by 1-naphthyl, 2-thiophenyl, or 1,1′-biphenyl and the corresponding products **3e**, **3f**, and **3g** were observed in 70%, 46%, and 30% yields, respectively. Unfortunately, when R^1

Table 2 Reaction scope using *p*-toluenethiophenol as the source of free radical[a,b]
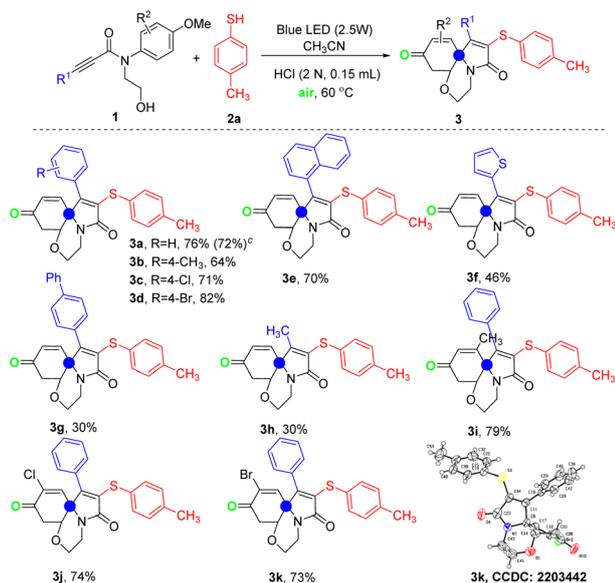

[a] Standard conditions: **1** (0.2 mmol), **2a** (0.3 mmol), HCl (2.0 N, 0.15 mL), air, in 2 mL of CH₃CN were stirred under blue LED (2.5 W) at 60 °C, 12 h. [b] Isolated yield based on **1**. [c] 1.0 mmol scale experiment of **1a**.

Table 3 Reaction scope for the synthesis of thio(sele)-containing spirotricycles[a,b]

[a] Standard conditions: **1** (0.2 mmol), **2** (0.3 mmol), HCl (2.0 N, 0.15 mL), air, in 2 mL of CH₃CN were stirred under blue LED (2.5 W) at 60 °C, 12 h. [b] Isolated yield based on **1**.

is methyl, the corresponding product **3h** was obtained with only 30% yield. Next, the influence of phenyl substituents R^2 on the reaction of *N*-arylpropamides was studied. It can be seen from the results that substrates containing methyl, chlorine, or bromine substituted could react smoothly and give the corresponding products **3i–k** in good yields. The structure of compound **3k** (CCDC: 2203442†) was identified by X-ray single-crystal diffraction (see the ESI† for details).

In order to extend the universality of the reaction substrates, the substrate with secondary alcohol or other primary alcohol was synthesized as the starting material (Table 3). The results showed that the substrate with secondary alcohol or other primary alcohol was also compatible for the reaction, leading to the corresponding products **3l**, **3m**, and **3n** in 76%, 74%, and 74% yields, respectively. Next, the influence of different thio-alcohols on the reaction was investigated. Using 4-chlor-obenzenethiol or naphthalene-2-thiol as the reaction substrate, the reaction proceeded smoothly and the corresponding products **3o** and **3p** were obtained in good yields. Unfortunately, using heterocyclic mercaptan and ethanethiol as the reaction substrates, the corresponding products could only be obtained in low yields of 5–38%. Happily, when phenylselenol was used as the substrate, the corresponding product **3t** was obtained in 62% yield under standard conditions. Notably, the reaction using the substrate with 3-propanol was retarded, leading to the corresponding product **3u** in only 10% yield. Finally, changing the primary alcohol to Ts protected amine, the reaction was still going on smoothly and the expected product **3v** was achieved in 36% yield.
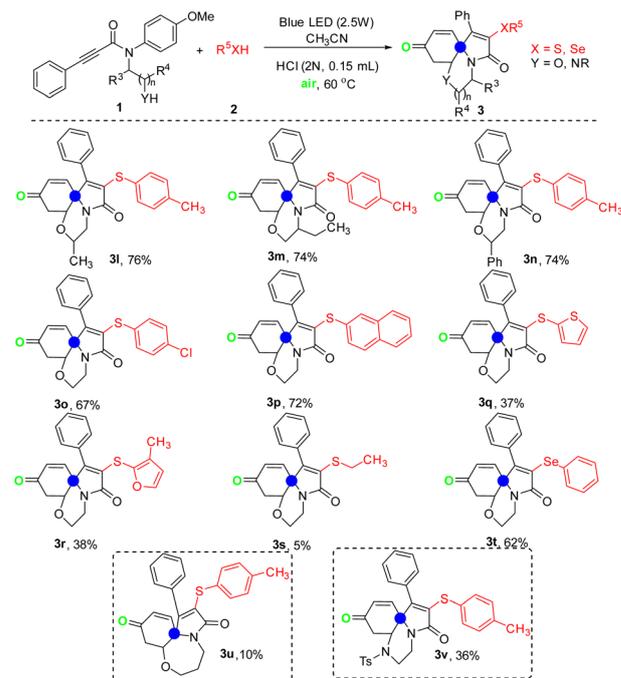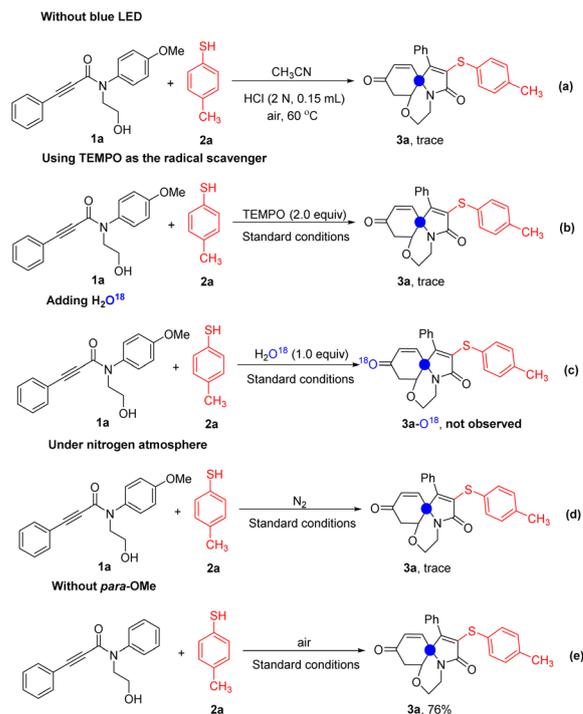

Scheme 3 Control experiments.

In order to shed light on the mechanism of this reaction, some control experiments were carried out (Scheme 3). First of all, the reaction could not be carried out normally without the blue LED (Scheme 3a). Next, the expected product **3a** could not be detected when 2.0 equiv of TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) was added to the reaction system (Scheme 3b). From this result, the reaction probably underwent a radical pathway. Furthermore, when adding 1.0 equiv of H_2O^{18} to the standard conditions, the O^{18} atom was not observed by LC-MS analysis in the product, which perhaps indicated that the oxygen of carbonyl was not derived from the water (Scheme 3c). Finally, the reaction did not work under N_2 atmosphere may be implied that the oxygen of carbonyl group came from the oxygen in the air (Scheme 3d). If the reaction was carried out with *N*-phenylproiolamides without a *para*-methoxy substituent on the *N*-substituted aryl moiety, the desired product **3a** was still obtained in 76% yield, which indicated that oxygen of carbonyl was derived from the air (Scheme 3e).

Based on the control experiments aforementioned above and the previous reports,[15,18] a plausible mechanism was proposed in Scheme 4. Initially, $^1O_2$ ($E = 2.2$ V) reacted with Cl^- ($E = 1.36$ V) producing chlorine radical in the presence of blue LED and air.[18b] Then chlorine radical undergoes HAT with thio(sele)phenol to give sulfur(selenium) radical **A** (route I).[18a] Of course, the sulfur(selenium) radical **A** could also be offered directly by the blue LED and air (route II). Intermediate **B** was formed through the α-addition of *N*-arylpropiolamides **1** to sulfur(selenium) radical **A**. Then, the key intermediate **C** was provided by radical ipso-cyclization. Next, the intermediate **C** was captured by molecular oxygen in para-site fashion to offer the intermediate **D**. Subsequently, under the action of proton acid, the key intermediate **E** was obtained through electron rearrangement, while releasing a molecule of methanol. When there was no methoxy group present in the reaction substrate, the required product **3a** was still obtained in 76% yield (Scheme 3e), indicating that intermediate **C** could still be captured by molecular oxygen, leading to electron rearrangement to obtain intermediate **E**. Finally, assisted by the additives, the intermediate **E** undergoes an intramolecular Michael-addition reaction, thus providing the final products **3**.
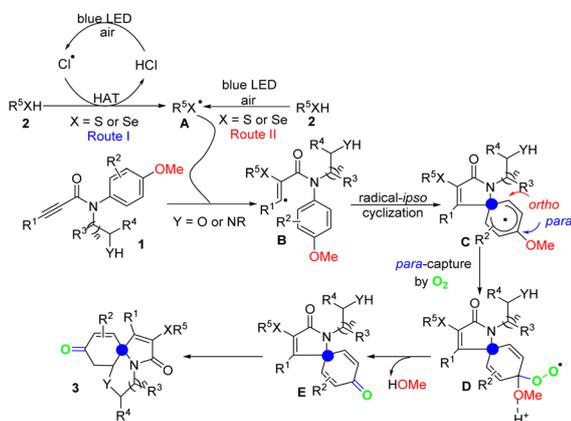
Scheme 4 Plausibe mechanism.

Conclusions

In conclusion, we have developed a general and convenient protocol for the blue LED-promoted chlorine radical-mediated spiro-tricyclization of *N*-arylpropiolamides with thiophenols under metal-free conditions. In this reaction, hydrochloric acid is used as the cheap promoter and air as the sustainable oxidant. Many functional groups tolerate the reaction conditions and produce a series of sulfur-containing benzo[*b*]pyrrolo [2,1-*c*][1,4]oxazine-3,9-diones with high efficiency and specific selectivity. Preliminary mechanistic studies indicated that the reaction undergoes LED-promoted chlorine radical-mediated spiro-cyclization and intramolecular Michael-addition reaction. Further studies on the visible light induced radical cyclization are currently ongoing.

Experimental

General methods and materials

Unless stated otherwise, reactions were conducted in dried glassware. Commercially available reagents and solvents were used as received. 300–400 mesh silica gel was used for flash column chromatography. Visualization on TLC was achieved by the use of UV light (254 nm). 400 MHz and 100 MHz were used to record the ^1H NMR and ^{13}C NMR spectra. Chemical shifts (δ ppm) were reported in parts per million, referring to either the internal standard of TMS or the residue of the deuterated solvents. The splitting pattern was described as follows: s for singlet, d for doublet, t for triplet, q for quartet, and m for multiplet. Coupling constants were reported in Hz. The high-resolution mass spectrum (HRMS) was performed on waters Xevo G2-S QTof mass spectrometer. The crystal of **3k** was measured on an Agilent Technologies Gemini single-crystal diffractometer and the solvent system for crystal growth is dichloromethane and petroleum ether.

Typical procedure for the synthesis of compound 3a

To a test tube were added *N*-(2-hydroxyethyl)-*N*-(4-methoxyphenyl)-3-phenylpropiolamide **1a** (0.20 mmol), 4-methylbenzenethiol **2a** (0.30 mmol, 1.50 equiv), CH_3CN (2.00 mL), and then HCl (0.15 mL, 2.00 mol L^{-1}) was added to the mixture. Then the mixture was stirred under air at 60 °C under 2.5 W blue LED irradiation for 12 hours until the complete consumption of the substrate. The mixture was treated with saturated $NaHCO_3$ (2.0 mL) and extracted with EA (2.0 mL × 3). The combined organic layer was dried with anhydrous Na_2SO_4. The solvent was removed under vacuum and the residue was purified by silica gel chromatography, using a mixture of petroleum ether/ethyl acetate to give the desired product **3a**.

Characterization data

1-Phenyl-2-(*p*-tolylthio)-5,6,7a,8-tetrahydro-3*H*,9*H*-benzo[*b*]pyrrolo[2,1-*c*][1,4]oxazine-3,9-dione (3a). Yellow solid (61.3 mg, 76%); M.p. = 170–173 °C; ^1H NMR (400 MHz, CDCl$_3$) δ 7.33–7.24 (m, 3H), 7.15 (d, $J = 7.9$ Hz, 2H), 7.08 (d, $J = 7.5$ Hz, 2H), 6.96 (d, $J = 7.7$ Hz, 2H), 6.41–6.34 (m, 2H), 4.26–4.23 (m, 1H), 3.90–3.85

(m, 1H), 3.72 (s, 1H), 3.36–3.30 (m, 1H), 3.17–3.11 (m, 1H), 2.36–2.24 (m, 1H), 2.24 (s, 3H), 1.87–1.82 (m, 1H); ^{13}C{^{1}H}NMR (100 MHz, CDCl$_3$) δ 194.4, 166.1, 153.5, 142.6, 137.8, 134.0, 133.7, 131.9, 129.7, 129.4, 128.7, 128.3, 127.5, 79.1, 66.2, 41.3, 38.8, 21.1; IR (KBr): 2950, 1688, 1640, 1495, 1070, 1044, 1020, 739, 621 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for C$_{24}$H$_{21}$NO$_3$NaS 426.1140; found: 426.1137.

1-(*p*-Tolyl)-2-(*p*-tolylthio)-5,6,7a,8-tetrahydro-3*H*,9*H*-benzo[*b*]pyrrolo[2,1-*c*][1,4]oxazine-3,9-dione (3b). Yellow solid (53.4 mg, 64%); M.p. = 144–147 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.12 (m, 4H), 6.97 (s, 4H), 6.37–6.34 (m, 2H), 4.24–4.23 (m, 1H), 3.86–3.84 (m, 1H), 3.69 (m, 1H), 3.33–3.28 (m, 1H), 3.14–3.08 (m, 1H), 2.35 (s, 1H), 2.31 (s, 3H), 2.24 (s, 3H), 1.93–1.89 (m, 1H); ^{13}C{^{1}H}NMR (100 MHz, CDCl$_3$) δ 194.5, 166.2, 154.1, 142.7, 139.7, 137.7, 134.0, 133.1, 131.7, 129.8, 129.5, 129.0, 128.1, 127.8, 79.2, 66.1, 41.3, 38.7, 21.3, 21.1; IR (KBr): 2917, 1493, 1273, 1170, 1060, 1013, 788, 765, 755, 662 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for C$_{25}$H$_{23}$NO$_3$NaS 440.1296; found: 440.1290.

1-(4-Chlorophenyl)-2-(*p*-tolylthio)-5,6,7a,8-tetrahydro-3*H*,9*H*-benzo[*b*]pyrrolo[2,1-*c*][1,4]oxazine-3,9-dione (3c). Yellow solid (62.1 mg, 71%); M.p. = 175–178 °C; ^{1}H NMR (400 MHz,CDCl$_3$) δ 7.20 (d, J = 8.0 Hz, 2H), 7.11 (d, J = 6.4 Hz, 2H), 6.96 (d, J = 8.8 Hz, 4H), 6.35 (s, 2H), 4.26–4.22 (m, 1H), 3.88–3.85 (m, 1H), 3.70 (s, 1H), 3.34–3.28 (m, 1H), 3.12–3.10 (m, 1H), 2.39–2.34 (m, 1H), 2.25 (s, 3H), 1.88–1.84 (m, 1H); ^{13}C{^{1}H}NMR (100 MHz, CDCl$_3$) δ 194.0, 165.8, 150.7, 142.5, 138.3, 135.6, 134.7, 134.1, 132.5, 130.2, 129.7, 128.9, 126.5, 79.0, 66.2, 66.1, 41.3, 38.8, 21.1; IR (KBr): 2924, 1693, 1488, 1398, 1384, 1071, 1012, 804, 760, 661 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for C$_{24}$H$_{20}$NO$_3$NaSCl 460.0750; found: 460.0751.

1-(4-Bromophenyl)-2-(*p*-tolylthio)-5,6,7a,8-tetrahydro-3*H*,9*H*-benzo[*b*]pyrrolo[2,1-*c*][1,4]oxazine-3,9-dione (3d). Yellow solid (79.1 mg, 82%); M.p. = 167–170 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.35 (d, J = 7.7 Hz, 2H), 7.11 (d, J = 7.5 Hz, 2H), 6.93 (d, J = 7.6 Hz, 2H), 6.89 (d, J = 7.7 Hz, 2H), 6.35 (s, 2H), 4.26–4.22 (m, 1H), 3.88–3.85 (m, 1H), 3.70 (s, 1H), 3.34–3.28 (m, 1H), 3.16–3.10 (m, 1H), 2.39–2.35 (m, 1H), 2.25 (s, 3H), 1.89–1.85 (m, 1H); ^{13}C{^{1}H}NMR (100 MHz, CDCl$_3$) δ 194.0, 165.8, 150.4, 142.5, 138.4, 134.7, 134.1, 132.5, 131.8, 130.7, 129.9, 129.7, 126.4, 123.8, 79.0, 66.1, 41.3, 38.8, 21.2; IR (KBr): 2916, 1693, 1398, 1385, 1107, 1067, 1012, 805, 787, 688, 660 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for C$_{24}$H$_{20}$NO$_3$NaSBr 504.0245; found: 504.0243.

1-(Naphthalen-1-yl)-2-(*p*-tolylthio)-5,6,7a,8-tetrahydro-3*H*,9*H*-benzo[*b*]pyrrolo[2,1-*c*][1,4]oxazine-3,9-dione (3e). Yellow solid (63.5 mg, 70%); M.p. = 206–209 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.77 (d, J = 5.7 Hz, 2H), 7.68 (d, J = 7.9 Hz, 1H), 7.61 (d, J = 8.9 Hz, 1H), 7.52 (s, 2H), 7.21 (m, 1H), 6.96 (d, J = 7.1 Hz, 1H), 6.82 (d, J = 7.5 Hz, 2H), 6.61 (m, 2H), 6.41 (d, J = 10.1 Hz, 1H), 6.32 (d, J = 9.8 Hz, 1H), 4.36 (m, 1H), 3.97–3.86 (m, 2H), 3.46–3.41 (m, 1H), 3.24–3.21 (m, 1H), 2.10 (s, 3H), 2.07 (s, 1H), 1.39–1.35 (m, 1H); ^{13}C{^{1}H}NMR (100 MHz, CDCl$_3$) δ 194.2, 165.9, 146.9, 142.9, 138.1, 136.3, 133.7, 133.3, 130.3, 129.2, 129.0, 128.8, 128.7, 128.3, 127.5, 127.2, 126.4, 124.4, 124.3, 78.8, 67.5, 66.2, 41.0, 38.9, 20.9; IR (KBr): 2973, 2861, 1685, 1490, 1442, 1385, 1103, 1064, 1052, 1016, 811, 792, 761, 649 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for C$_{28}$H$_{23}$NO$_3$NaS 476.1296; found: 476.1298.

1-(Thiophen-2-yl)-2-(*p*-tolylthio)-5,6,7a,8-tetrahydro-3*H*,9*H*-benzo[*b*]pyrrolo[2,1-*c*][1,4]oxazine-3,9-dione (3f). Yellow solid (37.7 mg, 46%); M.p. = 115–118 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.40 (s, 1H), 7.20 (s, 2H), 7.07 (s, 1H), 7.01 (s, 3H), 6.46 (s, 1H), 6.41 (s, 1H), 4.23–4.20 (m, 1H), 3.86–3.83 (m, 1H), 3.67 (s, 1H), 3.32–3.26 (m, 1H), 3.13–3.07 (m, 1H), 2.46–2.42 (m, 1H), 2.26 (s, 3H), 2.18–2.14 (m, 1H); ^{13}C{^{1}H}NMR (100 MHz, CDCl$_3$) δ 194.6, 165.8, 146.3, 141.8, 137.9, 135.4, 133.6, 131.6, 131.5, 130.0, 129.7, 129.16, 127.6, 79.6, 66.0, 65.8, 41.3, 38.8, 21.2; IR (KBr): 2970, 2920, 1683, 1487, 1397, 1384, 1281, 1101, 1060, 797, 760, 709, 700, 649 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for C$_{22}$H$_{19}$NO$_3$NaS$_2$ 432.0704; found: 432.0697.

1-([1,1′-Biphenyl]-4-yl)-2-(*p*-tolylthio)-5,6,7a,8-tetrahydro-3*H*,9*H*-benzo[*b*]pyrrolo[2,1-*c*][1,4]oxazine-3,9-dione (3g). Yellow solid (28.8 mg, 30%); M.p. = 91–94 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.52 (d, J = 17.6 Hz, 5H), 7.45 (s, 2H), 7.38 (s, 1H), 7.18 (s, 3H), 6.96 (s, 2H), 6.43 (s, 2H), 4.30–4.27 (m, 1H), 3.91–3.87 (m, 1H), 3.77 (s, 1H), 3.37–3.33 (m, 1H), 3.20–3.14 (m, 1H), 2.42–2.38 (m, 1H), 2.23 (s, 3H), 2.02–1.98 (m, 1H); ^{13}C{^{1}H}NMR (100 MHz, CDCl$_3$) 194.4, 166.2, 152.6, 142.7, 142.3, 139.7, 137.9, 134.1, 133.9, 132.1, 130.8, 129.7, 128.9, 127.8, 127.2, 127.0, 79.2, 66.2, 41.4, 38.8, 21.1; IR (KBr): 2975, 2918, 1686, 1487, 1437, 1385, 1277, 1098, 1061, 760, 730, 730, 693 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for C$_{30}$H$_{25}$NO$_3$NaS 502.1453; found: 502.1448.

1-Methyl-2-(*p*-tolylthio)-5,6,7a,8-tetrahydro-3*H*,9*H*-benzo[*b*]pyrrolo[2,1-*c*][1,4]oxazine-3,9-dione (3h). Yellow solid (20.5 mg, 30%); M.p. = 160–163 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.25 (d, J = 6.6 Hz, 2H), 7.08 (d, J = 7.1 Hz, 2H), 6.35 (d, J = 10.0 Hz, 1H), 6.18 (d, J = 9.9 Hz, 1H), 4.21–4.18 (m, 1H), 3.88–3.86 (s, 1H), 3.64 (m, 1H), 3.32–3.26 (m, 1H), 3.13–3.07 (m, 1H), 2.87–2.75 (m, 2H), 2.29 (s, 3H), 2.07 (s, 3H); ^{13}C{^{1}H}NMR (100 MHz, CDCl$_3$) δ 194.2, 166.6, 154.8, 144.7, 137.5, 133.1, 132.1, 130.7, 129.9, 128.8, 78.5, 66.3, 66.0, 41.9, 38.5, 21.1, 13.8; IR (KBr): 2918, 2816, 1691, 1601, 1490, 1398, 1283, 1105, 1062, 801, 744 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for C$_{19}$H$_{19}$NO$_3$NaS 364.0983; found: 364.0984.

11-Methyl-1-phenyl-2-(*p*-tolylthio)-5,6,7a,8-tetrahydro-3*H*,9*H*-benzo[*b*]pyrrolo[2,1-*c*][1,4]oxazine-3,9-dione (3i). Yellow solid (66.0 mg, 79%); M.p. = 141–143 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.29 (m, 3H), 7.13 (d, J = 7.3 Hz, 2H), 6.97 (m, 4H), 6.27 (s, 1H), 4.26–4.23 (m, 1H), 3.85–3.82 (m, 1H), 3.66 (s, 1H), 3.35–3.29 (m, 1H), 2.92–2.86 (m, 1H), 2.33–2.28 (m, 1H), 2.23 (s, 3H), 1.85 (s, 3H), 1.79 (s, 1H); ^{13}C{^{1}H}NMR (100 MHz, CDCl$_3$) δ 194.2, 166.6, 153.7, 150.5, 137.8, 134.0, 132.6, 131.9, 131.8, 129.7, 129.6, 128.7, 127.9, 79.6, 68.6, 65.9, 41.3, 38.6, 21.1, 18.2; IR (KBr): 2877, 2915, 1705, 1676, 1493, 1436, 1385, 1346, 1276, 1103, 1065, 870, 813, 778, 769, 723, 710, 647 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for C$_{25}$H$_{23}$NO$_3$NaS 440.1296; found: 440.1291.

10-Chloro-1-phenyl-2-(*p*-tolylthio)-5,6,7a,8-tetrahydro-3*H*,9*H*-benzo[*b*]pyrrolo[2,1-*c*][1,4]oxazine-3,9-dione (3j). Yellow solid (64.8 mg, 74%); M.p. = 165–168 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.30 (d, J = 7.7 Hz, 3H), 7.15 (d, J = 6.8 Hz, 2H), 7.03 (d, J = 6.5 Hz, 2H), 6.95 (d, J = 7.1 Hz, 2H), 6.58 (s, 1H), 4.27–4.24 (m, 1H), 3.89–3.87 (m, 1H), 3.70 (m, 1H), 3.36–3.30 (m, 1H), 3.21–3.16 (m, 1H), 2.54–2.49 (m, 1H), 2.24 (s, 3H), 1.91–1.86 (m,

1H); ^{13}C{^{1}H}NMR (100 MHz, CDCl$_3$) δ 192.17, 166.90, 155.67, 142.1, 135.1, 134.0, 133.0, 132.4, 131.0, 129.4, 129.1, 129.0, 128.7, 128.1, 127.9, 127.8, 126.8, 82.1, 72.8, 68.1, 52.5, 44.7, 17.8; IR (KBr): 2912, 2859, 1694, 1489, 1440, 1398, 1385, 1098, 1063, 802, 605 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for C$_{24}$H$_{20}$NO$_3$NaSCl 460.0750; found: 460.0742.

10-Bromo-1-phenyl-2-(p-tolylthio)-5,6,7a,8-tetrahydro-3H,9H-benzo[b]pyrrolo[2,1-c][1,4]oxazine-3,9-dione (3k). Yellow solid (70.4 mg, 73%); M.p. = 183–185 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.29 (d, J = 6.8 Hz, 3H), 7.14 (d, J = 5.1 Hz, 2H), 7.03 (s, 2H), 6.94 (d, J = 5.7 Hz, 2H), 6.85 (s, 1H), 4.26–3.23 (m, 1H), 3.89–3.86 (m, 1H), 3.71 (s, 1H), 3.34–3.29 (m, 1H), 3.21–3.15 (m, 1H), 2.56–2.52 (m, 1H), 2.23 (s, 3H), 1.91–1.87 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 186.4, 165.8, 151.8, 142.8, 138.1, 134.2, 132.3, 131.5, 129.7, 129.6, 128.9, 128.2, 127.9, 126.9, 78.9, 68.2, 66.1, 41.0, 38.8, 21.1; IR (KBr): 2960, 2854, 1697, 1492, 1439, 1384, 1339, 1275, 1127, 1097, 1062, 1011, 997, 805, 775, 711, 687 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for C$_{24}$H$_{20}$NO$_3$NaS 504.0245; found: 504.0240.

10-Bromo-1-phenyl-2-(p-tolylthio)-5,6,7a,8-tetrahydro-3H,9H-benzo[b]pyrrolo[2,1-c][1,4]oxazine-3,9-dione (3l). Yellow solid (63.5 mg, 76%); M.p. = 173–175 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.14 (d, J = 7.5 Hz, 2H), 7.07 (d, J = 6.9 Hz, 2H), 6.95 (d, J = 7.4 Hz, 2H), 6.37 (d, J = 10.4 Hz, 1H), 6.33 (d, J = 10.5 Hz, 1H), 4.4–4.21 (m, 1H), 3.77 (s, 1H), 3.46–3.35 (m, 1H), 2.75–2.69 (m, 1H), 2.35–2.31 (m, 1H), 2.23 (s, 3H), 1.85–1.81 (m, 1H), 1.13 (d, J = 5.9 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, CDCl$_3$) δ 194.5, 166.1, 153.7, 142.6, 137.7, 134.0, 133.5, 132.0, 131.9, 129.6, 129.4, 128.6, 128.3, 127.6, 78.7, 72.3, 65.7, 44.6, 41.3, 21.1, 17.9; IR (KBr): 2973, 2900, 2875, 1700, 1635, 1490, 1439, 1385, 1272, 1109, 1045, 1014, 791, 753 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for C$_{25}$H$_{23}$NO$_3$NaS 440.1296; found: 440.1292.

5-Ethyl-1-phenyl-2-(p-tolylthio)-5,6,7a,8-tetrahydro-3H,9H-benzo[b]pyrrolo[2,1-c][1,4]oxazine-3,9-dione (3m). Yellow solid (61.2 mg, 74%); M.p. = 166–169 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.26 (m, 3H), 7.13 (d, J = 7.1 Hz, 2H), 7.00 (d, J = 6.4 Hz, 2H), 6.92 (d, J = 6.9 Hz, 2H), 6.43 (d, J = 9.8 Hz, 1H), 6.23 (d, J = 10.0 Hz, 1H), 4.25–4.15 (m, 1H), 3.85–3.82 (m, 1H), 3.71 (s, 1H), 3.43–3.41 (m, 1H), 2.36–2.32 (m, 1H), 2.22 (s, 3H), 1.85–1.81 (m, 1H), 1.70–1.69 (m, 2H), 0.95 (t, J = 6.5 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, CDCl$_3$) δ 194.2, 167.3, 153.4 (s), 143.9, 137.8, 133.6, 132.1, 131.9, 129.6, 129.2, 128.6, 128.3, 127.3, 79.3, 68.7, 65.8, 51.7, 41.3, 24.7, 21.1, 11.0; IR (KBr): 3053, 2965, 2917, 2875, 1706, 1685, 1490, 1384, 1318, 1269, 1118, 1077, 1044, 1032, 1010, 809, 764, 678, 703 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for C$_{26}$H$_{25}$NO$_3$NaS 454.1453; found: 454.1446.

1,6-Diphenyl-2-(p-tolylthio)-5,6,7a,8-tetrahydro-3H,9H-benzo[b] pyrrolo[2,1-c][1,4]oxazine-3,9-dione (3n). Yellow solid (70.9 mg, 74%); M.p. = 90–93 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.32 (d, J = 5.1 Hz, 10H), 7.21 (d, J = 6.4 Hz, 1H), 7.15 (s, 2H), 7.00 (s, 1H), 6.46 (s, 2H), 4.48–4.39 (m, 2H), 4.00 (s, 1H), 3.03–2.93 (m, 1H), 2.49–2.45 (m, 1H), 2.27 (s, 3H), 1.96–1.92 (m, 1H); ^{13}C{^{1}H}NMR (100 MHz, CDCl$_3$) δ 194.4, 166.1, 153.4, 142.6, 137.9, 137.5, 134.2, 133.7, 132.0, 131.9, 129.7, 129.5, 128.7, 128.6, 128.4, 128.3, 127.4, 125.8, 79.0, 77.7, 65.7, 44.9, 41.3, 21.2; IR (KBr): 2919, 2854, 1686, 1493, 1392, 1063, 1013, 752,

698 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for C$_{30}$H$_{25}$NO$_3$NaS 502.1453; found: 502.1453.

2-((4-Chlorophenyl)thio)-1-phenyl-5,6,7a,8-tetrahydro-3H,9H-benzo[b]pyrrolo[2,1-c][1,4]oxazine-3,9-dione (3o). Yellow solid (56.8 mg, 67%); M.p. = 176–179 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.44–7.24 (m, 4H), 7.15 (s, 2H), 7.11 (s, 2H), 7.06 (d, J = 6.1 Hz, 2H), 6.36 (s, 2H), 4.23–4.21 (m, 1H), 3.87–3.84 (m, 1H), 3.71 (s, 1H), 3.33–3.28 (m 1H), 3.16–3.10 (m, 1H), 2.34–2.31 (m, 1H), 1.85–1.80 (m, 1H). ^{13}C{^{1}H}NMR (100 MHz, CDCl$_3$) δ 194.1, 165.8, 154.7, 142.2, 134.2, 133.8, 132.9, 132.8, 131.7, 129.8, 129.7, 129.0, 128.8, 128.2, 79.0, 66.4, 66.1, 41.2, 38.8; IR (KBr): 3062, 2927, 2853, 1689, 1475, 1401, 1383, 1105, 1069, 1013, 818, 755, 698, 660 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for C$_{23}$H$_{18}$NO$_3$NaSCl 446.0594; found: 446.0584.

2-(Naphthalen-2-ylthio)-1-phenyl-5,6,7a,8-tetrahydro-3H,9H-benzo[b]pyrrolo[2,1-c][1,4]oxazine-3,9-dione (3p). Yellow solid (63.3 mg, 72%); M.p. = 167–169 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.73 (s, 2H), 7.64 (s, 2H), 7.43 (s, 2H), 7.32 (s, 1H), 7.20 (s, 3H), 7.09 (s, 2H), 6.40 (s, 2H), 4.26 (m, 1H), 3.88 (m, 1H), 3.76 (s, 1H), 3.34 (m, 1H), 3.15 (m, 1H), 2.35 (m, 1H), 1.83 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$) δ 194.3, 166.1, 154.5, 142.5, 134.1, 133.3, 132.4, 131.8, 131.0, 129.5, 128.6, 128.5, 128.2, 127.6, 127.4, 126.5, 126.4, 79.1, 66.4, 66.2, 41.3, 38.8; IR (KBr): 2327, 2313, 1712, 1679, 1384, 1098, 1065, 1010, 824, 752, 703 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for C$_{27}$H$_{21}$NO$_3$NaS 462.1104; found: 462.1135.

2-((3-Methylfuran-2-yl)thio)-1-phenyl-5,6,7a,8-tetrahydro-3H,9H-benzo[b]pyrrolo[2,1-c][1,4]oxazine-3,9-dione (3r). Yellow solid (29.9 mg, 38%); M.p. = 161–163 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.35–7.26 (m, 3H), 7.03 (d, J = 6.6 Hz, 3H), 6.36–6.24 (m, 2H), 6.18–6.10 (m, 1H), 4.28–4.25 (d, J = 13.3 Hz, 1H), 3.90–3.87 (m, 1H), 3.74–3.69 (m, 1H), 3.37–3.31 (m, 1H), 3.18–3.11 (m, 1H), 2.34–2.30 (m, 1H), 2.12 (s, 3H), 1.83–1.78 (m, 1H). ^{13}C{^{1}H}NMR (100 MHz, CDCl$_3$) δ 194.3, 166.2, 156.1, 150.8, 142.6, 140.4, 133.9, 133.6, 131.7, 129.3, 128.5, 128.1, 115.2, 105.1, 78.9, 66.2, 66.1, 41.3, 38.7, 11.8; IR (KBr): 2925, 2865, 2322, 1690, 1384, 1275, 1179, 1275, 1179, 1095, 1052, 801, 754, 707 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for C$_{22}$H$_{19}$NO$_3$NaS 416.0932; found: 416.0934.

2-(Ethylthio)-1-phenyl-5,6,7a,8-tetrahydro-3H,9H-benzo[b] pyrrolo[2,1-c][1,4]oxazine-3,9-dione (3s). Yellow solid (3.4 mg, 5%); M.p. = 106–109 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.40 (d, J = 1.7 Hz, 3H), 7.18 (m, 2H), 6.37 (s, 2H), 4.30 (m, 1H), 3.91 (m, 1H), 3.71 (s, 1H), 3.35 (m, 1H), 3.17 (m, 1H), 2.99 (m, 2H), 2.36 (m, 1H), 1.87 (m, 1H), 1.16 (t, J = 6.1 Hz, 3H); ^{13}C{^{1}H}NMR (100 MHz, CDCl$_3$) δ 194.4, 151.1, 142.8, 133.9, 133.3, 132.5, 129.6, 128.9, 128.3, 79.2, 66.1, 66.0, 41.3, 38.6, 25.1, 15.1; IR (KBr): 2968, 2920, 2319, 1689, 1385, 1098, 1070, 848, 766, 728, 710 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for C$_{19}$H$_{19}$NO$_3$NaS 364.0983; found: 364.0988.

1-Phenyl-2-(phenylselanyl)-5,6,7a,8-tetrahydro-3H,9H-benzo[b] pyrrolo[2,1-c][1,4]oxazine-3,9-dione (3t). Yellow solid (54.1 mg, 62%); M.p. = 155–158 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.32 (d, J = 6.8 Hz, 2H), 7.27 (d, J = 6.6 Hz, 1H), 7.23 (d, J = 6.9 Hz, 2H), 7.14 (d, J = 6.5 Hz, 1H), 7.08 (d, J = 6.9 Hz, 2H), 7.00 (d, J = 6.5 Hz, 2H), 6.47–6.19 (m, 2H), 4.28–4.24 (m, 1H), 3.88–3.85 (m, 1H), 3.72 (s, 1H), 3.35–3.30 (m, 1H), 3.18–3.11 (m, 1H),

2.34–2.29 (m, 1H), 1.83–1.78 (m, 1H); $^{13}C\{^{1}H\}$NMR (100 MHz, CDCl$_3$) δ 194.3, 167.0, 156.2, 142.5, 134.0, 133.9, 132.5, 129.4, 129.0, 128.7, 128.0, 127.9, 126.9, 78.9, 67.4, 66.2, 41.2, 38.9; IR (KBr): 1712, 1698, 1385, 1093, 1060, 742, 656 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for C$_{23}$H$_{19}$NO$_3$NaSe 460.0428; found: 460.0427.

1-Phenyl-2-(*p*-tolylthio)-6,7,8a,9-tetrahydro-3*H*,5*H*,10*H*-benzo[*b*] pyrrolo[2,1-*c*][1,4]oxazepine-3,10-dione (3u). Yellow solid (8.4 mg, 10%); M.p. = 154–158 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.35–7.25 (m, 3H), 7.15 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 6.9 Hz, 2H), 6.95 (d, J = 7.9 Hz, 2H), 6.41–6.39 (m, 1H), 6.35–6.32 (m, 1H), 4.21–4.18 (m, 2H), 3.78 (d, J = 2.3 Hz, 1H), 3.52–3.45 (m, 1H), 3.23–3.16 (m, 1H), 2.38–2.33 (m, 1H), 2.25 (s, 3H), 2.11–2.02 (m, 1H), 1.94–1.85 (m, 1H), 1.78–1.72 (m, 1H). $^{13}C\{^{1}H\}$NMR (100 MHz, CDCl$_3$) δ 194.6, 167.4, 153.4, 143.2, 137.8, 134.5, 132.6, 132.0, 129.6, 129.4, 128.7, 128.1, 127.6, 85.8, 71.6, 70.3, 42.7, 37.4, 27.1, 21.1; IR (KBr): 2946, 1695, 1682, 1492, 1433, 1405, 1338, 1308, 1193, 1107, 1013, 950, 811, 747, 624, 652 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for C$_{25}$H$_{23}$NO$_3$NaS 440.1296; found: 440.1298.

1-Phenyl-2-(*p*-tolylthio)-7-tosyl-6,7,7a,8-tetrahydro-3*H*-pyrrolo [1,2-*d*]quinoxaline-3,9(5*H*)-dione (3v). Yellow solid (40.1 mg, 36%), M.p. = 216–220 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.59 (d, J = 8.0 Hz, 2H), 7.37–7.25 (m, 5H), 7.12 (d, J = 7.8 Hz, 2H), 7.07 (d, J = 7.4 Hz, 2H), 6.94 (d, J = 7.8 Hz, 2H), 6.45 (d, J = 10.1 Hz, 1H), 6.37 (d, J = 10.1 Hz, 1H), 4.37–4.32 (m, 1H), 3.91–3.86 (m, 1H), 3.80–3.70 (m, 1H), 3.51–3.44 (m, 1H), 3.14–3.08 (m, 1H), 2.71–2.66 (m, 1H), 2.46 (s, 3H), 2.24 (s, 3H), 2.05–2.00 (m, 1H). $^{13}C\{^{1}H\}$NMR (100 MHz, CDCl$_3$) δ 193.9, 166.6, 154.2, 144.9, 144.6, 138.0, 135.9, 133.5, 132.9, 132.3, 131.1, 130.3, 129.6, 128.8, 128.2, 126.9, 126.8, 64.2, 57.0, 41.7, 40.5, 37.4, 21.7, 21.1; IR (KBr): 2326, 1741, 1641, 1385, 1170, 1166, 1093, 818, 665 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for C$_{31}$H$_{28}$N$_2$-O$_4$NaS$_2$ 579.1388; found: 579.1392.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

Notes and references

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