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Article

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Elemental Sulfur-Incorporated Cyclizations of Pyrrolidines Leading to Thienopyrroles

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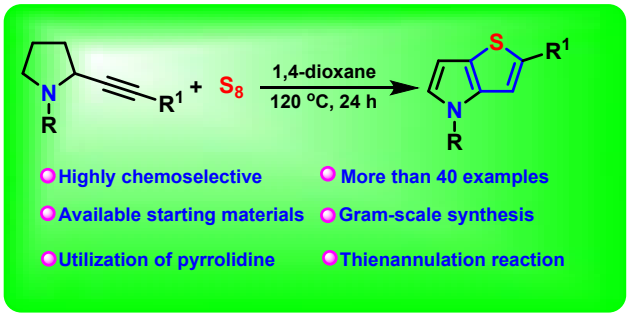


Abstract: We report, herein, the synthesis of thieno[3,2-*b*]pyrroles from the direct oxidative [4+1] cyclization of 2-alkynyl pyrrolidines with elemental sulfur. This transformation likely originates from electrophilic attack at the β-position of pyrrolidine followed by an intramolecular thienannulation to deliver the desired product. Mechanistic investigation suggests that the present reaction involves the formation of dihydrothieno[3,2-*b*]pyrrole as an intermediate.

Keywords: thieno[3,2-*b*]pyrrole, elemental sulfur, oxidative annulation, thienannulation reaction.

INTRODUCTION

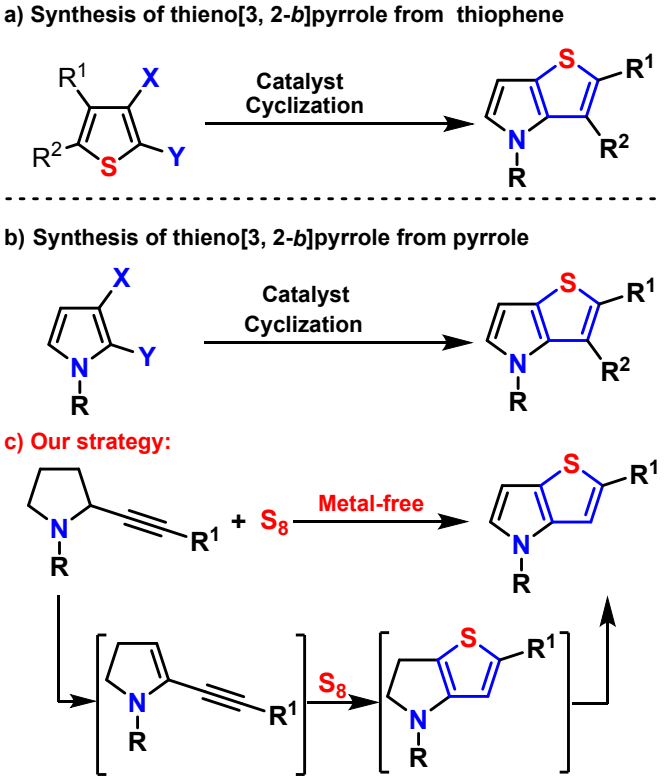
Thienopyrroles are molecules that contain thiophene and pyrrole rings and are used as structural cores for important components of natural products, organic optoelectronic

materials, agrochemicals and pharmaceuticals.[1] Of particular interest are thieno[3,2-*b*]pyrrole-based anti-inflammatory agents, immunomodulators, and bioisosteric analogues of hallucinogens, due to their inhibitory effects on MCP-1. Hence, there has been great interest in developing new strategies for the synthesis of thieno[3,2-*b*]pyrrole in the past few decades.[2] In particular, research has been focused on synthesizing thieno[3,2-*b*]pyrroles *via* the direct functionalization of the thiophene ring (Scheme **1a**).[3-6] Despite considerable advances, this approach has suffered from harsh reaction conditions and low yields for the desired product. Furthermore, it requires the utilization of a multistep process and the construction of a special substrate. An alternative route is the elemental sulfur-incorporated annulate functionalization of the pyrrole ring (Scheme **1b**). However, the synthesis of thieno[3,2-*b*]pyrrole *via* the latter route remains to be explored. Direct functionalization of pyrrole rings for thieno[3,2-*b*]pyrrole synthesis is challenging since the electron-rich and relatively low-aromatic pyrrole rings can lead to multiple side reactions and increase the reaction complexity under oxidative conditions. Consequently, the development of effective methods to synthesize thieno[3,2-*b*]pyrroles remains highly demanding.

We hypothesize that the utilization of pyrrolidine as an initial skeleton can be used to overcome the above limitation (Scheme **1c**). Recent work has shown that α-alkyne functionalized pyrrolidines can be easily obtained from widely accessible proline.[7] Furthermore, elemental sulfur is a promising oxidant and electrophile owing to its numerous oxidation states.[8] Motivated by these promising advancements in the

synthesis of S-containing compounds,[9-18] we explored the possibility of synthesizing thieno[3,2-*b*]pyrroles by incorporating elemental sulfur and pyrrolidine. The first step involved the synthesis of thiophene *via* oxidative annulation using elemental sulfur as the oxidant. After the thienannulation reaction, further dehydrogenative aromatization delivers the final product. In this route, elemental sulfur not only serves as an electrophile but also functions as an oxidant.

Scheme 1. The Different Strategies Used for the Synthesis of Thieno[3,2-*b*]pyrroles.

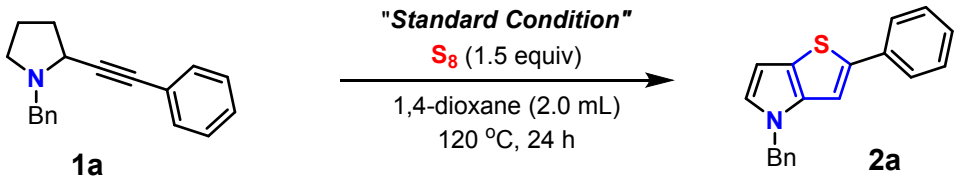


RESULTS AND DISCUSSION

To verify our hypothesis, we first focused on the synthesis of thieno[3,2-*b*]pyrrole from 1-benzyl-2-(phenylethynyl)-pyrrolidine (**1a**) and elemental sulfur. After considerable efforts, the cyclization was achieved by heating the mixture of **1a** and S_8 in 1,4-dioxane at 120 °C for 24 hours. The desired product **2a** was obtained in 74%

yield (Table 1, entry 1). When the base was added, a lower yield for the product was observed (Table 1, entry 2). No other additives were required. Both the reaction temperature and reaction time were found to have a crucial effect on the formation of **2a** (Table 1, entries 3-4). Increasing the reaction time and temperature led to the positive results. Thus, decreasing the amount of elemental sulfur in 1,4-dioxane (2 mL) resulted in dramatically decreased yield for **2a** (Table 1, entry 5). However, using a lower amount of dioxane and elemental sulfur, the final product was obtained in 62%-78% yields (Table 1, entries 6 and 7). In addition, using nonpolar solvents under similar conditions resulted in trace to moderate yields (Table 1, entries 8 and 9). Meanwhile, relatively lower yields were observed in DMF, pyridine, and *N*-methylpiperidine (Table 1, entry 10). Interestingly, when *N*-methylmorpholine was used instead of 1, 4-dioxane, the reaction proceeded smoothly to afford the desired product **2a** in 85% yield (Table 1, entry 11). When 1-benzyl-2-(phenylethynyl)-pyrrolidine (**1a**) was exposed to air, the corresponding product **2a** resulted in a moderate yield (Table 1, entry 12) as 1-benzyl-2-(phenylethynyl)-pyrrolidine (**1a**) was easy to decompose in air. The optimized condition can be summarized as follows: **1a** (0.30 mmol), $\mathbf{S_8}$ (0.45 mmol), *N*-methylmorpholine (2.0 mL), 120 °C, 24 h under N_2 atmosphere.

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



1a **2a**

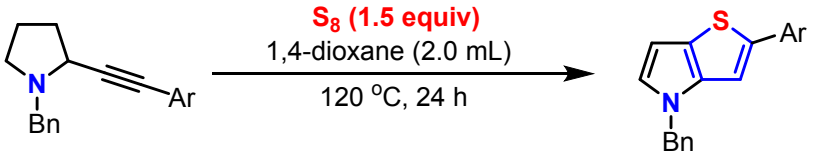
entry	variation from the standard condition	yield (%)
1	none	74
2	K_2CO_3, NaO^tBu were added	0, 7
3	100 °C,110 °C instead of 120 °C	17, 30
4	36 h at 100 °C, 110 °C, 120 °C	64, 64, 63
5	S_8 (0.50, 1.0 equiv) in 1,4-dioxane (2.0 mL)	41, 43
6	S_8 (0.75 equiv) in 1,4-dioxane (1.0, 1.5 mL)	62, 78
7	S_8 (1.0 equiv) in 1,4-dioxane (1.0 mL)	73
8	THF, Toluene, DME and Anisole instead of 1,4-dioxane	55, 37, 57, trace
9	*tert*-Butyl methyl ether, tetraethylene glycol dimethyl ether instead of 1,4-dioxane	trace, trace
10	DMF, Pyridine, N-methylpiperidine and instead of 1,4-dioxane	53, trace, trace
11	N-methylmorpholine instead of 1,4-dioxane	85
12	in air	48

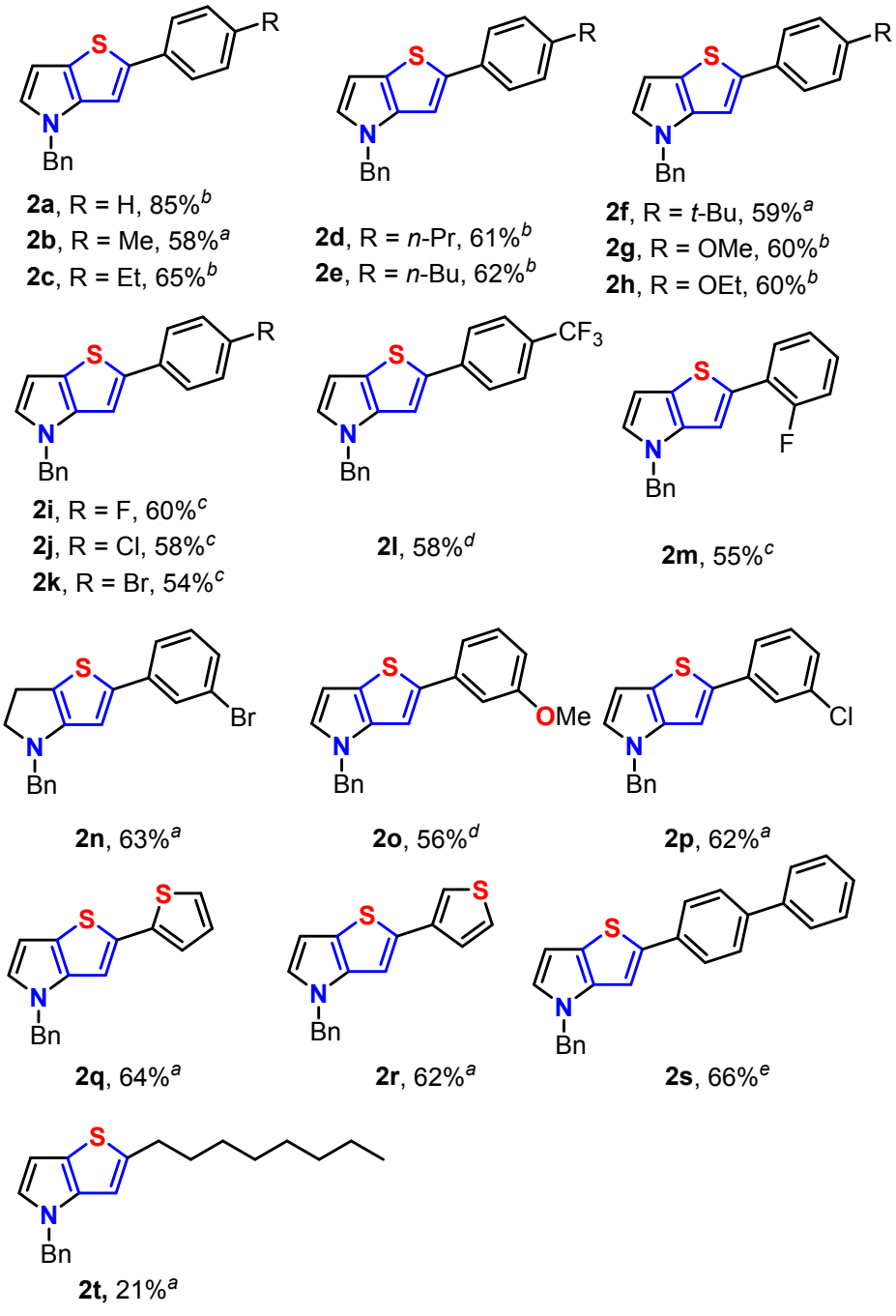
[a] Standard conditions: **1a** (0.30 mmol), S_8 (1.5 equiv), 1,4-dioxane (2.0 mL), N_2, 120 °C, 24 h.

With the optimum conditions identified, we investigated the substrate scope for this oxidative cyclization by elemental sulfur to construct thieno[3,2-*b*]pyrrole derivatives (Scheme 2). During the process of condition optimization, we have found that N-methylmorpholine was the best solvent for the elemental sulfur incorporated cyclization of 1-benzyl-2-(phenylethynyl)pyrrolidine (**1a**), 1-benzyl-2-((4-methoxyphenyl)ethynyl)pyrrolidine (**1g**) and 1-benzyl-2-((4-ethoxyphenyl)ethynyl)pyrrolidine (**1h**). Then, 1,4-dioxane was found

to be more efficient than *N*-methylmorpholine in the synthesis of other thienopyrroles. A series of electron-donating pyrrolidines in the 4-position of the benzene ring were found to be compatible with oxidative cyclization, providing the corresponding products in 54-82% yields (**2a**-**2h**). The structures of **2b** and **2h** were unambiguously confirmed by single-crystal X-ray diffraction analysis.[19] Substitution on the 4-position of the benzene ring, such as fluoro, chloro, bromo, and trifluoromethyl groups, under the optimum conditions identified above led to the generation of the final products in good yields (**2i**-**2l**). When an *ortho* substituent was introduced to the elemental sulfur incorporating the pyrrolidine ring, the reaction proceeded smoothly to afford the desired product in 55% yield (**2m**). Excitingly, when **1n** was subjected to optimized conditions, 4-benzyl-2-(3-bromophenyl)-5,6-dihydro-4*H*-thieno[3,2-*b*]pyrrole (**2n**) was obtained in 63% yield. Other *meta* substituents were found to completely convert to the desired thieno[3,2-*b*]pyrroles (**2o** and **2p**). Additionally, thiophene-substituted substrates could be installed without decreasing the final product yield (**2q** and **2r**). Furthermore, a biphenyl-substituted substrate was also found to be amenable to this transformation, which resulted in a 66% yield (**2s**). Finally, 1-benzyl-2-(dec-1-yn-1-yl)pyrrolidine was evaluated under the optimized condition, providing the desired products in 21% yield (**2t**). Overall, little adjustments to the reaction conditions were necessary to deliver the desired thieno[3,2-*b*]pyrroles in good yields.

Scheme 2. Scope for 1-Benzyl-2-(phenylethynyl)pyrrolidine Derivatives.[a]





[a] Reaction conditions: **1** (0.30 mmol), S_8 (1.5 equiv), 1,4-dioxane (2.0 mL), N_2, 120 °C, 24 h.

[b] S_8 (1.5 equiv), *N*-methylmorpholine (2.0 mL).

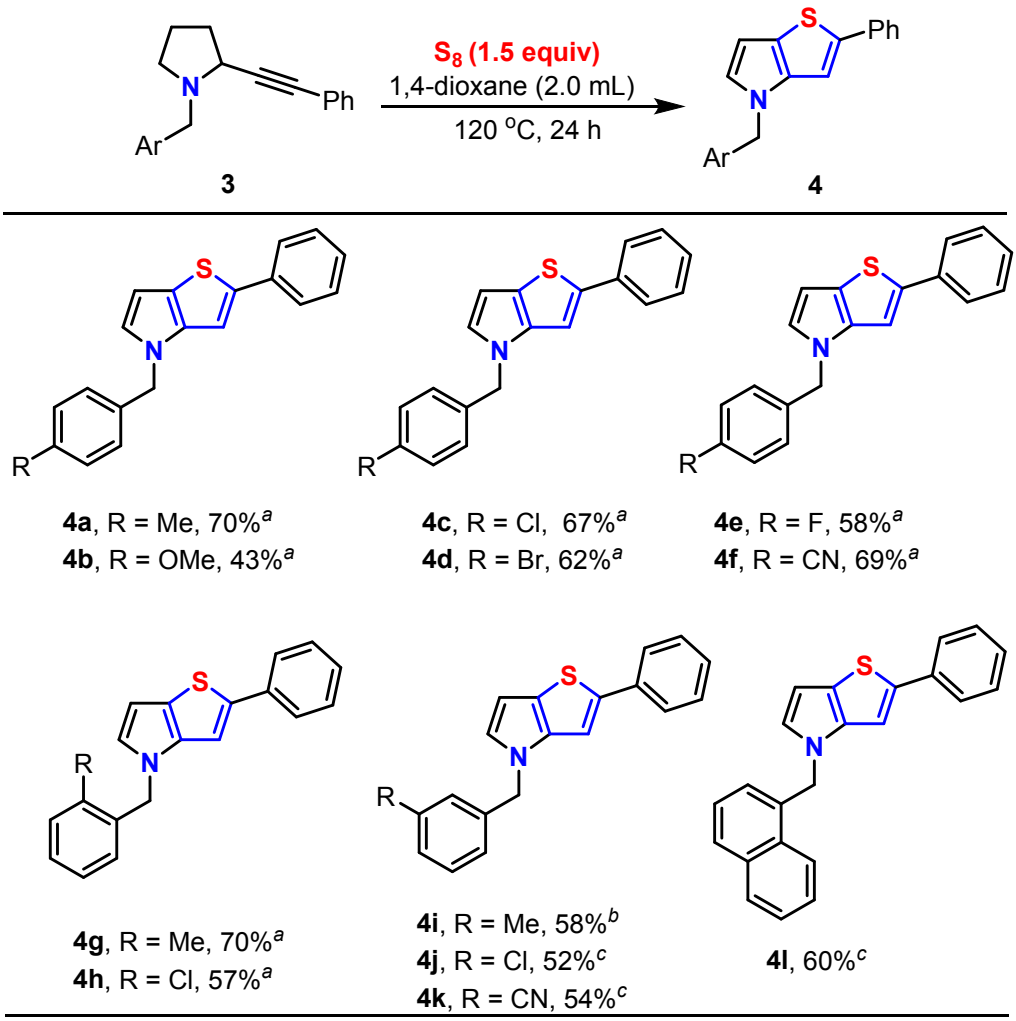
[c] S_8 (1.0 equiv), 1,4-dioxane (1.0 mL).

[d] 115 °C, 24 h.

[e] 120 °C, 36 h.

After synthesizing thieno[3,2-*b*]pyrroles, we turned our efforts towards exploring the effect of an *N*-substituent at the benzene ring (Scheme 3). Pyrrolidines with either electron-donating groups (4-Me and 4-OMe) or electron-withdrawing groups (4-F, 4-Cl, 4-Br and 4-CN) were found to react smoothly with elemental sulfur to deliver the corresponding thieno[3,2-*b*]pyrroles in 43-70% yields (**4a-4f**). Notably, N-substituents at the 3-position of the benzene ring were found to be suitable for oxidative cyclization, affording the final products in 70% and 57% yields, respectively (**4g** and **4h**). Meanwhile, a range of *N*-benzyl pyrrolidines bearing different substituents at the *meta*-position of the phenyl ring were well tolerated, which provided various products in good yields (**4i-4k**). In addition, this oxidative cyclization was also found to proceed successfully with a pyrrolidine bearing naphthalene group, leading to the desired product in 60% yield (**4l**).

Scheme 3. Scope for 1-Benzyl-2-(phenylethynyl)pyrrolidine Derivatives.[a]



[a] Reaction conditions: **3** (0.30 mmol), S_8 (1.5 equiv), 1,4-dioxane (2.0 mL), N_2, 120 °C, 24 h.

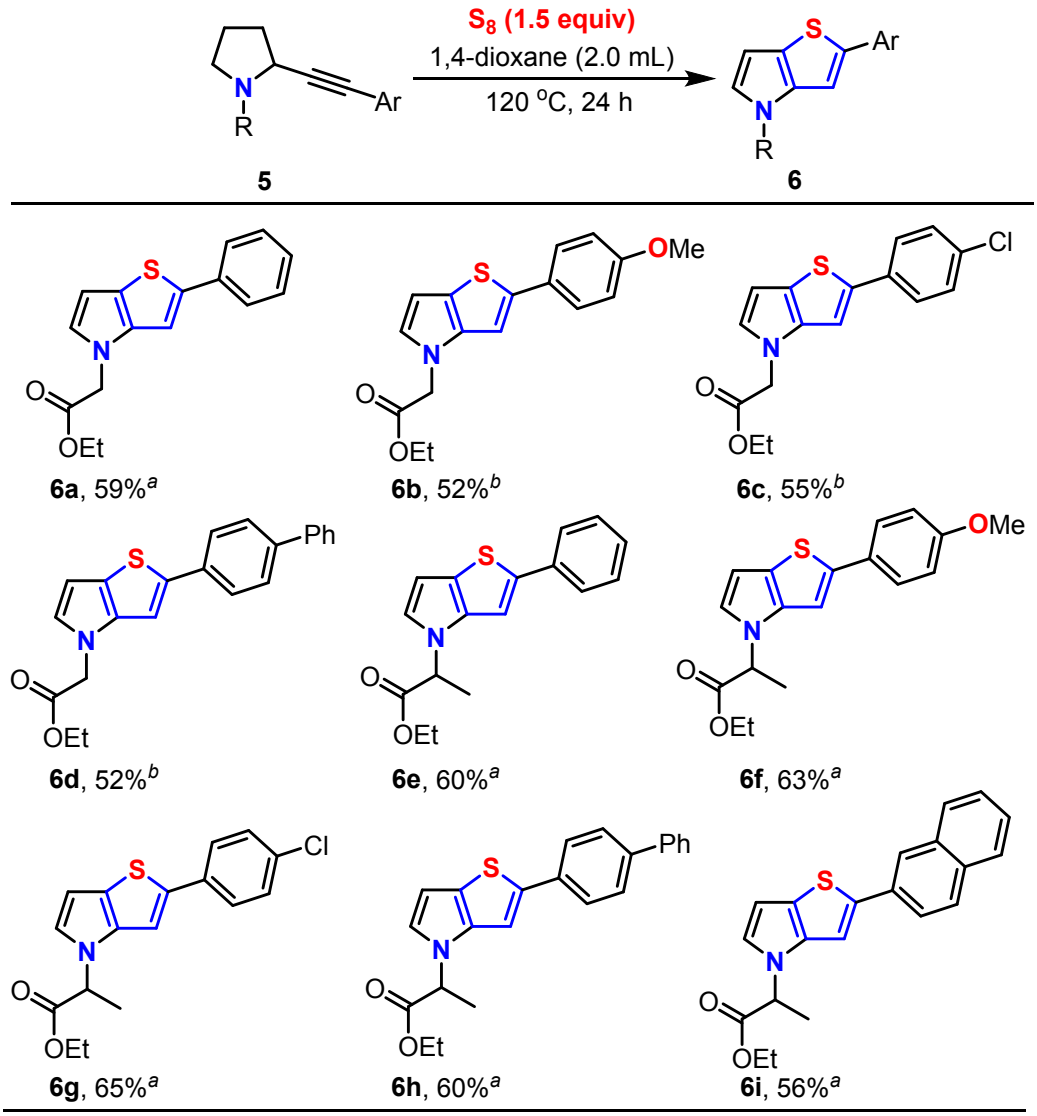
[b] S_8 (1.5 equiv), *N*-methylmorpholine (2.0 mL).

[c] S_8 (1.0 equiv), 1,4-dioxane (1.0 mL).

Encouraged by these results, we next aimed to expand the scope for *N*-substituent pyrrolidines bearing an ethyl acetate group (Scheme 4). A variety of *N*-substituent pyrrolidines bearing an ethyl acetate group were successfully utilized to perform the oxidative cyclization of aliphatic amine, forming the corresponding products in good yields (**6a-6d**). Furthermore, the reaction with ethyl 2-(2-phenyl-4*H*-thieno[3,2-*b*]pyrrol-4-yl)propanoates bearing electron-donating and

electron-withdrawing groups proceeded smoothly to generate the targeted products in 56%-65% yields (**6e**-**6i**).

Scheme 4. Scope for 1-Benzyl-2-(phenylethynyl)pyrrolidine Derivatives.[a]

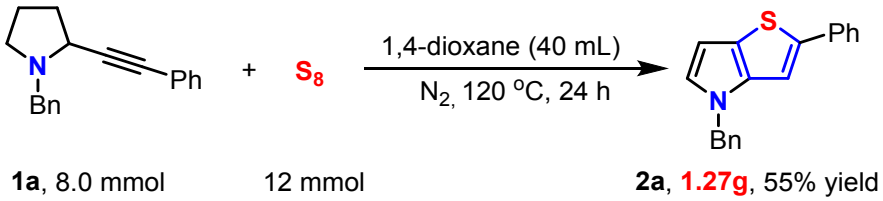


[a] Reaction conditions: **5** (0.30 mmol), $\mathbf{S_8}$ (1.0 equiv), 1,4-dioxane (1.0 mL), N_2, 120 °C, 24 h.

[b] $\mathbf{S_8}$ (1.5 equiv), *N*-methylmorpholine (2.0 mL).

To explore the practicality of this strategy, a gram-scale experiment was carried out (Scheme 5). The desired product was obtained in 55% yield, which demonstrated that this protocol was also readily scalable and practical.

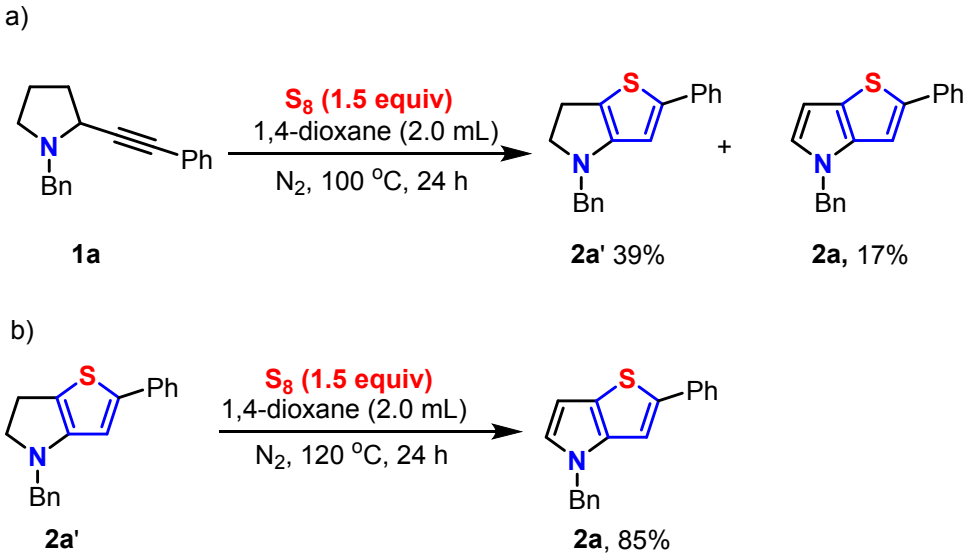
Scheme 5. Gram-Scale Experiment.



1a, 8.0 mmol 12 mmol **2a**, 1.27g, 55% yield

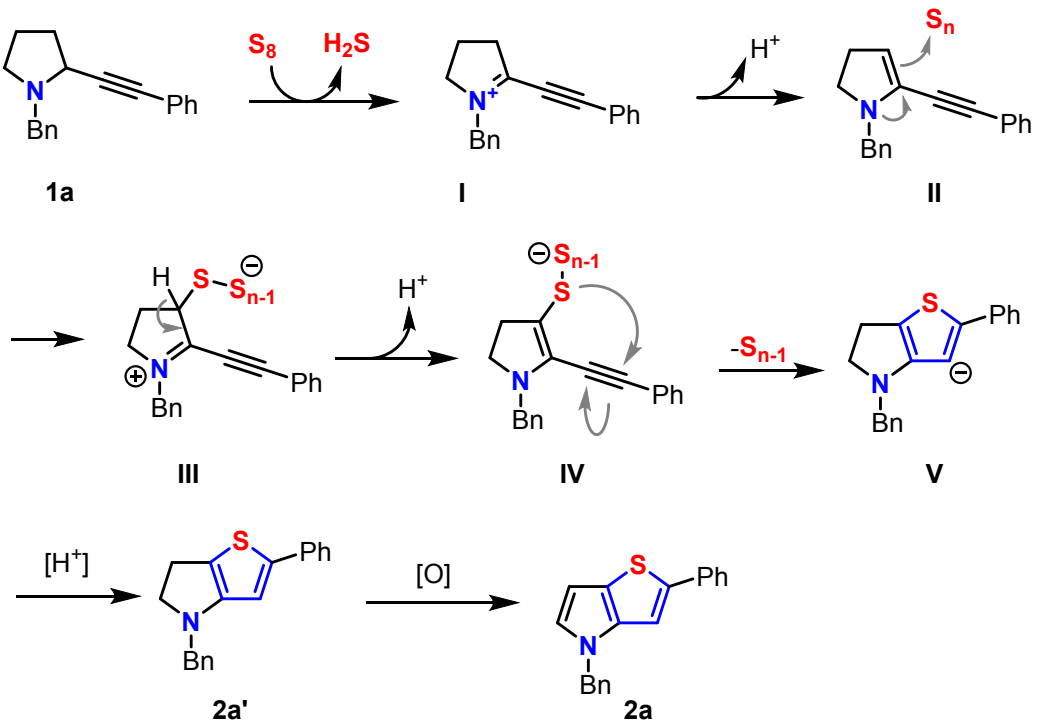
To better understand the mechanism for the functionalization of pyrrolidine, some control experiments were performed (Scheme 6). An EPR experiment for the thienannulation reaction was conducted under the optimized condition, with no EPR signal observed (see SI for more details). This result indicated that a free radical process may not be involved in the present thienannulation reaction of aliphatic amine. When the thienannulation reaction of 1-benzyl-2-(phenylethynyl)pyrrolidine (**1a**) was carried out at 110 °C for 24 h, 4-benzyl-2-phenyl-5,6-dihydro-4*H*-thieno[3,2-*b*]pyrrole (**2a'**) was unexpectedly observed in 39% yield (Scheme **6a**). Then, **2a'** was subjected to the standard condition, and the targeted product was obtained in 85% yield (Scheme **6b**). This result demonstrated that **2a'** was most likely the intermediate of this transformation.

Scheme 6. Control Experiments.



Based on the results of this work, a plausible pathway is proposed (Scheme 7). Initially, **1a** undergoes oxidation to form the intermediate **I**, followed by the loss of H^+ to give the intermediate **II**. Electrophilic sulfuration of intermediate **II** generated intermediate **III**. The cation at the β-position of pyrrolidine is easily stabilized by the conjugation of the propargylic group. Subsequently, intermediate **III** undergoes H^+ elimination to afford the common intermediate **IV**. A nucleophilic attack of the sulfur anion on the alkynyl group easily occurs, leading to intermediate **V**, furnished by the elimination of elemental sulfur ($\mathbf{S_{n-1}}$). After the protonation and aromatization, the final product **2a** is released.

Scheme 7. Possible Reaction Mechanism.



CONCLUSION

In summary, we have reported a new strategy for the synthesis of thieno[3,2-*b*]pyrroles *via* elemental sulfur incorporated pyrrolidine rings. The reaction occurs at the β-position of pyrrolidine to deliver the desired product, which is furnished by the electrophilic attack of elemental sulfur and an intramolecular cyclization reaction. We also demonstrated that this transformation can be extended to explore the functionalization of pyrrolidine with various substrates and shows good reaction efficiency on the gram scale. Notably, the utilization of elemental-promoted oxidative cyclization of pyrrolidine can provide valuable information for the further design of S-containing compounds.

EXPERIMENTAL SECTION

General Information. All the solvents and other reagents were purchased from commercial suppliers without further purification. All reactions were performed in N_2 atmosphere. The substituted pyrrolidines **1**, **3** and **5** were prepared in accordance with the reported literature.[7] ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded using a Bruker Avance/600 (^1H: 600 MHz, $^{13}C\{^1H\}$: 150 MHz at 25 ºC) or Bruker Avance/400 (^1H: 400 MHz, $^{13}C\{^1H\}$: 100 MHz at 25 ºC) and TMS as internal standard. ^1H and ^{19}F NMR multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), quartet (q), multiplet (m), and broad resonance (br). All high-resolution mass spectra (HRMS) were measured with a mass spectrometer by using electrospray ionization (ESI-oa-TOF). Melting points were measured by a melting point apparatus equipped with a thermometer and used uncorrected. All reactions were monitored by thin-layer chromatography (TLC) through GF254 silica gel-coated plates. Flash chromatography was conducted on silica gel (200-300 mesh, purchased from Sinopharm Chemical Reagent Co., Ltd). Di-*tert*-butyl peroxide (97%) was purchased from Sinopharm Chemical Reagent Co., Ltd.

General procedure for the synthesis of substituted pyrrolidines (1, **3** and **5):**

General procedure (A):[7a] CuBr (0.045 mmol, 6.5 mg) was added to a solution of *N,N,N′,N′*-tetramethylethylenediamine (13.5 μL, 0.09 mmol) in toluene (2.0 mL). The mixture was then stirred for 10 min under N_2 atmosphere. Next, benzylproline (61.6 mg, 0.30 mmol), ethynylbenzene (49.4 μL, 0.45 mmol) and *tert*-butyl peroxide (77.2 μL, 0.42 mmol) were injected into a Schlenk tube with a syringe under N_2 atmosphere. The contents of the Schlenk tube were then allowed to stir at 110 °C by

using a heating mantle for 12 h followed by cooling to room temperature. The reaction mixture was diluted with ethyl acetate and filtered through a short florisil column eluting with ethyl acetate. The residue was concentrated under *vacuum*, purified by chromatography on silica gel and then eluted with petroleum ether/ethyl acetate as an eluent to obtain the desired product **1a**.

General procedure (B):[7b] (4-methylbenzyl)proline (65.8 mg, 0.30 mmol), ethynylbenzene (65.9 μL, 0.60 mmol) and $Cu_2(OH)_2CO_3$ (6.6 mg, 0.03 mmol) were mixed in a 25 mL flame-dried Schlenk tube equipped with a stir bar and then the tube was sealed. Next, the Schlenk tube was purged three times with N_2. Then, toluene (2.0 mL) and DBU (134.5 μL, 0.90 mmol) was injected into the Schlenk tube with a syringe under N_2 atmosphere. The contents of the Schlenk tube were then allowed to stir at 110 °C with a heating mantle for 24 h followed by cooling to room temperature. The reaction mixture was then diluted with ethyl acetate and filtered through a short florisil column eluting with ethyl acetate. Next, the residue was concentrated under *vacuum*, purified by chromatography on silica gel and then eluted with petroleum ether/ethyl acetate as an eluent to obtain the desired product **3a**.

General procedure (C):[7c] *L*-proline (51.8 mg, 0.45 mmol), and CuBr (6.5 mg, 0.045 mmol) were mixed in a 25 mL flame-dried Schlenk tube equipped with a stir bar and then the tube was sealed. Next, the Schlenk tube was purged three times with N_2. Then, ethyl glyoxalate (41.6 μL, 0.42 mmol), *N,N*-diisopropylethylamine (14.9 μL, 0.09 mmol) ethynylbenzene (33.0 μL, 0.30 mmol) and toluene (1.5 mL) were injected into the Schlenk tube with a syringe under N_2 atmosphere. The contents of the

Schlenk tube were then allowed to stir at 110 °C by using a heating mantle for 12 h followed by cooling to room temperature. Next, the reaction mixture was diluted with ethyl acetate and filtered through a short florisil column eluting with ethyl acetate. The residue was concentrated under *vacuum*, purified by chromatography on silica gel and then eluted with petroleum ether/ethyl acetate as an eluent to obtain the desired product **5a**.

1-Benzyl-2-(phenylethynyl)pyrrolidine (1a). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 54.8 mg, 70% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (q, J = 4.0 Hz, 2H), 7.39 (dd, J = 8.0, 1.2 Hz, 2H), 7.33-7.28 (m, 5H), 7.26-7.22 (m, 1H), 4.06 (d, J = 16.0 Hz, 1H), 3.63-3.58 (m, 2H), 2.81-2.75 (m, 1H), 2.57-2.51 (m, 1H), 2.21-2.12 (m, 1H), 2.07-1.76 (m, 3H). ESI-MS (M): 261.

1-Benzyl-2-(p-tolylethynyl)pyrrolidine (1b). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 51.9 mg, 63% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (dd, J = 8.0, 1.4 Hz 2H), 7.36-7.29 (m, 4H), 7.26-7.22 (m, 1H), 7.11 (d, J = 8.0 Hz, 2H), 4.07 (d, J = 12.0 Hz, 1H), 3.63-3.58 (m, 2H), 2.81-2.75 (m, 1H), 2.58-2.52 (m, 1H), 2.34 (s, 3H), 2.19-2.12 (m, 1H), 2.05-1.88 (m, 2H), 1.83-1.76 (m, 1H). ESI-MS (M): 275.

1-Benzyl-2-((4-ethylphenyl)ethynyl)pyrrolidine (1c). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 50.3 mg, 58% yield. ^{1}H NMR (400 MHz,

$CDCl_3$) δ 7.41-7.38 (m, 4H), 7.33 (td, J = 8.0, 4.0 Hz, 2H), 7.27 (t, J = 2.0 Hz, 1H), 7.15 (dd, J = 8.0, 4.0 Hz, 2H), 4.08 (d, J = 12.0 Hz, 1H), 3.63-3.58 (m, 2H), 2.82-2.76 (m, 1H), 2.66 (q, J = 8.0 Hz, 2H), 2.58-2.52 (m, 1H), 2.20-2.13 (m, 1H), 2.08-1.89 (m, 2H), 1.86-1.77 (m, 1H), 1.24 (t, J = 6.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 144.3, 138.8, 131.7, 129.3, 128.2, 127.8, 127.0, 120.6, 87.9, 85.1, 57.2, 54.5, 51.5, 31.7, 28.8, 22.0, 15.4. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{21}H_{24}N$ ($M+H^+$): 290.1903; found 290.1903.

1-Benzyl-2-((4-propylphenyl)ethynyl)pyrrolidine (1d). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 50.0 mg, 55% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.42-7.37 (m, 3H), 7.33 (td, J = 8.0, 4.0 Hz, 2H), 7.28-7.23 (m, 2H), 7.13 (d, J = 8.0 Hz, 2H), 4.08 (d, J = 12.0 Hz, 1H), 3.63 (q, J = 6.7 Hz, 2H), 2.82-2.76 (m, 1H), 2.59 (td, J = 8.0, 2.0 Hz, 3H), 2.20-2.13 (m, 1H), 2.06-1.91 (m, 2H), 1.85-1.78 (m, 1H), 1.64 (q, J = 5.3 Hz, 2H), 0.94 (t, J = 8.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 142.8, 138.9, 131.7, 129.3, 128.5, 128.2, 127.0, 120.6, 88.0, 85.1, 57.2, 54.5, 51.5, 38.0, 31.7, 24.4, 22.1, 13.8. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{22}H_{26}N$ ($M+H^+$): 304.2060; found 304.2060.

1-Benzyl-2-((4-butylphenyl)ethynyl)pyrrolidine (1e). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 50.4 mg, 53% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 (td, J = 8.0, 4.0 Hz, 4H), 7.21 (td, J = 8.0, 4.0 Hz, 2H), 7.13 (t, J = 8.0 Hz, 1H), 7.01 (d, J = 8.0 Hz, 2H), 3.96 (d, J = 12.0 Hz, 1H), 3.52-3.47 (m, 2H),

2.70-2.64 (m, 1H), 2.51-2.40 (m, 3H), 2.08-2.00 (m, 1H), 1.96-1.77 (m, 2H), 1.72-1.65 (m, 1H), 1.50-1.44 (m, 2H), 1.27-1.21 (m, 2H), 0.82 (t, J = 8.0 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 141.9, 137.8, 130.6, 128.2, 127.3, 127.1, 125.9, 119.5, 86.9, 84.1, 56.1, 53.4, 50.4, 34.5, 32.4, 30.6, 21.3, 21.0, 12.9. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{28}N$ ($M+H^+$): 318.2216; found 318.2213.

1-Benzyl-2-((4-(tert-butyl)phenyl)ethynyl)pyrrolidine (1f). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 52.3 mg, 55% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.37 (m, 4H), 7.34-7.29 (m, 4H), 7.25-7.22 (m, 1H), 4.06 (d, J = 12.0 Hz, 1H), 3.62-3.57 (m, 2H), 2.80-2.74 (m, 1H), 2.57-2.51 (m, 1H), 2.20-2.11 (m, 1H), 2.06-1.88 (m, 2H), 1.84-1.75 (m, 1H), 1.31 (s, 9H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 151.2, 138.8, 131.5, 129.3, 128.2, 127.0, 125.3, 120.4, 88.0, 85.1, 57.2, 54.5, 51.5, 34.8, 31.7, 31.2, 22.1. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{28}N$ ($M+H^+$): 318.2216; found 318.2217.

1-Benzyl-2-((4-methoxyphenyl)ethynyl)pyrrolidine (1g). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 52.4 mg, 60% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (dd, J = 8.0, 4.0 Hz, 4H), 7.31 (td, J = 6.0, 4.0 Hz, 2H), 7.24-7.22 (m, 1H), 6.83 (dd, J = 4.0, 4.0 Hz, 2H), 4.07 (d, J = 12.0 Hz, 1H), 3.80 (s, 3H), 3.58 (q, J = 9.3 Hz, 2H), 2.81-2.75 (m, 1H), 2.54-2.48 (m, 1H), 2.20-2.11 (m, 1H), 2.06-1.86 (m, 2H), 1.83-1.73 (m, 1H). ESI-MS (M): 291.

1-Benzyl-2-((4-ethoxyphenyl)ethynyl)pyrrolidine (1h). The title compound was

prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 53.1 mg, 58% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45-7.38 (m, 4H), 7.32 (t, J = 6.0 Hz, 2H), 7.25 (t, J = 6.0 Hz, 1H), 6.83 (dd, J = 6.0, 6.0 Hz, 2H), 4.08-4.01 (m, 3H), 3.61-3.56 (m, 2H), 2.80-2.76 (m, 1H), 2.54-2.50 (m, 1H), 2.19-2.13 (m, 1H), 2.05-1.99 (m, 1H), 1.95-1.89 (m, 1H), 1.83-1.77 (m, 1H), 1.41 (t, J = 9.0 Hz, 3H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 158.8, 134.1, 133.1, 129.3, 128.2, 127.0, 115.4, 114.4, 87.1, 84.9, 63.5, 57.2, 54.6, 51.5, 31.7, 22.0, 14.8. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{21}H_{24}NO$ ($M+H^+$): 306.1852; found 306.1851.

1-Benzyl-2-((4-fluorophenyl)ethynyl)pyrrolidine (1i). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 54.4 mg, 65% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 (t, J = 6.0 Hz, 2H), 7.38 (d, J = 12.0 Hz, 2H), 7.32 (t, J = 6.0 Hz, 2H), 7.25 (d, J = 6.0 Hz, 1H), 7.00 (t, J = 9.0 Hz, 2H), 4.05 (d, J = 12.0 Hz, 1H), 3.61-3.56 (m, 2H), 2.80-2.76 (m, 1H), 2.55-2.51 (m, 1H), 2.18-2.13 (m, 1H), 2.05-1.99 (m, 1H), 1.94-1.89 (m, 1H), 1.83-1.77 (m, 1H). ESI-MS (M): 279.

1-Benzyl-2-((4-chlorophenyl)ethynyl)pyrrolidine (1j). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 53.1 mg, 60% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.47-7.42 (m, 4H), 7.35-7.30 (m, 4H), 7.26-7.22 (m, 1H), 3.94 (d, J = 16.0 Hz, 1H), 3.62-3.54 (m, 2H), 2.66-2.60 (m, 1H), 2.50-2.46 (m, 1H), 2.16-2.07 (m, 1H), 1.92-1.71 (m, 3H); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 139.3, 133.6, 133.5,

129.2, 129.1, 128.6, 127.3, 121.9, 90.8, 83.9, 56.9, 54.3, 51.5, 31.7, 22.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{19}ClN$ ($M+H^+$): 296.1201; found 296.1205.

1-Benzyl-2-((4-bromophenyl)ethynyl)pyrrolidine (1k). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 59.0 mg, 58% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.54 (dt, J = 12.0, 2.0 Hz, 2H), 7.36 (dd, J = 4.0, 4.0 Hz, 2H), 7.32-7.28 (m, 4H), 7.25-7.21 (m, 1H), 3.94 (d, J = 12.0 Hz, 1H), 3.59-3.52 (m, 2H), 2.65-2.59 (m, 1H), 2.49-2.43 (m, 1H), 2.14-2.05 (m, 1H), 1.92-1.82 (m, 1H), 1.81-1.68 (m, 2H); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 139.3, 133.8, 132.1, 129.1, 128.6, 127.3, 122.3, 122.1, 90.9, 84.0, 56.9, 54.3, 51.5, 31.7, 22.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{19}BrN$ ($M+H^+$): 340.0695; found 340.0690.

1-Benzyl-2-((4-(trifluoromethyl)phenyl)ethynyl)pyrrolidine (1l). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 54.3 mg, 55% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56-7.51 (m, 4H), 7.37 (d, J = 8.0 Hz, 2H), 7.31 (td, J = 8.0, 4.0 Hz, 2H), 7.24 (d, J = 4.0 Hz, 1H), 4.04 (d, J = 12.0 Hz, 1H), 3.62-3.58 (m, 2H), 2.81-2.75 (m, 1H), 2.58-2.52 (m, 1H), 2.23-2.13 (m, 1H), 2.07-1.77 (m, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 138.7, 132.0, 129.2, 128.3, 127.2 (d, J = 17.2 Hz), 125.2 (q, J = 4.0 Hz), 91.7, 83.7, 57.3, 54.4, 51.7, 31.6, 22.1. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{19}F_3N$ ($M+H^+$): 330.1464; found 330.1463.

1-Benzyl-2-((2-fluorophenyl)ethynyl)pyrrolidine (1m). The title compound was prepared according to the general procedure (A) and purified by flash column

chromatography to give a yellow liquid, 44.4 mg, 53% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.40 (m, 3H), 7.35-7.27 (m, 4H), 7.12-7.06 (m, 2H), 4.06 (d, J = 12.0 Hz, 1H), 3.69-3.65 (m, 2H), 2.82-2.75 (m, 1H), 2.65-2.59 (m, 1H), 2.23-2.14 (m, 1H), 2.10-1.91 (m, 2H), 1.87-1.79 (m, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.9 (J = 253 Hz), 138.8, 133.6, 129.6 (J = 8.1 Hz), 129.3, 128.2, 127.0, 123.9 (J = 3.0 Hz), 115.5 (J = 21.2 Hz), 112.0 (J = 15.2 Hz), 94.2, 78.4, 57.0, 54.4, 51.4, 31.6, 22.0. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{19}FN$ ($M+H^+$): 280.1496; found 280.1495.

1-Benzyl-2-((3-bromophenyl)ethynyl)pyrrolidine (1n). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 52.9 mg, 52% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (t, J = 2.0 Hz, 1H), 7.42 (dd, J = 8.0, 4.0 Hz, 1H), 7.36 (td, J = 8.0, 4.0 Hz, 3H), 7.31 (td, J = 8.0, 4.0 Hz, 2H), 7.25-7.22 (m, 1H), 7.16 (t, J = 6.0 Hz, 1H), 4.02 (d, J = 12.0 Hz, 1H), 3.59 (q, J = 6.7 Hz, 2H), 2.79-2.73 (m, 1H), 2.58-2.52 (m, 1H), 2.20-2.11 (m, 1H), 2.05-1.76 (m, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 138.7, 134.5, 131.1, 130.3, 129.7, 129.2, 128.3, 127.1, 125.4, 122.1, 90.4, 83.6, 57.3, 54.4, 51.6, 31.6, 22.1. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{19}BrN$ ($M+H^+$): 340.0695; found 340.0694.

1-Benzyl-2-((3-methoxyphenyl)ethynyl)pyrrolidine (1o). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 41.9 mg, 48% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (dd, J = 8.0, 4.0 Hz, 2H), 7.33 (td, J = 6.0, 4.0 Hz, 2H), 7.28-7.27 (m,

1H), 7.25-7.21 (m, 1H), 7.07 (d, J = 8.0 Hz, 1H), 7.00 (d, J = 4.0 Hz, 1H), 6.89-6.86 (m, 1H), 4.08 (d, J = 12.0 Hz, 1H), 3.82 (s, 3H), 3.64-3.59 (m, 2H), 2.83-2.77 (m, 1H), 2.59-2.53 (m, 1H), 2.21-2.14 (m, 1H), 2.09-1.90 (m, 2H), 1.86-1.79 (m, 1H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 159.3, 138.8, 129.3, 129.2, 128.2, 127.0, 124.4, 124.3, 116.7, 114.5, 88.7, 84.9, 57.3, 55.3, 54.5, 51.6, 31.6, 22.1. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{22}NO$ ($M+H^+$): 292.1696; found 292.1696.

1-Benzyl-2-((3-chlorophenyl)ethynyl)pyrrolidine (1p). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 44.3 mg, 50% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J = 4.0 Hz, 1H), 7.38 (dd, J = 8.0, 4.0 Hz, 2H), 7.33-7.29 (m, 3H), 7.28-7.19 (m, 3H), 4.03 (d, J = 12.0 Hz, 1H), 3.62-3.57 (m, 2H), 2.79-2.74 (m, 1H), 2.58-2.52 (m, 1H), 2.20-2.11 (m, 1H), 2.05-1.74 (m, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 138.7, 134.1, 131.7, 129.9, 129.5, 129.2, 128.3, 127.1, 125.2, 90.3, 83.7, 57.3, 54.4, 51.6, 31.7, 22.1. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{19}ClN$ ($M+H^+$): 296.1201; found 296.1196.

1-Benzyl-2-(thiophen-2-ylethynyl)pyrrolidine (1q). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 41.7 mg, 52% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (dd, J = 8.0, 4.0 Hz, 2H), 7.28 (td, J = 8.0, 4.0 Hz, 2H), 7.23-7.18 (m, 1H), 7.16-7.13 (m, 2H), 6.90 (q, J = 4.0 Hz, 1H), 4.01 (d, J = 12.0 Hz, 1H), 3.59-3.54 (m, 2H), 2.75-2.70 (m, 1H), 2.53-2.47 (m, 1H), 2.16-2.07 (m, 1H), 2.03-1.95 (m, 1H), 1.93-1.69 (m, 2H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 138.9, 131.7, 129.3, 128.4, 127.1, 127.0, 126.7,

123.5, 93.0, 78.2, 57.4, 54.7, 51.7, 31.7, 22.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{18}NS$ ($M+H^+$): 268.1154; found 268.1149.

1-Benzyl-2-(thiophen-3-ylethynyl)pyrrolidine (1r). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 44.1 mg, 55% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.37 (m, 3H), 7.31 (td, J = 6.0, 2.0 Hz, 2H), 7.27-7.22 (m, 2H), 7.12 (d, J = 4.0 Hz, 1H), 4.06 (d, J = 12.0 Hz, 1H), 3.62-3.57 (m, 2H), 2.81-2.75 (m, 1H), 2.57-2.51 (m, 1H), 2.20-2.11 (m, 1H), 2.06-1.97 (m, 1H), 1.95-1.86 (m, 1H), 1.84-1.74 (m, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 138.6, 130.1, 129.3, 128.3, 128.3, 127.1, 125.2, 122.4, 88.2, 80.1, 57.2, 54.5, 51.5, 31.6, 22.1. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{18}NS$ ($M+H^+$): 268.1154; found 268.1157.

2-([1,1'-Biphenyl]-4-ylethynyl)-1-benzylpyrrolidine (1s). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 70.8 mg, 70% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (dd, J = 8.0, 4.0 Hz, 2H), 7.60-7.55 (m, 4H), 7.49-7.43 (m, 4H), 7.40-7.34 (m, 3H), 7.31-7.27 (m, 1H), 4.12 (d, J = 12.0 Hz, 1H), 3.66 (q, J = 6.7 Hz, 2H), 2.86-2.81 (m, 1H), 2.62-2.56 (m, 1H), 2.25-2.17 (m, 1H), 2.13-2.04 (m, 1H), 2.01-1.94 (m, 1H), 1.90-1.81 (m, 1H). ESI-MS (M): 337.

1-Benzyl-2-(dec-1-yn-1-yl)pyrrolidine (1t). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 40.1 mg, 45% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.27 (m, 4H), 7.25-7.21 (m, 1H), 4.02 (d, J = 12.0 Hz, 1H), 3.48 (d, J = 16.0 Hz, 1H),

3.32-3.28 (m, 1H), 2.74-2.69 (m, 1H), 2.44-2.38 (m, 1H), 2.23 (td, J = 7.2, 2.0 Hz, 2H), 2.10-2.00 (m, 1H), 1.92-1.67 (m, 3H), 1.57-1.50 (m, 2H), 1.45-1.38 (m, 2H), 1.32-1.19 (m, 10H), 0.87 (t, J = 6.0 Hz, 3H). ESI-MS (M): 297.

1-(4-Methylbenzyl)-2-(phenylethynyl)pyrrolidine (3a). The title compound was prepared according to the general procedure (B) and purified by flash column chromatography to give a yellow liquid, 53.6 mg, 65% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52-7.49 (m, 2H), 7.36-7.31 (m, 5H), 7.17 (d, J = 8.0 Hz, 2H), 4.07 (dd, J = 12.0, 4.0 Hz, 1H), 3.65-3.61 (m, 2H), 2.85-2.79 (m, 1H), 2.61-2.55 (m, 1H), 2.38 (s, 3H), 2.25-2.15 (m, 1H), 2.12-1.91 (m, 2H), 1.88-1.79 (m, 1H). ESI-MS (M): 275.

1-(4-Methoxybenzyl)-2-(phenylethynyl)pyrrolidine (3b). The title compound was prepared according to the general procedure (C) and purified by flash column chromatography to give a yellow liquid, 24.4 mg, 28% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 (d, J = 6.0 Hz, 2H), 7.33-7.31 (m, 5H), 6.87 (d, J = 6.0 Hz, 2H), 4.00 (d, J = 12.0 Hz, 1H), 3.80 (s, 3H), 3.59-3.56 (m, 2H), 2.80-2.76 (m, 1H), 2.56-2.52 (m, 1H), 2.19-2.13 (m, 1H), 2.06-2.01 (m, 1H), 1.96-1.89 (m, 1H), 1.84-1.77 (m, 1H). ESI-MS (M): 291.

1-(4-Chlorobenzyl)-2-(phenylethynyl)pyrrolidine (3c). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 53.1 mg, 60% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.35 (m, 2H), 7.24-7.21 (m, 6H), 7.17 (d, J = 12.0 Hz, 1H), 3.93 (d, J = 12.0 Hz, 1H), 3.53-3.50 (m, 2H), 2.71-2.65 (m, 1H), 2.50-2.45 (m, 1H), 2.14-2.05 (m, 1H), 1.99-1.81 (m, 2H), 1.78-1.69 (m, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ

136.2, 131.7, 130.7, 129.5, 127.3, 127.2, 127.0, 122.2, 87.3, 84.2, 55.4, 53.4, 50.5, 30.6, 21.0. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{19}ClN$ ($M+H^+$): 296.1201; found 296.1204.

1-(4-Bromobenzyl)-2-(phenylethynyl)pyrrolidine (3d). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 62.2 mg, 61% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.32 (m, 4H), 7.32-7.25 (m, 5H), 3.99 (d, J = 16.0 Hz, 1H), 3.63-3.58 (m, 2H), 2.79-2.74 (m, 1H), 2.61-2.55 (m, 1H), 2.22-2.12 (m, 1H), 2.07-1.90 (m, 2H), 1.88-1.77 (m, 1H). ESI-MS (M): 340.

1-(4-Fluorobenzyl)-2-(phenylethynyl)pyrrolidine (3e). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 54.4 mg, 65% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (q, J = 4.0 Hz, 2H), 7.39-7.36 (m, 2H), 7.34-7.31 (m, 3H), 7.04-7.00 (m, 2H), 4.04 (d, J = 12.0 Hz, 1H), 3.61 (td, J = 6.0, 4.0 Hz, 2H), 2.81-2.76 (m, 1H), 2.59-2.53 (m, 1H), 2.24-2.15 (m, 1H), 2.10-1.90 (m, 2H), 1.88-1.78 (m, 1H). ESI-MS (M): 279.

4-((2-(Phenylethynyl)pyrrolidin-1-yl)methyl)benzonitrile (3f). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 48.9 mg, 57% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 8.0 Hz, 2H), 7.51 (d, J = 8.0 Hz, 2H), 7.44-7.42 (m, 2H), 7.31 (t, J = 4.0 Hz, 3H), 4.08 (d, J = 12.0 Hz, 1H), 3.69-3.61 (m, 2H), 2.80-2.74 (m, 1H), 2.60-2.54 (m, 1H), 2.23-2.14 (m, 1H), 2.08-1.91 (m, 2H), 1.88-1.79 (m, 1H); ^{13}C{^{1}H}

NMR (101 MHz, $CDCl_3$) δ 144.8, 132.1, 131.7, 129.6, 128.3, 128.2, 123.1, 119.0, 110.8, 88.1, 85.4, 56.9, 54.6, 51.7, 31.7, 22.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{19}N_2$ ($M+H^+$): 287.1543; found 287.1549.

1-(2-Methylbenzyl)-2-(phenylethynyl)pyrrolidine (3g). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 52.0 mg, 63% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.49 (dd, J = 8.0, 4.0 Hz, 2H), 7.38 (td, J = 4.0, 4.0 Hz, 1H), 7.36-7.32 (m, 3H), 7.19 (t, J = 4.0 Hz, 3H), 4.13 (d, J = 12.0 Hz, 1H), 3.64 (t, J = 6.0 Hz, 1H), 3.57 (d, J = 12.0 Hz, 1H), 2.86-2.80 (m, 1H), 2.58-2.53 (m, 1H), 2.47 (s, 3H), 2.25-2.16 (m, 1H), 2.09-2.01 (m, 1H), 2.00-1.90 (m, 1H), 1.88-1.79 (m, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 137.4, 137.3, 131.7, 130.2, 129.6, 128.3, 127.9, 127.0, 125.6, 123.5, 89.2, 84.7, 55.2, 55.0, 51.8, 31.8, 22.2, 19.3. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{22}N$ ($M+H^+$): 276.1747; found 276.1744.

1-(2-Chlorobenzyl)-2-(phenylethynyl)pyrrolidine (3h). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 48.7 mg, 55% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.54-7.50 (m, 1H), 7.45-7.42 (m, 2H), 7.33 (d, J = 8.0 Hz, 1H), 7.30-7.25 (m, 3H), 7.23-7.18 (m, 1H), 7.15 (td, J = 8.0, 4.0 Hz, 1H), 4.13 (dd, J = 14.0, 4.0 Hz, 1H), 3.82 (dd, J = 16.0, 4.0 Hz, 1H), 3.68 (td, J = 6.0, 4.0 Hz, 1H), 2.88-2.82 (m, 1H), 2.60-2.53 (m, 1H), 2.22-2.13 (m, 1H), 2.08-1.97 (m, 1H), 1.96-1.87 (m, 1H), 1.84-1.74 (m, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 136.8, 134.2, 131.8, 130.9, 129.5, 128.3, 128.1, 128.0, 126.7, 123.5, 88.9, 85.0, 55.0, 54.0, 51.8, 31.8, 22.3.

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{19}ClN$ ($M+H^+$): 296.1201; found 296.1208.

1-(3-Methylbenzyl)-2-(phenylethynyl)pyrrolidine (3i). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 41.3 mg, 50% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.40 (m, 2H), 7.27-7.25 (m, 3H), 7.19-7.15 (m, 3H), 7.03 (dd, J = 4.0, 4.0 Hz, 1H), 4.01 (dt, J = 12.0, 2.0 Hz 1H), 3.59-3.52 (m, 2H), 2.79-2.72 (m, 1H), 2.56-2.49 (m, 1H), 2.30 (d, J = 2.4 Hz, 3H), 2.19-2.09 (m, 1H), 2.05-1.83 (m, 2H), 1.82-1.73 (m, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 138.5, 137.8, 131.8, 130.1, 128.3, 128.1, 128.0, 127.8, 126.4, 123.4, 88.7, 85.1, 57.2, 54.6, 51.6, 31.6, 22.0, 21.4. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{22}N$ ($M+H^+$): 276.1747; found 276.1748.

1-(3-Chlorobenzyl)-2-(phenylethynyl)pyrrolidine (3j). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 59.5 mg, 67% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.42 (m, 2H), 7.40 (t, J = 4.0 Hz, 1H), 7.31-7.27 (m, 3H), 7.25 (dd, J = 4.0, 4.0 Hz, 1H), 7.23-7.20 (m, 2H), 4.01 (d, J = 12.0 Hz, 1H), 3.61-3.56 (m, 2H), 2.79-2.73 (m, 1H), 2.56-2.50 (m, 1H), 2.21-2.12 (m, 1H), 2.07-1.87 (m, 2H), 1.85-1.75 (m, 1H). ESI-MS (M): 296.

3-((2-(Phenylethynyl)pyrrolidin-1-yl)methyl)benzonitrile (3k). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 51.5 mg, 60% yield. ^{1}H NMR (400 MHz,

$CDCl_3$) δ 7.72 (t, J = 2.0 Hz, 1H), 7.64 (dt, J = 8.0, 2.0 Hz, 1H), 7.54 (dt, J = 8.0, 2.0 Hz, 1H), 7.45-7.39 (m, 3H), 7.33-7.30 (m, 3H), 4.06 (d, J = 12.0 Hz, 1H), 3.68-3.62 (m, 2H), 2.80-2.74 (m, 1H), 2.61-2.55 (m, 1H), 2.24-2.15 (m, 1H), 2.09-1.92 (m, 2H), 1.90-1.79 (m, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 139.5, 132.4, 131.5, 130.7, 129.7, 128.0, 127.3, 127.1, 122.0, 118.0, 111.3, 87.0, 84.4, 84.4, 55.4, 53.5, 50.6, 30.6, 21.1. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{19}N_2$ ($M+H^+$): 287.1543; found 287.1538.

1-(Naphthalen-1-ylmethyl)-2-(phenylethynyl)pyrrolidine (3l). The title compound was prepared according to the general procedure (A) and purified by flash column chromatography to give a yellow liquid, 56.9 mg, 61% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 8.0 Hz, 1H), 7.91 (dd, J = 8.0, 4.0 Hz, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.60-7.51 (m, 5H), 7.49-7.45 (m, 1H), 7.42-7.35 (m, 3H), 4.71 (dd, J = 12.0, 4.0 Hz, 1H), 3.93 (dd, J = 14.0, 4.0 Hz, 1H), 3.70 (td, J = 8.0, 4.0 Hz, 1H), 2.91-2.85 (m, 1H), 2.65-2.58 (m, 1H), 2.28-2.19 (m, 1H), 2.15-2.06 (m, 1H), 2.01-1.81 (m, 2H). ESI-MS (M): 311.

Ethyl 2-(2-(phenylethynyl)pyrrolidin-1-yl)acetate (5a). The title compound was prepared according to the general procedure (C) and purified by flash column chromatography to give a yellow liquid, 43.9 mg, 57% yield. ^1H NMR (400 MHz, DMSO-d_6) δ 7.43-7.39 (m, 2H), 7.38-7.35 (m, 3H), 4.09 (q, J = 8.0 Hz, 2H), 3.87 (q, J = 4.0 Hz, 1H), 3.54 (d, J = 16.0 Hz, 1H), 3.39 (d, J = 16.0 Hz, 1H), 2.82-2.76 (m, 1H), 2.71-2.66 (m, 1H), 2.17-2.08 (m, 1H), 1.90-1.71 (m, 3H), 1.19 (t, J = 6.0 Hz, 3H). ESI-MS (M): 257.

Ethyl 2-(2-((4-methoxyphenyl)ethynyl)pyrrolidin-1-yl)acetate (5b). The title compound was prepared according to the general procedure (C) and purified by flash column chromatography to give a yellow liquid, 55.1 mg, 64% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, J = 8.0 Hz, 2H), 6.81 (d, J = 8.0 Hz, 2H), 4.21-4.15 (m, 2H), 3.90 (q, J = 4.0 Hz, 1H), 3.79 (s, 3H), 3.63 (d, J = 20.0 Hz, 1H), 3.46 (d, J = 16.0 Hz, 1H), 2.95-2.89 (m, 1H), 2.80-2.75 (m, 1H), 2.26-2.18 (m, 1H), 2.04-1.95 (m, 2H), 1.90-1.82 (m, 1H), 1.27 (t, J = 6.0 Hz, 3H). ESI-MS (M): 287.

Ethyl 2-(2-((4-chlorophenyl)ethynyl)pyrrolidin-1-yl)acetate (5c). The title compound was prepared according to the general procedure (C) and purified by flash column chromatography to give a yellow liquid, 52.4 mg, 60% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (dd, J = 8.0, 4.0 Hz, 2H), 7.17 (dd, J = 8.0, 4.0 Hz, 2H), 4.14-4.07 (m, 2H), 3.83 (td, J = 6.0, 2.0 Hz, 1H), 3.55 (dd, J = 20.0, 4.0 Hz, 1H), 3.38 (dd, J = 16.0, 4.0 Hz, 1H), 2.86-2.81 (m, 1H), 2.74-2.67 (m, 1H), 2.19-2.10 (m, 1H), 1.98-1.84 (m, 2H), 1.82-1.75 (m, 1H), 1.19 (td, J = 8.0, 2.0 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 170.7, 134.0, 132.9, 128.5, 121.6, 89.1, 83.9, 60.6, 54.3, 53.6, 51.7, 31.8, 22.4, 14.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{16}H_{19}ClNO_2$ ($M+H^+$): 292.1099; found 292.1097.

Ethyl 2-(2-([1,1'-biphenyl]-4-ylethynyl)pyrrolidin-1-yl)acetate (5d). The title compound was prepared according to the general procedure (C) and purified by flash column chromatography to give a yellow liquid, 53.9 mg, 54% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (dt, J = 4.0, 2.0 Hz, 2H), 7.55-7.48 (m, 4H), 7.44 (td, J = 8.0, 4.0 Hz, 2H), 7.37-7.33 (m, 1H), 4.24-4.18 (m, 2H), 3.97 (q, J = 4.0 Hz, 1H), 3.67 (d, J =

16.0 Hz, 1H), 3.51 (d, *J* = 16.0 Hz, 1H), 2.97-2.92 (m, 1H), 2.85-2.79 (m, 1H), 2.30-2.22 (m, 1H), 2.11-1.85 (m, 3H), 1.29 (t, *J* = 8.0 Hz, 3H). ESI-MS (M): 333.

Ethyl 2-(2-(phenylethynyl)pyrrolidin-1-yl)propanoate (5e). The title compound was prepared according to the general procedure (C) and purified by flash column chromatography to give a yellow liquid, 43.9 mg, 54% yield. ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.41-7.36 (m, 5H), 4.13-4.08 (m, 2H), 3.90 (t, *J* = 6.0 Hz, 1H), 3.67 (q, *J* = 8.0 Hz, 1H), 2.78 (t, *J* = 6.0 Hz, 2H), 2.15-2.09 (m, 1H), 1.87-1.72 (m, 3H), 1.31 (d, *J* = 6.0 Hz, 3H), 1.19 (t, *J* = 6.0 Hz, 3H). ESI-MS (M): 271.

Ethyl 2-(2-((4-methoxyphenyl)ethynyl)pyrrolidin-1-yl)propanoate (5f). The title compound was prepared according to the general procedure (C) and purified by flash column chromatography to give a yellow liquid, 47.0 mg, 52% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.23 (m, 2H), 6.74-6.69 (m, 2H), 4.12-4.06 (m, 2H), 4.00-3.91 (m, 1H), 3.69 (dd, *J* = 8.0, 4.0 Hz, 4H), 2.88-2.56 (m, 2H), 2.18-2.07 (m, 1H), 1.95-1.72 (m, 3H), 1.34 (t, *J* = 8.0 Hz, 3H), 1.20-1.15 (m, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 174.1, 173.4, 159.3, 159.3, 133.0, 115.3, 115.2, 113.8, 113.7, 87.1, 86.0, 84.8, 84.5, 60.5, 60.2, 59.9, 57.5, 55.1, 52.8, 51.6, 49.5, 46.8, 32.2, 31.7, 22.4, 22.3, 17.7, 16.9, 14.3, 14.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{18}H_{24}NO_3$ ($M+H^+$): 302.1751; found 302.1746.

Ethyl 2-(2-((4-chlorophenyl)ethynyl)pyrrolidin-1-yl)propanoate (5g). The title compound was prepared according to the general procedure (C) and purified by flash column chromatography to give a yellow liquid, 45.8 mg, 50% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29 (t, *J* = 6.0 Hz, 2H), 7.21 (dd, *J* = 6.0, 6.0 Hz, 2H), 4.17-4.13 (m,

2H), 4.06-3.97 (m, 1H), 3.73-3.40 (m, 1H), 2.93-2.84 (m, 1H), 2.82-2.63 (m, 1H), 2.21-2.15 (m, 1H), 2.00-1.81 (m, 3H), 1.40 (t, J = 6.0 Hz, 3H), 1.23 (td, J = 6.0, 6.0 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 173.9, 173.2, 133.9, 133.8, 132.8, 128.4, 128.4, 121.7, 121.6, 89.8, 89.0, 83.7, 83.4, 60.5, 60.2, 59.7, 57.5, 52.6, 51.4, 49.6, 46.8, 32.1, 31.7, 22.4, 22.3, 17.6, 16.9, 14.3, 14.1. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{21}ClNO_2$ ($M+H^+$): 306.1255; found 306.1252.

Ethyl 2-(2-([1,1'-biphenyl]-4-ylethynyl)pyrrolidin-1-yl)propanoate (5h). The title compound was prepared according to the general procedure (C) and purified by flash column chromatography to give a yellow liquid, 52.1 mg, 50% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 8.0 Hz, 2H), 7.54-7.49 (m, 4H), 7.42 (t, J = 8.0 Hz, 2H), 7.34 (t, J = 6.0 Hz, 1H), 4.24-4.18 (m, 2H), 4.09 (t, J = 6.0 Hz, 1H), 3.82 (q, J = 8.0 Hz, 1H), 3.01-2.94 (m, 1H), 2.89-2.84 (m, 1H), 2.29-2.21 (m, 1H), 2.08-1.86 (m, 3H), 1.47 (t, J = 6.0 Hz, 3H), 1.31-1.26 (m, 3H). ESI-MS (M): 347.

Ethyl 2-(2-(naphthalen-2-ylethynyl)pyrrolidin-1-yl)propanoate (5i). The title compound was prepared according to the general procedure (C) and purified by flash column chromatography to give a yellow liquid, 50.1 mg, 52% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 4.0 Hz, 1H), 7.80-7.73 (m, 3H), 7.49-7.45 (m, 3H), 4.24-4.09 (m, 3H), 3.87-3.51 (m, 1H), 3.02-2.91 (m, 1H), 2.89-2.71 (m, 1H), 2.31-2.22 (m, 1H), 2.12-1.85 (m, 3H), 1.48 (q, J = 5.3 Hz, 3H), 1.31-1.26 (m, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 174.2, 173.6, 133.0, 132.7, 131.4, 131.4, 128.7, 128.6, 127.9, 127.8, 127.7, 127.7, 126.5, 126.5, 126.5, 126.5, 120.6, 120.5, 89.1, 88.1, 85.4, 85.1, 60.7, 60.4, 60.0, 57.7, 52.9, 51.7, 49.7, 47.0, 32.3, 31.8, 22.5, 22.4, 17.8,

17.1, 14.4, 14.3. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{21}H_{24}NO_2$ ($M+H^+$): 322.1802; found 322.1801.

General procedure for the synthesis of thieno[3,2-*b*]pyrrole (2, 4 and 6): 1-benzyl-2-(phenylethynyl)pyrrolidine **1b** (82.6 mg, 0.30 mmol) and elemental sulfur (115.2 mg, 0.45 mmol) were mixed in a 50 mL flame-dried Young-type tube equipped with a stir bar and then the tube was sealed. Next, the Schlenk tube was purged three times with N_2. Then, 1,4-dioxane (2.0 mL) was injected into the Schlenk tube with a syringe under N_2 atmosphere. The contents of the Schlenk tube were then allowed to stir at 120 °C by using a heating mantle for 24 h. After cooling down to room temperature, the residue was concentrated under *vacuum*, purified by chromatography on silica gel and then eluted with petroleum ether/ethyl acetate as an eluent to obtain the desired product **2b** in 58% yield.

1-benzyl-2-(phenylethynyl)pyrrolidine **1a** (78.4 mg, 0.30 mmol) and elemental sulfur (115.2 mg, 0.45 mmol) were mixed in a 50 mL flame-dried Schlenk tube equipped with a stir bar and then the tube was sealed. Next, the Schlenk tube was purged three times with N_2. Then, N-methylmorpholine (2.0 mL) was injected into the Schlenk tube with a syringe under N_2 atmosphere. The contents of the Schlenk tube were then allowed to stir at 120 °C by using a heating mantle for 24 h. After cooling down to room temperature, the residue was concentrated under *vacuum*, purified by chromatography on silica gel and then eluted with petroleum ether/ethyl acetate as an eluent to obtain the desired product **2a** in 85% yield.

The general procedure for the gram scale synthesis of 2a.

1-benzyl-2-(phenylethynyl)pyrrolidine **1a** (2.09 g, 8.0 mmol) and elemental sulfur (3.07 g, 12 mmol) were combined in a 100 mL flame-dried Schlenk tube equipped with a stir bar, and then the tube was sealed. Next, the Schlenk tube was purged three times with a N_2 balloon. Then, 1,4-dioxane (40 mL) was injected into the Schlenk tube with a syringe under N_2 atmosphere. The contents of the Schlenk tube were then allowed to stir at 120 °C in an oil bath for 24 h. After cooling to room temperature, the residue was concentrated in *vacuum*. Then, the residue was purified by chromatography on silica gel and eluted with petroleum ether/ethyl acetate as an eluent to afford the desired product **2a** in 55% yield.

The general procedure for 4-benzyl-2-phenyl-5,6-dihydro-4*H*-thieno[3,2-*b*]pyrrole (2a').

1-benzyl-2-(phenylethynyl)pyrrolidine **1a** (78.4 mg, 0.30 mmol), and elemental sulfur (115.2 mg, 0.45 mmol) were mixed in a 25 mL flame-dried Schlenk tube equipped with a stir bar, and then the tube was sealed. Next, the Schlenk tube was purged three times with N_2. Then, 1,4-dioxane (2.0 mL) was injected into the Schlenk tube with a syringe under N_2 atmosphere. The contents of the Schlenk tube were then allowed to stir at 110 °C by using a heating mantle for 24 h. After cooling down to room temperature, the residue was concentrated under *vacuum*, purified by chromatography on silica gel and then eluted with petroleum ether/ethyl acetate as an eluent to obtain the desired product **2a** and 2**a'** in 17% and 39% yields, respectively.

4-Benzyl-2-phenyl-5,6-dihydro-4H-thieno[3,2-b]pyrrole (2a'). The title compound was prepared according to the general procedure and purified by flash column

chromatography to give a yellow liquid, 34 mg, 39% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (dd, J = 8.0, 4.0 Hz, 2H), 7.42 (d, J = 8.0 Hz, 2H), 7.38-7.30 (m, 5H), 7.22 (td, J = 10.0, 4.0 Hz, 1H), 6.66 (s, 1H), 4.13 (s, 2H), 3.49 (t, J = 10.0 Hz, 2H), 2.99 (t, J = 8.0 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.3, 146.6, 138.4, 135.4, 128.8, 128.5, 127.3, 127.1, 125.1, 119.1, 109.6, 59.2, 58.1, 29.7, 27.9. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{18}NS$ ($M+H^+$): 292.1154; Found 292.1156.

The aromatization of 2a'. 4-benzyl-2-phenyl-5,6-dihydro-4*H*-thieno[3,2-*b*]pyrrole (87.4 mg, 0.30 mmol) and elemental sulfur (115.2 mg, 0.45 mmol) were combined in a 50 mL flame-dried Young-type tube equipped with a stir bar, and then the tube was sealed. Next, the Schlenk tube was purged three times with N_2. Then, 1,4-dioxane (2.0 mL) was injected into the Schlenk tube with a syringe under N_2 atmosphere. The contents of the Schlenk tube were then allowed to stir at 120 °C by using a heating mantle for 24 h. After cooling to room temperature, the residue was concentrated in *vacuum*. Then, the residue was purified by chromatography on silica gel and eluted with petroleum ether/ethyl acetate as an eluent to afford the desired product **2a** in 85% yield.

EPR experiment procedure for interaction of 4-benzyl-2-phenyl-5,6-dihydro-4*H*-thieno[3,2-*b*]pyrrole (1a) with elemental sulfur. 1-benzyl-2-(phenylethynyl)pyrrolidine (78.4 mg, 0.30 mmol) and elemental sulfur S_8 (115.2 mg, 0.45 mmol) were combined in a 50 mL flame-dried Young-type tube equipped with a stir bar, and then the tube was sealed. Next, the Schlenk tube was purged three times with N_2. Then, 1,4-dioxane (2.0 mL) was injected into the

Schlenk tube with a syringe under N_2 atmosphere. The contents of the Schlenk tube were then allowed to stir at 120 °C by using a heating mantle for 1.0 h. Then, DMPO was added to the mixture and preserved in liquid nitrogen for EPR examination. No organic radical was observed.

4-Benzyl-2-phenyl-4H-thieno[3,2-b]pyrrole (2a). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a black green solid, 73.7 mg, 85% yield; m.p. 84-87 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (dd, J = 8.0, 4.0 Hz, 2H), 7.25-7.18 (m, 5H), 7.13 (dd, J = 8.0, 4.0 Hz, 1H), 7.08 (td, J = 6.0, 4.0 Hz, 2H), 6.93 (d, J = 0.8 Hz, 1H), 6.78 (d, J = 4.0 Hz, 1H), 6.33 (d, J = 4.0 Hz, 1H), 5.12 (s, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 142.3, 140.3, 137.4, 135.9, 128.9, 128.8, 127.9, 127.1, 127.0, 126.2, 125.5, 123.1, 106.6, 101.1, 52.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{16}NS$ ($M+H^+$): 290.0998; Found 290.0997.

4-Benzyl-2-(p-tolyl)-4H-thieno[3,2-b]pyrrole (2b). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a green solid, 52.7 mg, 58% yield; m.p. 78-81 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.0 Hz, 2H), 7.36-7.29 (m, 3H), 7.20-7.14 (m, 4H), 6.99 (s, 1H), 6.87 (d, J = 4.0 Hz, 1H), 6.42 (d, J = 3.2 Hz, 1H), 5.24 (s, 2H), 2.35 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 142.6, 140.3, 137.4, 136.8, 133.1, 129.5, 128.8, 127.8, 127.0, 125.8, 125.4, 122.7, 106.1, 101.1, 52.2, 21.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{18}NS$ ($M+H^+$): 304.1154; found 304.1151.

4-Benzyl-2-(4-ethylphenyl)-4H-thieno[3,2-b]pyrrole (2c). The title compound was

prepared according to the general procedure and purified by flash column chromatography to give a brown solid, 61.8 mg, 65% yield; m.p. 70-73 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (dd, J = 8.0, 4.0 Hz, 2H), 7.36-7.29 (m, 3H), 7.20-7.17 (m, 4H), 6.99 (s, 1H), 6.87 (d, J = 2.8 Hz, 1H), 6.42 (d, J = 2.8 Hz, 1H), 5.24 (s, 2H), 2.65 (q, J = 8.0 Hz, 2H), 1.25 (t, J = 8.0 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 143.2, 142.6, 140.3, 137.4, 133.3, 128.8, 128.3, 127.8, 127.0, 125.8, 125.5, 122.7, 106.1, 101.1, 52.2, 28.6, 15.6. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{21}H_{20}NS$ ($M+H^+$): 318.1311; found 318.1310.

4-Benzyl-2-(4-propylphenyl)-4H-thieno[3,2-b]pyrrole (2d). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a yellowish-brown solid, 61.6 mg, 61% yield; m.p. 62-64 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (dd, J = 8.0, 4.0 Hz, 2H), 7.35-7.28 (m, 3H), 7.19-7.14 (m, 4H), 6.99 (d, J = 0.4 Hz, 1H), 6.87 (d, J = 4.0 Hz, 1H), 6.42 (d, J = 4.0 Hz, 1H), 5.24 (s, 2H), 2.58 (t, J = 8.0 Hz, 2H), 1.65 (q, J = 8.0 Hz, 2H), 0.95 (t, J = 8.0 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 142.6, 141.6, 140.3, 137.4, 133.3, 128.9, 128.8, 127.8, 127.0, 125.8, 125.3, 122.7, 106.1, 101.1, 52.2, 37.7, 24.5, 13.8. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{22}H_{22}NS$ ($M+H^+$): 332.1467; found 332.1468.

4-Benzyl-2-(4-butylphenyl)-4H-thieno[3,2-b]pyrrole (2e). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a black green solid, 64.2 mg, 62% yield; m.p. 133-136 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (dd, J = 8.0, 4.0 Hz, 2H), 7.35-7.29 (m, 3H),

7.20-7.14 (m, 4H), 6.99 (d, J = 0.8 Hz, 1H), 6.79 (d, J = 2.8 Hz, 1H), 6.42 (dd, J = 2.8, 0.8 Hz, 1H), 5.24 (s, 2H), 2.61 (t, J = 8.0 Hz, 2H), 1.63-1.58 (m, 2H), 1.37 (q, J = 8.0 Hz, 2H), 0.94 (t, J = 8.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 141.6, 140.8, 139.3, 136.3, 132.2, 127.8, 126.8, 126.0, 124.8, 124.3, 121.6, 105.1, 100.0, 51.2, 34.3, 32.5, 21.3, 12.9. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{24}NS$ ($M+H^+$): 346.1624; found 346.1618.

4-Benzyl-2-(4-(tert-butyl)phenyl)-4H-thieno[3,2-b]pyrrole (2f). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a yellow solid, 61.1 mg, 59% yield; m.p. 132-136 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 7.52 (dd, J = 8.0, 4.0 Hz, 2H), 7.39-7.30 (m, 5H), 7.20 (dd, J = 8.0, 4.0 Hz, 2H), 7.00 (d, J = 0.4 Hz 1H), 6.88 (d, J = 4.0 Hz, 1H), 6.43 (dd, J = 4.0, 0.4 Hz, 1H), 5.24 (s, 2H), 1.34 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 150.1, 142.5, 140.3, 137.4, 133.1, 128.8, 127.8, 127.1, 125.9, 125.7, 125.2, 122.8, 106.2, 101.1, 52.2, 34.6, 31.3. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{24}NS$ ($M+H^+$): 346.1624; found 346.1623.

4-Benzyl-2-(4-methoxyphenyl)-4H-thieno[3,2-b]pyrrole (2g). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a yellow liquid, 57.4 mg, 60% yield; ^1H NMR (400 MHz, $CDCl_3$) δ 7.49 (dd, J = 8.0, 4.0 Hz, 2H), 7.35-7.29 (m, 3H), 7.18 (dd, J = 8.0, 1.4 Hz, 2H), 6.91 (d, J = 4.0 Hz, 2H), 6.87 (dd, J = 8.0, 4.0 Hz, 2H), 6.42 (d, J = 4.0 Hz, 1H), 5.23 (s, 2H), 3.82 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.9, 142.3, 140.3, 137.4, 128.8, 128.8, 127.8, 127.0, 126.7, 125.6, 122.3, 114.2, 105.7, 101.1, 55.4, 52.2.

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{18}NOS$ ($M+H^+$): 320.1104; found 320.1099.

4-Benzyl-2-(4-ethoxyphenyl)-4H-thieno[3,2-b]pyrrole (2h). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a yellow solid, 59.9 mg, 60% yield; m.p. 101-103 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 (dd, J = 8.0, 4.0 Hz, 2H), 7.36-7.28 (m, 3H), 7.18 (dd, J = 8.0, 1.6 Hz, 2H), 6.91-6.85 (m, 4H), 6.42 (d, J = 4.0 Hz, 1H), 5.23 (s, 2H), 4.05 (q, J = 8.0 Hz, 2H), 1.43 (t, J = 8.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.2, 142.4, 140.3, 137.4, 128.8, 128.6, 127.8, 127.0, 126.7, 125.6, 122.3, 114.8, 105.6, 101.1, 63.6, 52.2, 14.9. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{19}NNaOS$ ($M+Na^+$): 356.1080; found 356.1082.

4-Benzyl-2-(4-fluorophenyl)-4H-thieno[3,2-b]pyrrole (2i). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a green liquid, 55.3 mg, 60% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.53-7.50 (m, 2H), 7.37-7.30 (m, 3H), 7.19 (dd, J = 8.0, 4.0 Hz, 2H), 7.06-7.02 (m, 2H), 6.95 (s, 1H), 6.89 (d, J = 3.2 Hz 1H), 6.43 (d, J = 4.0 Hz, 1H), 5.24 (s, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.0 (J = 242 Hz), 141.2, 140.2, 137.3, 132.2 (J = 10.1 Hz), 128.9, 127.9, 127.1 (J = 10.1 Hz), 126.1, 123.0, 115.8, 115.6, 106.6, 101.1, 52.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -115.4 ppm. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{15}FNS$ ($M+H^+$): 308.0904; found 308.0905.

4-Benzyl-2-(4-chlorophenyl)-4H-thieno[3,2-b]pyrrole (2j). The title compound was prepared according to the general procedure and purified by flash column

chromatography to give a yellow liquid, 56.2 mg, 58% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (dd, J = 8.0, 4.0 Hz, 2H), 7.34-7.28 (m, 5H), 7.18 (dd, J = 8.0, 4.0 Hz, 2H), 6.99 (s, 1H), 6.90 (d, J = 3.2 Hz, 1H), 6.43 (d, J = 4.0 Hz, 1H), 5.24 (s, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 140.9, 140.2, 137.2, 134.4, 132.5, 128.9, 128.9, 127.9, 127.0, 126.5, 126.4, 123.4, 106.9, 101.1, 52.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{15}ClNS$ ($M+H^+$): 324.0608; found 324.0609.

4-Benzyl-2-(4-bromophenyl)-4H-thieno[3,2-b]pyrrole (2k). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a yellow solid, 59.5 mg, 54% yield; m.p. 94-97 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.40 (m, 4H), 7.36-7.29 (m, 3H), 7.18 (dd, J = 8.0, 4.0 Hz, 2H), 7.00 (s, 1H), 6.90 (d, J = 2.8 Hz, 1H), 6.43 (d, J = 4.0 Hz, 1H), 5.24 (s, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 140.8, 140.2, 137.2, 134.8, 131.8, 128.9, 127.9, 127.0, 126.8, 126.5, 123.4, 120.5, 106.9, 101.1, 52.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{15}BrNS$ ($M+H^+$): 368.0103; found 368.0107.

4-Benzyl-2-(4-(trifluoromethyl)phenyl)-4H-thieno[3,2-b]pyrrole (2l). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a yellowish-brown solid, 62.1 mg, 58% yield; m.p. 116-119 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 8.0 Hz, 2H), 7.57 (d, J = 8.0 Hz, 2H), 7.38-7.31 (m, 3H), 7.19 (dd, J = 8.0, 1.8 Hz, 2H), 7.10 (s, 1H), 6.94 (d, J = 4.0 Hz, 1H), 6.46 (d, J = 4.0 Hz, 1H), 5.26 (s, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 140.2, 139.3, 137.1, 128.9, 128.0, 127.1 (J = 10.1 Hz), 125.8 (q, J = 3.3 Hz), 125.2, 124.3, 107.9, 101.2, 52.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.4 ppm. HRMS

(ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{15}F_3NS$ ($M+H^+$): 358.0872; found 358.0871.

4-Benzyl-2-(2-fluorophenyl)-4H-thieno[3,2-b]pyrrole (2m). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a yellowish-brown solid, 50.7 mg, 55% yield; m.p. 64-68 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 (td, J = 8.0, 2.0 Hz, 1H), 7.36-7.31 (m, 3H), 7.30-7.27 (m, 1H), 7.21-7.08 (m, 5H), 6.91 (d, J = 4.0 Hz, 1H), 6.45 (d, J = 4.0 Hz, 1H), 5.25 (s, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.0 (J = 253 Hz), 140.4, 137.3, 135.0, 128.8, 128.3 (J = 3.0 Hz), 127.9 (J = 9.1 Hz), 127.1, 126.6, 124.4 (J = 3.0 Hz), 116.2 (J = 23.2 Hz), 110.4 (J = 10.1 Hz), 101.0, 52.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.2 ppm. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{15}FNS$ ($M+H^+$): 308.0904; found 308.0906.

4-Benzyl-2-(3-bromophenyl)-5,6-dihydro-4H-thieno[3,2-b]pyrrole (2n). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a yellow solid, 70.1 mg, 63% yield; m.p. 162-165 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (t, J = 2.0 Hz 1H), 7.41 (t, J = 8.0 Hz, 4H), 7.35 (t, J = 8.0 Hz, 3H), 7.18 (t, J = 8.0 Hz, 1H), 6.66 (s, 1H), 4.14 (s, 2H), 3.50 (t, J = 8.0 Hz, 2H), 3.02 (t, J = 8.0 Hz, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 144.6, 138.2, 137.4, 130.3, 129.8, 128.5, 128.4, 127.9, 127.4, 123.6, 122.9, 110.2, 59.2, 58.0, 27.9. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{17}BrNS$ ($M+H^+$): 370.0260, found 370.0259.

4-Benzyl-2-(3-methoxyphenyl)-4H-thieno[3,2-b]pyrrole (2o). The title compound was prepared according to a general procedure and purified by flash column

chromatography to give the yellowish-brown solid, 53.5 mg, 56% yield; m.p. 73-76 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.27 (m, 3H), 7.23 (t, J = 4.0 Hz, 1H), 7.17-7.14 (m, 3H), 7.09 (t, J = 2.0 Hz, 1H), 7.01 (d, J = 0.8 Hz, 1H), 6.87 (d, J = 4.0 Hz, 1H), 6.78-6.75 (m, 1H), 6.41 (dd, J = 4.0, 0.8 Hz, 1H), 5.21 (s, 2H), 3.82 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.9, 142.1, 140.2, 137.3, 137.3, 129.8, 128.9, 127.9, 127.0, 126.2, 123.2, 118.1, 112.4, 111.1, 106.8, 101.1, 55.3, 52.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{18}NOS$ ($M+H^+$): 320.1104; found 320.1108.

4-Benzyl-2-(3-chlorophenyl)-4H-thieno[3,2-b]pyrrole (2p). The title compound was prepared according to a general procedure and purified by flash column chromatography to give the yellow solid, 60.0 mg, 62% yield; m.p. 99-102 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (t, J = 2.0 Hz, 1H), 7.34 (dt, J = 8.0, 2.0 Hz, 1H), 7.27-7.21 (m, 3H), 7.15 (d, J = 8.0 Hz, 1H), 7.10-7.07 (m, 3H), 6.95 (d, J = 4.0 Hz, 1H), 6.82 (d, J = 4.0 Hz, 1H), 6.35 (dd, J = 4.0, 0.3 Hz, 1H), 5.15 (s, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 140.5, 140.2, 137.7, 137.2, 134.7, 130.0, 128.9, 127.9, 127.0, 126.7, 126.7, 125.2, 123.7, 123.5, 107.3, 101.2, 52.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{15}ClNS$ ($M+H^+$): 324.0608, found 324.0605.

4-Benzyl-2-(thiophen-2-yl)-4H-thieno[3,2-b]pyrrole (2q). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a yellowish-brown solid, 56.6 mg, 64% yield; m.p. 69-72 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.30 (m, 3H), 7.19-7.12 (m, 4H), 6.99 (q, J = 2.7 Hz, 1H), 6.91 (s, 1H), 6.88 (d, J = 4.0 Hz, 1H), 6.41 (d, J = 4.0 Hz, 1H), 5.22 (s, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 139.8, 139.1, 137.3, 135.2, 128.9, 127.9, 127.7,

127.0, 126.2, 123.6, 122.9, 107.2, 101.1, 52.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{14}NS_2$ ($M+H^+$): 296.0562; found 296.0561.

4-Benzyl-2-(thiophen-3-yl)-4H-thieno[3,2-b]pyrrole (2r). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a brown solid, 54.9 mg, 62% yield; m.p. 91-94 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 7.32-7.28 (m, 3H), 7.25-7.23 (m, 3H), 7.15 (dd, J = 8.0, 4.0 Hz, 2H), 6.87 (s, 1H), 6.85 (d, J = 4.0 Hz, 1H), 6.39 (d, J = 4.0 Hz, 1H), 5.20 (s, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 139.9, 137.3, 137.2, 137.1, 128.8, 127.8, 127.0, 126.0, 126.0, 125.9, 122.3, 118.4, 106.7, 101.0, 52.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{14}NS_2$ ($M+H^+$): 296.0562; found 296.0563.

2-([1,1'-Biphenyl]-4-yl)-4-benzyl-4H-thieno[3,2-b]pyrrole (2s). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a brown solid, 72.3 mg, 66% yield; m.p. 160-163 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 7.65-7.57 (m, 6H), 7.45 (t, J = 8.0 Hz, 2H), 7.37-7.30 (m, 4H), 7.20 (dd, J = 8.0, 4.0 Hz, 2H), 7.08 (d, J = 0.40 Hz 1H), 6.90 (d, J = 3.2 Hz, 1H), 6.45 (dd, J = 4.0, 0.80 Hz, 1H), 5.26 (s, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 140.9, 139.6, 139.3, 138.6, 136.3, 133.8, 127.8, 127.8, 126.8, 126.4, 126.2, 126.0, 125.8, 125.2, 124.7, 122.2, 105.6, 100.1, 51.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{25}H_{19}N$ NaS ($M+Na^+$): 388.1130; found 388.1129.

4-Benzyl-2-octyl-4H-thieno[3,2-b]pyrrole (2t). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a brown liquid, 20.4 mg, 21% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.31-7.25 (m,

4H), 7.15 (dd, *J* = 8.0, 4.0 Hz, 2H), 6.78 (d, *J* = 4.0 Hz, 1H), 6.49 (s, 1H), 6.35 (d, *J* = 4.0 Hz, 1H), 5.16 (s, 1H), 2.76 (t, *J* = 8.0 Hz, 2H), 1.67-1.61 (m, 2H), 1.29-1.23 (m, 10H), 0.88 (t, *J* = 6.0 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 144.8, 139.2, 137.6, 128.7, 127.7, 127.0, 124.4, 121.2, 107.6, 100.8, 52.1, 31.9, 31.8, 31.4, 29.4, 29.3, 29.2, 22.7, 14.1. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{21}H_{28}NS$ ($M+H^+$): 326.1929; found 326.1937.

4-(4-Methylbenzyl)-2-phenyl-4H-thieno[3,2-b]pyrrole (4a). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a yellowish-brown liquid, 63.7 mg, 70% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 8.0, 4.0 Hz, 2H), 7.35 (t, *J* = 8.0 Hz, 2H), 7.25-7.21 (m, 1H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 7.06 (s, 1H), 6.89 (d, *J* = 4.0 Hz, 1H), 6.43 (d, *J* = 4.0, 0.60 Hz, 1H), 5.20 (s, 2H), 2.35 (s, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 142.2, 140.3, 137.6, 135.9, 134.3, 129.5, 128.8, 127.1, 126.9, 126.1, 125.4, 123.1, 106.7, 101.0, 52.0, 21.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{18}NS$ ($M+H^+$): 304.1154; found 304.1155.

4-(4-Methoxybenzyl)-2-phenyl-4H-thieno[3,2-b]pyrrole (4b). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a reddish brown liquid, 41.2 mg, 43% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 (d, *J* = 6.0 Hz, 2H), 7.36 (t, *J* = 9.0 Hz, 2H), 7.24 (t, *J* = 9.0 Hz, 1H), 7.15 (d, *J* = 6.0 Hz, 2H), 7.05 (s, 1H), 6.88 (d, *J* = 6.0 Hz, 3H), 6.42 (d, *J* = 3.0 Hz, 1H), 5.17 (s, 2H), 3.80 (s, 3H); $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 159.3, 142.2, 140.2, 135.9, 129.3, 128.8, 128.5, 126.9, 126.0, 125.4, 123.1, 114.2, 106.7, 101.0,

55.3, 51.8. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{17}NOS$ ($M+H^+$): 320.1104, found 320.1107.

4-(4-Chlorobenzyl)-2-phenyl-4H-thieno[3,2-b]pyrrole (4c). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a green solid, 64.9 mg, 67% yield; m.p. 87-90 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 7.57 (dd, J = 8.0, 4.0 Hz, 2H), 7.37-7.29 (m, 4H), 7.25-7.21 (m, 1H), 7.10 (d, J = 8.0 Hz, 2H), 7.01 (s, 1H), 6.86 (d, J = 2.8 Hz, 1H), 6.44 (d, J = 4.0 Hz, 1H), 5.21 (s, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 142.6, 140.1, 135.8, 135.7, 133.7, 129.0, 128.8, 128.3, 127.0, 125.9, 125.4, 123.3, 106.3, 101.4, 51.5. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{15}ClNS$ ($M+H^+$): 324.0608; found 324.0600.

4-(4-Bromobenzyl)-2-phenyl-4H-thieno[3,2-b]pyrrole (4d). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a yellowish-brown solid, 68.2 mg, 62% yield; m.p. 122-123 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, J = 8.0, 0.60 Hz, 2H), 7.45 (d, J = 8.0 Hz, 2H), 7.35 (t, J = 8.0 Hz, 2H), 7.25-7.22 (m, 1H), 7.03 (t, J = 6.0 Hz, 3H), 6.86 (d, J = 4.0 Hz, 1H), 6.41 (d, J = 4.0 Hz, 1H), 5.17 (s, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 142.7, 140.2, 136.4, 135.8, 132.0, 128.9, 128.6, 127.1, 126.0, 125.5, 123.3, 121.8, 106.4, 101.4, 51.6. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{15}BrNS$ ($M+H^+$): 368.0103; found 368.0108.

4-(4-Fluorobenzyl)-2-phenyl-4H-thieno[3,2-b]pyrrole (4e). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a black green solid, 53.4 mg, 58% yield; m.p. 62-63 ^oC. ^1H

NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, J = 8.0, 4.0 Hz, 2H), 7.35 (t, J = 8.0 Hz, 2H), 7.25-7.22 (m, 1H), 7.18-7.14 (m, 2H), 7.05-7.00 (m, 3H), 6.87 (d, J = 4.0 Hz, 1H), 6.42 (dd, J = 3.2, 0.60 Hz, 1H), 5.20 (s, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.3 (J = 242 Hz), 142.5, 140.1, 135.7, 133.1 (J = 10.1 Hz), 128.8, 128.7 (J = 10.1 Hz), 127.0, 125.9, 125.4, 123.2, 115.7 (J = 20.2 Hz), 106.4, 101.2, 51.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.2 ppm. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{15}FNS$ ($M+H^+$): 308.0904; found 308.0901.

4-((2-Phenyl-4H-thieno[3,2-b]pyrrol-4-yl)methyl)benzonitrile (4f). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a black green solid, 65.0 mg, 69% yield; m.p. 84-86 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 8.0 Hz, 2H), 7.56 (dd, J = 8.0, 1.4 Hz, 2H), 7.35 (td, J = 8.0, 4.0 Hz, 2H), 7.22 (t, J = 8.0 Hz, 3H), 6.98 (s, 1H), 6.87 (d, J = 4.0 Hz, 1H), 6.48 (d, J = 4.0 Hz, 1H), 5.29 (s, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 143.1, 142.8, 140.1, 135.6, 132.7, 128.9, 127.3, 127.2, 126.0, 125.5, 123.5, 118.5, 111.8, 106.1, 101.9, 51.6. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{15}N_2S$ ($M+H^+$): 315.0950; found 315.0949.

4-(2-Methylbenzyl)-2-phenyl-4H-thieno[3,2-b]pyrrole (4g). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a yellowish-brown solid, 63.8 mg, 70% yield; m.p. 158-161 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 (dd, J = 8.0, 1.6 Hz, 2H), 7.34 (t, J = 8.0 Hz, 2H), 7.24-7.22 (m, 2H), 7.20-7.15 (m, 2H), 7.00 (d, J = 4.0 Hz, 1H), 6.95 (d, J = 8.0 Hz, 1H), 6.80 (d, J = 4.0 Hz, 1H), 6.43 (dd, J = 2.8, 0.80 Hz, 1H), 5.23 (s, 2H), 2.31

(s, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 141.1, 139.3, 135.0, 134.8, 134.0, 129.5, 127.7, 127.0, 126.9, 125.8, 125.4, 124.9, 124.3, 121.9, 105.6, 100.0, 49.4, 18.0. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{18}NS$ ($M+H^+$): 304.1154; found 304.1153.

4-(2-Chlorobenzyl)-2-phenyl-4H-thieno[3,2-b]pyrrole (4h). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a yellow solid, 55.2 mg, 57% yield; m.p. 59-62 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, J = 8.0, 0.60 Hz, 2H), 7.42 (dd, J = 8.0, 1.2 Hz, 1H), 7.35 (t, J = 8.0 Hz, 2H), 7.25-7.21 (m, 2H), 7.17 (td, J = 8.0, 1.2 Hz, 1H), 7.08 (d, J = 0.40 Hz, 1H), 6.90 (d, J = 4.0 Hz, 1H), 6.82 (dd, J = 8.0, 1.6 Hz, 1H), 6.46 (dd, J = 4.0, 0.60 Hz, 1H), 5.35 (s, 2H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 142.6, 140.3, 135.8, 135.1, 132.5, 129.6, 129.1, 128.8, 128.4, 127.4, 127.0, 126.3, 125.4, 123.2, 106.5, 101.5, 49.7. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{15}ClNS$ ($M+H^+$): 324.0608; found 324.0612.

4-(3-Methylbenzyl)-2-phenyl-4H-thieno[3,2-b]pyrrole (4i). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a yellowish-brown solid, 52.7 mg, 58% yield; m.p. 125-128 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, J = 8.0, 1.4 Hz, 2H), 7.35 (t, J = 8.0 Hz, 2H), 7.23 (t, J = 8.0 Hz, 2H), 7.11 (d, J = 8.0 Hz, 1H), 7.06 (s, 1H), 7.00 (t, J = 8.0 Hz, 2H), 6.89 (d, J = 4.0 Hz, 1H), 6.43 (d, J = 3.2 Hz, 1H), 5.20 (s, 2H), 2.33 (s, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 142.2, 140.3, 138.6, 137.3, 135.9, 128.8, 128.7, 128.6, 127.8, 126.9, 126.1, 125.4, 124.2, 123.0, 106.6, 101.0, 52.2, 21.5. HRMS

(ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{18}NS$ ($M+H^+$): 304.1154; found 304.1151.

4-(3-Chlorobenzyl)-2-phenyl-4H-thieno[3,2-b]pyrrole (4j). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a yellowish-brown solid, 50.4 mg, 52% yield; m.p. 115-118 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 7.57 (dd, J = 8.0, 1.2 Hz, 2H), 7.35 (t, J = 8.0 Hz, 2H), 7.27 (d, J = 1.2 Hz, 1H), 7.25-7.18 (m, 3H), 7.03 (d, J = 0.80 Hz, 2H), 6.88 (d, J = 4.0 Hz, 1H), 6.45 (dd, J = 2.8, 0.60 Hz, 1H), 5.21 (s, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 142.7, 140.2, 139.4, 135.7, 134.8, 130.2, 128.8, 128.1, 127.0, 126.0, 125.4, 125.0, 123.3, 106.3, 101.5, 51.6. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{19}H_{15}ClNS$ ($M+H^+$): 324.0608; found 324.0603.

3-((2-Phenyl-4H-thieno[3,2-b]pyrrol-4-yl)methyl)benzonitrile (4k). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a black green liquid, 50.9 mg, 54% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.59-7.55 (m, 3H), 7.45-7.41 (m, 2H), 7.35 (t, J = 8.0 Hz, 3H), 7.25-7.22 (m, 1H), 6.99 (d, J = 0.40 Hz, 1H), 6.87 (d, J = 4.0 Hz, 1H), 6.48 (dd, J = 2.4, 0.80 Hz, 1H), 5.27 (s, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 143.2, 140.1, 139.1, 135.6, 131.6, 131.1, 130.2, 129.8, 128.9, 127.2, 125.9, 125.5, 123.6, 118.5, 113.1, 106.0, 101.9, 51.3. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{15}N_2S$ ($M+H^+$): 315.0950; found 315.0949.

4-(Naphthalen-1-ylmethyl)-2-phenyl-4H-thieno[3,2-b]pyrrole (4l). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a yellowish-brown solid, 61.0 mg, 60% yield; m.p.

81-84 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00-7.97 (m, 1H), 7.94-7.91 (m, 1H), 7.84 (d, J = 8.0 Hz, 1H), 7.59-7.54 (m, 4H), 7.41 (t, J = 8.0 Hz, 1H), 7.34 (td, J = 8.0, 4.0 Hz, 2H), 7.25-7.20 (m, 1H), 7.09 (td, J = 4.0, 4.0 Hz, 2H), 6.87 (d, J = 4.0 Hz, 1H), 6.46 (d, J = 4.0 Hz, 1H), 5.71 (s, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 142.4, 140.5, 135.8, 133.7, 132.4, 130.9, 129.0, 128.8, 128.7, 126.9, 126.8, 126.2, 126.1, 125.6, 125.4, 125.4, 123.1, 122.6, 106.6, 101.2, 50.1. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{18}NS$ ($M+H^+$): 340.1154; found 340.1151.

Ethyl 2-(2-phenyl-4H-thieno[3,2-b]pyrrol-4-yl)acetate (6a). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a brown liquid, 50.4 mg, 59% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.61 (d, J = 12.0 Hz, 2H), 7.37 (t, J = 9.0 Hz, 2H), 7.24 (d, J = 12.0 Hz, 1H), 7.14 (s, 1H), 6.86 (d, J = 6.0 Hz 1H), 6.45 (d, J = 3.0 Hz, 1H), 4.77 (s, 2H), 4.25 (q, J = 8.0 Hz, 2H), 1.30 (t, J = 9.0 Hz, 3H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 168.3, 142.9, 140.5, 135.8, 128.8, 127.0, 126.5, 125.5, 123.3, 106.1, 101.9, 61.8, 49.8, 14.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{16}H_{16}NO_2S$ ($M+H^+$): 286.0896; found 286.0894.

Ethyl 2-(2-(4-methoxyphenyl)-4H-thieno[3,2-b]pyrrol-4-yl)acetate (6b). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a brown liquid, 49.1 mg, 52% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.53 (d, J = 6.0 Hz, 2H), 7.01 (s, 1H), 6.91 (d, J = 6.0 Hz, 2H), 6.83 (d, J = 6.0 Hz, 1H), 6.43 (d, J = 6.0 Hz, 1H), 4.76 (s, 2H), 4.25 (q, J = 6.0 Hz, 2H), 3.83 (s, 3H), 1.29 (t, J = 6.0 Hz, 3H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 168.4,

158.9, 142.9, 140.5, 128.7, 126.8, 126.0, 122.5, 114.3, 105.2, 101.8, 61.8, 55.4, 49.8, 14.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{18}NO_3S$ ($M+H^+$): 316.1002; found 316.1003.

Ethyl 2-(2-(4-chlorophenyl)-4H-thieno[3,2-b]pyrrol-4-yl)acetate (6c). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a brown liquid, 52.6 mg, 55% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52 (d, J = 6.0 Hz, 2H), 7.32 (d, J = 6.0 Hz, 2H), 7.10 (s, 1H), 6.86 (d, J = 6.0 Hz, 1H), 6.44 (d, J = 6.0 Hz, 1H), 4.76 (s, 2H), 4.24 (q, J = 8.0 Hz, 2H), 1.29 (t, J = 6.0 Hz, 3H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 168.3, 141.4, 140.4, 134.3, 132.6, 128.9, 126.8, 126.6, 123.6, 106.5, 101.9, 61.9, 49.7, 29.7, 14.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{16}H_{15}ClNO_2S$ ($M+H^+$): 320.0507; found 320.0506.

Ethyl 2-(2-([1,1'-biphenyl]-4-yl)-4H-thieno[3,2-b]pyrrol-4-yl)acetate (6d). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a brown solid, 56.3 mg, 52% yield; m.p. 93-96 ^{o}C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.68 (d, J = 12.0 Hz, 2H), 7.64-7.60 (m, 4H), 7.46 (t, J = 9.0 Hz, 2H), 7.34 (td, J = 6.0, 0.80 Hz, 1H), 7.18 (s, 1H), 6.87 (d, J = 3.0 Hz, 1H), 6.46 (d, J = 3.0 Hz, 1H), 4.78 (s, 2H), 4.26 (q, J = 8.0 Hz, 2H), 1.30 (t, J = 6.0 Hz, 3H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 168.3, 142.5, 140.6, 139.7, 134.8, 128.8, 127.5, 127.3, 126.9, 126.6, 125.8, 123.4, 106.2, 101.9, 61.8, 49.8, 14.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{22}H_{20}NO_2S$ ($M+H^+$): 362.1209; found 362.1205.

Ethyl 2-(2-phenyl-4H-thieno[3,2-b]pyrrol-4-yl)propanoate (6e). The title compound

was prepared according to the general procedure and purified by flash column chromatography to give a green liquid, 53.8 mg, 60% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.62 (d, J = 6.0 Hz, 2H), 7.37 (t, J = 9.0 Hz, 2H), 7.24 (d, J = 12.0 Hz, 1H), 7.20 (s, 1H), 6.97 (d, J = 3.0 Hz, 1H), 6.43 (d, J = 3.0 Hz, 1H), 4.96 (q, J = 6.0 Hz, 1H), 4.21 (q, J = 8.0 Hz, 2H) 1.81 (d, J = 12.0 Hz, 3H), 1.25 (t, J = 9.0 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 170.9, 142.4, 139.5, 135.8, 128.8, 127.0, 125.5, 124.0, 123.4, 106.8, 101.6, 61.7, 56.4, 17.8, 14.1. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{18}NO_2S$ ($M+H^+$): 300.1053; found 300.1050.

Ethyl 2-(2-(4-methoxyphenyl)-4H-thieno[3,2-b]pyrrol-4-yl)propanoate (6f). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a yellow liquid, 62.2 mg, 63% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (dd, J = 6.0, 2.4 Hz, 2H), 7.08 (s, 1H), 6.94 (d, J = 3.0 Hz, 1H), 6.92 (dd, J = 6.0, 3.0 Hz, 2H), 6.42 (d, J = 3.0 Hz, 1H), 4.94 (q, J = 8.0 Hz, 1H), 4.20 (q, J = 8.0 Hz, 2H), 3.84 (s, 3H), 1.81 (d, J = 6.0 Hz, 3H), 1.25 (t, J = 9.0 Hz, 3H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 170.9, 158.9, 142.4, 139.5, 128.7, 126.8, 123.5, 122.6, 114.3, 105.9, 101.5, 61.7, 56.4, 55.4, 17.8, 14.1. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{18}H_{20}NO_3S$ ($M+H^+$): 330.1158; found 330.1156.

Ethyl 2-(2-(4-chlorophenyl)-4H-thieno[3,2-b]pyrrol-4-yl)propanoate (6g). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a brown liquid, 64.9 mg, 65% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.53 (dd, J = 6.0, 1.8 Hz, 2H), 7.32 (d, J = 6.0, 1.8 Hz, 2H), 7.17 (s, 1H), 6.98 (d, J = 6.0 Hz, 1H), 6.43 (d, J = 3.0 Hz, 1H), 4.94 (q, J = 6.0 Hz, 1H), 4.20

(q, J = 6.0 Hz, 2H), 1.81 (d, J = 6.0 Hz, 3H), 1.25 (t, J = 9.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 170.8, 140.9, 139.4, 134.4, 132.6, 129.0, 126.6, 124.3, 123.7, 107.2, 101.6, 61.8, 56.4, 17.8, 14.1. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{17}ClNO_2S$ ($M+H^+$): 334.0663; found 334.0664.

Ethyl 2-(2-([1,1'-biphenyl]-4-yl)-4H-thieno[3,2-b]pyrrol-4-yl)propanoate (6h). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a black green solid, 67.5 mg, 60% yield; m.p. 105-108 ^oC. ^1H NMR (600 MHz, $CDCl_3$) δ 7.69 (d, J = 6.0 Hz, 2H), 7.64-7.60 (m, 4H), 7.46 (t, J = 9.0 Hz, 2H), 7.36 (t, J = 9.0 Hz, 1H), 7.25 (s, 1H), 6.99 (d, J = 6.0 Hz, 1H), 6.45 (d, J = 3.0 Hz, 1H), 4.97 (q, J = 6.0 Hz, 1H), 4.21 (q, J = 8.0 Hz, 2H), 1.83 (d, J = 6.0 Hz, 3H), 1.26 (t, J = 9.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 170.9, 142.0, 140.6, 139.7, 139.6, 134.9, 128.8, 127.5, 127.3, 126.9, 125.8, 124.1, 123.5, 106.8, 101.6, 61.8, 56.4, 17.8, 14.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{22}NO_2S$ ($M+H^+$): 376.1366; found 376.1365.

Ethyl 2-(2-(naphthalen-2-yl)-4H-thieno[3,2-b]pyrrol-4-yl)propanoate (6i). The title compound was prepared according to the general procedure and purified by flash column chromatography to give a brown solid, 58.6 mg, 56% yield; m.p. 63-66 ^oC. ^1H NMR (600 MHz, $CDCl_3$) δ 8.04 (d, J = 1.8 Hz, 1H), 7.85-7.80 (m, 3H), 7.77 (dd, J = 9.0, 6.0 Hz, 1H), 7.48 (td, J = 6.0, 1.2 Hz, 1H), 7.44 (td, J = 9.0, 1.2 Hz, 1H), 7.34 (s, 1H), 7.00 (d, J = 6.0 Hz, 1H), 6.47 (d, J = 6.0 Hz, 1Hz), 4.99 (q, J = 6.0 Hz, 1H), 4.22 (q, J = 8.0 Hz, 2H), 1.83 (d, J = 6.0 Hz, 3H), 1.26 (t, J = 6.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 170.9, 142.4, 139.6, 133.8, 133.3, 132.6, 128.4, 127.9, 127.7,

126.5, 125.7, 124.2, 124.1, 123.6, 123.4, 107.3, 101.6, 61.8, 56.4, 17.9, 14.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{21}H_{20}NO_2S$ ($M+H^+$): 350.1209; found 350.1211.

Associated content

Supporting Information

X-ray crystallography data and CIF file, ^1H and $^{13}C\{^1H\}$ NMR spectra of all compounds. The SI is available free of charge on the ACS Publications website.

Crystal structure data for **2b** (CIF)

Crystal structure data for **2h** (CIF)

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Notes

The authors declare no competing financial interest.

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(19) CCDC 1946767 (**2b**) and 1946766 (**2h**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.