Iodocyclization of *N*-[2-(Methylthio)phenyl]propiolamides: Selective Synthesis of 3-Iodo-1,5-benzothiazepin-4-ones

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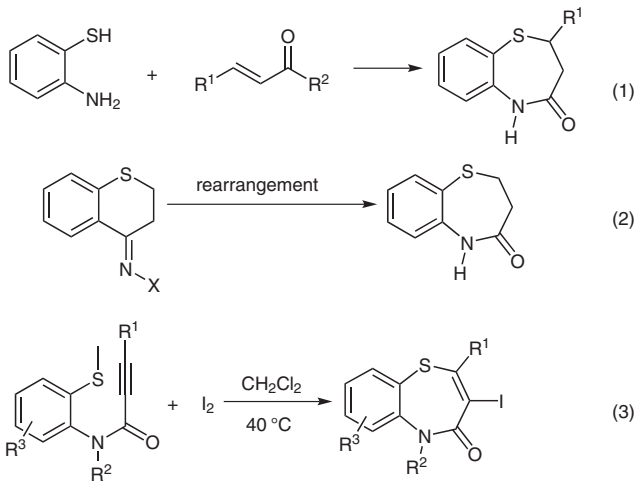
Abstract: A selective method for the synthesis of 3-iodo-1,5-benzothiazepin-4-ones via the intramolecular iodocyclization of *N*-[2-(methylthio)phenyl]propiolamides has been developed. In the presence of I_2, iodocyclizations of *N*-[2-(methylthio)phenyl]propiolamides were conducted smoothly to afford the corresponding 3-iodo-1,5-benzothiazepin-4-ones in moderate to good yields.

Key words: iodine, iodide, iodocyclization, *N*-[2-(methylthio)phenyl]propiolamide, 3-iodo-1,5-benzothiazepin-4-one

1,5-Benzothiazepin-4-one scaffolds are extremely versatile structural units for drug lead discovery due to their wide range of activity against different families of target.[1] A number of 1,5-benzothiazepin-4-one compounds,[2–5] such as diltiazem,[3] clentiazem,[4] and thiazesim[5], have been clinically used as drugs. Although considerable efforts have been devoted to the development of efficient methods for the synthesis of 1,5-benzothiazepin-4-ones,[6–8] the majority are focused on (1) the addition/cyclization of *o*-aminothiophenol with α,β-unsaturated carbonyls or β-halo acids (Scheme 1, Equation 1),[7] and (2) ring enlargement of *N*-halothiochromen-4-imines via Beckmann or Schmidt-type rearrangements (Scheme 1, Equation 2).[8] To the best of our knowledge, the construction of benzothiazepine skeleton by the electrophilic cyclization reaction still remains an unexplored area. Recently, Flynn's group and Larock's group independently reported the electrophilic cyclizations of 2-ethynylphenylsulfanes to synthesize benzo[*b*]thiophenes and iodothiochromenones.[9,10] These results prompted us to examine the feasibility of synthesizing 1,5-benzothiazepin-4-ones by the electrophilic cyclization reaction. After a series of trials, we found that 3-iodo-1,5-benzothiazepin-4-ones could be obtained by electrophilic cyclization of *N*-[2-(methylthio)phenyl]propiolamides with I_2 in moderate to good yields (Scheme 1, Equation 3). Here, we report our results in detail.

The reactions of *N*-methyl-*N*–[2-(methylthio)phenyl]-3-phenylpropiolamide (**1a**) with various iodine reagents were conducted to screen the optimal reaction conditions, and the results are summarized in Table 1. Initially, three iodine reagents were investigated. While treatment of **1a** with ICl or NIS in CH_2Cl_2 at room temperature for 24 hours afforded the target product **2a** in low yields (Table 1, entries 1 and 2), I_2 provided the target product **2a** in 72% yield after 12 hours (entry 3). It is noteworthy that the structure of **2a** was unambiguously confirmed by the X-ray single-crystal diffraction analysis (Figure 1). Subsequently, the effect of reaction temperature was evaluated (entries 3 and 4). We were delighted to find that the yield of **2a** could be increased to 81% at reflux (40 °C, entry 4). The results showed that the addition of K_2CO_3 did not affect the reaction (entry 5), and 2 equivalents of I_2 reduced the yield (entry 6). Finally, three other solvents, MeCN, methanol, and $MeNO_2$ were evaluated, and they were less effective than CH_2Cl_2 (entries 7–9).



Scheme 1 Synthesis of 1,5-benzothiazepin-4-ones

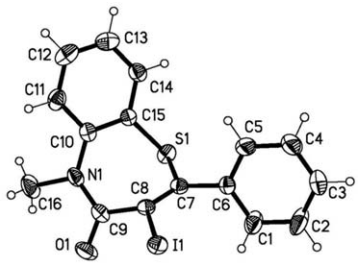


Figure 1 ORTEP Diagram of the single-crystal X-ray structure of compound **2a**. Selected bond lengths (Å): O(1)–C(15), 1.218(4); N(1)–C(15), 1.375(4); N(1)–C(14), 1.403(4); N(1)–C(16), 1.452(4); C(1)–C(2), 1.375(5); C(1)–C(6), 1.396(5); C(2)–C(3), 1.370(6); C(3)–C(4), 1.375(6); C(4)–C(5), 1.375(6); C(5)–C(6), 1.401(5); C(6)–C(7), 1.458(5); C(7)–C(8), 1.345(5); C(8)–C(9), 1.468(5); C(8)–C(15), 1.490(5); C(9)–C(10), 1.375(5); C(9)–C(14), 1.394(5); C(10)–C(11), 1.382(5); C(11)–C(12), 1.380(6); C(12)–C(13), 1.384(5); C(13)–C(14), 1.376(5).

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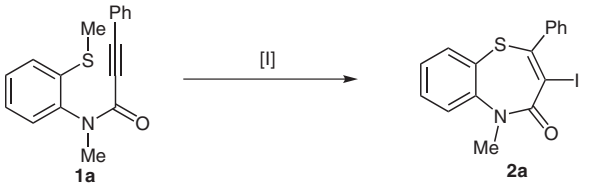
Table 1 Screening Optimal Conditions for the Cyclization of **1a**[a]



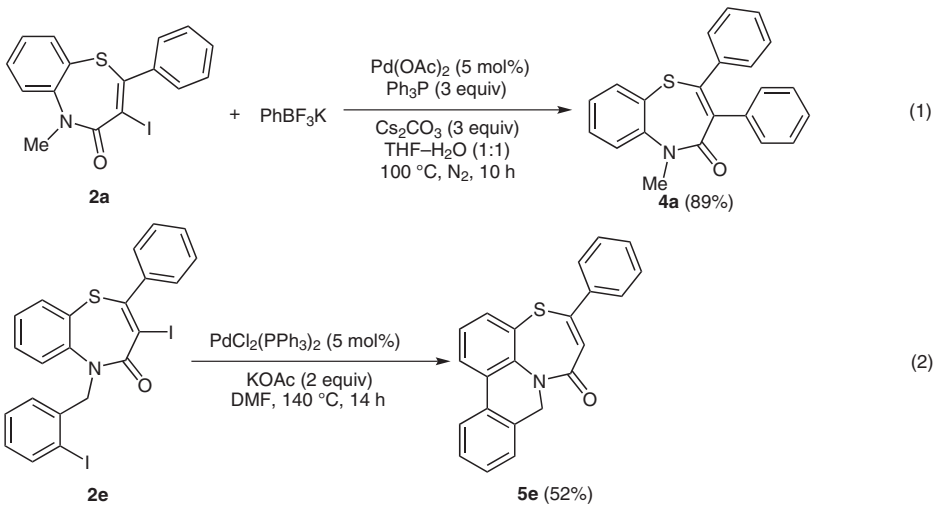
Entry	[I] (equiv)	Solvent	Temp (°C)	Time (h)	Isolated yield (%)
1	ICl (1.5)	CH_2Cl_2	25	24	22
2	NIS (1.5)	CH_2Cl_2	25	24	30
3	I_2 (1.5)	CH_2Cl_2	25	12	72
4	I_2 (1.5)	CH_2Cl_2	40	12	81
5[b]	I_2 (1.5)	CH_2Cl_2	40	12	80
6	I_2 (2.0)	CH_2Cl_2	40	12	51
7	I_2 (1.5)	MeCN	40	12	18
8	I_2 (1.5)	MeOH	40	12	16
9	I_2 (1.5)	$MeNO_2$	40	12	40

[a] Reaction conditions: **1a** (0.2 mmol), [I], and solvent (2 mL).
[b] K_2CO_3 (2 equiv) was added.

With the optimal conditions in hand, we next explored the scope of arylpropiolamides for the intramolecular iodocyclization reaction (Table 2). As shown in Table 2, a variety of amides **1b–q** were examined in the presence of I_2 and CH_2Cl_2. We found that the reaction could not occur when the *N*-methyl group was replaced by a hydrogen atom or an acetyl group (entries 1 and 2). To our delight, both *N*-benzyl-*N*-[2-(methylthio)phenyl]-3-phenylpropiolamide (**1d**) and *N*-(2-iodobenzyl)-*N*-[2-(methylthio)phenyl]-3-phenylpropiolamide (**1e**) are suitable substrates for the reaction with I_2 in moderate yields (entries 3 and 4). Substituents at the terminal alkyne of propiolamides were subsequently evaluated. The results demonstrated that both electronics and sterics affected the reaction to some extent. Substrates **1f** and **1h–k**, bearing *para*-substituted aryl groups, underwent the cyclization with I_2 smoothly to afford the *endo-dig*-products, exclusively, in moderate to good yields (entries 5 and 7–10). However, amines **1g** and **1l**, having an *ortho*- or *meta*-substituted aryl group, provided a mixture of an *endo-dig*-product and an *exo-dig*-product (entries 6 and 11). It is noteworthy that the electron-deficient groups at the terminal alkyne disfavor the reaction. Although a heteroaryl alkyne **1m** underwent reaction, it gave a mixture of the products **2m** and **3m** in a low total yield (entry 12). Gratifyingly, substrates **1n** or **1o**, bearing an aliphatic group at the terminal alkyne, afforded the desired products in good yields (entries 13 and 14). The reaction of *N*-methyl-*N*-[2-(methylthio)phenyl]propiolamide (**1p**), a terminal alkyne, with I_2 was also successful to afford the target product **2p** in 46% yield together with the *exo-dig*-product **3p** in 11% yield (entry 15). It was interesting to observe that *N*-[5-(trifluoromethyl)-2-(methylthio)phenyl]-*N*-methyl-3-phenylpropiolamide (**1q**) could undergo the reaction smoothly with I_2 in 58% yield (entry 16).

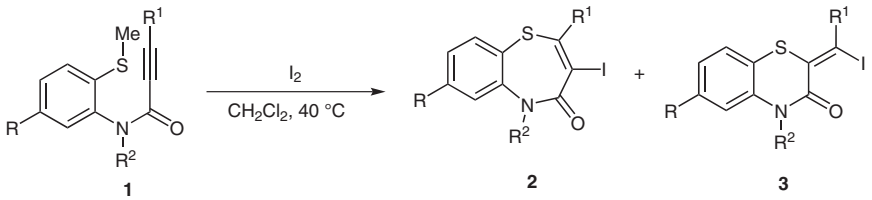
The iodocyclization products have several functional groups, such as iodo and olefin groups, which provide an attractive and useful route to introduce new groups for the synthesis of natural products. For example, a phenyl group was introduced at the 3-position of 1,5-benzothiazepin-4-one by treatment of 3-iodo-5-methyl-2-phenylbenzo[*b*][1,4]thiazepin-4(5*H*)-one (**2a**) with $PhBF_3K$, $Pd(OAc)_2$, Ph_3P, and Cs_2CO_3 to afford **4a** (Scheme 2, Equation 1).[11] To our delight, palladium-catalyzed intramolecular oxidative coupling reaction of 5-(2-iodobenzyl)-3-iodo-2-phenylbenzo[*b*][1,4]thiazepin-4(5*H*)-one (**2e**) was also carried out smoothly to afford the tetracyclic heterocycle **5e** in 52% yield (Scheme 2, Equation 2).[12]

In summary, we have developed a novel intramolecular iodocyclization reaction method for the synthesis of 3-iodo-1,5-benzothiazepin-4-ones. In the presence of I_2, a variety of *N*-[2-(methylthio)phenyl]propiolamides successfully underwent the iodocyclization reaction to afford selectively 3-iodo-1,5-benzothiazepin-4-ones in moderate to good yields.



Scheme 2

Table 2 Iodocyclization of *N*-[2-(Methylthio)phenyl]propiolamides **1**[a]



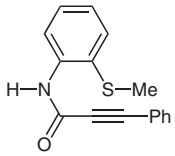
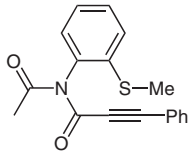
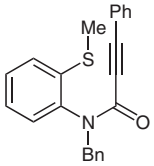
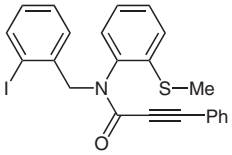
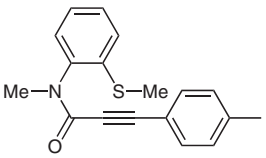
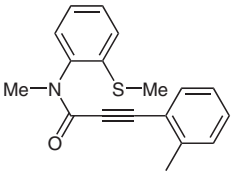
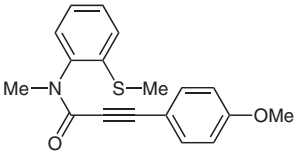
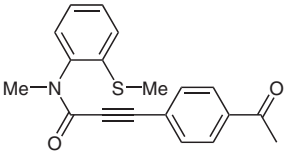
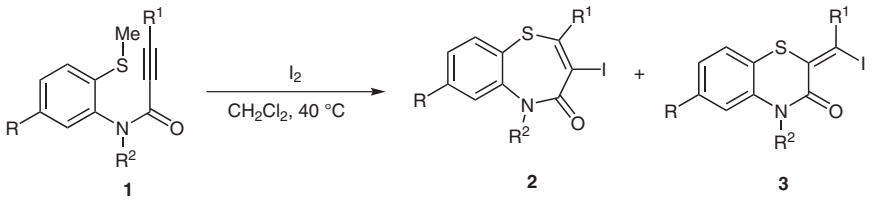
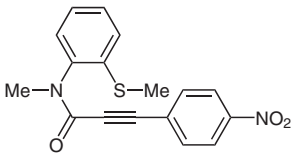
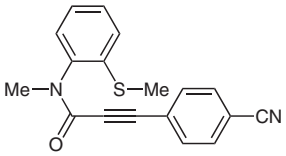
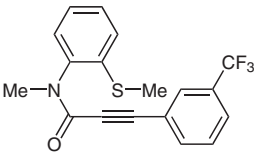
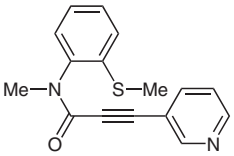
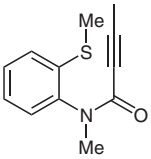
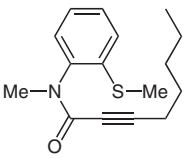
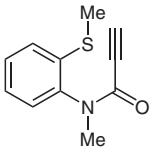
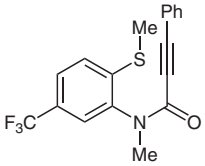
Entry	Propiolamide		Time (h)	Isolated yield of product(s) (%)	
				2	**3**
1	**1b**		24	trace (**2b**)	0 (**3b**)
2	**1c**		24	trace (**2c**)	0 (**3c**)
3	**1d**		12	65 (**2d**)	0 (**3d**)
4	**1e**		12	62 (**2e**)	0 (**3e**)
	1f		12	77 (**2f**)	0 (**3f**)
6[b]	**1g**		12	37 (**2g**)	37 (**3g**)
7	**1h**		24	trace (**2h**)	0 (**3h**)
8	**1i**		12	60 (**2i**)	0 (**3i**)

Table 2 Iodocyclization of *N*-[2-(Methylthio)phenyl]propiolamides **1**[a] (continued)



Entry	Propiolamide		Time (h)	Isolated yield of product(s) (%)	
				2	**3**
9	**1j**		24	48 (**2j**)	0 (**3j**)
10	**1k**		24	34 (**2k**)	0 (**3k**)
11	**1l**		12	18 (**2l**)	61 (**3l**)
12	**1m**		24	20 (**2m**)	16 (**3m**)
13	**1n**		12	86 (**2n**)	0 (**3n**)
14	**1o**		12	81(**2o**)	0 (**3o**)
15[b]	**1p**		12	46 (**2p**)	11 (**3p**)
16	**1q**		12	58 (**2q**)	0 (**3q**)

[a] Reaction conditions: **1** (0.2 mmol), I_2 (0.3 mmol), and CH_2Cl_2 (2 mL) at 40 °C.
[b] The mixture of **2** and **3** can not be isolated, and the ratio was confirmed by ^1H NMR spectroscopy.

Melting points are uncorrected. NMR spectroscopy was performed on a Bruker-300 spectrometer operating at 300 MHz (^{1}H NMR) and 75 MHz (^{13}C NMR). TMS was used an internal standard and $CDCl_3$ was used as the solvent. Mass spectrometric analysis was performed on GC-MS analysis (Shimadzu GCMS-QP2010).

N-[2-(Methylthio)phenyl]propiolamides 1;[13] General Procedure

To a solution of 2-(methylthio)aniline (696.0 mg, 5 mmol) and propiolic acid (364.3 mg, 5.2 mmol) in CH_2Cl_2 (6 mL) was added gradually a solution of both DCC (1.07 g, 5.2 mmol) and DMAP (12.2 mg, 0.1 mmol) in CH_2Cl_2 (6 mL) at 0 °C, and then the mixture was stirred at r.t. for 4 h. After completion of the reaction, aq sat. NaCl (10 mL) was added, and the aqueous phase was extracted with CH_2Cl_2 (5 × 5 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under vacuo. The residue was purified by flash column chromatography on silica gel using EtOAc–hexane (1:5) as eluent to give the pure product, which was treated with MeI (1.42 g, 10 mmol) in the presence of NaH (240 mg, 10 mmol) to afford *N*-methyl-*N*-[2-(methylthio)phenyl]propiolamide.

This product was used for the Sonagashira cross-coupling reaction as follows. A mixture of *N*-methyl-*N*-[2-(methylthio)phenyl]propiolamide (102.7 mg, 0.5 mmol), ArI (0.5 mmol), CuI (9.5 mg, 0.05 mmol), $PdCl_2(PPh_3)_2$ (17.5 mg, 0.025 mmol), Et_3N (3 mL) and THF (3 mL) was heated at 60 °C for 6–24 h under N_2 until complete consumption of starting material as monitored by TLC. The precipitate was filtered, and the organic solution was evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel (hexane–EtOAc) to give the corresponding *N*-[2-(methylthio)phenyl]propiolamide **1**.

For the preparation of **1q**, 5-trifluoromethyl-2(methylthio)aniline was used as the starting aniline. For the preparation of **1b** no MeI was used, and for **1c**–**e**, MeI was replaced by the respective alkylating reagent.

N-Methyl-*N*-[2-(methylthio)phenyl]-3-phenylpropiolamide (1a)

Yield: 89%; light yellow solid; mp 80.9–83.2 °C.

IR (KBr): 2919, 2210, 1640, 1362 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.39 (m, 1 H), 7.31–7.18 (m, 6 H), 7.05 (d, *J* = 7.1 Hz, 2 H), 3.31 (s, 3 H), 2.46 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ =154.8, 140.4, 139.1, 132.5, 129.8, 129.3, 129.2, 128.2, 125.9, 125.4, 120.5, 89.8, 82.5, 34.7, 15.0.

LRMS (EI, 70 eV): *m*/*z* (%) = 281 (M$^+$, 5), 234 (92), 129 (100).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{15}NOS$ (M$^+$): 281.0874; found: 281.0871.

N-[2-(Methylthio)phenyl]-3-phenylpropiolamide (1b)

Yield: 91%; yellow solid; mp 88.2–90.7 °C.

IR (KBr): 3318, 2914, 2207, 1658, 1378 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.67 (br s, 1 H), 8.34 (d, *J* = 7.7 Hz, 1 H), 7.63–7.61 (m, 2 H), 7.53–7.30 (m, 5 H), 7.14–7.08 (m, 1 H), 2.42 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.0, 137.9, 133.1, 132.7, 130.4, 129.0, 128.6, 128.2, 125.0, 121.1, 119.9, 85.9, 83.5, 19.2.

LRMS (EI, 70 eV): *m*/*z* (%) = 267 (M$^+$, 11), 234 (15), 220 (32), 129 (100).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{13}NOS$ (M$^+$): 267.0718; found: 267.0717.

N-Acetyl-*N*-[2-(methylthio)phenyl]-3-phenylpropiolamide (1c)

Yield: 85%; white solid; mp 110.9–113.2 °C.

IR (KBr): 2914, 2215, 1640, 1628, 1360 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.53–7.49 (m, 1 H), 7.41–7.37 (m, 2 H), 7.32–7.25 (m, 4 H), 7.12 (d, *J* = 7.2 Hz, 2 H), 2.68 (s, 3 H), 2.46 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.0, 154.6, 139.2, 136.5, 133.1, 130.8, 130.4, 129.9, 128.4, 126.8, 125.9, 119.5, 94.2, 82.8, 27.1, 15.5.

LRMS (EI, 70 eV): *m*/*z* (%) = 309 (M$^+$, 8), 294 (19), 267(16), 220 (18), 129 (100).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{15}NO_2S$ (M$^+$): 309.0824; found: 309.0820.

N-Benzyl-*N*-[2-(methylthio)phenyl]-3-phenylpropiolamide (1d)

Yield: 88%; white solid; mp 101.3–103.5 °C.

IR (KBr): 2931, 2211, 1633, 14352, 1380, 694 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.28 (m, 8 H), 7.24–7.19 (m, 2 H), 7.08–7.04 (m, 3 H), 6.81 (d, *J* = 7.7 Hz, 1 H), 5.64 (d, *J* = 14.3 Hz, 1 H), 4.25 (d, *J* = 14.3 Hz, 1 H), 2.47 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.8, 139.2, 136.7, 132.6, 130.9, 129.4, 129.1, 128.6, 128.5, 128.4, 128.2, 127.6, 126.0, 124.9, 120.5, 90.2, 82.6, 50.2, 15.2.

LRMS (EI, 70 eV): *m*/*z* (%) = 357 (M$^+$, 10), 310 (49), 129 (74), 91 (100).

HRMS (EI): *m*/*z* calcd for $C_{23}H_{19}NOS$ (M$^+$): 357.1187; found: 357.1185.

N-(2-Iodobenzyl)-*N*-[2-(methylthio)phenyl]-3-phenylpropiolamide (1e)

Yield: 67%; yellow solid; mp 104.2–106.3 °C.

IR (KBr): 2922, 2211, 1630, 1341, 1370, 752 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 7.8 Hz, 1 H), 7.52–7.50 (m, 1 H), 7.34–7.30 (m, 5 H), 7.26–7.23 (m, 1 H), 7.20–7.16 (m, 3 H), 7.08–7.05 (m, 2 H), 5.63 (d, *J* = 14.8 Hz, 1 H), 4.62 (d, *J* = 14.8 Hz, 1 H), 2.47 (s, 3 H), 2.29 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.9, 139.5, 139.3, 139.1, 138.1, 135.8, 132.6, 130.8, 130.6, 129.9, 129.3, 128.5, 128.2, 126.3, 125.1, 120.3, 100.1, 90.6, 82.4, 53.8, 15.4.

LRMS (EI, 70 eV): *m*/*z* (%) = 483 (M$^+$, 1), 436 (27), 356 (97), 308 (22), 217 (38), 129 (100).

HRMS (EI): *m*/*z* calcd for $C_{23}H_{18}INOS$ (M$^+$): 483.0154; found: 483.0150.

N-Methyl-*N*-[2-(methylthio)phenyl]-3-*p*-tolylpropiolamide (1f)

Yield: 70%; light yellow solid; mp 82.3–85.0 °C.

IR (KBr): 2920, 2209, 1638, 1360 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41–7.38 (m, 1 H), 7.31–7.23 (m, 3 H), 7.27–7.18 (m, 3 H), 7.01 (d, *J* = 8.0 Hz, 2 H), 6.95 (d, *J* = 8.0 Hz, 2 H), 3.31 (s, 3 H), 2.45 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ =154.9, 140.5, 140.3, 139.1, 132.5, 129.3, 129.2, 129.0, 125.9, 125.4, 117.3, 90.3, 82.1, 34.7, 21.6, 15.0.

LRMS (EI, 70 eV): *m*/*z* (%) = 295 (M$^+$, 7), 248 (88), 143 (100).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{17}NOS$ (M$^+$): 295.1031; found: 295.1029.

N-Methyl-*N*-[2-(methylthio)phenyl]-3-*o*-tolylpropiolamide (1g)

Yield: 51%; pale yellow oil.

IR (neat): 2924, 2212, 1687, 1375, 765 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41–7.36 (m, 1 H), 7.29–7.21 (m, 5 H), 7.08–7.04 (m, 2 H), 3.31 (s, 3 H), 2.46 (s, 3 H), 1.87 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.9, 141.4, 140.3, 139.1, 133.3, 129.8, 129.3, 129.2, 126.6, 125.9, 125.6, 125.5, 120.4, 88.5, 86.3, 34.8, 19.9, 14.9.

LRMS (EI, 70 eV): *m*/*z* (%) = 295 (M^+, 5), 280 (22), 248 (100), 143 (56), 115 (76).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{17}NOS$ (M^+): 295.1031; found: 295.1030.

3-(4-Methoxyphenyl)-*N*-methyl-*N*-[2-(methylthio)phenyl]propiolamide (1h)
Yield: 59%; light yellow solid; mp 103.0–105.5 °C.

IR (KBr): 2925, 2201, 1632, 1471, 680 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.51–7.46 (m, 1 H), 7.32–7.28 (m, 3 H), 7.00 (d, *J* = 8.4 Hz, 2 H), 6.72 (d, *J* = 8.4 Hz, 2 H), 3.77 (s, 3 H), 3.31 (s, 3 H), 2.46 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.8, 155.1, 140.5, 139.1, 134.3, 129.3, 129.1, 125.8, 125.4, 113.9, 112.3, 90.5, 81.8, 55.3, 34.6, 15.0.

LRMS (EI, 70 eV): *m*/*z* (%) = 323 (M^+, 9), 276 (91), 171 (100).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{17}NO_2S$ (M^+): 311.0980; found: 311.0978.

3-(4-Acetylphenyl)-*N*-methyl-*N*-[2-(methylthio)phenyl]propiolamide (1i)
Yield: 55%; light yellow solid; mp 101.0–103.1 °C.

IR (KBr): 2924, 2219, 1685, 1631, 1469, 678 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.80 (d, *J* = 8.4 Hz, 2 H), 7.47–7.41 (m, 1 H), 7.32–7.22 (m, 3 H), 7.16 (d, *J* = 8.4 Hz, 2 H), 3.33 (s, 3 H), 2.56 (s, 3 H), 2.47 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.1, 154.4, 139.9, 139.1, 137.4, 132.6, 129.4, 129.2, 128.3, 125.8, 125.4, 125.1, 88.3, 84.8, 30.9, 26.7, 14.9.

LRMS (EI, 70 eV): *m*/*z* (%) = 323 (M^+, 9), 276 (91), 171 (100).

HRMS (EI): *m*/*z* calcd for $C_{19}H_{17}NO_2S$ (M^+): 323.0980; found: 323.0979.

***N*-Methyl-*N*-[2-(methylthio)phenyl]-3-(4-nitrophenyl)propiolamide (1j)**
Yield: 78%; light yellow solid; mp 126.1–127.9 °C.

IR (KBr): 3092, 2224, 1645, 1507, 708 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.09 (d, *J* = 8.6 Hz, 2 H), 7.47–7.42 (m, 1 H), 7.33–7.22 (m, 5 H), 3.33 (s, 3 H), 2.48 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.9, 147.9, 139.8, 139.2, 133.2, 129.5, 129.2, 127.2, 125.8, 125.4, 123.5, 86.6, 86.3, 34.7, 14.9.

LRMS (EI, 70 eV): *m*/*z* (%) = 326 (M^+, 5), 279 (100), 233 (34), 136 (46).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{14}N_2O_3S$ (M^+): 326.0725; found: 326.0723.

3-(4-Cyanophenyl)-*N*-methyl-*N*-[2-(methylthio)phenyl]propiolamide (1k)
Yield: 81%; light yellow solid; mp 123.3–125.2 °C.

IR (KBr): 2924, 2220, 1648, 1349, 760 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.52 (d, *J* = 8.5 Hz, 2 H), 7.45–7.41 (m, 1 H), 7.33–7.24 (m, 3 H), 7.17 (d, *J* = 8.5 Hz, 2 H), 3.33 (s, 3 H), 2.48 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.0, 139.8, 139.1, 132.8, 131.9, 129.5, 129.1, 125.8, 125.4, 125.2, 117.9, 113.1, 86.9, 85.6, 34.7, 14.9.

LRMS (EI, 70 eV): *m*/*z* (%) = 306 (M^+, 4), 273 (13), 259 (100), 154 (32), 136 (34).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{14}N_2OS$ (M^+): 306.0827; found: 306.0825.

***N*-Methyl-*N*-[2-(methylthio)phenyl]-3-[3-(trifluoromethyl)phenyl]propiolamide (1l)**
Yield: 71%; light yellow oil.

IR (neat): 2930, 2219, 1639, 1457, 1337, 770 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.53–7.51 (m, 1 H), 7.40–7.36 (m, 1 H), 7.29–7.22 (m, 6 H), 3.32 (s, 3 H), 2.45 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.3, 140.0, 139.2, 135.3, 129.4, 129.3, 129.2, 128.9, 127.2 (q, $J_{C,F}$ = 270.8 Hz), 126.3, 126.2, 125.7, 125.4, 121.9, 87.7, 83.6, 34.6, 14.8.

LRMS (EI, 70 eV): *m*/*z* (%) = 349 (M^+, 7), 302 (100), 197 (38), 136 (34).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{14}F_3NOS$ (M^+): 349.0748; found: 349.0745.

***N*-Methyl-*N*-[2-(methylthio)phenyl]-3-(pyridin-3-yl)propiolamide (1m)**
Yield: 45%; light yellow oil.

IR (neat): 2818, 2214, 1640, 1310, 740 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.50–8.52 (m, 1 H), 8.18–8.20 (m, 1 H), 7.46–7.31 (m, 2 H), 7.29–7.18 (m, 4 H), 3.31 (s, 3 H), 2.46 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.2, 153.0, 149.9, 139.9, 139.3, 139.1, 129.5, 129.2, 125.8, 125.4, 122.9, 117.7, 86.0, 85.3, 34.6, 14.9.

LRMS (EI, 70 eV): *m*/*z* (%) = 282 (M^+, 4), 281 (7), 249 (14), 235 (100), 130 (54).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{14}N_2OS$ (M^+): 282.0827; found: 282.0826.

***N*-Methyl-*N*-[2-(methylthio)phenyl]but-2-ynamide (1n)**
Yield: 80%; yellow solid; mp 60.2–63.1 °C.

IR (KBr): 2910, 2208, 1630, 1351, 771 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.35 (m, 1 H), 7.29–7.27 (m, 1 H), 7.25–7.19 (m, 2 H), 3.24 (s, 3 H), 2.45 (s, 3 H), 1.71 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.8, 140.3, 138.6, 129.0, 127.9, 125.8, 125.3, 88.7, 73.9, 34.6, 14.9, 3.8.

LRMS (EI, 70 eV): *m*/*z* (%) = 219 (M^+, 2), 172 (100), 136 (29).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{13}NOS$ (M^+): 219.0718; found: 219.0716.

***N*-Methyl-*N*-[2-(methylthio)phenyl]oct-2-ynamide (1o)**
Yield: 85%; light yellow oil.

IR (neat): 2927, 2895, 2211, 1649, 1324, 785 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.34–7.33 (m, 1 H), 7.29–7.27 (m, 1 H), 7.19–7.17 (m, 2 H), 3.23 (s, 3 H), 2.45 (s, 3 H), 2.05 (t, *J* = 7.0 Hz, 2 H), 1.17–1.10 (m, 3 H), 1.01–0.99 (m, 3 H), 0.81 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.8, 140.4, 138.7, 129.0, 128.9, 125.7, 125.3, 92.8, 74.8, 34.5, 30.3, 27.1, 21.9, 18.5, 14.9, 13.8.

LRMS (EI, 70 eV): *m*/*z* (%) = 260 ($M^+ - CH_3$, 38), 228 (100), 178 (26), 136 (30).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{21}NOS$ (M^+): 275.1344; found: 275.1341.

N-Methyl-N-[2-(methylthio)phenyl]propiolamide (1p)
Yield: 95%; yellow solid; mp 51.8–53.4 °C.

IR (KBr): 3002, 2918, 2205, 1630 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.41–7.37 (m, 1 H), 7.28–7.20 (m, 3 H), 3.25 (s, 3 H), 2.71 (s, 1 H), 2.47 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.5, 139.6, 138.8, 129.4, 129.0, 125.8, 125.5, 78.1, 76.2, 34.7, 14.8.

LRMS (EI, 70 eV): *m*/*z* (%) = 205 (M^+, 6), 158 (100), 136 (34).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{11}NOS$ (M^+): 205.0561; found: 205.0560.

N-Methyl-N-[2-(methylthio)-5-(trifluoromethyl)phenyl]-3-phenylpropiolamide (1q)
Yield: 51%; colorless oil.

IR (neat): 2916, 2209, 1646, 1339, 675 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.65–7.60 (m, 1 H), 7.56 (s, 1 H), 7.37–7.20 (m, 4 H), 7.10–7.06 (m, 2 H), 3.33 (s, 3 H), 2.50 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.5, 144.8, 139.9, 132.5, 130.1, 128.6, 128.3, 127.2 (q, $J_{C,F}$ = 247.5 Hz), 126.3, 125.8, 125.6, 120.0, 90.4, 81.9, 34.3, 14.4.

LRMS (EI, 70 eV): *m*/*z* (%) = 349 (M^+, 4), 303 (11), 302 (53), 129 (100).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{14}F_3NOS$ (M^+): 349.0748; found: 349.0745.

Iodocyclization of *N*-[2-(Methylthio)phenyl]propiolamides 1 with I_2; General Procedure
A mixture of *N*-[2-(methylthio)phenyl]propiolamide **1** (0.2 mmol) and I_2 (76.2 mg, 0.3 mmol) was stirred in CH_2Cl_2 (2 mL) at 40 °C for the indicated time (Table 2) until complete consumption of starting material as monitored by TLC and GC analysis. After completion of the reaction, aq sat. $Na_2S_2O_3$ (10 mL) was added, and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under vacuo. The residue was purified by flash column chromatography on silica gel using EtOAc–hexane (1:5) as eluent to give the product **2** or a mixture of **2** and **3** (Table 2).

3-Iodo-5-methyl-2-phenylbenzo[*b*][1,4]thiazepin-4(5*H*)-one (2a)
Light yellow solid; mp 144.1–145.0 °C.

IR (KBr): 2923, 1638, 1474, 1347, 683 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 7.7 Hz, 1 H), 7.48–7.41 (m, 4 H), 7.38–7.23 (m, 4 H), 3.58 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.8, 149.9, 144.2, 140.9, 136.1, 132.6, 130.3, 129.4, 128.9, 128.3, 126.1, 124.7, 92.0, 38.6.

LRMS (EI, 70 eV): *m*/*z* (%) = 393 (M^+, 13), 266 (100), 226 (32).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{12}INOS$ (M^+): 392.9684; found: 392.9682.

5-Benzyl-3-iodo-2-phenylbenzo[*b*][1,4]thiazepin-4(5*H*)-one (2d)
Light yellow solid; mp 123.7–124.5 °C.

IR (KBr): 2931, 1632, 1439, 1380, 696 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.63 (d, *J* = 7.6 Hz, 1 H), 7.50 (m, 2 H), 7.44–7.17 (m, 11 H), 5.41 (d, *J* = 15.3 Hz, 1 H), 5.16 (d, *J* = 15.3 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.0, 149.7, 142.9, 140.6, 137.0, 136.5, 132.9, 130.2, 129.5, 128.9, 128.6, 128.3, 127.6, 127.5, 126.2, 124.8, 91.2, 54.2.

LRMS (EI, 70 eV): *m*/*z* (%) = 469 (M^+, 5), 342 (19), 129 (18), 91 (100).

HRMS (EI): *m*/*z* calcd for $C_{22}H_{16}INOS$ (M^+): 468.9997; found: 468.9996.

3-Iodo-5-(2-iodobenzyl)-2-phenylbenzo[*b*][1,4]thiazepin-4(5*H*)-one (2e)
Yellow solid; mp179.8–181.0 °C.

IR (KBr): 2922, 1632, 1339, 1376, 757 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 7.8 Hz, 1 H), 7.66 (d, *J* = 7.5 Hz, 1 H), 7.56–7.51 (m, 3 H), 7.40–7.35 (m, 6 H), 7.22–7.16 (m, 1 H), 6.96 (m, 1 H), 5.36 (d, *J* = 16.4 Hz, 1 H), 5.19 (d, *J* = 16.4 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.9, 149.7, 143.1, 140.5, 138.3, 138.1, 136.3, 134.0, 131.4, 130.5, 129.5, 129.3, 128.6, 127.9, 127.4, 126.6, 125.2, 123.2, 97.9, 90.7, 59.5.

LRMS (EI, 70 eV): *m*/*z* (%) = 595 (M^+, 4), 468 (100), 341 (23), 217 (88).

HRMS (EI): *m*/*z* calcd for $C_{22}H_{15}I_2NOS$ (M^+): 594.8964; found: 594.8963.

3-Iodo-5-methyl-2-*p*-tolylbenzo[*b*][1,4]thiazepin-4(5*H*)-one (2f)
Light yellow solid; mp 189.3–191.0 °C.

IR (KBr): 2920, 1638, 1360, 759 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 7.3 Hz, 1 H), 7.47–7.38 (m, 4 H), 7.27–7.18 (m, 3 H), 3.58 (s, 3 H), 2.38 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.9, 150.0, 144.2, 139.7, 137.9, 136.0, 132.6, 130.2, 129.0, 128.9, 126.0, 124.7, 91.1, 38.6, 21.5.

LRMS (EI, 70 eV): *m*/*z* (%) = 407 (M^+, 10), 280 (100), 240 (30).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{14}INOS$ (M^+): 406.9841; found: 406.9840.

3-Iodo-5-methyl-2-*o*-tolylbenzo[*b*][1,4]thiazepin-4(5*H*)-one (2g) and 2-[(*E*)-Iodo(*o*-tolyl)methylidene]-4-methyl-2*H*-benzo[*b*][1,4]thiazin-3(4*H*)-one (3g)
2g/3g = 1:1; pale yellow oil.

IR (neat): 2910, 1688, 1380, 760 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.55–7.50 (m, 3 H), 7.47–7.41 (m, 4 H), 7.28–7.19 (m, 1 H), 3.59 (s, 3 H), 2.35 (s, 1.5 H), 2.00 (s, 1.5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.9, 151.7, 150.7, 143.9, 142.2, 135.6, 134.8, 134.4, 132.7, 130.3, 129.0, 127.4, 126.1, 124.8, 96.6, 96.0, 39.2, 38.7, 20.0, 19.6.

LRMS (EI, 70 eV): *m*/*z* (%) = 407 (M^+, 23), 280 (100), 115 (46).

2-(4-Acetylphenyl)-3-iodo-5-methylbenzo[*b*][1,4]thiazepin-4(5*H*)-one (2i)
Light yellow solid; mp 204.0–205.2 °C.

IR (KBr): 2926, 1683, 1633, 1476, 1261, 678 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.98 (d, *J* = 8.2 Hz, 2 H), 7.65 (d, *J* = 7.7 Hz, 1 H), 7.56 (d, *J* = 8.2 Hz, 2 H), 7.51–7.45 (m, 2 H), 7.28 (m, 1 H), 3.60 (s, 3 H), 2.64 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.3, 166.5, 148.9, 145.5, 144.0, 137.3, 135.8, 132.6, 130.5, 129.1, 128.4, 126.3, 124.9, 93.6, 38.7, 26.7.

LRMS (EI, 70 eV): *m*/*z* (%) = 435 (M^+, 24), 308 (64), 266 (100).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{14}INO_2S$ (M^+): 434.9790; found: 434.9789.

3-Iodo-5-methyl-2-(4-nitrophenyl)benzo[*b*][1,4]thiazepin-4(5*H*)-one (2j)
Light yellow solid; mp 179.7–185.5 °C.

IR (KBr): 3094, 1647, 1510, 1342, 704 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.28 (d, *J* = 8.4 Hz, 2 H), 7.42 (d, *J* = 8.4 Hz, 2 H), 7.31–7.28 (m, 1 H), 7.16–7.03 (m, 3 H), 3.62 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.1, 149.6, 147.7, 138.0, 129.4, 127.8, 126.0, 125.8, 123.9, 123.7, 121.3, 117.7, 97.9, 33.2.

LRMS (EI, 70 eV): *m*/*z* (%) = 438 (M^+, 100), 311 (71), 236 (64).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{11}IN_2O_3S$ (M^+): 437.9535; found: 437.9533.

4-(3-Iodo-5-methyl-4-oxo-4,5-dihydrobenzo[*b*][1,4]thiazepin-2-yl)benzonitrile (2k)
Light yellow solid; mp 217.3–220.2 °C.

IR (KBr): 2917, 1644, 1346, 754 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 7.8 Hz, 2 H), 7.34 (d, *J* = 7.8 Hz, 2 H), 7.31–7.27 (m, 1 H), 7.14–7.01 (m, 3 H), 3.59 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.2, 147.8, 138.0, 132.1, 131.6, 129.1, 127.7, 126.0, 123.8, 121.4, 118.2, 117.6, 112.7, 98.5, 33.1.

LRMS (EI, 70 eV): *m*/*z* (%) = 418 (M^+, 100), 291 (81).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{11}IN_2OS$ (M^+): 417.9637; found: 417.9637.

3-Iodo-5-methyl-2-[3-(trifluoromethyl)phenyl]benzo[*b*][1,4]thiazepin-4(5*H*)-one (2l)
Light yellow solid; mp 95.0–97.3 °C.

IR (KBr): 2924, 1634, 1454, 1331, 762 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.74 (s, 1 H), 7.67–7.62 (m, 3 H), 7.54–7.42 (m, 3 H), 7.29–7.24 (m, 1 H), 3.59 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.5, 148.4, 144.1, 141.6, 135.7 132.6, 131.5, 131.0, 130.5, 130.2, 127.2 (q, $J_{C,F}$ = 270.8 Hz), 126.3, 126.0, 125.9, 124.9, 93.6, 38.6.

^{19}F NMR (282 MHz, $CDCl_3$): δ = –62.9 (s).

LRMS (EI, 70 eV): *m*/*z* (%) = 461 (M^+, 20), 334 (100), 294 (38).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{11}F_3INOS$ (M^+): 460.9558; found: 460.9557.

2-{(*E*)-Iodo[3-(trifluoromethyl)phenyl]methylidene}-4-methyl-2*H*-benzo[*b*][1,4]thiazin-3(4*H*)-one (3l)
Pale yellow oil.

IR (neat): 2917, 2932, 1657, 1329, 1126, 695 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.60–7.27 (m, 5 H), 7.14–7.08 (m, 2 H), 7.08–7.00 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.5, 144.1, 138.1, 131.8, 130.5, 128.8, 127.4, 126.0, 125.8 (q, J_{C-F} = 270.0 Hz), 125.6, 125.2, 123.7, 121.8, 117.6, 117.2, 99.4, 33.1.

^{19}F NMR (282 MHz, $CDCl_3$): δ = –62.7 (s).

LRMS (EI, 70 eV): *m*/*z* (%) = 461 (M^+, 100), 334 (79).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{11}F_3INOS$ (M^+): 460.9558; found: 460.9558.

3-Iodo-5-methyl-2-(pyridin-3-yl)benzo[*b*][1,4]thiazepin-4(5*H*)-one (2m)
Light yellow solid; mp 196.5–199.9 °C.

IR (KBr): 2818, 1633, 1351, 752 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.75 (s, 1 H), 8.60 (m, 1 H), 7.82 (m, 1 H), 7.65 (d, *J* = 7.8 Hz, 1 H), 7.50–7.44 (m, 2 H), 7.37–7.25 (m, 2 H), 3.59 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.4, 150.0, 149.7, 146.8, 144.0, 137.0, 136.5, 135.6, 132.6, 130.6, 126.3, 124.9, 130.0, 94.2, 38.7.

LRMS (EI, 70 eV): *m*/*z* (%) = 394 (M^+, 100), 267 (84).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{11}IN_2OS$ (M^+): 393.9637; found: 393.9636.

2-[(*E*)-Iodo(pyridin-3-yl)methylidene]-4-methyl-2*H*-benzo[*b*][1,4]thiazin-3(4*H*)-one (3m)
Pale yellow oil.

IR (neat): 2923, 2841, 1653, 1345, 1137, 750, 706 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.59–8.52 (m, 2 H), 7.68 (m, 1 H), 7.38–7.27 (m, 2 H), 7.14–7.11 (m, 2 H), 7.08–7.00 (m, 1 H), 3.60 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.5, 149.8, 148.7, 139.5, 138.1, 136.4, 127.6, 126.1, 125.6, 123.8, 123.0, 121.6, 117.6, 97.3, 33.1.

LRMS (EI, 70 eV): *m*/*z* (%) = 394 (M^+, 100), 267 (84).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{11}IN_2OS$ (M^+): 393.9637; found: 393.9637.

3-Iodo-2,5-dimethylbenzo[*b*][1,4]thiazepin-4(5*H*)-one (2n)
Yellow solid; mp 117.2–118.1 °C.

IR (KBr): 2920, 1632, 1357, 760 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.50–7.32 (m, 3 H), 7.18–7.13 (m, 1 H), 3.52 (s, 3 H), 2.35 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.2, 148.7, 144.1, 135.1, 132.7, 130.1, 125.8, 124.5, 94.1, 38.8, 31.4.

LRMS (EI, 70 eV): *m*/*z* (%) = 331 (M^+, 35), 204 (100), 164 (74).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{10}INOS$ (M^+): 330.9528; found: 330.9527.

3-Iodo-5-methyl-2-pentylbenzo[*b*][1,4]thiazepin-4(5*H*)-one (2o)
Light yellow oil.

IR (neat): 2927, 1641, 1474, 1300, 762 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.49 (d, *J* = 7.7 Hz, 1 H), 7.47–7.31 (m, 2 H), 7.17–7.14 (m, 1 H), 3.52 (s, 3 H), 2.66–2.51 (m, 2 H), 1.68–1.56 (m, 2 H), 1.33–1.24 (m, 4 H), 0.87 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.3, 152.8, 144.3, 135.6, 132.7, 129.9, 125.8, 124.4, 93.5, 43.6, 38.7, 31.0, 26.5, 22.4, 13.9.

LRMS (EI, 70 eV): *m*/*z* (%) = 387 (M^+, 10), 260 (100), 220 (53).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{18}INOS$ (M^+): 387.0154; found: 387.0153.

3-Iodo-5-methylbenzo[*b*][1,4]thiazepin-4(5*H*)-one (2p) and 2-[(*E*)-Iodomethylidene]-4-methyl-2*H*-benzo[*b*][1,4]thiazin-3(4*H*)-one (3p)
2p/3p = 4.2:1; yellow solid; mp 52.8–56.4 °C.

IR (KBr): 2918, 1630, 1346, 1252, 745 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.96 (s, 0.2 H), 7.33 (s, 0.8 H), 7.32–7.24 (m, 2 H), 7.11–7.03 (m, 2 H), 3.55 (s, 2.4 H), 3.51 (s, 0.6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.2, 138.1, 127.5, 126.2, 123.7, 121.6, 117.5, 116.7, 90.4, 82.9, 32.5, 32.4.

LRMS (EI, 70 eV): *m*/*z* (%) = 317 (M^+, 100), 190 (24), 162 (21), 109 (34).

3-Iodo-5-methyl-2-phenyl-7-(trifluoromethyl)benzo[*b*][1,4]thiazepin-4(5*H*)-one (2q)
White solid; mp 157.9–159.6 °C.

IR (KBr): 2916, 1643, 1339, 1128, 670 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 8.0 Hz, 1 H), 7.65 (s, 1 H), 7.51–7.38 (m, 6 H), 3.60 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.5, 148.8, 144.7, 140.5, 139.9, 134.2, 132.0, 130.5, 129.9, 128.7, 127.4 (q, $J_{C,F}$ = 270.6 Hz), 122.6, 120.5, 92.0, 39.5.

^{19}F NMR (282 MHz, $CDCl_3$): δ = –62.7 (s).

LRMS (EI, 70 eV): *m*/*z* (%) = 461 (M^+, 8), 334 (100), 294 (43), 129 (60).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{11}F_3INOS$ (M^+): 460.9558; found: 460.9555.

5-Methyl-2,3-diphenylbenzo[*b*][1,4]thiazepin-4(5*H*)-one (4a)
A mixture of **2a** (78.6 mg, 0.2 mmol), potassium phenyltrifluoroborate (38.6 mg, 0.21 mmol), $Pd(OAc)_2$ (2.5 mg, 0.01 mmol), Ph_3P (105 mg, 0.4 mmol), Cs_2CO_3 (195.5 mg, 0.6 mmol) in THF–H_2O (10:1; 5.5 mL) was stirred under N_2 at 100 °C for 10 h. Then brine (10 mL) was added and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane–EtOAc) to afford **4a**; yield: 61.0 mg (89%); white solid; mp 156.2–158.2 °C.

IR (KBr): 3010, 2912, 1637, 1367, 743, 690 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 7.8 Hz, 1 H), 7.34–7.24 (m, 7 H), 7.15–7.06 (m, 6 H), 3.55 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.2, 145.0, 144.9, 138.5, 137.9, 137.4, 136.5, 132.7, 130.1, 130.0, 129.7, 128.3, 127.9, 127.8, 127.5, 125.6, 124.9, 37.4.

LRMS (EI, 70 eV): *m*/*z* (%) = 343 (M^+, 20), 283 (33), 226 (100), 121 (81).

HRMS (EI): *m*/*z* calcd for $C_{22}H_{17}NOS$ (M^+): 343.1031; found: 343.1030.

5-Phenyl[1,4]thiazepino[2,3,4-*de*]phenanthridin-7(9*H*)-one (5e)
A mixture of **2e** (59.5 mg, 0.1 mmol), $PdCl_2(PPh_3)_2$ (4 mg, 0.005 mmol), KOAc (20 mg, 0.2 mmol) in DMF (2 mL) was stirred under N_2 at 140 °C for 14 h. Then brine (10 mL) was added and the aqueous phase extracted with Et_2O (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexane–EtOAc) to afford the desired product **5e**; yield: 17.8 mg (52%); light yellow solid; mp 210.0–212.2 °C.

IR (KBr): 2925, 1628, 1342, 1370, 761 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.83–7.73 (m, 4 H), 7.61 (d, *J* = 7.8 Hz, 1 H), 7.43–7.25 (m, 7 H), 6.40 (s, 1 H), 6.07 (d, *J* = 14.6 Hz, 1 H), 4.20 (d, *J* = 14.6 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.5, 150.7, 139.2, 137.8, 134.7, 132.3, 132.2, 131.5, 131.2, 129.9, 128.5, 128.4, 128.2, 127.8, 126.3, 126.1, 125.4, 123.7, 123.5, 45.2.

LRMS (EI, 70 eV): *m*/*z* (%) = 341 (M^+, 64), 312 (71), 280 (100), 129 (49).

HRMS (EI): *m*/*z* calcd for $C_{22}H_{15}NOS$ (M^+): 341.0874; found: 341.0874.

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