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One-pot synthesis of 1,4-dihydro-3,1-benzoxazine-2-thiones by the reaction of 2-lithiophenyl isothiocyanates with aldehydes or ketones

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ABSTRACT

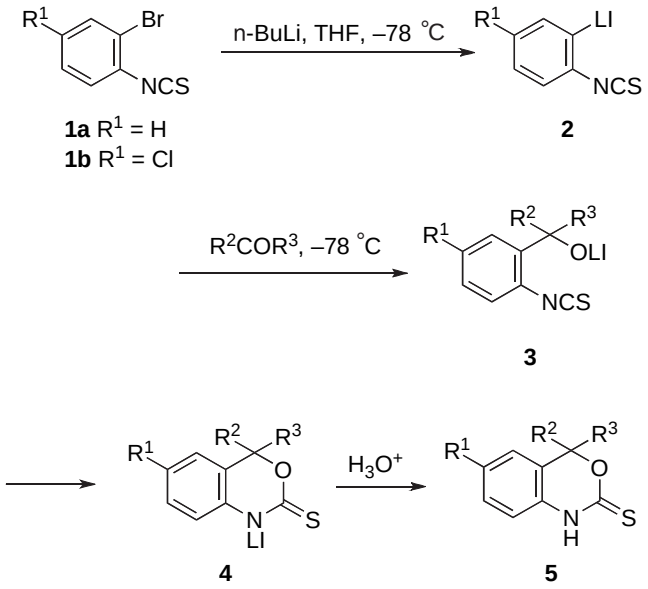
An efficient one-pot method for the synthesis of 4-monosubstituted and 4,4-disubstituted 1,4-dihydro-3,1-benzoxazine-2-thiones has been developed. Treatment of 2-bromophenyl isothiocyantes with butyllithium in THF at −78 °C generates 2-lithiophenyl isothiocyanates, which are allowed to react with various carbonyl compounds, including aldehydes, ketones, and butanolide, to give the corresponding desired products in moderate to good yields.

1. Introduction

Certain compounds having the 1,4-dihydro-3,1-benzoxazine-2-thione skeleton have been reported to exhibit a broad spectrum of biological activity.[1] This class of heterocycles has been synthesized by the treatment of the respective 1,4-dihydro-3,1-benzoxazin-2-one derivatives with Lawesson's reagent at rather high temperatures.[1a,b,d] To the best of our knowledge no one-pot syntheses from readily available starting materials have been reported. In this paper, we wish to report an efficient one-pot method for the preparation of 1,4-dihydro-3,1-benzoxazine-2-thiones carrying one or two substituents at the 4-position. We found that treatment of 2-bromophenyl isothiocyanates with butyllithium generated 2-lithiophenyl isothiocyanates and that their reaction with various aldehydes or ketones gave1,4-dihydro-3,1-benzoxazine-2-thiones.[2] We report as well the synthesis of 1,4-dihydrospiro[3,1-benzoxazine-4,2′-tetrahydrofuran]-2-thiones utilizing butanolide in place of aldehydes or ketones.

2. Results and discussion

The synthesis of 4-monosubstituted and 4,4-disubstituted 1,4-dihydro-3,1-benzoxazine-2-thiones **5** from 2-bromophenyl isothiocyanates **1** via 2-lithiophenyl isothiocyanates **2** is illustrated in Scheme 1. One of the starting materials, 2-bromophenyl isothiocyanate **1a**, was commercially available. The other starting material, 2-bromo-4-chlorophenyl isothiocyanate **1b**, was easily prepared from commercially available 2-bromo-4-chlorobenzenamine. This aniline derivative was transformed into 2-bromo-4-



Scheme 1.

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chlorophenyl isocyanide by the standard N-formylation with formic acid[3] followed by the dehydration of the resulting formamide with phosphoryl chloride in the presence of triethylamine.[4] This isocyanide was then converted into the corresponding isothiocyanate **1b** on treatment with sulfur in the presence of a catalytic amount of selenium and excess triethylamine under conditions reported by Fujiwara et al.[5]

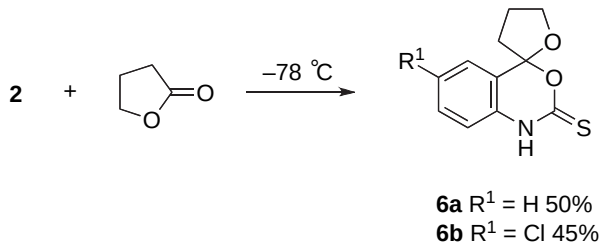
The new 2-lithiophenyl isothiocyanates **2** were readily generated by the treatment of 2-bromophenyl isothiocyanates **1** with an equimolar amount of butyllithium in THF at −78 °C. These lithium intermediates were immediately allowed to react with aldehydes or ketones to form lithium 2-isocyanatobenzyloxide intermediates **3**. These intermediates quickly cyclized intramolecularly by the attack of the alkoxide oxygen on the isothiocyanate carbon to give 1-lithio-1,4-dihydro-3,1-benzoxazine-2-thione intermediates **4**, which gave, after the usual aqueous workup followed by purification by recrystallization, 4-monosubstituted or 4,4-disubstituted 1,4-dihydro-3,1-benzoxazine-2-thiones **5** in satisfactory yields. The addition of carbonyl compounds 5 min later on treatment of **1** with butyllithium resulted in formation of complex mixtures of products containing rather lower yields of the desired products. This implies that the generation of the lithium intermediates was accomplished rapidly and that they were unstable and decomposed even at −78 °C. Both aliphatic and aromatic carbonyl compounds proved suitable for the present preparation. The isolated yields of the desired products range from 50 to 79% as summarized in Table 1.

Table 1
Preparation of 1,4-Dihydro-3,1-benzoxazine-2-thiones **5**

Entry	**1**	R^2COR^3	**5** (Yield/%)[a]
1	**1a**	EtCHO	**5a** (69)
2	**1a**	PhCHO	**5b** (77)
3	**1a**	3-ClC_6H_4CHO	**5c** (73)
4	**1a**	3-$MeOC_6H_4CHO$	**5d** (74)
5	**1a**	Naphthalene-1-carboxaldehyde	**5e** (71)
6	**1a**	EtCOMe	**5f** (69)
7	**1a**	Cyclohexanone	**5g** (71)
8	**1a**	PhCOMe	**5h** (79)
9	**1a**	1-(Thiophen-2-yl)ethanone	**5i** (76)
10	**1a**	PhCOPh	**5j** (50)
11	**1b**	EtCHO	**5k** (65)
12	**1b**	4-ClC_6H_4CHO	**5l** (76)
13	**1b**	Cyclohexanone	**5m** (69)
14	**1b**	PhCOMe	**5n** (53)

[a] Isolated yields.

Subsequently, we found that when 2-lithiophenyl isothiocyanates **2** were treated with butanolide under the same conditions as described above for the preparation of **5**, a similar addition/cyclization sequence occurred to afford the corresponding 1,4-dihydrospiro[3,1-benzoxazine-4,2′-tetrahydrofuran]-2-thiones **6** in moderate yields as shown in Scheme 2. Unfortunately, however, several attempts to prepare 1,4-dihydrospiro[3,1-benzoxazine-4,2′-tetrahydropyran]-2-thiones using pentanolide were unsuccessful; the reactions gave considerably more complex mixtures of products. This is probably due to less reactivity of this lactone toward the lithium intermediates **2** compared to butanolide.



Scheme 2.

In conclusion, we have developed a novel method for the preparation of 1,4-dihydro-3,1-benzoxazine-2-thiones using the reaction of 2-lithiophenyl isothiocyanates with aldehydes, ketones, or a lactone. The present method may find some value in organic synthesis, because: (1) this is the first generation of 2-lithiophenyl isothiocyanates; (2) the starting materials are readily available; (3) the operations are very simple.

3. Experimental

3.1. General

All melting points were obtained on a Laboratory Device MEL-TEMP II melting apparatus and are uncorrected. IR spectra were determined with a Shimadzu FTIR-8300 spectrophotometer as KBr disks. ^{1}H NMR spectra were determined using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 500 MHz or a JEOL LA400 FT NMR spectrometer operating at 400 MHz. ^{13}C NMR spectra were determined using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 125 MHz or a JEOL LA400 FT NMR spectrometer operating at 100 MHz. Low-resolution MS spectra (CI) were measured with a JEOL JMS AX505 HA spectrometer. TLC was carried out on a Merck Kieselgel 60 PF_{254}. Column chromatography was performed using Wako Gel C-200E. All of the organic solvents used in this study were dried over appropriate drying agents and distilled prior to use.

3.2. Starting materials

All chemicals used in this study are commercially available.

3.2.1. N-(2-Bromo-4-chlorophenyl)formamide. This compound was prepared in 87% yield by the standard N-formylation of 2-bromo-4-chlorobenzeneamine with formic acid in toluene under azeotropic conditions;[3] a pale-yellow solid; mp 147 °C (hexane/THF) (lit.,[6] 154 °C); IR 3246, 1695, 1665 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.45 (dd, J=8.7, 2.0 Hz, 1H), 7.79 (d, J=2.0 Hz, 1H), 8.03 (d, J=8.7 Hz, 1H), 8.34 (s, 1H), 9.83 (s, 1H).

3.2.2. 1-Bromo-5-chloro-2-isocyanobenzene. This compound was prepared in 75% yield by dehydration of the above formamide with $POCl_3$/Et_3N in THF at 0 °C;[4] a pale-yellow solid; mp 38–40 °C (hexane/Et_2O); IR (KBr) 2128 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (dd, J=8.7, 2.0 Hz, 1H), 7.39 (d, J=8.7 Hz, 1H), 7.68 (d, J=2.0 Hz, 1H). Anal. Calcd for C_7H_3BrClN: C, 38.84; H, 1.40; N, 6.47. Found: C, 38.82; H, 1.43; N, 6.33.

*3.2.3. 1-Bromo-5-chloro-2-isothiocyanatobenzene (**1b**).* This compound was prepared in 86% yield by treating the above isocyanide with sulfur in the presence of catalytic amount of selenium and Et_3N in THF at room temperature;[5] a white solid; mp 21–23 °C (hexane); IR (KBr) 2068 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, J=8.3 Hz, 1H), 7.27 (dd, J=8.3, 2.5 Hz, 1H), 7.59 (d, J=2.5 Hz, 1H). Anal. Calcd for $C_7H_3BrClNS$: C, 33.83; H, 1.22; N, 5.63. Found: C, 33.78; H, 1.20; N, 5.53.

3.3. Typical procedure for the preparation of 1,4-dihydro-3,1-benzoxazine-2-thiones 5 and 6

*3.3.1. 4-Ethyl-1,4-dihydro-3,1-benzoxazine-2-thione (**5a**).* To a stirred solution of **1a** (0.21 g, 1.0 mmol) in THF (4 mL) at −78 °C was added *n*-BuLi (1.6 M solution in hexane; 1.0 mmol) dropwise. After 1 min propanal (58 mg, 1.0 mmol) was added and stirring was

continued for an additional 15 min. The mixture was diluted with Et_2O (10 mL) and saturated aqueous NH_4Cl (10 mL) was added. The layers were separated and aqueous layer was extracted with AcOEt twice (10 mL each). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated by evaporation. The residue was triturated with Et_2O/hexane (1:9, 10 mL), and the precipitate was collected by filtration and recrystallized from hexane/$CHCl_3$ to give **5a** (0.11 g, 59%); a pale-yellow solid; mp 90–92 °C; IR (KBr) 3173, 1622, 1169 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.09 (t, J=7.3 Hz, 3H), 1.99–2.11 (m, 2H), 5.40 (t, J=6.0 Hz, 1H), 6.89 (dd, J=7.8, 0.9 Hz, 1H), 7.09 (d, J=7.8 Hz, 1H), 7.16 (ddd, J=7.8, 7.3, 0.9 Hz, 1H), 7.30 (ddd, J=7.8, 7.3, 0.9 Hz, 1H), 9.66 (br s, 1H); ^{13}C NMR (125 Hz, $CDCl_3$) δ 8.77, 27.97, 82.29, 114.02, 121.17, 124.43, 125.08, 129.24, 132.28, 184.81; MS m/z 194 ($[M+1]^+$, 100). Anal. Calcd for $C_{10}H_{11}NOS$: C, 62.15; H, 5.74; N, 7.25. Found: C, 61.87; H, 5.77; N, 7.13.

*3.3.2. 4-Phenyl-1,4-dihydro-3,1-benzoxazine-2-thione (**5b**).* A pale-yellow solid; mp 187–190 °C (hexane/$CHCl_3$); IR (KBr) 3175, 1618, 1163 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.40 (s, 1H), 6.88 (d, J=7.3 Hz, 1H), 6.92 (d, J=7.8 Hz, 1H), 7.12 (ddd, J=7.8, 7.3, 1.4 Hz, 1H), 7.32–7.37 (m, 3H), 7.40–7.42 (m, 3H), 9.48 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 82.47, 113.77, 121.21, 125.13, 126.04, 128.00, 128.86, 129.48, 129.74, 132.80, 136.53, 184.68; MS m/z 242 ($[M+1]^+$, 100). Anal. Calcd for $C_{14}H_{11}NOS$: C, 69.68; H, 4.59; N, 5.80. Found: C, 69.43; H, 4.31; N, 6.01.

*3.3.3. 4-(3-Chlorophenyl)-1,4-dihydro-3,1-benzoxazine-2-thione (**5c**).* A pale-yellow solid; mp 159–161 °C (hexane/$CHCl_3$); IR (KBr) 3173, 1620, 1159 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.36 (s, 1H), 6.89 (d, J=7.8 Hz, 1H), 6.95 (d, J=7.8 Hz, 1H), 7.15 (dd, J=7.8, 7.3 Hz, 1H), 7.28 (d, J=7.3 Hz, 1H), 7.33–7.40 (m, 4H), 9.60 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 81.49, 113.99, 120.50, 125.34, 125.89, 126.17, 128.05, 129.71, 130.04, 130.18, 132.72, 134.86, 138.47, 184.31; MS m/z 276 ($[M+1]^+$, 100). Anal. Calcd for $C_{14}H_{10}ClNOS$: C, 60.98; H, 3.66; N, 5.08. Found: C, 60.86; H, 3.55; N, 5.06.

*3.3.4. 4-(3-Methoxyphenyl)-1,4-dihydro-3,1-benzoxazine-2-thione (**5d**).* A pale-yellow solid; mp 185–187 °C (hexane/$CHCl_3$); IR (KBr) 3181, 1618, 1153 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.80 (s, 3H), 6.34 (s, 1H), 6.91–6.94 (m, 5H), 7.12 (t, J=7.3 Hz, 1H), 7.26–7.35 (m, 2H), 9.63 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.34, 82.29, 113.38, 113.72, 115.07, 120.20, 121.17, 125.14, 126.07, 129.75, 129.89, 132.76, 137.97, 159.91, 184.67; MS m/z 272 ($[M+1]^+$, 100). Anal. Calcd for $C_{15}H_{13}NO_2S$: C, 66.40; H, 4.83; N, 5.16. Found: C, 66.24; H, 4.65; N, 5.24.

*3.3.5. 4-(Naphthalen-1-yl)-1,4-dihydro-3,1-benzoxazine-2-thione (**5e**).* A pale-yellow solid; mp 175–178 °C (hexane/$CHCl_3$); IR (KBr) 3175, 1618, 1165 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.73 (d, J=7.8 Hz, 1H), 6.99 (d, J=8.2 Hz, 1H), 7.05 (dd, J=7.8, 7.3 Hz, 1H), 7.06 (s, 1H), 7.33–7.36 (m, 2H), 7.45 (dd, J=8.2, 7.3 Hz, 1H), 7.52–7.55 (m, 2H), 7.92–7.94 (m, 2H), 8.06–8.08 (m, 1H), 9.59 (br s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 78.76, 114.22, 121.03, 124.44, 124.67, 125.22, 125.56, 126.15, 126.71, 127.07, 128.78, 129.58, 130.14, 130.67, 132.32, 133.52, 133.74, 183.46; MS m/z 292 ($[M+1]^+$, 100). Anal. Calcd for $C_{18}H_{13}NOS$: C, 74.20; H, 4.50; N, 4.81. Found: C, 74.11; H, 4.21; N, 4.58.

*3.3.6. 4-Ethyl-4-methyl-1,4-dihydro-3,1-benzoxazine-2-thione (**5f**).* A pale-yellow solid; mp 98–100 °C (hexane/$CHCl_3$); IR (KBr) 3179, 1620, 1190 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.95 (t, J=7.3 Hz, 3H), 1.74 (s, 3H), 2.02–2.06 (m, 2H), 6.98 (d, J=7.3 Hz, 1H), 7.08 (d, J=7.3 Hz, 1H), 7.15 (td, J=7.3, 0.9 Hz, 1H), 7.28 (td, J=7.3, 1.4 Hz, 1H), 10.46 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 8.06, 26.31, 33.71, 88.06, 114.18, 123.87, 124.87, 125.22, 128.97, 131.66, 184.10; MS m/z 208 ($[M+1]^+$, 100). Anal. Calcd for $C_{11}H_{13}NOS$: C, 63.74; H, 6.32; N, 6.76. Found: C, 63.81; H, 6.30; N, 6.51.

*3.3.7. 1′,4′-Dihydrospiro[cyclohexane-1,4′-[3,1]benzoxazine]-2′-thione (**5g**).* A pale-yellow solid; mp 149–151 °C (hexane/$CHCl_3$); IR (KBr) 3150, 1618, 1175 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.21–1.37 (m, 1H), 1.66–1.77 (m, 4H), 1.83–1.86 (m, 1H), 1.96–2.05 (m, 2H), 2.21–2.23 (m, 2H), 6.99 (dd, J=7.8, 0.9 Hz, 1H), 7.13–7.17 (m, 2H), 7.23–7.29 (m, 1H), 10.59 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.75, 24.87, 35.25, 85.60, 114.21, 123.02, 125.33, 126.97, 128.85, 131.72, 184.02; MS m/z 234 ($[M+1]^+$, 100). Anal. Calcd for $C_{13}H_{15}NOS$: C, 66.92; H, 6.48; N, 6.00. Found: C, 66.89; H, 6.41; N, 5.96.

*3.3.8. 4-Methyl-4-phenyl-1,4-dihydro-3,1-benzoxazine-2-thione (**5h**).* A pale-yellow solid; mp 194–196 °C (hexane/$CHCl_3$); IR (KBr) 3171, 1620, 1178 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.09 (s, 3H), 6.97 (d, J=7.8 Hz, 1H), 7.22–7.37 (m, 8H), 10.21 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.95, 87.14, 114.31, 125.07, 125.11, 125.43, 125.49, 128.43, 128.45, 129.54, 132.26, 142.11, 184.45; MS m/z 256 ($[M+1]^+$, 100). Anal. Calcd for $C_{15}H_{13}NOS$: C, 70.56; H, 5.13; N, 5.49. Found: C, 70.28; H, 5.05; N, 5.45.

*3.3.9. 4-Methyl-4-(thiophen-2-yl)-1,4-dihydro-3,1-benzoxazine-2-thione (**5i**).* A pale-yellow solid; mp 139–141 °C (hexane/$CHCl_3$); IR (KBr) 3169, 1620, 1177 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.21 (s, 3H), 6.82 (d, J=2.9 Hz, 1H), 6.89 (dd, J=4.9, 3.9 Hz, 1H), 6.99 (d, J=7.8 Hz, 1H), 7.19–7.32 (m, 3H), 7.36 (ddd, J=7.8, 7.3, 1.4 Hz, 1H), 10.25 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.54, 84.46, 114.27, 124.58, 125.15, 125.30, 126.07, 126.56, 126.80, 129.90, 132.06, 146.10, 183.73; MS m/z 262 ($[M+1]^+$, 100). Anal. Calcd for $C_{13}H_{11}NOS_2$: C, 59.74; H, 4.24; N, 5.36. Found: C, 59.53; H, 4.20; N, 5.28.

*3.3.10. 4,4-Diphenyl-1,4-dihydro-3,1-benzoxazine-2-thione (**5j**)*[7]. A white solid; mp 226–228 °C (hexane/$CHCl_3$); IR (KBr) 3169, 1614, 1178 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 6.68 (dd, J=7.8, 1.4 Hz, 1H), 7.07–7.09 (m, 4H), 7.11 (d, J=7.8 Hz, 1H), 7.15 (ddd, J=7.8, 7.3, 1.4 Hz, 1H), 7.39–7.43 (m, 7H), 12.34 (br s, 1H).

*3.3.11. 6-Chloro-4-ethyl-1,4-dihydro-3,1-benzoxazine-2-thione (**5k**).* A white solid; mp 127–129 °C (hexane/$CHCl_3$); IR (KBr) 3165, 1618, 1159 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.10 (t, J=7.3 Hz, 3H), 2.04 (quint, J=7.3 Hz, 2H), 5.37 (t, J=7.3 Hz, 1H), 6.92 (d, J=8.8 Hz, 1H), 7.09 (d, J=2.4 Hz, 1H), 7.27 (dd, J=8.8, 2.4 Hz, 1H), 10.37 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.74, 27.85, 81.74, 115.29, 122.84, 124.65, 129.33, 130.25, 130.90, 184.50; MS m/z 228 ($[M+1]^+$, 100). Anal. Calcd for $C_{10}H_{10}ClNOS$: C, 52.75; H, 4.43; N, 6.15. Found: C, 52.72; H, 4.68; N, 6.19.

*3.3.12. 6-Chloro-4-(4-chlorophenyl)-1,4-dihydro-3,1-benzoxazine-2-thione (**5l**).* A pale-yellow solid; mp 199–203 °C (hexane/THF); IR (KBr) 3163, 1614, 1155 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 6.68 (s, 1H), 7.10 (d, J=8.8 Hz, 1H), 7.11 (d, J=2.4 Hz, 1H), 7.35 (d, J=8.8 Hz, 2H), 7.45 (dd, J=8.8, 2.4 Hz, 1H), 7.52 (d, J=8.8 Hz, 2H), 12.45 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 79.00, 116.17, 122.82, 125.47, 128.24, 129.04, 129.22, 129.64, 131.79, 133.96, 136.31, 182.84; MS m/z 310 ($[M+1]^+$, 100). Anal. Calcd for $C_{14}H_9Cl_2NOS$: C, 54.21; H, 2.92; N, 4.52. Found: C, 53.92; H, 2.88; N, 4.49.

*3.3.13. 6′-Chloro-1′,4′-dihydrospiro[cyclohexane-1,4′-[3,1]benzoxazine]-2′-thione (**5m**).* A pale-yellow solid; mp 203–206 °C (hexane/$CHCl_3$); IR (KBr) 3156, 1616, 1178 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.26–1.38 (m, 1H), 1.65–1.75 (m, 4H), 1.83–1.88 (m, 1H), 1.92–2.05 (m, 2H), 2.19–2.23 (m, 2H), 6.89 (d, J=8.3 Hz, 1H), 7.15 (d, J=2.4 Hz, 1H), 7.24 (dd, J=8.3, 2.4 Hz, 1H), 10.27 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 20.66, 24.77, 35.13, 85.28, 115.38, 123.54,

128.63, 128.90, 130.34, 130.43, 183.76; MS *m*/*z* 268 ($[M+1]^+$, 100). Anal. Calcd for $C_{13}H_{14}ClNOS$: C, 58.31; H, 5.27; N, 5.23. Found: C, 58.25; H, 5.25; N, 5.11.

*3.3.14. 6-Chloro-4-methyl-4-phenyl-1,4-dihydro-3,1-benzoxazine-2-thione (**5n**).* A white solid; mp 214–215 °C (hexane/THF); IR (KBr) 3158, 1616, 1176 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 2.02 (s, 3H), 7.04 (d, *J*=8.3 Hz, 1H), 7.24 (d, *J*=7.3 Hz, 2H), 7.31 (t, *J*=7.3 Hz, 1H), 7.36 (t, *J*=7.3 Hz, 2H), 7.47 (dd, *J*=8.3, 2.0 Hz, 1H), 7.68 (d, *J*=2.0 Hz, 1H), 12.32 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 27.67, 85.50, 116.23, 125.05, 125.18, 127.23, 128.33, 128.526, 128.534, 129.55, 131.42, 142.17, 182.96; MS *m*/*z* 290 ($[M+1]^+$, 100). Anal. Calcd for $C_{15}H_{12}ClNOS$: C, 62.17; H, 4.17; N, 4.83. Found: C, 62.14; H, 4.14; N, 4.60.

*3.3.15. 1,4-Dihydrospiro[3,1-benzoxazine-4,2′-tetrahydrofuran]-2-thione (**6a**).* A pale-yellow solid; mp 99–102 °C (hexane/$CHCl_3$); IR (KBr) 3169, 1620, 1167 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.18–2.25 (m, 1H), 2.38–2.44 (m, 1H), 2.47–2.56 (m, 1H), 2.59–2.64 (m, 1H), 4.20–4.24 (m, 1H), 4.39–4.43 (m, 1H), 7.02 (d, *J*=7.8 Hz, 1H), 7.19 (ddd, *J*=7.8, 7.3, 1.4 Hz, 1H), 7.34 (d, *J*=7.8 Hz, 1H), 7.36 (ddd, *J*=7.8, 7.3, 1.4 Hz, 1H), 10.57 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.53, 37.61, 70.38, 112.65, 114.34, 120.09, 124.29, 125.22, 130.54, 133.11, 182.83; MS *m*/*z* 222 ($[M+1]^+$, 100). Anal. Calcd for $C_{11}H_{11}NO_2S$: C, 59.71; H, 5.01; N, 6.33. Found: C, 59.65; H, 4.85; N, 6.14.

*3.3.16. 6-Chloro-1,4-dihydrospiro[3,1-benzoxazine-4,2′-tetrahydrofuran]-2-thione (**6b**).* A pale-yellow solid; mp 129–131 °C (hexane/$CHCl_3$); IR (KBr) 3153, 1618, 1165 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.17–2.26 (m, 1H), 2.32–2.39 (m, 1H), 2.46–2.57 (m, 1H), 2.59–2.66 (m, 1H), 4.20–4.26 (m, 1H), 4.39–4.44 (m, 1H), 6.94 (d, *J*=7.8 Hz, 1H), 7.33 (d, *J*=2.4 Hz, 1H), 7.33 (dd, *J*=7.8, 2.4 Hz, 1H), 10.33 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.52, 37.81, 70.67, 112.14, 115.62, 121.82, 124.61, 130.33, 130.62, 131.71, 182.57; MS *m*/*z* 256 ($[M+1]^+$, 100). Anal. Calcd for $C_{11}H_{10}ClNO_2S$: C, 51.66; H, 3.94; N, 5.48. Found: C, 51.73; H, 4.04; N, 5.54.

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Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2010.10.010.

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