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ONE-POT SYNTHESIS OF 4,5-DIHYDRO-3,1-BENZOXAZEPINE-2(1*H*)-THIONES FROM 2-(2-ISOCYANOPHENYL)ETHANOLS *VIA* THE CORRESPONDING ISOTHIOCYANATES

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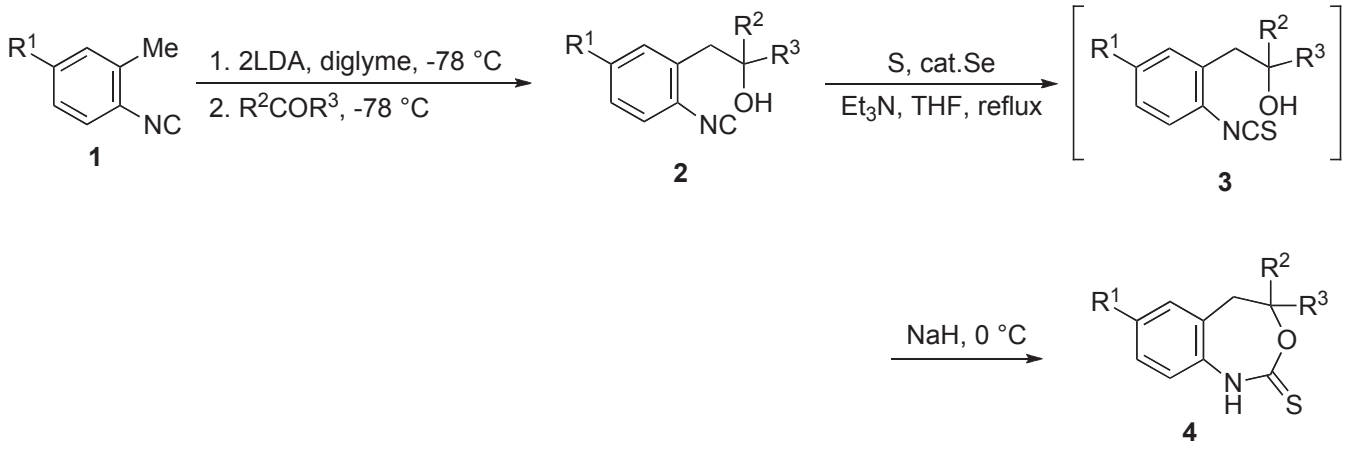
Abstract – An efficient method for the preparation of 4,5-dihydro-3,1-benzoxazepine-2(1*H*)-thiones under mild conditions has been developed. 2-(2-Isocyanophenyl)ethanols, easily accessible by treating 1-isocyano-2-(lithiomethyl)benzenes with aldehydes or ketones, were converted into the corresponding isothiocyanates on treatment with sulfur in the presence of a catalytic amount of selenium and excess triethylamine. These isothiocyanato alcohols were then treated with sodium hydride to give 4,5-dihydro-3,1-benzoxazepine-2(1*H*)-thione derivatives in one pot.

Compounds having the 4,5-dihydro-3,1-benzoxazepine-2(1*H*)-thione structure are an important class of molecules, because this structure is found in some biologically active compounds.[1] However, very few practical methods for the preparation of the 4,5-dihydro-3,1-benzoxazepine-2(1*H*)-thione derivatives have been reported. Suda *et al*. have reported on the conversion of 4,5-dihydro-3,1-benzoxazepin-2(1*H*)-one derivatives into the corresponding thione derivatives by the treatment with Lawesson's reagent.[1c] In this paper, we describe a facile synthesis of 4,5-dihydro-3,1-benzoxazepine-2(1*H*)-thiones from 1-isocyano-2-methylbenzenes *via* a three-step procedure.

The synthesis of 4,5-dihydro-3,1-benzoxazepine-2(1*H*)-thione derivatives (**4**) from 1-isocyano-2-methylbenzenes (**1**), *via* 2-(2-isocyanophenyl)ethanols (**2**), is illustrated in Scheme 1. The requisite isocyano alcohols (**2**) were prepared by the lithiation of **1** with LDA followed by the reaction with aldehydes or ketones according to the procedure reported by Ito *et al*.[2,3] The yields of **2** are generally good (Table 1). The reaction could be applicable to aldehydes and ketones carrying α-hydrogens, such as propanal, acetone, cyclohexanone, and acetophenone (Entries 1 and 4–6). However, as can be seen from Entries 8 and 9, the yields of the products (**2j**) and (**2k**) from 1-isocyano-2,4-dimethylbenzene are somewhat lower than those of the others. This may be ascribed to simultaneous slight lithiation of

4-methyl group.



Scheme 1

Table 1. Preparations of 4,5-Dihydro-3,1-benzoxazepine-2(1*H*)-thione Derivatives (**4**) *via* 2-(2-Isocyanophenyl)ethanols (**2**)

Entry	R^1	R^2	R^3	**2** (Yield/%)[a]	**4** (Yield/%)[a]
1	H	H	Et	**2a** (86)[b]	**4a** (78)
2	H	H	Ph	**2b** (97)[b]	**4b** (85)
3	H	H	thiophen-2-yl	**2c** (93)	**4c** (0)
4	H	Me	Me	**2d** (88)[b]	**4d** (66)
5	H	-$(CH_2)_5$-		**2e** (94)	**4e** (87)
6	H	Me	Ph	**2f** (84)	**4f** (61)
7	H	Ph	Ph	**2g** (88)	**4g** (0)
8	Me	H	Ph	**2h** (67)	**4h** (80)
9	Me	H	4-MeC_6H_4	**2i** (64)	**4i** (89)
10	Cl	H	naphthalen-2-yl	**2j** (74)	**4j** (62)
11	Cl	H	4-ClC_6H_4	**2k** (70)	**4k** (61)
12	OMe	H	Ph	**2l** (81)	**4l** (86)
13	OMe	H	3-$MeOC_6H_4$	**2m** (97)	**4m** (85)

[a] Isolated yields. [b] The synthesis of these compounds has been reported by Ito *et al*.[2,3]

Compounds (**2**) thus obtained were converted into the corresponding isothiocyanates (**3**) on treatment with sulfur in the presence of a catalytic amount of selenium and excess Et_3N in THF at reflux temperature under the same conditions as reported by Fujiwara *et al*.[4] These isothiocyanates were then, without isolation, treated with an equimolar amount of sodium hydride at 0 °C to generate the corresponding sodium alkoxide intermediates, which cyclized by the attack of the alkoxide oxygen on the isothiocyanate carbon. The cyclization proceeded immediately and cleanly. The completion of each step of the sequence was monitored by TLC (silica gel) analyses. The usual aqueous workup and subsequent purification by recrystallization of the crude products afforded the desired products (**4**) in one pot from **2**. The results are summarized in Table 1. The yields are fair to good as a whole. The 4,4-disubsutituted

derivatives (**4d-f**) could also be obtained in generally good yields (Entries 4-6). However, in the reaction of 1-(2-isocyanophenyl)-2,2-diphenylethan-2-ol (**2g**) (Entry 7), its clean conversion into the corresponding isothiocyanates (**3g**) could be confirmed by TLC analysis, but treatment of this isothiocyanate with sodium hydride resulted in the formation of a complex mixture of products, in which only trace of the desired product (**4g**) was detected as a mixture with structurally undefined products by ^{1}H NMR. This result may be ascribed to the crowdedness at the 4-position of the product due to two phenyl groups. The reaction of 2-(2-isocyanophenyl)-1-(thiophen-2-yl)ethanol (**2c**) was also gave a similar result (Entry 3), though the reaction for this is unclear.

In conclusion, we have demonstrated that 2-(2-isocyanophenyl)ethanols can been utilized for the one-pot synthesis of 4,5-dihydro-3,1-benzoxazepine-2(1*H*)-thiones. Since the method employs readily available starting materials and is experimentally simple, it may be of value in organic synthesis.

EXPERIMENTAL

The melting points were obtained on a Laboratory Devices MEL-TEMP II melting apparatus and are uncorrected. IR spectra were determined with a Shimadzu FTIR-8300 spectrophotometer. The ^{1}H NMR spectra were determined using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 500 MHz. The ^{13}C NMR spectra were determined using TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer operating at 125 MHz. Low- and high-resolution MS spectra (EI, 70 eV) were measured by 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.

Starting Materials. 1-Isocyano-2-methylbenzenes (**1**) were prepared according to the procedure reported previously by Ito *et al*.[5] All other chemicals used in this study were commercially available.

2-(2-Isocyanophenyl)ethanols (2). These compounds were prepared by treating the respective 1-isocyano-2-lithiomethybenzenes, generated from 1-isocyano-2-methylbenzenes (**1**) and LDA, with aldehydes or ketones according to the procedure reported by Ito *et al*.[2] Physical, spectral, and analytical data for new compounds follow.

2-(2-Isocyanophenyl)-1-(thiophen-2-yl)ethanol (2c): a yellow oil; R_f 0.35 (1:4 EtOAc–hexane); IR (neat) 3412, 2120 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.20 (d, J = 3.9 Hz, 1H), 3.12 (dd, J = 13.7, 8.3 Hz, 1H), 3.20 (dd, J = 13.7, 5.3 Hz, 1H), 5.26–5.30 (m, 1H), 6.95–6.98 (m, 2H), 7.26–7.35 (m, 4H), 7.38 (d, J = 7.8 Hz, 1H). HR-MS. Calcd for $C_{13}H_{11}NOS$: M, 229.0561. Found: *m/z* 229.0533.

1-[(2-Isocyanophenyl)methyl]cyclohexanol (2e): a pale-yellow oil; R_f 0.36 (1:4 THF–hexane); IR (neat) 3466, 2120 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.27 (s, 1H), 1.53–1.63 (m, 10H), 2.93 (s, 2H), 7.26 (td, J = 7.8, 1.8 Hz, 1H), 7.34 (td, J = 7.8, 1.4 Hz, 1H), 7.38 (dd, J = 7.8, 1.8 Hz, 1H), 7.39 (dd, J = 7.8, 1.4 Hz, 1H). HR-MS. Calcd for $C_{14}H_{17}NO$: M, 215.1310. Found: *m/z* 215.1316.

1-(2-Isocyanophenyl)-2-phenylpropan-2-ol (2f): a pale-yellow oil; R_f 0.32 (1:5 THF–hexane); IR (neat) 3445, 2122 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.63 (s, 3H), 1.79 (s, 1H), 3.16 (d, *J* = 13.7 Hz, 1H), 3.30 (d, *J* = 13.7 Hz, 1H), 7.14–7.16 (m, 1H), 7.24–7.36 (m, 7H), 7.44 (dd, *J* = 7.3, 1.4 Hz, 1H). HR-MS. Calcd for $C_{16}H_{15}NO$: M, 237.1154. Found: *m/z* 237.1170.

1-(2-Isocyanophenyl)-2,2-diphenylethan-2-ol (2g): a pale-yellow oil; R_f 0.33 (1:6 THF–hexane); IR (neat) 3412, 2122 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.28 (s, 1H), 3.78 (s, 2H), 6.76 (d, *J* = 7.8 Hz, 1H), 7.08 (td, *J* = 7.8, 0.9 Hz, 1H), 7.15 (t, *J* = 7.8 Hz, 1H), 7.24–7.39 (m, 11H). HR-MS. Calcd for $C_{21}H_{17}NO$: M, 299.1310. Found: *m/z* 299.1308.

2-(2-Isocyano-5-methylphenyl)-1-phenylethanol (2h): a yellow oil; R_f 0.33 (1:5 THF–hexane); IR (neat) 3418, 2118 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.95 (d, *J* = 3.2 Hz, 1H), 2.34 (s, 3H), 3.04 (dd, *J* = 13.7, 9.1 Hz, 1H), 3.17 (dd, *J* = 13.7, 4.1 Hz, 1H), 5.00–5.03 (m, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 7.09 (s, 1H), 7.26 (d, *J* = 7.8 Hz, 1H), 7.30 (tt, *J* = 7.3, 1.8 Hz, 1H), 7.36 (td, *J* = 7.3, 1.8 Hz, 2H), 7.41 (dd, *J* = 7.3, 1.8 Hz, 2H). HR-MS. Calcd for $C_{16}H_{15}NO$: M, 237.1154. Found: *m/z* 237.1129.

2-(2-Isocyano-5-methylphenyl)-1-(4-methylphenyl)ethanol (2i): colorless crystals; mp 100–102 °C (hexane–Et_2O); IR (KBr) 3350, 2118 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.87 (d, *J* = 3.2 Hz, 1H), 2.34 (s, 3H), 2.36 (s, 3H), 3.03 (dd, *J* = 13.7, 9.1 Hz, 1H), 3.15 (dd, *J* = 13.7, 4.1 Hz, 1H), 4.97–5.00 (m, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 7.12 (s, 1H), 7.17 (d, *J* = 7.8 Hz, 2H), 7.26 (d, *J* = 7.8 Hz, 1H), 7.31 (d, *J* = 7.8 Hz, 2H). Anal. Calcd for $C_{17}H_{17}NO$: C, 81.24; H, 6.82; N, 5.57. Found: C, 81.11; H, 6.77; N, 5.53.

2-(5-Chloro-2-isocyanophenyl)-1-(naphthalen-2-yl)ethanol (2j): a pale-yellow solid; mp 106–108 °C (hexane–CH_2Cl_2); IR (KBr) 3412, 2141 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.06 (d, *J* = 3.4 Hz, 1H), 3.14 (dd, *J* = 13.7, 8.6 Hz, 1H), 3.25 (dd, *J* = 13.7, 4.0 Hz, 1H), 5.16–5.20 (m, 1H), 7.26 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.31 (d, *J* = 8.6 Hz, 1H), 7.38 (d, *J* = 2.3 Hz, 1H), 7.47–7.52 (m, 2H), 7.54 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.83–7.88 (m, 4H). Anal. Calcd for $C_{19}H_{14}ClNO$: C, 74.15; H, 4.58; N, 4.55. Found: C, 74.16; H, 4.62; N, 4.40.

2-(5-Chloro-2-isocyanophenyl)-1-(4-chlorophenyl)ethanol (2k): a yellow solid; mp 79–81 °C (hexane–Et_2O); IR (KBr) 3354, 2124 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.01 (d, *J* = 2.9 Hz, 1H), 3.03 (dd, *J* = 14.3, 9.2 Hz, 1H), 3.13 (dd, *J* = 14.3, 4.0 Hz, 1H), 4.97–5.00 (m, 1H), 7.26 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.30–7.35 (m, 6H). Anal. Calcd for $C_{15}H_{11}Cl_2NO$: C, 61.67; H, 3.79; N, 4.79. Found: C, 61.44; H, 3.93; N, 4.50.

2-(2-Isocyano-5-methoxyphenyl)-1-phenylethanol (2l): a pale-yellow solid; mp 62–63 °C (hexane–Et_2O); IR (KBr) 3420, 2118 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.00 (d, *J* = 2.9 Hz, 1H), 3.06 (dd, *J* = 13.7, 9.1 Hz, 1H), 3.17 (dd, *J* = 13.7, 4.4 Hz, 1H), 3.77 (s, 3H), 5.00–5.04 (m, 1H), 6.75 (s, 1H), 6.77 (d, *J* = 7.8 Hz, 1H), 7.30–7.42 (m, 6H). Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.80; H, 6.06; N, 5.67.

2-(2-Isocyano-5-methoxyphenyl)-1-(3-methoxyphenyl)ethanol (2m): a yellow oil; R_f 0.26 (1:3 EtOAc–hexane); IR (neat) 3418, 2118 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.97 (d, *J* = 3.4 Hz, 1H), 3.05 (dd, *J* =

13.7, 8.6 Hz, 1H), 3.17 (dd, *J* = 13.7, 4.0 Hz, 1H), 3.78 (s, 3H), 3.81 (s, 3H), 4.98–5.01 (m, 1H), 6.75–6.85 (m, 3H), 6.97 (s, 1H), 6.98 (d, *J* = 7.8 Hz, 1H), 7.26–7.32 (m, 2H). HR-MS. Calcd for $C_{17}H_{17}NO_3$: M, 283.1208. Found: *m/z* 283.1183.

Typical Procedure for the Preparation of 4,5-Dihyro-3,1-benzoxazepine-2(1*H*)-thiones (4). 4-Ethyl-4,5-dihyro-3,1-benzoxazepine-2(1*H*)-thione (4a). A mixture of **2a** (0.27 g, 1.5 mmol), Et_3N (0.38 g, 3.8 mmol), sulfur (58 mg, 1.8 mmol), and selenium (3.6 mg, 45 μmol) in THF (5 mL) was stirred at reflux temperature for 1 h. After cooling to 0 ˚C, NaH (60% in oil; 72 mg, 1.8 mmol) was added, and stirring was continued for an additional 30 min at the same temperature. Saturated aqueous NH_4Cl (10 mL) was added and organic materials were extracted with AcOEt three times (10 mL each), and the combined extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated by evaporation. The residual solid was recrystallized from hexane-CH_2Cl_2 to give **4a** (0.24 g, 78 %); a beige solid; mp 88–90 ˚C (hexane–CH_2Cl_2); IR (KBr) 3181, 1153 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.09 (t, *J* = 7.3 Hz, 3H), 1.72–1.80 (m, 1H), 1.89–1.97 (m, 1H), 3.10 (dd, *J* = 16.4, 1.4 Hz, 1H), 3.21 (dd, *J* = 16.4, 8.2 Hz, 1H), 4.60–4.64 (m, 1H), 6.99 (dd, *J* = 7.8, 0.9 Hz, 1H), 7.08 (td, *J* = 7.8, 0.9 Hz, 1H), 7.12 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.21 (td, *J* = 7.8, 1.4 Hz, 1H), 9.53 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 9.83, 28.19, 39.05, 86.82, 119.79, 124.93, 127.38, 127.86, 130.48, 136.44, 188.90; MS *m/z* 207 (M^+, 17), 177 (30), 162 (100). Anal. Calcd for $C_{11}H_{13}NOS$: C, 63.74; H, 6.32; N, 6.76. Found: C, 63.70; H, 6.42; N, 6.70.

4-Phenyl-4,5-dihyro-3,1-benzoxazepine-2(1*H*)-thione (4b): a pale-yellow solid; mp 147–149 ˚C (hexane–EtOAc); IR (KBr) 3160, 1148 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.31 (dd, *J* = 16.9, 2.3 Hz, 1H), 3.54 (dd, *J* = 16.9, 7.8 Hz, 1H), 5.80 (dd, *J* = 7.8, 2.3 Hz, 1H), 7.07 (td, *J* = 7.3, 0.9 Hz, 1H), 7.20 (d, *J* = 7.3, 1.4 Hz, 1H), 7.23 (td, *J* = 7.3, 1.4 Hz, 1H), 7.30 (dd, *J* = 7.3, 0.9 Hz, 1H), 7.36 (t, *J* = 7.3 Hz, 1H), 7.40 (t, *J* = 7.3 Hz, 2H), 7.47 (d, *J* = 7.3 Hz, 2H), 11.64 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 40.47, 85.89, 120.43, 124.52, 126.37, 127.50, 128.07, 128.39, 128.45, 130.62, 137.03, 139.48, 187.83; MS *m/z* 255 (M^+, 7.0), 225 (45), 210 (100). Anal. Calcd for $C_{15}H_{13}NOS$: C, 70.56; H, 5.13; N, 5.49. Found: C, 70.68; H, 5.17; N, 5.37.

4,4-Dimethyl-4,5-dihyro-3,1-benzoxazepine-2(1*H*)-thione (4d): beige crystals; mp 144–146 ˚C (hexane–CH_2Cl_2); IR (KBr) 3175, 1153 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.52 (s, 6H), 3.06 (s, 2H), 7.02 (d, *J* = 7.8 Hz, 1H), 7.14–7.18 (m, 2H), 7.25–7.29 (m, 1H), 9.85 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 27.74, 44.68, 92.70, 119.99, 125.75, 128.09, 128.93, 130.49, 136.66, 188.37; MS *m/z* 207 (M^+, 48), 132 (100). Anal. Calcd for $C_{11}H_{13}NOS$: C, 63.74; H, 6.32; N, 6.76. Found: C, 63.69; H, 6.25; N, 6.76.

Spiro[cyclohexane-1,4'-4,5-dihyro-3,1-benzoxazepine-2(1*H*)-thione] (4e): yellow crystals; mp 153–155 ˚C (hexane–CH_2Cl_2); IR (KBr) 3160, 1167 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.31–2.04 (m, 10H), 3.04 (s, 2H), 7.02 (d, *J* = 7.8 Hz, 1H), 7.13–7.15 (m, 2H), 7.23–7.26 (m, 1H), 9.99 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 22.02, 25.19, 36.04, 43.47, 93.95, 119.88, 125.58, 127.93, 128.26, 130.61, 136.66, 188.37; MS *m/z* 247 (M^+, 20), 172 (100). Anal. Calcd for $C_{14}H_{17}NOS$: C, 67.98; H, 6.93; N, 5.66. Found: C, 67.83; H, 6.62; N,

5.49.

4-Methyl-4-phenyl-4,5-dihyro-3,1-benzoxazepine-2(1*H*)-thione (4f): a beige solid; mp 111–113 °C (hexane–CH_2Cl_2); IR (KBr) 3165, 1144 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.84 (s, 3H), 3.48 (d, *J* = 16.0 Hz, 1H), 3.52 (d, *J* = 16.0 Hz, 1H), 6.88 (d, *J* = 7.8 Hz, 1H), 7.05–7.06 (m, 2H), 7.14–7.22 (m, 2H), 7.266 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.273 (t, *J* = 7.8 Hz, 2H), 7.36 (d, *J* = 7.8 Hz, 1H), 9.67 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 30.60, 45.05, 94.31, 119.67, 124.74, 125.45, 127.58, 127.95, 128.00, 128.33, 130.74, 136.40, 142.64, 187.80; MS *m/z* 269 (M^+, 8.5), 209 (62), 194 (100). Anal. Calcd for $C_{16}H_{15}NOS$: C, 71.34; H, 5.61; N, 5.20. Found: C, 71.25; H, 5.61; N, 5.13.

7-Methyl-4-phenyl-4,5-dihyro-3,1-benzoxazepine-2(1*H*)-thione (4h): a white solid; mp 126–128 °C (hexane–CH_2Cl_2); IR (KBr) 3185, 1161 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.29 (s, 3H), 3.26 (dd, *J* = 16.8, 1.8 Hz, 1H), 3.59 (dd, *J* = 16.8, 8.7 Hz, 1H), 5.67 (dd, *J* = 8.7, 1.8 Hz, 1H), 6.83 (d, *J* = 8.4 Hz, 1H), 6.92 (d, *J* = 1.4 Hz, 1H), 7.04 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.35–7.43 (m, 5H), 9.14 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 20.57, 41.87, 86.48, 119.94, 126.04, 127.16, 128.66 (two overlapped C's), 128.70, 131.01, 134.02, 134.96, 138.65, 188.31; MS *m/z* 269 (M^+, 6.1), 209 (100). Anal. Calcd for $C_{16}H_{15}NOS$: C, 71.34; H, 5.61; N, 5.20. Found: C, 71.14; H, 5.50; N, 5.04.

7-Methyl-4-(4-methylphenyl)-4,5-dihyro-3,1-benzoxazepine-2(1*H*)-thione (4i): colorless crystals; mp 158–160 °C (hexane–CH_2Cl_2); IR (KBr) 3175, 1161 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.28 (s, 3H), 2.36 (s, 3H), 3.24 (dd, *J* = 16.0, 1.8 Hz, 1H), 3.59 (dd, *J* = 16.0, 9.2 Hz, 1H), 5.64 (dd, *J* = 9.2, 1.8 Hz, 1H), 6.87 (d, *J* = 8.2 Hz, 1H), 6.91 (d, *J* = 1.8 Hz, 1H), 7.02 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.19 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 9.41 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 20.58, 21.15, 41.81, 86.42, 119.83, 126.05, 127.16, 128.61, 129.35, 131.08, 134.02, 134.89, 135.70, 138.56, 188.48; MS *m/z* 283 (M^+, 5.0), 223 (100). Anal. Calcd for $C_{17}H_{17}NOS$: C, 72.05; H, 6.05; N, 5.66. Found: C, 72.06; H, 6.13; N, 5.63.

7-Chloro-4-(naphthalen-2-yl)-4,5-dihyro-3,1-benzoxazepine-2(1*H*)-thione (4j): a pale-yellow solid; mp 171–173 °C (EtOAc); IR (KBr) 3219, 1165 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.43 (dd, *J* = 16.7, 1.7 Hz, 1H), 3.66 (dd, *J* = 16.7, 9.2 Hz, 1H), 5.99 (dd, *J* = 9.2, 1.7 Hz, 1H), 7.31–7.36 (m, 3H), 7.53–7.56 (m, 2H), 7.61 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.91–8.00 (m, 4H), 11.77 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 40.49, 85.43, 122.10, 124.27, 125.27, 126.51, 126.53, 127.39, 127.61, 128.01, 128.23, 128.25, 130.06, 130.28, 132.51, 132.73, 136.05, 136.65, 187.68; MS *m/z* 339 (M^+, 5.0), 273 (100). Anal. Calcd for $C_{19}H_{14}ClNOS$: C, 67.15; H, 4.15; N, 4.12. Found: C, 66.87; H, 4.27; N, 3.84.

7-Chloro-4-(4-chlorophenyl)-4,5-dihyro-3,1-benzoxazepine-2(1*H*)-thione (4k): a yellow solid; mp 120–122 °C (hexane–EtOAc); IR (KBr) 3183, 1153 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.28 (dd, *J* = 16.7, 2.3 Hz, 1H), 3.53 (dd, *J* = 16.7, 8.6 Hz, 1H), 5.69 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.91 (d, *J* = 8.6 Hz, 1H), 7.11 (d, *J* = 2.3 Hz, 1H), 7.22 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.34 (d, *J* = 8.6 Hz, 2H), 7.38 (d, *J* = 8.6 Hz, 2H), 9.12–9.37 (br, 1H); ^{13}C NMR ($CDCl_3$) δ 41.43, 85.71, 121.50, 127.52, 128.42, 128.81, 129.15, 130.47, 130.68, 134.95, 135.02, 136.70, 188.50; MS *m/z* 322 (M^+, 8.6), 262 (100). Anal. Calcd for $C_{15}H_{11}Cl_2NOS$: C,

55.57; H, 3.42; N, 4.32. Found: C, 55.66; H, 3.40; N, 4.21.

7-Methoxy-4-phenyl-4,5-dihyro-3,1-benzoxazepine-2(1*H*)-thione (4l): colorless needles; mp 177–178 °C (EtOAc); IR (KBr) 3183, 1153 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.28 (dd, *J* = 16.7, 2.3 Hz, 1H), 3.56 (dd, *J* = 16.7, 8.6 Hz, 1H), 3.73 (s, 3H), 5.69 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.61 (d, *J* = 2.7 Hz, 1H), 6.77 (dd, *J* = 8.6, 2.7 Hz, 1H), 6.96 (d, *J* = 8.6 Hz, 1H), 7.32–7.41 (m, 5H), 9.52 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 41.97, 55.65, 86.76, 113.46, 115.58, 121.46, 126.17, 128.83 (two overlapped C's), 129.12, 130.10, 138.75, 156.94, 188.14; MS *m*/*z* 285 (M^+, 25), 225 (100). Anal. Calcd for $C_{16}H_{15}NO_2S$: C, 67.34; H, 5.30; N, 4.91. Found: C, 67.29; H, 5.30; N, 4.95.

7-Methoxy-4-(3-methoxyphenyl)-4,5-dihyro-3,1-benzoxazepine-2(1*H*)-thione (4m): a pale-yellow solid; mp 149–150 °C (hexane–EtOAc); IR (KBr) 3160, 1148 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.27 (dd, *J* = 16.7, 2.3 Hz, 1H), 3.47 (dd, *J* = 16.7, 8.6 Hz, 1H), 3.70 (s, 3H), 3.75 (s, 3H), 5.71 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.82–6.84 (m, 2H), 6.92 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.03 (d, *J* = 7.8 Hz, 1H), 7.06 (d, *J* = 2.3 Hz, 1H), 7.20 (d, *J* = 7.8 Hz, 1H), 7.31 (t, *J* = 7.8 Hz, 1H), 11.56 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 40.34, 55.12, 55.31, 85.91, 112.05, 113.10, 113.76, 115.13, 118.42, 121.81, 129.54, 129.76, 130.53, 141.15, 156.02, 159.23, 186.95; MS *m*/*z* 315 (M^+, 8.7), 255 (100). Anal. Calcd for $C_{17}H_{17}NO_3S$: C, 64.74; H, 5.43; N, 4.44. Found: C, 64.52; H, 5.42; N, 4.33.

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