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AN EFFICIENT SYNTHESIS OF BENZENE FUSED SIX-, SEVEN- AND EIGHT-MEMBERED RINGS CONTAINING NITROGEN AND SULFUR BY BENZYNE RING CLOSURE REACTION

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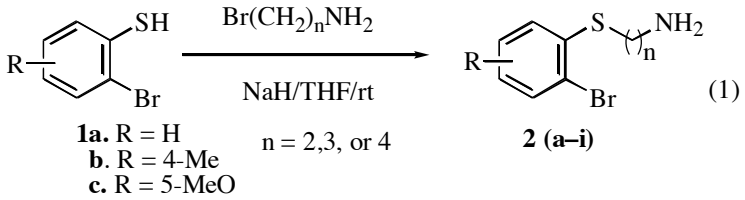
Abstract- 3,4-Dihydro-2-*H*-benzo[1,4]thiazines (**3a–c**), 2,3,4,5-tetrahydro[*b*]-[1,4]thiazapines (**3d–f**) and 2,3,4,5-tetrahydro-2*H*-benzo[*b*][1,4]thiazocines (**3g–i**) were prepared by the cyclization of the respective 2-bromophenylsulfanyl derivatives of ethylamine (**1a–c**), propylamine (**2d–f**) and butylamine (**2g–i**).

A major portion of our research for the past several years has been concerned with the use of benzyne chemistry in preparing new heterocycles. For example, we have prepared new heterocycles by nucleophilic addition to arynes possessing charged substituents,[1] by the reaction of benzyne with Barton esters,[2] and by Diels-Alder's cycloaddition reactions involving 4-haloarynes with furan,[3] selenoureas,[4] and *N,N*-diethylthiocarbamic acid *S*-*o*-tolyl esters.[5] Recently, we turned our attention to the use of benzyne ring closure reactions in preparation of benzene fused six-membered, seven-membered-, and eight-membered heterocycles for several reasons. First, many of these heterocycles function as CNS and cardiovascular agents. Compounds such as diazepam (an auxiolytic 1,4-benzodiazepine,[6] nefopam (an anagesic 1*H*-2,5-benzoxazocine),[7] and diltiazam (a calcium channel blocker)[8] are representative of such agents with clinically interesting biological activity. Second, although many five- and six-membered rings have been prepared by benzyne ring closure reactions,[9] no seven-membered ring and only one eight-membered ring which contains a single nitrogen atom have been prepared by this route.

We were thus particularly interested in preparing 3,4-dihydro-2*H*-benzo[1,4]thiazines, 2,3,4,5-tetrahydrobenzo[*b*][1,4]thiazepines, and 2,3,4,5-tetrahydro-2*H*-benzo[*b*][1,4]thiazocines. Since the nitrogen and sulfur atoms of the heterocylic portion of these compounds are on adjacent carbons of the benzene fused ring, they should, in principle, be capable of being synthesized by aryne ring closure reactions. Furthermore, of the sulfur and nitrogen containing seven-membered and eight-membered rings, only the unsubstituted 2,3,4,5-tetrahydrobenzo[*b*][1,4]thiazepine (**3d***)* is known.[10–13]

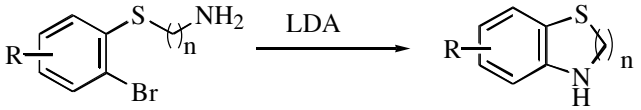
We selected 2-bromophenylsulfanyl derivatives of ethylamine (**2a–c**), propylamine (**2d–f**) and butylamine (**2g–i**) to be the aryne precursors. They were prepared according to equation 1 by the reaction



(1)

of the respective 2-bromobenzenethiol (**1a-c**) with the HBr salts of 2-bromoethyl-, 3-bromopropyl- and 4-bromobutylamine and NaH and THF at room temperature. The first two amines are commercially available whereas 4-bromobutylamine was prepared by treatment of 4-aminobutyl alcohol with HBr (48%).[14]

Next, as shown in equation 2 and Table 1, compounds (**2a–c**) underwent cyclization with LDA to give



(2)

3,4-dihydro-2*H*-benzo[1,4]thiazines (**3a–c**) in 87–93% yields. However, and more importantly, compounds (**2d–f**) afforded seven-membered rings (**3d–f**) and **2g–i** gave eight-membered rings (**3g–i**) in yields of 85–95% and 64–70%, respectively. The products were identified on the basis of ^{1}H NMR and ^{13}C NMR spectroscopy and, in the case of **3e**, by X-Ray crystallography. An ORTEP drawing of **3e** is shown below in Figure 1.

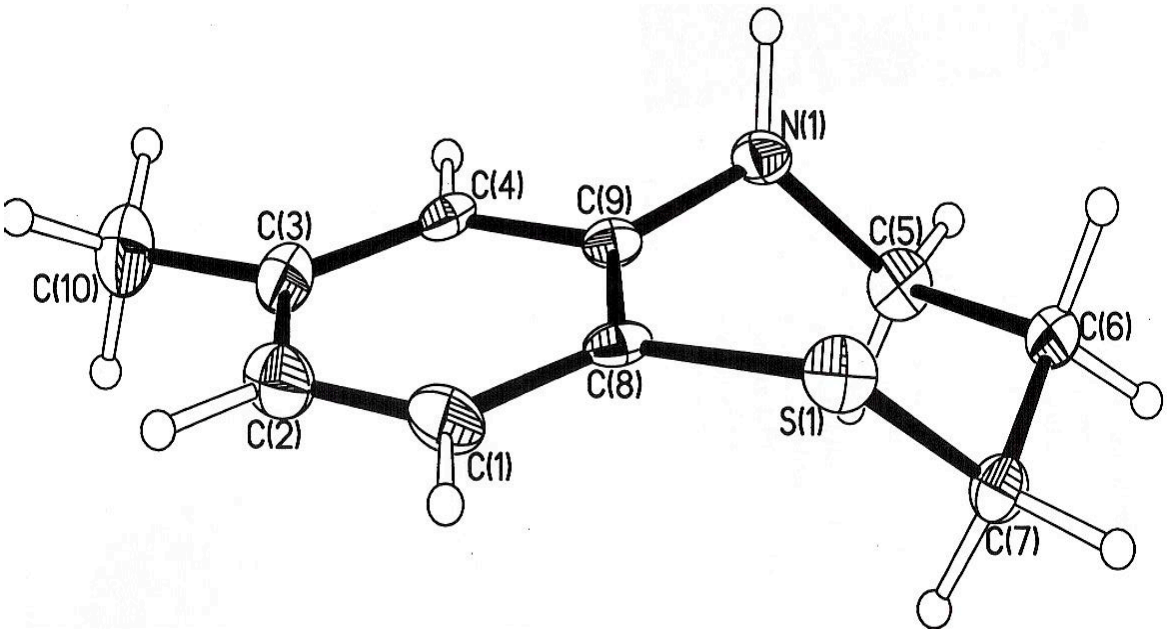


Figure 1 ORTEP drawing of compound (**3e**)

On the basis of entropy, one might expect the formation of seven- and especially eight-membered rings to be disfavored. Indeed this expectation might be one of the major reasons why aryne ring closure reactions have not been applied to such rings. However, the use of the sterically demanding base LDA and the non-nucleophilic solvent THF enables the ring closure reaction to occur.

Conclusions

In conclusion, we have found benzyne ring closure reactions to be a valuable method for the preparation of six-, seven- and eight-membered rings possessing nitrogen and sulfur atoms. Of the compounds reported here, only the parent seven-membered ring compound (**3d**) was previously known. The yield of **3d** reported in Table 1 is higher than those from previous methods which generally involved a ring expansion of thio-4-chromanones[13] or the corresponding oximes by reduction[12] or N-deoxygenation.[11] Thus, the high yields and the facile synthesis of substituted 2-bromobenzenethiols from the corresponding bromoanilines[15] shown in this study suggest that the benzyne ring closure reaction is the method of choice for the preparation of the titled compounds.

EXPERIMENTAL

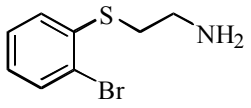
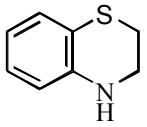
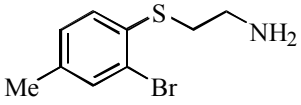
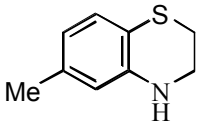
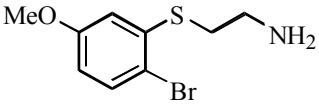
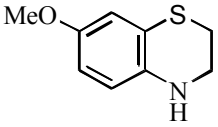
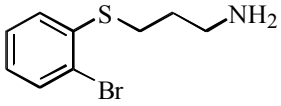
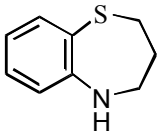
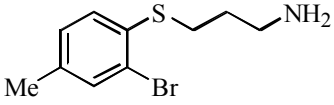
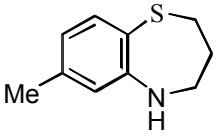
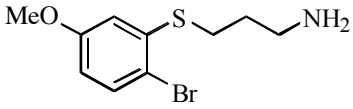
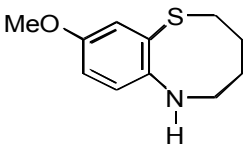
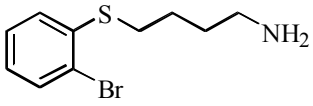
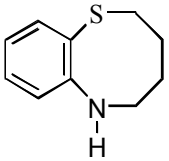
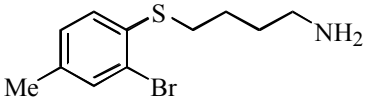
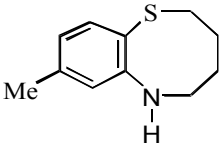
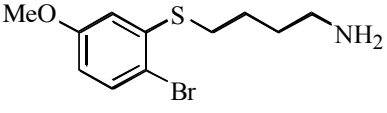
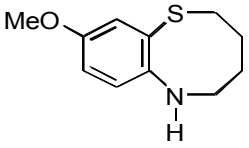
General Data Melting points were taken on a Melt-Temp capillary apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz Bruker AVANCE DRX-400 Multi-nuclear NMR spectrometer. Chemical shift are reported in reference to TMS as internal standard. HMRS were measured by the Washington University Mass Spectrometry Resource, an NIH Research Resource (Grant No.P41RR0954). Routine MS were recorded on a Hewlett-Packard GC/MS Model GCD Series II. THF was freshly distilled using sodium-benzophenone method and all reactions were monitored by TLC. Concentrations were performed by rotary evaporator using water aspirator system. Low pressure chromatography was carried out by applying air pressure to pyrex column packed with silica gel 60 (0.040-0.063 mm particle size, 230-400 mesh). Na_2SO_4 was used as drying agent. The solvents, reagents, and starting materials, including 2-bromobenzenethiol (**1a**) were purchased from commercial sources. 2-Bromo-4-methyl- (**1b**), and 2-bromo-6-methoxybenzenethiol (**1c**) were prepared as follows.

Procedure for the synthesis of 2-bromobenzenethiols (1b,c)

A mixture of 2-bromo-4-methylaniline or 2-bromo-6-methoxyaniline (26.8 mmol), concd HCl (5 mL) and ice (10 g) was cooled at –5 °C and slowly treated with solution of sodium nitrite (1.88 g, 26.8 mmol) in water (10 mL), the temperature being maintained below 0 °C . The cold solution of the diazonium salt was added dropwise (1 h) to a stirring aqueous (10 mL) solution of potassium ethyl xanthate (8.6 g, 53.7 mmol) maintained at 70–78 °C. After stirring for an additional 1 h, the mixture was cooled to rt, the pH of the solution adjusted to 8 by the addition of $NaHCO_3$, and extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with water, dried over Na_2SO_4, and the solvent evaporated

to give an oily residue. The residue was mixed with a solution of 6 g of KOH in 30 mL of ethanol then hydrolyzed by refluxing for 12 h under nitrogen atmosphere. After the evaporation of the solvent, the

Table 1 Preparation of Compounds (**3a-i**)

Entry	**2**	Aryne Precursor	Yield, %	**3**	Product	Yield, %
1	**a**		84	**a**		89
2	**b**		79	**b**		93
3	**c**		82	**c**		87
4	**d**		87	**d**		85
5	**e**		84	**e**		95
6	**f**		82	**f**		92
7	**g**		67	**g**		68
8	**h**		74	**h**		70
9	**i**		80	**i**		64

reaction mixture was diluted with water, and the resulting solution was washed with ether. The aqueous layer was acidified by the slow addition of 3N sulfuric acid and extracted with CH_2Cl_2. The CH_2Cl layer was washed with water, dried over Na_2SO_4 and the solvent evaporated. The resulting crude product was purified by column chromatography with hexane as eluent to give **1b** and **1c** in nearly quantitative

yields.[15]

General procedure for the synthesis of 2-(bromophenylsulfanyl)amines (2a–i)

To a well stirred solution of NaH (60% suspension in hexanes, 0.25g, 10.5 mmol) and THF (10 mL) kept under argon atmosphere at rt, the appropriate 2-bromobenzenethiol (2.6 mmol) in THF (5 mL) was slowly added through a needle-syringe system. The reaction mixture was stirred for 30 min then the appropriate 2-bromoethylamine hydrobromide salt (39 mmol) was added in small portions under continuous argon purging. After the addition of the salt, the reaction mixture was stirred for another 6 h. Then ice-water was added at 0 °C, and the mixture extracted with CH_2Cl_2 (3x75 mL). The combined CH_2Cl_2 extracts were washed with water, dried over Na_2SO_4, and the solvent removed under reduced pressure. The resulting crude product (**2a–i**), which was purified by column chromatography using 5% ethyl acetate-hexane as eluent. The physical and spectral properties for **2a–i** are shown below.

2-(2-Bromophenylsulfanyl)ethylamine (2a)

This compound was obtained as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 1.44 (s, 2H, -NH_2), 3.01(t, *J* = 5.7 Hz, 2H, -CH_2), 3.08 (t, *J* = 5.7 Hz, 2H, -CH_2), 7.06 (dd, *J* = 7.0, 7.4 Hz, 1H, Ar-H-6), 7.31(m, 2H, Ar-H-4, Ar-H-5), 7.57 (d, *J* = 7.6 Hz, 1H, Ar-H-3). ^{13}C NMR ($CDCl_3$) δ 37.6, 40.9, 124.8, 127.4 128.2, 129.3, 133.5, 137.5. MS (EI) *m/z*, (relative intensity): 233 (M^+, 7), 231 (M^+, 7), 204 [(M^+–CH_2NH), 100], 202 [(M^+–CH_2NH), 100], 152 [(M^+–Br), 53]. *Anal.* Calcd for C_7H_8NBrS: C, 38.55; H, 3.70; N, 6.42. Found: C, 38.66; H, 3.79; N, 6.45.

2-(2-Bromo-4-methylphenylsulfanyl)ethylamine (2b)

This compound was obtained as a viscous liquid. ^{1}H NMR ($CDCl_3$) δ 1.45(br s, 2H, -NH_2), 2.31(s, 3H, -CH_3), 2.93 (t, *J* = 6.0 Hz, 2H, -CH_2), 3.02 (t, *J* = 5.8 Hz, 2H, -CH_2), 7.08 (d, *J* = 7.8 Hz, 1H, Ar-H-6), 7.25 (dd, *J* = 2.5, 7.8 Hz, 1H, Ar-H-5), 7.42 (d, *J* = 2.5 Hz, 1H, Ar-H-3). ^{13}C NMR ($CDCl_3$) δ 21.0, 38.6, 41.1, 124.8, 129.1, 130.7, 133.5, 134.1, 138.2. MS (EI) *m/z*, (relative intensity): 247 (M^+, 2), 245 (M+2), 234 [(M^+–CH_2NH), 37], 232 [(M^+–CH_2NH), 37], 166 [(M^+–Br), 100]. *Anal.* Calcd for $C_8H_{10}NBrS$: C, 41.39; H, 4.34; N, 6.03. Found: C, 41.51; H, 4.40; N, 6.21.

2-(2-Bromo-5-methoxyphenylsulfanyl)ethylamine (2c)

This compound was obtained as a light yellow oil. ^{1}H NMR ($CDCl_3$) δ 1.43 (br s, 2H, -NH_2), 3.01 (t, *J* = 5.8 Hz, 2H, -CH_2), 3.05 (t, *J* = 5.8 Hz, 2H, -CH_2), 3.81(s, 3H, -OMe), 6.62(dd, *J* = 2.4, 8.6 Hz, 1H, Ar-H-4), 6.88 (d, *J* = 2.4 Hz, 1H, Ar-H-6), 7.45 (d, *J* = 8.6 Hz, 1H, Ar-H-3). ^{13}C NMR ($CDCl_3$) δ 33.8, 39.5, 55.7, 113.5, 115.3, 116.0, 133.9, 136.6, 159.5. MS (EI) *m/z*, (relative intensity): 263 (M^+, 3), 261 (M^+, 3), 182 [(M^+–79), 100]. *Anal.* Calcd for $C_8H_{10}NOBrS$: C, 38.72; H, 4.06; N, 5.64. Found: C, 38.66; H, 4.11; N, 5.41.

3-(2-Bromophenylsulfanyl)propylamine (2d)

This compound was obtained as a viscous liquid. ^{1}H NMR ($CDCl_3$) δ 1.28 (br s, 2H, -NH_2), 1.87 (m, 2H, -CH_2), 2.88 (m, 2H, -CH_2), 3.01(t, J = 6.1 Hz, 2H, -CH_2),7.03 (dd, J = 2.4 Hz, 7.8 Hz, 1H, Ar-H-6), 7.27 (m, 2H, Ar-H-5, H-6), 7.55 (d, J = 7.7 Hz, 1H, Ar-H-3). ^{13}C NMR ($CDCl_3$) δ 30.7, 32.6, 41.5, 123.9, 126.8, 128.1, 128.3, 133.4, 138.5. MS (EI) *m/z*, (relative intensity): 247 $(M)^+$, 9), 245 (M^+, 9), 166 [(M^+–Br), 34], 57 [$(CH_2CH_2CH_2NH)^+$, 100]. *Anal.* Calcd for $C_8H_{10}NBrS$: C, 41.39; H, 4.34; N, 6.03. Found: C, 41.44; H, 4.41; N, 6.05.

3-(2-Bromo-4-methylphenylsulfanyl)propylamine (2e)

This compound was obtained as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 1.27 (br s, 2H, -NH_2), 1.82(m, 2H, -CH_2), 2.31 (s, 3H, -CH_3), 2.87 (m, 2H, -CH_2), 2.98 (t, J = 6.3 Hz, 2H, -CH_2), 7.08 (d, J = 7.9 Hz, 1H, Ar-6H), 7.21 (dd, J = 2.5, 7.9 Hz, 1H, Ar-5H), 7.41 (d, J = 2.5 Hz, 1H, Ar-H-3). ^{13}C NMR δ ($CDCl_3$) 20.9, 31.3, 32.8, 41.5, 124.6, 129.0, 129.5, 134.0, 134.4, 137.6. MS (EI) *m/z*, (relative intensity): 261 (M^+, 4), 259 (M^+, 4), 194 (M^+, 20), 57 [$(CH_2CH_2CH_2NH)^+$, 100]. *Anal.* Calcd for $C_9H_{12}NBrS$: C, 43.91; H, 4.91; N, 5.69. Found: C, 43.98; H, 4.77; N, 5.55.

3-(2-Bromo-5-methoxyphenylsulfanyl)propylamine (2f)

This compound was isolated as a white powder, mp 134-135 °C (EtOAc/hexanes). ^{1}H NMR ($CDCl_3$) δ 1.69 (br s, 1H, -NH_2), 1.89 (m, 2H, -CH_2), 2.89 (m, 2H, -CH_2), 3.01 (t, J = 6.4 Hz, 2H, -CH_2), 3.81 (s, 3H, -OMe), 6.60 (dd, J = 2.4, 8.0 Hz, 1H, Ar-H-4), 6.84 (d, J = 2.4 Hz, 1H, Ar-H-6), 7.42 (d, J = 8.0 Hz, 1H, Ar-H-3). ^{13}C NMR ($CDCl_3$) δ 30.5, 30.7, 40.4, 55.8, 112.4, 114.3, 114.8, 133.7, 138.8, 159.5. MS (*m/z*) (relative intensity): 277 (M^+, 4), 275 (M^+, 4), 196 [(M^+–Br), 100]. *Anal.* Calcd for $C_9H_{12}NOBrS$: C, 41.23; H, 4.61; N, 5.34. Found: C, 41.18; H, 4.69; N, 5.19.

4-(2-Bromophenylsulfanyl)butylamine (2g)

This compound was isolated as a yellow viscous liquid. ^{1}H NMR ($CDCl_3$) δ 1.29 (br s, 1H, -NH_2), 1.66 (m, 2H, -CH_2), 1.77 (m, 2H, -CH_2), 2.88 (m, 2H, -CH_2), 3.48 (t, J = 6.4 Hz, 2H -CH_2), 7.08 (dd, J = 2.5, 7.8 Hz, 1H, Ar-H-6), 7.28 (dd, J = 7.8, 8.0 Hz, 1H, Ar-H-5), 7.43 (dd, J = 7.8, 8.0 Hz, 1H, Ar-H-4), 7.59 (d, J = 7.8 Hz, 1H, Ar-H-3). ^{13}C NMR ($CDCl_3$) δ 21.5, 40.0, 40.4, 40.6, 127.9, 128.1, 129.2, 131.8, 133.6, 137.3. MS (EI) *m/z*, (relative intensity): 261 (M^+, 4), 259. (M^+, 4), 180 [(M^+–Br), 16], 56 ([$CH_2CH_2CH_2N]^+$, 100). *Anal.* Calcd for $C_9H_{12}NBrS$: C, 43.91; H, 4.91; N, 5.69. Found: C, 43.69; H, 4.98; N, 5.67.

4-(2-Bromo-4-methylphenylsulfanyl)butylamine (2h)

This compound was isolated as a yellow viscous liquid. ^{1}H NMR ($CDCl_3$) δ 1.52(br s, 1H, -NH_2), 1.74 (m, 4H, -CH_2x2), 2.31 (s, 3H, -CH_3), 2.73 (m, 2H, -CH_2), 2.93 (t, J = 6.2, Hz, 2H, -CH_2), 7.07(dd, J = 2.7, 7.7 Hz, 1H, Ar-H-5), 7.18 (d, J = 7.7 Hz, 1H, Ar-H-6), 7.40 (d, J = 2.6 Hz, 1H, Ar-H-3). ^{13}C NMR ($CDCl_3$) δ 20.9, 27.1, 30.5, 33.6, 51.2, 124.3, 129.0, 129.1, 133.9, 134.8, 137.3. MS (EI) *m/z*, (relative

intensity): 275 (M^+, 1), 273 (M^+, 1), 194 [(M^+–Br), 100]. *Anal.* Calcd for $C_{10}H_{14}NBrS$: C, 46.16; H, 5.42; N, 5.38. Found: C, 46.31; H, 5.41; N, 5.46.

4-(2-Bromo-4-methoxyphenylsulfanyl)butylamine (2i)

This compound was isolated as a colorless viscous liquid. ^{1}H NMR ($CDCl_3$) δ 1.32 (s, 1H, -NH_2), 1.74(m, 4H, -CH_2x2), 2.89 (m, 2H, -CH_2), 3.12 (t, *J* = 6.4 Hz, 2H, -CH_2), 3.90 (s, 3H, -OMe), 6.64 (d, *J* = 2.7 Hz, 1H, Ar-H-6), 6.94 (dd, *J* = 2.7, 8.0 Hz, 1H, Ar-H-4), 7.45 (d, *J* = 8.0 Hz, 1H, Ar-H-3). ^{13}C NMR ($CDCl_3$) δ 29.4, 30.6, 30.7, 40.5, 55.9, 112.1, 114.3, 114.8, 133.7, 138.8, 159.6. MS (EI) *m/z*, (relative intensity): 291 (M^+, 3), 289 (M^+, 3), 210 [(M^+–Br), 40], 73 (100). *Anal.* Calcd for $C_{10}H_{14}NOBrS$: C, 43.49; H, 5.11; N, 5.07. Found: C, 43.38; H, 5.22; N, 5.19.

Typical procedure for the synthesis of 3a–3i

Diisopropylamine (0.5 mL, 5 mmol) was added through a needle syringe system to a well stirred solution of THF (5 mL) and *n*-BuLi (2.4 mL of 1.6 M solution in hexanes, 3.8 mmol) kept at –78 °C under argon atmosphere. The reaction mixture was then cooled to –20 °C and kept at that temperature for 45 min. The reaction mixture was the cooled to –78 °C and a solution of the appropriate 2-(2-bromophenyl-sulfanyl)amine (1.3 mmol) in THF (5 mL) was slowly added to the reaction mixture which was allowed to warm to rt. After stirring for 5 h, a saturated NH_4Cl solution was added, and the resulting mixture was extracted with ethyl acetate, and the extract was washed with water, and dried (Na_2SO_4). The solvent was removed and the remaining crude product was purified by column chromatography using silica gel (400 mesh) and 10% ethyl acetate-hexane. The physical and spectral properties of **3a–i** are given below.

3,4-Dihydro-2*H*-benzo[1,4]thiazine (3a)

This compound was isolated as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 3.07 (t, *J* = 5.0 Hz, 2H, -CH_2), 3.65 (t, *J* = 5.0 Hz, 2H, -CH_2), 4.00 (br s, 1H, -NH), 6.48 (dd, *J* = 1.8, 7.9 Hz, 1H, Ar-H-5), 6.63 (dd, *J* = 7.4 Hz, 7.5 Hz, 1H, Ar-H-7), 6.96 (dd, *J* = 7.4, 7.8 Hz, 1H, Ar-H-6), 7.00 (dd, *J* = 1.7, 7.8 Hz, 1H, Ar-H-8). ^{13}C NMR ($CDCl_3$) δ 26.5, 42.7, 115.8, 118.5, 125.9, 127.1, 128.1, 128.9. HRMS calcd for C_8H_9NS: 151.046. Found: 151.047. *Anal.* Calcd for C_8H_9NS: C, 63,54; H, 6.00; N, 9.26. Found: C, 63.66; H, 6.07; N, 9.36.

6-Methyl-3,4-dihydro-2*H*-benzo[1,4]thiazine (3b)

This compound was isolated as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 2.21 (s, 3H, -CH_3), 3.06 (t, *J*=6.2 Hz, 2H, -CH_2), 3.60 (t, *J*=6.2 Hz, 2H, -CH_2), 3.94 (br s, 1H, -NH), 6.31 (d, *J* = 2.2 Hz, 1H, Ar-H-5), 6.47 (dd, *J* = 2.2, 7.6 Hz, 1H, Ar-H-7), 6.89 (d, *J* = 7.6 Hz, 1H, Ar-H-8). ^{13}C NMR ($CDCl_3$) δ 21.4, 26.5, 42.9, 116.4, 119.6, 127.9, 130.2, 135.8, 141.9. HRMS calcd for $C_9H_{11}NS$: 165.061. Found: 165.060. *Anal:* Calcd for $C_9H_{11}NS$: C, 65.41; H, 6.71; N, 8.48. Found: C, 65.32; H, 6.61; N, 8.56.

7-Methoxy-3,4-dihydro-2*H*-benzo[1,4]thiazine (3c)

This compound was isolated as a light yellow oil. ^{1}H NMR ($CDCl_3$) δ 3.10 (t, J = 5.1 Hz, 2H, -CH_2), 3.59 (t, J = 5.1 Hz, 2H, -CH_2), 3.73 (br s, 1H, -NH), 3.75 (s, 3H, -OMe), 6.45 (dd, J = 2.6, 8.5 Hz, 1H, Ar-H-6), 6.52 (d, J = 2.6 Hz, 1H, Ar-H-8), 6.60 (d, J = 8.5 Hz, 1H, Ar-H-5). ^{13}C NMR ($CDCl_3$) δ 38.4, 53.9, 55.6, 110.3, 113.5, 113.6, 133.3, 140.1, 150.1. HRMS calcd for $C_9H_{11}NOS$: 181.056. Found: 181.058. *Anal.* Calcd for $C_9H_{11}NOS$: C, 59.64; H, 6.12; N, 7.73. Found: C, 59.80; H, 6.18; N, 7.83.

2,3,4,5-Tetrahydrobenzo[*b*][1,4]thiazepine (3d)

This compound was isolated as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 2.10 (m, 2H, -CH_2), 2.86 (m, 2H, -CH_2), 3.30 (t, J = 5.4 Hz, 2H, -CH_2), 3.90 (br s, 1H, -NH), 6.76 (d, J = 7.0 Hz, 1H, Ar-H-6), 6.81(dd, J =7.0, 7.5 Hz, 1H, Ar- H-8), 7.07 (dd, J = 7.2, 7.5 Hz, 1H, Ar-H-7), 7.40 (d, J = 7.2 Hz, 1H, Ar-H-9). ^{13}C NMR ($CDCl_3$) δ 32.2, 33.4, 47.6, 120.4, 121.3, 125.5, 128.9, 133.3, 152.1. HRMS calcd for $C_9H_{11}NS$: 165.061. Found: 165.063. *Anal*. Calcd for $C_9H_{11}NS$: C, 65.41; H, 6.71; N, 8.48. Found: C, 65.49; H, 6.81; N, 8.57.

7-Methyl-2,3,4,5-tetrahydrobenzo[*b*][1,4]thiazepine (3e)

This compound was isolated as a colorless needles, mp 48–49 °C (EtOAc/hexanes). ^{1}H NMR ($CDCl_3$) δ 2.09 (m, 2H, -CH_2), 2.26 (s, 3H, -CH_3), 2.79 (m, 2H, -CH_2), 3.24 (m, 2H, -CH_2), 3.91 (br s, 1H, -NH), 6.59 (d, J = 2.8 Hz, 1H, Ar-H-6), 6.63 (dd, J = 2.8,7.6 Hz, 1H, Ar-H-8), 7.28 (d, J = 7.6 Hz, 1H, Ar-H-9). ^{13}C NMR ($CDCl_3$) δ 21.3 32.4, 33.7, 47.9, 121.2, 122.4, 122.4, 133.3, 138.4, 152.1. HRMS calcd for $C_{10}H_{13}NS$: 179.077. Found: 179.075. *Anal.* Calcd for $C_{10}H_{13}NS$: C, 66.99; H, 7.31; N, 7.81. Found: C, 67.18; H, 7.40; N, 7.88.

8-Methoxy-2,3,4,5-tetrahydrobenzo[*b*][1,4]thiazepine (3f)

This compound was isolated as a yellow oil. ^{1}H NMR ($CDCl_3$) δ 2.01(m, 2H, -CH_2), 2.78 (m, 2H, -CH_2), 3.14 (t, J = 5.0 Hz, 2H, -CH_2), 3.75 (br s, 1H, -NH), 3.77 (s, 3H, -OMe), 6.69 (dd, J = 2.3, 8.4 Hz, 1H, Ar-H-7), 6.77 (d, J = 8.4 Hz, 1H, Ar-H-6), 7.04 (d, J = 2.3 Hz, 1H, Ar-H-9). ^{13}C NMR ($CDCl_3$) δ 32.5, 34.0, 48.5, 56.0, 114.7, 117.9, 122.0, 128.1, 146.2, 154.5. HRMS. calcd for $C_{10}H_{13}NOS$: 195.072. Found: 195.074. *Anal*. Calcd for $C_{10}H_{13}NOS$: C, 61.50; H, 6.71; N, 7.17. Found: C, 67.12; H, 7.40; N, 7.91.

3,4,5,6-Tetrahydro-2*H*-benzo[*b*][1,4]thiazocine (3g)

This compound was isolated as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 1.36 (m, 2H, -CH_2), 2.01 (m, 2H, CH_2), 3.06 (m, 2H, -CH_2), 3.64 (m, 2H, -CH_2), 3.95 (br s, 1H, -NH), 6.73 (d, J = 7.7 Hz, 1H, Ar-H-7), 6.80 (dd, J = 7.6, 7.8 Hz, 1H, Ar-H-9), 7.06 (dd, J = 7.7, 7.8 Hz, 1H, Ar-H-8), 7.38 (d, J = 7.6 Hz, 1H, Ar-H-10). ^{13}C NMR ($CDCl_3$) δ 30.2, 40.5, 41.7, 46.6, 120.1, 121.3, 124.0, 128.3, 133.7, 152.3. HRMS calcd for $C_{10}H_{13}NS$: 179.077. Found: 179.079. *Anal.* Calcd for $C_{10}H_{13}NS$: C, 66.99; H, 7.31; N, 7.81. Found: C, 66.89; H, 7.30; N, 7.90.

8-Methyl-3,4,5,6-tetrahydro-2*H*-benzo[*b*][1,4]thiazocine (3h)

This compound was isolated as a yellow oil. ^{1}H NMR ($CDCl_3$) δ 1.34 (m, 2H, -CH_2), 2.03 (m, 2H, -CH_2), 2.26 (s, 3H, -CH_3), 2.99 (m, 2H, -CH_2), 3.58 (m, 2H, -CH_2), 3.87 (br s, 1H, -NH), 6.57 (d, *J* = 1.2 Hz, 1H, Ar-H-7), 6.64 (dd, *J* = 1.2, 7.6 Hz, 1H, Ar-H-9), 7.28 (d, *J* = 7.6 Hz, 1H, Ar-H-10). ^{13}C NMR ($CDCl_3$) δ 15.2, 28.8, 30.1, 34.5, 51.2, 112.9, 116.5, 117.9, 127.5, 142.1, 133.9. HRMS calcd for $C_{11}H_{15}NS$: 193.093. Found: 193.096. *Anal.* Calcd for $C_{11}H_{15}NS$: C, 68.35; H, 7.82; N, 7.25. Found: C, 68.40; H, 7.88; N, 7.30.

9-Methoxy-3,4,5,6-tetrahydro-2*H*-benzo[*b*][1,4]thiazocine (3i)

This compound was isolated as a yellowish oil. ^{1}H NMR ($CDCl_3$) δ 1.33 (m, 2H, -CH_2), 2.14 (m, 2H, -CH_2), 2.98 (m, 2H, -CH_2), 3.68 (m, 2H, -CH_2), 3.77 (br s, 1H, -NH), 3.92 (s, 3H, -OMe), 6.77(d, J = 7.8 Hz, 1H, Ar-H-7), 6.79 (dd, J = 2.6, 7.8 Hz, 1H, Ar-H-8), 7.28 (d, J = 2.6 Hz, 1H, Ar-H-10). ^{13}C NMR ($CDCl_3$) δ 28.0, 29.1, 34.5, 51.2, 55.6, 113.1, 116.3, 118.0, 127.5, 142.1, 155.9. HRMS calcd for $C_{11}H_{15}NOS$: 209.087. Found: 209.089. *Anal.* Calcd for $C_{11}H_{15}NOS$: C, 63.12; H, 7.22; N, 6.69. Found: C, 63.22; H, 7.31; N, 6.61.

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