

## **Catalyst-Free Synthesis of 2,3-dihydro-1,5-benzothiazepines in Renewable and Biodegradable Reaction Medium**

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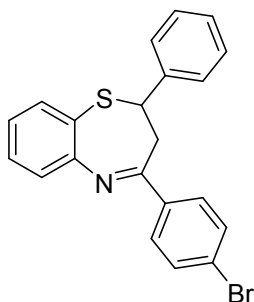
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## **Experimental Section**

### **General procedure for the synthesis of 2,3-dihydro-1,5- benzothiazepine .**

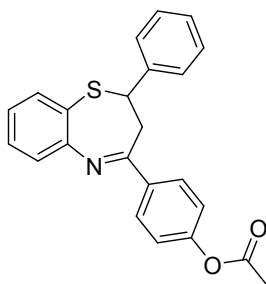
10 mL Glycerol was added to a round bottom and then respective Chalcone (1mmol) and 2-aminothiophenol(1mmol) as reactant were added under stirring at 70°C catalyst free condition. It was allowed to stir till completion of the reaction. Progress of the reaction was monitored by TLC the product was precipitated by addition of 10 mL of H<sub>2</sub>O. After that products were separated by simple filtration.

### 2-Phenyl-4-(4-bromophenyl)-2,3-dihydro-1,5-benzothiazepine (3a)



mp 135 °C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): = 3.07 (t,  $J = 12.7$  Hz, 1 H), 3.25 (dd,  $J = 4.9, 13.0$  Hz, 1 H), 4.94 (dd,  $J = 4.8, 12.4$  Hz, 1 H), 7.12 (td,  $J = 1.5, 7.5$  Hz 1 H), 7.26-7.33 (m, 6 H), 7.49 (td,  $J = 1.5, 7.6$  Hz 1 H), 7.64 (d,  $J = 8.6$  Hz, 3 H), 7.95 (d,  $J = 8.6$  Hz, 2 H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 37.72 (C), 60.52 (CH<sub>2</sub>), 123.64 (C), 125.32 (CH), 126.27 (CH), 128.07 (CH), 128.79 (CH), 129.33 (CH), 129.78 (CH), 133.11 (CH), 135.29 (CH), 141.61 (C), 153.19 (C), 166.92 (C).

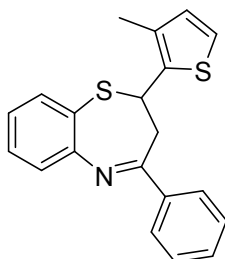
### 4-(4-acetoxyphenyl)-2-phenyl-2,3-dihydro-1,5-benzothiazepine (3b)



142-143 °C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): = 2.34 (s, 3 H), 3.03 (t,  $J = 12.8$  Hz, 1 H), 3.26 (dd,  $J = 4.8, 13.0$  Hz, 1 H), 4.96 (dd,  $J = 4.8, 13.0$  Hz, 1 H), 7.16 (td,  $J = 1.4, 7.5$  Hz, 1 H), 7.25-7.33 (m, 8 H), 7.46-7.54 (m, 1 H), 7.65 (dd,  $J = 1.4, 7.7$  Hz, 1 H), 8.12 (d,  $J = 8.8$  Hz, 2

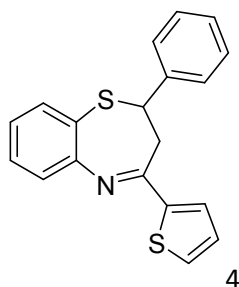
H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 21.213 ( $\text{CH}_3$ ), 36.4 ( $\text{CH}_2$ ), 60.4 ( $\text{CH}$ ), 122.9 ( $\text{CH}$ ), 125.4 ( $\text{CH}$ ), 126.6 ( $\text{CH}$ ), 127.7 ( $\text{CH}$ ), 128.6 ( $\text{CH}$ ), 129.8 ( $\text{CH}$ ), 136.1 ( $\text{CH}$ ), 146.0 ( $\text{C}$ ), 152.3 ( $\text{C}$ ), 154.0 ( $\text{C}$ ), 166.0 ( $\text{C}$ ), 169.2 ( $\text{C}$ ). IR (KBr): 1598, 1755, 2917  $\text{cm}^{-1}$ . MS (ESI):  $m/z = 374.43$  ( $\text{MH}^+$ ). Anal. Calcd. for  $\text{C}_{23}\text{H}_{19}\text{NO}_2\text{S}$ : C, 73.97; H, 5.13; N, 3.75, found: C, 74.07; H, 5.16; N, 3.74.

### 2-(3-Methylthiophen-2-yl)-4-phenyl-2,3-dihydro-1,5-benzothiazepine (3c)



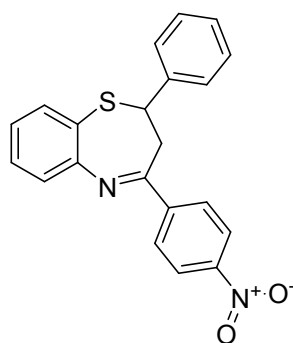
mp 121-124  $^{\circ}\text{C}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  2.24 (s, 3 H), 2.97 (t,  $J = 12.8$  Hz, 1 H), 3.35 (dd,  $J = 4.9, 12.9$  Hz, 1 H), 5.34 (dd,  $J = 4.8, 12.5$  Hz, 1 H), 6.83 (d,  $J = 5.1$  Hz, 1 H), 7.05 (d,  $J = 5.0$  Hz, 1 H), 7.15 (t,  $J = 7.5$  Hz, 1 H), 7.33 (d,  $J = 8.9$  Hz, 1 H), 7.45-7.63 (m, 5 H), 8.08 (d,  $J = 7.9$  Hz, 2 H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 16.04 ( $\text{CH}_3$ ), 38.38 ( $\text{CH}_2$ ), 53.58 ( $\text{CH}$ ), 121.91 ( $\text{CH}$ ), 125.53 ( $\text{CH}$ ), 126.59 ( $\text{CH}$ ), 128.54 ( $\text{CH}$ ), 128.85 ( $\text{CH}$ ), 129.32 ( $\text{CH}$ ), 129.87 ( $\text{CH}$ ), 130.36 ( $\text{CH}$ ), 132.52 ( $\text{CH}$ ), 135.87 ( $\text{CH}$ ). MS (ESI):  $m/z = 336.36$  ( $\text{MH}^+$ ). IR (KBr): 1608, 2918  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{20}\text{H}_{17}\text{NS}_2$ : C, 71.60; H, 5.11; N, 4.18, found: C, 71.63; H, 5.12; N, 4.17.

### 2-Phenyl-4-(Thiophen-2-yl)-2,3-dihydro-1,5-benzothiazepine (3d)



mp 122 - 125 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): = 3.04 (t, *J* = 12.6 Hz, 1 H), 3.24 (dd, *J* = 4.7, 12.8 Hz, 1 H), 5.01 (dd, *J* = 4.7, 12.0 Hz, 1 H), 7.06-7.16 (m, 2 H), 7.17- 7.33 (m, 6 H), 7.35-7.44 (m, 1 H), 7.52-7.59 (m, 3 H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz): 38.7 (CH<sub>2</sub>), 60.1 (CH), 123.6 (C), 125.4 (CH), 127.1 (CH), 128.0 (CH), 128.6 (CH), 129.7 (CH), 133.1 (CH), 135.5 (CH), 143.4 (C), 164.5 (C). IR (KBr): 1605, 2920 cm<sup>-1</sup>. Anal. Calcd for C<sub>19</sub>H<sub>15</sub>NS<sub>2</sub>: C, 70.99; H, 4.70; N, 4.36, found: C, 71.13; H, 4.72; N, 4.35.

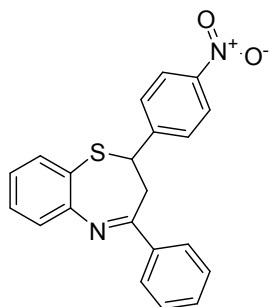
#### 4-(4-Nitrophenyl)-2-phenyl-2,3-dihydro-1,5-benzothiazepine (3e)



mp 122 - 124 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400MHz): = 3.12 (t, *J* = 13.1 Hz, 1 H), 3.27 (dd, *J* = 5.0, 13.2 Hz, 1 H), 5.02 (dd, *J* = 5.0, 12.0 Hz, 1 H), 7.17 (dt, *J* = 1.5, 7.5 Hz, 1 H), 7.23-7.36 (m, 6

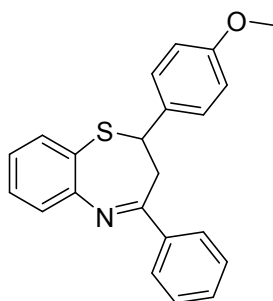
H), 7.52 (dt,  $J = 1.5, 7.6$  Hz, 1 H), 7.65 (dd,  $J = 1.5, 7.7$  Hz, 1 H), 8.17-8.26 (m, 2 H), 8.32-8.35 (m 2 H).

**2-(4-Nitrophenyl)-4-phenyl-2,3-dihydro-1,5-benzothiazepine (3f)**



mp 184-186°C  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz): = 3.07 (t,  $J = 12.7$  Hz, 1 H), 3.41 (dd,  $J = 4.9, 12.8$  Hz, 1 H), 5.06 (dd,  $J = 4.8, 12.5$  Hz, 1 H), 7.21-7.24 (m, 1 H), 7.46-7.64 (m, 8 H), 8.16 (d,  $J = 8.7$  Hz, 2 H).

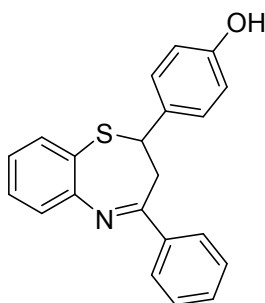
**2-(4-Methoxyphenyl)-4-phenyl-2,3-dihydro-1,5-benzothiazepine (3g)**



mp 126-127 °C  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400MHz): = 3.07 (t,  $J = 12.7$  Hz, 1 H), 3.32 (dd,  $J = 4.7, 12.9$  Hz, 1 H), 3.83 (s, 3 H), 4.96 (dd,  $J = 4.7, 12.5$  Hz, 1 H), 6.85 (d,  $J = 11.15$  Hz, 2 H),

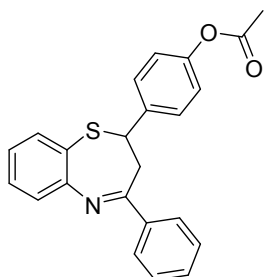
7.17 (t,  $J = 7.5$  Hz, 1 H), 7.25 (d,  $J = 8.6$  Hz, 2 H), 7.34 (d,  $J = 7.9$  Hz, 1 H), 7.48 – 7.55 (m, 4 H), 7.62 (d,  $J = 7.6$  Hz, 1H), 8.08 (d,  $J = 7.15$  Hz, 2 H).

**2-(4-Hydroxyphenyl)-4-phenyl-2,3-dihydro-1,5-benzothiazepine (3h)**



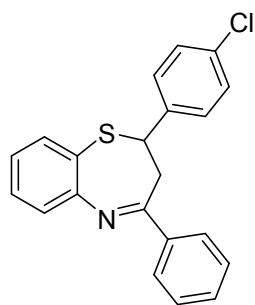
mp 132-134 °C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): = 3.03 (t,  $J = 12.7$  Hz, 1 H), 3.26 (dd,  $J = 4.8$ , 12.9 Hz, 1 H), 4.93 (dd,  $J = 4.7$ , 12.5 Hz, 1 H), 5.12 (bs, 1 H), 6.78 (d,  $J = 8.5$  Hz, 2 H), 7.16-7.23 (m, 3 H), 7.37 (d,  $J = 8.5$  Hz, 1 H), 7.44- 7.53 (m, 4 H), 7.65 (dd,  $J = 1.5$ , 7.7 Hz, 1 H), 8.08 (m, 2 H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 36.97 ( $\text{CH}_2$ ), 60.12 (CH), 115.58 (CH), 122.09 (C), 127.45 (CH), 127.73 (CH), 131.15 (CH), 136.54 (C), 141.56 (C), 153.24 (C). IR (KBr): 1595, 2923, 3351  $\text{cm}^{-1}$ . MS (ESI):  $m/z = 332.24$  ( $\text{MH}^+$ ). Anal. Calcd. for  $\text{C}_{21}\text{H}_{17}\text{NOS}$ : C, 76.10; H, 5.17; N, 4.23, found: C, 76.23; H, 5.13; N, 4.21.

**2-(4-acetoxyphenyl)-4-phenyl-2,3-dihydro-1,5-benzothiazepine (3i)**



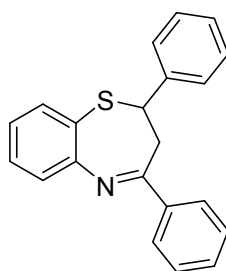
$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): = 2.34 (s, 3 H), 3.04 (t,  $J$  = 12.8 Hz, 1 H), 3.30 (dd,  $J$  = 4.7, 12.9 Hz, 1 H), 4.96 (dd,  $J$  = 4.7, 12.6 Hz, 1 H), 7.02 (d,  $J$  = 8.4 Hz, 2 H), 7.14 (t,  $J$  = 7.3 Hz, 1 H), 7.31-7.37 (m, 3 H), 7.46-7.68 (m, 5 H), 8.05 (d,  $J$  = 8.19 Hz, 2 H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz): 23.17 ( $\text{CH}_3$ ), 37.75 ( $\text{CH}_2$ ), 57.76 (CH), 121.83 (CH), 123.79 (C), 125.52 (CH), 127.24 (CH), 127.54 (CH), 128.83 (CH), 129.92 (CH), 132.40 (CH), 134.87 (CH), 136.86 (C), 143.59 (C), 150.08 (C), 151.91 (C), 169.23 (C), 170.47 (C). IR (KBr): 1600, 1745, 2916  $\text{cm}^{-1}$ . MS (ESI):  $m/z$  = 373.7. Anal. Calcd. for  $\text{C}_{23}\text{H}_{19}\text{NO}_2\text{S}$ : C, 73.97; H, 5.13; N, 3.75, found: C, 74.13; H, 5.12; N, 3.72.

### 2-(4-Chlorophenyl)-4-phenyl-2,3-dihydro-1,5-benzothiazepine (3j)



mp 126-128 °C  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): = 3.05 (t,  $J$  = 12.8 Hz, 1 H), 3.32 (dd,  $J$  = 4.8, 12.8 Hz, 1 H), 4.98 (dd,  $J$  = 4.8, 12.8 Hz, 1 H), 7.17 (t,  $J$  = 7.4 Hz, 1 H), 7.25-7.33 (m, 5 H), 7.45-7.56 (m, 3 H), 7.62 (d,  $J$  = 7.6 Hz, 2 H), 8.58 (d,  $J$  = 7.6 Hz, 2 H). Isolated Yield: 319 mg, 73.0%.

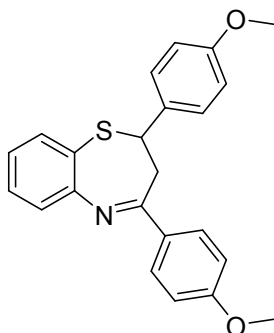
### 2,4-Diphenyl-2,3-dihydro-1,5-benzothiazepine (3k)





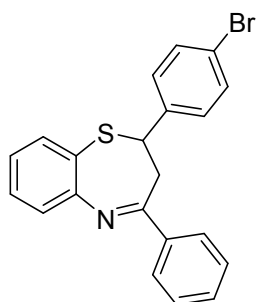
mp 115-117 °C <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 3.05 (t, *J* = 12.6 Hz, 1 H), 3.34 (dd, *J* = 4.7, 13.1 Hz, 1 H), 4.98 (dd, *J* = 4.5, 12.0 Hz, 1 H), 7.10-7.18 (m, 1H), 7.27-7.32 (m, 5 H), 7.42-7.53 (m, 4 H), 7.60 (d, *J* = 6.1 Hz, 2 H), 8.06 (d, *J* = 7.5 Hz, 2 H).

**2-(4-Methoxyphenyl)-4-(4-methoxyphenyl)-2,3-dihydro-1,5-benzothiazepine (3l)**



Yellow solid; mp 105- 106 °C <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): = 3.03 (t, *J* = 12.8 Hz, 1 H), 3.22 (dd, *J* = 4.5, 13.0 Hz, 1 H), 3.77 (s, 3 H), 4.03 (s, 3 H), 4.96 (dd, *J* = 4.3, 12.1 Hz, 1 H), 6.80 (d, *J* = 8.3 Hz, 2 H), 6.97 (d, *J* = 8.4 Hz, 2 H), 7.10 (t, *J* = 7.5 Hz, 1 H), 7.18-7.27 (m, 3 H), 7.45 (t, *J* = 7.5 Hz, 1 H), 7.56 (d, *J* = 8.4 Hz, 1 H), 8.01 (d, *J* = 7.6 Hz, 2 H).

**2-(4-Bromophenyl)-4-phenyl-2,3-dihydro-1,5-benzothiazepine (3m)**



Pale yellow solid; mp 117-120 °C  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz): = 3.00 (t,  $J = 12.8\text{Hz}$ , 1 H), 3.26 (dd,  $J = 4.8, 12.9\text{ Hz}$ , 1 H), 4.95 (dd,  $J = 4.8, 12.5\text{ Hz}$ , 1 H), 7.16-7.21 (m, 3 H), 7.30 (dd,  $J = 1.2, 7.9\text{ Hz}$ , 1 H), 7.46-7.58 (m, 6 H), 7.62 (dd,  $J = 1.3, 7.7\text{ Hz}$ , 1 H), 8.03 (d,  $J = 8.0\text{ Hz}$ , 2 H).