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## SYNTHESIS OF NEW 1, 2-DIPHENYL-4, 5-DIHYDRO-3H-3-BENZAZEPINES

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**Abstract** – 1,2-Diphenyl-4,5-dihydro-3H-3-benzazepine derivatives (**2a-d**) were synthesized *via* cyclization reaction of *N*-[2-(2-iodophenyl)ethyl]- $\alpha$ -phenylphenacylamines (**5a-c**) and (**5e**) with *n*-C<sub>4</sub>H<sub>9</sub>Li, followed by dehydration of the cyclization products, 1,2-diphenyl-1-hydroxy-3-methyl-2,3,4,5-tetrahydro-1H-3-benzazepines (**4a-d**) with trifluoromethanesulfonic acid.

### INTRODUCTION

Tamoxifen is a well established estrogen antagonist and one of the most used anti-breast cancer drug.<sup>1,2</sup> This triarylethylene compound is today the drug of choice for palliative therapy of advanced breast cancer.<sup>3</sup> However, side effects including endometrial carcinoma are also sometimes observed as a major adverse consequence of drug treatment.<sup>4</sup>

In order to overcome these defects, in recent years, much attention has been paid to the design of novel alternate scaffolds for estrogen antagonists such as 4,5-diphenyl-2,3-dihydro-1-benzoxepines,<sup>5</sup> 3,4-diphenyl-quinolines and isoquinolines,<sup>6</sup> 1,2-diphenyl-1,2,3,4-tetrahydroisoquinolines,<sup>7</sup> 2-phenyl-1-phenyloxynaphthalenes,<sup>8</sup> and 2,3-diphenylindenes.<sup>9</sup>

We have reported the synthesis and biological evaluation of 3,4-diphenyl-2-methyl-1,2-dihydroisoquinoline (**1a**)<sup>10</sup> and the 7-phenolic compound (**1b**).<sup>11</sup> Compounds (**1a,b**) were found to have nearly equipotent anti-proliferative activities to that of tamoxifen against human mammary carcinoma MCF-7 cell line.

On the basis of these facts, 1,2-diphenyl-4,5-dihydro-3H-3-benzazepine (**2a**) having a novel structure is an interesting compound in the biological and synthetic points of view (Figure 1). We now report a convenient synthesis of **2a** and the substituted compounds (**2b-d**) on the 1-phenyl group.

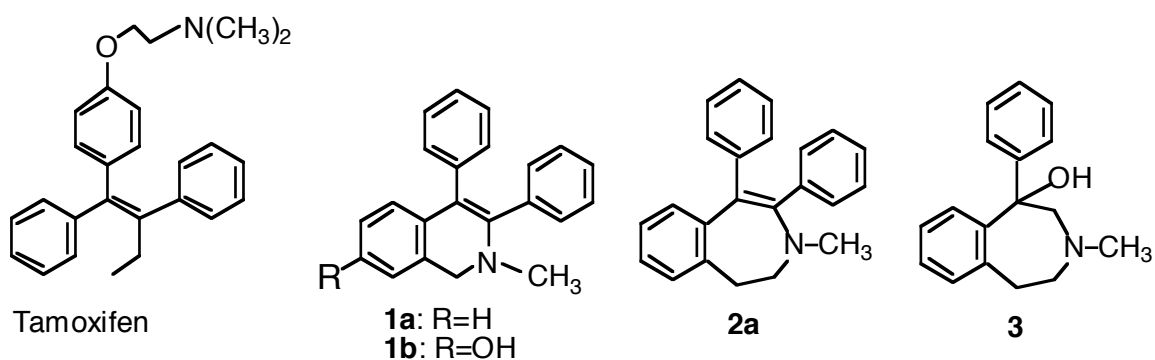
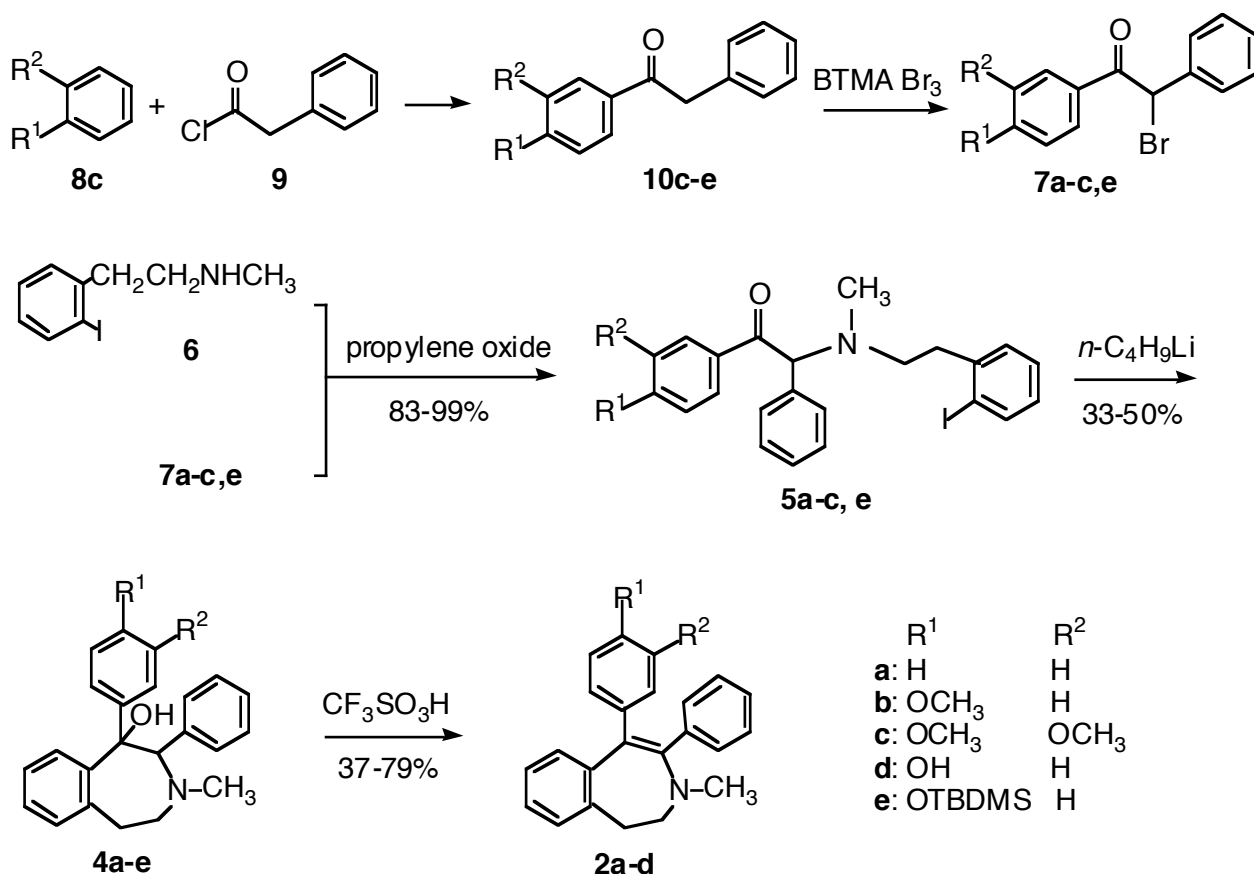


Figure 1



Scheme 1

## RESULTS AND DISCUSSION

In our previous papers, we reported the synthesis of 3,4-diphenyl-1,2-dihydroisoquinolines (**1a,b**)<sup>10,11</sup> by acidic dehydration of the corresponding 3,4-diphenyl-4-hydroxy-1,2,3,4-tetrahydroisoquinolines, which were prepared by intramolecular Barbier reaction of *N*-(2-iodobenzyl)phenacylamines with *n*-butyllithium (*n*-C<sub>4</sub>H<sub>9</sub>Li). Recently, we reported<sup>12</sup> the synthesis of the phenolic derivatives of 1-hydroxy-1-phenyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine (**3**) by cyclization of *N*-[2-(2-iodophenyl)-

ethyl]phenacylamines with  $n\text{-C}_4\text{H}_9\text{Li}$ . Thus, we carried out the synthesis of 4,5-dihydro-1,2-diphenyl-3-methyl-3*H*-3-benzazepines (**2a-d**) by dehydration of 1,2-diphenyl-1-hydroxy-3-methyl-2,3,4,5-tetrahydro-1*H*-3-benzazepines (**4a-d**) with trifluoromethanesulfonic acid ( $\text{CF}_3\text{SO}_3\text{H}$ ) as shown in Scheme 1. The compounds **4a-c** were synthesized by intramolecular Barbier reaction of the key intermediates, *N*-[2-(2-iodophenyl)ethyl]- $\alpha$ -phenylphenacylamines (**5a-c**) with  $n\text{-C}_4\text{H}_9\text{Li}$  in 33-43 % yields. The singlet signal ( $\delta$  4.65) of C2-H in the  $^1\text{H-NMR}$  spectrum of **4a** showed a single diastereomer, which may be formed due to the steric hindrance between an  $\alpha$ -phenyl group and a phenyl group of the phenacylamine in **5a**. Compounds (**5a-c**) were prepared by condensation of *N*-methyl-2-(2-iodophenyl)ethylamine (**6**) with  $\alpha$ -phenylphenacyl bromides (**7a-c**) in the presence of propylene oxide in high yields. The bromides (**7a**),<sup>13</sup> (**7b**),<sup>10</sup> and (**7c**) were obtained by bromination of benzyl phenyl ketones (**10a-c**) with benzyltrimethylammonium tribromide (BTMA  $\text{Br}_3$ ) according to the method reported by us.<sup>10</sup> The ketone (**10c**) was prepared by Friedel-Crafts reaction of veratrole (**8c**) with phenylacetyl chloride (**9**).

The phenolic 1-hydroxy-1,2-diphenyl-3-benzazepine (**4d**) was obtained by deprotection of the *t*-butyldimethylsilyl (TBDMS) group of compound (**4e**) with tetrabutylammonium fluoride (TBAF). Compound (**4e**) was prepared in the same way as **4a-c** as follows. Protection of the phenolic group of benzyl phenyl ketone (**10d**) with *t*-butyldimethylsilyl chloride (TBDMSCl) and then bromination of the product (**10e**) with BTMA  $\text{Br}_3$  gave an  $\alpha$ -phenylphenacyl bromide (**7e**). The condensation of **7e** with **6** afforded a key intermediate (**5e**), which was treated with  $n\text{-C}_4\text{H}_9\text{Li}$  to give **4e** in 50% yield.

It is interesting to note that the yields (33-50%) of 1,2-diphenyl-1-hydroxy-3-benzazepines (**4**) in the cyclization reaction of *N*-[2-(2-iodophenyl)ethyl]- $\alpha$ -phenylphenacylamines (**5**) with  $n\text{-C}_4\text{H}_9\text{Li}$  in this study are higher than those (15-32%) of the phenolic derivatives protected with TBDMS of 1-hydroxy-1-phenyl-3-benzazepine (**3**) in cyclization of *N*-[2-(2-iodophenyl)ethyl]phenacylamines reported in our previous paper.<sup>12</sup> The higher yields of **4** may be attributed to the restriction of conformational freedom by the  $\alpha$ -phenyl group in **5**.

In conclusion, a cyclization reaction of *N*-[2-(2-iodophenyl)ethyl]- $\alpha$ -phenylphenacylamines (**5**) with  $n\text{-C}_4\text{H}_9\text{Li}$ , followed by dehydration reaction of the products (**4**) in this study provides an applicable method for the preparation of 1,2-diphenyl-4,5-dihydro-3*H*-3-benzazepine derivatives (**2**).

## EXPERIMENTAL

**General** All melting points are given as uncorrected values. High-resolution mass (HR-MS) spectra were recorded on a JEOL JMS-D 300 spectrometer.  $^1\text{H-NMR}$  spectra were recorded on a JEOL JNM-FX 200 spectrometer with TMS as a standard.

**Benzyl 3,4-Dimethoxyphenyl Ketone (10c)**  $\text{AlCl}_3$  (3.00 g, 22.5 mmol) was added to a mixture

of veratrole (**8c**) (6.31 mL, 49.5 mmol) and phenylacetyl chloride (**9**) (1.98 mL, 15 mmol) for 10 min and the mixture was stirred for 30 min at rt. The mixture was poured into a solution of 36 % HCl (5 mL) and ice-cold H<sub>2</sub>O (50 mL) and the mixture was extracted with CHCl<sub>3</sub> (100 mL x 3). The extract was washed with brine (50 mL), dried over MgSO<sub>4</sub>, and evaporated to give a pale brown oil. This was subjected to column chromatography on SiO<sub>2</sub> with *n*-hexane-AcOEt (5 : 1) to afford **10c** as colorless needles (from *n*-hexane) (3.57 g, 92.9 %), mp 76-78°C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.66 (1H, d, *J*=8.4 Hz), 7.55 (1H, s), 7.29 (5H, m), 6.88 (1H, d, *J*=8.4 Hz), 4.24 (2H, s), 3.93 (3H, s), 3.90 (3H, s). HR-MS *m/z*: Calcd for C<sub>16</sub>H<sub>16</sub>O<sub>3</sub>: 256.1100 (M<sup>+</sup>). Found: 256.1077. *Anal.* Calcd for C<sub>16</sub>H<sub>16</sub>O<sub>3</sub>: C, 74.98; H, 6.29. Found: C, 75.02; H, 6.39.

**Benzyl 4-(*t*-Butyldimethylsilyloxy)phenyl Ketone (10e)** A mixture of **10d** (0.76 g, 3.59 mmol), TBDMSCl (0.82 g, 5.38 mmol), and imidazole (0.54 g, 8.97 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (20 mL) was stirred for 2 h at rt. The mixture was washed with brine (50 mL x 3), dried over MgSO<sub>4</sub>, and evaporated to give **10e** as colorless plates (from EtOH) (1.13 g, 96.4 %), mp 97.5-99°C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.93 (2H, d, *J*=8.7 Hz), 7.27 (5H, m), 6.86 (2H, d, *J*=8.7 Hz), 4.22 (2H, s), 0.98 (9H, s), 0.23 (6H, s). HR-MS *m/z*: Calcd for C<sub>20</sub>H<sub>26</sub>O<sub>2</sub>Si: 326.1702 (M<sup>+</sup>). Found: 326.1703. *Anal.* Calcd for C<sub>20</sub>H<sub>26</sub>O<sub>2</sub>Si: C, 73.57; H, 8.03. Found: C, 73.27; H, 7.99.

**3,4-Dimethoxy- $\alpha$ -phenylphenacyl Bromide (7c)** BTMA Br<sub>3</sub><sup>10</sup> (3.04 g, 7.80 mmol) was added to a solution of **10c** (2.00 g, 7.80 mmol) in CH<sub>2</sub>Cl<sub>2</sub>-CH<sub>3</sub>OH (5:2) (35 mL). The mixture was refluxed for 5 h and evaporated *in vacuo*. H<sub>2</sub>O (80 mL) was added to the residue and the mixture was extracted with CHCl<sub>3</sub> (70 mL x 3). The extract was washed with H<sub>2</sub>O, dried over MgSO<sub>4</sub>, and evaporated *in vacuo* to give a pale brown oil. This was purified by column chromatography on SiO<sub>2</sub> with CHCl<sub>3</sub> to afford **7c** as pale yellow plates (from *n*-hexane) (1.24 g, 47.3%), mp 117-118°C. <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.61 (1H, d, *J*=8.4 Hz), 7.55 (1H, s), 7.53 (2H, d, *J*=7.5 Hz), 7.35 (3H, m), 6.85 (1H, d, *J*=8.4 Hz), 6.38 (1H, s), 3.93 (3H, s), 3.90 (3H, s). HR-MS *m/z*: Calcd for C<sub>16</sub>H<sub>15</sub>O<sub>3</sub>Br: 334.0205 (M<sup>+</sup>). Found: 334.0216. *Anal.* Calcd for C<sub>16</sub>H<sub>15</sub>O<sub>3</sub>Br: C, 57.33; H, 4.51. Found: C, 57.20; H, 4.61.

**4-(*t*-Butyldimethylsilyloxy)- $\alpha$ -phenylphenacyl Bromide (7e)** In the same way as **10c**, compound (**10e**) (1.00 g, 3.06 mmol) was treated with BTMA Br<sub>3</sub> (1.43 g, 3.68 mmol) to give **7e** as a pale yellow oil (0.54 g, 43.3 %). <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.91 (2H, d, *J*=9.0 Hz), 7.53 (2H, d, *J*=7.5 Hz), 7.35 (3H, m), 6.85 (1H, d, *J*=9.0 Hz), 6.34 (1H, s), 0.97 (9H, s), 0.22 (6H, s). HR-MS *m/z*: Calcd for C<sub>20</sub>H<sub>25</sub>O<sub>2</sub>BrSi: 404.0807 (M<sup>+</sup>). Found: 404.0766.

***N*-[2-(2-Iodophenyl)ethyl]-*N*-methyl- $\alpha$ -phenylphenacylamine (5a)** A solution of **6** (1.622 g, 6.19 mmol),  $\alpha$ -phenylphenacyl bromide (**7a**) (1.42 g, 5.15 mmol), and propylene oxide (3 mL) in dioxane (40 mL) was heated at 110°C for 1.5 h. The mixture was evaporated and H<sub>2</sub>O (50 mL) was added to the residue. The mixture was basified with 25 % NaOH and extracted with CHCl<sub>3</sub> (50 mL x 3). The extract was washed with H<sub>2</sub>O, dried over MgSO<sub>4</sub>, and evaporated to give a pale brown oil. This was subjected to column chromatography on SiO<sub>2</sub> with CHCl<sub>3</sub>-acetone (100:1) to afford **5a** as a pale yellow oil (2.04 g, 87.0 %). <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 7.99 (2H, d, *J*=7.2 Hz), 7.74 (1H, d, *J*=7.8 Hz), 7.47-7.36 (5H, m), 7.28 (3H,

m), 7.20 (1H, t-like,  $J=7.5$  Hz), 7.09 (1H, d,  $J=7.5$  Hz), 6.84 (1H, m), 5.19 (1H, s), 2.90 (4H, m), 2.49 (3H, s). HR-MS  $m/z$ : Calcd for  $C_{23}H_{22}NOI$ : 455.0747 ( $M^+$ ). Found: 455.0709.

Compounds (**5b,c** and **5e**) were prepared in the same way as **5a**.

***N*-[2-(2-Iodophenyl)ethyl]-4-methoxy-*N*-methyl- $\alpha$ -phenylphenacylamine (**5b**)** Reaction of **6** (1.32 g, 5.03 mmol) with **7b** (1.28 g, 4.19 mmol) and propylene oxide (2.57 mL) in dioxane (20 mL) gave **5b** as a pale yellow oil (2.10 g, 98.0 %).  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ : 8.01 (2H, d,  $J=8.7$  Hz), 7.73 (1H, d  $J=7.7$  Hz), 7.38-7.25 (5H, m), 7.20 (1H, t-like,  $J=7.5$  Hz), 7.09 (1H, d,  $J=7.5$  Hz), 6.84 (2H, d,  $J=8.7$  Hz), 5.13 (1H, s), 3.81 (3H, s), 2.93-2.61 (4H, m), 2.48 (3H, s). HR-FABMS  $m/z$ : Calcd for  $C_{24}H_{25}NO_2I$ : 486.0931 ( $M+H$ ). Found: 486.0923.

**3,4-Dimethoxy-*N*-[2-(2-iodophenyl)ethyl]-*N*-methyl- $\alpha$ -phenylphenacylamine (**5c**)** Reaction of **6** (1.03 g, 3.93 mmol) with **6c** (0.80 g, 2.93 mmol) and propylene oxide (2.01 mL) in dioxane (28 mL) gave **5c** as an amorphous (1.18 g, 99.4 %).  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ : 7.73 (1H, d,  $J=8.4$  Hz), 7.70 (1H, d  $J=8.6$  Hz), 7.57 (1H, d,  $J=1.8$  Hz), 7.40-7.23 (5H, m), 7.20 (1H, dd,  $J=7.5$  and 7.7 Hz), 7.09 (1H, d,  $J=7.7$  Hz), 6.84 (2H, t-like,  $J=7.5$  Hz), 6.79 (1H, d,  $J=8.4$  Hz), 5.15 (1H, s), 3.90 (3H, s), 3.88 (3H, s), 2.97-2.61 (4H, m), 2.49 (3H, s). HR-FABMS  $m/z$ : Calcd for  $C_{25}H_{27}NO_3I$ : 516.1031 ( $M+H$ ). Found: 516.1026.

**4-*t*-Butyldimethylsilyloxy-*N*-[2-(2-iodophenyl)ethyl]-*N*-methyl- $\alpha$ -phenylphenacylamine (**5e**)**

Reaction of **6** (0.426 g, 1.63 mmol) with **7e** (0.52 g, 1.29 mmol) and propylene oxide (0.85 mL) in dioxane (6 mL) gave **5e** as a pale yellow oil (0.628 g, 83.3 %).  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ : 7.94 (2H, d,  $J=8.7$  Hz), 7.73 (1H, d  $J=7.8$  Hz), 7.38 (5H, m), 7.20 (1H, t-like,  $J=7.5$  Hz), 7.08 (1H, d,  $J=7.8$  Hz), 6.84 (2H, t-like,  $J=7.5$  Hz), 6.77 (2H, d,  $J=8.7$  Hz), 5.12 (1H, s), 2.96-2.62 (4H, m), 2.47 (3H, s), 0.96 (9H, s), 0.20 (6H, s). HR-MS  $m/z$ : Calcd for  $C_{29}H_{36}NO_2ISi$ : 585.1560. Found: 585.1537.

**1-Hydroxy-3-methyl-1,2-diphenyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine (**4a**)**  $n$ - $C_4H_9Li$  (3.13 mL of 1.53 M solution in  $n$ -hexane, 4.79 mmol) were added to a solution of **5a** (1.452 g, 3.19 mmol) in dry THF (30 mL) under argon atmosphere at  $-78^\circ C$ . The mixture was stirred for 30 min at rt.  $H_2O$  (30 mL) was added and the mixture was extracted with ether (50 mL x 3). The extract was dried over  $MgSO_4$  and evaporated to give a pale brown oil. This was subjected to column chromatography on  $SiO_2$  with  $n$ -hexane-AcOEt (10:1) to afford **4a** as a pale yellow oil (0.450 g, 42.8 %).  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ : 7.48 (1H, d,  $J=7.5$  Hz), 7.40 (2H, d,  $J=7.2$  Hz), 7.30-7.09 (9H, m), 6.78 (2H, d,  $J=7.7$  Hz), 4.65 (1H, s), 3.01-2.61 (4H, m), 2.18 (3H, s). HR-MS  $m/z$ : Calcd for  $C_{23}H_{23}NO$ : 329.1780 ( $M^+$ ). Found: 329.1770.

1-Hydroxy-3-benzazepines (**4b,c**) and (**4e**) were prepared in the same way as **4a**.

**1-Hydroxy-1-(4-methoxyphenyl)-3-methyl-2-phenyl-2,3,4,5-tetrahydro-1*H*-3-benzazepine (**4b**)**

Compound (**5b**) (0.50 g, 1.03 mmol) was reacted with  $n$ - $C_4H_9Li$  (1.04 mL of 1.53 M solution in  $n$ -hexane, 1.58 mmol) in dry THF (8 mL). The crude product was purified by column chromatography on  $SiO_2$  with  $n$ -hexane-AcOEt (5:1) to give **4b** as a pale yellow oil (0.123 g, 33.2 %).  $^1H$ -NMR ( $CDCl_3$ )  $\delta$ : 7.52 (1H, d,

$J=7.5$  Hz), 7.33 (2H, d,  $J=8.7$  Hz), 7.21-7.10 (6H, m), 6.83 (2H, d,  $J=8.7$  Hz), 6.75 (2H, d,  $J=7.2$  Hz), 4.62 (1H, s), 3.78 (3H, s), 3.01-2.59 (4H, m), 2.18 (3H, s). HR-MS  $m/z$ : Calcd for  $C_{24}H_{25}NO_2$ : 359.1886 ( $M^+$ ). Found: 359.1888.

**1-(3,4-Dimethoxyphenyl)-1-hydroxy-3-methyl-2-phenyl-2,3,4,5-tetrahydro-1H-3-benzazepine (4c)**

Compound (**5c**) (0.41 g, 0.80 mmol) was reacted with  $n\text{-C}_4\text{H}_9\text{Li}$  (0.78 mL of 1.53 M solution in  $n$ -hexane, 1.20 mmol) in dry THF (2.5 mL). The crude product was purified by column chromatography on  $\text{SiO}_2$  with  $\text{CHCl}_3$ -acetone (20:1) to give **4c** as a pale brown amorphous (0.108 g, 34.9 %).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.47 (1H, d,  $J=7.3$  Hz), 7.20-7.10 (6H, m), 6.99 (1H, d,  $J=2.0$  Hz), 6.91 (1H, dd,  $J=8.5$  and 2.0 Hz), 6.79 (2H, d,  $J=7.2$  Hz), 6.78 (1H, d,  $J=8.5$  Hz), 4.58 (1H, s), 3.84 (3H, s), 3.78 (3H, s), 3.10-2.63 (4H, m), 2.19 (3H, s). HR-MS  $m/z$ : Calcd for  $C_{25}H_{27}NO_3$ : 389.1991 ( $M^+$ ). Found: 389.2004.

**1-[4-(*t*-Butyldimethylsilyloxy)phenyl]-1-hydroxy-3-methyl-2-phenyl-2,3,4,5-tetrahydro-1H-3-benzazepine (4e)**

Compound (**5e**) (0.48 g, 0.83 mmol) was reacted with  $n\text{-C}_4\text{H}_9\text{Li}$  (0.76 mL of 1.53 M solution in  $n$ -hexane, 1.16 mmol) in dry THF (2.5 mL). The crude product was purified by column chromatography on  $\text{SiO}_2$  with  $n$ -hexane-AcOEt (15:1) to give **4e** as a pale yellow oil (0.19 g, 50.0 %).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.49 (1H, d,  $J=7.5$  Hz), 7.40-7.09 (10H, m), 6.74 (2H, d,  $J=8.8$  Hz), 4.59 (1H, s), 3.00-2.83 (2H, m), 2.71-2.60 (2H, m), 2.17 (3H, s), 0.90 (9H, s), 0.17 (6H, s). HR-MS  $m/z$ : Calcd for  $C_{29}H_{37}NO_2\text{Si}$ : 459.2593 ( $M^+$ ). Found: 459.2579.

**1-Hydroxy-1-(4-hydroxyphenyl)-3-methyl-2-phenyl-2,3,4,5-tetrahydro-1H-3-benzazepine (4d)**

A solution of TBAF (1.20 mL of 1.0 M solution in THF, 1.20 mmol) in dry THF (1.2 mL) was added to a solution of **4e** (0.184 g, 0.40 mmol) in dry THF (3 mL) under ice-cooling. The mixture was stirred for 30 min.  $\text{H}_2\text{O}$  (70 mL) was added and the mixture was extracted with  $\text{CHCl}_3$  (100 mL x 3). The extract was washed with  $\text{H}_2\text{O}$ , dried over  $\text{MgSO}_4$ , and evaporated to give a pale brown oil. This was purified by column chromatography on  $\text{SiO}_2$  with  $\text{CHCl}_3$ -acetone (10:1) to give **4d** as a pale yellow amorphous (0.081 g, 58.5 %).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.48 (1H, d,  $J=7.5$  Hz), 7.32-7.10 (8H, m), 6.75 (2H, d,  $J=7.5$  Hz), 6.63 (2H, d,  $J=8.3$  Hz), 4.62 (1H, s), 3.12-2.63 (4H, m), 2.16 (3H, s). HR-MS  $m/z$ : Calcd for  $C_{23}H_{23}NO_2$ : 345.1729 ( $M^+$ ). Found: 345.1729.

**3-Methyl-1,2-diphenyl-4,5-dihydro-3H-3-benzazepine (2a)**  $\text{CF}_3\text{SO}_3\text{H}$  (0.162 ml, 1.82 mmol) was added to a solution of **4a** (0.120 g, 0.37 mmol) in dry benzene (5 mL) and the mixture was refluxed for 30 min at  $100^\circ\text{C}$ . The reaction mixture was made basic with 5 % NaOH and extracted with  $\text{CHCl}_3$  (70 mL x 3). The extract was washed with  $\text{H}_2\text{O}$ , dried over  $\text{MgSO}_4$ , and evaporated *in vacuo* to give **2a** as a pale yellow solid (0.089 g, 78.5 %).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.17 (1H, m), 7.00 (12H, m), 6.85 (1H, m), 3.49 (2H, m), 3.11 (2H, m), 2.42 (3H, s). HR-MS  $m/z$ : Calcd for  $C_{23}H_{21}N$ : 311.1674 ( $M^+$ ). Found: 311.1646.

1, 2-Diphenyl-3-benzazepines (**2b-d**) were prepared in the same way as **2a**.

**1-(4-Methoxyphenyl)-3-methyl-2-phenyl-4,5-dihydro-3H-3-benzazepine (2b)** Compound **4b**

(0.093 g, 0.26 mmol) was reacted with  $\text{CF}_3\text{SO}_3\text{H}$  (0.114 mL, 1.29 mmol) in benzene (5 mL) for 30 min at  $100^\circ\text{C}$ . The crude product was purified by column chromatography on  $\text{SiO}_2$  with *n*-hexane-AcOEt (5:1) to give **2b** as a pale yellow solid (0.033 g, 36.9 %).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.18 (1H, m), 7.09 (4H, m), 7.05-7.00 (3H, m), 6.91 (2H, d,  $J=8.5$  Hz), 6.88 (1H, m), 6.59 (2H, d,  $J=8.5$  Hz), 3.70 (3H, s), 3.49 (2H, m), 3.10 (2H, m), 2.41 (3H, s). HR-MS  $m/z$ : Calcd for  $\text{C}_{24}\text{H}_{23}\text{NO}$ : 341.1779 ( $\text{M}^+$ ). Found: 341.1809.

**1-(3,4-Dimethoxyphenyl)-3-methyl-2-phenyl-4,5-dihydro-3H-3-benzazepine (2c)** Compound (**4c**) (0.041 g, 0.11 mmol) was reacted with  $\text{CF}_3\text{SO}_3\text{H}$  (0.082 mL, 0.55 mmol) in benzene (3.5 mL) for 30 min at  $90^\circ\text{C}$ . The crude product was purified by column chromatography on  $\text{SiO}_2$  with *n*-hexane-AcOEt (10:1) to give **2c** as a pale yellow solid (0.0153 g, 37.7 %).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.18 (1H, m), 7.10-7.01 (7H, m), 6.92 (1H, m), 6.58-6.52 (3H, m), 3.77 (3H, s), 3.65 (3H, s), 3.46 (2H, m), 3.08 (2H, m), 2.43 (3H, s). HR-MS  $m/z$ : Calcd for  $\text{C}_{25}\text{H}_{25}\text{NO}_2$ : 371.1886 ( $\text{M}^+$ ). Found: 371.1858.

**1-(4-Hydroxyphenyl)-3-methyl-2-phenyl-4,5-dihydro-3H-3-benzazepine (2d)** Compound (**4d**) (0.017 g, 0.048 mmol) was reacted with  $\text{CF}_3\text{SO}_3\text{H}$  (0.021 mL, 0.24 mmol) in benzene (1.0 mL) for 30 min at  $90^\circ\text{C}$ . The crude product was purified by column chromatography on  $\text{SiO}_2$  with *n*-hexane-AcOEt (5:1) to give **2d** as a pale yellow oil (0.0083 g, 52.9 %).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.18 (1H, m), 7.10-6.70 (7H, m), 6.88 (1H, m), 6.85 (2H, d,  $J=8.5$  Hz), 6.51 (2H, d,  $J=8.5$  Hz), 3.48 (2H, m), 3.09 (2H, m), 2.40 (3H, s). HR-MS  $m/z$ : Calcd for  $\text{C}_{23}\text{H}_{21}\text{NO}$ : 327.1623 ( $\text{M}^+$ ). Found: 327.1592.

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