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# THE REACTION OF 2-((TRIMETHYLSILYL)METHYL)-2H-TETRAZOLES WITH ALDEHYDES AND KETONES IN THE PRESENCE OF 1,8-DIAZABICYCLO[5.4.0]UNDEC-7-ENE

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Abstract – 2-((Trimethylsilyl)methyl)-2*H*-tetrazoles were treated with aldehydes and ketones in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to give 2-(2-hydroxyethyl)-2*H*-tetrazoles. This simple procedure offers a valuable strategy for the preparation of 2-(hydroxyethyl)-2*H*-tetrazoles.

### **INTRODUCTION**

Tetrazoles and their derivatives constitute an interesting subclass of heterocycles with a variety of applications.<sup>1</sup> Tetrazole derivatives have been shown to play an important role in biochemistry and medicinal chemistry.<sup>2</sup> Recently, 2-alkyltetrazole derivatives were shown to have interesting biological properties such as antimicrobial and anticonvulsant activities.<sup>3</sup>

(Trimethylsilyl)acetonitrile<sup>4</sup> and ethyl (trimethylsilyl)acetate<sup>5</sup> are widely used building blocks for easily introducing alkyl, alkylidene, and acyl groups at the  $\alpha$ -position of silicon atoms. In the case of 2-((trimethylsilyl)methyl)-2*H*-tetrazoles, a few examples have been reported.<sup>6</sup> Ogata and co-workers<sup>6a</sup> reported the reaction of 1-((trimethylsilyl)methyl)-1*H*-tetrazole with benzophenone using *t*-BuOK gave the rearranged product, 5-(diphenylhydroxymethyl)-1-methyl-1*H*-tetrazole, instead of 1-(hydroxyethyl)-tetrazole. The reaction of 2-((trimethylsilyl)methyl)-2*H*-tetrazoles with aldehydes using *t*-BuLi was reported and they afforded 2-alkenyltetrazoles as Peterson olefination products.<sup>6b,c</sup> The alkylation of 1,5- and 2,5-substituted tetrazoles without TMS group was also reported,<sup>7</sup> which afforded the corresponding alkylated product, but they used *t*-BuLi as a base. This report describes the reactivity of 2-((trimethyl-silyl)methyl)-2*H*-tetrazoles using DBU as a simple synthetic procedure of 2-(hydroxyethyl)-2*H*-tetrazoles.

### **RESULTS AND DISCUSSION**

Initially, 5-phenyl-2-((trimethylsilyl)methyl)-2*H*-tetrazole (**1a**), which can be purchased from Kanto Chemical Co., Ltd. or synthesized from 5-phenyltetrazole and (chloromethyl)trimethylsilane by Ogata's procedure,<sup>6a</sup> and benzaldehyde were selected as reaction substrates, and the resulting products were studied under various reaction conditions (Table 1). The treatment of **1a** with benzaldehyde in the presence of tetrabutylammonium fluoride (TBAF) in THF gave the desired product **2a**<sup>8</sup> in low yield (23%) and a desilylated product **3**<sup>9</sup> with a 60% yield (entry 1). The reaction was repeated in the presence of KOAc, which has been used in reactions of (trimethylsilyl)acetonitrile with benzaldehyde,<sup>4e</sup> to afford **2a** in low yield (17%) with recovery of **1a** (entry 2). Because the electron-withdrawing character of the tetrazole ring is weaker than that of cyanide, stronger bases were evaluated. Compound **1a** hardly reacted with benzaldehyde using Na<sub>2</sub>CO<sub>3</sub> did not reach completion (entry 4), but the reaction using K<sub>2</sub>CO<sub>3</sub> afforded **2a** in 76% yield and **3** in 19% yield (entry 5). However, when the same reaction was carried out with NaOH, the yield of **2a** decreased significantly (62%, entry 6). The use of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as an organic base gave **2a** and **3** in 87% and 13% yields, respectively (entry 7). In the use of catalytic amount of DBU (0.1 equiv), **2a** also was obtained with increase of **3** (entry 8).

### Table 1. The reaction of 1a with benzaldehyde



				2a	3					2a	3
Entry	Base	(equiv)	Solvent	Yield	$l(\%)^a$	Entry	Base	(equiv)	Solvent	Yield	$(\%)^a$
1	TBAF	(2)	THF	23	60	7	DBU	(1)	NMP	87	13
2	KOAc	(1)	NMP	$17^{b}$	6	8 <sup>e</sup>	DBU	(0.1)	NMP	76	21
3	Li <sub>2</sub> CO <sub>3</sub>	(1)	NMP	4 <sup><i>c</i></sup>	trace	9	pyridine	(1)	NMP	no rea	action
4	Na <sub>2</sub> CO <sub>3</sub>	(1)	NMP	$47^d$	4	10	Et <sub>3</sub> N	(1)	NMP	no rea	action
5	K <sub>2</sub> CO <sub>3</sub>	(1)	NMP	76	19	11	DIPEA	(1)	NMP	no rea	action
6	NaOH	(1)	NMP	62	19						

<sup>a</sup> Isolated Yield. <sup>b</sup> Starting material was recovered in 70% yield. <sup>c</sup> Starting material was recovered in 90% yield.

<sup>d</sup> Starting material was recovered in 31% yield. <sup>e</sup> Reaction time was 48 h.

Compound **1a** did not react with benzaldehyde in the presence of other organic bases such as pyridine,  $Et_3N$ , and *N*,*N*-diisopropylethylamine (DIPEA) (entries 9–11). The reaction proceeded well in *N*-methylpyrrolidone (NMP), DMSO, DMF, MeCN, and THF as a solvent (Table 2, entries 1–5). In the use of MeOH and *t*-BuOH, desilylated product **3** was obtained as a main product (entries 6, 7).



 Table 2. The reaction of 1a with benzaldehyde in several solvents

<sup>*a*</sup> Yield was determined by HPLC. <sup>*b*</sup> Isolated yield.

The results for the reaction of **1a** with aldehydes and ketones in the presence of DBU under optimized conditions are summarized in Table 3. Aromatic aldehydes having electron-donating or -withdrawing groups reacted smoothly to provide the desired products **2b–2f** in good yields (64–88%) (entries 2–6). The reaction of 2-methoxybenzaldehyde afforded the product **2g** in low yield (32%) (entry 7). Reaction with cinnamaldehyde also gave the desired product **2h** (entry 8). Aliphatic aldehydes also provided the desired products in good yields (79–82%) (entries 9, 10). Conversely, reactions with ketones proceeded but the yields of desired products (**2k–2m**) were low (18–43%), and the desilylated product **3** was obtained as a side product (entries 11–13).

Next, the reactions of various 2-((trimethylsilyl)methyl)-2*H*-tetrazoles (**1b**–**1d**) with benzaldehyde were examined. Although the reaction of 5-amino-2-((trimethylsilyl)methyl)-2*H*-tetrazole (**1b**) resulted in a low yield (Table 4, entry 1), reactions with 5-methyl-2-((trimethylsilyl)methyl)-2*H*-tetrazole (**1c**) and 2-((trimethylsilyl)methyl)-2*H*-tetrazole (**1d**) gave the corresponding adducts in good yields (entries 2, 3). In a similar manner, 1-(2-chlorophenyl)-2-(2*H*-tetrazol-2-yl)ethanol<sup>3a</sup> (**4d**), which is intermediate of

investigational drug with anticonvulsant activity, was synthesized with a 79% yield by the reaction of 1d with 2-chlorobenzaldehyde (entry 4).

Ph	1) R <sup>1</sup> R <sup>2</sup> C=O (1.1 equiv) DBU (1.0 equiv) NMP, 35 °C, 19 h	Ph V, N _1	Ph
N-NTMS	2) HCl aq., rt, 0.5 h	Ň=Ń R' +R <sup>2</sup> OH	N-N Me
1a		2	3

Table 3. The reaction of 1a with aldehydes and ketones

Entry	<b>D</b> <sup>1</sup>	<b>P</b> <sup>2</sup>	Viold	$(0/a)^{a}$	Entry	<b>D</b> <sup>1</sup>	<b>P</b> <sup>2</sup>	Viald	$(0/)^{a}$
Entry	K	Λ	Tielu	(70)	Entry	K	K	Tielu	(/0)
1	Н	Ph	<b>2a</b> 87	<b>3</b> 13	8	Н	PhCH=CH	<b>2h</b> 85	<b>3</b> 12
2	Н	$4-CO_2MeC_6H_4$	<b>2b</b> 64	<b>3</b> 30	9	Н	<sup>n</sup> Pr	<b>2i</b> 82	<b>3</b> 17
3	Н	$4-BrC_6H_4$	<b>2c</b> 88	<b>3</b> 9	10	Н	<sup>i</sup> Pr	<b>2j</b> 79	<b>3</b> 21
4	Н	$4-ClC_6H_4$	<b>2d</b> 84	<b>3</b> 10	$11^{b}$	Me	Et	<b>2k</b> 18	<b>3</b> 70
5	Н	$2-ClC_6H_4$	<b>2e</b> 81	<b>3</b> 11	$12^{b}$	Me	Ph	<b>21</b> 43	<b>3</b> 49
6	Н	4-MeOC <sub>6</sub> H <sub>4</sub>	<b>2f</b> 82	<b>3</b> 15	13 <sup>b</sup>	Ph	Ph	<b>2m</b> 39	<b>3</b> 43
7	Н	2-MeOC <sub>6</sub> H <sub>4</sub>	<b>2g</b> 32	<b>3</b> 66					

<sup>*a*</sup> Isolated Yield. <sup>*b*</sup> Reaction time was 48 h.

### Table 4. The reaction of 1b-1d with benzaldehydes

R		1) A E N	Aldehyde (1.1 equiv) DBU (1.0 equiv) IMP, 35 °C, 19 h	N,	R N N N-N OH			
N–N	-TMS	2) H	ICI aq., rt, 0.5 h		×-{			
1					4			
Entry	1	R	Aldehyde	Х	Yield	(%) <sup>a</sup>		
1	1b	$\mathrm{NH}_2$	benzaldehyde	Н	<b>4</b> a	36		
2	1c	Me	benzaldehyde	Н	<b>4</b> b	84		
3	1d	Н	benzaldehyde	Н	<b>4</b> c	79		
4	1d	Н	2-Cl-benzaldehyde	Cl	<b>4</b> d	79		

<sup>a</sup> Isolated Yield.

In conclusion, this report demonstrates that 2-((trimethylsilyl)methyl)-2*H*-tetrazoles may be used as building blocks for 2-alkyltetrazoles by reactions with aldehydes and ketones. This simple synthetic procedure provides a valuable means of preparing a wide variety of 2-(hydroxyethyl)-2*H*-tetrazoles.

### **EXPERIMENTAL**

Melting points were uncorrected. IR spectra were recorded using an attenuated total reflectance measurement. <sup>1</sup>H-NMR spectra were recorded at 400 MHz and <sup>13</sup>C-NMR spectra were recorded at 100 MHz with tetramethylsilane as an internal standard. High resolution mass spectra were recorded on a time-of-flight instrument using electrospray ionization method. Column chromatography was performed with silica gel 60N (40–100  $\mu$ m, spherical, neutral). All materials and solvents were purchased and used without further purification.

### **Typical Procedure for Preparation of Products 2, 3, and 4.**

### 1-Phenyl-2-(5-phenyl-2*H*-tetrazol-2-yl)ethanol<sup>8</sup> (2a) and 2-methyl-5-phenyl-2*H*-tetrazole<sup>9</sup> (3)

DBU (0.50 mmol) was added to the mixture of 5-phenyl-2-((trimethylsilyl)methyl)-2*H*-tetrazole (**1a**) (0.50 mmol) and benzaldehyde (0.55 mmol) in dry NMP (0.5 mL). The mixture was stirred at 35 °C for 19 h. Hydrochloric acid (1.0 mol/L) was added to the reaction mixture and the mixture was stirred at room temperature for 0.5 h. Water was added to the reaction mixture and the mixture was extracted with AcOEt. The organic layer was washed with water, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford the **2a** (87%) and **3** (13%).

**2a:** white solid; mp 97–98 °C (*n*-hexane-CHCl<sub>3</sub>, lit.<sup>8</sup> 100.5–102 °C); IR (ATR) 3234 cm<sup>-1</sup>; <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$  3.02 (1H, d, *J* = 3.6 Hz, OH), 4.86 (1H, d, *J* = 5.2 Hz, N-CH<sub>2</sub>-), 4.87 (1H, d, *J* = 7.2 Hz, N-CH<sub>2</sub>-), 5.35-5.45 (1H, m, -CH-OH), 7.37-7.57 (8H, m, aromatic protons), 8.12-8.20 (2H, m, aromatic protons); <sup>13</sup>C-NMR (CDCl<sub>3</sub>)  $\delta$  59.9, 72.3, 125.9, 126.8, 126.9, 128.6, 128.8, 128.8, 130.4, 139.4, 165.0; HRMS (ESI) calcd for C<sub>15</sub>H<sub>15</sub>N<sub>4</sub>O [M+H]<sup>+</sup> 267.1246, found 267.1246.

**3:** colorless crystals; mp 51 °C (*n*-hexane); <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$  4.41 (3H, s, CH<sub>3</sub>), 7.44-7.53 (3H, m, aromatic protons), 8.12-8.19 (2H, m, aromatic protons); <sup>13</sup>C-NMR (CDCl<sub>3</sub>)  $\delta$  39.5, 126.8, 127.4, 128.9, 130.3, 165.3; HRMS (ESI) calcd for C<sub>8</sub>H<sub>9</sub>N<sub>4</sub> [M+H]<sup>+</sup> 161.0827, found 161.0826.

### Methyl 4-(1-hydroxy-2-(5-phenyl-2H-tetrazol-2-yl)ethyl)benzoate (2b):

White solid; mp 110–111 °C (*n*-hexane-CHCl<sub>3</sub>); IR (ATR) 3356, 1712 cm<sup>-1</sup>; <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$  3.15-3.70 (1H, bs, OH), 3.93 (3H, s, CH<sub>3</sub>), 4.86 (1H, d, J = 6.8 Hz, N-CH<sub>2</sub>-), 4.86 (1H, d, J = 5.2 Hz, N-CH<sub>2</sub>-), 5.46 (1H, dd, J = 5.6, 6.8 Hz, -CH-OH), 7.47-7.52 (3H, m, aromatic protons), 7.55 (2H, d, J = 8.0 Hz, aromatic protons), 8.07 (2H, d, J = 8.0 Hz, aromatic protons), 8.10-8.15 (2H, m, aromatic protons); <sup>13</sup>C-NMR (CDCl<sub>3</sub>)  $\delta$  52.3, 59.6, 72.1, 126.0, 126.9, 129.0, 129.6, 130.2, 130.5, 130.6, 144.1, 165.3, 166.6; HRMS

(ESI) calcd for  $C_{17}H_{17}N_4O_3$  [M+H]<sup>+</sup> 325.1301, found 325.1308.

# 1-(4-Bromophenyl)-2-(5-phenyl-2*H*-tetrazol-2-yl)ethanol (2c):

Colorless crystals; mp 131–132 °C (EtOH); IR (ATR) 3307 cm<sup>-1</sup>; <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$  3.12 (1H, d, *J* = 4.0 Hz, OH), 4.83 (1H, d, *J* = 7.2 Hz, N-CH<sub>2</sub>-), 4.83 (1H, d, *J* = 5.6 Hz, N-CH<sub>2</sub>-), 5.32-5.42 (1H, m, -CH-OH), 7.32-7.38 (2H, m, aromatic protons), 7.48-7.57 (5H, m, aromatic protons), 8.12-8.18 (2H, m, aromatic protons); <sup>13</sup>C-NMR (CDCl<sub>3</sub>)  $\delta$  59.7, 71.8, 126.9, 127.0, 127.4, 129.0, 129.2, 130.6, 134.6, 137.7, 165.4; HRMS (ESI) calcd for C<sub>15</sub>H<sub>14</sub>N<sub>4</sub>OBr [M+H]<sup>+</sup> 345.0351, found: 345.0356.

# 1-(4-Chlorophenyl)-2-(5-phenyl-2*H*-tetrazol-2-yl)ethanol<sup>3b</sup> (2d):

Colorless crystals; mp 129–130 °C (EtOH, lit.<sup>3b</sup> 120–121 °C); IR (ATR) 3303 cm<sup>-1</sup>; <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$  3.12 (1H, bs, OH), 4.83 (1H, d, J = 6.8 Hz, N-CH<sub>2</sub>-), 4.84 (1H, d, J = 5.2 Hz, N-CH<sub>2</sub>-), 5.38 (1H, t, J = 5.8 Hz, -CH-OH), 7.37-7.44 (4H, m, aromatic protons), 7.48-7.53 (3H, m, aromatic protons), 8.12-8.18 (2H, m, aromatic protons); <sup>13</sup>C-NMR (CDCl<sub>3</sub>)  $\delta$  59.6, 71.9, 122.8, 126.9, 127.0, 127.7, 129.0, 130.6, 132.1, 138.2, 165.4; HRMS (ESI) calcd for C<sub>15</sub>H<sub>14</sub>N<sub>4</sub>OCl [M+H]<sup>+</sup> 301.0856, found: 301.0859.

# 1-(2-Chlorophenyl)-2-(5-phenyl-2H-tetrazol-2-yl)ethanol (2e):

Colorless crystals; mp 89–90 °C (EtOH); IR (ATR) 3248 cm<sup>-1</sup>; <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$  3.33 (1H, d, *J* = 4.0 Hz, OH), 4.77 (1H, dd, *J* = 8.8, 14.0 Hz, N-CH<sub>2</sub>-), 5.01 (1H, dd, *J* = 2.4, 13.6 Hz, N-CH<sub>2</sub>-), 5.74-5.80 (1H, m, -CH-OH), 7.28-7.38 (2H, m, aromatic protons), 7.41 (1H, dd, *J* = 1.6, 7.6 Hz, aromatic proton), 7.47-7.53 (3H, m, aromatic protons), 7.68 (1H, dd, *J* = 1.6, 7.6 Hz, aromatic proton), 8.12-8.18 (2H, m, aromatic protons); <sup>13</sup>C-NMR (CDCl<sub>3</sub>)  $\delta$  58.1, 69.3, 126.9, 127.1, 127.4, 127.5, 128.9, 129.7, 129.7, 130.5, 131.8, 136.7, 165.3; HRMS (ESI) calcd for C<sub>15</sub>H<sub>14</sub>N<sub>4</sub>OCl [M+H]<sup>+</sup> 301.0856, found: 301.0859.

# 1-(4-Methoxyphenyl)-2-(5-phenyl-2*H*-tetrazol-2-yl)ethanol<sup>6b</sup> (2f):

White solid; mp 84–85 °C (*n*-hexane-CHCl<sub>3</sub>); IR (ATR) 3367 cm<sup>-1</sup>; <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ 2.98 (1H, d, *J* = 3.2 Hz, OH), 3.82 (3H, s, CH<sub>3</sub>), 4.77-4.88 (2H, m, N-CH<sub>2</sub>-), 5.31-5.38 (1H, m, -CH-OH), 6.93 (2H, d, *J* = 8.8 Hz, aromatic protons), 7.47-7.53 (3H, m, aromatic protons), 8.12-8.18 (2H, m, aromatic protons); <sup>13</sup>C-NMR (CDCl<sub>3</sub>)  $\delta$  55.4, 59.9, 72.1, 114.3, 126.9, 127.2, 127.3, 128.9, 130.5, 131.4, 159.9, 165.2; HRMS (ESI) calcd for C<sub>16</sub>H<sub>17</sub>N<sub>4</sub>O<sub>2</sub> [M+H]<sup>+</sup> 297.1352, found: 297.1362. **1-(2-Methoxyphenyl)-2-(5-phenyl-2***H***-tetrazol-2-yl)ethanol (2g):** 

# A colorless oil; IR (ATR) 3369 cm<sup>-1</sup>; <sup>1</sup>H-NMR (CDCl<sub>3</sub>) $\delta$ 3.35 (1H, d, *J* = 6.8 Hz, OH), 3.91 (3H, s, CH<sub>3</sub>), 4.87-4.99 (2H, m, N-CH<sub>2</sub>-), 5.50-5.57 (1H, m, -C*H*-OH), 6.94 (1H, d, *J* = 8.0 Hz, aromatic proton), 7.00 (1H, dt, *J* = 0.1, 7.4 Hz, aromatic proton), 7.33 (1H, dt, *J* = 0.1, 8.0 Hz, aromatic proton), 7.43 (1H, dt, *J* = 0.2, 7.6 Hz, aromatic proton), 7.47-7.53 (3H, m, aromatic protons), 8.12-8.18 (2H, m, aromatic protons); <sup>13</sup>C-NMR (CDCl<sub>3</sub>) $\delta$ 55.4, 58.6, 69.6, 110.5, 121.1, 126.9, 127.1, 127.3, 127.3, 128.9, 129.6, 130.3, 156.4, 165.1; HRMS (ESI) calcd for C<sub>16</sub>H<sub>17</sub>N<sub>4</sub>O<sub>2</sub> [M+H]<sup>+</sup> 297.1352, found: 297.1363.

### (E)-4-Phenyl-1-(5-phenyl-2H-tetrazol-2-yl)but-3-en-2-ol (2h):

Colorless crystals; mp 136–137 °C (EtOH); IR (ATR) 3425 cm<sup>-1</sup>; <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$  2.85 (1H, d, *J* = 4.0 Hz, OH), 4.76-4.88 (2H, m, N-CH<sub>2</sub>-), 4.96-5.03 (1H, m, -CH-OH), 6.26 (1H, dd, *J* = 6.4, 16.0 Hz, -C*H*=CH-Ph), 6.79 (1H, d, *J* = 16.0 Hz, -CH=CH-Ph), 7.26-7.41 (5H, m, aromatic protons), 7.46-7.52 (3H, m, aromatic protons), 8.12-8.18 (2H, m, aromatic protons); <sup>13</sup>C-NMR (CDCl<sub>3</sub>)  $\delta$  58.4, 71.0, 126.3, 126.7, 126.9, 127.1, 128.3, 128.7, 128.9, 130.5, 133.3, 135.8, 165.3; HRMS (ESI) calcd for C<sub>17</sub>H<sub>17</sub>N<sub>4</sub>O [M+H]<sup>+</sup> 293.1402, found: 293.1399.

# 1-(5-Phenyl-2H-tetrazol-2-yl)pentan-2-ol (2i):

A colorless oil; IR (ATR) 3381 cm<sup>-1</sup>; <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$  0.98 (3H, t, *J* = 7.0 Hz, CH<sub>3</sub>), 1.44-1.64 (4H, m, CH<sub>3</sub>-CH<sub>2</sub>-CH<sub>2</sub>-), 2.67 (1H, d, *J* = 5.2 Hz, OH), 4.22-4.32 (1H, m, -CH-OH), 4.63 (1H, dd, *J* = 8.0, 14.0 Hz, N-CH<sub>2</sub>-), 4.73 (1H, dd, *J* = 3.0, 14.0 Hz, N-CH<sub>2</sub>-), 7.47-7.54 (3H, m, aromatic protons), 8.12-8.18 (2H, m, aromatic protons); <sup>13</sup>C-NMR (CDCl<sub>3</sub>)  $\delta$  13.9, 18.6, 36.3, 58.8, 69.8, 126.9, 127.2, 128.9, 130.5, 165.2; HRMS (ESI) calcd for C<sub>12</sub>H<sub>17</sub>N<sub>4</sub>O [M+H]<sup>+</sup> 233.1402, found: 233.1386.

# 3-Methyl-1-(5-phenyl-2H-tetrazol-2-yl)butan-2-ol (2j):

A colorless oil; IR (ATR) 3381 cm<sup>-1</sup>; <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$  1.07 (6H, d, J = 6.8 Hz, CH<sub>3</sub>), 1.82 (1H, oct, J = 6.5 Hz, (CH<sub>3</sub>)<sub>2</sub>CH-), 2.64 (1H, d, J = 4.8 Hz, OH), 3.98-4.07 (1H, m, -CH-OH), 4.67 (1H, dd, J = 8.4, 14.0 Hz, N-CH<sub>2</sub>-), 4.77 (1H, dd, J = 3.2, 14.0 Hz, N-CH<sub>2</sub>-), 7.44-7.54 (3H, m, aromatic protons), 8.10-8.19 (2H, m, aromatic protons); <sup>13</sup>C-NMR (CDCl<sub>3</sub>)  $\delta$  17.5, 18.7, 31.8, 57.0, 74.7, 126.9, 127.2, 128.9, 130.5, 165.2; HRMS (ESI) calcd for C<sub>12</sub>H<sub>17</sub>N<sub>4</sub>O [M+H]<sup>+</sup> 233.1402, found: 233.1395.

### 2-Methyl-1-(5-phenyl-2*H*-tetrazol-2-yl)butan-2-ol (2k):

A colorless oil; IR (ATR) 3430 cm<sup>-1</sup>; <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$  1.02 (3H, t, J = 7.6 Hz, CH<sub>2</sub>CH<sub>3</sub>), 1.22 (3H, s, CH<sub>3</sub>), 1.53 (2H, q, J = 7.6 Hz, CH<sub>2</sub>CH<sub>3</sub>), 2.83 (1H, s, OH), 4.66 (1H, d, J = 14.0 Hz, N-CH<sub>2</sub>-), 4.71 (1H, d, J = 14.0 Hz, N-CH<sub>2</sub>-), 7.45-7.54 (3H, m, aromatic protons), 8.11-8.21 (2H, m, aromatic protons); <sup>13</sup>C-NMR (CDCl<sub>3</sub>)  $\delta$  9.0, 23.9, 32.3, 61.7, 72.5, 126.9, 127.1, 128.9, 130.5, 165.2; HRMS (ESI) calcd for C<sub>12</sub>H<sub>17</sub>N<sub>4</sub>O [M+H]<sup>+</sup> 233.1402, found: 233.1400.

# 2-Phenyl-1-(5-phenyl-2H-tetrazol-2-yl)propan-2-ol (2l):

A colorless oil; IR (ATR) 3419 cm<sup>-1</sup>; <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ 1.59 (3H, s, CH<sub>3</sub>), 3.70 (1H, s, OH), 4.90 (1H, d, J = 14.0 Hz, N-CH<sub>2</sub>-), 5.00 (1H, d, J = 14.0 Hz, N-CH<sub>2</sub>-), 7.25-7.38 (3H, m, aromatic protons), 7.46-7.54 (5H, m, aromatic protons), 8.08-8.15 (2H, m, aromatic protons); <sup>13</sup>C-NMR (CDCl<sub>3</sub>)  $\delta$  27.4, 63.1, 74.1, 124.8, 126.9, 127.8, 128.6, 128.9, 130.6, 143.3, 165.1; HRMS (ESI) calcd for C<sub>16</sub>H<sub>17</sub>N<sub>4</sub>O [M+H]<sup>+</sup> 281.1402, found: 281.1394.

# 1,1-Diphenyl-2-(5-phenyl-2*H*-tetrazol-2-yl)ethanol (2m):

Colorless needles; mp 149–150 °C (EtOH); IR (ATR) 3472 cm<sup>-1</sup>; <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ 4.84 (1H, s, OH),

5.39 (2H, s, N-CH<sub>2</sub>-), 4.71 (1H, d, J = 14.0 Hz, N-CH<sub>2</sub>-), 7.22-7.35 (6H, m, aromatic protons), 7.44-7.54 (7H, m, aromatic protons), 8.03-8.10 (2H, m, aromatic protons); <sup>13</sup>C-NMR (CDCl<sub>3</sub>)  $\delta$  61.5, 77.9, 126.1, 126.8, 126.9, 127.9, 128.5, 128.9, 130.6, 142.5, 164.8; HRMS (ESI) calcd for C<sub>21</sub>H<sub>19</sub>N<sub>4</sub>O [M+H]<sup>+</sup> 343.1559, found: 343.1546.

### 2-(5-Amino-2H-tetrazol-2-yl)-1-phenylethanol (4a):

Colorless crystals; mp 141–142 °C (CHCl<sub>3</sub>); IR (ATR) 3436, 3305 cm<sup>-1</sup>; <sup>1</sup>H-NMR (DMSO-*d<sub>6</sub>*)  $\delta$ 4.42-4.54 (2H, m, N-CH<sub>2</sub>-), 5.05-5.09 (1H, m, -*CH*-OH), 5.78 (1H, d, *J* = 5.2 Hz, OH), 5.98 (2H, s, NH<sub>2</sub>), 7.26-7.40 (5H, m, aromatic protons); <sup>13</sup>C-NMR (DMSO-*d<sub>6</sub>*)  $\delta$  58.8, 70.7, 126.0, 127.6, 128.2, 141.7, 166.8; HRMS (ESI) calcd for C<sub>9</sub>H<sub>12</sub>N<sub>5</sub>O [M+H]<sup>+</sup> 206.1042, found: 206.1043.

### 2-(5-Methyl-2*H*-tetrazol-2-yl)-1-phenylethanol (4b):

White solid; mp 61 °C (*n*-hexane-CHCl<sub>3</sub>); IR (ATR) 3351 cm<sup>-1</sup>; <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ 2.56 (3H, s, CH<sub>3</sub>), 3.01 (1H, d, *J* = 3.6 Hz, OH), 4.76 (1H, d, *J* = 6.4 Hz, N-CH<sub>2</sub>-), 4.76 (1H, d, *J* = 5.6 Hz, N-CH<sub>2</sub>-), 5.28-5.33 (1H, m, -CH-OH), 7.33-7.47 (5H, m, aromatic protons); <sup>13</sup>C-NMR (CDCl<sub>3</sub>)  $\delta$  10.9, 59.5, 72.5, 125.9, 128.7, 128.9, 139.3, 163.1; HRMS (ESI) calcd for C<sub>10</sub>H<sub>13</sub>N<sub>4</sub>O [M+H]<sup>+</sup> 205.1089, found: 205.1077.

### 1-Phenyl-2-(2H-tetrazol-2-yl)ethanol (4c):

A colorless oil; IR (ATR) 3410 cm<sup>-1</sup>; <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ 2.90 (1H, d, *J* = 3.6 Hz, OH), 4.84 (1H, dd, *J* = 4.4, 13.8 Hz, N-CH<sub>2</sub>-), 4.89 (1H, dd, *J* = 8.0 13.8 Hz, N-CH<sub>2</sub>-), 5.32-5.40 (1H, m, -CH-OH), 7.34-7.48 (5H, m, aromatic protons), 8.55 (1H, s, H-5); <sup>13</sup>C-NMR (CDCl<sub>3</sub>)  $\delta$  59.7, 72.5, 125.9, 128.9, 129.0, 139.2, 152.9; HRMS (ESI) calcd for C<sub>9</sub>H<sub>11</sub>N<sub>4</sub>O [M+H]<sup>+</sup> 191.0933, found: 191.0932.

# 1-(2-Chlorophenyl)-2-(2*H*-tetrazol-2-yl)ethanol<sup>3a</sup> (4d):

Colorless crystals; mp 71–72 °C (*n*-hexane-CHCl<sub>3</sub>); IR (ATR) 3346 cm<sup>-1</sup>; <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$  3.24 (1H, d, J = 4.0 Hz, OH), 4.79 (1H, dd, J = 8.4, 14.0 Hz, N-CH<sub>2</sub>-), 4.99 (1H, dd, J = 2.6, 13.8 Hz, N-CH<sub>2</sub>-), 5.70-5.76 (1H, m, -CH-OH), 7.27-7.43 (2H, m, aromatic protons), 7.41 (1H, dd, J = 1.6, 7.6 Hz, aromatic proton), 7.63 (1H, dd, J = 2.0, 7.6 Hz, aromatic proton), 8.55 (1H, s, H-5); <sup>13</sup>C-NMR (CDCl<sub>3</sub>)  $\delta$  58.0, 69.2, 127.3, 127.5, 129.7, 129.8, 131.8, 136.6, 152.9; HRMS (ESI) calcd for C<sub>9</sub>H<sub>10</sub>N<sub>4</sub>OCl [M+H]<sup>+</sup> 225.0543, found: 225.0527.

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