

## GREEN SYNTHESIS OF 5-SUBSTITUTED-1*H*-1,2,3,4-TETRAZOLES AND 1-SUBSTITUTED-1*H*-1,2,3,4-TETRAZOLES VIA [3+2] CYCLOADDITION BY REUSABLE IMMOBILIZED AlCl<sub>3</sub> ON $\gamma$ -Al<sub>2</sub>O<sub>3</sub>

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**Abstract** – We report the effectiveness of the surface modified  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> which is reusable, efficient, catalytic, safe and environmentally acceptable procedure for the conversion of both alkyl and aryl nitriles into the corresponding 5-substituted-1*H*-1,2,3,4-tetrazoles *via* [3+2] cycloaddition with sodium azide in excellent yields at mild reaction conditions (50 °C). The catalyst also afforded 1-substituted-1*H*-1,2,3,4-tetrazoles by the reaction of amines, sodium azide and triethyl orthoformate. The catalyst could be recycled and was reused eleven runs without losing its activity.

The nitrile moiety is very useful functional group that can be transformed to many other interesting functional groups like acyl, carboxyl, formyl and carbamoyl, *etc*<sup>1</sup> which are stable and pharmacologically important intermediates. Since last eighty years, organic cyanides occupied the major laboratory curiosities and are continuing owing to the possibilities of conversion of cyanides into useful active heterocycles of biological importance. On the other hand, heterocyclic chemistry is been playing major role in synthetic organic chemistry and heterocycles are the most important constituents of drug candidates.<sup>2</sup> We have thoroughly scanned the literature and it is found that more than 90 percent of new drug molecules, drug intermediates and other bio-molecules are heterocycles. Among other hetero atoms nitrogen is unique which stands first and most contributor and backbone of heterocycles and many potent bio-molecules.

5-Substituted-1*H*-1,2,3,4-tetrazoles and the derivatives are metabolically stable and possess potent biological activities such as antibacterial,<sup>3</sup> antifungal,<sup>4</sup> anti-inflammatory,<sup>5</sup> antiallergic,<sup>6</sup> antiviral,<sup>7</sup> anti-biotic,<sup>8</sup> analgesic,<sup>9</sup> antineoplastic,<sup>10</sup> antihypertensive,<sup>11</sup> antiulcer,<sup>12</sup> anti-tuberculosis<sup>13</sup> and anti-cancer activities.<sup>14</sup> It is also well documented in the literature that the derivatives of tetrazoles to be stimulators

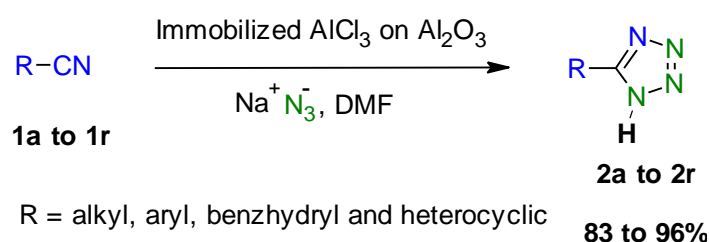
of growth hormone release<sup>15</sup> and are studied as metallo-protease inhibitors.<sup>16</sup> It is also evident from the literature that, tetrazole family is being utilized as new energetic materials owing to good thermal stability of tetrazoles due to aromatic ring system (5-azido-1*H*-tetrazole).<sup>17</sup> It is worth noting that, numerous derivatives of medicinally important tetrazole drugs have been approved by the FDA.<sup>18</sup> Owing to their wide applications of complexes of tetrazoles with Ni(II), Cu(II), Co(II), Zn(II) and low toxicity of tetrazoles attracted synthetic chemists and biologists in synthesizing the metal derivatives of tetrazoles.<sup>19</sup> Synthesis of 5-substituted-1*H*-1,2,3,4-tetrazoles is therefore attracting chemistry community. The classical method of obtaining 5-substituted-1*H*-tetrazoles include the proton acid-catalyzed cycloaddition of nitriles and hydrazoic acid normally involves a dangerous potential explosion with large excess amounts of harmful hydrazoic acid.<sup>20</sup> Since then, many attempts have been made to synthesize 5-substituted-1*H*-1,2,3,4-tetrazoles using catalytic systems of [3+2] cycloaddition reactions between sodium azide and nitriles. Among them, FeCl<sub>3</sub>-SiO<sub>2</sub>,<sup>21</sup> CdCl<sub>2</sub>,<sup>22</sup> Et<sub>3</sub>N·HCl,<sup>23</sup> Pd(PPh<sub>3</sub>)<sub>4</sub>,<sup>24</sup> TBAF,<sup>25</sup> BF<sub>3</sub>·OEt<sub>2</sub>,<sup>26</sup> Zn/Al hydrotalcite,<sup>27</sup> Zn(II) salts,<sup>28</sup> mesoporous Zn-S nanospheres,<sup>29</sup> nanocrystalline-ZnO,<sup>30</sup> nano-Zn-Cu alloy,<sup>31</sup> Cu<sub>2</sub>O,<sup>32</sup> ZrOCl<sub>2</sub>·8 H<sub>2</sub>O<sup>33</sup> and BaWO<sub>4</sub><sup>34</sup> are the important ones. Synthesis of 5-substituted-1*H*-tetrazoles is also achieved employing microwave irradiation,<sup>35</sup> under solvent free conditions,<sup>36</sup> micellar media,<sup>37</sup> ionic liquids<sup>38</sup> and using natural natrolite zeolites.<sup>39</sup> B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub>,<sup>40</sup> AgNO<sub>3</sub><sup>41</sup> and AlPO-5-based microspheres<sup>42</sup> are the recent reagents used for this reaction.

But most of the reported procedures use temperatures at 100 °C or above, longer reaction time, stringent conditions, expensive and toxic metal catalysts (e.g., Pd(PPh<sub>3</sub>)<sub>4</sub> is costly and air sensitive), tedious work-ups and unable or unsatisfactory recovery of catalyst. Also we could not reproduce the results obtained with the catalysts CdCl<sub>2</sub>, Cu<sub>2</sub>O, TBAF, Et<sub>3</sub>N·HCl and AgNO<sub>3</sub> though the procedure seems simple and the other reagents employed are not commercially and easily available.

In view of the importance of tetrazoles as described above, we are interested in developing easy procedure involving commercially, readily available and reusable catalyst which works at mild reaction conditions affording high yields. In recent years, surface modification of inorganic catalysts and their effective utilization for organic syntheses has attracted attention of synthetic chemists. AlCl<sub>3</sub> is one of the prime members of Friedel-Crafts catalysts that are widely used in petroleum refining and pharmaceutical industries. AlCl<sub>3</sub> plays a major role in alkylation, acylation, alkene isomerization, cracking and polymerization processes. It should be noted that researchers of late, avoid using AlCl<sub>3</sub> because of drawbacks such as its corrosiveness, difficulty in separating the used/unreacted catalyst from products and production of a large amount of waste. Previous report for the synthesis of 5-substituted-1*H*-1,2,3,4-tetrazoles uses stoichiometric amounts of AlCl<sub>3</sub> which is not supporting to handle in bulk scale, involves tedious work-up procedure and producing waste material affecting

environment.<sup>43</sup> A promising improvement of traditional AlCl<sub>3</sub> catalysts is the immobilization of AlCl<sub>3</sub> on a support and it is been playing important role in organic transformations such as Friedel-Crafts alkylation, acylation, polymerization and in the preparation of functionalized ethers.<sup>44</sup> Immobilization of AlCl<sub>3</sub> can easily be achieved on supports such as Al<sub>2</sub>O<sub>3</sub>, SiO<sub>2</sub> and MCM-41. Recently, immobilized AlCl<sub>3</sub> over both Al<sub>2</sub>O<sub>3</sub> and SiO<sub>2</sub> have been studied for the isomerization of  $\alpha$ -pinene into camphene, limonene and terpinolene and the report indicates AlCl<sub>3</sub>/ $\gamma$ -Al<sub>2</sub>O<sub>3</sub> is superior to AlCl<sub>3</sub>/SiO<sub>2</sub> in terms of catalytic activity.<sup>45</sup> Very recently, toluene is converted into *p*-toluic acid by AlCl<sub>3</sub>/Al<sub>2</sub>O<sub>3</sub> under mild conditions with less byproducts.<sup>46</sup>

Provoked by these results and in continued interest in employing immobilized AlCl<sub>3</sub> on  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> for catalyzing organic synthesis,<sup>47</sup> herein we report the clean synthesis of 5-substituted-1*H*-1,2,3,4-tetrazoles. Initially we chose the reaction of 1 mmol of 4-methoxybenzotrile (**1b**) with sodium azide (3 mmol) in presence of immobilized AlCl<sub>3</sub> on  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> (100 mg) at 50 °C. After usual work-up and characterization revealed the product was found to be 5-(4-methoxyphenyl)-1*H*-1,2,3,4-tetrazole (**2b**) in 94% yield. Later, the reaction was standardized with various amounts of immobilized AlCl<sub>3</sub> on  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> loading and the effect of unmodified  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> was also studied under same reaction conditions to compare the results between modified and unmodified  $\gamma$ -Al<sub>2</sub>O<sub>3</sub>, the results are presented in Table 1. It is clear from Table 1 that, surface modification of Al<sub>2</sub>O<sub>3</sub> with AlCl<sub>3</sub> is necessary to catalyze the reaction and unmodified Al<sub>2</sub>O<sub>3</sub> was found to be almost inactive for this reaction. The method was then extended to various phenyl, benzyl, aliphatic and heterocyclic nitriles to prepare the corresponding 5-substituted-1*H*-1,2,3,4-tetrazoles (**2a-2r**) and the approach was successful with the reaction being efficient and proceed with excellent yields at 50 °C as shown in Scheme 1 and the results are presented in Table 2.



**Scheme 1**

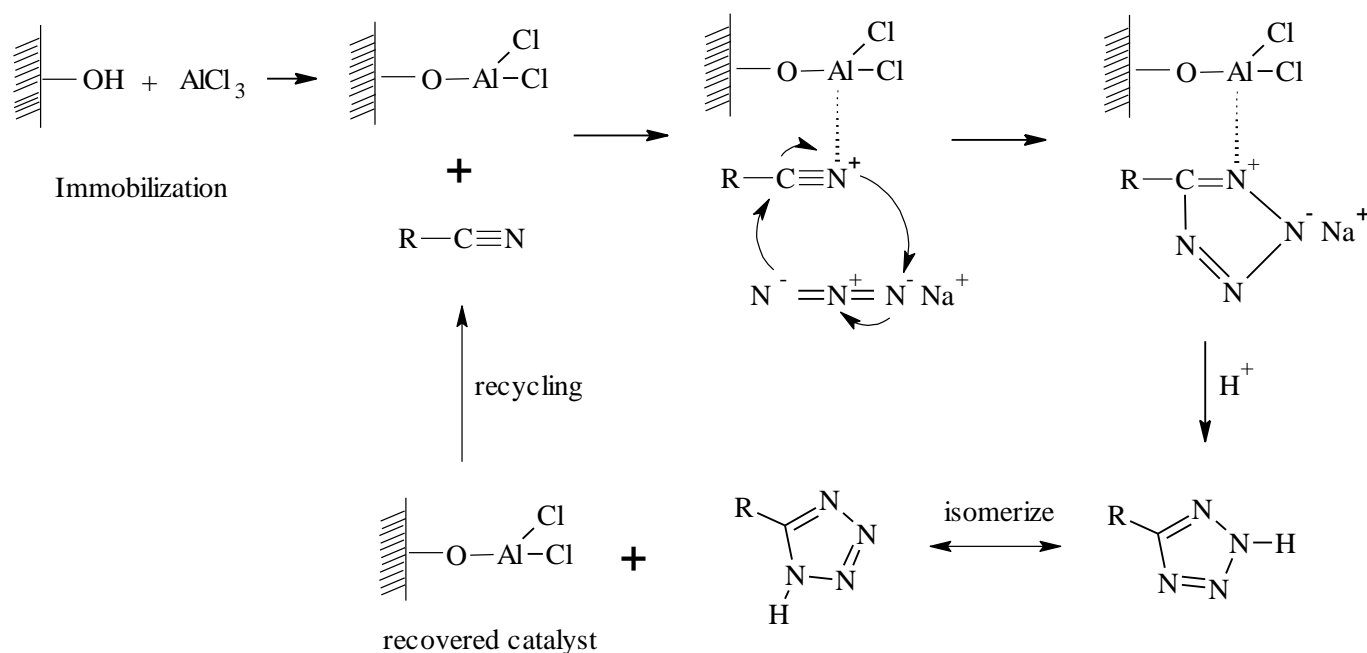
The plausible mechanism for the catalytic activity of immobilized AlCl<sub>3</sub> on  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> for the formation of 5-substituted-1*H*-1,2,3,4-tetrazoles is proposed as shown in Scheme 2. Inspired by these results and previous reports for the preparation of 1-substituted-1*H*-1,2,3,4-tetrazoles by the reaction of amines, sodium azide and triethyl orthoformate with various catalysts,<sup>48</sup> it was planned to employ immobilized AlCl<sub>3</sub> on  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> to check the suitability of the catalyst for the preparation of

1-substituted-1*H*-1,2,3,4-tetrazoles by the reaction of amines (**3s-3w**), sodium azide and triethyl orthoformate. It was found that the same reaction conditions holds good to obtain a series of 1-substituted-1*H*-1,2,3,4-tetrazoles (**4s-4w**) in excellent yields as shown in Scheme 3 and the results are presented in Table 3.

**Table 1.** Results of the amounts of immobilized AlCl<sub>3</sub> on  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> and unmodified  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> at 50 °C<sup>a</sup>

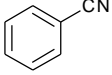
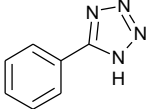
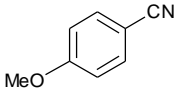
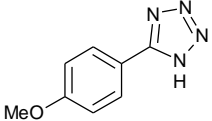
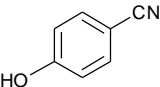
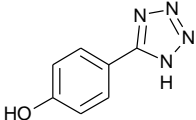
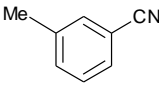
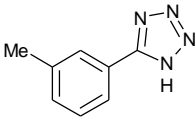
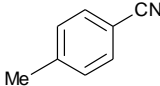
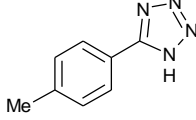
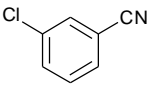
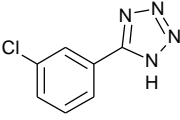
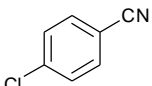
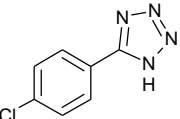
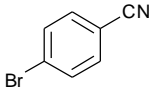
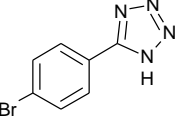
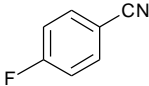
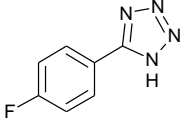
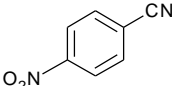
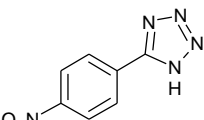
Entry	Catalyst loaded (mg) Modified/Unmodified	Reaction time (h)	Yield (%) Modified/Unmodified
1	05	10/24	12/Trace
2	10	10/24	35/Trace
3	15	10/24	44/Trace
4	20	10/24	62/Trace
5	25	10/24	74/Trace
6	30	1.5/24	94/Trace
7	40	1.5/24	94/Trace
8	50	1.5/24	94/Trace
9	60	1.5/48	94/<5%
10	70	1.5/48	94/<5%
11	80	1.5/48	94/<5%
12	90	1.5/24	94/<5%
13	100	1.5/24	94/<5%
14	no catalyst	18/24	trace/trace

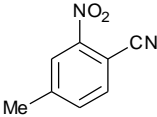
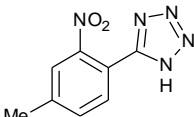
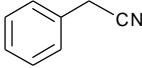
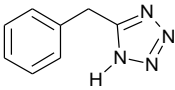
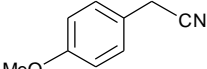
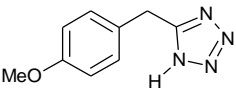
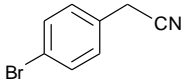
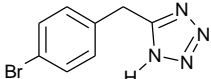
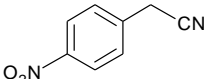
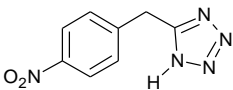
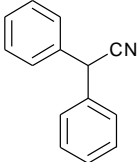
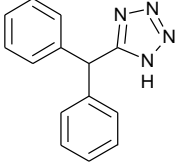
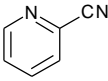
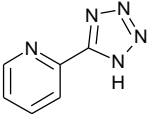
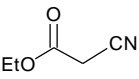
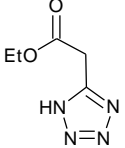
<sup>a</sup>Reaction of 4-methoxybenzotrile **1a** (1 mmol) and sodium azide (3 mmol) in DMF (4 mL) in the presence of various quantities of both immobilized AlCl<sub>3</sub> on  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> and unmodified  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> was studied.



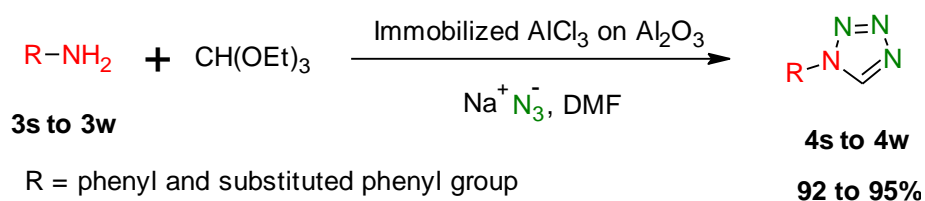
**Scheme 2**

**Table 2.** Immobilized AlCl<sub>3</sub> on  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> catalyzed synthesis of 5-substituted-1*H*-1,2,3,4-tetrazoles (**2**) by the reaction of nitriles (**1**) and sodium azide in DMF at 50 °C

Entry	Nitrile ( <b>1</b> )	Product ( <b>2</b> )	Time (h)	Yield (%) <sup>a</sup>
a			1.5	94
b			1.5	94
c			2.0	96
d			1.5	95
e			1.5	96
f			1.5	95
g			1.5	96
h			1.5	94
i			1.5	93
j			1.5	95

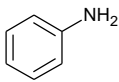
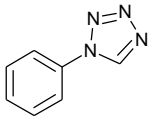
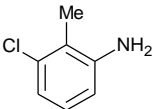
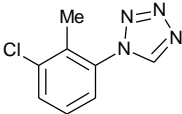
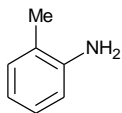
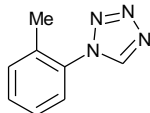
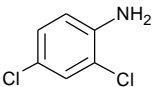
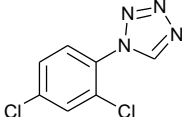
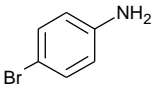
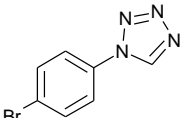
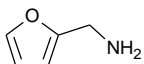
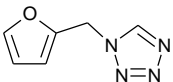
k			2.5	95
l			2.0	92
m			2.0	95
n			2.0	92
o			2.0	89
p			2.5	92
q			2.0	95
r			3.0	83

<sup>a</sup>Isolated yields after column purification



**Scheme 3**

**Table 3.** Immobilized AlCl<sub>3</sub> on  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> catalyzed synthesis of 1-substituted-1*H*-1,2,3,4-tetrazoles by the reaction of amines, triethyl orthoformate and sodium azide in DMF at 50 °C

Entry	Amine (3)	Product (4)	Time (h)	Yield (%) <sup>a</sup>
s			1.0	94
t			1.0	95
u			1.0	94
v			1.0	92
w			1.0	94
x			1.0	92

<sup>a</sup>Isolated yields after column purification

In summary, we have demonstrated an elegant method for the syntheses of a wide variety of both 5-substituted-1*H*-1,2,3,4-tetrazoles and 1-substituted-1*H*-1,2,3,4-tetrazoles in the presence of immobilized AlCl<sub>3</sub> on  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> under mild reaction conditions at shorter duration. The products of this environmentally friendly procedure were analytically pure, in addition, the process allowed reuse of the catalyst whilst still maintaining excellent yields of the product; this procedure is therefore very versatile, superior to previous reports and will be of great interest to the synthetic chemistry community.

## EXPERIMENTAL

### MATERIALS AND METHODS

All the nitriles, amines and sodium azide were of analytical grade and purified wherever necessary according to standard procedures prior to use. All other solvents and reagents were of reagent grade and purified/distilled prior to use. TLC's were run on pre-coated silica gel on aluminum plates obtained from Whatmann Inc. All reactions were performed at 50 °C. Melting points were obtained with Büchi B-540 apparatus and IR spectra were recorded on Bruker- TENSOR-FTIR spectroscopy. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded on Bruker Avance 400 and 100 MHz spectrometer respectively, chemical shifts were reported in (ppm) with TMS as internal standard. Elemental analyses were performed on Perkin Elmer – 2004. Yields refer to the isolated products after purification by column chromatography using 70–230 mesh silica gel.

#### Preparation of the Catalyst: Immobilization of AlCl<sub>3</sub> on $\gamma$ -Al<sub>2</sub>O<sub>3</sub>

AlCl<sub>3</sub> generated by the reaction of CCl<sub>4</sub> and  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> at 600 °C was carried to the reactor containing activated  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> and reacted for 3 h at 400 °C, the excess AlCl<sub>3</sub> was removed by flushing with Nitrogen at 400 °C for 1 h. The reaction product was cooled and stored under vacuum.

#### Typical Procedure for the Preparation of 5-Substituted-1*H*-1,2,3,4-tetrazoles (2a-2r).

**5-(4-Methoxyphenyl)-1*H*-1,2,3,4-tetrazole (2a).** To the mixture of 4-methoxybenzotrile (0.133 g, 1 mmol) and sodium azide (0.193 g, 3 mmol) in DMF (4 mL) was added immobilized AlCl<sub>3</sub> on  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> (30 mg) and the mixture heated to 50 °C with stirring and the completion of reaction was observed by the disappearance of starting material (nitrile) on TLC in 1.5 h. The solid catalyst was separated by filtration and washed off with EtOAc (5 mL X 3), the filtrate was treated with 4N HCl (10 mL) and stirring was continued for 10 min. The organic layer was washed successively with water, brine, dried over anhydrous MgSO<sub>4</sub> and the solvent was evaporated off under vacuum to get crude solid which was purified by column chromatography on silica gel eluting with a mixture of EtOAc/petroleum ether (40:60) to give pure 5-(4-methoxyphenyl)-1*H*-1,2,3,4-tetrazole (0.172 g, 94%) as colourless crystals (mp 231–232 °C); IR (KBr)  $\nu$ = 3210–3292, 1292, 1184, 1035, 823, 750 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  3.86 (3 H, s), 7.11 (2 H, d, *J* = 9.0 Hz), 7.93 (2 H, d, *J* = 9.0 Hz) ppm.

#### Typical Procedure for the Preparation of 1-Substituted-1*H*-1,2,3,4-tetrazoles (4s-4w).

To a mixture of amine (1 mmol), sodium azide (3 mmol) and triethyl orthoformate (1.25 mmol) in DMF (4 mL) was added immobilized AlCl<sub>3</sub> on  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> (30 mg) and the mixture heated to 50 °C with stirring. The completion of reaction was observed by the disappearance of starting material (amine) on TLC in 1 h. The solid catalyst was separated by filtration and washed off with EtOAc (5 mL X 3), The combined filtrate was evaporated to dryness at reduced pressure to afford crude which was purified by column chromatography on silica gel eluting with EtOAc/petroleum ether (30%) to give the corresponding



1-substituted-1*H*-1,2,3,4-tetrazole in pure form.

### Recycling the catalyst

On completion of each reaction, the reaction mixture was filtered off and washed with EtOAc (5 mL X 3), the solid catalyst was again washed with 10 mL of MeCN and was dried by rotary evaporation and the catalyst reused directly for the next run. The recovered catalyst was utilized for five subsequent reactions without any loss in catalytic activity. When the catalyst was filtered off, washed successively with EtOAc, MeCN and acetone (4 X 10 mL) and activated at 400 °C under Nitrogen stream, the results of eleven subsequent reactions did not have significant changes in terms of yield and purity of the products.

### Characterization data

**5-Phenyl-1*H*-1,2,3,4-tetrazole (2a):** Colorless crystals, mp 215–216 °C (Lit.<sup>49</sup> 214–216 °C); IR (KBr):  $\nu$  = 3124, 3044, 2982, 2911, 2834, 2692, 2606, 2557, 2488, 1613, 1563, 1485, 1409, 1163, 1056 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 7.61 (s, 3H, Ph), 8.05 (s, 2H, Ph); <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 124.6, 127.5, 129.9, 131.6, 155.7.

**5-(4-Methoxyphenyl)-1*H*-1,2,3,4-tetrazole (2b):** Colorless crystals, mp 156–157 °C (Lit.<sup>50</sup> 156–157 °C); IR (KBr):  $\nu$  = 3145, 3101, 3060, 2986, 2921, 2868, 2737, 2647, 1613, 1505, 1470, 1394, 1293, 1262, 1189, 1056, 1041, 923, 827, 751, 653, 522 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 3.85 (s, 3H), 7.15 (d, *J* = 8.8 Hz, 2H), 7.98 (d, *J* = 8.8 Hz, 2H).

**5-(4-Hydroxyphenyl)-1*H*-1,2,3,4-tetrazole (2c):** Colorless crystals, mp 234–235 °C (Lit.<sup>51</sup> 234–235 °C); IR (KBr):  $\nu$  = 3252, 3101, 3066, 3019, 3000-2200, 1615, 1599, 1511, 1466, 1413, 1282, 832, 752, 514 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 6.97 (d, 2H, *J* = 8.4 Hz, Ph), 7.87 (d, 2H, *J* = 8.8 Hz, Ph), 10.20 (brs, OH); <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 115.0, 116.6, 129.2, 155.2, 160.5.

**5-(*m*-Tolyl)-1*H*-1,2,3,4-tetrazole (2d):** Colorless crystals, mp 57–58 °C (Lit.<sup>52</sup> 55–58 °C); IR (KBr):  $\nu$  = 3120, 3061, 2912, 2871, 2753, 2617, 2491, 1728, 1605, 1486, 1150, 1064, 1038, 802, 741 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 2.6 (s, 3H), 7.32-7.47 (m, 2H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.85 (s, 1H).

**5-(*p*-Tolyl)-1*H*-1,2,3,4-tetrazole (2e):** Colorless crystals, mp 248–250 °C (Lit.<sup>53</sup> 248–249 °C); IR (KBr):  $\nu$  = 3062, 2983, 2961, 2472, 2400, 2972, 1590, 1492, 823 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 2.38 (s, 3H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.96 (d, *J* = 8.4 Hz, 2H).

**5-(3-Chlorophenyl)-1*H*-1,2,3,4-tetrazole (2f):** Colorless crystals, mp 113–114 °C (Lit.<sup>54</sup> 110–115 °C); IR (KBr):  $\nu$  = 3453, 3069, 2534, 2435, 1562, 1473, 1105, 893 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.43-7.50 (m, 2H), 7.92 (d, *J* = 7.6 Hz, 1H), 8.21 (s, 1H).

**5-(4-Chlorophenyl)-1*H*-1,2,3,4-tetrazole (2g):** Colorless crystals, mp 262–263 °C (Lit.<sup>50</sup> 261–263 °C); IR (KBr):  $\nu$  = 3415, 3068, 2997, 2930, 2816, 2726, 1619, 1489, 1459, 1436, 1384, 1352, 1162, 1100, 1054, 831 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 7.68 (d, 2H, *J* = 8.4 Hz), 8.05 (d, 2H, *J* = 8.8 Hz). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 123.5, 129.2, 130.0, 136.4, 155.3.

**5-(4-Bromophenyl)-1H-1,2,3,4-tetrazole (2h):** Pale yellow crystals, mp 267–268 °C (Lit.<sup>54</sup> 268–269 °C); IR (KBr):  $\nu = 3461, 3082, 3002, 2747, 1602, 1483, 1164, 1067, 994 \text{ cm}^{-1}$ ;  $^1\text{H NMR}$  (400 MHz, DMSO- $d_6$ ):  $\delta$ : 7.6 (d,  $J = 8.4 \text{ Hz}$ , 2H), 8.2 (d,  $J = 8.4 \text{ Hz}$ , 2H).

**5-(4-Fluorophenyl)-1H-1,2,3,4-tetrazole (2i):** Colorless crystals, mp 210–211 °C (Lit.<sup>54</sup> 210 °C); IR (KBr):  $\nu = 3074, 2925\text{--}2415 \text{ (br)}, 1610, 1500, 842 \text{ cm}^{-1}$ ;  $^1\text{H NMR}$  (400 MHz, DMSO- $d_6$ ):  $\delta$ : 7.47 (t,  $J = 8.8 \text{ Hz}$ , 2H), 8.07–8.11 (m, 2H).

**5-(4-Nitrophenyl)-1H-1,2,3,4-tetrazole (2j):** Yellow crystals, mp 220–221 °C (Lit.<sup>50</sup> 219–221 °C); IR: (KBr)  $\nu = 3448, 3334, 3235, 3109, 3080, 2974, 2900, 2819, 2659, 1562, 1532, 1488, 1357, 1340, 1315, 1143, 1106, 995, 867, 853, 730, 710 \text{ cm}^{-1}$ ;  $^1\text{H NMR}$  (400 MHz, DMSO- $d_6$ ):  $\delta$ : 8.31 (d, 2H,  $J = 8.4 \text{ Hz}$ , Ph), 8.46 (d, 2H,  $J = 8.8 \text{ Hz}$ , Ph);  $^{13}\text{C NMR}$  (100 MHz, DMSO- $d_6$ ):  $\delta$ : 125.1, 128.6, 131.0, 149.2, 155.9.

**5-(2-Nitro-4-methylphenyl)-1H-1,2,3,4-tetrazole (2k):** Yellow crystals, mp 180–182 °C (Lit.<sup>54</sup> 180–182 °C); IR: (KBr)  $\nu = 3073 \text{ (m, C-H)}, 2983, 2942, 1607, 1468, 943, 869 \text{ cm}^{-1}$ ;  $^1\text{H NMR}$  (400 MHz, DMSO- $d_6$ ):  $\delta$ : 2.49 (s, 3H), 7.68–7.75 (m, 2H), 8.2 (s, 1H).

**5-Benzyl-1H-1,2,3,4-tetrazole (2l):** Colorless crystals, mp 123–124 °C (Lit.<sup>50</sup> 123–125 °C); IR (KBr)  $\nu = 3109, 3031, 2984, 2945, 2863, 2778, 2704, 2594, 1768, 1707, 1638, 1549, 1533, 1494, 1457, 1241, 1108, 1074, 772, 734, 695 \text{ cm}^{-1}$ ;  $^1\text{H NMR}$  (400 MHz, DMSO- $d_6$ ):  $\delta$ : 4.28 (s, 2H), 7.25–7.27 (m, 3H), 7.31–7.35 (m, 2H).

**5-(4-Methoxybenzyl)-1H-1,2,3,4-tetrazole (2m):** Yellow crystals, mp 231–232 °C (Lit.<sup>54</sup> 231–232 °C); IR (KBr):  $\nu = 3428, 3064, 2993, 2877, 2483, 1617, 1283, 1180, 1019, 841 \text{ cm}^{-1}$ ;  $^1\text{H NMR}$  (400 MHz, DMSO- $d_6$ ):  $\delta$ : 7.22 (d,  $J = 8.4 \text{ Hz}$ , 2H), 6.84 (d,  $J = 8.8 \text{ Hz}$ , 2H), 4.16 (s, 2H), 3.80 (s, 3H).

**5-(4-Bromobenzyl)-1H-1,2,3,4-tetrazole (2n):** Colorless crystals, mp 268–269 °C (Lit.<sup>54</sup> 268–269 °C); IR (KBr)  $\nu = 3089, 3063, 2996, 2900, 2844, 2761, 2729, 2633, 1652, 1604, 1560, 1482, 1431, 1405, 1157, 1076, 1054, 1018, 829, 744, 502 \text{ cm}^{-1}$ ;  $^1\text{H NMR}$  (400 MHz, DMSO- $d_6$ ):  $\delta$ : 7.80 (d, 2H,  $J = 9.5 \text{ Hz}$ , Ph), 7.95 (d, 2H,  $J = 9.5 \text{ Hz}$ , Ph).

**5-(4-Nitrobenzyl)-1H-1,2,3,4-tetrazole (2o):** Yellow crystals, mp 219–220 °C (Lit.<sup>51</sup> 219–220 °C); IR (KBr)  $\nu = 3452, 3319, 3206, 3068, 2910, 2653, 1562, 1496, 1345, 1143, 992, 851 \text{ cm}^{-1}$ ;  $^1\text{H NMR}$  (400 MHz, DMSO- $d_6$ ):  $\delta$ : 8.28 (d, 2H,  $J = 8.4 \text{ Hz}$ ), 8.44 (d, 2H,  $J = 8.8 \text{ Hz}$ );  $^{13}\text{C NMR}$  (100 MHz, DMSO- $d_6$ ):  $\delta$ : 125.1, 128.5, 131.1, 149.2, 155.7.

**5-Benzhydryl-1H-1,2,3,4-tetrazole (2p):** Colorless crystals, mp 164–165 °C (Lit.<sup>55</sup> 164–165 °C); IR (KBr):  $\nu = 3084, 2093\text{--}2483 \text{ (brs)}, 1602, 1491, 1267, 828 \text{ cm}^{-1}$ ;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$ : 5.75 (s, 1H), 7.23–7.31 (m, 4H), 7.37–7.45 (m, 6H).

**5-(2-Pyridyl)-1H-1,2,3,4-tetrazole (2q):** Colorless crystals, mp 211–213 °C (Lit.<sup>50</sup> 210–213 °C); IR (KBr):  $\nu = 3088, 3060, 2960, 2930, 2865, 2735, 2691, 2621, 2583, 1729, 1601, 1557, 1483, 1445, 1404, 1284, 1158, 1068, 1024, 955, 795, 743, 726, 703, 637, 496 \text{ cm}^{-1}$ ;  $^1\text{H NMR}$  (400 MHz, DMSO- $d_6$ ):  $\delta$ : 7.65

(s, 1H), 8.10 (s, 1H), 8.24 (d, 1H,  $J = 6.4$  Hz), 8.81 (s, 1H);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ )  $\delta$ : 123.1, 126.7, 138.7, 144.0, 150.6, 155.3.

**(1H-1,2,3,4-Tetrazol-5-yl)ethylacetate (2r)**: Colorless crystals, mp 130–131 °C (Lit.<sup>54</sup> 130–132 °C); IR (KBr):  $\nu = 3475, 3092, 3072, 1747, 1610, 1568, 1450, 830$ ;  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$ : 1.22 (t, 3H  $J = 8.1$  Hz), 4.15 (q, 2H,  $J = 8.1$  Hz), 4.19 (s, 2H).

**1-Phenyl-1H-1,2,3,4-tetrazole (4a)**: Yellow crystals, mp 64–65 °C (Lit.<sup>56</sup> 64–65 °C); IR (KBr):  $\nu = 3051, 1677$  (C=N), 1588, 1488;  $^1\text{H}$  NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$ : (7.07-7.34 (m, 5H, Ar), 8.20 (s, 1H).

**1-(2-Methyl-3-chlorophenyl)-1H-1,2,3,4-tetrazole (4b)**: Colorless crystals, mp 95–96 °C (Lit.<sup>56</sup> 95–96 °C); IR (KBr):  $\nu = 1588, 1579, 1473, 1381, 1244, 1172, 1062, 895$  cm<sup>-1</sup>;  $^1\text{H}$  NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$ : 2.23 (s, 3H), 7.22 (d,  $J = 8.0$  Hz, 1H), 7.34 (t,  $J = 8.0$  Hz, 1H), 7.55 (d,  $J = 8.0$  Hz, 1H), 8.52 (s, 1H) ppm;  $^{13}\text{C}$  NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$ : 15.18, 124.69, 127.47, 131.80, 132.87, 133.87, 136.40, 143.18.

**1-(2-Methylphenyl)-1H-1,2,3,4-tetrazole (4c)**: Colorless crystals, mp 153–155 °C (Lit.<sup>57</sup> 150–153 °C); IR (KBr):  $\nu = 3015$  (C-H, sp<sup>2</sup> stretch, Ar), 2870 (C-H, sp<sup>3</sup> stretch), 1664 (C=N), 1488, 1590 (C=C) cm<sup>-1</sup>;  $^1\text{H}$  NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$ : 2.33 (s, 3H), 7.02-7.03 (d, 1H), 7.05-7.07 (d, 1H,  $J = 8$  Hz), 7.18-7.22 (t, 2H,  $J = 7$  Hz), 8.08 (s, 1H);  $^{13}\text{C}$  NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$ : 17.94, 117.68, 123.43, 127.00, 128.71, 130.72, 144.10, 147.78.

**1-(2,4-Dichlorophenyl)-1H-1,2,3,4-tetrazole (4d)**: Colorless crystals, mp 146–147 °C (Lit.<sup>56</sup> 146 °C); IR (KBr):  $\nu = 1587, 1508, 1436, 1256, 1207, 861$  cm<sup>-1</sup>;  $^1\text{H}$  NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$ : 7.58 (dd,  $J = 2.8$  Hz, 8.4 Hz, 1H), 7.66 (d,  $J = 8.4$  Hz, 1H), 7.96 (d,  $J = 2.4$  Hz, 1H), 8.96 (s, 1H) ppm.  $^{13}\text{C}$  NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$ : 120.45, 123.34, 132.25, 133.00, 134.81, 134.89, 140.69.

**1-(3,5-Dichlorophenyl)-1H-1,2,3,4-tetrazole (4e)**: Colorless crystals, mp 127–128 °C (Lit.<sup>56</sup> 128 °C); IR (KBr):  $\nu = 3151, 3019, 1659, 1576, 1481, 1460, 1215, 1088, 998$  cm<sup>-1</sup>;  $^1\text{H}$  NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$ : 6.92-6.94 (s, 2H), 7.40-7.42 (d, 2H,  $J = 8$  Hz), 8.09 (s, 1H);  $^{13}\text{C}$  NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$ : 116.43, 120.76, 132.01, 143.99, 149.29.

**1-(2-Furylmethyl)-1H-1,2,3,4-tetrazole (4f)**: Colorless crystals, mp 85–86 °C (Lit.<sup>56</sup> 85 °C); IR (KBr):  $\nu = 1522, 1479, 1352, 1274, 1165, 1016, 922$  cm<sup>-1</sup>;  $^1\text{H}$  NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$ : 5.71 (s, 2H), 6.52-6.59 (m, 1H), 6.73-6.81 (m, 1H), 7.49-7.53 (m, 1H), 8.72 (s, 1H);  $^{13}\text{C}$  NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$ : 44.96, 111.24, 111.43, 142.69, 144.39, 145.80.

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