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Comproportionation based Cu(I) catalyzed [3+2] cycloaddition of nitriles and sodium azide

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Abstract: A simple and convenient procedure for synthesis of 5-substituted 1*H*-tetrazoles using various nitriles and sodium azide in the presence of a catalytic amount of Cu-powder and anhydrous CuSO₄ in DMF solvent in good to high yields is reported. The reaction plausibly proceeds involving active Cu(I) catalyst which is formed due to comproportionation of the Cu(II)/Cu(0) couple and in situ formation of a Cu(I) azide species. Process safety RC (reaction calorimetry) study was also performed to understand the exothermicity during the reaction.

Keywords: Cu(I) catalyst, cycloaddition, tetrazole, azide

Introduction

Tetrazole is an impressive functionality with diverse applications in medicinal chemistry. ^[1] Interest in tetrazole chemistry is found to be extremely important due to the fact that it acts as stable carboxylic acid surrogate that offers superior pharmacokinetic profile to the parent molecule. ^[2] Such an advancement led to the discovery of angiotensin II antagonists. ^[3]

This functionality has also been frequently exploited as lipophilic spacers, ligands,

precursors of a variety of nitrogen containing heterocycles in coordination chemistry^[4&5] and in material sciences including photography, information recording systems, and explosives^[6]

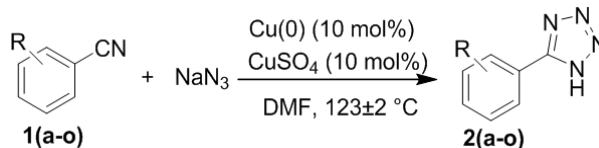
Most widely practiced synthesis of 5-substituted 1*H*-tetrazoles is [3+2] cycloaddition reaction involving nitriles and azides. A number of synthetic protocols with variations are precedented. ^[6] In most instances, sodium azide (NaN₃) has been used as an inorganic azide source in combination with ammonium halides (Cl⁻ and Br⁻) as an additive employing dipolar

aprotic solvents.^[6&7] In some cases, Brønsted⁸ or Lewis acids,^[9] or stoichiometric amounts of Zn(II) salts^[10] have been reported as suitable additives to afford the desired azide–nitrile addition process. As an alternative to inorganic azide salts, trimethylsilyl,^[11] trialkyltin^[12] and organoaluminum azides^[13] have been introduced as comparatively safer azide sources and these have the advantage of being soluble in organic solvents. Unfortunately, with very few exceptions, all of these methods require longer reaction times in combination with higher reaction temperatures.

Heterogeneous catalysis is a very attractive strategy as it allows the production and easy separation of large quantities of products with the use of catalyst. Recently, several heterogeneous catalytic systems were reported, for example, nanocrystalline ZnO,^[14a] Zn/Al hydrotalcite,^[14b] Zn hydroxyapatite^[14c], Cu-Zn alloy,^[14d] and Cu₂O,^[15a] CuO,^[15b] tungstate salts^[16] as catalysts, mesoporous ZnS nanospheres,^[17] reusable catalyst CuFe₂O₄ nanoparticles,^[18] CoY Zeolite,^[19] montmorillonite K-10,^[20] and Fe (HSO₄)₃,^[21] InCl₃,^[22] and Phosphomolybdic acid (H₃Mo₁₂O₄₀P),^[23] have been reported as catalyst for the synthesis of 5-substituted 1H tetrazoles. Organic azides e.g. triethyl ammonium azide²⁴ and NaN₃ in the presence of the acidic resin amberlyst-15,^[25a] Recently, AgNO₃,^[25b] DMAP acetate,^[25c] have also been reported to achieve similar cycloaddition reaction.

The development of a catalytic synthetic method for the preparation of tetrazole molecules still remains a fascinating research area. Reports for synthesis of triazoles using Cu(I) species are well documented.^[28] The utilization of Cu(I) species for synthesis of tetrazoles gaining significant interest. Herein we utilized precedent based strategy to prepare Cu(I) species *in situ* by using Cu(0) and Cu²⁺.^[29&30] Considering this approach we attempted the synthesis of 5-substituted 1H-tetrazoles **2** by using the catalytic potential

of Cu-powder [Cu(0)] and anhydrous CuSO₄ via [3+2] cycloaddition reaction involving the corresponding nitriles **1** and sodium azide in DMF solvent (Scheme 1).

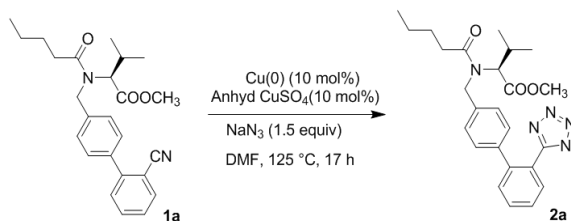


Scheme 1. Synthesis of 1H-tetrazoles by Cu (I)-catalyzed cycloaddition

Results and Discussion

Initially, we focused on the synthesis of API (active pharmaceutical ingredients) related tetrazole intermediates like valsartan intermediate **2a** and irbesartan **2b** by using different catalytic systems. Substrate **1a** was selected for the model studies to examine the catalytic potential of different systems (Table 1). First set of reaction was conducted using Cu and CuSO₄ individually in presence of DMF solvent and NaN₃ as azide source (entry 1 and 2, Table 1). We did not obtain promising results hence we adopted the reported conditions,^[15a, 15b & 27] for the synthesis of valsartan intermediate **2a**, (Table 1; entries 5, 6 and 7), and observed less yields and low *ee*%.

Table 1. Optimization of reaction conditions for synthesis of 5-substituted 1H-tetrazoles.^a



^aReaction conditions: **1a** (2.46 mmol), metal catalysts each (10 mol %), NaN₃ (3.69 mmol), TMSN₃ (3.69 mmol), Solvent (10 mL) at 123±2 °C; ^bIsolated yields; ^c Determined by chiral HPLC; NA-analysis not performed

Entry	Copper source	Azide source	Solvent	Yield (%) ^b	Time/h	ee (%) ^c
1	Cu(0)	NaN ₃	DMF	40	24	NA
2	CuSO ₄	NaN ₃	DMF	35	24	NA
3	Cu(0)+CuSO₄	NaN₃	DMF	85	17	88
4	Cu(0)+CuSO ₄	NaN ₃	DMSO	80	17	87
5	Cu ₂ O	TMSN ₃ [15a, c]	DMF/MeOH	55	24	78
6	CuO	NaN ₃ [15b]	DMF	45	24	72
7	CuSO ₄ ·5H ₂ O	NaN ₃ [27]	DMSO	65	24	75
8	Cu ₂ O	NaN ₃	DMF	38	24	NA

We made efforts to understand the importance of solubility on reaction progress. We examined this by performing cycloaddition reaction between **1a** and NaN₃, to obtain tetrazole **2a** (Table 1) in different solvents e.g. DMF and DMSO. Among these two solvents, DMF along with 1.5 equivalent of NaN₃, 10 mol% Cu-powder and 10 mol% of anhydrous CuSO₄ afforded the product in good yields (85%) with 88% *ee* at 123±2 °C in 17 h and the results are summarized in Table 1.

Based on this promising result, we started investigating the catalytic potential of above mentioned catalytic system for the synthesis of aromatic and alkyl tetrazoles.

In order to establish its generality for broader application of this method, we selected a variety of structurally divergent nitriles **1** to understand the scope of the Cu(I) catalyzed/promoted [3+2] cycloaddition to form 5-substituted 1*H*-tetrazole with Cu(0) powder (10mol%) with anhydrous CuSO₄ (10 mol%), the results are presented in Table 2. The reactions of the aryl nitrile, bearing electron donating substituent in *para* position and *ortho* position of aromatic ring, afforded the corresponding tetrazole in similar yields when compared with electron withdrawing substituent (Table 2). Benzyl nitriles containing *p*-, *o*-, *m*-methoxy group also offered the tetrazoles **2j**, **2k** and **2l** in moderate to high yields and alkyl nitriles offered corresponding tetrazole **2o** in

lower yields. On the other hand this method has proven to be noteworthy when compared with the reported methods²⁷ for synthesis of sterically hindered structures like sartans (Table 2, entries: **2a**, **2b**, and **2c**).

Process Safety Studies

Since the literature on hazards associated with the process to synthesize **2** is unavailable therefore reaction calorimetry (RC) studies were performed for the synthesis of tetrazoles **2** (Figure 2, 3, 4 and 5). Based on this study, it was possible to recommend process change in operation during scale-up.

The reaction of **1d** (85.36 mmol) with NaN₃ (128.0 mmol) in the presence of Cu-powder (10 mol%) and CuSO₄ (10 mol%), in DMF (100 mL) was studied for heat of reaction and adiabatic temperature rise by using calorimeter equipped with 4-blade propeller agitator having 0.06 m diameter with 300 rpm. Comparison of the batch temperature profile inside the reactor (Tr) with the reactor jacket temperature profile (Tj) in isothermal mode revealed that the reaction was instantaneous with insignificant heat evolution. We studied the heat evolution from 33 °C to 123 °C at a rate of 0.5 °C /min.

The reaction mass temperature was elevated to 134.44 °C from 123 °C which was evident from the insignificant deviation between Tr and Tj.

For 10 g of **1d**, the heat of reaction/process (H_r) for the batch size taken in RC1e indicates that the estimated adiabatic temperature rise was 11.4 °C. [31]

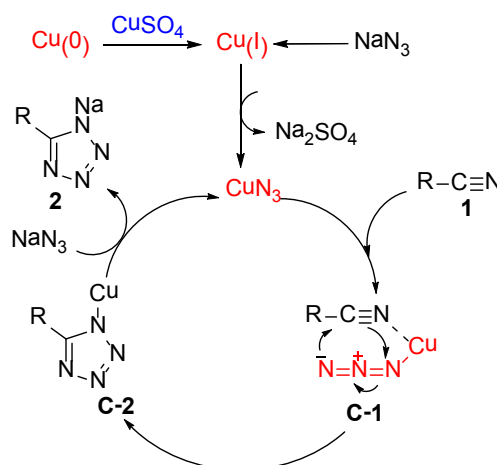
Likewise, during the maintenance at 123 °C from 3h, the adiabatic temperature rise was observed to be 6.49 °C (see supporting). Based on this it was concluded that the generation of CuN_3 from $\text{Cu}(0)$ and CuSO_4 , followed by tetrazole formation is slightly exothermic in nature over formation of **2**.

Therefore, an impetus was given to ensure the rate of heat was controlled throughout the course of the reaction and efficient jacket cooling was recommended. RC experiment involving RSD (Rapid Screening Device) indicated the degree of explosivity which was found to be violent at >250 °C (see supporting). As a result, we were limited to conduct all our experiments featured in the work at 123 ± 2 °C only. Moreover, RC studies indicate that this chemistry/process as such is safe to practice.

Mechanistically, based on the precedented literature [15a,15c,28,30] it is understood that, *in situ* generation of $\text{Cu}(\text{I})$ by comproportionation of $\text{Cu}(0)$ and CuSO_4 may lead to cyclo addition. The $\text{Cu}(\text{I})$ reacts with NaN_3 to produce the CuN_3 (at any given point of time CuN_3 will not be left unreacted as we understood that the rate of cycloaddition event is much faster than comproportionation; therefore the safety concerns associated with CuN_3 can be well estimated). Thus, resulting CuN_3 reacts with the $\text{C}\equiv\text{N}$ bond of nitrile by [3+2] cycloaddition to generate the intermediate C-2 *via* C-1 complex. Transmetalation of Cu with sodium in intermediate C-2 was achieved by using NaN_3 as shown in Figure 1. To support this mechanism, the reaction of **1** with NaN_3 in DMF was conducted and we found that the reaction did not proceed at all in the absence of the Cu/CuSO_4 catalyst. [15a, 15c]

Figure 1. A plausible mechanism for the

formation of 5-substituted 1H-tetrazole.



In conclusion, we have developed a comproportionation based $\text{Cu}(\text{I})$ catalyzed/promoted efficient cycloaddition reaction involving an array of diverse nitriles and azide to obtain pharmaceutically relevant molecules. This method has advantage over the use of isolated CuN_3 in cycloaddition reactions which is not safe to handle.

General procedure for the synthesis of tetrazole **2**

The procedure for the synthesis of the tetrazole **2** is representative. A mixture of nitrile **1d** (8.53 mmol, 1.0 equiv), sodium azide (12.8 mmol, 1.5 equiv), Cu -powder (10 mol%), anhydrous CuSO_4 (10 mol%) and DMF (10 mL) was taken in a round-bottom flask and stirred at 123 ± 2 °C until complete conversion of the starting material, which was monitored by TLC. After completion of the reaction, the reaction mixture was cooled to room temperature and diluted the reaction mass with water (20 mL) at 25-35 °C. The reaction mass containing excess metal azide traces was safely decomposed by adding sodium nitrite (6.4 mmol)²⁶ and 5N aqueous hydrochloric acid (50 mL) at 5-10 °C, and the unwanted salts were removed by filtration through celite and the filtrate was treated with ethyl acetate (2x50 mL). The resultant organic

RC1e study

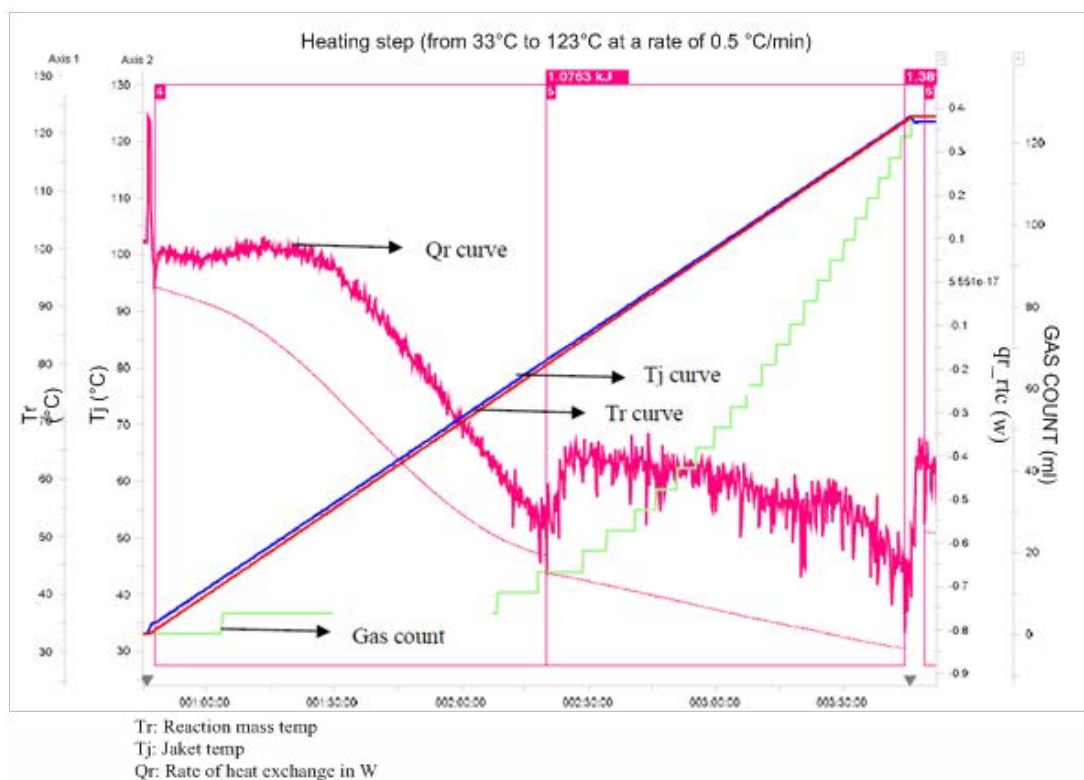


Figure 2. RC study graphical representation. Comparison of the batch temperature profile inside the reactor (Tr) with the reactor jacket temperature profile (Tj) in isothermal mode.

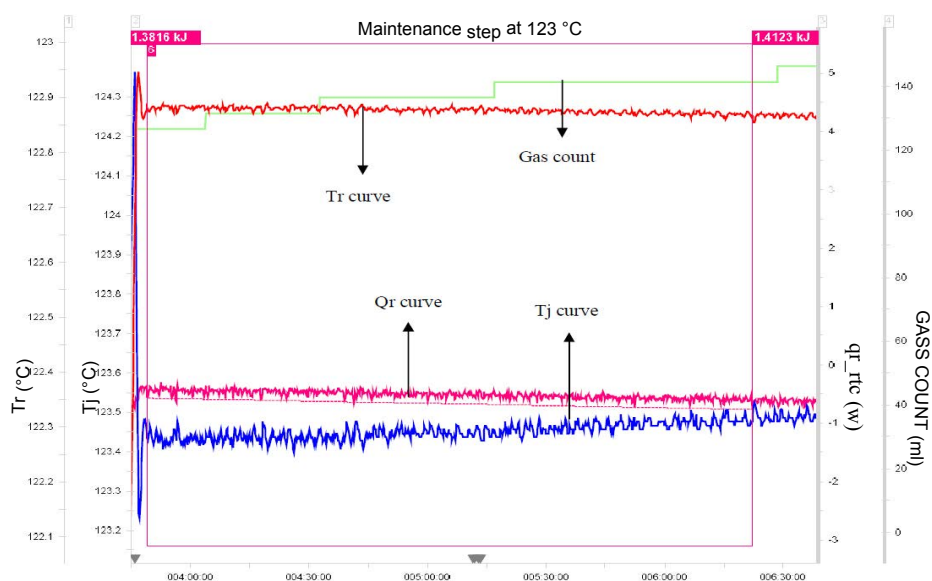


Figure 3. Maintenance at 123 °C ($123 \pm 2^\circ\text{C} \approx 123^\circ\text{C}$) for 3h represents the adiabatic temperature rise.

Rapid Screening Device Data

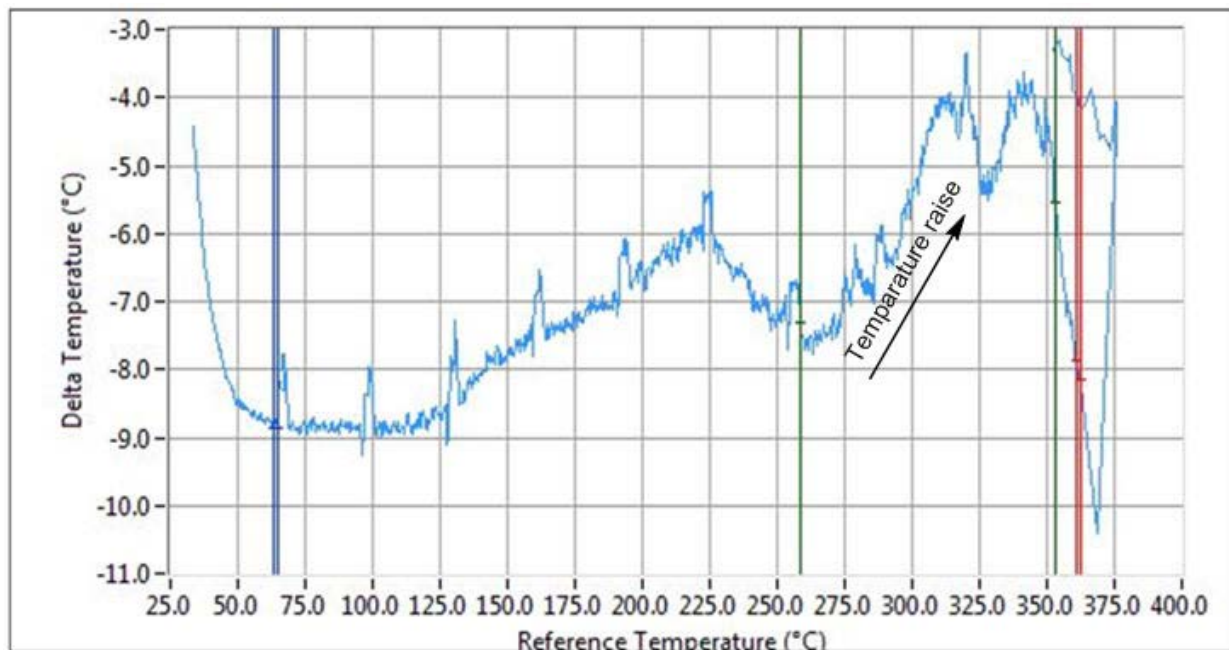


Figure 4. Temperature difference as a function of reference temperature (RSD data). [RC experiment involving RSD (Rapid Screening Device) indicated the degree of explosivity which was found to violent at 250 °C.]

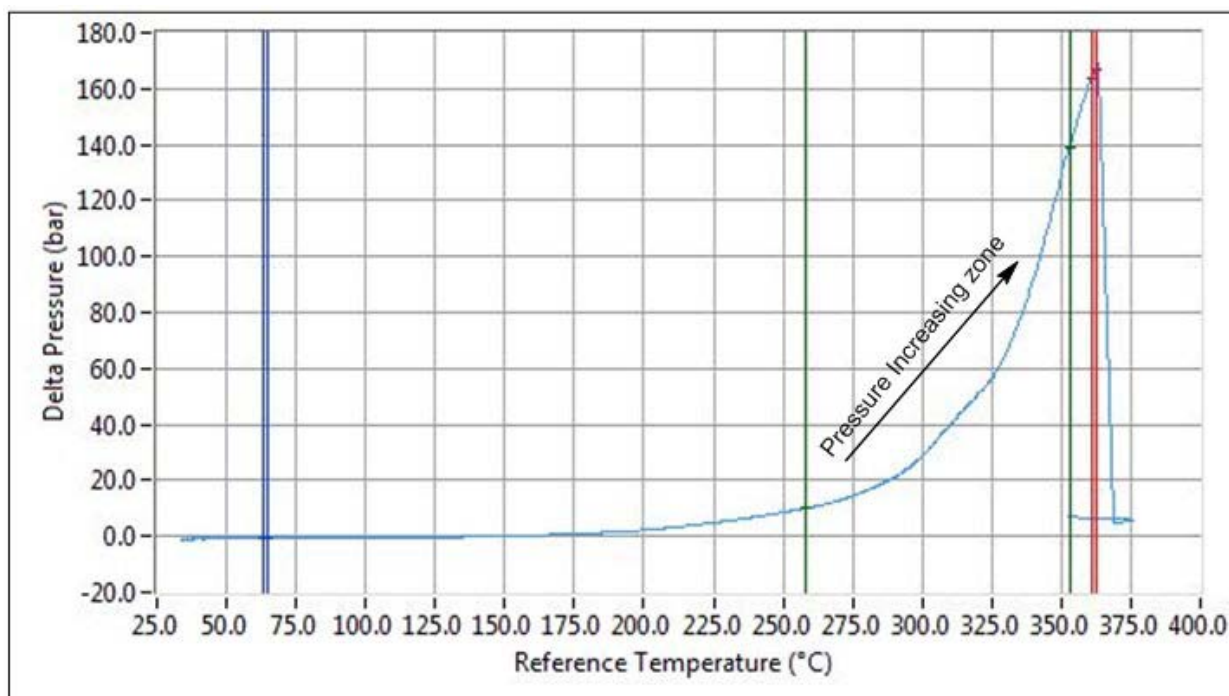
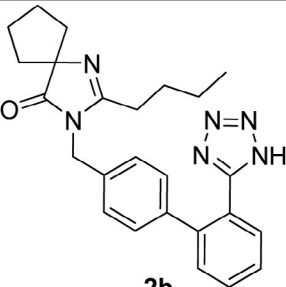
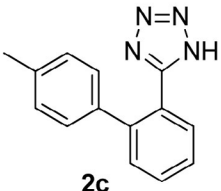
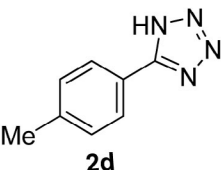
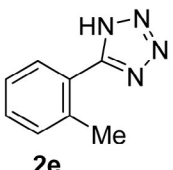
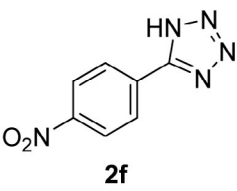
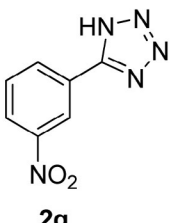
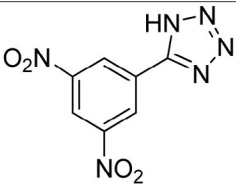
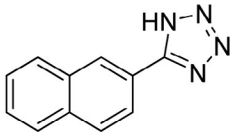
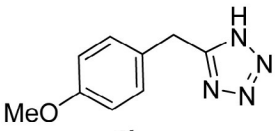
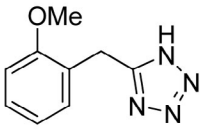
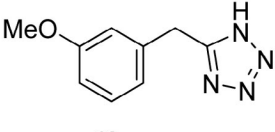
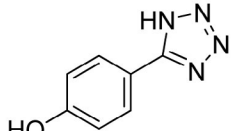
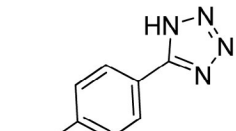
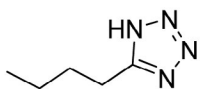


Figure 5. Pressure difference as a function of reference temperature (RSD data).

Table 2 Cu(0)/Cu(II)-catalyzed synthesis of 5-substituted 1*H*-tetrazoles **2**^a.

Entry	Product	Time/h	Yield (%) ^b
1	 2b	17	78 ^c
2	 2c	16	85
3	 2d	1.5	95
4	 2e	3.0	85
5	 2f	1.5	95
6	 2g	1.5	90

7	 2h	1.0	95
8	 2i	2.0	92
9	 2j	15	80
10	 2k	17	75
11	 2l	15	80
12	 2m	12	80
13	 2n	12	85
14	 2o	5	50

^aReaction conditions: Reactions were carried out on a 1.0 g scale of **1** with NaN₃ (1.5 equiv) in the presence of Cu(0) (10 mol%) and CuSO₄ (10 mol%) in DMF (10 mL) at 123±2 °C; ^bIsolated yields; ^cyield after column purification.

layer was separated and the aqueous layer was extracted with ethyl acetate (30 mL). The combined organic layer was washed with 10 % aq. NaCl solution (2x50 mL) and dried over anhydrous Na₂SO₄ and concentrated to give a crude product, which was isolated using chilled water after 3-4 h maintenance, and eventually filtered off to give desired product **2 (b-n)**. Whereas compound **2a** and **2o** were isolated by dissolving the reaction mass in ethyl acetate and hexane (1:9) and the solution was maintained for 3 h at 0-5 °C to obtain the product.

(S)-Methyl N-((2'-(1H-tetrazol-5-yl)-[1,1'-biphenyl]-4-yl)methyl)-N-pentanoyl-L-valinate (2a)

Pale-yellow solid (Yield: 85%). FT-IR (KBr) 3451, 2962, 2933, 2873, 2743, 1739, 1617, 1467, 1206 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): (major rotamer) δ 8.00-7.05 (m, 8H), 4.94-4.89 (2H, m), 4.29-4.25 (d, *J* = 15.5 Hz, 1H), 3.47 (s, 3H), 2.61-2.17 (m, 3H), 1.42-1.23 (m, 4H), 0.99-0.82 (m, 9H). (minor rotamer) δ 8.00-7.05 (m, 8H), 4.68-4.57 (2H, m), 4.08-4.05 (d, *J* = 15.5 Hz, 1H), 3.41 (s, 3H), 2.61-2.17 (m, 3H), 1.42-1.23 (m, 4H), 0.99-0.82 (m, 9H); ¹³C NMR (400 MHz, CDCl₃): (major rotamer): δ 174.9, 171.3, 154.8, 141.0, 137.9, 136.9, 131.1, 130.8, 129.4, 128.0, 127.3, 126.0, 123.1, 66.0, 52.9, 48.0, 33.4, 27.7, 27.5, 26.9, 22.4, 19.8, 18.7, 13.8. (minor rotamer) δ 174.8, 170.3, 155.3, 137.7, 131.1, 130.7, 129.0, 128.0, 122.8, 61.7, 51.9, 45.6, 33.4, 27.7, 27.3, 22.4, 19.8, 18.6; EI-Mass: *m/z* 450.4 [M+H]⁺.

3-((2'-(1H-Tetrazol-5-yl)biphenyl-4-yl)methyl)-2-butyl-1,3-diazaspiro[4.4]non-1-en-4-one (Irbesartan) (2b)

White solid (Yield: 78 %). FT-IR (KBr) 3434.3, 2959.6, 2871.5, 2437.8, 1731.6, 1618.1, 1405.9, 756.2 cm⁻¹; ¹H NMR (400 MHz, DMSO): 7.69(m, 2H), 7.59 (m, 2H), 7.09 (s, 4H), 4.69(s, 2H), 2.31(t, *J*=7.36 Hz, 2H), 1.8-1.68 (m, 7H), 1.67-1.65 (t, *J* = 8.52 Hz, 2H), 1.4-1.5 (q, *J* = 7.6 Hz, 2H), 1.28-1.23 (m, 2H), 0.78 (t, *J* = 14.68 Hz, 3H); ¹³C NMR (100 MHz, DMSO): δ 186.1,

161.6, 155.5, 141.5, 138.8, 136.8, 131.5, 131.1, 131.0, 129.7, 128.3, 126.7, 123.9, 76.3, 42.7, 37.3, 27.9, 27.0, 25.9, 22.0, 14.1; EI-Mass: *m/z* 429 [M+H]⁺.

5-(4'-Methylbiphenyl-2-yl)-1H-tetrazole (2c)

White solid (Yield: 85 %). FT-IR (KBr) 3430.1, 2981.5, 2901.4, 2717.4, 2610.0, 1776.3, 1601, 1566.3, 1480, 1250.7, 753.6 cm⁻¹; ¹H NMR (400 MHz, DMSO): 7.69 (m, 2H), 7.57(m, 2H), 7.12(d, *J* = 7.8 Hz, 2H), 6.98(d, *J* = 8.0 Hz, 2H), 2.28(s, 3H); ¹³C NMR (100 MHz, DMSO): δ 155.1(br), 141.5, 136.8, 136.3, 131.1, 130.6, 130.5, 128.9, 128.6, 127.5, 123.4, 20.6; EI-Mass: *m/z* 237 [M+H]⁺.

5-*p*-Tolyl-1H-tetrazole (2d)

White solid (Yield: 95 %). FT-IR (KBr) 2688.8, 2543.5, 1887.1, 1615.6, 1572.9, 1499.3, 1160.8, 1052.5, 987.3, 821.1, 740.0 cm⁻¹; ¹H NMR (400 MHz, DMSO): δ 7.93 (d, *J* = 8.04 Hz, 2H), 7.44 (d, *J* = 7.8 Hz, 2H), 2.40 (s, 3H); ¹³C NMR (100 MHz, DMSO): δ 155.1, 141.2, 129.9, 126.9, 121.4, 21.0; EI-Mass: *m/z* 161 [M+H]⁺.

5-*o*-Tolyl-1H-tetrazole (2e)

White solid (Yield: 85 %). FT-IR (KBr) 2967.3, 2712, 2603, 1603.9, 1558, 1486.6, 1157.1, 1055, 742.8 cm⁻¹; ¹H NMR (400 MHz, DMSO): δ 7.70 (d, *J* = 1.21 Hz, 2H), 7.50-7.37 (m, 3H), 2.48 (s, 3H); ¹³C NMR (100 MHz, DMSO): δ 155.4, 137.1, 131.3, 130.7, 129.4, 126.3, 123.9, 20.5; EI-Mass: *m/z* 161 [M+H]⁺.

5-(4-Nitrophenyl)-1H-tetrazole (2f)

Pale-yellow solid (Yield: 95 %). FT-IR (KBr) 3445.5, 2906.6, 2669.3, 2565.2, 1531.4, 1342.6, 1086.3, 993.0, 722.6 cm⁻¹; ¹H NMR (400 MHz, DMSO): δ 8.46 (d, *J* = 8.84 Hz, 2H), 8.32 (d, *J* = 8.92 Hz, 2H); ¹³C NMR (100 MHz, DMSO): δ 155.7, 148.7, 130.9, 128.2, 124.6; EI-Mass: *m/z* 190 [M-H]⁻.

5-(3-Nitrophenyl)-1H-tetrazole (2g)

Pale-yellow solid (Yield: 90%). FT-IR (KBr) 3392, 3079.8, 2630.8, 1656.5, 1527.6, 1346.7,

1015.1, 735.2 cm^{-1} ; ^1H NMR (400 MHz, DMSO): δ 8.85 (s, 1H), 8.49 (d, $J = 7.81$ Hz, 1H), 8.44 (d, $J = 9.76$ Hz, 1H), 7.93 (t, $J = 8.01$ Hz, 1H); ^{13}C NMR (100 MHz, DMSO): δ 153.8, 148.2, 133.7, 132.4, 131.6, 124.9, 119.3; EI-Mass: m/z 190 $[\text{M}-\text{H}]^-$.

5-(3,5-Dinitrophenyl)-1H-tetrazole (2h)

Pale-yellow solid (Yield: 95%). FT-IR (KBr) 3415.1, 3098.2, 2882.8, 2739.4, 1537.4, 1348.9, 1088.3, 918.7, 722.5 cm^{-1} ; ^1H NMR (400 MHz, DMSO): δ 9.16 (s, 2H), 8.97 (s, 1H); ^{13}C NMR (100 MHz, DMSO): δ 154.8, 148.7, 127.9, 126.8, 120.2; EI-Mass: m/z 235 $[\text{M}-\text{H}]^-$.

5-(Naphthalen-2-yl)-1H-tetrazole (2i)

White solid (Yield: 92 %) FT-IR (KBr) 3056.4, 2750.7, 2627.9, 1564.7, 1414.6, 1077.5, 1012.9, 913.3, 760.4 cm^{-1} ; ^1H NMR (400 MHz, DMSO): δ 8.68 (s, 1H), 8.14-8.09 (m, 3H), 8.04-8.02 (m, 1H), 7.68-7.62 (m, 2H); ^{13}C NMR (100 MHz, DMSO): δ 155.6 (br), 133.8, 132.6, 129.2, 128.6, 127.8, 127.8, 127.2, 127.0, 123.7, 121.7; EI-Mass: m/z 195 $[\text{M}-\text{H}]^-$.

5-(4-Methoxybenzyl)-1H-tetrazole (2j)

Pale-brown solid (Yield: 80 %). FT-IR (KBr) 2961.8, 2839.9, 2721.6, 1608.5, 1511.4, 1247.9, 1174.2, 1051.9, 1028.1, 841, 831, 753 cm^{-1} ; ^1H NMR (400 MHz, DMSO): δ 16.24 (br, 1H), 7.20 (d, $J = 8.56$ Hz, 2H), 6.90 (d, $J = 8.56$ Hz, 2H), 4.20 (s, 2H), 3.72 (s, 3H); ^{13}C NMR (100 MHz, DMSO): δ 158.7, 130.2, 128.2, 114.6, 114.3, 55.5, 28.5; EI-Mass: m/z 191 $[\text{M}+\text{H}]^+$.

5-(2-Methoxybenzyl)-1H-tetrazole (2k)

Pale-brown solid (Yield: 75 %). FT-IR (KBr) 2978., 2841.8, 2618.1, 1600, 1565, 1495.8, 1253.9, 1046, 764.4 cm^{-1} ; ^1H NMR (400 MHz, DMSO): δ 15.99 (br, 1H), 7.3 (t, $J = 8.68$ Hz, 1H), 7.2 (d, $J = 7.36$ Hz, 1H), 7.03 (d, $J = 7.81$ Hz, 1H), 6.93 (t, $J = 7.41$ Hz, 1H), 4.19 (s, 2H), 3.7(s, 3H); ^{13}C NMR (100 MHz, DMSO): δ 156.9, 130.1, 128.7, 123.6, 120.4, 111.0, 55.4, 23.9; EI-Mass: m/z 191 $[\text{M}+\text{H}]^+$.

5-(3-Methoxybenzyl)-1H-tetrazole (2l)

Pale-brown solid (Yield: 80 %). FT-IR (KBr) 2848.3, 2735.8, 2617.5, 1693, 1581.2, 1485.4, 1287.8, 1154, 1045.4, 927.8, 757.1 cm^{-1} ; ^1H NMR (400 MHz, DMSO): δ 16.18 (br, 1H), 7.27 (t, $J = 7.88$ Hz, 1H), 6.87-6.81 (m, 3H), 4.26(s, 2H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, DMSO): δ 159.5, 137.4, 129.8, 120.8, 114.5, 112.5, 55.1, 28.9; EI-Mass: m/z 189 $[\text{M}-\text{H}]^-$.

4-(1H-Tetrazol-5-yl)phenol (2m)

White solid (Yield: 80 %). FT-IR (KBr) 3928.4, 3104.9, 3063.4, 2935.7, 2620.2, 1605.9, 1503.9, 1255.2, 1078.6, 842.6, 742.7 cm^{-1} ; ^1H NMR (400 MHz, DMSO): δ 10.17 (br, 1H), 7.87 (d, $J = 8.81$ Hz, 2H), 6.96 (d, 2H, $J = 8.76$ Hz); ^{13}C NMR (100 MHz, DMSO): δ 160.6, 155.2(br), 129.2, 116.6, 115.1; EI-Mass: m/z 161 $[\text{M}-\text{H}]^-$.

5-(4-Methoxyphenyl)-1H-tetrazole (2n)

White solid (Yield: 85 %). FT-IR (KBr) 3430.6, 3082.4, 2933.3, 2747.5, 1612.5, 1502, 1261, 1028, 852.2, 609.8 cm^{-1} ; ^1H NMR (400 MHz, DMSO): δ 8.01 (d, $J = 8.76$ Hz, 2H), 7.18 (d, $J = 8.76$ Hz, 2H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, DMSO): δ 161.5, 154.8(br), 128.6, 116.3, 114.8, 55.4; EI-Mass: m/z 175 $[\text{M}-\text{H}]^-$.

5-Butyl-1H-tetrazole (2o)

Pale-yellow semi solid (Yield: 50 %) FT-IR (KBr) 2960, 1583, 1550, 1467, 1260, 1108 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 3.14 (t, $J = 7.61$ Hz, 2H), 1.88 (p, $J = 7.21$ Hz, 2H), 1.43 (sextet, $J = 7.21$ Hz, 2H), 0.94 (t, $J = 7.2$, 3H); ^{13}C NMR (100 MHz, DMSO): δ 156.9, 29.6, 23.1, 22.1, 13.5; EI-Mass: m/z 127 $[\text{M}+\text{H}]^+$.

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