WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 11, Issue 3, 1091-1104. Review Article ISSN 2277– 7105

COMPARATIVE STUDY OF VARIOUS SYNTHETIC METHODS OF 1,2,3-TRIAZOLES VIA CLICK REACTION: A MINI REVIEW

Omprakash S. Chavan*

Department of Chemistry, Badrinarayan Barwale College, Jalna, Maharashtra, India-431213.

Article Received on
06 January 2022,

Revised on 26 January 2022,
Accepted on 16 Feb. 2022

DOI: 10.20959/wjpr20223-23333

***Corresponding Author**
Dr. Omprakash S. Chavan
Department of Chemistry,
Badrinarayan Barwale
College, Jalna, Maharashtra,
India-431213.

ABSTRACT

Different derivatives of azides are condensed with different derivatives of terminal alkynes via click condensation reaction to form respective derivatives of 1,2,3-triazoles in various reaction conditions. Present paper deals with the comparative study of synthesis of derivatives of 1,2,3-triazoles with respect to yield, reaction time and reaction conditions. All products (3a-m) are characterized by spectral data and elemental analysis.

KEYWORDS: *1,2,3-triazoles, Click reaction, Different synthetic route, Comparative study. Green method, MWI, USI.*

1. INTRODUCTION

Chemistry is one of the branches of science which is continuously developing for making human life easy in the area of medicine, dyes, paints, polymers and agriculture etc. In the chemistry, organic chemistry have some precise importance due to the carbocyclic combinations that contains at smallest one ring which may be aromatic or aliphatic in environment and those which have at least one atom other than carbon are called heterocyclic compounds. Nitrogen, Sulphur and Oxygen containing five and six member heterocycles retained the curiosity of researchers during the decades of historical enlargement of organic synthesis.

Heterocyclic compounds found essential for plant and animal kingdom by playing an essential role in biochemical developments. Hence Heterocyclic compound have involved the attention of scientist over the years due to their pharmaceutical values.[1] They are important to life as, vitamins, proteins, hormones contain aromatic heterocyclic system.[2]

Nitrogen containing drugs also play an important role in field of medicinal chemistry. In the synthetic organic chemistry, many molecules have strong pharmaceutical activities due to presence of Nitrogen as a hetero atom.[3]

Triazole including 1,2,3-triazole and 1,2,4-triazole as occupy an significant position in medicinal chemistry attribute to their various biological activities,[4] antifungal and antioxidant Properties,[5] antimicrobial[6] and anti TB agent,[7] a number of of them have been recycled in clinical practice. Compounds having the 1,2,3-triazole moiety can be synthesized over click-chemistry, which is rapid responses with good yields allowing the synthesis of a great derivatives multiplicity by making minor changes in the reagents. The copper-catalyzed 1,3-dipolar cycloaddition reaction among an azide and an alkyne is extensively used for the synthesis of compounds through the 1,2,3-triazole ring with substituents in position 4.[8] Other procedure for the synthesis of this class of compounds is the reaction of an azide using methylenic activated compounds, using different catalysts producing a triazole with substituents in positions 4 and 5.[9]

In continuation of our research interest,[10-14] the current work represents the comparative study of synthesis of 1,2,3-troazoles by click reaction as a mini review using different procedures and its influence with various aspects like yield, reaction time and conditions.

2. Experimental section

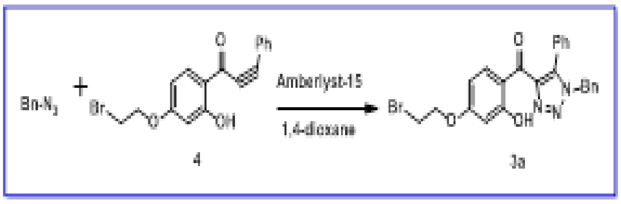
General

The melting points of the compounds were determined in open head capillary and are uncorrected. The IR spectra of the compounds were verified in the region of 4000-400 cm^{-1} by using KBr pallet on FT-IR Perkin spectrophotometer. 1H NMR spectra were recorded on a DRX-300 Bruker FT-NMR spectrophotometer in $CDCl_3$/DMSO-d_6. The standards of chemical shift are expressed in δ ppm as a unit. All the compounds were checked for purity by thin layer chromatography (TLC). The Sonicator was used with 300 watts power of 230 V AC suppliers.

Synthesis of 1, 2, 3-triazole derivatives (3a) mediated by Amberlyst-15 as resin catalyst.[15]

Previously synthesized compounds 1-[(4-2-bromoethoxy-2-hydroxyphenyl)]-3-phenylprop-2-yne-1-one (4) (1 equiv.), dry 1, 4-dioxane, benzyl azide (4 equiv.) and Amberlyst-15 (10% w/w) acidic resin are added in rbf at room temperature. After 16-36 h at 80°C, crude product is filtered in order to remove Amberlyst-15, washed, recrystallized and collect in pure form.

As shown in Scheme 1.

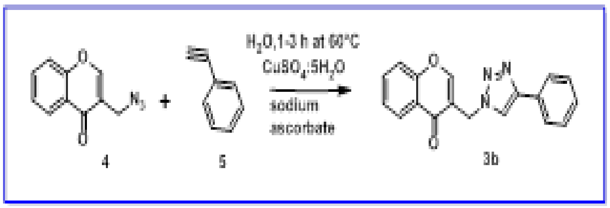


Scheme 1: Synthesis of 1, 2, 3-triazoles (3a) mediated by Amberlyst-15 as resin catalyst (2-hydroxy-4-(2-bromoethoxyphenyl)[5-phenyl-1-(phenyl methyl) -1H-1,2,3-triazol-4-yl]- methanone (3a):

A yellowish white solid. (Yield 58 %); IR (neat) 3032, 2965, 1619, 1591, 1485, 1455, 1355, 1213, 1127, 909 cm^{-1} ; ^{1}H-NMR (CDCl$_3$, 500 MHz) δ 12.69 (br. s, 1H, OH), 8.83 (d, J=9.29 Hz, 1H, Ar), 7.54-7.51 (m, 1H, Ar), 7.47 (t, J=7.34 Hz, 2H, Ar), 7.30 (dd, J=5.38, 1.96 Hz, 2H, Ar), 7.25 (dd, J=6.85, 1.47 Hz, 2H, Ar), 7.06 (dd, J=7.34, 1.96 Hz, 2H, Ar), 6.54 (dd, J=9.29, 2.45 Hz, 1H, Ar), 6.42 (d, J=2.45 Hz, 1H, Ar), 5.46 (s, 2H, benzylic CH$_2$), 4.35 (t, J=6.36 Hz, 2H, OCH$_2$), 3.66 (t, J=6.36 Hz, 2H, CH$_2$Br); ^{13}C-NMR (CDCl$_3$, 125 MHz) δ 188.2 (C=O), 166.6 (COH), 164.6 (C-OH), 143.6 (C-triazol), 141.5 (C-triazol), 136.0 (Ar), 134.5 (Ar), 130.1 (Ar), 129.7 (2C-Ar), 128.8 (2C-Ar), 128.7 (2C-Ar), 128.5(2C-Ar), 127.6 (Ar), 126.3 (Ar), 114.0 (Ar), 107.8 (Ar), 101.4 (Ar), 67.7 (CH$_2$O), 52.0 (CH$_2$-Bn), 28.3(CH$_2$Br). GC-MS (EI): calc. $C_{24}H_{20}BrN_3O_3$: 477.07. Found: 477.0 (M$^+$), m/z 450.09 (-N$_2$), 306.01, 242.96, 137.06, 108.97, 91.03 (100).

Synthesis of 1,2,3-triazole derivatives (3b) by conventional method in presence of Catalyst [16]

Azide (4) (1 equiv), aliphatic/aromatic alkynes (5) (1.3 equiv) in t-butanol (3ml),copper sulfate pentahydrate (20mol%), sodium ascorbate (20mol%) and distilled water (3ml) were stirred for 1–3 h at 60°C. After completion of the reaction (monitored by TLC), obtained was purified over silica gel column chromatography and collet triazole derivatives (3b). As shown in Scheme 2.



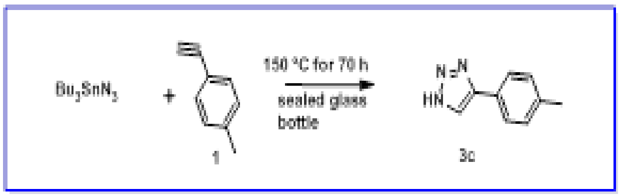
Scheme 2: Synthesis of 1,2,3-triazoles (3b) by conventional method in presence of

Catalyst 3-((4-phenyl-1H-1,2,3-triazol-1-yl)methyl)-4H-chromen-4-one(3b):

Yellow solid; (Yield 90%); mp=154–155°C; IR ($CHCl_3$, cm^{-1}) νmax=3685, 3357, 3022, 2923, 2402, 1649, 1523, 1469, 1423, 1353, 1216, 1030, 927, 765, 671; ^{1}HNMR (400MHz, $CDCl_3$) δ=5.48(s,2H), 7.30–7.34(m, 1H), 7.39–7.51(m,4H), 7.70–7.74 (m,1H), 7.83(d, J=7.3Hz,2H), 8.15(s,1H), 8.22(s,1H), 8.24(dd, J=8.0, 1.6Hz,1H); ^{13}CNMR (100MHz, $CDCl_3$) δ=176.7(CO), 156.5(C), 155.8(CH), 134.4 (CH, 2carbons), 130.1 (C), 128.8 (CH, 2 carbons), 128.3 (CH), 125.8 (CH, 3 carbons), 123.8 (C), 121.3 (C), 119.1 (C), 118.4 (CH, 2carbons), 45.5 (CH_2); HRMS(ESI) m/z=Calcd for $C_{18}H_{13}O_2N_3$ $[M^+H]^+$ 304.1081, found 304.1086.

Synthesis of 1,2,3-triazole derivatives (3c) by conventional method without any Catalyst [17][18]

A mixture of tri-n-butyl tin azide with the appropriate alkyne was heated at 150ºC for 70 h in a sealed glass bottle. The resulting solution was purified by column chromatography and recrystallized from to give the desired triazole. As shown in Scheme 3.



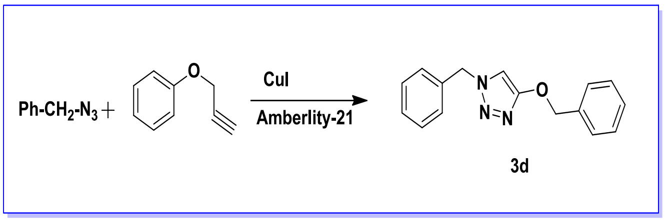
Scheme 3: Synthesis of 1,2,3-triazoles (3c) by conventional method without any Catalyst

4-(4-Methylphenyl)-1H (2H)-[1,2,3]triazole (3c):

Yellow solid, (Yield 40%); m.p. 139−141 ºC. ^{1}H NMR (200 MHz, DMSO-d_6): δ = 14.91 (sw, 1 H, NH), 8.08 (s, 1 H, H-5), 7.61 (d, 3Jo,m = 7.8 Hz, 2 H, Ho), 7.11 (d, 3Jo,m = 7.8 Hz, 2 H, Hm), 2.21 (s, 3 H, CH_3) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ = 147.4 (C-4), 137.7 (Cp), 129.3 (Cm, C-5), 129.1 (Cipso), 125.4 (Co), 20.8 (CH_3) ppm. ESI-MS: m/z (%) = 182 $[M^{++}Na]$; 160 $[M^{++}1]$. Anal. Calcd. for $C_9H_9N_3$: C, 67.90; H, 5.70, N, 26.40. Found: C, 67.81; H, 5.75; N, 26.49.

Synthesis of 1,2,3-triazole derivatives (3d) by flash method technic[19]

The azide and alkyne were placed together in an open small test tube. Amberlyst A-21, CuI (1.35 mmol/g, 30 mg, 0.040 mmol, 8% mol) was added at on one occasion and recovered product after evaporation of the solvent. As shown in Scheme 4.

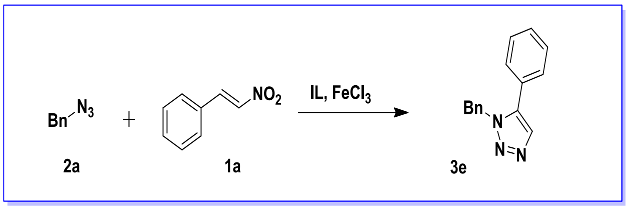


Scheme 4: Synthesis of 1, 2, 3-triazoles (3d) by flash method technic 1-Benzyl-4-(phenoxymethyl) triazole (3d):

Prepared from 66 mg (0.50 mmol) propargyl phenyl ether and 73 mg (0.55 mmol) benzyl azide. The product was obtained as a white solid. (Yield 99 %); $C_{16}H_{15}N_3O$, M = 265.31 g/mol^{-1}; mp: 119-121°C; FTIR: ν 3132, 3016, 2970, 2920, 2866, 1588, 1488, 1239, 1222 and 1052 cm^{-1}; ^{1}H-NMR: δ 5.17 (s, 2H), 5.51 (s, 2H), 6.95 (m, 3H), 7.26 (m, 4H), 7.33 (m,3H) and 7.44 (s, 1H) ppm; ^{13}C-NMR: δ 54.2, 62.0, 114.8, 121.3, 128.1, 128.8 , 129.1, 129.5, 134.5, 144.6 and 158.2 ppm; LC-MS: ELSD pur. 92 %, UV pur. 100 %; Rt = 9.56 min; m/z: 266 ($[M^+H]^+$).

Synthesis of 1,2,3-triazole derivatives (3e) by Ionic Liquid Catalyzed method[20]

In round bottom flask, ionic liquid (5 mL), $FeCl_3$ (20 mol%), (E)-nitro styrene (1a) (1 eq.), and azide (2a)(2 eq.) were sited. The reaction was conducted at 100 ◦C. The resulting solution was purified by column chromatography and recrystallized from to give the desired triazole (3e). As shown in Scheme 5.

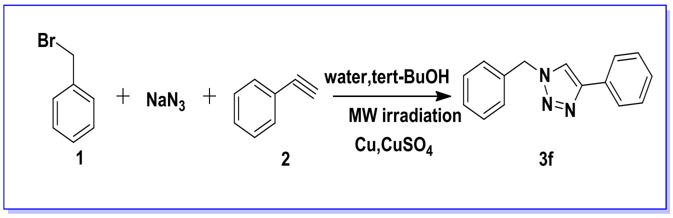


Scheme 5: Synthesis of 1, 2, 3-triazoles (3e) by Ionic Liquid Catalyzed method 1-Benzyl-5-phenyl-1,2,3-triazole (3e):

(Yield 95 %); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) 5.55 (s, 2H, CH2), 7.05–7.12 (m, 2H, Ar), 7.22–7.33 (m, 5H, Ar), 7.38–7.48 (m, 3H, Ar), 7.75 (s, 1H, CH). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) 51.83, 126.97, 127.17, 128.16, 128.82, 128.92, 128.95, 129.50, 133.30, 135.53, 138.15. ESI (+)-MS: m/z [M $^+$ H] calcd for $C_{15}H_{14}N_3$ is 236.1182, found: 236.0952.

Synthesis of 1,2,3-triazole derivatives (3f) by Nonconventional or MWI technique[21][22]

An appropriate halide (1) terminal alkyne (2) and sodium azide (1.1 mmol) in a 1:1 mixture of water and tert-butyl hydroxide. (1.5 mL each) then added the copper wire (50 mg), copper sulphate solution (1N, 200 µL), The mixture was then irradiated for MWirradiation power of 100 W. The resulting solution was purified by column chromatography and recrystallized from to give the desired triazole. As shown in Scheme 6.



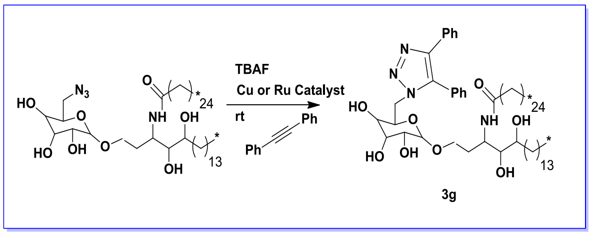
Scheme 6: Synthesis of 1,2,3-triazoles (3f) by Nonconventional or MWI technique

Synthesis of 1-benzyl-4-phenyl-1H-1,2,3-triazole (3f):

(Yield 90%); ^{1}H NMR (300 MHz, $CDCl_3$ + CD_3OD): δ = 5.46 (s, 2H), 7.25 – 7.39 (m, 8H), 7.67 (s, 1H), 7.77 (d, 2H, J = 7.3 Hz) ppm. ^{13}C NMR (75 MHz, $CDCl_3$ + CD_3OD): δ = 53.8, 119.6, 125.4, 127.7, 127.9, 128.4, 128.6, 128.8, 130.4, 134.6, 147.9 ppm. DEPT (75 MHz, $CDCl_3$ + CD_3OD): δ = -54.5, 120.2, 126.1, 128.4, 128.6, 129.1, 129.3, 129.5 ppm. EI - MS [M^+]: 235 (100%).

Synthesis of 1,2,3-triazole derivatives (3g) by using Quaternary Ammonium Salt at RT method[23][24]

Tetra-n-butyl ammonium fluoride (TBAF- quaternary ammonium salt), azide, diphenylacetylene and 2-(trimethylsilyl) phenyl trifluoromethane sulfonate in THF. After stirring the resulting mixture overnight at room temperature, by flash column chromatography afforded benzotriazole as a white solid. As shown in Scheme 7.



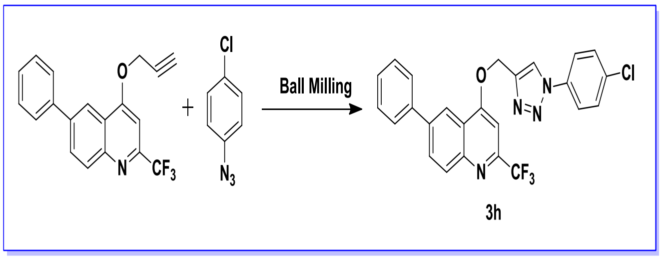
Scheme 7: Synthesis of 1,2,3-triazoles (3g) by using Quaternary Ammonium Salt at RT method

Triazole (3g):

A colourless paste (18 mg, 72%): Rf = 0.28 (15% MeOH in $CHCl_3$); IR (neat) 3370s br (O-H), 2920s, 2851s, 2460w, 1711w, 1630s (C=O), 1557w, 1467s, 1356w, 1242w, 1230m, 1092w, 1084w, 1076s, 1053m, 1046s, 767m, 757m; ^{1}H NMR (300 MHz, $CDCl_3$:CD_3OD, 2:1): 0.84 (app. t, 6H, J 7.2), 1.13-1.34 (stack, 68H), 1.42-1.69 (stack, 4H), 2.11 (app. t, 2H, J 7.7 Hz), 3.45-3.53 (stack, 2H), 3.57 (dd, 1H, J 10.5, 5.7 Hz), 3.58-3.77 (stack, 3H), 3.85-3.89 (m, 1H), 4.09-4.21 (stack, 2H), 4.36-4.41 (stack, 2H), 4.81 (d, 1H, J 2.4 Hz), 7.19-7.28 (m, 2H), 7.30-7.38 (m, 2H), 7.39-7.45 (m, 2H), 7.45-7.52 (stack, 4H), exchangeable protons not observed; ^{13}C NMR (75 MHz, $CDCl_3$:CD_3OD, 2:1): 14.6 (CH_3), [23.3, 26.1, 26.6, 30.0, 30.1, 30.4, 32.6, 33.4, 37.1 (CH_2, some overlapping alkyl resonances)], 48.9 (CH_2), 50.7 (CH), 67.7 (CH_2), 69.4 (CH), 70.1 (CH), 70.2 (CH), 70.6 (CH), 72.6 (CH), 75.4 (CH), 100.3 (CH), 126.8 (CH), 127.6 (CH), 128.4 (CH), 129.4 (CH), 130.18 (CH), 130.22 (CH), 131.2 (quat. C), 132.5 (quat. C), 144.0 (quat. C), 175.0 (quat. C), one quaternary carbon not observed due to resonance overlap; m/z (TOF ES$^+$) 1083.8 ([M$^+$Na]$^+$, 100%); HRMS m/z (TOF ES$^+$) 1083.8062. $C_{64}H_{108}N_4NaO_8$ requires 1083.8065.

Synthesis of 1,2,3-triazole derivatives (3h) by Ball milling method[25][26]

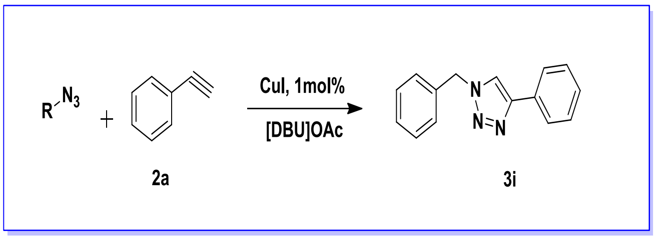
Alkynes and the corresponding aryl azide with $Cu(OAc)_2$ and two 7 mm diameter stainless steel balls. and the closed vessel was positioned in the IST500 mill after 3.5 h at 30 Hz milling and then crude product purified by column chromatography. As shown in Scheme 8.



Scheme 8: Synthesis of 1,2,3-triazoles (3h) by Ball milling method Crystal data for 3h: (Yield 57%); 0.763 × 0.424 × 0.155 mm^3; $C_{25}H_{16}ClF_3N_4O$, Mr = 480.87, triclinic, space group P-1 (No. 2); a = 8.0775(4) Å, b = 10.3530(5) Å, c = 13.7751(6) Å, α = 82.383(4)°, β = 74.062(4)°, γ = 84.946(4)°, V = 1096.29(9) Å3; Z = 2; ρ = 1.457 g cm^{-3}, μ(Mo Kα) = 0.226 mm^{-1}; θmax =27.999°, 19408 reflections measured, 5276 unique reflections and 3932 with $I \geq 2\sigma(I)$, Rint = 0.0337; Final R indices [$(I > 2\sigma(I))$]: R = 0.0538, wR = 0.1453, [all data]: R = 0.0729, wR = 0.1603, S = 1.180 for 334 parameters and 23 restraints, largest diff. peak and hole 0.335/−0.403 e Å$^{-3.}$

Synthesis of 1,2,3-triazole derivatives (3i) by Solvent free technique[27]

To a clean oven dried round bottom flask alkyne azide CuBr and [DBU]OAc (400 µl) were taken and stirred until mixture solidifies. After completion of the reaction the product is directly subjected to column chromatography afforded the desired triazole product. As shown in Scheme 9.

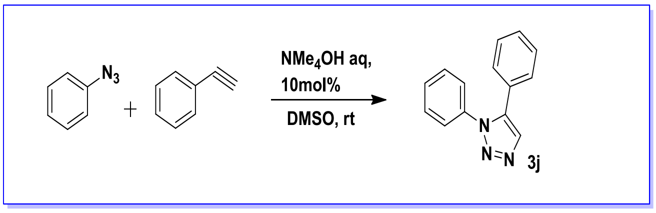


Scheme 9: Synthesis of 1,2,3-triazoles (3i) by Solvent free technique 1-Benzyl-4-phenyl-1H-1,2,3-triazole (3i):

White solid; (Yield 98 %); mp 127-130°C, ^{1}H NMR (600 MHz,) δ 7.80 (d, J = 8.1 Hz, 2H), 7.67 (s, 1H), 7.44 – 7.35 (m, 5H), 7.31 (t, J = 6.5 Hz, 3H), 5.57 (s, 2H). ^{13}C NMR (150 MHz, $CDCl_3$): δ148.32, 130.61, 129.25, 128.89, 128.25, 128.16, 125.78, 119.56, 54.32. MS (ESI) m/z: 236.16 $[M^+ H]^+$, cal. 236.11.

Synthesis of 1,2,3-triazole derivatives (3j) by Transition-Metal-Free Catalytic technique[28]

To a stirred DMSO solution of aryl alkyne and aryl azide, tetramethylammonium hydroxide or benzyl trimethylammonium hydroxide. After addition of base catalyst, the reaction mixture was stirred at room temperature under an atmosphere of N_2 (g) and monitored either by TLC. where the desired product could not be isolated by filtration, it was extracted with EtOAc. followed by flash column chromatography. As shown in Scheme 10.

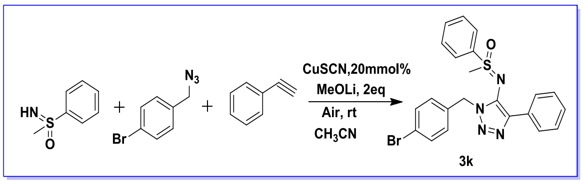


Scheme 10: Synthesis of 1,2,3-triazoles (3j) by Transition-Metal-Free Catalytic technique 1,5-Diphenyl-1H-1,2,3-triazole (3j):

Isolated as an off-white solid by vacuum filtration: (Yield 87%); mp 113–114 °C (lit.113–114 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.46–7.32 (m, 8H), 7.26–7.22 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.7, 136.6, 133.4, 129.3, 129.2, 128.8, 128.6, 126.7, 125.2; HRMS (ESI-TOF) (m/z): $[M^+H]^+$ calcd for $C_{14}H_{12}N_3$, 222.1026; found, 222.1038.

Synthesis of 1,2,3-triazole derivatives (3k) by Transition-Metal-Catalytic technique[29]

Azides, terminal alkynes, sulfoximines CuSCN, and MeOLi were added in dry MeCN and stirred for 12 h at room temperature in air. After the reaction was completed, crude product was purified with flash chromatography, as shown in Scheme 11.

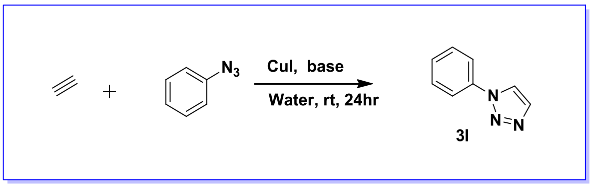


Scheme 11: Synthesis of 1, 2, 3-triazoles (3k) by Transition-Metal-Catalytic technique ((1-(4-bromobenzyl)-4-phenyl-1H-1, 2, 3-triazol-5-yl)imino) (methyl) (phenyl)-l6-ulfanone (3k):

shallow yellow oil, (75.5 mg, 81% yield.) ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 – 7.84 (m, 2 H), 7.69 – 7.67 (m, 2H), 7.59 – 7.56 (m, 1H), 7.44 – 7.39 (m, 6H), 7.32 – 7.28 (m, 1H), 7.22 – 7.20 (m, 2H), 5.60 – 5.53 (m, 2 H), 3.05 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.4, 137.3, 134.9, 134.8, 133.9, 131.6, 129.7, 129.4, 128.4, 127.7, 127.4, 126.8, 121.8, 50.2, 44.6. HRMS (ESI) m/z: $[M^+ H]^+$ Calcd for $C_{22}H_{20}BrN_4OS$, 467.0536; Found: 467.0533.

Synthesis of 1, 2, 3-triazole derivatives (3l) by water as a Green solvent technique[30][31]

Azide, Et3N, water and CuI were added successively with acetylene gas and the mixture was stirred at room temperature for 24 h. After completion of the reaction, the resulting solution was purified by column chromatography and recrystallized from to give the desired triazole. As shown in Scheme 12.

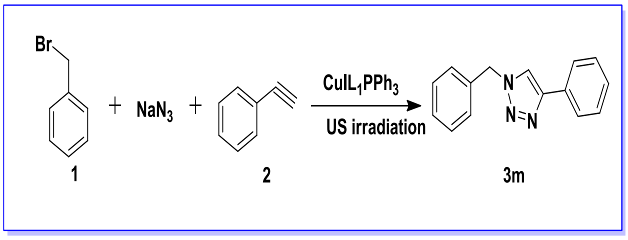


Scheme 12: Synthesis of 1,2,3-triazoles (3l) by water as a Green solvent technique 1-Phenyl-1H-1,2,3-triazole(3l):

White solid; (Yield 90%); mp 52–53°C; ^{1}H NMR ($CDCl_3$): δ 8.04 (s, 1H), 7.82 (s, 1H), 7.73 (d, J = 8.0 Hz, 2H), 7.52 (m, 3H); ^{13}C NMR ($CDCl_3$): δ 136.8, 134.2, 129.5, 128.5, 121.7, 120.4.

***Synthesis of 1, 2, 3-triazole derivatives (3m) by using Ultrasonic Irradiation as a Green technique*[32]**

A mixture of the alkyl halide, sodium azide, terminal alkyne and CuIL1PPh$_3$ complex in distilled water was placed two-neck flask. The mixture was directly irradiated with an ultrasonic probe at 60°C and maintained at this temperature for 30 min. The resulting precipitate was filtered, washed with water and then purified by flash chromatography to afford the pure 1,2,3-triazoles 1,4-disubstituted (3m). As shown in Scheme 13.



Scheme 13: Synthesis of 1,2,3-triazoles (3m) by using Ultrasonic Irradiation1-Benzyl-4-phenyl-1H-1,2,3-triazole (3m):

white solid (Yield 85%); mp 132−133 °C . ^{1}H NMR (400 MHz, CDCl$_3$): δ = 5.57 (s, 2H), 7.29−7.33 (m, 3H), 7.35−7.41 (m, 5H), 7.66 (s,1H), 7.81 (d, J=7.2Hz, 2H) ppm. ^{13}C NMR (101 MHz, CDCl$_3$): δ = 54.2(CH$_2$), 119.5(CH),125.7(CH), 128.1 (CH), 128.2 (CH), 128.8 (CH), 129.1 (CH), 130.5 (C), 134.7(C), 148.2(C) ppm. HRMS (ESI$^+$): calcd for $C_{15}H_{14}N_3^+$ 236.1182 [M$^+$H]$^+$; found 236.1188.

Table 1: Reaction condition, Time, Temperature and Yield of Compounds 3a-3m.

Comp.	Time with temp.	Yield in %	Reaction Conditions
3a	16-36 hr at 80 °C	58	Amberlyst-15, 1,4-Dioxane
3b	1-3 hr, at 60 °C	90	Sod. Ascorbate, CuSO$_4$:5H$_2$O
3c	70 hr at 150 °C	40	Heated in a sealed glass bottle
3d	5 min at RT	99	Amberlyst-A-21, Neat, copper (I) iodide.
3e	2 to 72 hr at 100 °C	95	Ionic Liquid, FeCl$_3$ Catalysed
3f	2- 5 min at 100 W	90	Copper sulphate solution, MWI,
3g	Overnight at RT,	69	QA Salt
3h	Grinding for 3.5 hr, 30Hz	57	Cu(OAc)$_2$, two 7 mm diameter SS balls
3i	Neat	98	CuBr(1mol%),

			[DBU]OAc (400 µl)
3j	2–12 hr, RT	87	NMe$_4$OH aq.,DMSO
3k	12 hr at RT	81	CuSCN, MeOLi ,MeCN
3l	24 hr at RT	90	CuI, water solvent
3m	60°C, 30 min	85	CuIL$_1$PPh$_3$ complex, USI, water

3. CONCLUSION

In conclusion, here we described comparative study of preparation of 1,2,3-Triazole Via Click reaction by several methods. Among which, this study prove that green synthetic method (3d) is most efficient via click reaction by simple, solvent free, Amberlyst-A-21 and copper (I) iodide catalyzed at normal room temperature are the merit of this reaction with 99 percent of yield is obtained within few minutes.

4. ACKNOWLEDGMENT

Author is thankful to the Principal, Badrinarayan Barwale College, Jalna-431213 for constant encouragement and providing necessary facilities for this work.

5. REFERENCES

1. Ameta, K.L.; Anshu Dandia, Green Chemistry: Synthesis of Bioactive Heterocycles, Springer, New Delhi, India, 2014. https://doi.org/10.1007/978-81-322-1850-0
2. Mulwad, V. V.; Bhushan P Langi, Atul C Chaskar, Synthesis of novel biologically active heterocyclic compounds from 2-oxo-2H-benzopyran-6-yl-imidazolidine, Acta Pol Pharm, 2011; 68(1): 39-47.
3. Kerru, N.; Lalitha Gummidi, Suresh Maddila, Kranthi Kumar Gangu and Sreekantha B. Jonnalagadda, A Review on Recent Advances in Nitrogen-Containing Molecules and Their Biological Applications, Molecules, 2020, 25(8): 1909. https://doi.org/10.3390/molecules25081909
4. Yi-Lei F.; Xing Ke, Min Liu, Coumarin–triazole Hybrids and Their Biological Activities, J. Hetero. Chem., 2018; 55(4): 791-802. https://doi.org/10.1002/jhet.3112.Nbngndgh
5. Shaikh, M.; Dnyaneshwar Subhedar, Firoz A Kalam Khan, Jaiprakash N. Sangshetti, 1,2,3-Triazole incorporated coumarin derivatives as potential antifungal and antioxidant agents, Chin. Chem. Lett., 2016; 27(2): 295-301. https://doi.org/10.1016/j.cclet.2015.11.003.

6. Kushwaha, N. K.; Lata, Subhash C. Jain, Design and synthesis of novel 2H-chromen-2-one derivatives bearing 1,2,3-triazole moiety as lead antimicrobials, Bioorg. & Med. Chem. Lett., 2014; 24(7): 1795-1801. https://doi.org/10.1016/j.bmcl.2014.02.027.
7. Ashish A.; Manohar V.Kulkarni, Shrinivas D. Joshi, Sheshagiri R. Dixit, One pot Click chemistry: A three component reaction for the synthesis of 2-mercaptobenzimidazole linked coumarinyl triazoles as anti-tubercular agents, Bioorg. & Med. Chem. Lett., 2016, 26(19): 4709-4713. https://doi.org/10.1016/j.bmcl.2016.08.045
8. Boechat, N.; V. F. Ferreira, S. B. Ferreira et al., Novel 1,2,3-triazole derivatives for use against mycobacterium tuberculosis H37Rv (ATCC 27294) strain, J. Med. Chem, 2011; 54(17): 5988–5999. https://doi.org/10.1021/jm2003624.
9. Zeghada, S.; G. Bentabed-Ababsa, A. Derdour et al., A combined experimental and theoretical study of the thermal cycloaddition of aryl azides with activated alkenes, Org. & Biomole. Chem., 2011; 9(11): 4295–4305. https://doi.org/10.1039/C1OB05176H
10. Bandgar, B.P.; Abasaheb V Patil, OS Chavan, Silica supported fluoroboric acid as a novel, efficient and reusable catalyst for the synthesis of 1, 5-benzodiazepines under solvent-free conditions, Journal of Molecular Catalysis A: Chemical, 2006, 256(1-2): 99-105. https://doi.org/10.1016/j.molcata.2006.04.024
11. Bandgar, B,P.; AV Patil, OS Chavan, VT Kamble, Regioselective ring opening of epoxides with thiols under solvent free and mild conditions using heterogeneous catalyst, Catalysis Communications, 2007; 8(7): 1065-1069. https://doi.org/10.1016/j.catcom.2006.10.003
12. Jadhav, S.A.; Mahesh G Shioorkar, Omprakash S Chavan, Aniket P Sarkate, Devanand B Shinde, Rapid and efficient one-pot microwave-assisted synthesis of 2-phenylimidazo[1,2-a]pyridines and 2-phenylimidazo[1,2-a]quinoline in water–PEG-400, Synthetic Communications, 2017; 47(4): 285-290. https://doi.org/10.1080/00397911.2016.1262040
13. Pardeshi, R.K.; Santosh A. Jadhav, Mahesh. G. Shioorkar, Omprakash S. Chavan, Aniket P. Sarkate, Mazahar Farooqui, Devanand. B. Shinde, An efficient microwave-assisted multi-component synthesis of rhodanine derivatives, Indian journal of heterocyclic chemistry, 2016; 25(3&4): 201-207.
14. Jadhav, S.A.; Mahesh Shioorkar, Omprakash Chavan, Aniket Sarkate, Devanand Shinde, Rajendra Pardeshi, Alum [$KAl(SO_4)2•12H_2O$] catalyzed microwave assisted synthesis of 5-arylidine-2-(methylthio)-thiazolone derivatives in water, European Journal of Chemistry, 2015; 6(4): 410-416. https://doi.org/10.5155/eurjchem.6.4.410-416.1312

15. Zhang, H.; Dao-Qing Dong, Zu-Li Wang, Direct Synthesis of N-Unsubstituted 4-Aryl-1,2,3-triazoles Mediated by Amberlyst-15, Synthesis, 2016; 48(01): 131-135.
16. Nalla V, Shaikh A, Bapat S, Vyas R, Karthikeyan M, Yogeeswari P, Sriram D, Muthukrishnan M., Identification of potent chromone embedded[1,2,3]-triazoles as novel anti-tuber cular agents. Royal Soc. Open Sci., 2018; 5: 171-175. https://doi.org/10.1098/rsos.171750
17. Cristina G. O.; Nadine Jagerovic, Pilar Goya, Ibon Alkorta, Jose Elguero, Rosa Cuberes, and Alberto Dordal, N-Substituted-1,2,3-triazoles: synthesis, characterization and evaluation as cannabinoid ligands, ARKIVOC, 2010; (ii): 127-147.
18. Mohamed R. A.; Efficient Eco-Friendly Solvent-Free Click Synthesis and Antimicrobial Evaluation of New Fluorinated 1,2,3-Triazoles and their Conversion into Schiff Bases, J. Braz. Chem. Soc., 2015; 26(10): 2105-2115. https://doi.org/10.5935/0103-5053.20150196
19. Ibtissem J.; Faouzi Meganem, Jean Herscovici and Christian Girard, “Flash” Solvent-free Synthesis of Triazoles Using a Supported Catalyst, Molecules, 2009; 14: 528-539. https://doi.org/10.3390/molecules14010528
20. Antonio De N.; Pedro Merino, Vincenzo Algieri, Monica Nardi, Maria Luisa Di Gioia, Beatrice Russo, Matteo Antonio Tallarida and Loredana Maiuolo, Synthesis of 1,5-Functionalized 1,2,3-Triazoles Using Ionic Liquid/Iron(III) Chloride as an Efficient and Reusable Homogeneous Catalyst, Catalysts, 2018; 8: 364-377. https://doi.org/10.3390/catal8090364
21. Appukkuttan, P.; Wim Dehaen, Valery V. Fokin, and Erik Van der Eycken, A Microwave-Assisted Click Chemistry Synthesis of 1,4-Disubstituted 1,2,3-Triazoles via a Copper(I)-Catalyzed Three-Component Reaction, Org. Lett., 2004; 6(23): 4223–4225. https://doi.org/10.1021/ol048341v.
22. Katritzky, A.R.; Sandeep K. Singh, Synthesis of C -Carbamoyl-1,2,3-triazoles by Microwave Induced 1,3-Dipolar Cycloaddition of Organic Azides to Acetylenic Amides, J. Org. Chem., 2002; 67(25): 9077–9079. https://doi.org/10.1021/jo026398u.
23. Peter J. J.; Lisa M. Graham, Erin L. Foster, Liam R. Cox, Steven A. Porcelli, Gurdyal S. Besra, New CD1d agonists: Synthesis and biological activity of 6″-triazole-substituted α-galactosyl ceramides, Bioorganic & Medicinal Chemistry Letters, 2012; 22(13): 4348-4352. https://doi.org/10.1016/j.bmcl.2012.05.009

24. Khan, I. A.; Matloob Ahmad, Sana Aslam, Muhammad Jawwad Saif, Ameer Fawad Zahoor, Syed Ali Raza Naqvi, Asim Mansha, Recent advances in the synthesis of triazole derivatives, AFINIDAD LXXII, 2015; 72(569): 64-77.
25. Tireli, M.; Silvija Maracic, Stipe Lukin, Marina Juribasic Kulcsar, Dijana Zilic, Mario Cetina, Ivan Halasz, Silvana Raic-Malic and Krunoslav Uzarevic, Solvent-free copper-catalysed click chemistry for the synthesis of N-heterocyclic hybrids based on quinoline and 1,2,3-triazole, Beilstein J. Org. Chem., 2017; 13: 2352–2363.
26. Mukherjee, M.; Sabir Ahammed, Sukalyan Bhadra and Brindaban C. Ranu, Solvent-free one-pot synthesis of 1,2,3-triazole derivatives by the ‘Click’ reaction of alkyl halides or aryl boronic acids, sodium azide and terminal alkynes over a Cu/Al O surface under ball-milling, Green Chem., 2013; 15: 389-397. https://doi.org/10.1039/C2GC36521A
27. Garg, A.; Debajit Borah, Priyanka Trivedi, Dipshikha Gogoi, Amrita Kashyap Chaliha, Abdul Aziz Ali, Dipak Chetia, Vinita Chaturvedi and Diganta Sarma, A simple workup free,solvent free approach to novel amino acid linked 1,4 disubstituted 1,2,3-triazoles as potent anti-TB agents, ACS Omega, 2020; 5(46): 29830–29837. https://doi.org/10.1021/acsomega.0c03862
28. Kwok, S. W.; Joseph R. Fotsing, Rebecca J. Fraser, Valentin O. Rodionov, Valery V. Fokin, Transition-Metal-Free Catalytic Synthesis of 1,5-Diaryl-1,2,3-triazoles, Org. Lett., 2010; 12(19): 4217–4219. https://doi.org/10.1021/ol101568d
29. Xua, J.; and Qiuling Song, Synthesis of fully-substituted 1,2,3-triazoles via copper(i)-catalysed three-component coupling of sulfoximines, alkynes and azides, Org. Chem. Front, 2017; 4: 938-942. https://doi.org/10.1039/C6QO00725B
30. Wu, L.; Bo Yan, Guo Yang and Yuxue Chen, Green synthesis of 1-monosubstituted 1,2,3-triazoles via ‘click chemistry’ in water, Heterocycl. Commun, 2013; 19(6): 397–400.https://doi.org/10.1515/hc-2013-0151
31. Alonso, F,; Yanina Moglie, Gabriel Radivoy, Miguel Yus, Multicomponent Synthesis of 1,2,3-Triazoles in Water Catalyzed by Copper Nanoparticles on Activated Carbon, Advanced Synthesis & Catalysis, 2010; 352(18): 3208-3214. https://doi.org/10.1002/adsc.201000637
32. Castillo, J. C.; Nestor-Fabian Bravo, Lenka-Victoria Tamayo, Paula-Daniela Mestizo, John Hurtado, Mario Macías, and Jaime Portilla, Water-Compatible Synthesis of 1,2,3-Triazoles under Ultrasonic Conditions by a Cu(I) Complex-Mediated Click Reaction, ACS Omega, 2020; 5: 30148−30159. https://doi.org/10.1021/acsomega.0c04592