

PREPARATION OF 1,2,3 –TRIAZOLE LINKED PIPERAZINE AND IMIDAZOLE DERIVATIVES VIA CLICK CHEMISTRY

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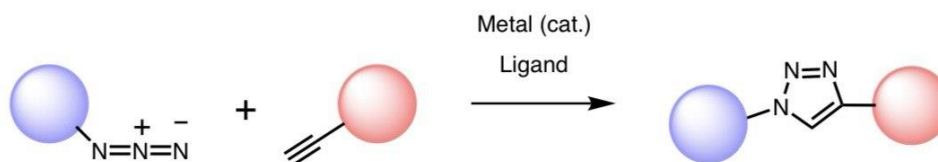
Abstract:

An efficient method has been developed for the synthesis of 1,2,3-triazole-linked piperazine, imidazole ring, through azido-alkyne using click chemistry. one of pair of chemical compounds known as piperazine, imidazole and triazoles of hetero compounds are profoundly receptive and are known to possess potent diverse actives liked analgesic, anti-HIV, anti-cancer, anti-bacterial and other. In conclusion numerous biological actions of 1,2,3-triazole derivative of heterocyclic compounds.

Keywords: click chemistry, piperazine, imidazole, 1,2,3—triazole.

Introduction

The 1,3-dipolar cycloaddition of an azide and an alkyne to 1,2,3-triazole is known as "click chemistry." as defined by the scientist (Sharpless) and his colleagues at the beginning of the twenty-first century the year 2001 at the Scripps Research Institute [1] is a collection of strong interactions and selectivity for the quick synthesis of novel substances [2]. This reaction has given a fresh perspective on chemical synthesis that comes next nature by binding small molecules with a, click reactions are standard with a range Wide and high productivity, simple to carry out and create only innocuous byproducts that are disposable Chromographic column.[3]

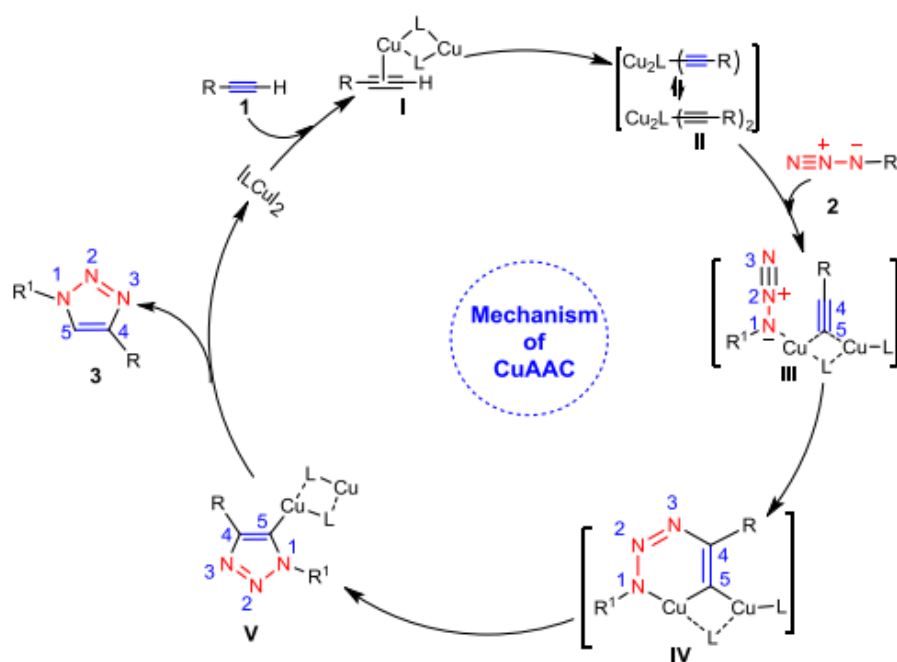


The cyclic addition reaction of 3,1-copper-catalyzed dipole (I) CuAAC (gradient mechanical) Includes copper in the first step where copper forms acetyl by coordination with alkyne,



In the second step, the azides are bonded with copper followed by the formation of an unconventional mineral cycle of Cu(II).

The intermediate then undergoes the decomposition of the ring to give copper a trisolvyl derivative, which gives when decomposed Proton product 1,2,3 – triazol required as in the diagram (1 – 1) [4,5]



Chemistry

In the first step, the synthesis of alkyne of piperazine and 5-cyano imidazole by treatment propargyl bromide, then prepare of 1,2,3-triazole through one pot reactions combining alkyne, benzyl chloride and sodium azide. Melting point (mp) were determined on stuart SMP30 digital advanced melting point Apparatus. Thin-layer chromatography (TLC) using aluminum sheets and benzene : methanol (4.5 :0.5). KBr discs were used to record IR spectra using a Shimadzu spectrophotometer. at faculty of education, department of chemistry, al-qadisiyah university. NMR spectra were recorded at faculty of science, al-basra university.

Prepare of 1,4-di(prop-2-yn-1-yl) piperazine 3

Dissolved piperazine (10mmol) in DMF (15 ml), and K_2CO_3 (5 equivalent 50mmol) were added at $0\text{ }^\circ\text{C}$. After 30 minutes, propargyl bromide was 2 equivalent (22 mmol) added to the reaction mixture and continue mixing to solution was left overnight at room temperature, and TLC verified that the reaction had finished before it was dumped over crushed ice. After forming a yellow precipitate, heated ethyl acetate was recovered and recrystallized. The result was produced with high yield of 84% [6,7]

Prepare of 1-(prop-2-yn-1-yl)-1H-imidazole-5-carbonitrile 4

Dissolved propargyl bromide (1.2 mmol) in (10ml) from DMF, added slowly to the mixture of 5-cyanoimidazole (1 mmol) and K_2CO_3 (2 mmol) dissolved in (5ml) of DMF for 10 hours at room temperature, stirring continuously, monitoring the reaction's completion using TLC, followed by washing the product with water and drying it.

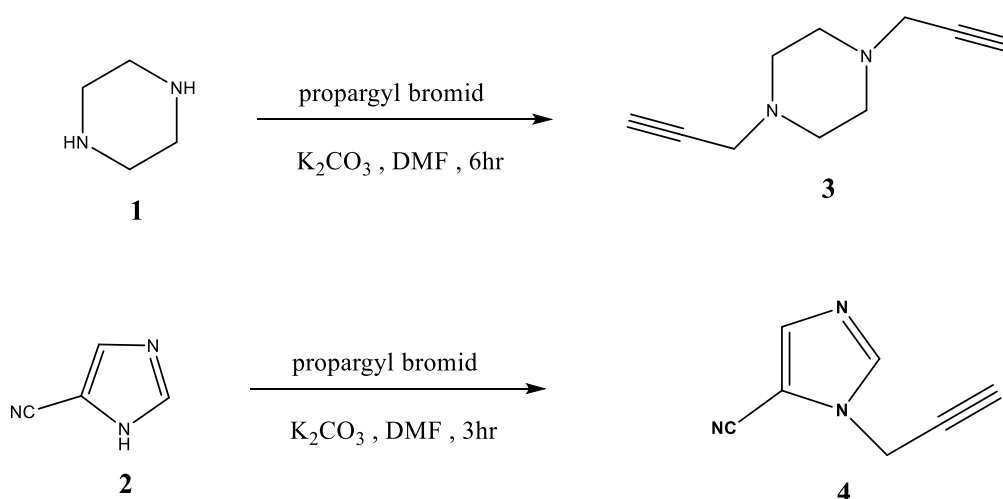
Preparation of 1,2,3-triazole derivatives by one pot reactions 5-8

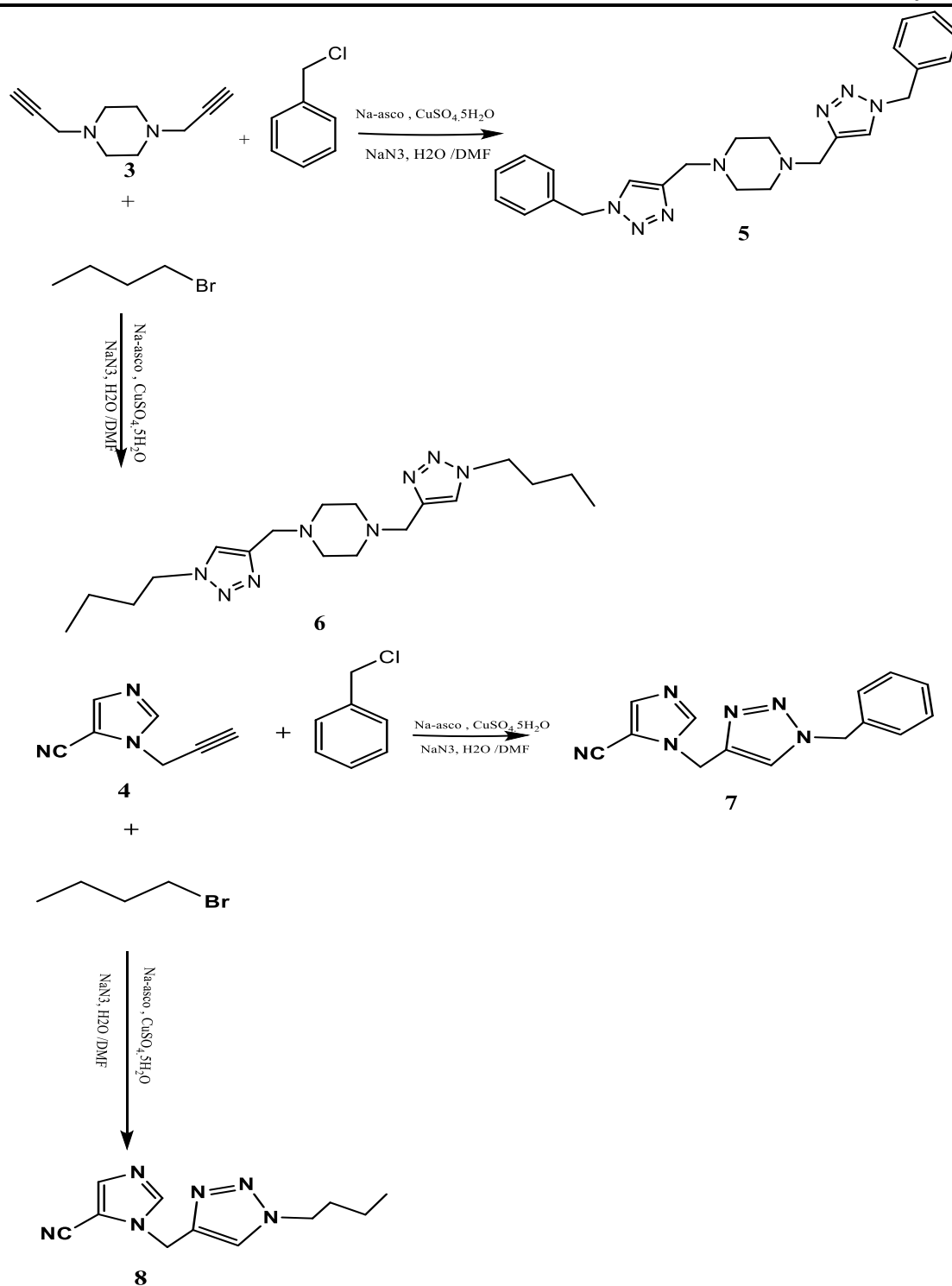
Dissolve (3.36mmol/1.68mmol) benzyl chloride / Bromo butane in a mixture of (6 ml) of ($H_2O:DMF$) at a ratio of (1:1) in a flask with a round bottom that is attached to a condenser, then add (3.36mmol/1.68mmol) of sodium azide dissolved in (3 ml) of distilled water. Leave the mixture for half an hour, then add (3.36mmol/1.68mmol) of compound 1,2 dissolved in (8 ml) of DMF. After that, add sodium ascorbate dissolved in a small amount of distilled water and Cupric sulfate pentahydrate. Stir the reaction at $65\text{ }^\circ\text{C}$ for (48-72) hr. Then cool the mixture with an ice bath and filter it to obtain a precipitate, which is purified with absolute ethanol.[8,9]

Results & Discussion

Through the use of click chemistry, the 1,2,3-triazole connected piperazine and 5-cyanoimidazole the work started by conversion of compounds (1,2) contain for N-H group treatment in DMF with propargyl bromide and K_2CO_3 present, it produced the compounds (3,4) in good to moderate yields.

The propargyl derivatives (3,4) were synthesized from which triazoles one pot reaction, where sodium azide is added to the alkyl halide first, and then after half an hour, the mixture is added to the propargyl derivative in the same vessel, By using sodium ascorbate and cooper sulfate in a regioselective manner, Cu(I)-catalyzed azide-alkyne cycloaddition produced 1,2,3-triazoles.





1,4-di(prop-2-yn-1-yl) piperazine 3 FT-IR spectrum showed the following bands cm^{-1} (neat): 3178 (C-H alkyne) stretching, 2985, 2850 (C-H aliphatic) stretching, 2127 (C≡C) stretching. ¹H NMR δ ppm: 2.98 (s, 8H), 3.4 (s, 2H), 4.1 (t, 4H). ¹³C NMR: δ 43.33, 56.01, 72.93, 78.58 ppm



1-(prop-2-yn-1-yl)-1H-imidazole-5-carbonitrile 4 FT-IR (KBr) 3128 (C-H alkyne), 2200 (C≡N), 2129 (C≡C), 1658 (C=N) cm^{-1} . ^1H NMR δ ppm: 8.6 (s, 2H), 9.2 (s, 2H), 4.45(s,2H),3.50(S,1H). ^{13}C NMR (75.5 MHz, CDCl_3 , δ): 116.3, 114.65, 123.57, 111.37, 138.3, 33.9, 67.9, 79.4 ppm.

1,4-bis((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)piperazine 5 FT-IR(KBr) 3032 (C-H aromatic), 2923, 2821 (C-H aliphatic), 2100 (N=N), 1615 (C=C) cm^{-1} . ^1H -NMR δ ppm: 7.17 (s, 2H), 7.11 (s, 2H), 5.54 (d, 2H), 7.78(s, 2H), 3.61 (s, 2H), 3.1 (d, 2H), 3.78 (t, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ : 128.6, 131.3, 129.7, 140.1, 54.1, 121.2, 130.3, 62.4.

1,4-bis((1-butyl-1H-1,2,3-triazol-4-yl)methyl)piperazine 6 FT-IR(KBr) 2923, 2821 (C-H aliphatic), 2140 (N=N), 1525 (C=C) cm^{-1} . ^1H -NMR δ : 0.9 (t, 3H), 1.46 (m, 2H), 2.65 (m, 2H), 8.2(s, 2H), 2.98 (s, 2H), 2.31 (d, 2H); ^{13}C NMR δ : 17.43, 24.62, 32.56, 61.0, 124.2, 130.7, 56.4, 55.3.

1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)-1H-imidazole-5-carbonitrile 7 FT-IR (KBr) 3030 (C-H aromatic), 2910, 2880 (C-H aliphatic), 1610 (C=N) cm^{-1} . ^1H NMR δ ppm: 7.86 (s, 1H), 9.21 (s, 1H), 5.73(s,1H),7.31(S,1H) 5.61 (s, 2H), 6.91(m, 5H). ^{13}C NMR δ : 117.1, 120.1, 131.5, 119.6, 130.0, 46.4, 123.6, 133.26, 127.6, 128.5, 57.8 ppm.

1-((1-butyl-1H-1,2,3-triazol-4-yl)methyl)-1H-imidazole-5-carbonitrile 8 FT-IR (KBr) 2910, 2880 (C-H aliphatic), 2181 (C≡N), 1721 (C=N) cm^{-1} . ^1H NMR δ : 1.45 (t, 3H), 3.4 (m, 2H), 4.1(m,2H),7.15(S,1H) 6.24 (s, 2H), 9.44 (s, 1H), 8.1 (s, 1H). ^{13}C NMR δ : 117.2, 113.87, 121.42, 139.3, 130.21, 46.2, 122.1, 55.2, 30.7, 22.5, 17.2 ppm.

Conclusions

The preparation of triazole compounds using copper-catalyzed addition reactions is a good method due to its high yield, selectivity, and efficiency. Additionally, the one-pot method is economical, saves time, and provides good yields of products.

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