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Design, Synthesis, And In Vitro Antibacterial, Cytotoxic, And Antifungal Studies For New Substitutes 2-Amino-4-Aryl-7-Propargyl Oxy-4H-Chromene-3-Carbonitriles By Effective Click Chemistry

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Abstract

A three-step procedure using sodium carbonate as a catalyst was used to manufacture a series of 2-amino-7-hydroxy-4H-chromene-3-carbonitriles **4a-c**. The solvent mixture used in the experiment was 96% ethanol and water, with a volume ratio of 1:20. A successful reaction between the corresponding hydroxyl chromenes derivatives and propargyl bromide resulted in the propargyl ether compounds **5a–c**, which are derived from chromene-3-carbonitriles. **5a–c** propargyl ethers and 1-azido-3-chlorobenzene were linked by 1H-1,2,3-triazole-tethered click chemistry to produce 4H-chromene-chlorophenyl conjugates **7a–c**. The ideal catalyst for this chemical reaction was CuI. From 77.68% to 82.33%, the yields of 1H-1,2,3-triazole were measured. The antimicrobial activity of each of the triazoles **7a-c** was examined in vitro. The following compounds were found to be efficient against several bacteria: B. subtilis (MCC 2010), S. aureus (MCC 2408), P. aeruginosa (MCC 2408), and E. coli (MCC 2412).

Keywords: 1H-1,2,3-Triazoles, 2-Amino-4H-chromene-3-carbonitriles, Propargyl ether, Antibacterial, Antifungal.

Introduction:

Due to their inherent conveniences and multiple benefits, multi-component coupling reactions (MCRs) are much sought after in the field of organic synthesis. The chemical transformation of three or more starting components is observed in the reactions indicated above, leading to the development of a product where the atoms from the starting materials are visible, either partially or entirely. An MCR is a method of synthesis that involves the assembly of components or parts by use of a succession of chemical reactions. Because of their essential biological actions, 4H-chromene derivatives and compounds containing a chromene moiety have remarkable applications in organic synthesis. Significant pharmacophores, these compounds are associated with a broad range of pharmacological actions. The compounds in issue have been discovered to exhibit antibacterial, hypolipidemic, anti-inflammatory, anti-proliferative, antioxidant, anticoagulant, antileishmanial, antitumor, cytotoxic, and anticancer actions, among other qualities [1,2]. Some heterocycles, such as 4H-pyran, 4H-chromene, and 1H-1,2,3-triazole, have recently demonstrated the ability to elicit interesting biological effects when combined [15,16]. Using appropriate 1-alkynes, click chemistry allows for the synthesis of the heterocyclic aromatic ring known as the 1H-1,2,3-triazole ring. Since the user has included a citation range in their content, it is already in an academic format. Implementing click chemistry via CuAAC (Copper(I)-catalyzed Alkyne-Azide Cycloaddition) requires the synthesis of 1-alkynes and organic azides. This study details a synthetic process for making 2-amino 4-aryl-7-propargyloxy-4H-chromene-3-carbonitriles with fluoro substituents from 2-amino-4-aryl-7-hydroxy-4H-chromene-3-carbonitriles. A typical product from this class is also tested for antibacterial properties.

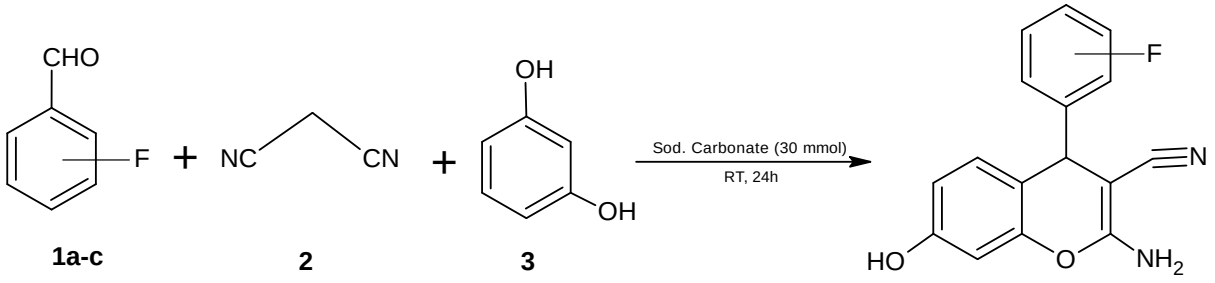
Experimental:

The reported melting points are unprocessed data obtained from an experimental procedure using the Myra melting point instrument, employing the open capillary method. The Brucker FT-IR Spectrometer was employed to get the infrared spectra of the KBr disc. The Bruker Avance II HD NMR 500MHz instrument was utilized to obtain ^{1}H NMR spectra in DMSO-d_6, with TMS serving as the internal reference compound. The Agilent LC-MS (ThermoScientific) instrument was utilized to obtain electrospray ionization (ESI) mass spectra in a methanol solvent. We received ultra-pure chemical reagents from the S. d. Fine Chemical Company located in India. All materials used for organic synthesis were of reagent grade. Analytical thin-layer chromatography (TLC) was performed using silica gel 60 WF254S aluminum sheets obtained from Merck, India. Visualization was achieved using UV light.

General procedure for the synthesis of 2-amino-4-aryl-7-hydroxy-4H-chromene-3-carbonitriles (4a-c):

A 30 mmol solution of sodium carbonate in 25 mL of water was combined with a mixture of fluoro-substituted benzaldehyde **1a-c** (10 mmol), malononitrile **2** (10 mmol), and resorcinol **3** (10 mmol) in a solution of water (25 mL) and 96% ethanol (1 mL). Under the monitoring of TLC, the reaction mixture was agitated for 24 hours at a temperature of 25 degrees Celsius. The compounds **4a-c** were obtained through recrystallization using a mixture of 96% ethanol and toluene

in a volume ratio of 1:1 or 2:1. The resulting mixture was filtered using suction and then washed with water until reaching a pH of 7.



1a-c **2** **3** **4a-c**

Where **a** = 2-fluoro, **b** = 3-fluoro, **c** =4-fluoro

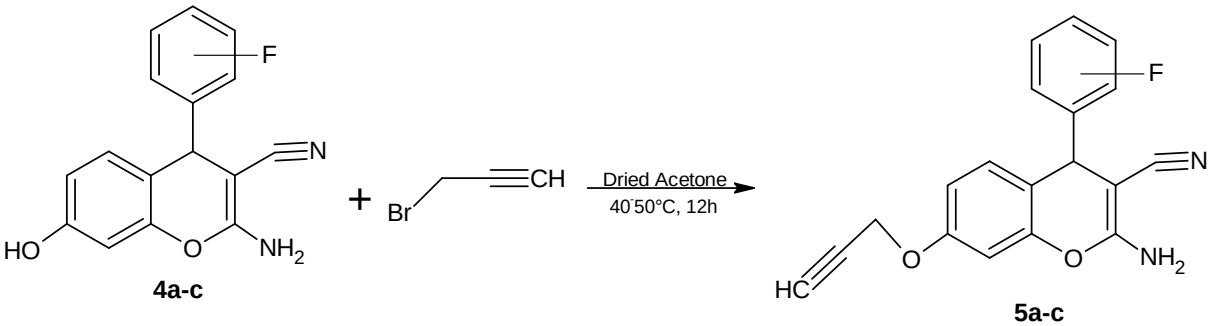
Scheme 1: Synthesis of 2-amino-4-aryl-7-hydroxy-4H-chromene-3-carbonitriles (**4a-c**)

2-amino-7-hydroxy-4-(2-fluorophenyl)-4H-1-benzopyran-3-carbonitrile (4a):
White crystals. From 2-fluorobenzaldehyde **1a** (20 mmol), malononitrile **2** (20 mmol), and resorcinol **3** (20 mmol). M. p. 187 °C (from 96% ethanol/toluene 2:1); IR (KBr), υ(cm^{-1}): 3330, 2962, 2230, 1604/1455, 1365, 1278; ^{1}H NMR (500 MHz, DMSO-d_6), δ (ppm): 9.578 (s, 1H, -OH), 7.215 (ddd, J = 8.20, 7.41, 1.27 Hz, 1H, Ar-H), 6.971 (s, 2H, -NH_2), 6.827-6.904 (m, 4H, Ar-H), 6.445 (dd, J = 7.93, 2.68 Hz, 1H, Ar-H), 6.376 (dd, J = 2.70, 0.43 Hz, 1H, Ar-H), 4.983 (s, 1H). ESI/HRMS: calcd. for $C_{17}H_{14}N_2O_3$, M = 294.36 Da, found: m/z 293.1446 $[M + H]^+$; Elemental anal., calcd: C, 69.38; H, 4.79; N, 9.52%; found: C, 69.30; H, 4.74; N, 9.36%.

2-amino-7-hydroxy-4-(3-fluorophenyl)-4H-1-benzopyran-3-carbonitrile (4b):
White crystals. From 3-fluorobenzaldehyde **1b** (20 mmol), malononitrile **2** (20 mmol), and resorcinol **3** (20 mmol). M. p. 189 °C (from 96% ethanol/toluene 2:1); IR (KBr), υ(cm^{-1}): 3305, 2925, 2227, 1603/1476, 1338, 1281; ^{1}H NMR (500 MHz, DMSO-d_6), δ (ppm): 10.024 (s, 1H, -OH), 7.615 (ddd, J = 8.19, 7.42, 1.25 Hz, 1H, Ar-H), 6.988 (s, 2H, -NH_2), 6.745-6.897 (m, 4H, Ar-H), 6.537 (dd, J = 7.95, 2.67 Hz, 1H, Ar-H), 6.379 (dd, J = 2.66, 0.41 Hz, 1H, Ar-H), 3.145 (s, 1H). ESI/HRMS: calcd. for $C_{17}H_{14}N_2O_3$, M = 294.36 Da, found: m/z 293.1446 $[M + H]^+$; Elemental anal., calcd: C, 69.38; H, 4.79; N, 9.52%; found: C, 69.30; H, 4.74; N, 9.36%.

2-amino-7-hydroxy-4-(4-fluorophenyl)-4H-1-benzopyran-3-carbonitrile (4c):
White crystals. From 4-fluorobenzaldehyde **1c** (20 mmol), malononitrile **2** (20 mmol), and resorcinol **3** (20 mmol). M. p. 195 °C (from 96% ethanol/toluene 2:1); IR (KBr), υ(cm^{-1}): 3303, 2928, 2226, 1601/1481, 1339, 1282; ^{1}H NMR (500 MHz, DMSO-d_6), δ (ppm): 10.356 (s, 1H, -OH), 7.578 (ddd, J = 8.22, 7.39, 1.19 Hz, 1H, Ar-H), 6.887 (s, 2H, -NH_2), 6.739-6.893 (m, 4H, Ar-H), 6.535 (dd, J = 7.95, 2.67 Hz, 1H, Ar-H), 6.376 (dd, J = 2.65, 0.40 Hz, 1H, Ar-H), 3.146 (s, 1H). ESI/HRMS: calcd. for $C_{17}H_{14}N_2O_3$, M = 294.36 Da, found: m/z 295.2345 $[M + H]^+$; Elemental anal., calcd: C, 69.38; H, 4.79; N, 9.52%; found: C, 69.22; H, 4.71; N, 9.35%.

General procedure for the synthesis of fluoro-substituted 2-amino-7-propargyloxy-4H-chromene-3-carbonitriles (5a-c):
A solution of 2-amino-4-aryl-7-hydroxy-4H-chromene-3-carbonitriles, properly substituted with fluorine groups, was treated with 15 mmol of anhydrous potassium carbonate. 4a-e, which is equivalent to 10 millimoles, dissolved in 25 mL of dried acetone. Subsequently, a solution of propargyl bromide 5 (containing 10 mmol and having a concentration of 80 wt.% in toluene) was slowly added to the mixture in the form of droplets. The reaction mixture was heated by agitation at a temperature of 50 □C in a water bath for a duration of 12 hours. Subsequently, the solvent was entirely evaporated under vacuum conditions at room temperature. The residue was treated with water to facilitate the dissolution of inorganic salts, specifically K_2CO_3 and KBr. The solid product, which had been separated, was subjected to filtration, followed by washing with water. It was then recrystallized from a combination of 96% ethanol and toluene (in ratios ranging from 1:1 to 1:2, by volumes). This process resulted in the production of propargyl ethers 5a-e of fluoro and methoxy-substituted 4H-chromene-3-carbonitriles.



Where F = **a** = 2-fluoro, **b** = 3-fluoro, **c** = 4-fluoro

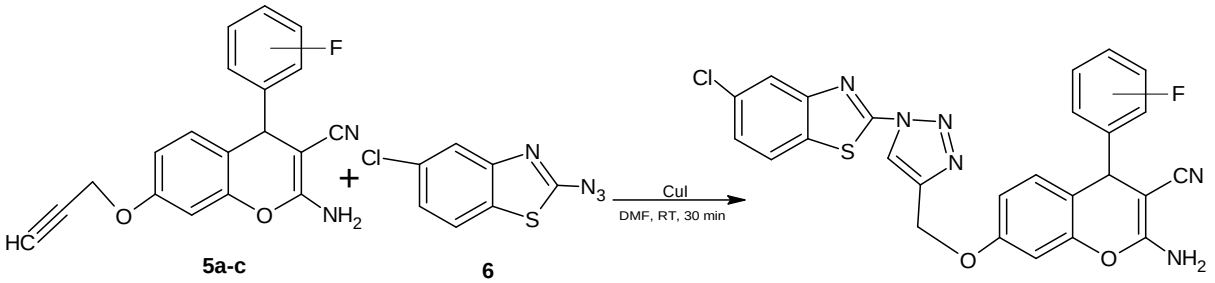
Scheme 2: Synthesis of fluoro substituted 2-amino-7-propargyloxy-4H-chromene-3-carbonitriles **(5a-c)**

2-amino-4-(2'-fluorophenyl)-7-propargyloxy-4H-chromene-3-carbonitrile (5a):
Brown crystals. From 2-amino-7-hydroxy-4-(2-fluorophenyl)-4H-1-benzopyran-3-carbonitrile **4a** (10 mmol), propargyl bromide (10 mmol), and anhydrous potassium carbonate (30 mmol). M. p. 189 °C (from 96% ethanol/toluene 2:1); IR (KBr), υ(cm^{-1}): 3178, 3110, 2963, 2227, 1582/1451, 1301, 1223, 1070, 741; ^{1}H NMR (500 MHz, DMSO-d_6), δ (ppm): 7.802-7.822 (s, 2H, -NH_2), 7.680-7.730 (dd, J = 7.88, 0.32 Hz, 2H, Ar-H), 7.620 (ddd, J = 7.99, 7.33, 1.51 Hz, 1H, Ar-H), 7.091-7.113 (m, 6H, Ar-H), 7.049-7.088 (dd, J = 2.39, 0.43 Hz, 2H, Ar-H), 5.291 (s, 2H, -CH_2-), 4.808 (s, 1H), 1.206 (s, 1H, CH). ESI/HRMS: calcd. for $C_{19}H_{13}N_2O_2F$, M = 320.32 Da, found: m/z 324.1477 $[M + H]^+$; Elemental anal., calcd: C, 71.24; H, 4.09; N, 8.75%; found: C, 70.88; H, 4.01; N, 8.69%.

2-amino-4-(3'-fluorophenyl)-7-propargyloxy-4H-chromene-3-carbonitrile (5b):
Brown crystals. From 2-amino-7-hydroxy-4-(3-fluorophenyl)-4H-1-benzopyran-3-carbonitrile **4b** (10 mmol), propargyl bromide (10 mmol), and anhydrous potassium carbonate (30 mmol). M. p. 193 °C (from 96% ethanol/toluene 2:1); IR (KBr), υ(cm^{-1}): 3113, 2979, 2932, 2288, 1603/1438, 1335, 1268, 1040, 740; ^{1}H NMR (500 MHz, DMSO-d_6), δ (ppm): 7.811-7.866 (s, 2H, -NH_2), 7.688-7.766 (dd, J = 7.11, 7.29 Hz, 2H, Ar-H), 7.666 (ddd, J = 7.66, 7.28, 1.49 Hz, 1H, Ar-H), 7.099-7.119 (m, 6H, Ar-H), 7.046-7.066 (dd, J = 2.33, 0.42 Hz, 2H, Ar-H), 5.288 (s, 2H, -CH_2-), 4.816 (s, 1H), 1.193 (s, 1H, CH). ESI/HRMS: calcd. for $C_{19}H_{13}N_2O_2F$, M = 320.32 Da, found: m/z 321.0546 $[M + H]^+$; Elemental anal., calcd: C, 71.24; H, 4.09; N, 8.75%; found: C, 70.96; H, 4.08; N, 8.71%.

2-amino-4-(4'-fluorophenyl)-7-propargyloxy-4H-chromene-3-carbonitrile (5c):
Brown crystals. From 2-amino-7-hydroxy-4-(4-fluorophenyl)-4H-1-benzopyran-3-carbonitrile **4c** (10 mmol), propargyl bromide (10 mmol), and anhydrous potassium carbonate (30 mmol). M. p. 196 °C (from 96% ethanol/toluene 2:1); IR (KBr), υ(cm^{-1}): 3115, 2937, 2227, 1604/1461, 1336, 1276, 1073, 740; ^{1}H NMR (500 MHz, DMSO-d_6), δ (ppm): 7.816-7.903 (s, 2H, -NH_2), 7.619-7.708 (dd, J = 7.11, 7.29 Hz, 2H, Ar-H), 7.718 (ddd, J = 7.61, 7.21, 1.45 Hz, 1H, Ar-H), 7.093-7.203 (m, 6H, Ar-H), 7.055-7.088 (dd, J = 2.29, 0.39 Hz, 2H, Ar-H), 5.267 (s, 2H, -CH_2-), 4.867 (s, 1H), 1.218 (s, 1H, CH). ESI/HRMS: calcd. for $C_{19}H_{13}N_2O_2F$, M = 320.32 Da, found: m/z 320.1456 $[M + H]^+$; Elemental anal., calcd: C, 71.24; H, 4.09; N, 8.75%; found: C, 71.03; H, 4.06; N, 8.62%.

General procedures for click chemistry of fluoro substituted 2-amino-4-aryl-7-propargyloxy-4H-chromene-3-carbonitriles with 1-azido-3-chlorobenzene (7a-c):
To prepare the reaction mixture, 25 mL of N, N-dimethylformamide (DMF) was added to 10-mmol of 2-amino-4-phenyl-7-propargyloxy-4H-chromene-3-carbonitrile **5a-c**, five mmol of CuI, and ten mmol of 1-azido-3-chlorobenzene **6**. To help the reactants dissolve, the mixture was gently stirred. The agitated reaction mixture was then supplemented with 50 mL of distilled water, successfully isolated a solid with a greenish-yellow color. Crystallization from a solvent mixture of 96% ethanol and toluene in a 2:1 by-volume ratio followed by filtration and washing with water was used to separate the solid components. The greenish-yellow solids known as compounds **7a–c** were produced as a by-product of this operation.



5a-c **6** **7a-c**

Where **a** = 2-fluoro, **b** = 3-fluoro, **c** =4-fluoro

Scheme 3: Synthesis of fluoro-substituted 2-amino-4-aryl-7-propargyloxy-4H-chromene-3-carbonitriles with 1-azido-3-chlorobenzene **(7a-c)**

2-Amino-4-(2′-fluorophenyl)-7-((5-chloro-1,3-benzothiazole)-1H-1,2,3-triazol-4-yl)methoxy)-4H-chromene-3-carbonitrile (7a):

Greenish yellow. From 2-amino-4-(2'-fluorophenyl)-7-propargyloxy-4H-chromene-3-carbonitrile **5a** (10 mmol), CuI (5 mmol), and 1-azido-3-chlorobenzene **6** (10 mmol). M. p. 209 °C (from 96% ethanol/toluene 2:1); IR (KBr), υ(cm^{-1}): 3311, 3053, 2201, 1595/1439, 1348, 1250, 1071, 738, 689; ^{1}H NMR (500 MHz, DMSO-d_6), δ (ppm): 7.340 (s, 2H, -NH_2), 7.549-7.620 (ddd, J = 8.10, 7.70, 1.50 Hz, 3H, Ar-H), 7.265-7.289 (dd, J = 2.52, 0.47 Hz, 1H, Ar-H), 7.182-7.552 (ddd, J = 8.29, 1.52, 0.50 Hz, 3H, Ar-H), 6.934 (ddt, J = 8.00, 4.31, 3.22 Hz, 1H, Ar-H), 6.779-6.924 (dd, J = 16.20, 8.05 Hz, 2H, -CH_2-), 4.920 (d, J = 7.78, 2.49 Hz, 1H, Ar-H). ESI/HRMS: calcd. for $C_{26}H_{16}N_6O_2ClSF$, M = 530.96 Da, found: m/z 530.1546 $[M + H]^+$; Elemental anal., calcd: C, 58.81; H, 3.04; N, 15.83%; found: C, 57.92; H, 3.02; N, 15.73%.

2-Amino-4-(3′-fluorophenyl)-7-((5-chloro-1,3-benzothiazole)-1H-1,2,3-triazol-4-yl)methoxy)-4H-chromene-3-carbonitrile (7b):

Greenish yellow. From 2-amino-4-(3'-fluorophenyl)-7-propargyloxy-4H-chromene-3-carbonitrile **5a** (10 mmol), CuI (5 mmol), and 1-azido-2-chlorobenzene **6** (10 mmol). M. p. 205 °C (from 96% ethanol/toluene 2:1); IR (KBr), υ(cm^{-1}): 3305, 3114, 2226, 1602/1462, 1408, 1338, 1268, 1072, 740, 680; ^{1}H NMR (500 MHz, DMSO-d_6), δ (ppm): 7.746 (s, 2H, -NH_2), 7.547 (dd, J = 7.83, 0.40 Hz, 3H, Ar-H), 7.203 (ddd, J = 8.43, 1.20, 0.53 Hz, 2H, Ar-H), 7.134 (ddd, J = 7.90, 7.69, 1.24 Hz, 2H, Ar-H), 6.773 (dd, J = 7.77, 0.41 Hz, 2H, Ar-H), 6.767 (ddd, J = 8.42, 1.20, 0.53 Hz, 2H, Ar-H), 5.210 (dd, J = 2.44, 0.39 Hz, 2H, Ar-H), 4.699 (s, 1H, Ali CH), 3.150 (s, 1H, Ali CH). ESI/HRMS: calcd. for $C_{26}H_{16}N_6O_2ClSF$, M = 530.96 Da, found: m/z 530.1546 $[M + H]^+$; Elemental anal., calcd: C, 58.81; H, 3.04; N, 15.83%; found: C, 58.37; H, 3.00; N, 15.76%.

2-Amino-4-(4′-fluorophenyl)-7-((5-chloro-1,3-benzothiazole)-1H-1,2,3-triazol-4-yl)methoxy)-4H-chromene-3-carbonitrile (7c):

Greenish yellow. From 2-amino-4-(4'-fluorophenyl)-7-propargyloxy-4H-chromene-3-carbonitrile **5e** (10 mmol), CuI (5 mmol), and 1-azido-2-chlorobenzene **6** (10 mmol). M. p. 211 °C (from 96% ethanol/toluene 2:1); IR (KBr), υ(cm^{-1}): 3339, 3295, 3080, 2193, 1592/1448, 1408, 1352, 1309, 1286, 1073, 732; ^{1}H NMR (500 MHz, DMSO-d_6), δ (ppm): 7.770 (s, 2H, -NH_2), 7.688 (ddd, J = 8.44, 1.20, 0.53 Hz, 2H, Ar-H), 7.575 (ddd, J = 7.99, 7.69, 1.24 Hz, 2H, Ar-H), 6.961 (dd, J = 7.80, 0.42 Hz, 3H, Ar-H), 6.646 (ddd, J = 8.43, 1.27, 0.56 Hz, 2H, Ar-H), 5.525 (dd, J = 2.48, 0.45 Hz, 2H, Ar-H), 4.754 (s, 1H, Ali CH), 3.168 (s, 1H, Ali CH). ESI/HRMS: calcd. for $C_{26}H_{16}N_6O_2ClSF$, M = 530.96 Da, found: m/z 530.1546 $[M + H]^+$; Elemental anal., calcd: C, 58.81; H, 3.04; N, 15.83%; found: C, 58.55; H, 3.03; N, 15.80%.

Biological assays:

In vitro antimicrobial activity:

In order to determine the antibacterial and antifungal activities of the synthesised 1H-1,2,3-triazoles 7a-e against both Gram-positive and Gram-negative bacterial species, they were tested in vitro. B. subtilis (MCC 2010) and S. aureus (MCC 2408) were the Gram-positive bacteria utilised in this investigation. Two examples of Gram-negative bacteria were Pseudomonas aeruginosa (MCC 2408) and Escherichia coli (MCC 2412). As described in our previous work [18], the minimum inhibitory concentration (MIC) approach was used to conduct the evaluations. Mueller-Hinton broth was used in the micro broth dilution procedure [19]. The substances being studied were dissolved in 1 mg/mL dimethyl sulfoxide (DMSO). Streptomycin and vancomycin were the drugs referenced in Table 1. Through the process of diluting the aforementioned test chemicals and benchmark medicines, solutions were produced with concentrations ranging from 400 to 0.78 millimolar (mM). To create the inoculum, a broth that had been incubated for four to six hours was diluted until its turbidity was similar to that of a 0.5 McFarland standard. The final concentration in the test tray was 5 x 105 CFU/mL, which was achieved by diluting the substance in broth media. The plates were left to incubate at 35°C for a full day. The concentration of the chemical that completely suppressed visible development was called the minimal inhibitory

concentration (MIC). The tests were repeated three times. In Table 1 you can see the MIC values for all the drugs that were tested and the reference medicine.

Antifungal action in vitro:Three fungal strains, including S. cerevisiae (MCC 1033) and Candida albicans (MCC 1439), were used to evaluate the antifungal activity of compounds 7a-e in vitro. According to what was previously stated [17], Saburoud's dextrose agar (Hi-Media) was used in the agar dilution procedure. To determine how well fluconazole worked against fungal infections, it was used as a pharmacological agent. For every chemical and reference medication that was tested, solutions were prepared at concentrations of 200, 100, 50, 25, 12.5, 6.25, 3.12, 1.56, and 0.78 mM. The concentration of each microbe was adjusted to 10 CFU/mL by making a suspension. The compounds under examination were diluted using agar plates before these suspensions were added. The incubation temperature was set at 35 □C for the plates. It took 72 hours to determine the minimum inhibitory concentrations (MICs) [18].

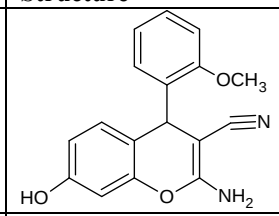
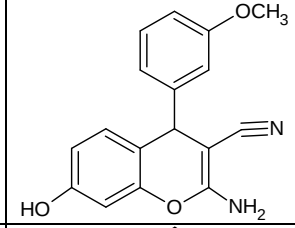
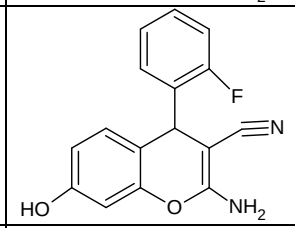
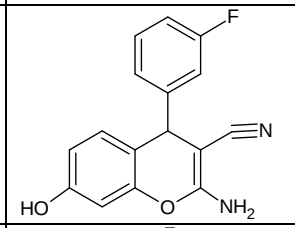
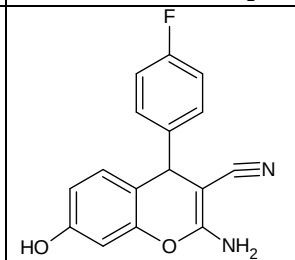
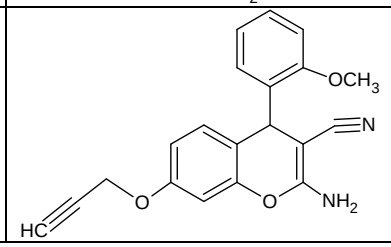
Finding the lowest inhibitory dosages of each antibiotic against commonly used fungal strains was the goal of the study. Three unique instances were used to conduct the experiments. The examined compounds and reference medications' minimum inhibitory concentration (MIC) values are shown in Table 2.

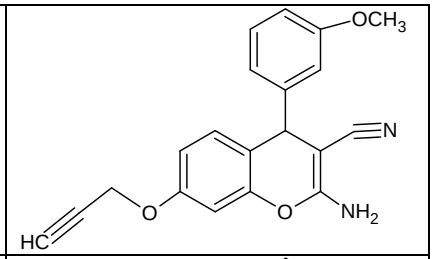
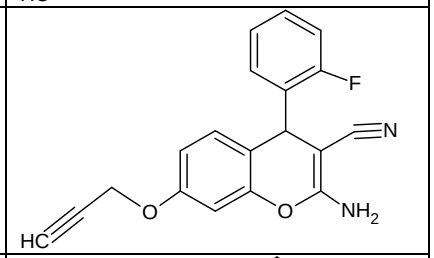
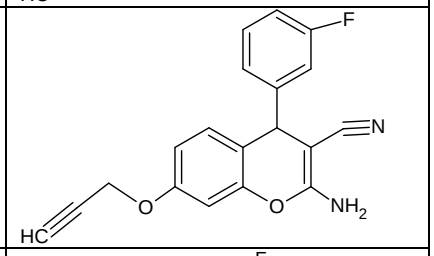
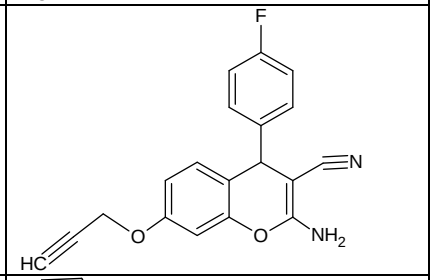
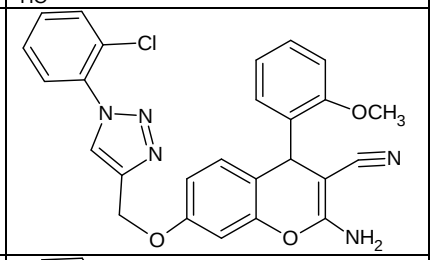
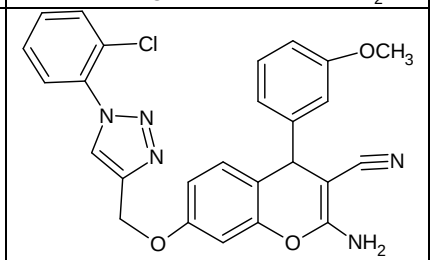
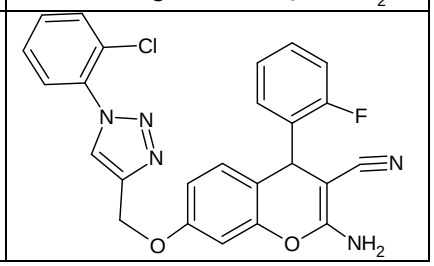
Discussion and Findings:A three-step process utilising substituted fluoro and methoxy benzaldehydes 1a-e, malononitrile 2, and resorcinol 3 was employed to synthesise 2-amino-4-aryl-7-hydroxyl-4H-chromene-3-carbonitriles 4a-e (Scheme 1). The experimental specifications for this three-step process called for a catalyst concentration of 30 mmol of sodium carbonate. As shown in Scheme 1 [19-21], the reaction was carried out for 24 hours at room temperature. At a volumetric ratio of 1:20, a co-solvent made of 96% ethanol was used. A range of 74.11 to 84.54% was observed in the isolated yields. Separate substituted 7-propargyl ethers 5a–e were produced by converting the 2-amino-4-aryl-7-hydroxy-4H-chromene-3-carbonitriles 4a–e described earlier.The 6-azido-2-chlorobenzene precursor was another one utilised in click chemistry. 2-Chlorobenzene and sodium azide were combined in either dried DMF or acetone water to produce this chemical [22–24]. To avoid the azide group's breakdown by water, dried acetone was used as a solvent. It was also much easier to extract acetone from the reaction mixture when acetone was used. A multi-gram scale synthesis of the crystalline solid of 1-azido-2-chlorobenzene 6 was accomplished.Current research indicates that several click chemistry catalysts have been found [25]. In order to find the optimal conditions for the click chemistry reaction with propargyl ether of 4H-chromene-3-carbonitriles 5a-e and 1-azido-2-chlorobenzene 6, a detailed investigation was carried out on the catalytic conditions of the CuI reaction with compound 7a-e and the aforementioned 1-azido-2-chlorobenzene (Scheme 3).An absorption band in the infrared spectrum ranging from 2928 to 2979 cm-1 was used to identify the hydroxyl group for 4H-chromenes 4a-e, and two additional absorption bands between 3300 and 3330 cm-1 were used to verify the existence of an amino group. There was a correlation between the nitrile functional group and absorption peaking at 2202-2230 cm-1. The 1H NMR spectra of chromenes 4a-e shared a proton's integral height at □ = 4.580-4.983 ppm, suggesting that this signal belonged to the proton at position 4. Possible applications of this signal include differentiating 4H-pyrans from 4H-chromenes. Additionally, the chemical shift at □ = 9.631-10.072 ppm proved the presence of the hydroxyl group at position 7 of the chromene ring. In chromenes 4a-e, a resonance signal was detected for the amino group at position 2 at □ = 6.384-7.205 ppm.7.-Propargyl ether 5a-e was structurally synthesised from 7-hydroxy-4H-chromes 4a-e, according to spectral data (IR, NMR, and MS). We utilised infrared and nuclear magnetic resonance spectra to search for the acetylenic unit that is present in the terminal triple bond of chromene propargyl ethers. Between 3300 and 3350 cm-1, the ethers' characteristic infrared absorption bands, which indicate the stretching vibration of the hydroxyl group, have vanished. The stretching vibrations of the CH and CC bonds were revealed by the simultaneous observation of absorption bands at 3380-3390 cm-1 and 2120-2100 cm-1. In the 2200-2180 cm-1 range, the nitrile group's absorption band was very strong, very near to the rather moderate CC absorption band. But two extra absorption bands in the 3450-3440 and 3280-3200 cm-1 regions of the 7-propargyloxy-4H-chromenes 5a-e IR spectra showed that the amino group was present. The infrared spectra of the first four 2-amino-4-aryl-7-hydroxy-4H-chromene-3-carbonitriles (a–e) showed comparable absorption bands. The data showed that the primary amino group at position 2 of the chromene ring's pyran moiety was O-alkylated instead of N-alkylated when the compound was reacting with propargyl bromides. The 1H NMR spectra of chromenes 5a-e confirmed this, as they did not exhibit any chemical shift in the hydroxyl group's region at position 7 (□ 9.63-10.72 ppm, singlet, 1H) and the amino group's region at position 2 (□ 7.624-7.902 ppm, singlet, 2H).The nitrile functional group's absorption band was 2225-2288 cm-1. The original 7-hydroxy chromene derivatives' 1H NMR spectra showed propargyl group signals, confirming the transformation. A proton's integral intensity falls inside the spectral area between □ 1.113 and 1.193 ppm, which was identified as the acetylenic proton in the o-propargyl group. The coupling constant of this signal was J = 2.18-2.56 Hz, and its interactions with the two methylene protons in the propargyl chain gave it a multiplicity of three. J = 2.62-2.77 Hz and □ = 3.266-3.309 ppm (in triplet) were determined to be the range of the methylene group resonance signal. A signal like this would travel downfield because of the diamagnetic action of an electronegative oxygen atom.

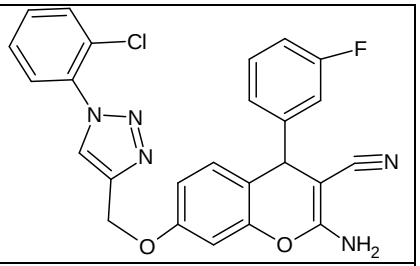
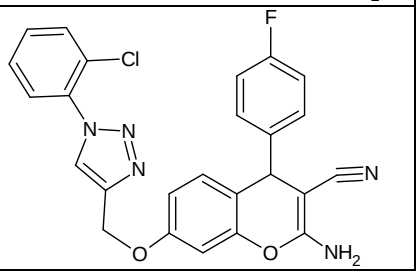
In the region of □ 5.290-5.302 ppm, shape resonance singlet signals were seen for the chromene ring proton at position 4, which is an allylic-type proton. The AMX spin pattern was matched chemically by three protonal interactions in the chromene benzene ring. H-5 proton had a ppm range of 7.102 to 7.123 in a doublet with J = 8.00 to 8.12 Hz, H-6 proton had a ppm range of 7.220 to 7.598 in a doublet of doublets with J = 0.39 to 0.43 and 7.8 to 7.9 Hz, and H-8 proton had a ppm range of 6.60 to 6.76 in a doublet with J = 1.90 to 2.33 Hz. Absorption bands between 1590 and 1607 cm-1, signs from carbon and proton resonances, and other evidence all pointed to the presence of aromatic rings.

Verification of the structural synthesis of 1-azido-2-chlorobenzene-substituted 2-amino-4-aryl-7-propargyloxy-4H-chromene-3-carbonitriles with fluoro and methoxy substituents A review of spectral data, including that from infrared, nuclear magnetic resonance, and mass spectrometry, lends credence to 7a-e. The acetylenic unit, consisting of a terminal triple bond, found in propargyl ethers of chromenes was the primary focus of the work. By analysing infrared and nuclear magnetic resonance spectra, this was achieved. A striking lack of absorption bands, particularly in the 2900–2950 cm-1 region, which is often linked to the stretching vibration of the acetylene group, was seen in the infrared spectra of these ethers. Two absorption bands were detected simultaneously in the 2150-2175 cm-1 spectral region. This stretching vibration of the N=N bond is responsible for these bands. On the other hand, 7a-e showed two extra absorption bands in the 3311-3380 cm-1 range in their infrared spectra, which means that these compounds include an amino group. Infrared spectra from the initial 5a-e also showed these regions of absorption. According to the data given, the acetylene group is involved in 1-azido-2-chlorobenzene reactions. The regions at □1.113-1.193 ppm (singlet, 1H) correspond to the acetylene group because there is no chemical shift there.

Table 1: Based on spectral studies, the structures of complexes are assigned as follows;

Comp Code	MW	Formula	MP	Structure
4a	294	$C_{17}H_{14}N_2O_3$	197	
4b	294	$C_{17}H_{14}N_2O_3$	192	
4c	282	$C_{16}H_{11}N_2O_2$	187	
4d	282	$C_{16}H_{11}N_2O_2$	189	
4e	282	$C_{16}H_{11}N_2O_2$	195	
5a	332	$C_{20}H_{16}N_2O_3$	196	

5b	332	$C_{20}H_{16}N_2O_3$	192	
5c	320	$C_{19}H_{19}N_2O_2F$	189	
5d	320	$C_{19}H_{19}N_2O_2F$	193	
5e	320	$C_{19}H_{19}N_2O_2F$	196	
7a	542	$C_{27}H_{19}N_6O_3Cl$	203	
7b	542	$C_{27}H_{19}N_6O_3Cl$	209	
7c	530	$C_{26}H_{16}N_6O_2F$	208	

7d	530	$C_{26}H_{16}N_6O_2F$	205	
7e	530	$C_{26}H_{16}N_6O_2F$	211	

Biological screening:

Antibacterial assays:
All the synthesized 1H-1,2,3-triazoles were screened for their in vitro antibacterial activity against two representative gram-positive bacteria, B. subtilis (MCC 2010), S. aureus (MCC 2408), and two representative Gram-negative bacteria, which were E. coli (MCC 2412), P. aeruginosa (MCC 2080). Antibacterial effectiveness was measured against streptomycin and vancomycin. Streptomycin and vancomycin are still used to treat a range of bacterial illnesses, with the former used to treat severe, life-threatening infections by Gram-positive bacteria that (are) refractory to other antibiotics. These latter drugs were used to treat life-threatening conditions brought on by Gram-negative bacteria like P. aeruginosa. Tabulated evaluations for items **7a-e** are provided there. **Table 2** shows that both low and high concentrations of the new molecules tested showed antibacterial action against the tested microorganisms. When compared to the MIC values of the reference chemical, practically all of the compounds tested exhibited low to moderate activity against the organisms used in the tests. Here are the MICs for these commonly used drugs: The MICs for ciprofloxacin (6.25 mM for Gram-positive bacteria) and for vancomycin (3.12 mM for Gram-negative bacteria) are, respectively. MIC values of 3.12-12.5 mM were found for certain 1H-1,2,3-triazoles against Gram-positive bacteria (B. subtilis, and S. aureus). Compounds **7d** (MIC = 3.12 mM), **7e** (MIC = 6.25 mM), and **7a** (MIC = 3.12 mM) were the most effective triazoles against B. subtilis. The minimum inhibitory concentrations (MICs) of **7a, 7c**, and **7d** against S. aureus were 3.12, 6.25, and 3.12 mM, respectively. With the exception of **7a, 7b, 7d**, and **7e** (MICs = 3.12 mM), the aforementioned triazoles exhibited more significant inhibitory activity than ciprofloxacin but less than vancomycin. Some others were less active against these bacteria with MIC values of 12.5-25 mM.

Antifungal assay:
The aforementioned 1H-1,2,3-triazoles **7a-e** were tested for their antifungal efficacy against a variety of fungal strains. These included Candida albicans (MCC 1439), and Saccharomyces cerevisiae (MCC 1039), reference included fluconazole. Fluconazole is an antifungal drug that belongs to the first generation of triazoles. Fluconazole had MIC values of 1.56, and 3.12 against the same two.
Table 3 displays the acquired results. Notably, the triazoles **7a-e** examined were more resistant to Candida albicans (MCC 1439) than fluconazole, but they were more active against S. cerevisiae. The MICs for **7b, 7c**, and **7d** were all less than 3.12-12.5 mM, making them all effective against S. cerevisiae. Inhibitory concentrations (MIC) of **7a** and **7e** against these fungi were as low as 1.56-3.12 mM.

Conclusion:

Williamson's ether synthesis was used to produce a sequence of 2-amino-4-aryl-7-propargyloxy-4H-chromene-3-carbonitriles (**5a-t**) from the equivalent 2-amino-7-hydroxy-4H-chromene-3-carbonitriles (**4a-e**). The K_2CO_3/acetone method was employed in these synthesis reactions involving propargyl bromide. This technique gave the ethers **5a-e** in excellent yields. The spectral studies help to confirm the structure of 2-amino-4-aryl-7-propargyloxy-4H-chromene-3-carbonitriles. By reacting with 1-azido-2-chlorobenzene using the CuI method, click chemistry was applied to these propargyl ethers. Research was done on the catalysts used in this chemical. Based on the data, it was clear that CuI was the best catalyst for the aforementioned chemical reaction. From 74.11 to 84.54%, 1H-1,2,3-triazoles **7a-7e** were produced. Inhibitory actions against selected Gram-positive and Gram-negative bacteria as well as yeasts were tested for

in all synthesized fluoro and methoxy-substituted 2-amino-4-aryl-7-propargyloxy-4H-chromene-3-carbonitriles with 1-azido-2-chlorobenzene conjugates. With MIC values between 3.12 and 12.5 mM, certain compounds showed considerable inhibitory action against the investigated bacteria. The MIC values of the triazoles **7c, 7d**, and **7e** against three clinical MRSA isolates ranged from 1.56 to 6.25 mM, respectively.

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