

Article

Unveiling Silver Catalysis to Access 5-Substituted Tetrazole Through [3+2]Cycloaddition Reaction, Utilizing Novel Silver Supramolecular Coordination Polymer-Based Catalyst: A New Green Horizon

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Abstract

A novel Ag(I) coordination polymer, $[Ag_2(bipy)(btca)]_n$, (**SCP 1**) was synthesized using 4,4'-bipyridyl (bipy) and 1,2,4,5-benzene-tetracarboxylic acid (H_4BTC). Characterization by FT-IR, $^1H/^{13}C$ NMR, and single-crystal X-ray diffraction confirmed its 3D network structure. The structure of **SCP 1** consists of two chains arranged in . . .ABAB. . . fashion. Chain A is one-dimensional, containing $[Ag(4,4'-bipy)]_n$ chain, while chain B is free, containing uncoordinated 1,2,4,5-benzene tetracarboxylate and water molecules. The stacking and argentophilic interactions extend the chain A of $[Ag(4,4'-bipy)]_n$ into a two-dimensional layer. In contrast, chain B of uncoordinated 1,2,4,5-benzene tetracarboxylate and water molecules form a 1-D chain through extensive hydrogen bonds between water molecules and BTC ions and between water molecules themselves. Chains A and B are connected through extensive hydrogen bonds, generating a three-dimensional network structure. This Silver I supramolecular coordination polymer (**SCP 1**) demonstrated high catalytic activity as a recyclable heterogeneous catalyst for the synthesis of 5-substituted 1H-tetrazoles via [3+2] cycloaddition of NaN_3 and terminal nitriles under solvent-free conditions in a Q-tube pressure reactor (yields: 94–99%). A mechanistic proposal involving cooperative Lewis acidic Ag(I) sites and Brønsted acidic -COOH groups facilitates the cycloaddition and protonation steps. **SCP 1** catalyst exhibits reusability up to 4 cycles without significant loss of activity. The structural stability of the **SCP 1** catalyst was assessed based on PXRD and FTIR analyses of the catalyst after usage, confirming its integrity during the recycling process.

Keywords: Q-tube; silver (I) supramolecular coordination polymer; 5-substituted tetrazole; green chemistry; sustainability



Academic Editor: Ken-ichi Fujita

Received: 30 July 2025

Revised: 25 September 2025

Accepted: 7 October 2025

Published: 10 October 2025

Citation: El-bendary, M.M.; Akhdhar, A.; Davaasuren, B.; Al-Bogami, A.S.; Saleh, T.S. Unveiling Silver Catalysis to Access 5-Substituted Tetrazole Through [3+2]Cycloaddition Reaction, Utilizing Novel Silver Supramolecular Coordination Polymer-Based Catalyst: A New Green Horizon. *Catalysts* **2025**, *15*, 969. <https://doi.org/10.3390/catal15100969>

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1. Introduction

Tetrazole is a ring-shaped, five-membered heterocyclic compound with one carbon atom and four nitrogen atoms. Tetrazoles have varied applications, serving as plant growth regulators in agriculture and as sweeteners in the food sector [1]. Tetrazole derivatives

are utilized in explosives, missile propellants, and gas generators for automotive airbags owing to their substantial energy release and non-toxic byproducts [2].

It plays an important role in medicinal chemistry due to its unique chemical properties [3]. Incorporating tetrazoles into various compounds results in different pharmacological effects, including anti-inflammatory [4], analgesic [5], anticonvulsant [6], anti-hypertensive [7], and antibacterial [8] properties, making it a vital building block in drug development. Due to their similarity to carboxylic acids, which demonstrates bioisosterism, tetrazoles exhibit superior pharmacokinetic properties. Notably, this modification can enhance drug stability, improve solubility, and increase the rate of breakdown in the body—key factors in the development of medications [9,10]. Figure 1 illustrates that many existing medications on the global market contain the tetrazole moiety. For instance, drugs aimed at lowering blood pressure include tetrazole-based antihypertensives such as valsartan and losartan [11,12].

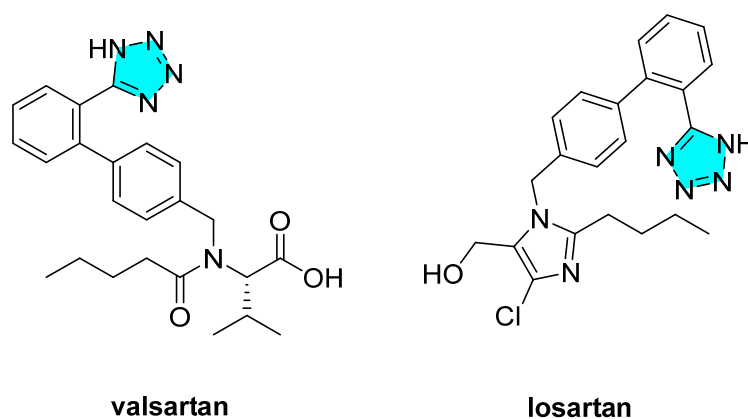
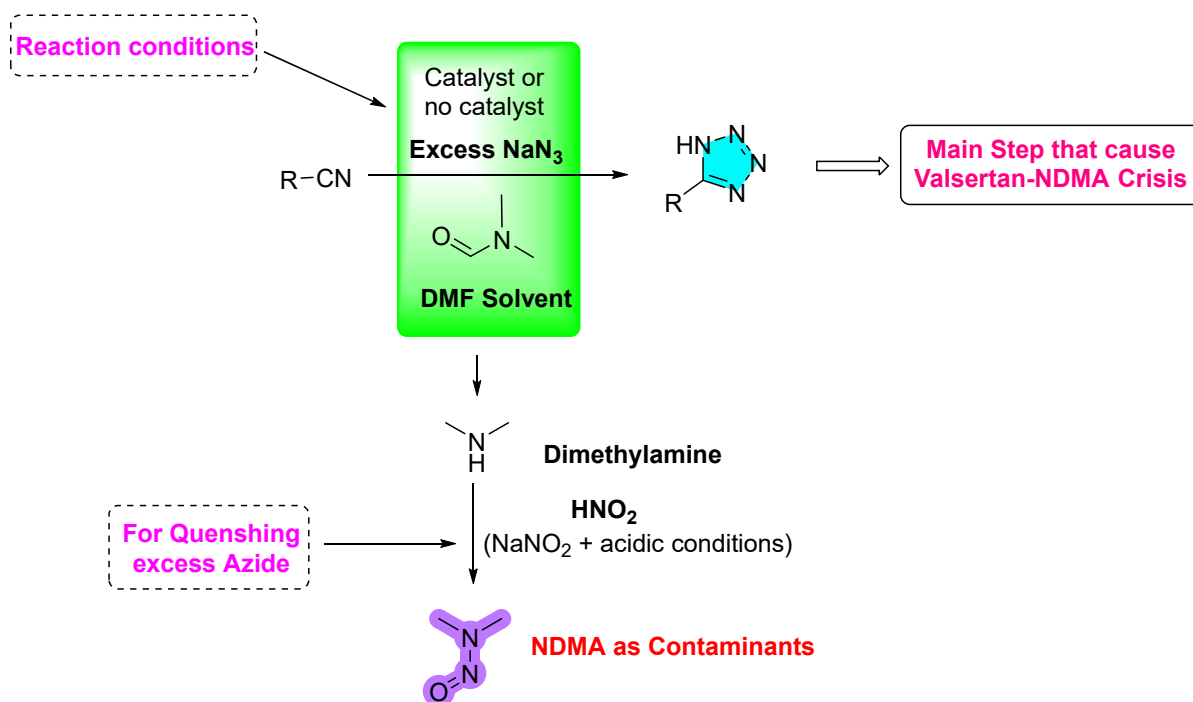


Figure 1. Tetrazole-based antihypertensive drugs.

The news surprised us that many batches of the Valestran medicine had to be recalled due to contamination with *N*-nitroso dimethylamine (NDMA), which the FDA classifies as a carcinogenic chemical. This ingredient is not used in its production, making the finding surprising [13]. As a result, testing revealed that the primary source of contamination was the main industrial process used during production (Scheme 1) [14]. NDMA formation occurs because of the procedure used to eliminate or quench the excess azide in the synthetic process that converts the cyano group into the tetrazole moiety. The main concern is that, although NDMA has been detected at low concentrations, these drugs are used to treat chronic diseases and can accumulate in the patient's body, leading to serious health risks. This situation has raised a red flag, prompting long-lasting reforms in medication manufacturing laws worldwide by exposing key shortcomings in pharmaceutical quality control and supply chain oversight [15,16].

The following table (Table 1) shows the different methods and catalytic systems used to synthesize tetrazoles from organic nitriles.

The above-reported literature (Table 1) showed significant differences in activity, selectivity, recyclability, and environmental friendliness for the synthesis of tetrazoles from organic nitriles. While microwave-assisted and heterogeneous catalyst systems often reduce reaction times and allow for easier product separation and higher yields, some suffer from high costs, limited substrate scope, or difficulties in catalyst recovery and reuse.



Scheme 1. Origin of NDMA in the synthetic process of nitrile to tetrazole.

Table 1. Diverse approaches for the synthesis of tetrazoles.

Catalyst	Reagent	Condition	Reference
Homogeneous	I_2 , DMF	Reflux, 6–18 h	[17]
	$\text{Et}_3\text{N.HCl}$, PhNO_2	MW, 100 °C	[18]
	AlCl_3 , ZnCl_2	200 °C, 3–10 min	[19]
	TMSCl , NMP	MW, 220 °C, 15–25 min	[20]
	$\text{Et}_3\text{N.HCl}$, DMF	MW, 130 °C, 2 h	[21]
	BiCl_3	1 h at 120–160 °C	[22]
Heterogeneous	$\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-LY-C-D-Pd}$	PEG-400, 100 °C, 0.5–2 h	[23]
	AMWCNTs-O-Cu(II)	DMF, 70 °C	[24]
	Ag-TiO ₂ and Ag-SiO ₂ nanostructures	DMF, 120 °C	[25]

On the other hand, green chemistry focuses on developing safer and more environmentally friendly chemical products and processes [26]. Crucial elements of green chemistry's homogeneous catalysis exhibit efficiency and reduced energy requirement. Because they are effective, versatile, and long-lasting, catalysts made of silver metal complexes are crucial for enhancing chemical processes. New catalyst applications and the introduction of a practical solution for the valsartan-NDMA crisis are being uncovered through their ongoing study. Furthermore, one application of green chemistry is the use of Q-tube pressure reactors in organic synthesis (Figure 2), enhancing efficiency, accelerating the rate of reaction, decreasing waste, and increasing safety [27–29].

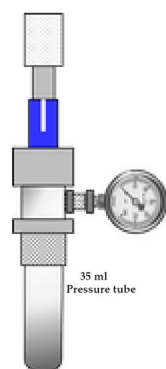


Figure 2. Q-Tube System.

Therefore, when catalysts are used in conjunction with a Q-tube, a synergistic effect is anticipated. In particular, a Q-tube reactor's reaction rate is sensitive to internal pressure. The activation energy needed to initiate the reaction decreases at higher pressures due to more frequent collisions between the reactant molecules [30], resulting in a highly efficient and environmentally friendly process. Considering all of the above and continuing to implement green procedures for various organic reactions [31–35], we introduce a novel silver supramolecular coordination polymer-based catalyst that overcomes the challenges of eliminating excess azides in the transformation of the nitrile group into tetrazole using Q-Tube technology as an energy-efficient reaction technique.

2. Results and Discussion

2.1. Crystal Structure of the $\{[Ag_4(4,4'-Bpy)_2] \cdot (BTC) \cdot 3H_2O\}$, **SCP 1**

The reaction of 4,4'-bipyridine (4,4'-bpy), 1,2,4,5-benzene tetracarboxylate (BTC), and silver nitrate at room temperature in water/acetonitrile/ammonia solvent affords the brown needle crystals of supramolecular coordination polymer (SCP) $\{[Ag_4(4,4'-bpy)_2] \cdot (BTC) \cdot 3H_2O\}$, (1). **SCP 1** is orthorhombic and crystallizes in the space group Cmce. Significant crystal data for **SCP 1** are listed in Table 2, while Table 3 shows bond lengths (Å) and bond angles (deg.).

Table 2. Crystal data and structure refinement for **SCP 1**.

Empirical Formula	$C_{30}H_{24}Ag_4N_4O_{11}$
Formula weight	1047.97
Temperature/K	293 (2)
Crystal system	orthorhombic
Space group	Cmce
a/Å	14.269 (2)
b/Å	22.673 (5)
c/Å	17.088 (3)
$\alpha/^\circ$	90
$\beta/^\circ$	90
$\gamma/^\circ$	90
Volume/Å ³	5528.3 (17)
Z	8
$\rho_{\text{calc}}/\text{cm}^3$	1.829
μ/mm^{-1}	1.480
F(000)	3048.0
Crystal size/mm ³	0.223 × 0.18 × 0.1
Radiation	MoK α (λ = 0.7107)
2 Θ range for data collection/ $^\circ$	5.84 to 54.988
Index ranges	−18 ≤ h ≤ 18, −29 ≤ k ≤ 29, −12 ≤ l ≤ 22

Table 2. Cont.

Empirical Formula	C ₃₀ H ₂₄ Ag ₄ N ₄ O ₁₁
Reflections collected	22,145
Independent reflections	3304 [R _{int} = 0.0648, R _{sigma} = 0.0403]
Data/restraints/parameters	3304/40/248
Goodness-of-fit on F ²	1.017
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0380, wR ₂ = 0.0855
Final R indexes [all data]	R ₁ = 0.0813, wR ₂ = 0.1040
Largest diff. peak/hole/e Å ^{−3}	0.69/−0.43

Table 3. Bond lengths (Å) and bond angles (deg) of the SCP 1.

Bond	Å d	Bond	Deg, °
Ag1–N1	2.123(4)	N1–Ag1–N2 ⁱ	180.0
Ag1–N2 ⁱ	2.132(3)	N3–Ag2–N4 ⁱⁱ	174.24 (12)
Ag2–N3	2.122(4)	Ag1–N2–C9	119.24 (3)
Ag2–N4 ⁱⁱ	2.140(4)	Ag2–N3–C14	122.31 (10)
O2–C1	1.256(3)	Ag2–N3–C10	119.86 (3)
C1–O1	1.245(4)	Ag1–N1–C4	120.50 (3)
Ag1–Ag1 ⁱ	3.635	Ag2–N4–C19	117.41 (7)
		Ag2–N4–C18	127.37 (7)

ⁱ = +X, 1/2 + Y, 1/2 − Z; ⁱⁱ = +X, −1/2 + Y, 1/2 − Z.

The molecular structure of **SCP 1** consists of four silver atoms, two 4,4'-bpy bridging ligands, one free 1,2,4,5-benzene tetracarboxylate molecule, and three waters of crystallization, Figure 3.

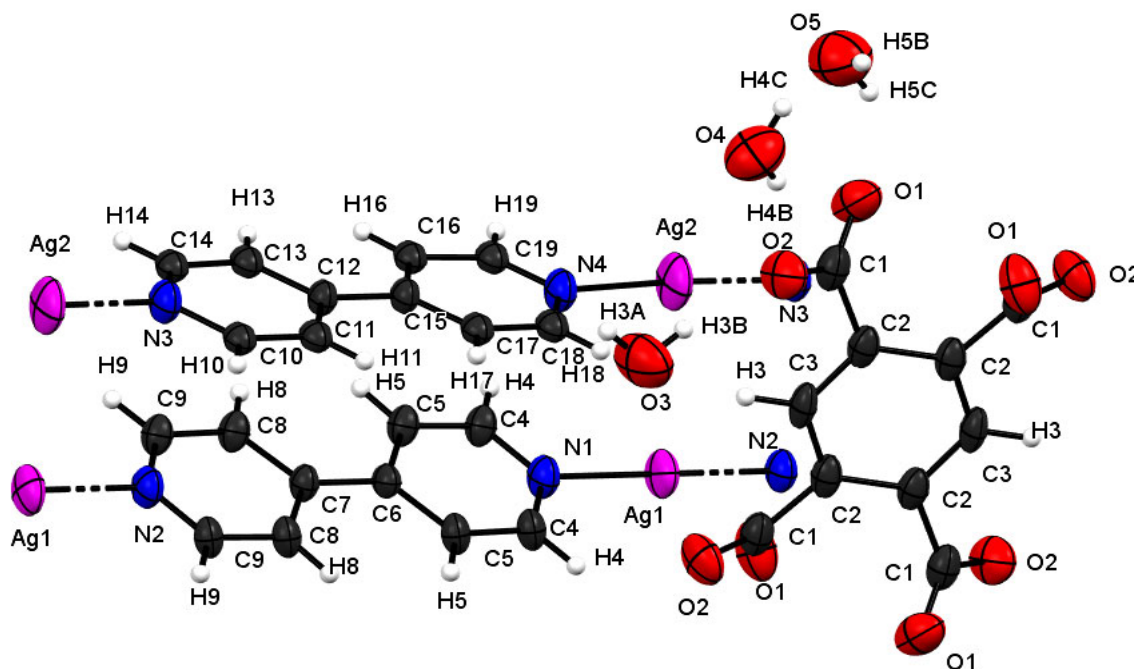


Figure 3. ORTEP plot showing the molecular structure of the SCP 1 with atom labeling scheme.

The silver atoms assume a slightly distorted linear geometry, where each silver atom is coordinated to two nitrogen atoms of two different 4,4'-bpy ligands, N1–Ag1–N2 = 180.0° and N3–Ag2–N4 = 174.24° (12). The silver atom is strongly bonded to nitrogen of two 4,4'-bpy bridging ligands; Ag1–N1, Ag1–N2 and Ag2–N3, Ag2–N4 are equal to 2.123(4)

Å, 2.123(4) Å 2.122 (4) and 2.140(4) Å, respectively, which are typical values for Ag-N coordination distances reported previously, [36–38]. The structure of **SCP 1** consists of two chains arranged in ...ABAB... fashion. Chain A is one-dimensional, containing $[\text{Ag}(4,4'\text{-bipy})]_n$ chain, while chain B is free, containing uncoordinated 1,2,4,5-benzene tetracarboxylate and water molecules. This chain of free BTC ions is nearly perpendicular to the 1-D chain of $[\text{Ag}(4,4'\text{-bipy})]_n$, as the free chain of BTC is out of the plane defined by the other $[\text{Ag}(4,4'\text{-bipy})]_n$ 1-D chain by an angle equals to 81.4° , Figure 4. The detailed analysis of the structure of chain A of $[\text{Ag}(4,4'\text{-bipy})]_n$ is stabilized by a strong face-to-face stacking interaction between the pyridyl ring of 4,4'-bpy defined by a centroid-centroid distance equal to 3.63 Å; (C8-C13 = 3.303 Å, C9-C14 = 3.315 Å, N2-N3 = 3.635 Å) [39].

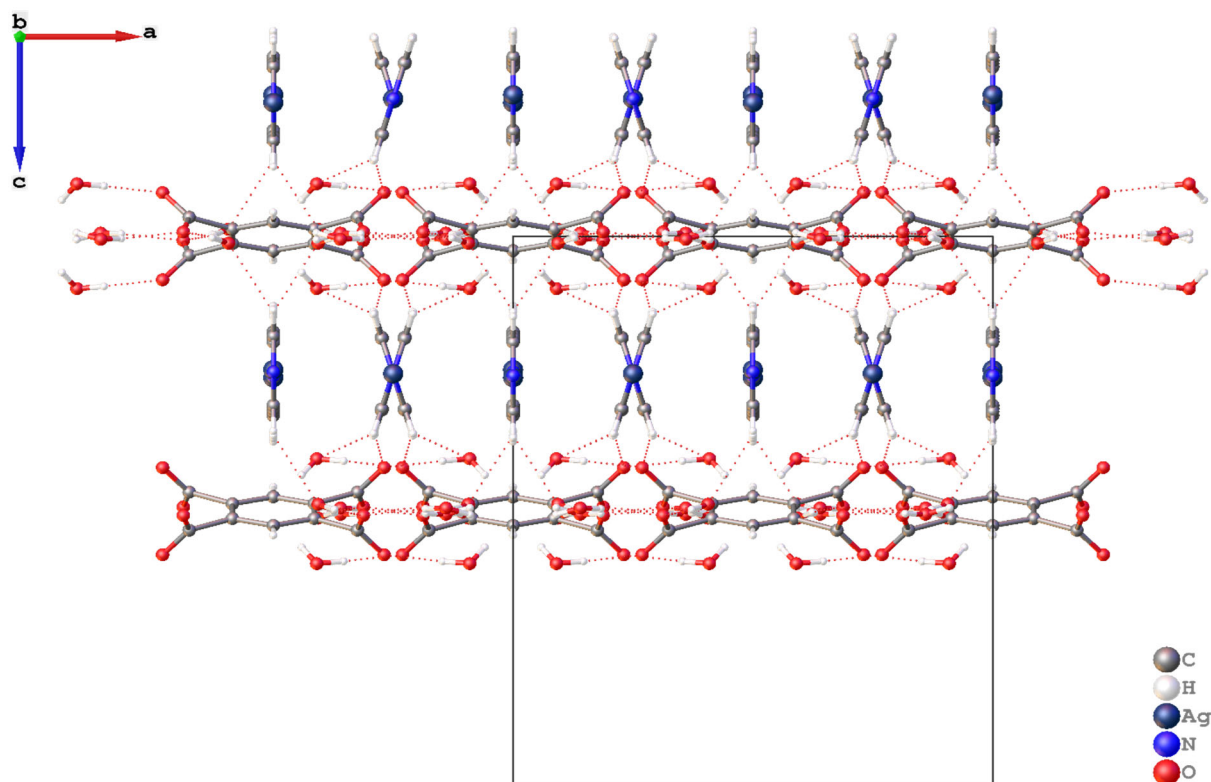


Figure 4. ...ABAB... plot showing hydrogen bonds between free BTC, water molecules chain with $[\text{Ag}(4,4'\text{-bipy})]_n$ chain in **SCP 1**.

Furthermore, given that the closest Ag-Ag separation distance is 3.635 Å, it can be concluded that there is some argentophilic interaction stabilizing the $[\text{Ag}(4,4'\text{-bipy})]_n$, Figure 5.

The π - π stacking and argentophilic interactions extend the $[\text{Ag}(4,4'\text{-bipy})]_n$ chain into a two-dimensional layer through Ag...Ag and pyridyl...pyridyl ring interactions. Therefore, these interactions define the overall packing arrangement. The chain B of uncoordinated 1,2,4,5-benzene tetracarboxylate (BTC) and water molecule ions forms a 1-D chain through extensive hydrogen bonds between water molecules and BTC ions and between water molecules themselves, O2-H4B = 1.995 Å, O5-H5B = 2.358 Å, and O1-H5C = 1.978 Å, Figure 6.

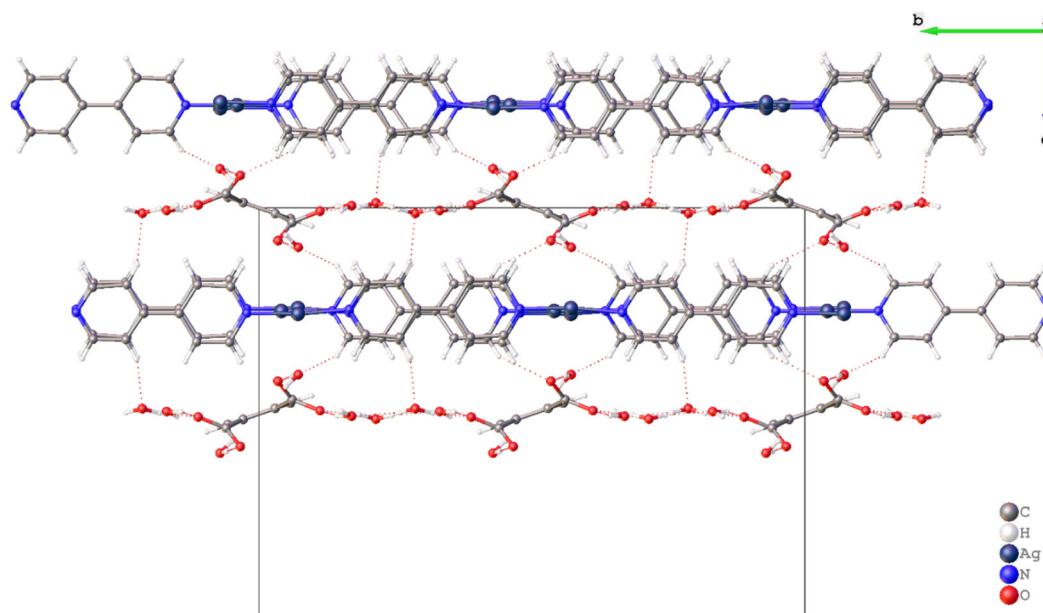


Figure 5. The packing diagram in the unit cell shows π - π stacking, argentophilic interactions, and hydrogen bonds between free BTC, water molecules, chain with $[\text{Ag}(4,4'\text{-bipy})]$ chain in SCP 1.

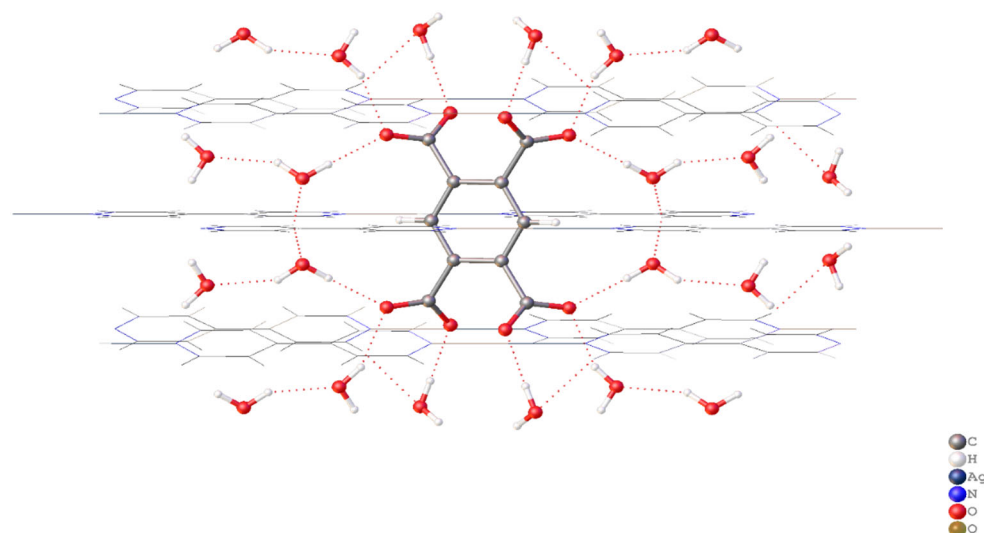


Figure 6. The 3D network structure of SCP 1 through hydrogen bonds.

The chains A and B are connected through extensive hydrogen bonds, generating a three-dimensional network structure Figures 4–6. The hydrogen bonds were established between the oxygen of BTC and water molecules with the hydrogen atoms of 4,4'-bpy in $[\text{Ag}(4,4'\text{-bipy})]_n$ layer [$\text{O1-H9} = 2.42\text{\AA}$, $\text{O1-H9A} = 2.55\text{\AA}$, $\text{O2-H8} = 2.762\text{\AA}$, and $\text{O5-H4} = 2.47\text{\AA}$]. Thus, BTC ions and water molecules might be regarded as the linkers of adjacent $[\text{Ag}(4,4'\text{-bipy})]_n$ layers and consolidate the structural framework through hydrogen bonding interactions. Thus, the extended structure of SCP 1 is a 3-D network via a combination of coordination bonds, hydrogen bonds, π - π stacking, and argentophilic interactions, creating channels that accommodate chain B of free BTC ions and water molecules, Figures 4–6.

2.2. Infrared Spectra

The IR spectrum of SCP 1 exhibits the bands characteristic of the carboxylate groups of H_4BTC and the bipodal ligand of 4,4'-bipy, Table 3. The SCP 1 shows strong bands of

the carboxylate groups at 1568 cm^{-1} and 1395 cm^{-1} for the antisymmetric and symmetric stretching vibrations, respectively. In the IR spectrum of **SCP 1**, the band due to the stretching vibrational frequency of the water molecules appears at 3395 cm^{-1} . Also, the IR spectrum of **SCP 1** shows the characteristic band of bending vibrations of the carboxylate group at 621 cm^{-1} . Moreover, the IR spectrum of **SCP 1** does not show the carbonyl stretching vibration band, confirming the involvement of the carboxylate group in strong intermolecular hydrogen bonds [40]. Noteworthy, we obtained SSNMR to explain this issue, in which ^1H SSNMR (cf. Supplementary Materials) revealed that the aromatic proton resonance ($\sim 7\text{ ppm}$) to protons on the bipyridyl and aromatic rings in our structure. The highly shielded -30 ppm signal likely corresponds to protons involved near the silver centers, perhaps from metal-coordinated ligands or hydride-like environments influenced by argentophilic interactions and unusual electronic shielding caused by the metal cluster environment. The signal around 39 ppm in our solid-state ^1H NMR spectrum is unusual for typical proton chemical shifts but can potentially be assigned in the context of a silver coordination complex, as the 39 ppm proton peak likely represents protons involved in strong hydrogen bonding within the lattice, experiencing pronounced deshielding caused by local electronic effects. Also, ^{13}C SSNMR (cf. Supplementary Materials) revealed that the deshielding or downfield ^{13}C SSNMR chemical shift of carbonyl carbon of carboxylic acid at 260 ppm upon H-bonding, and this is in line with the reported literature [41], as this is a widely observed phenomenon, and this downfield shift is commonly used as a spectroscopic ruler for H-bonding.

In the IR spectrum of **SCP 1** the band at 3037 cm^{-1} corresponds to $\nu_{\text{CH(arom.)}}$. The bands at 1478 , 741 , and 663 cm^{-1} were assigned to δ_{CH} and γ_{CH} of the ligands ($4,4'$ -bipy and H_4BTC), respectively, Table 3. These bands show shifts to lower wavenumbers than the vibrational frequencies of the free ligand ($4,4'$ -bipy) due to the formation of hydrogen bonds between the oxygen atoms of BTC ions and the hydrogen atoms in the other acceptor sites of the $[\text{Ag}(4,4'\text{-bipy})]$ chain, Table 4. In contrast, the bands at 1568 and 1458 cm^{-1} correspond to $\nu_{\text{C=N}}$ and $\nu_{\text{C=C}}$ of $4,4'$ -bipy and H_4BTC ligands, respectively, in **SCP 1**. Furthermore, the IR spectrum of **SCP 1** shows, also shows strong bands due to skeletal and C-C vibrations of the ligands at 1218 , 1134 , 1076 , and 1000 cm^{-1} .

Table 4. The wavenumbers (cm^{-1}) of different vibrational modes of $4,4'$ -bipy ligand and **SCP 1**.

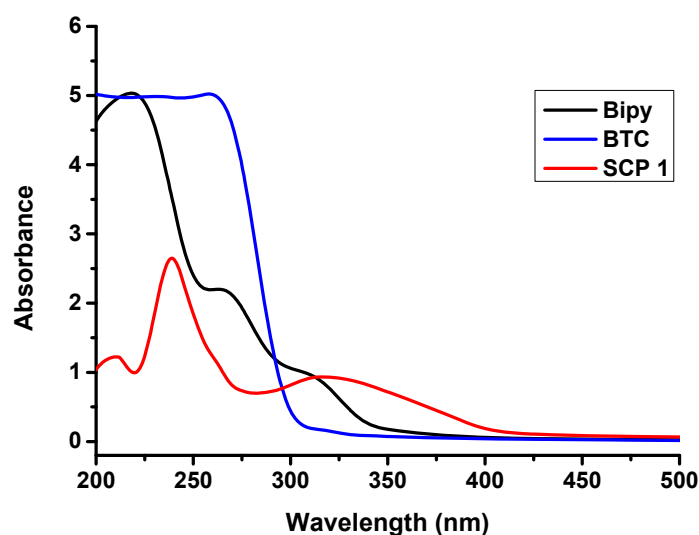
Compound	$\nu_{(\text{H}_2\text{O})}$	$\nu_{(\text{CH})}$ (Arom.)	$\nu_{(\text{C=N})}$ and $\nu_{(\text{C=C})}$ (Aromatic)	$\nu_{\text{asy.}(\text{COO}^-)}$ $\nu_{\text{sym.}(\text{COO}^-)}$ $\delta_{(\text{COO}^-)}$	Skeletal and C-C Vibrs. of L	δ_{CH} of L	γ_{CH} of L
$4,4'$ -bipy	-	3075 w	1604 s	1590 s 1406 s 674 m	1236 w–1155 m 1097 w–1039 m	1484 w	783 m 674 w
SCP 1	3395 br	3037 w	1568 s 1458 m	1568 s 1395 s 621 m	1218 w–1134 m 1076 w–1000 m	1478 w	741 m 663 w

2.3. Electronic Absorption and Emission Spectra

The electronic absorption spectra of free ligands ($4,4'$ -bipy, H_4BTC) and **SCP 1** were measured in DMF with concentration $1 \times 10^{-5}\text{ M}$ at room temperature, Table 5 and Figure 7. The electronic absorption spectrum of $4,4'$ -bipy shows three absorption peaks at 219 , 268 , and 315 nm corresponding to $^1\text{L}_a \leftarrow ^1\text{A}$, $^1\text{L}_b \leftarrow ^1\text{A}$, and $n\text{-}\pi^*$ transitions, respectively [42].

Table 5. The electronic absorption and emission spectra of the 4,4'-bpy, BTC ligands and SCP 1.

		λ_{abs} (nm)		λ_{em} (nm)		
BTC	4,4'-bpy	1	Assignment	4,4'-bpy	1	Assignment
-	219	210	$^1L_a \leftarrow ^1A$	378 ^b	435–457 ^b	Close lying π - π^* transition
260	268	240	$^1L_b \leftarrow ^1A$		486	Intra-ligand emission π - π^*
-	315	310–335 ^b	MLCT n - π^*		532	MLCT or (MC) transitions

^b = broad.**Figure 7.** UV absorption spectra of 4,4'-bipy, BTC ligands and SCP 1.

The n - π^* transition in the free ligand disappears on HCl addition. Also, the bands due to n - π^* transitions disappear in the spectrum of **SCP 1** due to the participation of the bipodal ligand (4,4'-bipy) in the coordination sphere of silver(I) ions [42], Figure 7, Table 5. At the same time, the electronic absorption spectrum of H_4 BTC exhibits only one absorption peak at 260 nm, which is assigned to $^1L_b \leftarrow ^1A$ transition. Furthermore, the electronic absorption spectrum of **SCP 1** in DMF exhibits two absorption bands at 210 and 240 nm assigned to $^1L_a \leftarrow ^1A$ and $^1L_b \leftarrow ^1A$, respectively, [42], Figure 7 and Table 5. The absorption spectrum of the **SCP 1** exhibits additional broadband at 310–355 nm corresponding to metal-to-ligand charge transfer (MLCT), where the charge is transferred from the silver(I) center to the unoccupied π^* -orbital of the ligand [43], Figure 7 and Table 5.

The emission spectra of 4,4'-bipy ligand and **SCP 1** were measured in DMF with an excitation wavelength of 290 nm at room temperature, Figure 8. The emission spectrum of 4,4'-bipy displays a well-developed broad peak at 378 nm, which corresponds to the lowest (π , π^*) and close lying (n , π^*) states [42]. On the other hand, the emission spectrum of free H_4 BTC does not show any emission bands under the used experimental conditions. At the same time, the emission spectrum of **SCP 1** exhibits a broad peak at 435–457 nm due to close lying π - π^* transition [44]. On the other hand, the emission spectrum of the **SCP 1** displays structural peaks of the bipodal ligand (4,4'-bipy) as well as additional bands at 486 and 532 nm which may be assigned to intra-ligand emission π - π^* transition and MLCT [43–45] or metal-centered transitions (MC) of the type $4d^{10} \rightarrow 4d^9 5s^1$ and $4d^{10} \rightarrow 4d^9 5p^1$ on the silver(I) center, respectively [43,45]. The emission spectrum of the **SCP 1** exhibits a high fluorescence intensity with a red shift compared to the 4,4'-bipy ligand by about 65 nm, moving from the UV to the visible region. Therefore, the luminescence behavior of 4,4'-bipy and **SCP 1** demonstrates a high degree of sensitivity to silver, making it a desirable candidate for a luminescent sensor.

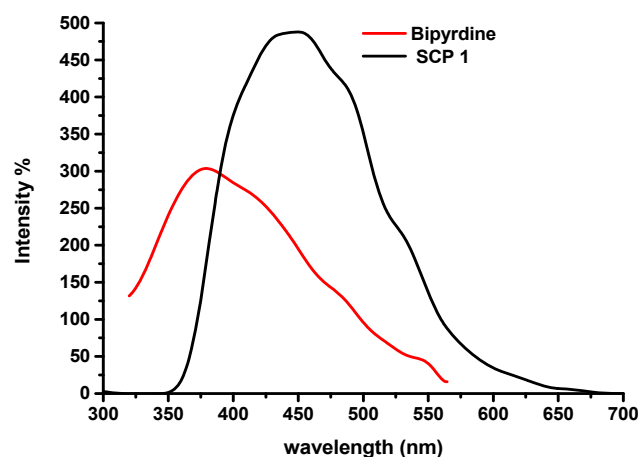
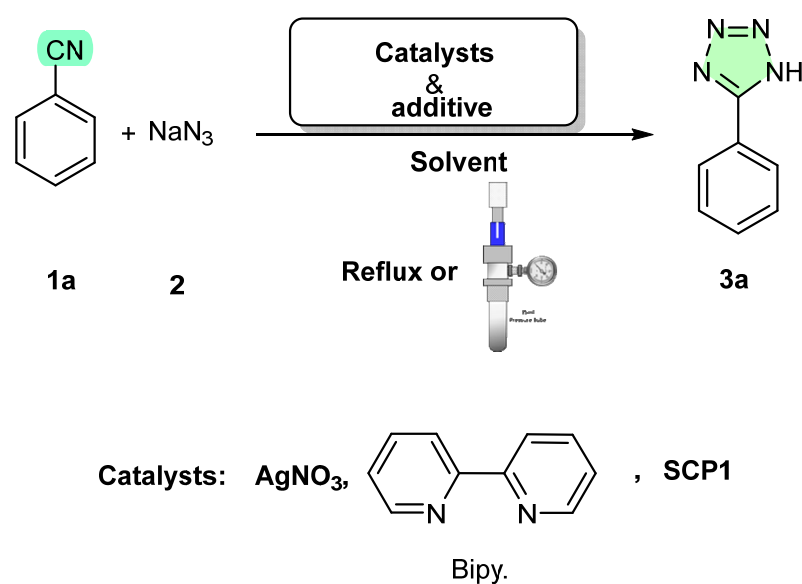


Figure 8. Emission spectra of 4,4'-bipyridine and SCP 1.

2.4. Catalytic Activity Study

The catalytic conversion of the nitrile group into tetrazole using a stoichiometric quantity of sodium azide has been optimized by an array of tests, as shown in Scheme 2. The reaction between the benzonitrile compound (**1a**) and sodium azide (**2**) was observed using different salts or complexes of silver(I). This reaction was used as a model to determine the most effective silver catalyst that could catalyze the reaction under both classical conditions and the Q-tube high-pressure system (Scheme 2). To facilitate this model reaction, the following silver catalysts are checked: silver nitrate, silver nitrate/bipy, and SCP {[Ag₄(4,4'-bpy)₂.(BTC).3H₂O)], (SCP 1), as shown in Table 5.



Scheme 2. Synthesis of 5-phenyl-1H-tetrazole derivative **3a** using silver catalysts.

The outcomes of the catalyzed reaction yield a singular isolable product in each instance, as analyzed by TLC. The compound is designated as 5-phenyl-1H-tetrazole derivative **3a** based on the acquired spectrum data (Scheme 2). The incorporation of an inorganic salt markedly enhanced the transformation efficiency in certain instances, as seen in Table 6. We examined sodium fluoride (NaF) and potassium tetrafluoroborate (KBF₄).

Table 6. Effect of different silver catalysts for the synthesis of 5-phenyl-1*H*-tetrazole derivative **3a**.

Entry	Catalyst	Additives	Classical Condition (Reflux)		Q-Tube High-Pressure Reactor	
			Time	Yield	Time	Yield
1	No catalyst	-	24 h	10%	4 h	17%
2	bipy	-	24 h	10%	4 h	17%
3	AgNO ₃	-	6 h	39%	90 min	67%
4	AgNO ₃ /bipy	-	3 h	61%	60 min	78%
5	AgNO ₃ /bipy	NaF	2 h	70%	60 min	84%
6	AgNO ₃ /bipy	KBF ₄	2 h	70%	60 min	84%
7	SCP1	-	1 h	80%	15 min	93%
8	SCP1	NaF	1 h	85%	15 min	99%
9	SCP1	KBF ₄	1 h	85%	15 min	99%

Table 6 indicates that the reaction illustrated in Scheme 2 can proceed without a catalyst (Entry 1), but it takes a very long time and yields an unacceptable result. In comparison to the classical conditions (reflux), the Q-tube high-pressure system for all the scanned catalysts outperformed the classical conditions [Entries 1–11]. The effect of ligand bipy was studied (entry 2), and it does not show any extra effect; it exhibits no catalytic effect. Silver nitrate gives relatively good results (entry 3). We are unable to implement it due to high cost and limited reaction scope, in addition to raising environmental issues due to its potential toxicity and accumulation in ecosystems. The good results obtained by the in situ complex formed between Bipy and silver nitrate (entry 4) push us to find the best results by utilizing inorganic fluoride salts (entries 5, 6). It was noticed that when we used NaF and KBF₄, the same results were obtained (entries 5, 6). Considering that tetrafluoroborate might undergo hydrolysis to give fluoride in situ, fluoride was thus chosen as the standard anion to conduct further investigations. Sodium fluoride was therefore selected as the salt for optimizing the conditions. The very good results obtained (entries 5, 6) suggest that the presence of a non-coordinating counter anion gives stability for the complex formed in situ [46]. The excellent results obtained by utilizing **SCP 1** in the presence of NaF (entry 8) under the Q-tube high-pressure system were considered the optimal catalyst, which achieved a quantitative yield in a very short reaction time, 15 min. Additionally, the other salt, potassium tetrafluoroborate, described in Entry 9, performed admirably same results when used as an additive, but we chose NaF to be the optimal choice due to its higher solubility, lower cost, and broader availability. Noteworthy, the principal and most vital function of NaF is to inhibit the development of insoluble, inactive silver azide (AgN₃) from any silver species leached from **SCP 1** by generating soluble silver-fluoride complexes. This guarantees that an adequate concentration of catalytically active Ag(I) species is maintained during the reaction [47–49]. Modulating Lewis acidity and generating basicity are secondary synergistic effects that enhance overall catalytic efficiency. The donation of F[−] may marginally diminish the Lewis acidity of Ag⁺, yet it can optimize it for activating the nitrile group (Ar-CN) to facilitate nucleophilic attack by N₃[−]. This activation reduces the energy barrier for the cycloaddition phase [47,50]. Furthermore, F[−] is a comparatively potent base (conjugate base of HF, pK_a approximately 3.17). It can deprotonate acidic sites within the framework, such as residual carboxylic acid groups from the 1,2,4,5-tetracarboxylic benzene ligand that remain uncoordinated, or water molecules coordinated to Ag⁺. This creates a moderately basic environment (HF or OH[−]), which might enhance the nucleophilicity of the azide anion (N₃[−]) and ease the last proton transfer step in the tetrazole production mechanism [51,52].

Afterwards, various concentrations of **SCP 1** catalyst were evaluated in a Q-Tube high-pressure reactor to optimize the catalyst's mole percent and solvent (Table 7).

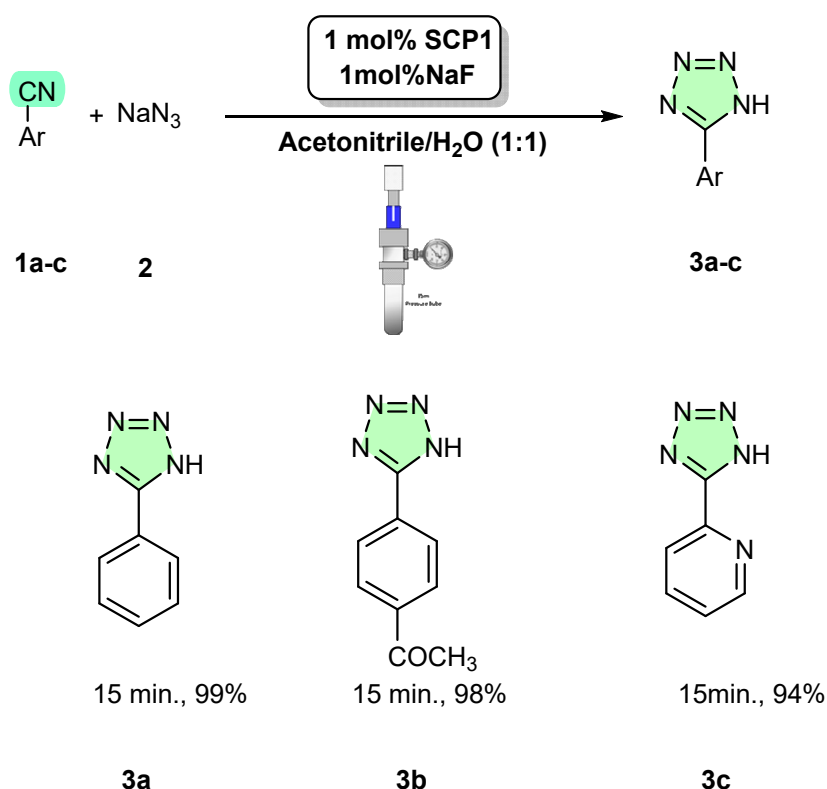
Table 7. Optimization of the Catalyst amount and the solvent used for the synthesis of 5-phenyl-1*H*-tetrazole derivative **3a** under the Q-tube high-pressure system.

Entry	Catalyst (mol %) *	Solvent	Time (min)	Yield
1	0.5	Acetonitrile (AcN.)	30	91%
2	1	AcN.	15	99%
3	1.5	AcN.	15	99%
4	1	AcN./water (1:1)	15	99%
5	1	water	45	84%
6	1	EtOH	30	90%
7	1	Cyclopentylmethyl ether	60	23%

* All of the experiments were performed in the presence of 1 mol % NaF.

It is evident from Table 7 results that 1 mol% of **SCP 1** was the ideal concentration (Entry 2), and that acetonitrile/water (1:1) solvent performed best when compared to ethanol, water, and cyclopentylmethylether. Even though AcN. Given the same outcomes for AcN./water, but due to cost and environmental impact, the acetonitrile-water mixture may be beneficial for both obtaining the best results and having the catalyst available for reuse.

The scope and generality of our optimized protocol have been extended to include other derivatives, as presented in Scheme 3.

**Scheme 3.** Scope and generality of our green protocol for the synthesis of 5-substituted tetrazole derivatives **3a-c**.

Our environmentally friendly methodology, which uses the Q-Tube system with **SCP 1** catalyst, shortened the reaction time for all compounds evaluated to just 15 min, as shown in Scheme 3. Another noteworthy finding is the high yield (94–99%) of 5-substituted tetrazole derivatives. Due to its three-dimensional, highly ordered structure, silver supramolecular coordination polymer **SCP 1** is superior to other forms (AgNO_3 and $\text{AgNO}_3/\text{Bipy.}$). As a result, there are more active sites for catalytic reactions than there would be with silver

nitrate due to its large specific surface area [53]. Catalytic efficiency and reproducibility can be limited by less predictable structures, nuclearity that varies, or aggregation (in situ formed complex of AgNO₃/Bipy), unlike **SCP 1**, which is synthesized with a well-defined and extended network structure that guarantees a uniform distribution of catalytic sites and stability throughout the material [54,55]. Using a Q-Tube pressure reactor in conjunction with **SCP 1** in this reaction has a synergistic effect for a number of reasons. One of these is that the Q-Tube reactor can achieve elevated pressure and temperature, which, as predicted by the Arrhenius equation (Equation (1)), greatly accelerates reaction rates and improves yields.

$$K = Ae^{-E_a/RT} \quad (1)$$

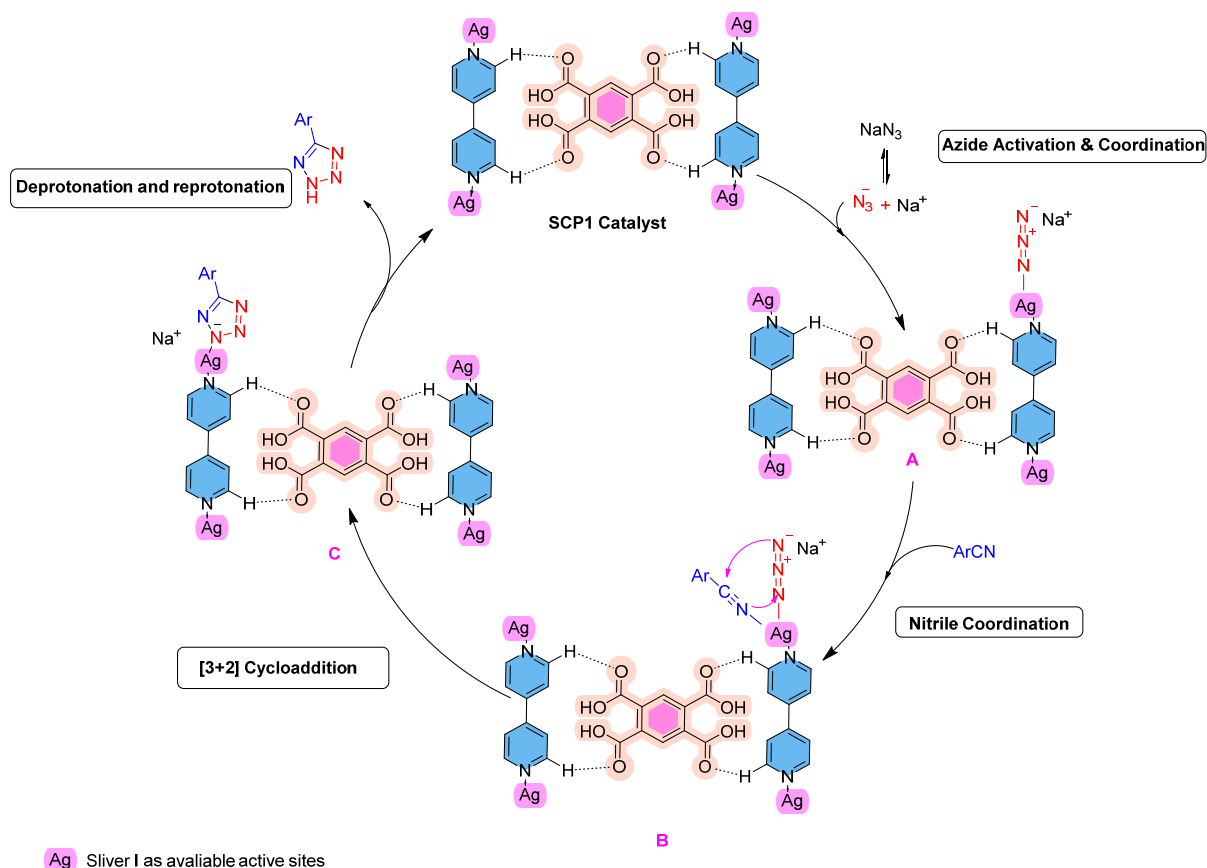
where R (8.3145 J/Kmol) is the gas constant, E_a is the activation energy, and K is the rate constant. On the other hand, T is the definition of temperature. The frequency of reactions is taken into consideration when calculating a frequency factor of A, with units of L.mol⁻¹s⁻¹ [56,57].

The Q-tube method enhances the solubility of reactants, which is particularly beneficial in our situation (we are using a mixed solvent, one of which is water). Additionally, it has been previously reported that a higher temperature is required to convert nitrile to tetrazole [52]. The solubility of reactants in the reaction fluid can be enhanced by increasing the pressure. The catalyst and reactants may have better interactions as a result of this. For reactions involving heterogeneous catalysts, the optimal configuration of a Q-tube reactor is crucial because it can optimize mass transfer rates among phases (e.g., solid, liquid, and gas) [58].

Analytical and spectroscopic investigations employing IR, ¹H, and ¹³C NMR techniques validated the structures of the synthesized compounds **3a–c**. In particular, the infrared spectrum of compound **3a** showed three peaks at 3310, 1603, and 1511 cm⁻¹, corresponding to the NH, C=N, and N=N functional groups, respectively. The structure of compound **3a** was confirmed when the band at 2224 cm⁻¹, due to the nitrile group of **1a**, disappeared. A unique D₂O exchangeable singlet at δ_H 16.02 ppm linked to the NH was found in the ¹H NMR spectra investigation, and five aromatic protons in the aromatic region, originating from the phenyl ring, were also identified. Referring to the Experimental part, the protons were resonated within their appropriate regions.

The utilization of **SCP 1** as a catalyst in the Q-Tube pressure reactor altered the reaction's behavior, necessitating the development of a mechanism, as illustrated in Scheme 4. The atypical structure of **SCP 1** contains specific carboxylic acid groups (-COOH) that remain protonated within the pores. This imparts local Brønsted acidity to the material, which is crucial for the observed catalytic activity. The suggested mechanism involves azide activation and the coordination stage. An azide ion (N₃⁻) approaches an available Ag(I) site in the **SCP 1**, subsequently forming a σ -complex as Ag(I) coordinates with the terminal nitrogen of N₃⁻ (Ag-N=N⁺=N⁻ or Ag-N⁻=N⁺=N) (Complex A). This coordination enhances the polarity of the azide, rendering the central nitrogen more electrophilic and the terminal nitrogen more nucleophilic. The subsequent step involves nitrile coordination, wherein the nitrogen of the nitrile coordinates to the identical Ag(I) center. This forms a bidentate complex whereby Ag(I) is coordinated to both N₃⁻ and R-CN (Complex B). This positions the reactants in proximity and activates the nitrile group by diminishing electron density via σ -coordination, so rendering the carbon more electrophilic. Subsequently, the activated terminal nitrogen of the azide, exhibiting high nucleophilicity, assaults the activated carbon of the nitrile, characterized by significant electrophilicity. This initiates a concerted or stepwise [3+2] cycloaddition within the Ag(I) coordination sphere (Complex C). A proximate protonated carboxylic acid group (-COOH) from the H₄BTC linker in the **SCP 1** releases protons (deprotonation). The -COOH group donates a proton to the

tetrazolato nitrogen (either N1 or N2, contingent upon the initial adduct isomer), resulting in the neutral 5-substituted 1H-tetrazole (product) that remains loosely associated with the site. Ultimately, the product release indicates that the neutral R-tetrazole product exhibits inferior adhesion to the Ag(I) site compared to the anionic intermediates. Additionally, A water molecule, or potentially the solvent or reaction medium, in the system reprotonates the deprotonated carboxylate ($-\text{COO}^-$) on the H_4BTC linker, reinstating the crucial $-\text{COOH}$ group (Reprotonation).



Scheme 4. Plausible mechanism for the synthesis of 5-substituted tetrazole derivatives **3a–c** catalyzed by **SCP 1**.

2.5. Recyclability of **SCP 1** Catalyst

The reaction was conducted under the previously specified optimized conditions. After each cycle, the catalyst was isolated using filtration, rinsed thrice with warm water, and subsequently dried for one hour at 80 °C before reuse. We believe the primary differentiating characteristic of this catalyst is its sustainability, in addition to its catalytic efficiency and environmental safety. This is demonstrated by its capacity for reuse up to four times while preserving consistent catalytic performance, as illustrated in Figure 9. This indicates that the architecture of the **SCP 1** catalyst is maintained by encapsulating leached Ag^+ within soluble $[\text{AgF}_n]^{(n-1)-}$ complexes. Sodium fluoride (NaF) may facilitate the redeposition of silver onto the framework or inhibit significant dissolution, hence assisting in the preservation of the catalyst's heterogeneity [59].

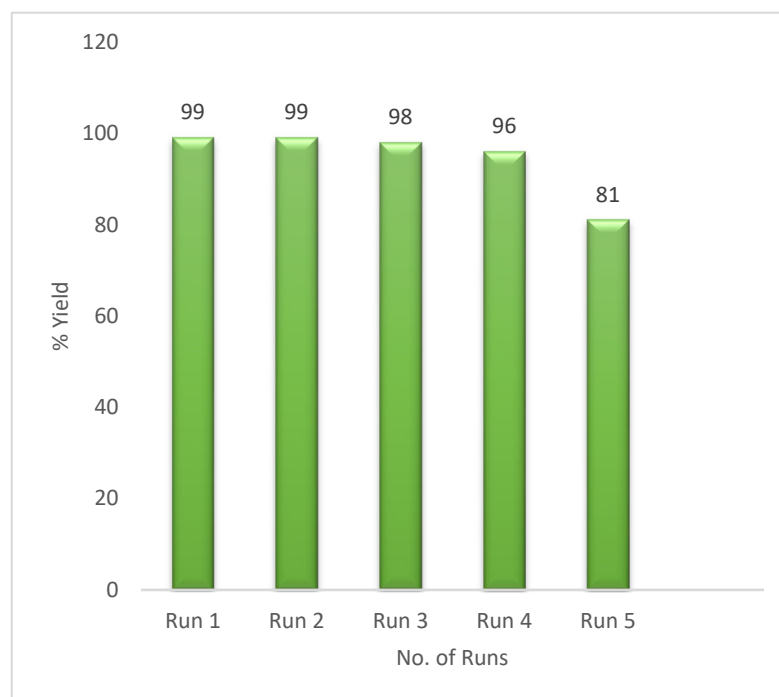


Figure 9. Recyclability of SCP 1 catalyst in the Synthesis of 5-substituted tetrazole derivatives **3a**.

To elucidate the observed decrease in catalytic activity after the fourth cycle, a comparative FT-IR analysis was performed for the catalyst samples before use (a), after the first use (b), and following the fifth use (c), as shown in Figure 10. The FT-IR spectra revealed no discernible differences among the three samples, indicating that the catalyst retains its functional groups throughout repeated catalytic cycles.

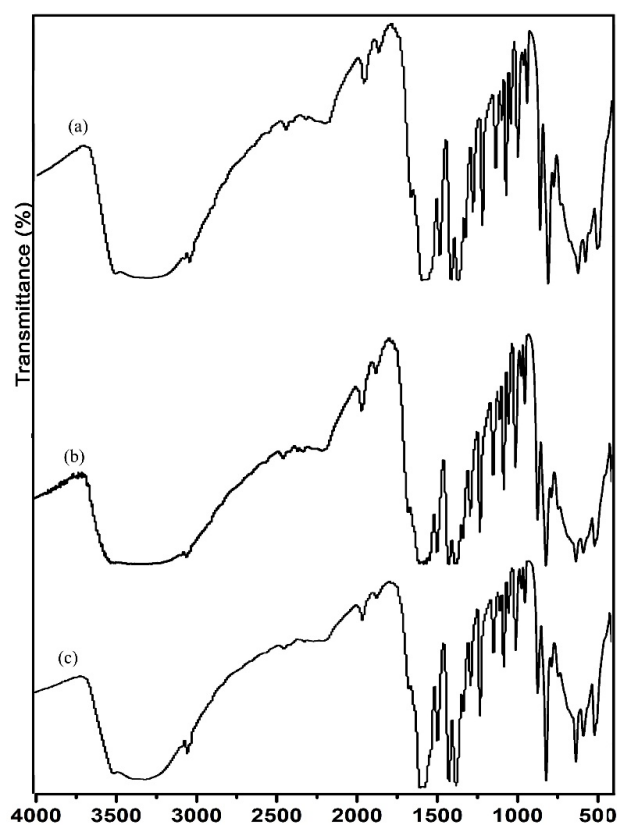


Figure 10. FT-IR of catalyst sample (a) before reaction, (b) after first use, (c) after fifth use.

In addition, to investigate the reason for the decline in catalytic activity after the fourth cycle, we obtained the PXRD pattern of the catalyst after the fifth use (Figure 11).

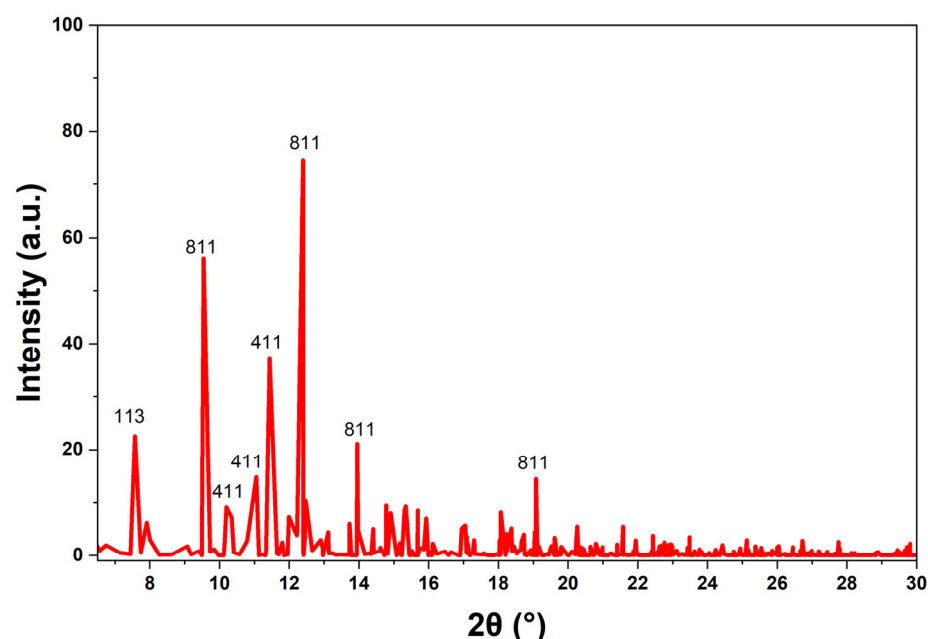


Figure 11. PXRD of the catalyst sample after the fifth use.

The XRD data suggest a well-defined crystalline phase, indicated by sharp and distinct diffraction peaks. This confirms that high crystallinity corresponds closely to the proposed molecular arrangement of the catalyst obtained by single crystal X-ray.

Morphological analysis by scanning electron microscopy (SEM) was conducted on the catalyst prior to reaction and after its fifth cycle of use (Figure 12). Comparative examination of the SEM images reveals that, before reaction (Figure 12a), the catalyst particles are relatively discrete, displaying distinct boundaries and well-defined individual shapes. In contrast, following the fifth use (Figure 12b), the catalyst exhibits a more agglomerated surface morphology, with particles appearing fused or clustered into larger, less distinct aggregates. This pronounced increase in aggregation and the diminished clarity of particle boundaries in the post-reaction SEM image indicate significant agglomeration, likely resulting from sintering or particle fusion during the reaction process. It is proposed that the observed decline in efficiency beyond the fourth cycle is attributable not only to agglomeration, but also to progressive catalyst attrition caused by material loss during repeated filtration and workup steps.

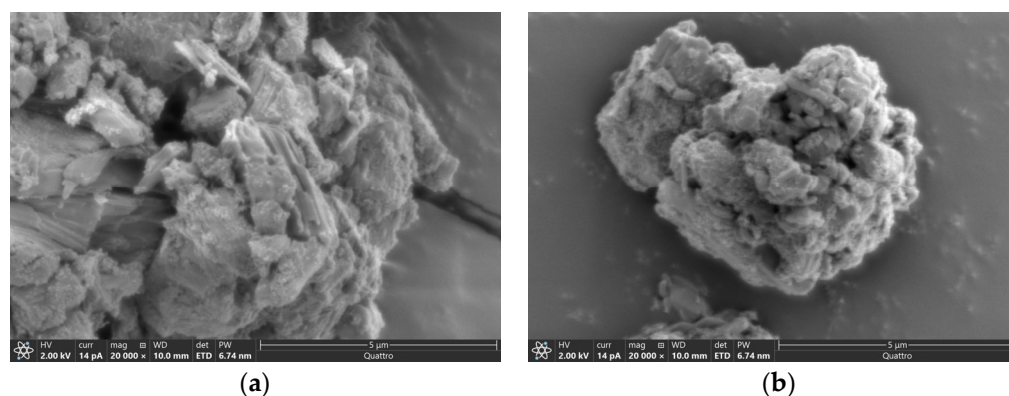


Figure 12. SEM of catalyst (a) before use (b) after fifth use.

3. Experimental

3.1. Chemicals and Reagents

All reagents, chemicals, and organic solvents were bought from commercial sources and utilized as received unless otherwise noted. All additional chemicals were acquired without further purification from Merck (Darmstadt, Germany), Sigma-Aldrich (St. Louis, MO, USA), or Acros Organics (part of Thermo Fisher Scientific, Waltham, MA, USA).

3.2. Instrumentation

Thin-layer chromatography was performed on Merck 60 GF254 silica gel plates pre-coated with a fluorescent indicator, with detection conducted via UV irradiation at 254 and 360 nm. The melting points were ascertained via the Stuart melting point apparatus without modifications. IR spectra were obtained using the Nicolet iS10 FT-IR spectrometer utilizing a Smart iTR, an ultrahigh-performance, adaptable attenuated total reflectance sampling accessory from Thermo Fisher Scientific (Madison, WI, USA). A Bruker Avance III 400 spectrometer (9.4 T, 400.13 MHz for ^1H , 100.62 MHz for ^{13}C) (Bruker, Billerica, MA, USA) equipped with a 5 mm BBFO probe was utilized to acquire NMR spectra at 298 K. Chemical changes (δ in ppm) are referenced against internal standards. Solid-State Nuclear Magnetic Resonance (NMR) Spectroscopy.

One-dimensional ^1H MAS and ^{13}C CP/MAS solid-state NMR spectra were recorded on Bruker AVANCE III spectrometers operating at 400 or 600 MHz resonance frequencies for ^1H . Experiments at 400 MHz employed a conventional double-resonance 4 mm CP/MAS probe, while experiments at 600 MHz utilized a 2.5 mm double-resonance probe. Dry nitrogen gas was utilized for sample spinning to prevent degradation of the samples.

The scanning electron microscope (SEM) of the catalyst morphology was examined using SEM in a Nova Nano SEM 240 unit. Elemental studies were conducted using a EuroVector C, H, N, and S analyser (EA3000 series). A Shimadzu (UV-3101 PC) (Shimadzu, Kyoto, Japan) spectrometer was employed to obtain electronic absorption spectra. The Cary Eclipse Fluorescence Spectrophotometer ($\lambda_{\text{ex}} = 290 \text{ nm}$) was employed to assess fluorescence spectra. Q-Tube-assisted reactions were performed in a Q-Tube-safe pressure reactor from Q Labtech (Washington, DC, USA) equipped with a cap/sleeve, pressure adapter (120 psi), needle, borosilicate glass tube, Teflon septum, and catch bottle.

3.3. Synthesis of **SCP** $\{[\text{Ag}_4(4,4'\text{-Bpy})_2] \cdot (\text{BTC}) \cdot 3\text{H}_2\text{O}\}$, (1)

A solution of AgNO_3 (0.08 g, 0.5 mmol) in 20 mL H_2O was added to a mixture solution of 4,4'-bipy (0.04 g, 0.25 mmol) in 20 mL acetonitrile and 1,2,4,5-benzenetetracarboxylic acid (H_4BTC) (0.054 g, 0.25 mmol) in 30 mL of 30% sodium hydroxide solution and stirred for 15 min. Brown precipitate was resulted, then concentrated ammonia solution was added dropwise with stirring to dissolve the precipitate and the solution became clear. Brown needle crystals **1** suitable for X-ray analysis were obtained in slow vaporization after standing at room temperature for two weeks. The crystals were filtered, washed with $\text{H}_2\text{O}/\text{CH}_3\text{CN}$, and dried in air (the yield was 70% concerning AgNO_3). Anal. Calcd for $\text{C}_{30}\text{H}_{24}\text{Ag}_4\text{N}_4\text{O}_{11}$: C, 34.38; H, 2.31; N, 5.35. Found: C, 34.89; H, 2.72; N, 5.15. IR (KBr, cm^{-1}): 3394 (br), 3047 (w), 1668 (s), 1568 (s), 1478 (w), 1395 (s), 1218(w), 1134 (m), 1076 (w), 1000 (m), 741(m), 702 (m), 663(w) and 621 (m).

3.4. Crystallographic Studies

Crystals were obtained by slow evaporation of the complex solution in water and acetonitrile. The collection of single-crystal X-ray diffraction data for the complex was carried out on a Bruker D8 Venture single-crystal X-ray diffractometer at 293 K, using Mo $\text{K}\alpha$ ($\lambda = 0.71073$) radiation. The crystal structure was solved using the SHELXT [60] structure

solution program and refined with SHELXL [60], implemented in the Olex2 [61] program package. The crystal structure refinement details for $C_{30}H_{24}Ag_4N_4O_{11}$ are listed in Table 1. Full crystallographic data can be found under the deposition number (CCDC 2478399): These data can be obtained free of charge via <https://www.ccdc.cam.ac.uk/structures/> (accessed on 1 August 2025) or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44-1223-336033.

PXRD was collected on a Bruker D8 Advance powder XRD diffractometer equipped with Cu (K α) radiation. The measurement was performed in the 2 θ range from 5 to 60 degrees with a 0.01-degree step size.

3.5. General Procedure for the Synthesis of 5-Substituted-1H-Tetrazoles via the [3+2] Cycloaddition Reaction

CAUTION! Organic azides are potentially explosive and should be handled with care. Even if no incident occurred on this scale, the cycloaddition can be highly exothermic and should not be attempted on a larger scale without being aware of explosion risks.

Method A

SCP 1 (1.0 mol %), sodium fluoride (1.0 mol%) in a mixture of acetonitrile/water (1:1) (20 mL) was added to nitrile (1.0 mmol), and sodium azide (1.0 mmol) in a 50 mL round-bottom flask. After reflux at 100 °C for the appropriate time, the progress of the reaction was monitored by TLC. After completion, the reaction was cooled to room temperature, and the reaction mixture was filtered to separate the catalyst. Then the filtrate was treated with cold water and then extracted with ethyl acetate (3 $\times$ 10 mL). The resultant organic layer was separated, washed with water, and dried over anhydrous sodium sulfate. The solvent of the extract was removed under reduced pressure with a rotary evaporator to obtain the product. The crude products were recrystallized from the appropriate solvent. The isolated products were authenticated with FT-IR and ^1H and ^{13}C NMR spectra.

Method B

The same mixture scale was placed in a Q-Tube at 120 °C/under the autogenic pressure (15 psi) for an appropriate time, as examined by TLC. The products were collected and worked up according procedure in Method A.

3.6. Physical and Spectroscopic Data of the Synthesized Compounds

5-Phenyl-1H-tetrazole (3a) [62].

White crystal. mp = 214–215 °C. Yield: 99%. FT-IR (KBr): ν_{max}/cm^{-1} : 3310 (NH), 1603 (C=N), 1511 (N=N). ^1H NMR (400 MHz, DMSO) δ 7.62–7.64 (m, 3H), 8.04–8.06 (m, 2H), 16.02 (br s, 1H, NH, D $_2$ O exchangeable), ^{13}C NMR (100 MHz, DMSO) δ 124.63, 127.43, 129.88, 131.76, 155.68.

5-(4-Acetyl phenyl)-1H-tetrazole (3b) [63].

Faint yellow solid. mp = 175–177 °C. Yield: 98%. FT-IR (KBr): ν_{max}/cm^{-1} : 3314 (NH), 1709 (CO), 1588 (C=N), 1506 (N=N). ^1H NMR (400 MHz, DMSO) δ 2.61 (s, 3H, CH $_3$), 8.11–8.13 (d, 2H, J = 7.4 Hz, ArH), 8.29–8.31 (d, 2H, J = 7.4 Hz, ArH), 16.02 (br s, 1H, NH, D $_2$ O exchangeable). ^{13}C NMR (100 MHz, DMSO) δ 27.26, 127.74, 129.51, 138.79, 155.51, 198.01.

2-(1H-Tetrazol-5-yl) pyridine (3c) [62].

White solid. mp 211–213 °C. Yield: 94%. FT-IR (KBr): ν_{max}/cm^{-1} 3289 (NH), 1602 (C=N), 1499 (N=N); ^1H NMR (400 MHz, DMSO) δ 7.64–7.66 (m, 1H, Py), 7.94–7.95 (m, 1H, Py), 8.22 (d, J = 6.4 Hz, 1H, Py), 8.51 (d, J = 6.0 Hz, 1H, Py); ^{13}C NMR (100 MHz, DMSO) δ 123.16, 126.73, 138.74, 144.00, 150.61, 155.34.

4. Conclusions

We successfully synthesized and characterized a novel 2D silver(I) coordination polymer, $[\text{Ag}_2(\text{bipy})(\text{btca})]_n$ (**SCP 1**), employing 4,4'-bipyridyl and 1,2,4,5-benzenetetracarboxylic acid. **SCP 1** functioned effectively as a reusable heterogeneous catalyst for the synthesis of 5-substituted 1H-tetrazoles, which hold significance in the medical field. This was accomplished via a Q-tube reactor in acetonitrile/water (1:1) solvent to combine terminal nitriles and sodium azide in a [3+2] cycloaddition reaction. The yields were quite high (94–99%). The significant novel concepts presented in this work are: 1. Stoichiometric Utilization of Azide, in which the reaction employs an equivalent quantity of sodium azide to the nitrile substrate. This eliminates the significant safety hazards and intricate purifying procedures associated with handling large quantities of NaN_3 . 2. DMF-Free and Safe Process: We circumvent the primary issue associated with conventional tetrazole syntheses by eliminating the use of DMF solvent. This inhibits the formation of N-nitrosodimethylamine (NDMA), a potent carcinogen, during the workup process. This occurs due to the quenching of surplus azide in DMF-based procedures. 3. The application of stoichiometric NaN_3 and a DMF-free methodology guarantees that the resultant 5-substituted 1H-tetrazole products are free from detrimental NDMA contamination from the outset. 4. The importance of inorganic salts that are used as additives, such as sodium fluoride, is discussed. This addresses a critical safety and regulatory concern for pharmaceutical applications. **SCP 1** exhibits robust and effective catalysis due to the synergistic interaction between its Ag(I) sites and Brønsted acidic -COOH groups, facilitating both cycloaddition and protonation processes, as shown in our mechanistic analysis. It is recyclable a minimum of four times.

Noteworthy, the combined use of **SCP 1** and Q-Tube reactor technology has successfully addressed major challenges in sustainable heterocyclic synthesis. The Q-Tube technology markedly reduced reaction time to 15 min. and enhanced the yield (up to 99%) by superior regulation of pressure and temperature, aligning with energy-efficient green chemistry principles.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/catal15100969/s1>, ^1H NMR (Solid State) of SCP1 Catalyst, ^{13}C NMR (Solid state) of SCP1 Catalyst.

Author Contributions: Conceptualization, T.S.S. and M.M.E.-b.; methodology, A.A.; software, T.S.S.; validation, T.S.S.; formal analysis, B.D. and A.S.A.-B.; investigation, A.A.; resources, M.M.E.-b.; data curation, T.S.S., A.A. and M.M.E.-b.; supervision, T.S.S. and M.M.E.-b.; project administration, T.S.S. and M.M.E.-b.; funding acquisition, M.M.E.-b. All authors have read and agreed to the published version of the manuscript.

Funding: This work was funded by the University of Jeddah, Jeddah, Saudi Arabia, under grant No. (UJ-24-DR-20424-1), Therefore, the authors thank the University of Jeddah for its technical and financial support.

Data Availability Statement: Data available on request.

Acknowledgments: I wish to express my sincere gratitude to Mohamed Mokhtar M. Mostafa, King Abdulaziz University, for their invaluable assistance and guidance in the X-ray diffraction (XRD) analysis during this study; I would also like to extend my sincere appreciation to Abdul-Hamid Emwas, Core Labs, King Abdullah University of Science and Technology (KAUST) for his expert assistance with the solid-state NMR experiments and the scanning electron microscopy (SEM) measurements during this work.

Conflicts of Interest: The authors declare no conflicts of interest.

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