# Catalytic Synthesis of 5-Substituted Tetrazoles: Unexpected Reactions and Products

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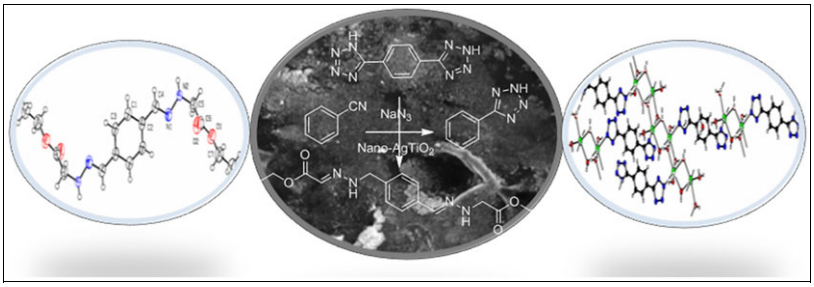



Tetrazoles are incredibly useful organic molecules with a wide range of applications from medicinal chemistry as carboxylic acid isosteres to high energy density materials in space research. In an effort to develop an easy protocol for the synthesis of tetrazoles from nitriles, we used nano-Ag-$TiO_2$ as an efficient heterogeneous catalyst for the reaction of various nitriles and sodium azide to afford 5-substituted tetrazoles in excellent yields. By this method, a wide variety of aryl nitriles underwent [3 + 2] cycloaddition to afford tetrazoles in excellent yields. Further reaction of tetrazoles with ethylchloroacetate resulted in the formation of expected products, except for a bis-tetrazole, which underwent ring opening and subsequent reaction to afford an unusual product. The bis-tetrazole also formed an unusual polymeric sodium complex in aq. NaOH solution. X-ray crystallography revealed a distorted octahedral geometry for the complex, which forms a three-dimensional network of chains interlinked by bis-tetrazole moieties through a network of H-bonds.



## INTRODUCTION

Tetrazole, a five-membered nitrogen heterocycle, scarce in nature has been of much scientific attention, owing to its rich and diverse chemical properties [1,2]. Most of the applications of this class of compounds are related to the acid–base properties of the tetrazole ring. In fact, the tetrazole acid fragment, $–CN_4H$, has similar acidity to the carboxylic acid group, $–CO_2H$, and is almost isosteric with it [1]. Due to the high enthalpy of formation, tetrazole decomposition results in the liberation of two nitrogen molecules and a significant amount of energy. Therefore, several tetrazole derivatives have been explored as explosives, propellant components for missiles and as gas generators for airbags in the automobile industry [3,4]. The four nitrogen atoms connected in succession may be involved in protolytic processes, and many physical, chemical, physicochemical, and biological properties of tetrazoles are closely related to their ability to behave as acids and bases [1,2,5].

Different synthetic methods and diverse studies are dedicated to tetrazoles, and a number of synthetic methods are already available, but there still exists a demand for improved and less tedious protocol which allows an effective transformation in the presence of a wide range of functional groups [2,6–12]. In recent years, there has been increasing emphasis on the use and design of environment friendly solid catalysts to reduce the amount of toxic waste. Heterogeneous catalysis is widely used in industrial applications because of the facile separation, which often results in lower operating costs. On the other hand, homogeneous catalysis has limited industrial applications due to the difficult and costly catalyst separation and recovery [13]. Different heterogenous catalytic systems have been employed for the synthesis of tetrazoles [2,14]. Most of these methods suffer from disadvantages such as the fact they require a large excess of sodium azide, higher temperatures, and longer reaction times. Nano-$TiO_2$ and nano-Ag have been used as catalysts separately [15,16], but with longer reaction times and tedious separation process. Sulfated titania has also been reported to be an efficient catalyst [14], but the more acidic nature of this catalyst hampers its use. Compared to Ag, nano Ag-$TiO_2$ is cost efficient and easily separable, and we used this catalyst for the synthesis of tetrazoles.

Moreover, derivatization of tetrazoles is being pursued to prepare diverse functionalized compounds for use in chemical industry. Alkylation is reported to be a simple and important route to prepare diverse tetrazole derivatives, and alkylation with alkyl halides, dialkyl sulphates, diazomethane, o-chloro carbonyl compounds, methyl chloromethyl ether, α-methylstyrene, etc. has been reported [17–20]. Normally, all these reactions have resulted in the synthesis of desired products. Our study for the first time reports the ring opening of 5-(4-2*H*-tetrazole-5-yl)-phenyl-1*H*-tetrazole on reaction with ethylchloroacetate. The ring opening and subsequent reaction with ethylchloroacetate resulted in the synthesis of an unexpected acetohydrazide product. The ring opening property of bis-tetrazole obtained in this study could be explored as a new synthetic route, or this compound can be used as a new starting scaffold for the preparation of diverse range of organic compounds. We also report a serendipitous synthesis of a rare polymeric bis-tetrazole-sodium complex obtained from the same bis-tetrazole.

## RESULTS AND DISCUSSION

First, we optimized the amount of nano Ag-$TiO_2$ catalyst required in the reaction between benzonitrile and sodium azide (Table 1; Scheme 1). The reaction conditions were standardized, and effects of solvents, temperature, and catalyst loading were investigated.

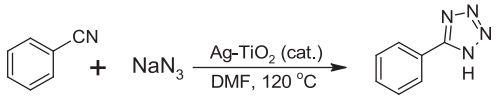
**Table 1**

Preparation of 5-phenyltetrazole using varying amounts of nano-Ag-$TiO_2$ at 120°C in DMF.

| Entry | Ag-$TiO_2$ (g) | Time (h) | Yield (%)[a] |
|---|---|---|---|
| 1 | 0.01 | 1 | 60 |
| 2 | 0.02 | 1 | 98 |
| 3 | 0.025 | 1 | 98 |
| 4 | 0.05 | 1 | 98 |
| 5 | No catalyst | 1 | 20 |
| 6 | Bare $TiO_2$ | 1 | 50 |
| 7[b] | Nano $TiO_2/SO_4^{2-}$ | 1.5 | 93 |
| 8[b] | 30 mol% Ag | 8 | 94 |
| 9[b] | Nano $TiO_2$ | 14 | 82 |

[a]Isolated yield.
[b]Results taken for comparison from the previous studies [14–16], respectively.

**Scheme 1.** General synthesis of 5-substituted tetrazoles using $AgTiO_2$ as catalyst.




Results revealed that the nature of solvents plays an important role.

Reactions in polar protic solvents such as methanol and ethanol (Table 2; entries 1 and 2) result in only 20% and 10% product formation while acetonitrile (Table 2; entry 3) gives 30% product. Other solvents such as tetrahydrofuran, chloroform, and 1,4-dioxane (Table 2; entries 4–6) also gave unsatisfactory results with no product formation after 24 h. Water was also not a suitable solvent for this reaction (Table 2; entry 7). Dimethylformamide (DMF) was found to be comparatively the best solvent for this reaction (Table 2; entry 8). Moderate to good yield is obtained on increasing the quantity of sodium azide from 1 to 1.5 equivalents. The optimum amount of Ag-$TiO_2$ was found to be 20 mg (Table 1) in the presence of nitrile (1 mmol) and sodium azide (1.5 mmol) in DMF (1 mL).

We next examined different benzonitriles possessing a wide range of functional groups to understand the scope and generality of the Ag-$TiO_2$ catalyzed reaction (Table 3). The nature of the substituent on the benzonitrile did not affect the reaction time. Due to the insignificant effect of the substituents on the reaction, the effect of electron withdrawing and releasing groups is not clear. Interestingly, 1,4-dicyanobenzene afforded a double addition product (Table 3; entry 10), contrary to the reported mono addition product in literature [14]. The double addition product offers a bis-tetrazole, in which two tetrazole rings are separated by a phenyl ring.

Demko and Sharpless reported that coordination of nitrile to the Lewis acidic $Zn^{2+}$ is the source of the catalytic effect in the formation of 1*H*-tetrazoles [12]. Subsequently, nucleophilic attack by azide followed by hydrolysis affords tetrazole. A plausible mechanism for Ag-$TiO_2$ catalyzed synthesis of tetrazoles could be thought to be driven by the coordination of the nitrile with the Lewis acid sites of Ag-$TiO_2$, which undergoes [3 + 2] cycloaddition with the readily available azide. A

**Table 2**

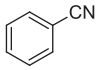
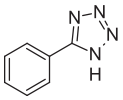
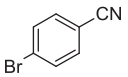
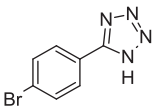
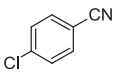
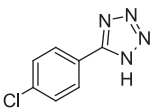
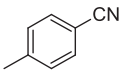
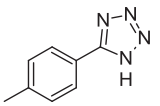
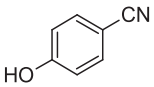
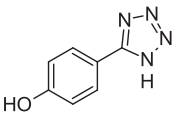
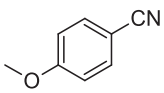
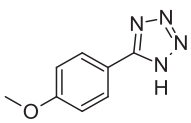
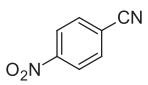
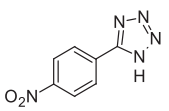
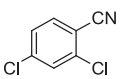
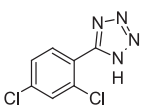
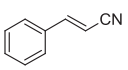
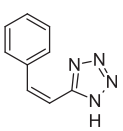
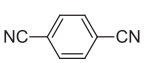
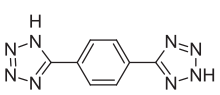
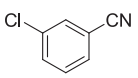
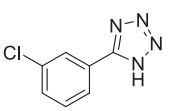
Effect of different solvents on the reaction.

| Entry[a] | Solvent | Time (h) | Yield (%)[b] |
|---|---|---|---|
| 1 | Methanol | 24 | 20 |
| 2 | Ethanol | 24 | 10 |
| 3 | Acetonitrile | 24 | 30 |
| 4 | THF | 24 | No reaction |
| 5 | Chloroform | 24 | No reaction |
| 6 | 1,4-dioxane | 24 | No reaction |
| 7 | $H_2O$ | 24 | No reaction |
| 8 | DMF | 1 | 98 |

[a]Reaction conditions: nitrile (1 mmol), sodium azide (1.5 mmol), catalyst (20 mg), and reflux.
[b]Isolated yield.

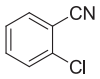
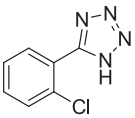
**Table 3**

Synthesis of different tetrazoles using Ag-$TiO_2$ as catalyst.

| Entry | Nitrile | Tetrazole | Yield (%)[b] | Ref. |
|---|---|---|---|---|
| 1 |  |  | 98 | Myznikov *et al*. [5] |
| 2 |  |  | 98 | Herr [1] |
| 3 |  |  | 98 | Najmeh *et al*. [7] |
| 4 |  |  | 93 | Najmeh *et al*. [7] |
| 5 |  |  | 93 | Myznikov *et al*. [5] |
| 6 |  |  | 96 | Myznikov *et al*. [5] |
| 7 |  |  | 98 | Myznikov *et al*. [5] |
| 8 |  |  | 95 | Herr [1] |
| 9 |  |  | 95 | Myznikov *et al*. [5] |
| 10 |  |  | 98 | Present study |
| 11 |  |  | 96 | Mona and Sepideh [14] |

(*Continues*)

**Table 3**
(*Continued*)

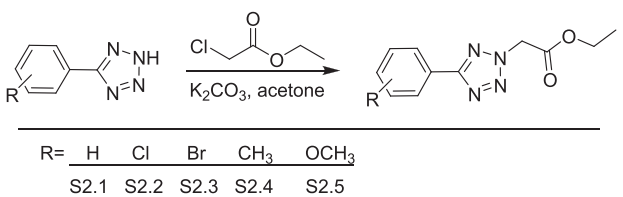
| Entry | Nitrile | Tetrazole | Yield (%)[b] | Ref. |
|---|---|---|---|---|
| 12 |  |  | 92 | Mona and Sepideh [14] |

[a]Reaction conditions: nitrile (1 mmol), sodium azide (1.5 mmol), and catalyst (20 mg), at 120°C in DMF;
[b]Isolated yield.

final acidification results in the precipitation of the product. The Ag-$TiO_2$ catalyst was recovered from the reaction mixture by simple filtration and washing with water and ethylacetate followed by drying in an oven at 100°C for 1 h. From each experiment, more than 95% of the Ag-$TiO_2$ catalyst was recovered. The recovered catalyst was reused three times without any loss of activity. The products were characterized by IR, $^1$H-NMR, $^{13}$C-NMR, ESI MS, and from melting points. The disappearance of one strong and sharp absorption band (CN stretching band), and the appearance of an NH stretching band in the IR spectra, was evident for the formation of 5-substituted 1*H*-tetrazoles. $^1$H-NMR, $^{13}$C-NMR, and ESI MS spectra also supported the formation of tetrazoles from nitriles as evidenced from the reported data [8,11,12,14]. The spectroscopic data of the bis-tetrazole **S1.1** (Table 3; entry 10) is given in Supporting Information.

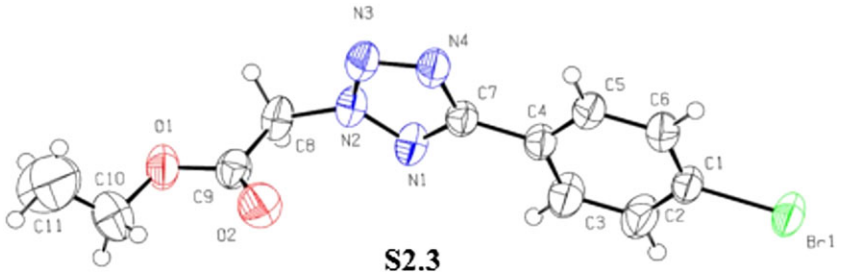
We further set out to synthesize some tetrazole derivatives by alkylation reaction using ethylchloroacetate. This route offers many structurally diverse polyfunctional tetrazole derivatives. Normally, the alkylation reaction is straight forward and results in the formation of desired products. Reaction of tetrazoles with ethylchloroacetate under standard conditions gave expected products (Scheme 2), which were confirmed by different spectroscopic techniques and X-ray crystallography as shown in Figure 1. The X-ray crystallography analysis shows that **S2.3** and **S2.5** crystallize in the common monoclinic space group P21/c with one molecule per asymmetric unit. In both structures, the molecules pack in columns with close proximity between neighboring aromatic rings, thus suggesting the existence of π…π interactions.

**Scheme 2.** Alkylation of tetrazoles and formation of expected products **S2.1**–**S2.5**.

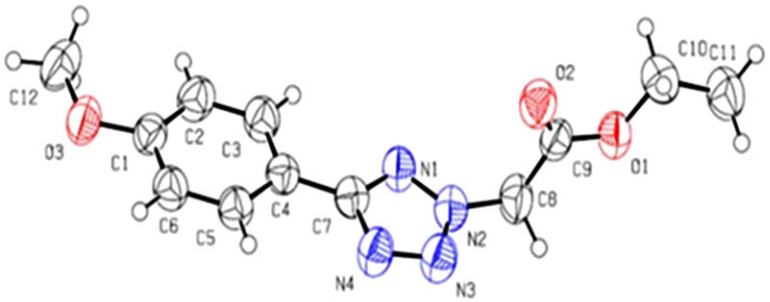



Alkylation of tetrazoles usually yields a mixture of N1 and N2 isomers, but the presence of substituents has a marked effect on deciding the ratio of the N1 and N2 isomer. "Electronic effects are dominant, with electron-donating substituents at C5 favouring alkylation at N1 while electron-withdrawing substituents favour N2." Besides, temperature and solvent can also lead to changes in the N1:N2 alkylation ratios. However, we exclusively got the N2 alkylated products for all mono-tetrazole derivatives. But the reaction of bis-tetrazole did not give the expected product, which underwent ring opening and subsequent reaction with ethylchloroacetate to afford an unusual bis-acetohydrazide product **S2.6** (Scheme 3). The same product was obtained regardless of the replacement of acetone as solvent with DMF or decreasing the temperature to 0°C. **S2.6** as shown in Figure 2 crystallizes in the triclinic P-1 space group, with half of a molecule in the asymmetric unit cell. The center of inversion lies in the center of the molecule. The central atoms are located in a common plane with the substituted carboxylic group lying almost perpendicular to the central plane. The short bond distance N1-C4 [1.262 Å] accounts for a double bond.

Due to the high enthalpy of formation, tetrazole decomposition results in the liberation of two nitrogen molecules and a significant amount of energy. As a general rule, the tetrazole ring can undergo cleavage in three different ways: (a) through the (N-1) (N-2) and (N-3) (N-4) bonds, releasing molecular nitrogen and forming a diazirine derivative; (b) through the (N-1) (C-5) and (N-3) (N-4) bonds; and (c) through (N-1) (N-2) and (N-4) (C-5) bonds. In the two latter cases, the precise nature of the products varies depending on the substituents present in the tetrazole ring, but one of the products is always an azide, which then can undergo subsequent reactions, most of times eliminating $N_2$ to form the nitrene that then can further react to form the final product. Literature data suggest that 2-substituted



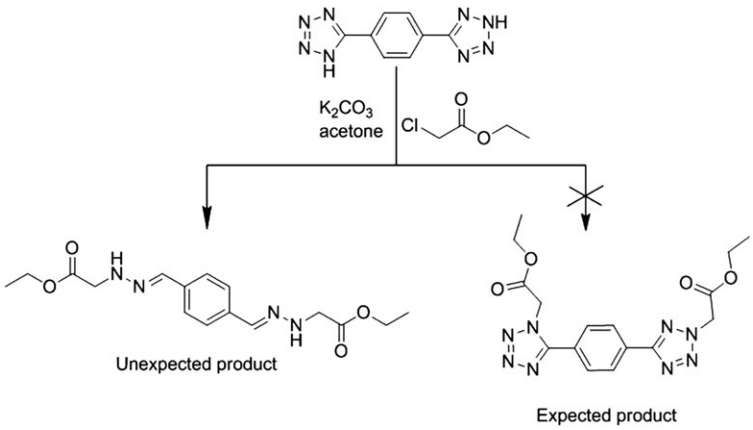

**S2.3**




**S2.5**

**Figure 1.** Oak Ridge thermal ellipsoid plot diagram of alkylated tetrazoles **S2.3** and **S2.5** drawn at the 50% probability level. [Color figure can be viewed at wileyonlinelibrary.com]

**Scheme 3.** Unexpected reaction of bis-tetrazole.




tetrazoles feature facile elimination of $N_2$ under a variety of experimental conditions to yield highly reactive nitrilimine intermediates (Scheme 4). These species undergo 1,3-dipolar cycloaddition reaction with dipolarophiles to yield diverse heterocyclic scaffolds [21,22].

The ring opening of tetrazoles has also been found to be substituent dependent where electron-deficient substituents at position 2 accelerate the rates and electron-donating moieties slow down the ring opening [26,27]. The presence of these groups at position 5 shows a reciprocal effect. But the overall effect of a substituent at position 2 on the rate of formation of nitrilimines is more profound than that of a group at position 5 of the tetrazoles ring [23,24].

The coordination compounds of alkali metals on the other hand are rare owing to their large size and small

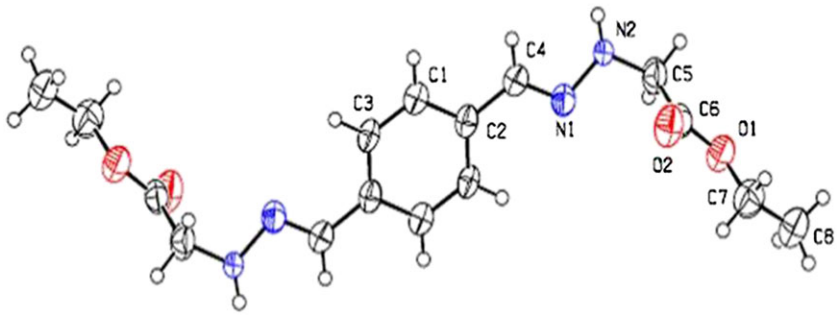
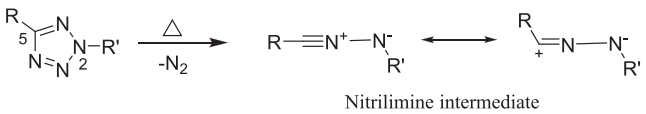



**Figure 2.** X-ray crystallographic structure of acetohydrazide product obtained after ring opening of bis-tetrazole **S2.6**. [Color figure can be viewed at wileyonlinelibrary.com]

**Scheme 4.** Ring opening of tetrazoles.




Nitrilimine intermediate

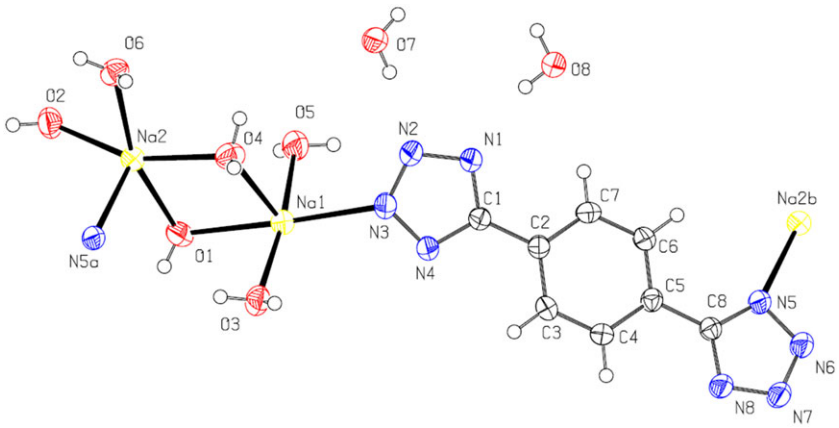



**Figure 3.** Oak Ridge thermal ellipsoid plot diagram of **S2.7** drawn at the 50% probability level. [Color figure can be viewed at wileyonlinelibrary.com]

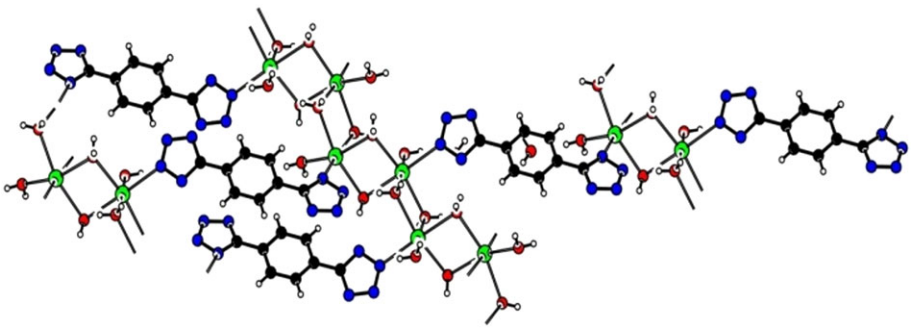


**Figure 4.** Packing diagram of **S2.7** showing the chain formation. [Color figure can be viewed at wileyonlinelibrary.com]

charge. Complexation of sodium and its higher congeners is an uncommon phenomenon, although not completely absent and in some crystalline solids, the coordination number ranges from 4 to 12 [25]. We obtained a bis-tetrazole (Table 3; entry 10) from the above synthetic procedure, which was found to be insoluble in common organic solvents except dimethyl sulfoxide (DMSO). However, the compound was found to be soluble in aq.

NaOH, and in keeping the solution for a few days, we obtained single crystals, which were resolved by X-ray single crystal structural analyses. Bis-tetrazole sodium complex (**S2.7**) crystallizes as an octohydrate in the triclinic space group P-1 with two sodium ions, two 5,5′-(1,4-phenylene)ditetrazolate ions, and eight water molecules in the asymmetric unit cell. The sodium ions have similar surroundings (Fig. 3). They all have a distorted octahedral coordination geometry defined by five oxygen atoms and one nitrogen atom from the organic moiety. The water molecules bridge the alkaline ions in ladder chains that run along the [011] direction. The bis-tetrazolate ions link the chains together, and the crystal cohesion is reinforced through a three-dimensional network of H-bonds (Fig. 4) (also see Tables S2 and S3). Further studies are in progress at present.

## CONCLUSIONS

In conclusion, we have developed an efficient method for the synthesis of 5-substituted (1*H*, 2*H*-tetrazoles) by treatment of nitriles with sodium azide in the presence of nano Ag-$TiO_2$ as catalyst. The significant advantages of this methodology are high yields, elimination of dangerous and harmful hydrazoic acid, a simple work-up procedure, and easy preparation and handling of the catalyst. The catalyst can be recovered by filtration and reused. Alkylation resulted in the ring opening and subsequent reaction of a bis-tetrazole with ethylchloroacetate to afford an acetohydrazide product, which crystallizes in the triclinic P-1 space group, with half of a molecule in the asymmetric unit cell as revealed by X-ray crystallography. This ring opening was not observed in mono-tetrazole derivatives. Importantly, a rare and new stable bis-tetrazole sodium complex was isolated for the first time, which forms a three dimensional network of chains interlinked by bis-tetrazole moieties through a network of H-bonds; properties desirable for high-energy density materials.

## EXPERIMENTAL

**General considerations.** All chemicals were purchased from Aldrich (Germany) and used as supplied unless otherwise indicated. Melting points (m.p.) were performed using a Mel-temp instrument, and the results are uncorrected. Reactions were monitored using thin-layer chromatography using commercially available precoated plates (Merck Kieselgel 60 F254 silica). Visualization was achieved with UV light at 254 nm or $I_2$ vapor staining.

**Measurements.** $^1$H and $^{13}$C-NMR spectra were recorded at room temperature on a Bruker AVANCE 500 NMR spectrometer using DMSO-$d_6$/$CDCl_3$ as solvent with tetramethylsilane as internal standard. Splitting patterns are designated as follows: s, singlet; d, doublet; dd, doublet of doublets; t, triplet; and m, multiplet. The ESI MS of all the compounds were recorded on a Bruker amazon SL (ion trap instrument).

**Synthesis of catalyst.** Bare $TiO_2$ and Ag-$TiO_2$ catalysts (1 wt % of Ag-$TiO_2$) were prepared by reported procedures (also see Fig. S3) [26,27].

**General procedure for the synthesis of 5-substituted (1*H*, 2*H*)-tetrazoles.** In a round-bottom flask, benzonitrile (1 mmol), sodium azide (1.5 mmol), and nano Ag-$TiO_2$ (20 mg) were charged. Then, the reaction mixture was stirred in distilled DMF (1 mL) at 120°C. The progress of the reaction was monitored by thin-layer chromatography (9:1 n-hexane: ethyl acetate). After completion of the reaction, the catalyst was separated by centrifugation and washed with doubly distilled water and acetone, and the solid was treated with 3N HCl (20 mL) under vigorous stirring. The aqueous solution finally obtained was extracted twice with ethyl acetate. The combined organic phase was washed with water and concentrated to precipitate the crude crystalline solid. All products were characterized by $^1$H-NMR, $^{13}$C-NMR, FTIR, and mass spectra, and the data for the known compounds were found to be identical with the literature [8,11,12,14]. Data for the newly synthesized tetrazoles are given in Supporting Information.

***5-[4-(2H-Tetrazol-5-yl)phenyl]-1H-tetrazole (S1.1).*** White solid; mp >250°C; $^1$H-NMR (DMSO-$d_6$) δ (ppm):: 8.04–8.24 (4H, m), 2.55 (1H, NH, br s), $^{13}$C-NMR (DMSO-$d_6$) δ (ppm): 162.5 (C=N), 136.6, 130.1; FTIR (ATR) $\nu_{max}$ ($cm^{-1}$): 3361 (N-H br stretch), 3000–2700 (C-H, Ar), 1587 (C=N), 1506 (C=C, Ar); ESI MS: *m/z*: 238.18 $[M + Na^+]^+$; 215.10 $[M + H]^+$ (Table 3; entry 11).

**Synthesis of substituted tetrazolyl-acetate derivatives.** Tetrazole (5-phenyl-2*H*-tetrazole) 1 mmol in dry acetone and $K_2CO_3$ (1.5 mmol) was added ethylchloroacetate (1 mmol) and refluxed for 12–24 h. In case of bis-tetrazole, 2 mmol of ethylchloroacetate was used. The reaction mixture was filtered hot, and the solvent was distilled off from the filtrate. The crude ester thus obtained was purified by recrystallization from ethanol.

***Ethyl 2-(5-phenyl-2H-tetrazol-2-yl)acetate (S2.1).*** Yield 62.5%; mp 145–147°C; IR $\nu_{max}$ ($cm^{-1}$): 3020 (C–H, Ar), 1722 (C=O), 1635 (C=N), 1584 (C=C, Ar); $^1$H-NMR (DMSO) δ (ppm): 7.98–7.45 (5H, m), 4.82 (2H, $CH_2$, s), 4.11 (2H, CH2, m); 1.38 (3H, $CH_3$, t); $^{13}$C-NMR (DMSO) δ (ppm): 165.0 (C=O) 160.5 (C=N), 137.7, 129.0, 126.8, 124.0, 64.5, 48.2, 16.2; ESI-MS *m/z*: [M + H] + 267.06.

***Ethyl 2-(5-(4-chlorophenyl)-2H-tetrazol-2-yl)acetate (S2.2).*** Yield 62.5%; mp 128–130°C; IR $\nu_{max}$ ($cm^{-1}$): 3028 (C–H, Ar), 1722 (C=O), 1635 (C=N), 1584

(C=C, Ar), 758 (C–Cl); $^1$H-NMR (DMSO) δ (ppm): 7.98–7.45 (4H, m), 4.82 (2H, CH2, s), 4.11 (2H, CH2, m); 1.38 (3H, CH3, t); $^{13}$C-NMR (DMSO) δ (ppm): 162.2 (C=O) 154.5 (C=N), 137.7, 126.0, 124.8, 122.0, 118.2, 64.5, 48.2, 16.2; ESI-MS *m/z*: [M + H] + 233.05.

***Ethyl 2-(5-(4-bromophenyl)-2H-tetrazol-2-yl)acetate (S2.3).*** Yield 62.5%; mp 130–132°C; IR $\nu_{max}$ ($cm^{-1}$): 3028 (C–H, Ar), 1722 (C=O), 1635 (C=N), 1584 (C=C, Ar), 758 (C–Br); $^1$H-NMR (DMSO) δ (ppm): 7.98–7.45 (4H, m), 4.82 (2H, CH2, s), 4.11 (2H, CH2, m); 1.38 (3H, CH3, t); $^{13}$C-NMR (DMSO) δ (ppm): 162.2 (C=O) 154.5 (C=N), 137.7, 126.0, 124.8, 122.0, 118.2, 64.5, 48.2, 16.2; ESI-MS *m/z*: [M + H] + 212.01.

***Ethyl 2-(5-(p-tolyl)-2H-tetrazol-2-yl)acetate (S2.4).*** Yield 62.5%; mp 145–147°C; IR $\nu_{max}$ ($cm^{-1}$): 3028 (C–H, Ar), 1722 (C=O), 1635 (C=N), 1584 (C=C, Ar), 758 (C–C); $^1$H-NMR (DMSO) δ (ppm): 7.98–7.45 (4H, m), 4.82 (2H, $CH_2$, s), 4.11 (2H, $CH_2$, m); 1.38 (3H, $CH_3$, t); $^{13}$C-NMR (DMSO) δ (ppm): 165.0 (C=O) 158.5 (C=N), 133.1, 129.8, 125.0, 64.5, 55.2, 24.6, 14.5; ESI-MS *m/z*: [M + H] + 247.14.

***Ethyl 2-(5-(4-methoxyphenyl)-2H-tetrazol-2-yl)acetate (S2.5).*** Yield 62.5%; mp 132–134°C; IR $\nu_{max}$ ($cm^{-1}$): 3028 (C–H, Ar), 1722 (C=O), 1635 (C=N), 1584 (C=C, Ar); $^1$H-NMR (DMSO) δ (ppm): 7.98–7.45 (4H, m), 4.82 (2H, CH2, s), 4.11 (2H, CH2, m); 1.38 (3H, CH3, t); $^{13}$C-NMR (DMSO) δ (ppm): 166.0 (C=O) 162.5 (C=N), 159.1 (C-O), 137.7, 124.8, 122.0, 64.5, 55.0, 50.2, 14.5; ESI-MS *m/z*: [M + H] + 263.10.

***Diethyl-1,4-phenylenebis (methanylylidene)-bis(hydrazine-2,1-diylidene)-diacetate (S2.6).*** Yield 62.5%; mp 158–160°C; IR $\nu_{max}$ ($cm^{-1}$): 3028 (C–H, Ar), 1722 (C=O), 1635 (C=N), 1584 (C=C, Ar); $^1$H-NMR (DMSO) δ (ppm): 8.45 (s, 1H, CH), 8.38 (s, 1H, CH), 8.25 (s, 2H, CH) 8.00 (s, 4H, Ar), 4.82 (2H, CH2, s), 4.11 (2H, CH2, m); 1.38 (3H, CH3, t); $^{13}$C-NMR (DMSO) δ (ppm): 165.0 (C=O) 154.5, 149.5 (C=N), 138.7, 129.8, 62.5, 13.2; ESI-MS *m/z*: [M + H] + 331.15.

**X-ray crystallography.** For the determination of the crystal structure by X-ray diffraction, a crystal of the aforementioned compounds were glued separately to a glass fiber and mounted on a Bruker APEX II diffractometer. Diffraction data were collected at room temperature 293(2) K using graphite monochromated MoKα (λ = 0.71073 Å). Absorption corrections were made using SADABS [28]. The structures were solved by direct methods using SHELXS-9725 and refined anisotropically (non-H atoms) by full-matrix least squares on F2 using the SHELXL-97 program [29]. PLATON [30] was used to analyze the structures and for figure plotting. Atomic coordinates, thermal parameters, and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre (CCDC). Any request to the CCDC for this material should quote the full literature citation and the reference numbers CCDC 1568228 (**S2.3**); 1568229 (**S2.5**); CCDC 1568226 (**S2.6**), and CCDC 1416396 (**S2.7**). Crystallographic details can be found in Tables S1, S2, S3, and S4.

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