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NOVEL 2*H*-1,2,3-TRIAZOLE SODIUM COMPLEX FROM *N*-[2-AMINO-1,2-DICYANOVINYL]ALKANAMIDES

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Abstract - Diazotization at 0 ^{o}C of *N*-[2-amino-1,2-dicyanovinyl]ethanamide **2a** or propanamide **2b** prepared from diaminomaleonitrile (DAMN) **1** using aqueous acetic acid and $NaNO_2$ solution furnished sodium complex **3**. The X-ray structure of the complex **3** showed that it is a 1:1 mixture of the neutral 2*H*-triazole heterocycle **4ii** and its anion deprotonated at the central (N) atom of the ring, together with a sodium counter ion and two coordinated water molecules. However, when the diazotization reaction was carried out in the presence of aqueous HCl, the product was 5-cyano-2*H*-[1,2,3]triazole-4-carboxylic acid amide monohydrate **4ii**. Diazotization of DAMN **1** using aqueous HCl furnished 1*H*-1,2,3-triazole-4,5-dicarbonitrile **5**, whereas with acetic acid there was no reaction, and hence no route analogous to that leading to complex **3**. The structure of both complex **3** and the triazole monohydrate **4ii** were solved using X-ray crystallography, and the compounds under study were fully characterized using spectroscopic techniques.

INTRODUCTION

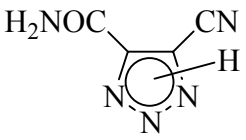
1,2,3-Triazole heterocycles have generated a great deal of interest notably in the last decade due to the important roles they have played in organic syntheses and the pharmaceutical industry.[1-4] Many methods were described for the synthesis of different 1,2,3-triazole systems bearing substituents on the *N*-1 and *N*-2 sites of the ring.[1-8] The most common of these processes is the cycloaddition of an alkyne to an azide.[4] Although a large number of 1,2,3-triazole derivatives were synthesized, annular tautomerism in these systems remains unresolved in spite of the extensive studies that were devoted to this phenomenon. In these investigations, researchers have used different characterization techniques including spectroscopic analyses, kinetic methods and ^{15}N NMR on various 1,2,3-triazole derivatives.[1-4,8,9]

In earlier work, we have shown that DAMN **1** is a versatile precursor for the synthesis of various heterocyclic compounds that have special importance in areas ranging from synthetic heterocycles and natural products to pharmaceuticals.[10-14] During our investigations on the synthesis of new heterocyclic-based AT_1-non-peptide angiotensin (II) receptor antagonists derived from DAMN **1**, we proved that alkylation of 1*H*-1,2,3-triazole-4,5-dicarbonitrile **5ii** gave two isomers.[14] Separation by HPLC using 50% aqueous acetonitrile showed that the major isomer is 2-alkyl-1,2,3-triazole-4,5-dicarbonitrile, thus confirming that the 2*H* tautomer of **5ii** was predominant in the reaction mixture.[14] The 1*H*-1,2,3-triazole-4,5-dicarbonitrile isomer **5ii** was more easily prepared by diazotization of DAMN **1** in aqueous HCl following the procedure reported by Hinkel *et.al*.[1] On the other hand, diazotization of *N*-[2-amino-1,2-dicyanovinyl]ethanamide **2a** by this approach furnished cyano-1,2,3-triazole carboxyamide. These findings prompted us to reinvestigate these procedures. In this paper, we report the structural characterization of 5-cyano-2*H*-[1,2,3]triazole-4-carboxylic acid amide monohydrate **4ii** and a direct method to synthesize its novel sodium complex **3**. The X-ray structure of compound **3** is presented.

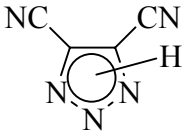
RESULTS AND DISCUSSION

SYNTHESIS AND CHARACTERIZATION

Hinkel and co-workers[1] have reported that the diazotization of *N*-[2-amino-1,2-dicyanovinyl]ethanamide **2a** and DAMN **1** in aqueous HCl solution gave cyano-[1,2,3]triazole carboxyamide **4i** and 1,2,3-triazole-4,5-dicarbonitrile **5i**, respectively. The two compounds are formally assigned the following structures:

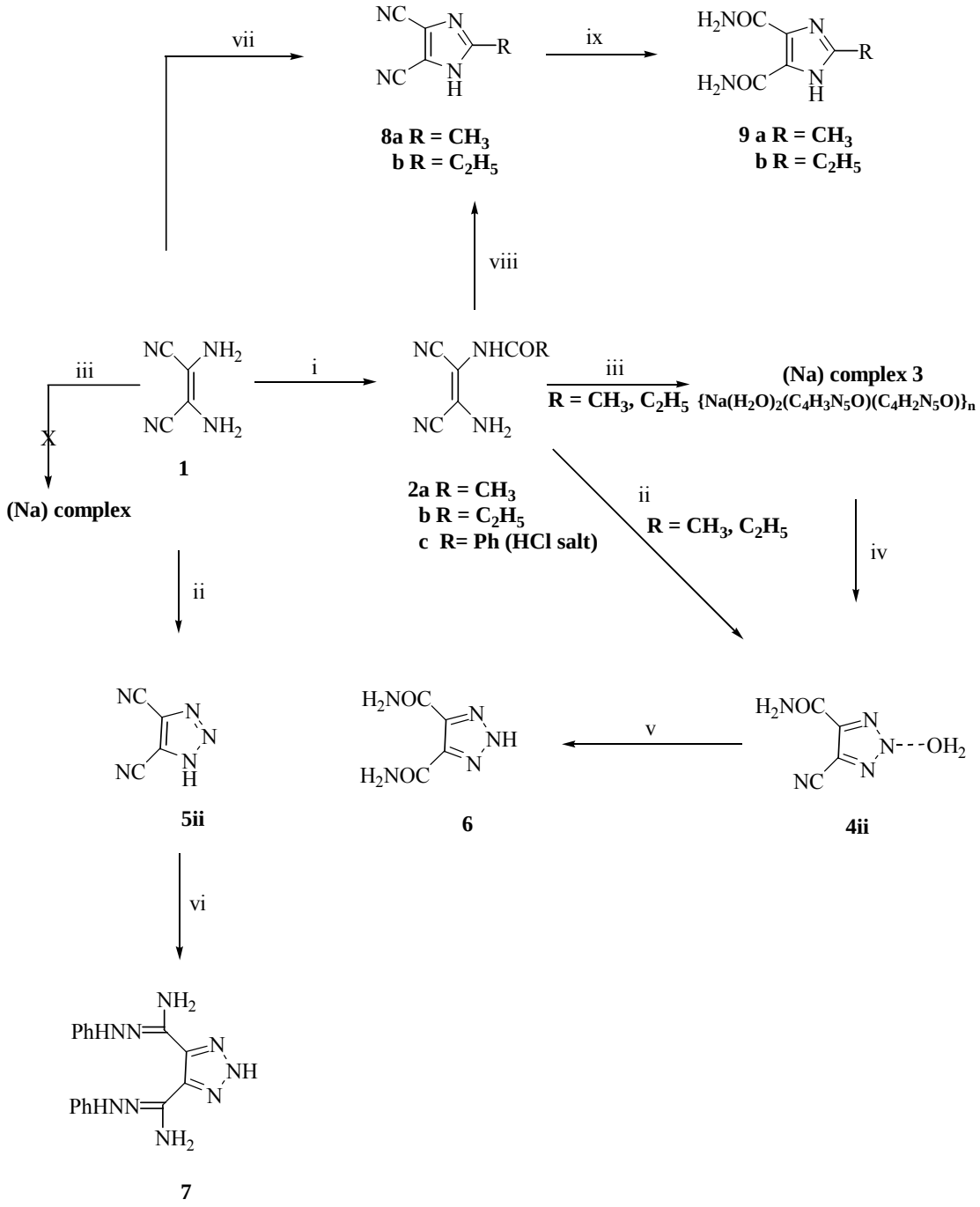


4i



5i

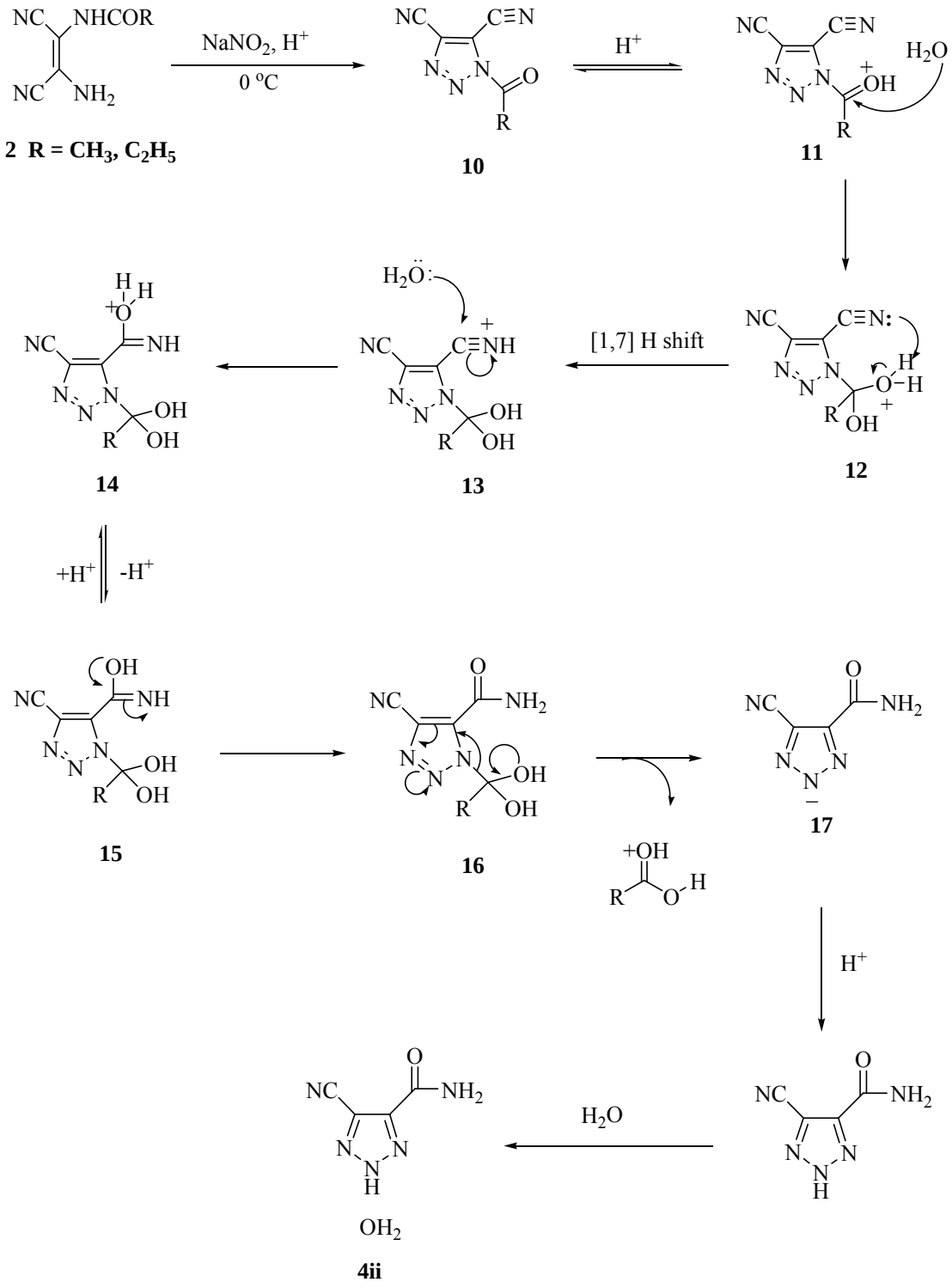
When the precursor, *N*-[2-amino-1,2-dicyanovinyl]ethanamide **2a,** was synthesized from DAMN **1** and subsequently diazotized using aqueous HCl at 0 ^{o}C, a white crystalline solid was obtained (Scheme 1, routes i, ii). Both melting point and elemental analysis agreed with the data reported for **4i**.[1] The ^{1}H NMR spectra of the crystalline material showed two singlets at δ 7.95 and 8.22, and a broad singlet at δ 15.90 ppm which disappeared on shaking with deuterium oxide. The ^{13}C NMR revealed four quaternary carbons, one of which was detected at 160.3 ppm assigned to the carbonyl group. The IR spectra also indicated the presence of a (C=O) stretching frequency at 1677 cm^{-1}. These results are consistent with the structure of the triazole heterocyclic ring system in **4ii**. We have previously noted that in order to distinguish between alternative feasible heterocyclic tautomers, it is often helpful to resort to an investigation of derivatives.[14] That the isomeric form of **4i** is the 2*H* tautomer **4ii** has been confirmed by x-ray analysis. The x-ray crystal structure (Figures 1,2) is that of the 5-cyano-2*H*-[1,2,3]triazole-4-carboxylic acid amide monohydrate **4ii**. Serendipitously, use of an acid (CH_3CO_2H) weaker than HCl for the diazotization of **2a** also afforded white crystals, but with a novel identity **3** (Scheme 1, iii). Although the MS and ^{13}C NMR spectra of these crystals were consistent with **4i**, the ^{1}H NMR showed a dramatic shift of the proton from δ = 15.90 to δ = 9.54 ppm, and the solubility, melting point and elemental analysis were also different from those of **4i**. An HMBC experiment performed on the isolated crystals showed no correlation between the proton at δ = 15.90 ppm and any of the four carbons. The two different diazotization conditions were also applied to the reaction of *N*-[2-amino-1,2-dicyanovinyl]propanamide **2b** which gave products analogous to those obtained from the ethanamide derivative **2a**. Under the experimental conditions described here, **2c** remained unreacted (Scheme 1, ii).



Scheme 1: i) **2a**: AcCl (1 equiv.), AcOEt, rt, 1.5 h, deionised water or acetic anhydride (2 equiv.), 5-10 min; **2b**: propanoic anhydride (1 equiv.), rt; 10 min; **2c**: benzoyl chloride (1 equiv.), AcOEt, rt, 1.5 h; ii) HCl/$NaNO_2$, 0 ^oC to rt, 1 h; iii) AcOH (aq), $NaNO_2$, 0 ^oC to rt; iv) HCl (aq.), rt; v) AcOH/HCl, reflux, 1 h; vi) $PhNHNH_2$, rt, 1 h; vii)

triethylorthoacetate/propionate (1.2-1.4 equiv.), $NaOCH_3$, anisole, water bath 100 ^oC, 2 h; viii) NaH (1 equiv.), DMF, reflux, 10-18 h; ix) $PhNHNH_2$, heat, 1 week, 50 ^oC.

An acceptable pathway describing the formation of the 2*H* tautomeric form and the attendant conversion of one of the two cyano moieties into an amide group during the diazotization of **2a** and **2b** to give **4ii** is outlined in Scheme 2. The X-ray structure of **2a** showed that the (C=O) of the acetamido group is on the same plane and facing the (C≡N) function of the same vinylic carbon.[10,14] Diazotization of **2a,** protonation of (C=O) and nucleophilic attack by the (H_2O) on the (C=O) carbon, subsequent thermally allowed sigmatropic [1,7] hydrogen shift, and further interaction with a second water molecule (Scheme 2, **10**-**14**) leads after rearrangement and de-acylation to the anion of the 2*H* isomeric form **17** of the triazole ring of **4ii**. The presence of this anion is crucial to the formation of both the monohydrate **4ii** and the novel sodium complex **3**. Besides, the amide group assists in the de-acylation process and in the stabilization of the incipient triazole anion **17**. The anion is also stabilized by the conjugative electron-withdrawing effect of the remaining (C≡N) group. Protonation of the anion **17** at the N-2 site provides the corresponding tautomer, the hydration of which gave the structure which was identified through x-ray analysis as **4ii**. Conversion of the remaining cyano group of **4ii** into a second amide functionality to give **6** requires further treatment (Scheme 1, v).



Scheme 2: Feasible mechanism for the formation of 5-cyano-2*H*-[1,2,3]triazole-4-carboxylic acid amide **4ii**.

Remarkably, when milder (aqueous CH_3CO_2H) acid conditions were used in the diazotization reaction, a portion of the stabilized triazole anion **17** persisted in the buffer-like (CH_3CO_2H/CH_3CO_2Na) medium to form an ion pair with the sodium counterion, and hence to generate complex **3** (Scheme 1, iii). As

expected, this triazole anion did not survive the much stronger (aqueous HCl) acid conditions (Scheme 1, ii), a fact further confirmed by the addition of aqueous HCl, which at room temperature, it helped decompose complex **3** into **4ii** (Scheme 1, iv). This observation also lends support to the possible involvement of the triazole anion **17** in the proposed reaction mechanism (Scheme 2). Besides, the diazotization of DAMN **1** in the presence of HCl resulted in the 1*H* triazole compound **5ii** (Scheme 1, ii). However, alternative use of aqueous CH_3CO_2H failed to furnish a (Na) complex analogues to **3**. It is to be noted that the 2*H* triazole tautomer formed both a monohydrate derivative and a (Na) complex derivative during diazotization (Scheme 2). The effect of solvent and temperature on the ratio of the 1*H* : 2*H* tautomers of the 1,2,3-triazole derivatives has been reported.[14]

Further, the molecular geometry of the monohydrate **4ii** indicates that the amide group as shown by x ray is essentially coplanar with the triazole ring, an observation that might be of interest with regards to the structure of triazoles. The x-ray structure also reveals that while the water (O) atom is coplanar with the ring, its (H) atoms are not; thus resulting in a 3D H-bond network. The hydrogen atom of the triazole ring, with its implication for the tautomeric heterocycle structure, was found in a clearly different location of the Fourier map (Figure 2), an indication of the presence of an N-H---O hydrogen bond between the 2*H* triazole ring and a water molecule (Figures 1-3).

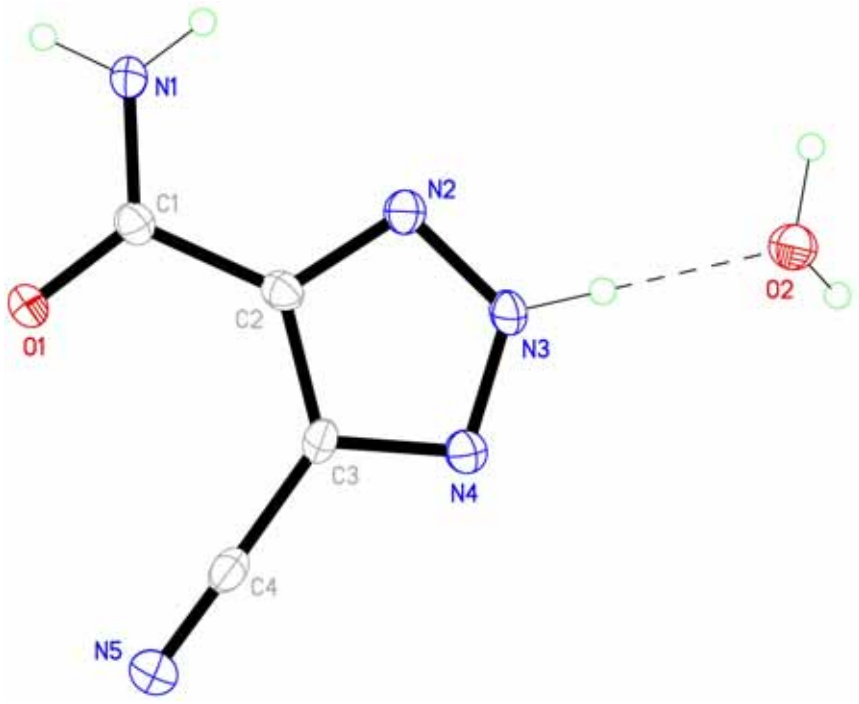


Figure 1. Molecular structure of 5-cyano-2*H*-[1,2,3]triazole-4-carboxylic acid amide monohydrate **4ii**.

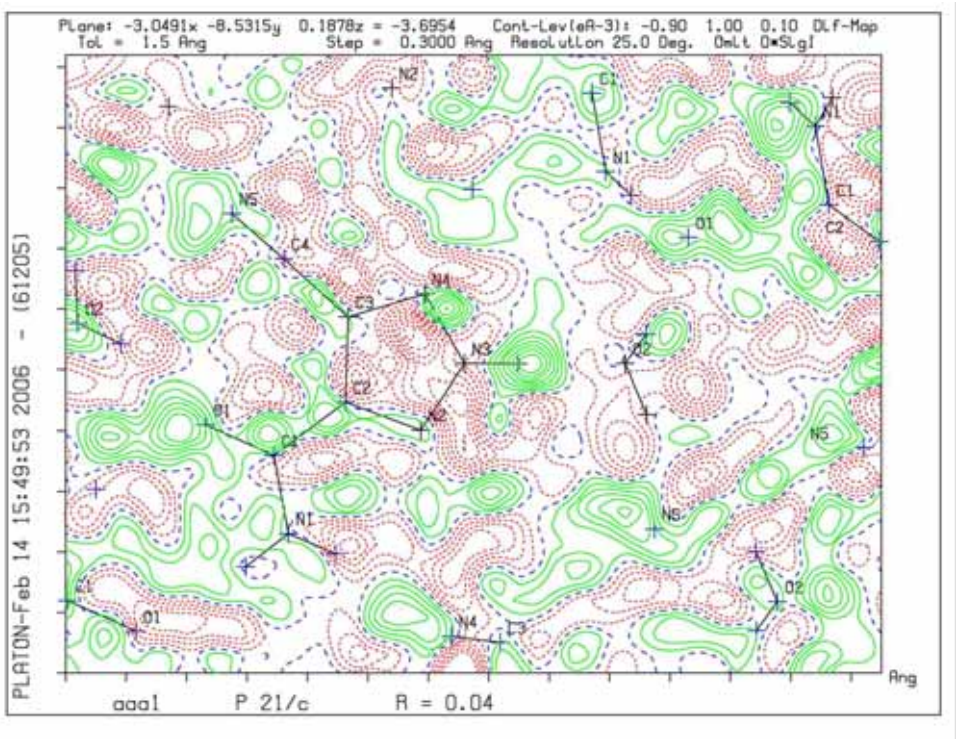


Figure 2. Fourier map showing location of ring N–H hydrogen atoms of **4ii.**

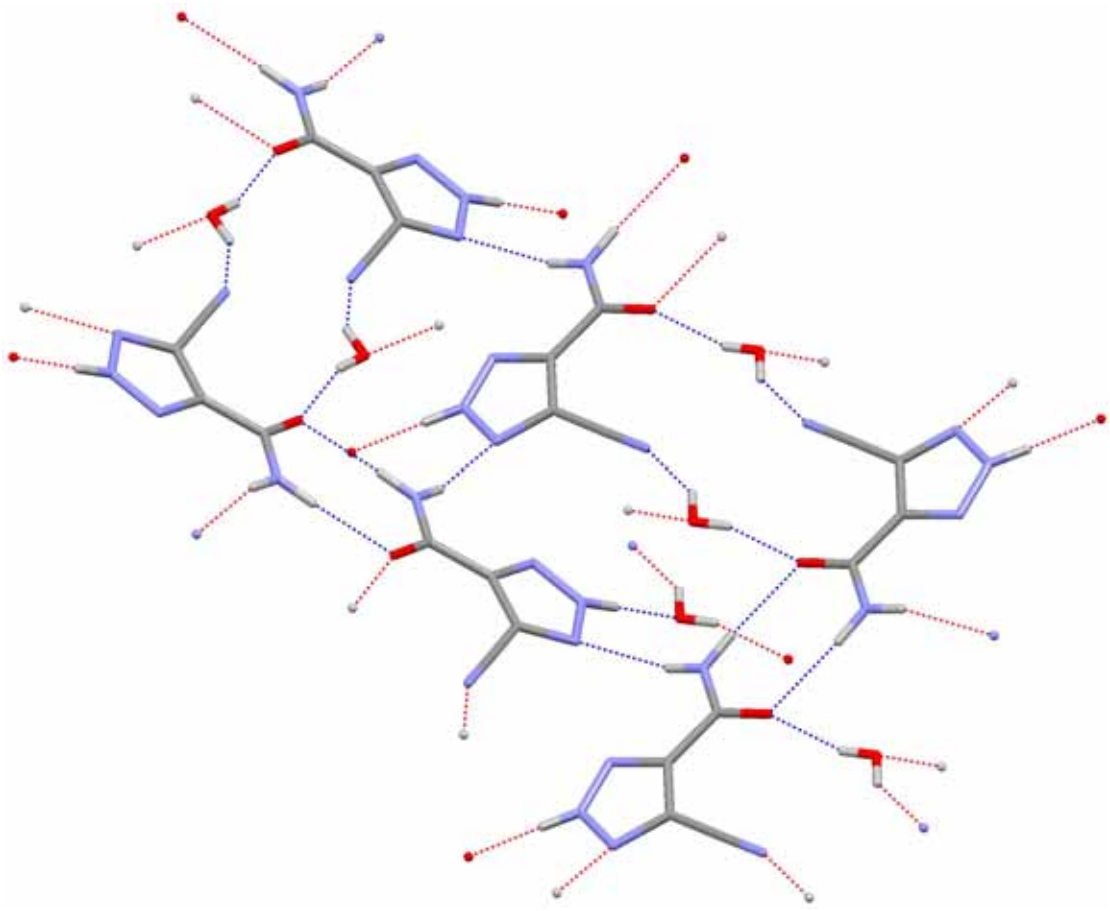


Figure 3. Part of the 3D hydrogen-bonded network in 5-cyano-2*H*-[1,2,3]triazole-4-carboxylic acid amide monohydrate **4ii.** Blue dashed lines indicate hydrogen bonds, red dashed lines indicate hydrogen bond continuation.

The present work on triazoles **4ii** and **5ii** was extended. First, triazole **4ii** in aqueous AcOH/HCl solution was refluxed for 1 h (Scheme1, v); the result was formation of a white precipitate with a molecular weight of 155 amu. IR analysis confirmed the disappearance of the cyano group, and ^{1}H and ^{13}C NMR spectra indicated formation of the dicarboximide **6**. In earlier work, we have shown that imidazoles **8a,b** can be synthesized from DAMN **1** (Scheme 1, vii)] or from **2a,b** (route viii)]. When these imidazoles are further hydrolyzed under mild basic conditions, in the presence of excess phenylhydrazine, and with gentle heating for several days, they are converted into the dicarboxylic acid amide **9a,b**. On the other hand, when the triazole **5ii** [prepared from DAMN **1** (Scheme 1, ii)] is treated with excess phenylhydrazine under conditions similar to those used with **8a,b**, a yellow precipitate was formed (Scheme 1, ii). The MS of this product showed a base peak at m/z = 77 and a peak at 335, the later with 55 % intensity. The ^{1}H NMR spectrum revealed the presence of two phenyl groups, a broad singlet at δ 8.19 ppm for 4H, and the ^{13}C NMR spectrum showed only 6 carbon signals. These results point to a symmetric structure compatible with the novel 2*H* tautomer **7**. Formation of an intermediate analogous to **7** during the transformation of **8** into **9** cannot be ruled out, but due to solubility effects the transience of this intermediate could not, however, be confirmed.

*X-RAY ANALYSIS OF COMPLEX **3***

The MS spectral data of **3** were similar to those of **4ii**. However, the ^{1}H NMR spectrum of one of the protons, the melting point, solubility, and the elemental analysis for C, H and N were widely different. The structures of the two compounds were finally established by an x-ray study of their crystal structure. Compound **3** is a $Na(H_2O)_2(C_4H_3N_5O)(C_4H_2N_5O)$ sodium complex (Figure 4) of a 1:1 mixture of the

neutral 2*H*-triazole and its anion **17**.

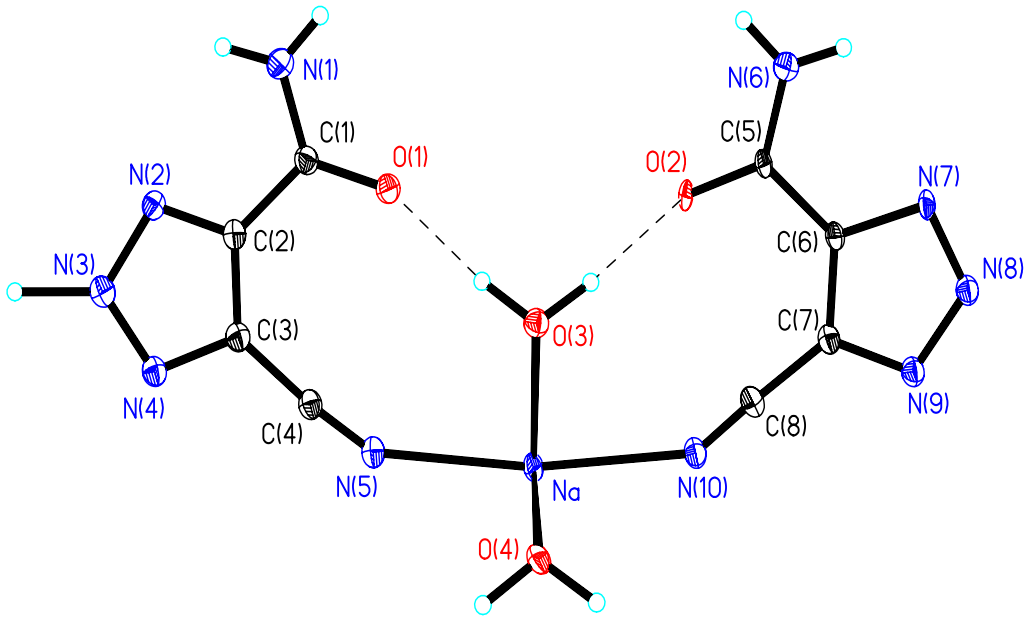


Figure 4: Molecular structure of sodium complex **3**.

In figure 5, sodium ions are linked into a chain by bridging water molecules, and the triazole rings are coordinated to sodium through their cyano groups. Water molecules act as hydrogen bond donors to oxygen and nitrogen atoms of the triazole rings. Amino groups are also hydrogen bonded to oxygen and nitrogen atoms of the rings. There is a strong hydrogen bond between the protonated and deprotonated ring central nitrogen atoms of the triazoles in adjacent chains in the structure, and this has been assumed to be symmetrical, a fact also is supported by the ^{13}C NMR spectrum which showed only 4 carbon signals (Figure 5).

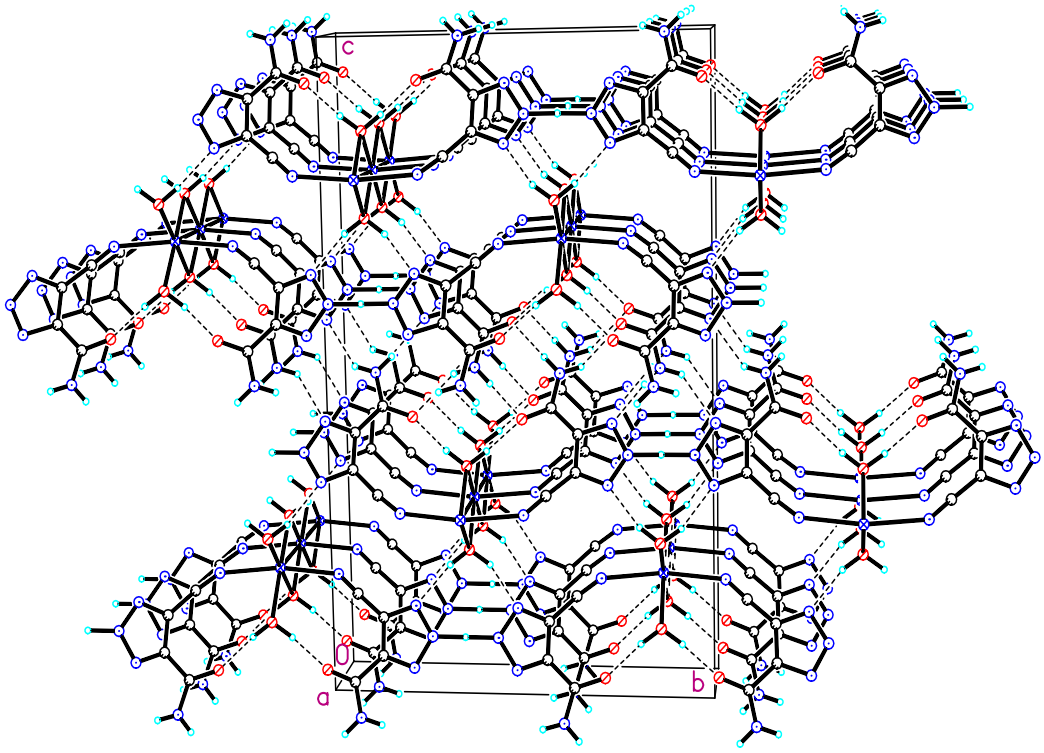


Figure 5: Extended polymeric coordination network of complex **3**.

CONCLUSION

This work describes a one pot synthesis of 2*H*-1,2,3-triazole sodium complex **3** starting from *N*-[2-ammonio-1,2-dicyanovinyl]alkanamide **2a,b**. The X-ray structures of both the sodium complex **3** and its free triazole monohydrate **4ii** demonstrate that the 2*H*-triazole is the predominant tautomer. The presence of an acyl group played a noticeable role in both hydrolysis of the cyano function and the formation of the 2*H* tautomer. These results suggest that a study of alkali and alkaline earth metal nitrites for diazotization beside those of sodium may be of interest.

EXPERIMENTAL

*CRYSTAL DATA AND STRUCTURE REFINEMENT OF COMPLEX **3***

Chemical formula (moiety) and (total) $C_{32}H_{36}N_{40}Na_4O_{16}$, formula weight 1328.97, temperature 120(2) K, radiation, wavelength synchrotron, 0.8462 Å, crystal system, spa e group monoclinic, $P2_1/c$, unit cell

parameters a = 3.574(2) Å, α = 90°, b = 15.647(11) Å, β = 91.835(9)°, c = 24.302(16) Å γ = 90°, cell volume 1358.3(15) $Å^3$, Z 1, calculated density 1.625 g/cm^3, absorption coefficient μ 0.159 mm^{-1}, F(000) 680, crystal colour and size colourless, 0.10 × 0.10 × 0.01 mm^3, reflections for cell refinement 2050 (θ range 4.0 to 29.9°), data collection method Bruker APEX2 CCD diffractometer, thin-slice ω scans, θ range for data collection 4.0 to 28.0°, index ranges h –3 to 3, k –17 to 17, l –26 to 26, completeness to θ = 28.0° 99.0 %, intensity decay 5%, reflections collected 7157, independent reflections 1897 (R_{int} = 0.0882), reflections with $F^2>2\sigma$ 1420, absorption correction none, structure solution direct methods, refinement method Full-matrix least-squares on F^2, weighting parameters a, b 0.1820, 48.1754, data / restraints / parameters 1897 / 196 / 209, final R indices [$F^2>2\sigma$] R1 = 0.1883, wR2 = 0.4655, R indices (all data) R1 = 0.2199, wR2 = 0.4888, goodness-of-fit on F^2 1.294, largest and mean shift/su 0.037 and 0.003, Largest diff. peak and hole 1.27 and –0.90 e $Å^{-3}$.

*CRYSTAL DATA AND STRUCTURE REFINEMENT OF TRIAZOLE **4ii***

Chemical formula (moiety) $C_4H_3N_5O·H_2O$, chemical formula (total) $C_4H_5N_5O_2$, formula weight 155.13, temperature 150(2) K, radiation, wavelength MoKα, 0.71073 Å, crystal system, space group monoclinic, $P2_1/c$, unit cell parameters a = 3.6073(9) Å α = 90°, b = 16.261(4) Å β = 97.960(6)°, c = 11.309(3) Å, γ = 90°, cell volume 657.0(3) $Å^3$, Z 4, calculated density 1.568 g/cm^3, absorption coefficient μ 0.129 mm^{-1}, F(000) 320, crystal colour and size colourless, 0.96 × 0.44 × 0.34 mm^3, reflections for cell refinement 2843 (θ range 2.2 to 28.2°), data collection method, Bruker SMART 1K CCD diffractometer thin-slice ω scans, θ range for data collection 2.2 to 25.0°, index ranges h –4 to 4, k 0 to 19, l 0 to 13, completeness to θ = 25.0° 95.8 %, reflections collected 1475, independent reflections 1491 (R_{int} = 0.0417), reflections with $F^2>2\sigma$ 1464, absorption correction semi-empirical from equivalents, Min. and max. transmission 0.886 and 0.957, structure solution direct methods, refinement method Full-matrix least-squares on F^2, weighting parameters a, b 0.0559, 0.6311, data / restraints / parameters 1491 / 0 / 122, final R indices [$F^2>2\sigma$] R1 = 0.0444, wR2 = 0.1190, R indices (all data) R1 = 0.0450, wR2 = 0.1197, goodness-of-fit on F^2 1.211, largest and mean shift/su 0.008 and 0.000, largest diff. peak and hole 0.24 and –0.30 e $Å^{-3}$.

INSTRUMENTATION AND TECHNIQUES

^1H and ^{13}C NMR spectra were recorded on a Bruker DPX 400 spectrometer at 400 and 100 MHz, $CDCl_3$, DMSO-d_6 or DMF-d_7 were used as solvents and TMS as internal standard. Mass spectra were recorded

on a VG Autospec Q spectrometer with a digital data output. IR analysis was recorded on RT-IR Perkin Elmer System 2000 using KBr discs. Melting points were determined using a Gallenkamp melting point apparatus and are uncorrected. TLC was performed on 0.25 mm pre-coated silica gel plates (Merck).

SYNTHESIS

Synthesis of *N*-[2-amino-1,2-dicyanovinyl]ethanamide 2a

Method (A)

A mixture of DAMN **1** (1.00 g, 9.26 mmol) and acetic anhydride was gently warmed (2.00 mL) until it dissolved into solution (5-10 minutes). On cooling, pale violet crystals were obtained. The crystals were filtered, washed with $CHCl_3$, and decolourized by refluxing the product in EtOH for 15 min in presence of charcoal; yield **2a:** (1.37 g, 9.13 mmol, 99%).

Method (B)

In a 50 mL round-bottomed flask a suspension of **1** (1.00 g, 9.26 mmol), and EtOAc (15.0 mL) was stirred at rt. Acetyl chloride (0.73 g, 9.26 mmol) was then added dropwise; the reaction is exothermic. TLC (9:1 v/v, $CHCl_3$: EtOH) showed the reaction to be complete within 1.5 h. The reaction mixture was filtered, washed with Et_2O, and the resultant yellow precipitate was then stirred in deionised water to furnish **2a**; yield: (1.2 g, 8.0 mmol, 86%), mp 164 °C, (Lit.,[1] mp 164 °C).

IR: 3524, 3316, 3200, 2999, 2251, 2212, 1695, 1530, 1395, 1367, 1303, 992 cm^{-1}.

^1H NMR (DMSO-d_6): δ/ppm = 1.93 (s, 3H, CH_3), 7.19 (s, 2H, NH_2), 9.14 (s, 1H, NH).

^{13}C NMR (DMSO-d_6): δ/ppm = 169.4, 127.35, 117.7, 114.7, 90.2, 23.4.

MS: m/z = $(M+1)^+$ 151, 50%, $(M\text{-}COCH_3)^+$ 108, 100%.

Anal. Calcd for $C_6H_6N_4O$ (150): C, 48.0; H, 4.0; N; 37.3. Found: C, 48.2; H, 4.0; N, 37.1.

Synthesis of *N*-[2-amino-1,2-dicyanovinyl]propanamide 2b

A mixture of **1** (1.00 g, 9.26 mmol) and propanoic anhydride (1.21 g, 9.3 mmol) was heated gently in a water bath at 50 °C for 10 min. The precipitate formed was filtered and washed with petroleum ether to afford **2b** as a white powder; yield: (1.30 g, 7.93 mmol, 86%), mp 165 °C.

IR: 3410, 3319, 3217, 2978, 2879, 2251, 2212, 1669, 1638, 1523, 1383, 1292, 1072 cm^{-1}.

^1H NMR (DMSO-d_6): δ/ppm = 1.00 (t, 3H, *J* 7.5 Hz, CH_3), 2.21 (q, 2H, *J* 7.5 Hz, CH_2), 7.16 (s, 2H, NH_2), 9.06 (s, 1H, NH).

^{13}C NMR (DMSO-d_6): δ/ppm = 173.1, 127.3, 117.9, 115, 90.6, 29.0, 10.0.

MS: m/z = M^+ 164, 15%, $(-COC_2H_5)^+$ 57, 100%.

Anal. Calcd for $C_7H_8N_4O$ (164): C, 51.2; H, 4.8; N, 34.1. Found: C, 51.0; H, 4.9; N, 34.2.

Synthesis of *N*1-[(*Z*)-2-ammonio-1,2-dicyano-1-ethenyl]benzamide chloride 2c

Benzoyl chloride (0.4 g, 2.78 mmol) was added to a suspension of DAMN **1** (0.30 g, 2.78 mmol) in EtOAc (10 mL) at rt. An exothermic reaction occurred and a yellow precipitate was formed immediately. The reaction mixture was allowed to stand (1.5 h), and the precipitate was then filtered and washed with petroleum ether to give **2c**; yield: (0.65 g, 2.6 mmol, 94%), mp 148 °C (dec.).

IR: 3437, 3031, 2250, 1689, 1651, 1580, 1561, 1450, 1212, 909 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ/ppm = 5.65 (brs, 3H, NH_3), 7.49 (t, 2H, *J* 7.4 Hz, ArH), 7.58 (t, 1H, *J* 7.3 Hz, ArH), 7.96 (d, 2H, *J* 7.4 Hz, ArH), 9.79 (s, 1H, NH).

^{13}C NMR (DMSO-d_6): δ/ppm = 166.22, 133.83, 133.16, 129.38, 129.09, 128.15, 117.99, 115.00, 90.52.

MS: m/z = $(M\text{-}HCl)^+$ 212, 70%, $(Ph+1)^+$, 77, 100%.

Anal. Calcd for $C_{11}H_9N_4OCl$ (248.5): C, 53.11; H, 3.62; N, 22.53. Found: C, 53.02; H, 3.72; N, 22.72.

Synthesis of sodium complex of 5-cyano-2*H*-[1,2,3]triazole-4-carboxylic acid amide hydrate 3

Compound **2a** (0.5 g, 3.3 mmol) or **2b** (0.54 g, 3.3 mmol) was stirred at 0 °C with a mixture of AcOH (0.4 g, 8.6 mmol) and water (2 mL), a solution of sodium nitrite (0.23 g, 3.3 mmol) in water (2 mL) was then added, and stirring was continued until the mixture warmed up to rt. The precipitate thus obtained was filtered and recrystallized from hot water to afford complex **3** as colourless needles; yield: (1.33 g, 1.00 mmol, 30 %), mp 270 °C.

IR: 3528, 3417, 2259, 1722, 1689, 1650, 1604, 1426, 1149, 559 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ/ppm = 3.95 (brs, O-H, H_2O), 7.53 (s, 1H, NH), 7.79 (s, 1H, NH), 9.54 (brs, 1H, NH).

^{13}C NMR (DMSO-d_6): δ/ppm = 162.15, 145.59, 119.47, 115.34.

MS: m/z = $(C_4HN_4O)^+$, 121, 100%.

Anal. Calcd for $C_{32}H_{36}N_{40}Na_4O_{16}$ (1328.97): C, 28.91; H, 2.71; N, 42.16. Found: C, 28.71; H, 2.71; N, 42.03.

Synthesis of 5-cyano-2*H*-[1,2,3]triazole-4-carboxylic acid amide monohydrate 4ii

Method (A)

Complex **3** (0.5 g, 0.38 mmol) was gently warmed for 5 min with an aqueous solution of 4 M HCl (5 mL). The precipitate was then filtered and recrystallised from acetone to afford **4ii** as colourless needles; yield: (0.41 g, 2.65 mmol, 82 %).

Method (B)

Compound **2a** (0.5 g, 3.3 mmol) or **2b** (0.54 g, 3.3 mmol) was stirred with a mixture of concentrated HCl (0.4 g, 11 mmol) and water (2 mL) at 0 ^{o}C, a solution of sodium nitrite (0.23 g, 3.3 mmol) in water (2 mL) was then added, and stirring was continued until the solution warmed up to rt. The precipitate formed was filtered off and recrystallized from hot water to afford **4ii** as colourless needles.

Yield: (0.36 g, 2.32 mmol, 70%), mp 220 °C.

IR: 3431, 3309, 3065, 2969, 2269, 1703, 1677, 1599, 1523, 1435, 1182, 1139, 989, 707, 565 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ/ppm = 7.95 (s, 1H, NH), 8.22 (s, 1H, NH), 15.90 (brs, 1H, NH).

^{13}C NMR (DMSO-d_6): δ/ppm = 160.31, 145.85, 121.25, 112.79.

MS: m/z = $(M\text{-}H_2O)^+$ 137, 30%, $(M\text{-}NH_2)^+$, 121, 100%.

Anal. Calcd for $C_4H_3N_5O$ (M 137): C, 35.04; H, 2.19; N, 51.09. Found: C, 34.80; H, 2.12; N, 50.8.

Synthesis of 1,2,3-triazole-4,5-dicarbonitrile 5ii

Compound **1** (1.0 g, 9.26 mmol) was stirred in aquoeus HCl (0.68 g, 18.6 mmol). The reaction mixture was cooled to 0 ^{o}C and a solution of sodium nitrite (0.7 g, 10 mmol) in water (2 mL) was added while stirring. After 1 h, a clear solution was formed which was extracted with Et_2O and crystallized to furnish **5ii**; yield: (0.77 g, 6.5 mmol, 70% yield), mp 145 °C.

IR: 3260, 2261, 1479, 1382, 1129, 791 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ/ppm = 10.10 (s, 1H, NH).

^{13}C NMR (DMSO-d_6): δ/ppm = 128.4, 123.2, 113.6.

MS: m/z = 119 $(M)^+$, 100%.

Anal. Calcd for C_4HN_5 (119): C, 40.3; H, 0.84; N; 58.8. Found: C, 40.3; H, 0.81; N, 59.2.

Synthesis of 2*H*-[1,2,3]triazole-4,5-dicarboxylic acid amide 6

Compound **4ii** (0.20 g, 1.29 mmol) was refluxed in an aqueous solution of AcOH (1 M), HCl (1 M), (1:1) (5 mL) for 1 h. The solution was cooled to rt, whereby compound **6** precipitated out as a white powder; yield: (0.17 g, 1.10 mmol, 85%), mp 300 °C.

IR: 3357, 3174, 1664, 1590, 1487, 1125, 996, 757 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 8.10 (s, 2H, NH_2), 8.48 (s, 1H, NH), 10.23 (s, 1H, NH), 16.47 (brs, 1H, NH).

^{13}C NMR (DMSO-d_6): δ = 164.87, 159.03, 138.62, 135.10.

MS: m/z = $(M)^+$ 155, 55%.

Anal. Calcd for $C_4H_5N_5O_2$ accurate mass: 155.0444. Found: 155.0494.

Synthesis of *N*4,*N*5-diphenyl-2*H*-1,2,3-triazole-4,5-dicarbohydrazonamide 7

A mixture of compound **5ii** (0.20 g, 1.68 mmol) and excess phenylhydrazine was stirred at rt for 1 h. The yellow precipitate thus obtained was filtered off and washed with petroleum ether to furnish **7**; yield: (0.36 g, 1.07 mmol, 64 %), mp 245 °C.

IR: 3383, 3264, 1663, 1629, 1601, 1495, 1252, 1139, 1051, 752 cm^{-1}.

^1H NMR (DMSO-d_6): δ/ppm = 6.70 (t, 2H, *J* 7.3 Hz, ArH), 6.77 (d, 4H, *J* 7.8 Hz, ArH), 7.07 (t, 4H, *J* 7.9 Hz, ArH), 8.19 (brs, 4H, 2 X NH_2), 8.36 (s, 2H, 2 X NH), 12.73 (brs, 1H, NH).

^{13}C NMR (DMSO-d_6): δ/ppm = 151.54, 147.81, 134.73, 130.06, 119.99, 113.59.

MS: m/z = $(M)^+$ 335, 55%; $(Ph+1)^+$, 77, 100%.

Anal. Calcd for $C_{16}H_{17}N_9$ (335): C, 57.31 ; H, 5.07 ; N, 37.61. Found: C, 57.13; H, 4.80; N, 37.42.

Synthesis of 2-methyl-1*H*-imidazole-4,5-dicarbonitrile 8a, and 2-ethyl-1*H*-imidazole-4,5-dicarbonitrile 8b

Method (A)

A mixture of **1** (5.0 g, 46.3 mmol) and, respectively, triethyl orthoacetate (9.75 g, 60.2 mmol) for **9** and triethyl orthopropionate (9.79 g, 55.6 mmol) for **9b** in anisole (60 mL) as solvent was heated in a water bath at 100 °C, with distillation continued of EtOH over a period of 2 h. Sodium metal (0.181 g, 7.87 mmol) in MeOH (5 mL) was then added, and heating was continued until no more alcohol distillate was obtained. The reaction mixture was filtered off while hot, and then cooled to afford imidazoles **8a** and **8b**.

Method (B)

A mixture of **2a** (0.5 g, 3.3 mmol) or **2b** (0.5 g, 3.0 mmol), each with an equimolar amount of NaH in DMF (15 mL) was refluxed for 10-18 hours. The mixture was then cooled and poured into water. The pH was adjusted to 7 and the resulting mixture was extracted with Et_2O to furnish **8a** or **8b**.

8a: *Method (A)*: yield: (4.3 g, 32.6 mmol, 70%); *Method (B)*: yield: (0.21 g, 1.6 mmol, 48%); mp 228 °C.
IR: 3414, 3162, 3006, 2893, 2750, 2641, 2536, 2236, 1581, 1520, 1394, 1299, 1145, 1039, 920, 770 cm^{-1}.
^1H NMR (d_7-DMF): δ/ppm = 2.49 (s, 3H, CH_3), 12.8 (brs, 1H, NH).
^{13}C NMR (d_7-DMF): δ/ppm = 152.1, 115.9, 111.9, 79.8, 14.1.
MS: m/z = $(M)^+$, 132, 100%.
Anal: Calcd for $C_6H_4N_4$ (132) accurate mass: 132.0431. Found: 132.0436.

8b: *Method (A)*: yield (4.5 g, 30.8 mmol, 67%); *Method (B)*: yield (0.12 g, 0.82 mmol, 27%); mp 184 °C.
IR: 3129, 2985, 2237, 1569, 1521, 1414, 1322, 1301, 1211, 1064, 1038 cm^{-1}.
^1H NMR (d_7-DMF): δ/ppm = 1.28 (t, 3H, *J* 7.7 Hz, CH_3), 2.80 (q, 4H, *J* 7.6 Hz, CH_2), 14.1 (brs, 1H, NH).
^{13}C NMR (d_7-DMF) δ/ppm = 157.0, 115.9, 112.1, 79.9, 22.3, 12.0.
MS: m/z= $(M+1)^+$ 147, 100%.
Anal. Calcd for $C_7H_6N_4$ (146): C, 57.5; H, 4.1; N, 38.4. Found: C, 57.5; H, 4.1; N, 38.4.

Synthesis of 2-methyl-1*H*-imidazole-4,5-dicarboxylic acid amide 9a, and 2-ethyl-1*H*-imidazole-4,5-dicarboxylic acid amide 9b

A mixture of imidazole **8a** (0.20 g, 1.5 mmol) or imidazole **8b** (0.20 g, 1.4 mmol) and an excess of phenylhydrazine was stirred at rt for one week, and during this time the mixture was heated daily for 8 h in a water bath (40-50 °C). At the end of this process, a solution of acetone in petroleum ether (1 : 3) was added, and the paste thus formed was triturated with CH_2Cl_2 and petroleum ether (1 :1) to give **9a** (pale green powder), and **9b** (cream precipitate).

9a: yield: (0.11 g, 0.65 mmol, 44 %); mp 298 °C.
IR: 3376, 3249, 1682, 1629, 1602, 1535, 1431, 1259, 1121 cm^{-1}.
^1H NMR (DMSO-d_6): δ/ppm = 2.29 (s, 3H, CH_3), 7.57 (s, 1H, NH), 7.68 (s, 1H, NH), 7.82 (s, 1H, NH), 10.43 (s, 1H, NH), 12.80 (s, 1H, NH).
^{13}C NMR (DMSO-d_6): δ/ppm = 166.80, 160.87, 145.88, 133.74, 129.15, 14.39.

MS: m/z = $(M)^+$ 168, 100%.

Anal. Calcd for $C_6H_8N_4O_2$ accurate mass: 168.0647. Found: 168.0648.

9b: yield: (0.15 g, 0.82 mmol, 59 %), mp 238 °C (dec.).

IR: 3429, 3255, 3073, 1661, 1542, 1468, 1435, 1383, 1305, 1249, 1049, 849 cm^{-1}.

^1H NMR (DMSO-d_6): δ/ppm = 1.18 (t, *J* 7.6 Hz, 3H, CH_3), 2.61 (q, *J* 7.6 Hz, 2H, CH_2), 7.61 (s, 1H, NH), 7.72 (s, 1H, NH), 7.80 (s, 1H, NH), 10.45 (s, 1H, NH), 12.81 (s, 1H, NH).

^{13}C NMR (DMSO-d_6): δ/ppm = 166.83, 160.93, 150.91, 133.56, 129.12, 21.86, 13.70.

MS: m/z = $(M)^+$ 182, 100%.

Anal. Calcd for $C_7H_{10}N_4O_2$ accurate mass: 182.0804. Found: 182.0801.

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15. Crystal data for complex **3**: (ref. CCDC 607415) can be obtained on request from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EW, UK. CCDC.
16. Crystal data for compound **4ii**: (ref. CCDC 607416) can be obtained on request from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EW, UK. CCDC.