Efficient synthesis of Triazolo[4,5-*d*]pyrimidine-7-carbonitriles and Imidazole-4,5-dicarbonitriles using Triethylorthoalkylates and their structural characterisation by Single-crystal x-ray diffraction

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Abstract

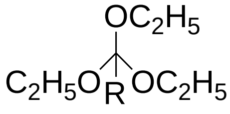
Cyclisation of 5-amino-1-(4-nitrophenyl)-1*H*-1,2,3-triazole-4-carbimidoyl cyanide and 3-amino-3-((*Z*)-2-cyano-2-phenylvinylamino)maleonitrile using either triethyl orthoformate or triethyl orthopropionate in dimethylformamide (DMF):1,4-dioxane (1:1 v/v) mixture under reflux conditions afforded 5-alkyl-3-(4-nitrophenyl)-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidine-7-carbonitriles and (*Z*)-1-(2-cyano-2-phenylvinyl)-2-alkyl-1*H*-imidazole-4,5-dicarbonitriles, respectively, in moderate to good yields. The structures of these novel compounds were confirmed with $^{1}H/^{13}C$ nuclear magnetic resonance (NMR), infrared spectroscopy (IR), and high-resolution mass spectroscopic methods. Two representative compounds from these molecules, namely 5-ethyl-3-(4-nitrophenyl)-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidine-7-carbonitrile and (*Z*)-1-(2-cyano-2-phenylvinyl)-1*H*-imidazole-4,5-dicarbonitrile, were further analysed by the single-crystal X-ray diffraction method. A comprehensive study of structural features and intermolecular interactions present among these heterocyclic compounds was carried out. The crystal data were further examined by a Hirshfeld surface analysis, which provided qualitative and quantitative information on various intermolecular interactions experienced within the crystal network.

Keywords: Crystal structure; hirshfeld surface analysis; imidazole; pyrimidine; triazole.

1. Introduction

Cyclisation reactions in synthetic heterocyclic chemistry are one of the most useful reactions that lead to different types of heterocyclic compounds, especially N-heterocyclic rings. Among the reagents used in these cyclisations, triethyl orthoalkylates (orthoesters) **1a-c**

$RC(OEt)_3$ are particularly significant (Woodward, 1950, Johnson, 1991, Alves *et al.*, 1990; Booth *et al.*, 1992; Al-Azmi *et al.*, 2003; Al-Azmi, 2015; Al-Azmi *et al.*, 2001; Al-Azmi & Kumari, 2009; Al-Azmi, 2005; Al-Azmi & Kalarikkal, 2013; Al-Azmi, 2020; Al-Azmi & Mahmoud, 2020) as they increase the ring by a carbon atom and the substituents on the carbon can be easily controlled by the right choice of an ortho-alkylate derivative. (Woodward, 1950; Johnson, 1991; Alves *et al.*, 1990; Booth *et al.*, 1992; Al-Azmi *et al.*, 2003; Al-Azmi, 2015; Al-Azmi *et al.*, 2001; Al-Azmi & Kumari, 2009; Al-Azmi, 2005, Al-Azmi & Kalarikkal; 2013, Al-Azmi, 2020; Al-Azmi & Mahmoud, 2020). The usual scenario in these types of cyclisation reactions is the attack of a nucleophile, mostly nitrogen, on the electrophilic ortho-alkylate carbon, causing the loss of two ethoxy groups as ethanol molecules. Consequently, this creates a highly electrophilic imidate carbon center that is susceptible to attack by nucleophiles.



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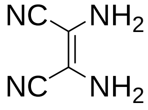
R a = H
b = CH_3
c = C_2H_5

In the last decades, triethyl orthoalkylates (orthoesters) have been broadly used by researchers worldwide, including our group, to synthesise many N-heterocycles, especially five- and six-membered rings that have various crucial applications. (Al-Azmi *et al.*, 2003; Al-Azmi, 2015; Al-Azmi *et al.*, 2001; Al-Azmi & Kumari, 2009; Al-Azmi, 2005; Al-Azmi & Kalarikkal, 2013; Al-Azmi, 2020; Al-Azmi & Mahmoud, 2020)

For the synthesis of N-heterocyclic rings, the utility of inexpensive and readily available triethyl orthoalkylates **1** is advantageous, as was demonstrated many times by our group. (Al-Azmi *et al.*, 2003; Al-Azmi, 2015; Al-Azmi *et al.*, 2001; Al-Azmi & Kumari, 2009; Al-Azmi, 2005; Al-Azmi & Kalarikkal, 2013; Al-Azmi, 2020; Al-Azmi & Mahmoud, 2020) The most exciting building block produced from triethyl orthoalkylates **1a** is (*Z*)-ethyl-(*N*)-[2-amino1,2-dicyanovinyl]formimidate **3** (commonly known as monoimidate), which can be prepared for excellent yield (80–90%) by refluxing a mixture of equimolar amounts of diaminomaleontrile (DAMN) **2** and triethyl orthoformate **1a** in 1,4-dioxane. (Woodward, 1950, Johnson, 1991) Monoimidate **3** normally reacts with a wide range of primary amines in the presence of a catalytic amount of anilinium hydrochloride to avert decomposition and to produce (*Z*)-*N*^{1}-(4-aryl)-*N*^{2}-[2-amino1,2-dicyanovinyl]formamidines **4**. (Woodward, 1950, Johnson, 1991; Alves *et al.*, 1990; Booth *et al.*, 1992; Al-Azmi *et al.*, 2003) Formamidine derivatives **4** are also reported to be excellent building blocks for several N-heterocycles, including imidazoles, purines, triazoles, pyrroles, and pyrimidines. (Alves *et al.*, 1990; Booth *et al.*, 1992; Al-Azmi *et al.*, 2003; Al-Azmi, 2015; Yildirim *et al.*, 2002) These compounds display fascinating applications, such as pharmaceutical, medicinal, and anticorrosive. (Al-Azmi *et al.*, 2003; Al-Azmi, 2015)

This prompts us to employ both 5-amino-1-(4-nitrophenyl)-1*H*-1,2,3-triazole-4-carbimidoyl cyanide, which has been prepared previously by our group (Al-Azmi & Kalarikkal, 2013), and the



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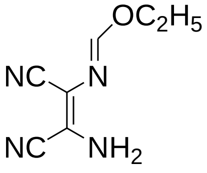

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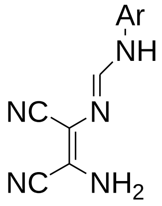

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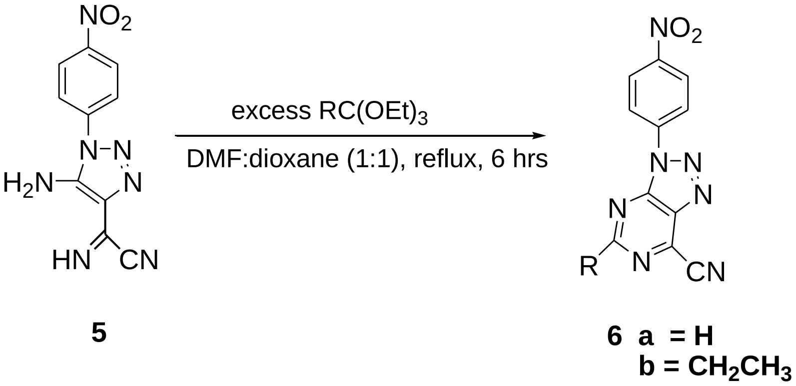
readily available 2-phenyl-3-oxopropanenitrile reagent (Al-Azmi & Kalarikkal, 2017) to synthesise new N-heterocyclic compounds by utilising their reaction with orthoesters **1**. To the best of our knowledge, this rather obvious approach has not been explored before.

In the present paper, we report the synthesis of new 5-alkyl-3-(4-nitrophenyl)-3*H*-[1,2,3]triazolo[4,5-*d*] pyrimidine-7-carbonitriles and (*Z*)-1-(2-cyano-2-phenylvinyl)-2-alkyl-1*H*-imidazole-4, 5-dicarbonitriles. The characterisation of these newly synthesised compounds, along with a detailed single-crystal X-ray diffraction analysis of two representative samples among them, is also presented and discussed.

2. Results and Discussion

2.1 Synthesis of Triazolopyrimidine and Imidazole dicarbonitrile Derivatives

The precursor molecule used for the synthesis of triazolopyrimidine compounds discussed in this work is 5-amino-1-(4-nitrophenyl)-1*H*-1,2,3-triazole-4-carbimidoyl cyanide **5**. This nitrophenyl derivative **5** is prepared after cyclisation of 2-(5-amino-1-(4-nitrophenyl)-1*H*-1,2,3-(triazol-4-yl)-2-iminoacetonitrile using a mixture of ethanol and a catalytic amount of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), as described in the literature. (Al-Azmi & Kalarikkal, 2013). The 4-nitrophenyl derivative **5** was used because it does not produce a mixture of the triazole-4-carbimidoyl cyanide and triazole-2-oxoacetonitrile, as do 4-methoxyphenyl, phenyl, 4-chlorophenyl, or 4-tolyl substituents. The synthesis of triazolopyrimidine derivatives (**6a** and **6b**) was carried out by refluxing triazole **5** with an excess of triethyl orthoformate **1a** or triethyl orthopropionate **1c** in a DMF:1,4-dioxane solvent mixture (1:1 v/v) for six hours, as depicted in Scheme 1. (Al-Azmi & Kumari, 2009) The details about the reaction workup and product purification are provided in the experimental section.



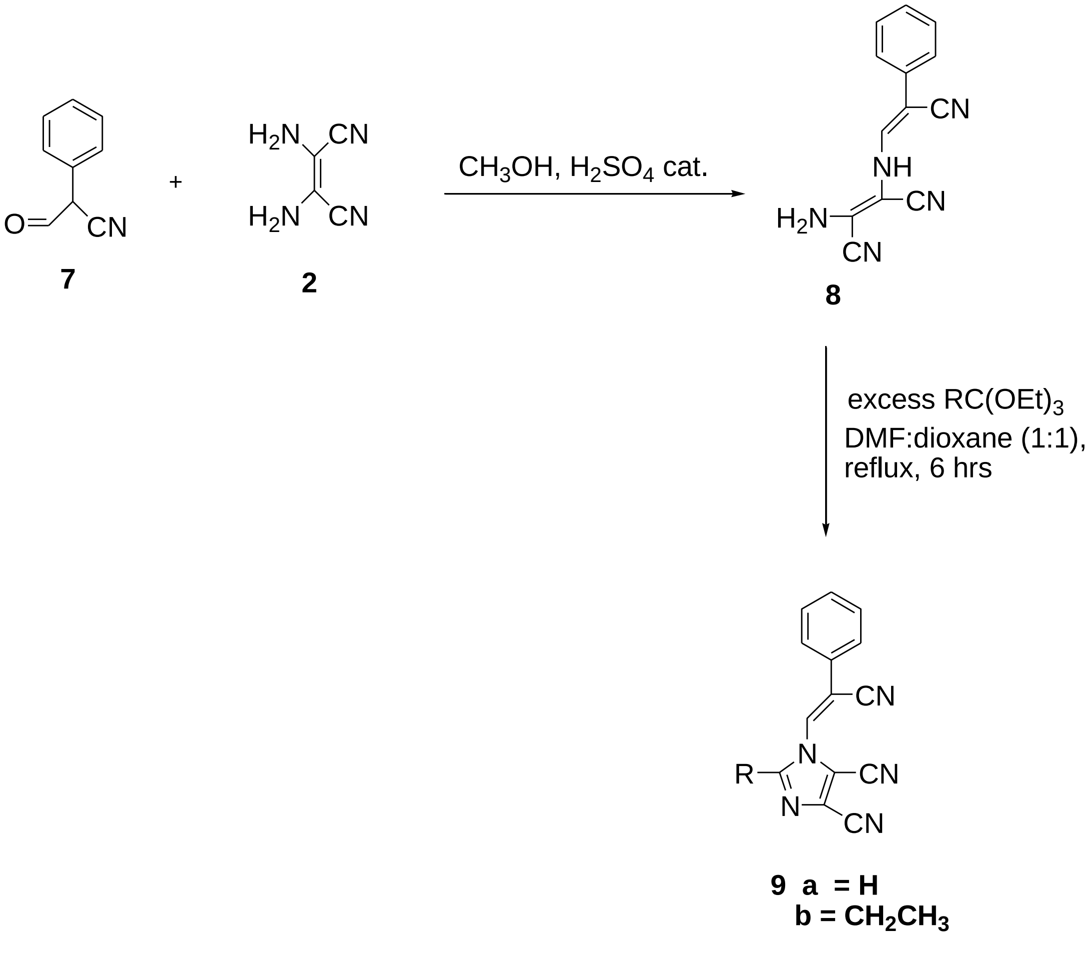
Scheme 1: Synthesis of triazolopyrimidine derivatives **6a** and **6b**

The ^{1}H NMR spectrum indicated the disappearance of both (NH) and NH_2 functions, and instead, both C<u>H</u> and C_2H_5 signals were detected at δ 9.41 parts per million (ppm), δ 1.38, and δ 2.94 ppm for **6a** and **6b**, respectively.

The Schiff base 3-amino-3-((*Z*)-2-cyano-2-phenylvinylamino)maleonitrile **8**, which is the precursor molecule for imidazole-4,5-dicarbonitriles **9a,b**, was prepared by reacting 2-phenyl-3-oxopropanitrile **7** with diaminomaleonitrile (DAMN) **2** in acetic acid, and the mixture was stirred for 24 hours at room temperature. The reaction provided the intended product as a green powder in good yield. The Schiff base structure was confirmed by the presence of three cyano functions in the infrared radiation (IR) and ^{13}C NMR spectra, while the ^{1}H NMR spectra indicated the presence of both NH and NH_2 proton signals.

Imidazole-4,5-dicarbonitriles **9a,b** were synthesised by reacting **8** with an excess of triethyl orthoformate **1a** or propionate **1c** under reflux conditions in the presence of a mixture of 1:1 DMF:1,4-dioxane for about six hours (Scheme 2). It is found that **9a** and **9b** are produced in 67% and 65% yields, respectively. The cyclisation was achieved when the ^{1}H NMR spectra of **9a** revealed the presence of hydrogen ($C\underline{H}$) at δ 8.89 ppm, and **9b** CH_2CH_3 protons appeared at δ 1.21 ppm and δ 2.84 ppm.

Al-Azmi described the preparation of 2-alkylimidazole-4,5-dicarbonitrile derivatives when (*Z*)-*N*^{1}-aryl-*N*^{2}-(2-amino-1,2-dicyanovinyl) formamidines were refluxed with triethyl orthoacetate **1b** or propionate **1c**. (Al-Azmi & Kumari, 2009)



Scheme 2: Synthesis of imdazole derivatives **9a** and **9b**.

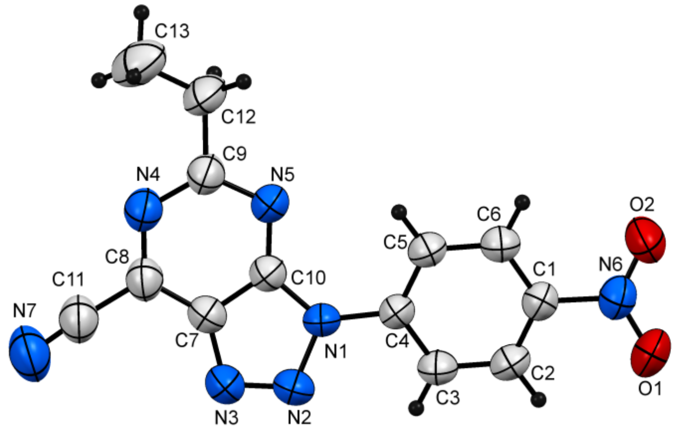
2.2 Single - Crystal X - Ray Diffraction Studies

Triazolopyrimidines occupy a vital place in the pharmaceutical field. They have been reported to act as angiotensin II receptor antagonists. (Nicolai *et al.*, 1994) It is also illustrated that derivatives of the triazolopyrimidine species, such as [1,2,4-oxadiazolyl]methyl-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidine, exhibit moderate to high antimicrobial activity. (El-Sayed *et al.*, 2012) Moreover, a series of 1,2,4-triazolopyrimidines were prepared and evaluated as antitumor agents using a DNA-binding assay on thin-layer chromatography (TLC) plates. (Hassan *et al.*, 2017) The 4,5-dicyanoimidazole analogues, on the other hand, have been reported as potential anticancer (Ali *et al.*, 2017), and additionally, they were involved in applications as photo-redox catalysts due to their push-pull characteristics. (Plaquet *et al.*, 2011, Hloušková & Bureš, 2017) Based on all these encouraging results, it is expected that the newly synthesised compounds reported in this work can have impressive applications in the pharmaceutical industry.

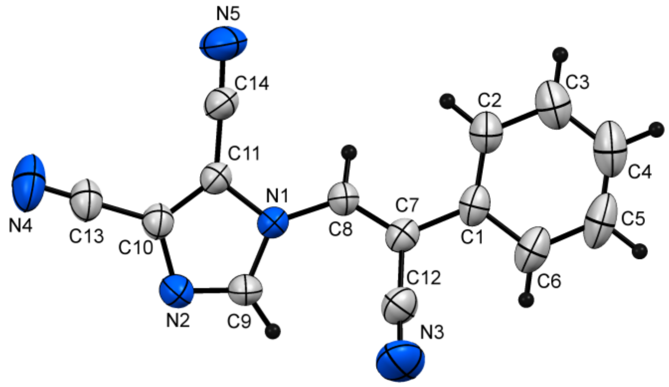
Before investigating the pharmaceutical applications, it is necessary to have a complete idea about the structural details with respect to the compound of interest. The bonding nature of the species, especially the presence of any supramolecular non-bonding interactions possible among such molecules, should also be investigated in detail. Such structural and non-bonding interaction studies provide an idea about the nature of the molecule and its affinity/reactivity toward target molecules in biomedical reactions. Thus, it is helpful to design suitable molecules for certain medicinal actions. A single-crystal X-ray diffraction analysis is considered the best method for such structural and interaction studies if the compound of interest is solid in nature and crystalline. Therefore, due to an interest in the pharmaceutical applications of triazolopyrimidines and imidazole-4,5-dicarbonitriles, we carried out a detailed crystal structure analysis of two representative samples (**6b** and **9a**) synthesised in the present work.

2.3 Structural Characterisations of Triazolopyrimidine **6b** and Imidazole dicarbonitrile **9a** by Single-Crystal X-Ray Diffraction

The crystal structures of triazolopyrimidine **6b** and imidazole dicarbonitrile **9a** are given in Figure 1, and their corresponding crystallographic data are provided in Table 1. The crystal data shows that both these molecules are not planar (Figure 2). The plane of nitrophenyl moiety of **6b** is twisted from the triazolopyrimidine plane by about 15°. At the same time, the distortion of planarity in imidazole dicarbonitrile is more pronounced in its crystal structure. It is found that the bridging nitrile spacer between the two aromatic moieties is oriented to a different plane. The nitrile spacer is twisted 32° from the substituted imidazole plane and about 27° from the other phenyl fragment plane.

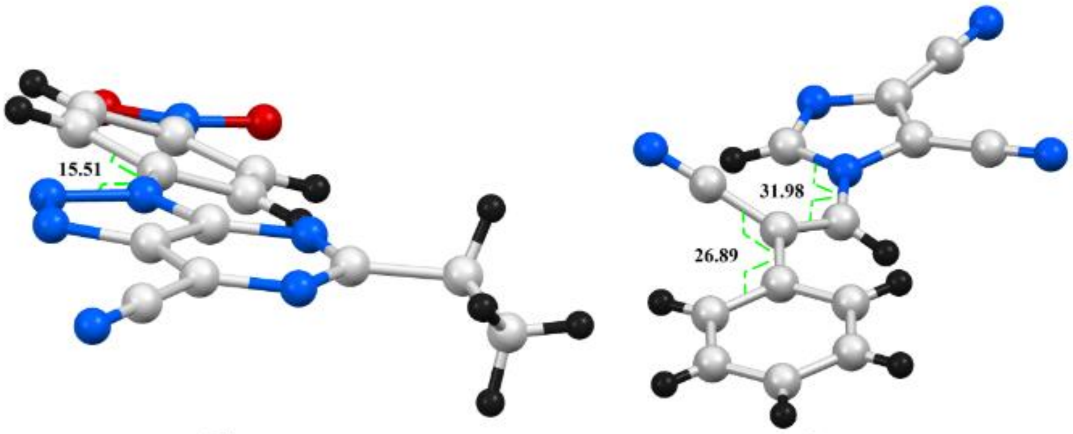


6b



9a

Fig. 1. Crystal structure (thermal ellipsoid representation; 50% probability) of 5-ethyl-3-(4-nitrophenyl)-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidine-7-carbonitrile **6b** and (*Z*)-1-(2-cyano-2-phenylvinyl)-1*H*-imidazole-4,5-dicarbonitrile **9a**.



6b **9a**

Fig. 2. Crystal structure of **6b** and **9a** showing the distortion from planarity.

Table 1. Experimental details and crystal data for compounds **6b** and **9a**.

Crystal sample	**6b**	**9a**
Chemical formula	$C_{13}H_9N_7O_2$	$C_{14}H_7N_5$
M_r	295.26	245.24
Crystal system, space group	Monoclinic, $P2_1/n$	Monoclinic, $C2/c$
Temperature (K)	293	150
a, b, c (Å)	10.300 (3), 8.923 (3), 14.672 (4)	14.3602 (16), 6.9255 (8) 25.895 (3)
β (°)	90.761 (7)	104.482 (8)
V (Å^3)	1348.3 (6)	2493.5 (5)
Z	4	8
Radiation type	Mo $K\alpha$	Mo $K\alpha$
μ (mm^{-1})	0.11	0.09
Crystal size (mm)	0.20 × 0.15 × 0.10	0.25 × 0.20 × 0.15
Diffractometer	Rigaku R-AXIS RAPID	Rigaku R-AXIS RAPID
Absorption correction	Multi-scan *ABSCOR* (Rigaku, 1995)	Multi-scan *ABSCOR* (Rigaku, 1995)
T_{min}, T_{max}	0.637, 0.989	0.559, 0.987
Number of measured, independent and observed [$I > 2\sigma(I)$] reflections	8548, 2689, 1082	9679, 2277, 1846
R_{int}	0.064	0.027
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.625	0.602
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.043, 0.129, 0.84	0.037, 0.111, 1.10
Number of reflections	2689	2277
Number of parameters	200	172
H-atom treatment	Constrained	Constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.17, −0.17	0.13, −0.15

2.4 Non-Bonding Interactions Within **6b** and **9a** Crystals

Both triazolopyrimidine **6b** and imidazole dicarbonitrile **9a** possess heterocyclic rings and terminal nitrogen or oxygen containing functional groups. This enables these molecules to engage efficient H-bonding/non-bonding interactions with their adjacent counterparts. Multiple H-bonding interactions are observed in the crystals of both **6b** and **9a**. In the case of triazolopyrimidine, most intermolecular supramolecular bonds are through C-H...N, C-H...C and C-H...O type interactions, whereas, for imidazole dicarbonitrile **9a**, such bonds are mainly through C-H...N interactions. The H-bonding/non-bonding observed among **6b,** and **9a** are depicted in Figure 3 and Figure 4, respectively, and their quantitative details are given in Table 2.

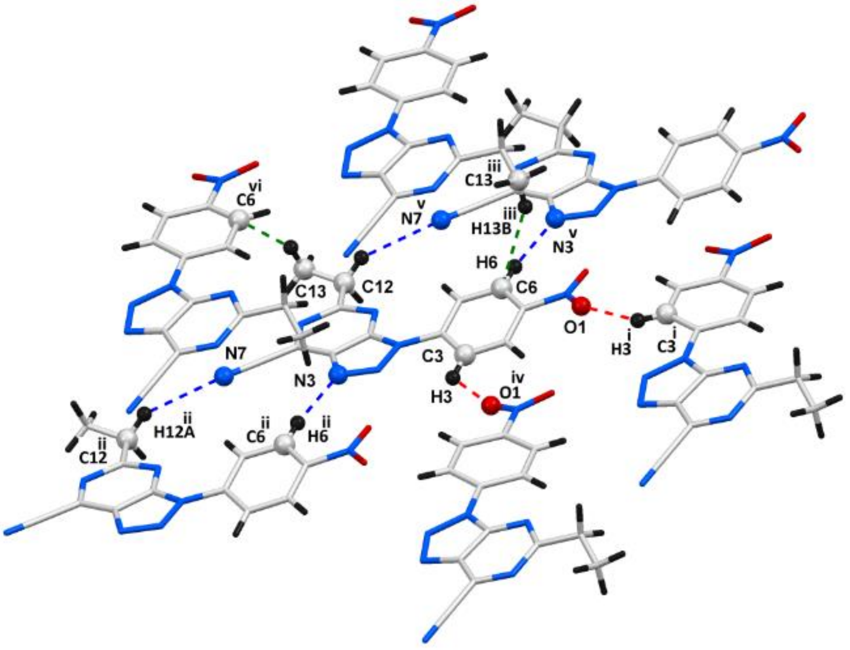


Fig. 3. H-bonding/non-bonding interactions in **6b** crystals. C-H---O, C-H---N and C-H---C interactions are represented by red, blue and green dotted lines, respectively (symmetry code: ([i]) 1/2-x, 1/2+y, 1/2-z; ([ii]) x, -1+y, z; ([iii]) 1/2-x, 1/2+y, 1.5-z; ([iv]) 1/2-x, -1/2+y, 1/2-z; ([v]) x, 1+y, z; ([vi]) 1/2-x, -1/2+y, 1.5-z).

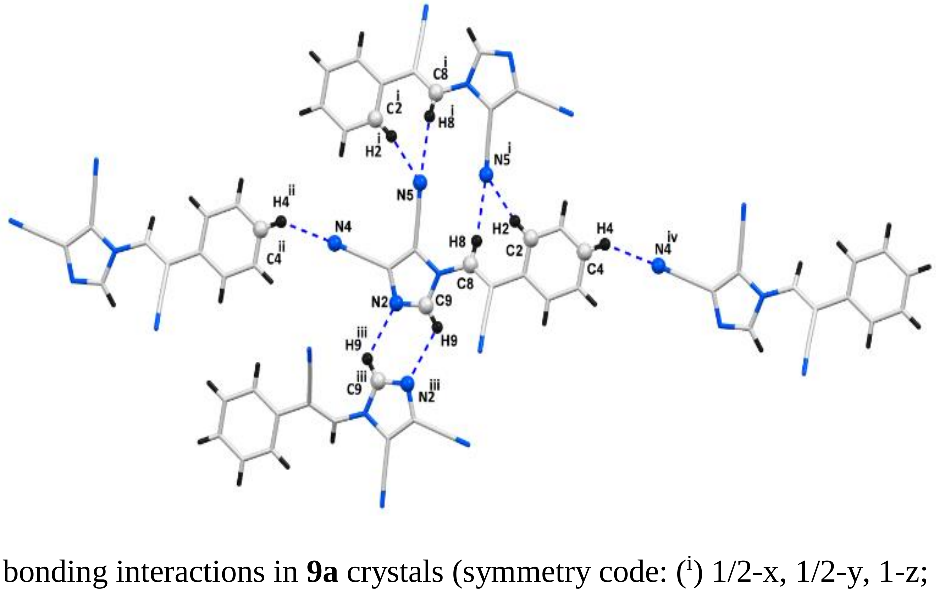


Fig. 4. H- bonding interactions in **9a** crystals (symmetry code: ([i]) 1/2-x, 1/2-y, 1-z; ([ii]) 1+x, y, z; ([iii]) 1-x, y, 1.5-z; ([iv]) -1+x, y, z).

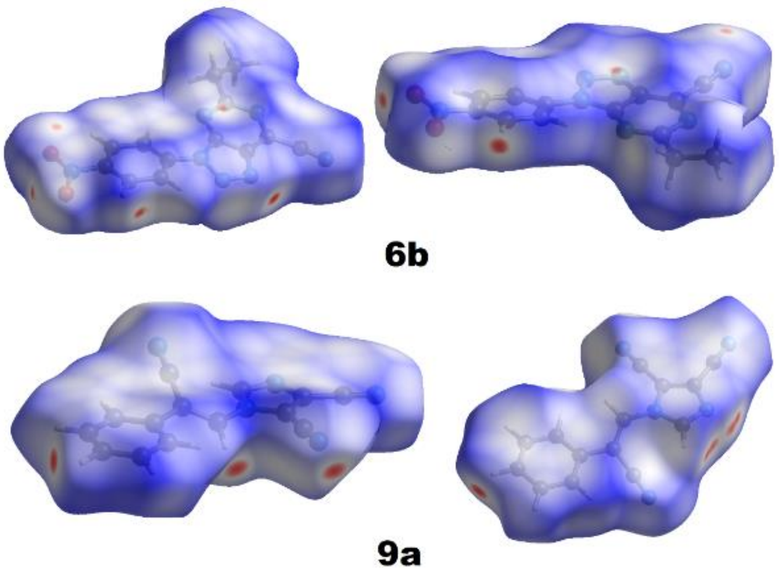
Table 2. Quantitative details of H-binding/non-bonding interactions among **6b** and **9a** crystals (symmetry codes: (^{i}) 1/2-x, 1/2+y, 1/2-z; (^{ii}) x, -1+y, z; (^{iii}) 1/2-x, 1/2+y, 1.5-z); (^{i}) 1/2-x, 1/2-y, 1-z; (^{ii}) 1+x, y, z; (^{iii}) 1-x, y, 1.5-z).

D-H...A	**D-H**	**H...A**	**D....A**	**D-H...A**
Triazolopyrimidine 6b				
C3^{i}-H3^{i}...O1	0.931	2.733	3.282(3)	118.6
C6^{ii}-H6^{ii}...N3	0.930	2.657	3.571(4)	167.45
C12^{ii}-H12A^{ii}...N7	0.970	2.756	3.620(4)	148.7
C13^{iii}-H13B^{iii}...C6	0.961	2.898	3.774(5)	152.2
Imidazole dicarbonitrile 9a				
C2^{i}-H2^{i}...N5	0.951	2.715	3.509(2)	141.48
C8^{i}-H8^{i}...N5	0.950	2.565	3.508(2)	171.73
C4^{ii}-H4^{ii}...N4	0.950	2.519	3.332(2)	143.6
C9^{iii}-H9^{iii}...N2	0.950	2.537	3.096(2)	117.78

Due to their ability to engage multiple H-bonding/non-bonding interactions, both **6b** and **9a** are supramolecularly attached to many neighbouring molecules. It is shown that each triazolopyrimidine molecule **6b** is non-covalently bonded with its six neighbouring counterparts and that each imidazole dicarbonitrile **9a** is bonded with four neighbours. Also, in the case of the triazolopyrimidine crystal, each molecule interacts with its nearest molecule by π-π interaction, which is demonstrated in the supporting information. This π-π interaction is achieved by the face-to-face attachment of two nitrophenyl fragments of **6b** molecules, which are oriented opposite each other.

2.5 Hirshfeld Surface Analysis of **6b** and **9a** Crystals

The Hirshfeld surfaces and the related two-dimensional (2D) fingerprint plots provide both qualitative and quantitative information about various intermolecular interactions experienced by a species in the crystal. The three-dimensional (3D) dnorm surface is useful to analyse and visualise the intermolecular interactions, and the 2D fingerprint plots offer a quantitative summarisation of the nature and type of various intermolecular contacts experienced by the molecules in the crystal network. (Spackman & Jayatilaka, 2009, McKinnon *et al.*, 2004; McKinnon *et al.*, 2007). The Hirshfeld surface, mapped with a dnorm function for triazolopyrimidine **6b** and imidazole dicarbonitrile **9a** molecules in their crystals, is shown in Figure 5, and the corresponding 2D finger plots are given in the supporting information. It should be noted that the red-coloured regions on the dnorm surface represent the intermolecular contacts closer than the sum of the Van der Waals radii, the white colour shows intermolecular distances close to van der Waals contacts with the dnorm equal to zero, and the blue region represents the longer contacts.


6b

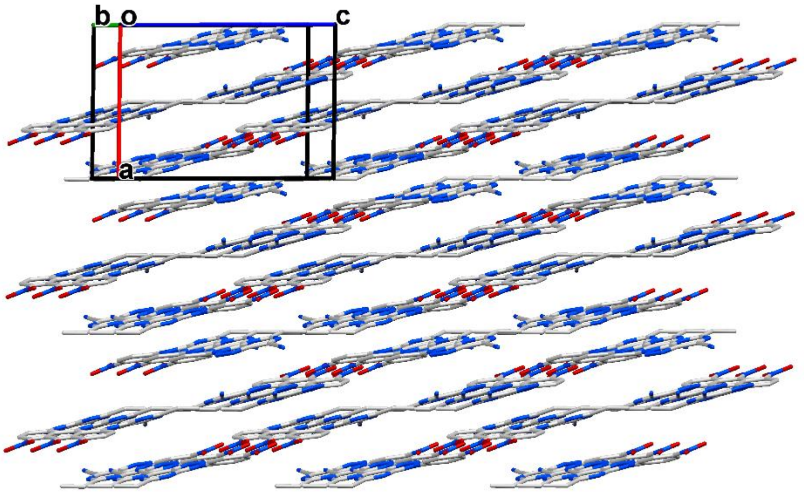
9a

Fig. 5. The Hirshfeld surface mapped with dnorms of **6b** and **9a** when viewing from two different directions.

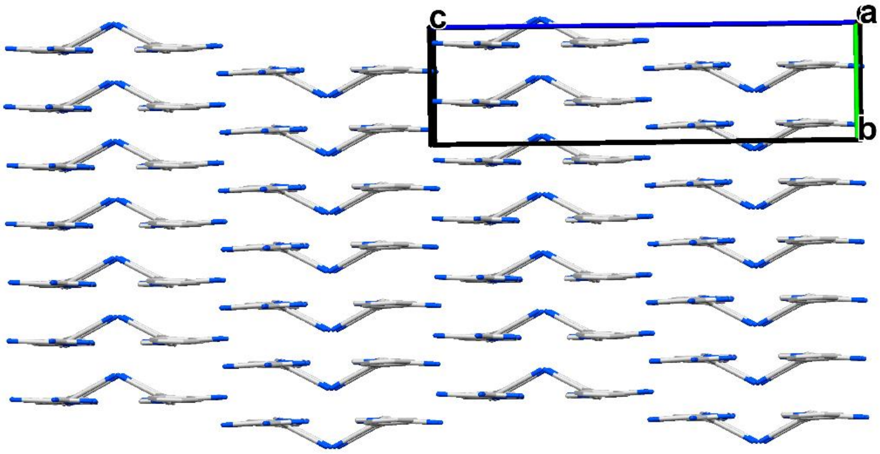
The red-dominated spots in the Hirshfeld surface of **6b** and **9a** are obviously the strong non-bonding interactions experienced in these systems – most of them are the H-bonding type already indicated in Figure 3 and Figure 4. There are also many white shades on the hydrosulphide (HS) surface, indicating additional moderately strong intermolecular contacts within the molecules in these crystals. The 2D fingerprint plots of triazolopyrimidine **6b** crystals show that the N...H interactions are the most significant interatomic interactions experienced by this molecule, with a considerable contribution of 29.8%. The C...H and O...H interactions are also significant in this system, with contributions of 18.3% and 15.0%, respectively. Other significant intermolecular interactions in this crystal are H...H (13.3%), N...C (5.9%), C...O (5.3%), N...O (5.0%) and N...N (4.7%). Other possible intermolecular contacts, such as C...C and O…O, are too low to count. In the case of imidazole dicarbonitrile **9a**, the 2D fingerprint shows that the N...H interactions are the most significant interatomic interactions, with a massive contribution of 45.8%. The C...C interaction is the second-highest significant interaction in this crystal, with a contribution of 16.4%, followed by the H...H interaction (14.9%) and the C...N interaction (10.0%). The contributions of other interactions are C...H (7.8 %) and N...N (5.1%). In short, excellent information about various interatomic interactions experienced by both **6b** and **9a** molecules within their crystals are obtained from the HS analysis.

2.6 Supramolecular Packing of **6b** and **9a** Crystals

As a result of multiple H-bonding/non-bonding interactions, the triazolopyrimidine **6b** and imidazole dicarbonitrile **9a** molecules formed a supramolecular network within their crystals with an interesting pattern. The packing pattern of these molecules in their crystals is depicted in Figure 6.



Triazolopyrimidine



Imidazole dicarbonitrile

Fig. 6. Packing pattern of triazolopyrimidine **6b** and imidazole dicarbonitrile **9a** molecules in their crystal network.

From its packing pattern, it is evident that the triazolopyrimidine molecule formed twisted one-dimensional polymers in the network, which is interesting in relation to various opto-electronic applications. On the other hand, the packing of imidazole dicarbonitrile **9a** molecules, a herringbone type assembly with oppositely oriented **9a** sets, is done in a zig-zag manner. The bridging nitrile spacer's orientation to a different plane against the aromatic planes in this molecule makes these packing patterns interesting. The packing features of both these molecules when viewing along different crystallographic directions are depicted in the supporting information.

3. Conclusion

We have demonstrated a simple and efficient method for cyclisation reactions using orthoesters to obtain pyrimidine and 4,5-dicyanoimidazole derivatives. With these economical and available reagents, the ability to introduce alkyl groups as substituents proved to be effective and productive. The obtained results are straightforward, and they play a valuable part in the synthesis of a series of nitrogen heterocyclic compounds, which are applicable in a group of different research/industrial areas. The single-crystal X-ray diffraction studies provide more insights into the structural aspects of these novel compounds; the existence of multiple supramolecular nonbonding interactions among these compounds suggest them to be very interesting species as functional materials – for example, pharmaceuticals. Application studies based on these novel heterocyclic compounds are being carried out in our lab.

4. Experimental

4.1 Material and methods

Infrared spectra were recorded using a Jasco FT-IR 6300 instrument. ^{1}H and ^{13}C NMR spectra were evaluated with a Bruker DPX instrument at 400/600 megahertz (MHz) for ^{1}H NMR and 100 MHz for ^{13}C NMR and dimethyl sulfoxide (DMSO)-d$_6$ as a solvent, with tetramethyl silane (TMS) as an internal standard. Chemical shifts were reported in parts per million. Mass spectra were measured using a GCeMS DFS Thermo spectrometer in electronic ionisation (EI) (70 electron volts [eV]) mode. Elemental analyses were performed using an Elementar Vario MICRO Cube Melting points were determined by using a Gallenkamp melting point apparatus and were uncorrected. The single-crystal X-ray diffraction analysis was made on a Rigaku R-AXIS RAPID diffractometer. The triazole was prepared following the previously reported procedure. (Al-Azmi and Kalarikkal, 2013).

4.2 Single-crystal data collection and structure refinement

Single crystals of triazolopyrimidine **6b** and imidazole dicarbonitrile **9a** were grown from hot ethanol and hot DCM, respectively (25.0 mg dissolved in 1.00 ml solvent) by slow solvent evaporation. Crystals suitable for diffraction analysis were obtained in one week. The single-crystal data analysis was made by a R-AXIS RAPID II Rigaku diffractometer using filtered Mo-Kα radiation. While the data collection from triazolopyrimidine **6b** crystals was done at room temperature, data collection from imidazole dicarbonitrile **9a** was performed under liquid nitrogen (150 K) using Oxford cryosystems (United Kingdom). The crystal data collection was carried out using Crystalclear (Rigaku, Japan), and data processing was done by CrystalStructure (Rigaku, Japan) software packages. The structure refinement was performed by SHELXL - 97. All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were placed at calculated positions and refined using a riding model. The molecular graphics and calculation of intermolecular interactions were carried out using Mercury (Version 3.6). The Hirshfeld surface analysis was performed using CrystalExplorer 17.1. (Turner, McKinnon, Wolff, Grimwood, Spackman, *et al.*, 2017).

4.3 General procedure for the synthesis of 5-alkyl-3-(4-nitrophenyl)-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidine-7-carbonitriles **6a**,**b**

Triazole **5** (1.00 mmol) was refluxed in a mixture of the excess of RC(OEt)$_3$ (R = H or C$_2$H$_5$) and DMF: dioxane 1:1 (1.00 mL) for six hours. The reaction mixture was filtered while hot and cooled to room temperature, the products were precipitated out, and they were then filtered off and recrystallised from hot ethanol.

3-(4-Nitrophenyl)-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidine-7-carbonitrile **6a**

Colourless crystals (68%), mp: 164-168 ^{o}C; ν_{max} (KBr)/cm^{-1} 3120, 2230, 1670, 1520, 1430, 1400, 1200, 1180, 845, 680, 640; ^{1}H NMR (DMSO-d$_6$, 600 MHz): δ 7.94 (d, 2H, J = 8.0 Hz, ArH), 8.39 (d, 2H, J = 8.0 Hz, ArH), 9.41 (s, 1H, CH);^{13}C NMR (DMSO-d$_6$): δ 116.6, 124.6, 125.4, 131.4, 132.1, 134.5, 135.3, 146.8, 152.9*;* *m/z* (EI) 267 (M^+); *m/z* (EI) 267.0504 (M^+, $C_{11}H_5N_7O_2$ requires 267.0505).

5-Ethyl-3-(4-nitrophenyl)-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidine-7-carbonitrile **6b**

Off-white crystals (71%), mp: 171-174 °C; ν_{max} (KBr)/cm^{-1} 3100, 2225, 1615, 1540, 1520, 1410, 1390, 1210, 1190, 1100, 945, 840, 800, 760; ^{1}H NMR (DMSO-d$_6$, 600 MHz): δ 1.38 (t, 3H, *J* = 7.2 Hz, $CH_2\underline{CH_3}$), 2.94 (q, 2H, *J* = 7.2 Hz, $\underline{CH_2}CH_3$), 7.91 (d, 2H, *J* = 8.2 Hz, ArH), 8.41 (d, 2H, *J* = 8.2, ArH); ^{13}C NMR (DMSO-d$_6$): δ 12.9, 32.1, 115.8, 124.9, 122.9, 131.8, 136.2, 137.7, 147.3, 153.6; m/z (EI) 295 (M^+); m/z (EI) 295.0818 (M^+, $C_{13}H_9N_7O_2$ requires 295.0818).

Synthesis of 3-Amino-3-((*Z*)-2-cyano-2-phenylvinylamino)maleonitrile **8**

A mixture of phenyl 3-oxopropanenitrile **7** (1.00 mmol), DAMN **2** (1.00 mmol) in CH_3CO_2H (10.00 mL was stirred at room temperature for 24 hrs. The green shiny powder formed was filtered off and was used without any further purification. (80%), mp: 207-210 °C decomp.; ν_{max} (KBr)/cm^{-1} 3419, 3333, 3270, 3218, 3057, 3025, 2924, 2222, 2208, 1652, 1626, 1602, 1470, 1443, 1376, 1345, 1319, 1286, 1264, 1240, 1193, 1159, 1076, 999; ^{1}H NMR (DMSO-d$_6$, 400 MHz): δ 7.14 (m, 1H, ArH), 7.29 (m, 6H, 4 ArH, 2H, NH_2), 7.48 (d, 1H, *J* = 10 Hz, CH), 8.65 (d, 1H, *J* = 10 Hz, NH); ^{13}C NMR (DMSO-d$_6$): δ 83.97, 93.57, 114.26, 116.90, 117.60, 123.71, 123.92, 126.13, 128.13, 128.99, 133.81, 144.68 m/z (EI) 235 (M^+) 100%; elemental analysis for $C_{13}H_9N_5$: C 66.38, H 3.83, N 29.79. Found: C 66.68, H 3.68, N 29.85%.

4.4 General Procedure for the Synthesis of (*Z*)-1-(2-cyano-2-phenylvinyl)-2-alkyl-1*H*-imidazole-4,5-dicarbonitriles **9a**,**b**

3-Amino-3-((*Z*)-2-cyano-2-phenylvinyl-amino) maleonitrile **8** (1.00 mmol) was refluxed in excess of $RC(OEt)_3$ R = H or C_2H_5 and DMF: dioxane 1:1 (1.00 mL) for six hours. The reaction mixture was filtered while hot and cooled to room temperature, the products were precipitated out, and they were then filtered off and recrystallised from hot DCM.

(*Z*)-1-(2-Cyano-2-phenylvinyl)-1*H*-imidazole-4,5-dicarbonitrile **9a**

Colourless crystals (67%), mp: 151-153 °C; ν_{max} (KBr)/cm^{-1} 3144, 3069, 3003, 2242, 2201, 1737, 1634, 1606, 1542, 1464, 1391, 1375, 1338, 1302, 1258, 1220, 1161, 1144, 1081, 1046, 1001, 918, 874, 768; ^{1}H NMR (DMSO-d$_6$, 400 MHz): 7.54 (m, 3H, ArH), 7.72 (m, 2 H, ArH), 8.43 (s, 1H, CH), 8.89 (s, 1H, CH), δ ^{13}C NMR (DMSO-d$_6$): δ 94.3, 113.9, 115.2, 118.4, 122.8, 123.7, 125.1, 126.6, 129.0, 133.2, 134.5, 147.3 , m/z (EI) 245 (M^+) 47%, 244, 100%; m/z (EI) 245.0701 (M^+, $C_{14}H_7N_5$ requires 245.0701).

(*Z*)-1-(2-Cyano-2-phenylvinyl)-2-ethyl-1*H*-imidazole-4,5-dicarbonitrile **9b**

Off-white crystals (65%), mp: 157-159 °C; ν_{max} (KBr)/cm^{-1} 3076, 2943, 2235, 2220, 2218, 1649, 1527, 1419, 1302, 1231, 1029, 1005, 941; ^{1}H NMR (DMSO-d$_6$, 400 MHz): δ 1.21 (t, 3H, *J* = 7.2 Hz, $CH_2\underline{CH_3}$), 2.84 (q, 2H, *J* = 7.2 Hz, $\underline{CH_2}CH_3$), 7.57 (m, 3H, ArH), 7.77 (m, 2H, ArH), 8.40 (s, 1H, CH); ^{13}C NMR (DMSO-d$_6$): δ 11.82, 21.56, 97.2, 114.5, 116.4, 117.9, 122.5, 123.1, 125.8, 127.7, 128.4, 134.0, 136.2, 146.3; m/z (EI) 273 (M^+) 84 %, 258, 100 %; m/z (EI) 273.1013 (M^+, $C_{16}H_{11}N_5$ requires 273.1014).

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Appendix A: Supplementary Material

Single-crystal data for compounds triazolopyrimidine **6b** (CCDC 993548) and imidazole dicarbonitrile **9a** (CCDC 2004526) have been deposited in Cambridge Crystallographic Data Centre. Supplementary data associated with this article can be found at http://www.ccdc.cam.ac.uk/conts/retrieving.html.

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