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Synthesis of 1,4,5-Trisubstituted-1,2,3-Triazoles *via* Coupling Reaction of Diaminomaleonitrile with Aromatic Diazonium Salts

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Abstract:

A mild procedure for the preparation of 2-(5-amino-1-aryl-1*H*-1,2,3-triazol-4-yl)-2-iminoacetonitriles and 2-(5-amino-1-aryl-1*H*-1,2,3-triazol-4-yl)-2-oxoacetonitriles was achieved by the reaction of diaminomaleonitrile and phenyl/substituted phenyl diazonium chlorides. 4-Nitrophenyl diazonium chloride afforded 2-amino-3-(3-(4-nitrophenyl)triaz-1-en-1-yl)maleonitrile. Triazole iminoacetonitrile and maleonitrile derivatives were reacted further with excess acetone and benzaldehyde with a catalytic amount of 1,8-diazabicyclo[5.4.0]undec-7-ene to yield 5-(5-imino-2,2-dimethyl-2,5-dihydrooxazol-4-yl)-3-aryl-3*H*-1,2,3-triazol-4-amine and (*E*)-*N*-benzylidene-5-(5-imino-2-aryl-2,5-dihydrooxazol-4-yl)-3-aryl-3*H*-1,2,3-triazol-4-amine, respectively. Two competitive reactions, i.e. nucleophilic substitution and nucleophilic addition, were observed when triazole oxoacetonitrile and maleonitrile derivatives were reacted with hydroxylamine hydrochloride in the presence of sodium acetate.

Key words: diazotization, diaminomaleonitrile, triazole, coupling, oxazole

INTRODUCTION

Since the synthesis of 1,2,3-triazoles from Huisgen 1,3-dipolar cycloaddition of azides and alkynes,[1] this class of heterocycles has gained great importance worldwide,[2-4] as they have found a wide range of applications as pharmaceuticals, catalysts and ligands in transition-based catalyst systems and molecular design.[2a,5-11] The strong demand for these interesting heterocyclic compounds has prompted several research groups to study new routes for their synthesis, particularly using 'click chemistry'. Several organic chemists have reported the preparation of

1,2,3-triazoles via the reaction of azides with not only terminal and internal alkynes but also calcium carbides[12] using various metal catalysts, such as copper,[4,13-22] palladium[23-25] and ruthenium.[26] Other researchers have described a transitionmetal-free catalytic synthesis procedure.[26-28]

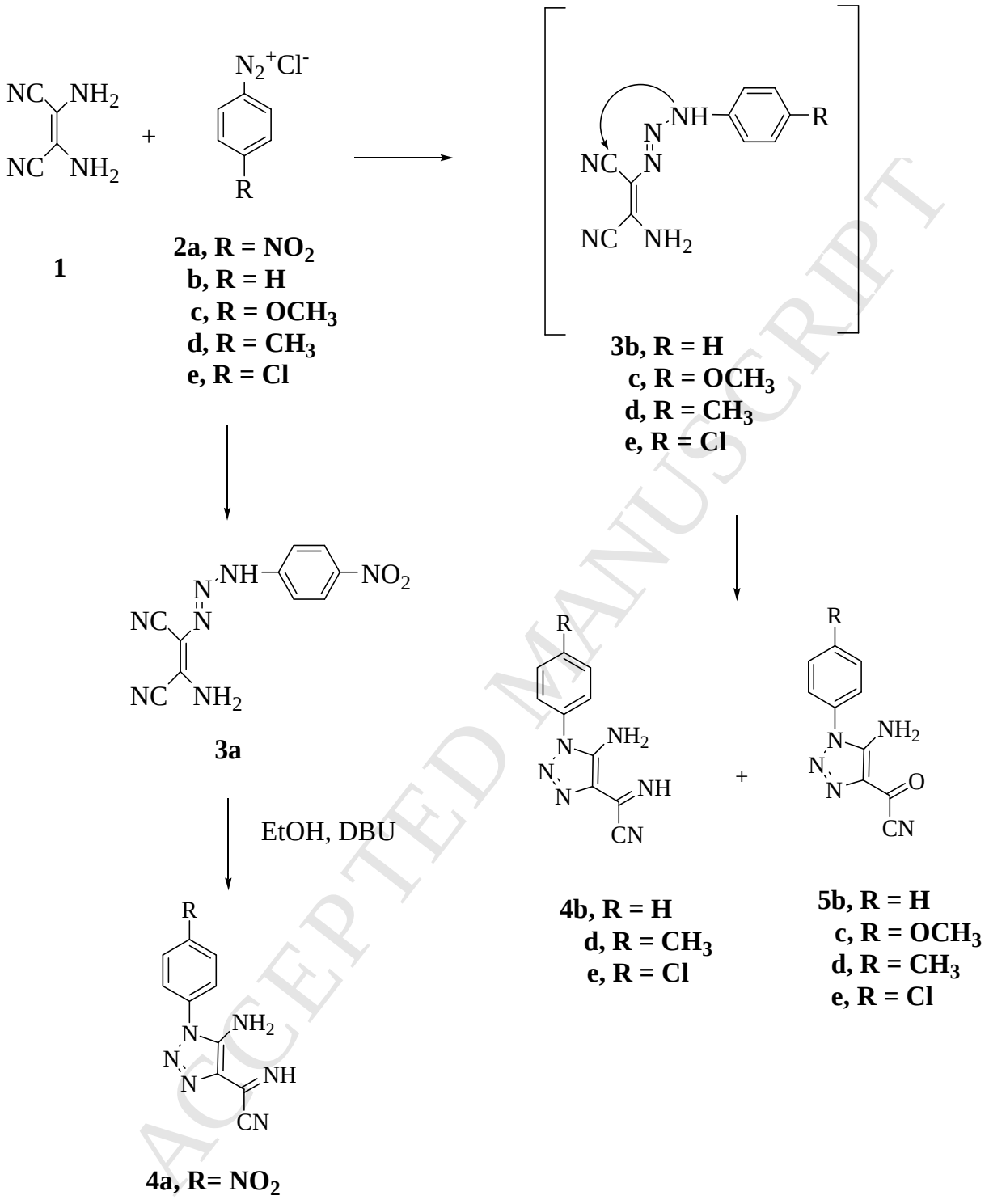
Wang *et al.*[26] obtained 1,4,5-trisubstituted 1,2,3-triazoles from a regiospecific synthesis procedure using enamide-azide cycloaddition. Cao and co-workers[14] showed that 1,4-disubstituted 1,2,3-triazoles could be obtained by a one-pot three-component reaction of primary alcohols, sodium azides and terminal alkynes utilising a Cu^{1}-catalyst. A recent paper by König *et al.*[13] described a solid-state synthesis protocol using a modified Wang resin for the synthesis of a series of substituted diaryltriazoles that have the potential to work as selective inhibitors for protein-protein interactions.

Amongst these reported procedures, azides appear to be the common reactant. However, in 1986 Vaughan reported an azide free route to 1,2,3-triazoles,[29] diazotisation of aryl amines followed by coupling with α-aminoacetonitrile gave cyanomethyltriazene derivatives which were cyclised to 1,2,3-triazoles using alumina as a catalyst. The extensive search for a mild, inexpensive and easily applicable approach continues to this day. Our group has investigated the chemistry of diaminomaleonitrile (DAMN) **1** for over a decade.[30a] Diazotisation of DAMN **1** or *N*-[2-amino-1,2-dicyanovinyl]alkanamides yields 4,5-disubstituted 1,2,3-triazoles.[30b] Our motivation for extending work in this area is based on further explorations of the reactions of DAMN **1** with aryl diazonium salts. Herein, we report a method for preparing 1,4,5-trisubstituted 1,2,3-triazoles *via* reaction of DAMN **1** with various aryl diazonium salts.

Results and Discussion

4-Nitrophenyl diazonium salt **2a** was freshly prepared[31a] and added to an ethanolic solution of DAMN **1**. A yellow solid was isolated by filtration from the reaction mixture and all spectroscopic analyses showed the expected 2-amino-3-(3-(4-nitrophenyl)triaz-1-en-1-yl)maleonitrile **3a** indicated in **Scheme 1**. Isolation of **3a** prompted us to prepare different derivatives that could be utilised as precursors in various transformations. Hence, phenyldiazonium salts **2b–e** were synthesised and allowed to react with DAMN **1** in ethanol. None of the isolated products showed an imine-NH– signal during ^{1}H NMR spectroscopy, and

the IR spectra obtained showed only a very weak CN peak in addition to a carbonyl function. Molecular ions detected in the mass spectra identified the triazoles **5b–e** shown in **Scheme 1**. Isolation of maleonitrile derivative **3a** from the 4-nitrophenyl diazonium salt could only result from the strong electron-withdrawing effect of the nitro group in the *para*-position of the benzene ring. This group reduces the electron density around the nitrogen atom in the N=N–NH– moiety, which survives cyclisation and, consequently, hydrolysis. Isolation of triazoles **5b–e** indicates that maleonitrile derivatives **3b–e** are formed as intermediates after the reaction of diazonium salts **2b–e** with DAMN **1**. Due to their instability, maleonitrile derivatives **3b–e** are cyclised to triazoles of type **4b-e**, which are hydrolysed spontaneously to give the more stable triazoles **5b–e**. Triazoles **5b–e** were characterized by spectroscopic data. All of them contain the alpha-ketonitrile group. In their ^{13}C NMR spectra, the carbonyl function of these groups appears at δ 160.3-156.7 ppm. This is not surprising as it has been reported before to appear at δ 164.7-167.6.[31b,c]



Scheme 1

In an attempt to obtain compounds **3b–e** and **4b–e**, the reaction conditions were modified, as shown in Table 1.

Table 1: Reaction conditions for the coupling of DAMN **1** with diazonium salts **2**

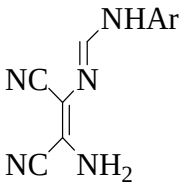
Entry	Diazonium salt	Reaction condition	Product	Yield
1	**2a**	DAMN, EtOH, rt	**3a**	44%
2	**2a**	DAMN, EtOH, rt, CH_3CO_2Na	**3a**	35%
3	**2a**	DAMN, EtOH, rt CH_3CO_2Na and ice	**Traces of 3a**	
4	**2b**	DAMN, EtOH, rt	**5b**	15%
5	**2b**	DAMN, EtOH, rt, CH_3CO_2Na	**5b**	12%
6	**2b**	DAMN, EtOH, rt, CH_3CO_2Na and ice	**Traces of 4b**	
7	**2c**	DAMN, EtOH, rt	**5c**	9%
8	**2c**	DAMN,EtOH, rt, CH_3CO_2Na	**decomposed**	
9	**2c**	DAMN, EtOH, rt CH_3CO_2Na and ice	**decomposed**	
10	**2d**	DAMN, EtOH, rt	**5d**	21%
11	**2d**	DAMN, EtOH, rt, CH_3CO_2Na	**5d**	7%
12	**2d**	DAMN, EtOH, rt, CH_3CO_2Na and ice	**Traces of 4d**	
13	**2e**	DAMN, EtOH, rt	**5e**	24%
14	**2e**	DAMN, EtOH, rt, CH_3CO_2Na	**5e**	13%
15	**2e**	DAMN, EtOH, rt, CH_3CO_2Na and ice	**Traces of 4e**	

Initially, all of the reactions were carried out in the presence of sodium acetate to prevent protonation of the amino groups in DAMN **1** prior to addition of the diazonium salts. Under these conditions, 4-nitrophenyl diazonium salt **2a** coupled with DAMN **1** to yield **3a**. However, when the same conditions were applied using diazonium salts **2b**, **d** and **e**, triazoles **5b**, **d** and **e** were obtained. Diazonium salt **2c**, on the other hand, decomposed. Ice, along with sodium acetate, was added to accelerate precipitation. All diazonium salt derivatives showed traces of the triazole **4,** except 4-methoxyphenyl diazonium chloride **2c**, which afforded a decomposed material; 4-nitrophenyl diazonium chloride **2a** gave only traces of **3a**. Attempts to isolate pure **4b, d** and **e** were unsuccessful. Diazonium salts **2b–e** may have formed triazoles **5b–e** mainly by

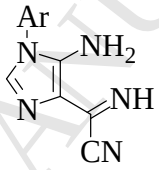
the effect of electron-releasing groups, which facilitate cyclisation and protonation of the imine function and thereby promote susceptibility of the compounds to hydrolysis.

We agree that the yields are relatively low, but from Table 1 it can be seen that the yields are affected by several factors i.e. the substituents on the aromatic diazonium salts, the presence of sodium acetate and addition of ice. Perhaps further future studies could lead to more interesting results.

The structure of the isolated maleonitrile **3a** resembles that of formamidine **6**; these amidines have been prepared extensively by our group[32-35] as well as other groups.[36-46] When a catalytic amount of DBU is added to formamidine **6** in ethanol, imidazoles of type **7** are formed in good yields.



6



7

Initially, the reaction of **3a** with acetone was stirred for several days, no products were detected as indicated by TLC. The use of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as a base catalyst came after we realized the resemblance between the structure of **3a** and formamidine **6**. In literature,[32-46] successful reactions of formamidines with other reagents were done using DBU as a catalyst. As a result, maleonitrile **3a** was treated with a catalytic amount of DBU in ethanol, forming a solid that was filtered, dried and identified as triazole **4a** based on its spectroscopic data. When **3a** was reacted with acetone in the presence of DBU, it formed a solid that, in its ^{1}H NMR spectrum, revealed incorporation of an acetone molecule. A molecular ion of 315 was further observed in the MS spectrum of the product. Similarly, when triazole **4a** reacted with acetone only, several spots in addition to the starting material were detected in TLC, unfortunately, these spots could not be identified. On the other hand, reaction of **4a** with acetone and a catalytic amount of DBU, furnished an identical solid to the one collected from the reaction of **3a** with acetone and DBU. Attempts to grow crystals suitable for X-ray analysis failed. Actually beside DBU, triethylamine and pyridine were also used as catalysts. Reaction of

maleonitrile **3a** and triazole **4a** with acetone in the presence of either triethylamine or pyridine for 7 days gave dark brown mixture which contained several unidentified spots as TLC showed. The crude brown solid collected from the reaction of diazonium chloride **2b** with DAMN **1** using sodium acetate in addition to ice showed spectral signals indicating that it could be assigned as triazole **4b**. Purification by DFC, column chromatography and recrystallisation with several solvents did not lead to isolation of this product. However, when acetone was added to the solid in the presence of DBU, an off-white powder with ^{1}H NMR and MS spectra indicative of the addition of an acetone molecule was obtained. Recrystallisation of this off-white solid from acetone gave good crystals for X-ray analysis, which showed the product to be 5-(5-imino-2,2-dimethyl-2,5-dihydrooxazol-4-yl)-3-phenyl-3*H*-1,2,3-triazol-4-amine **8b**, shown in **Fig. 1**.[47]

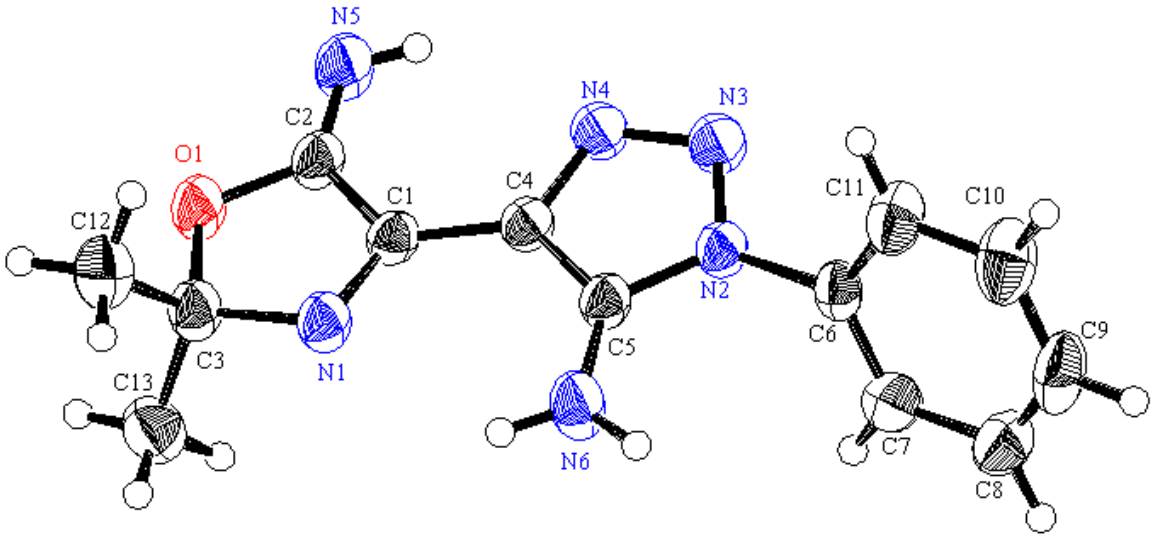
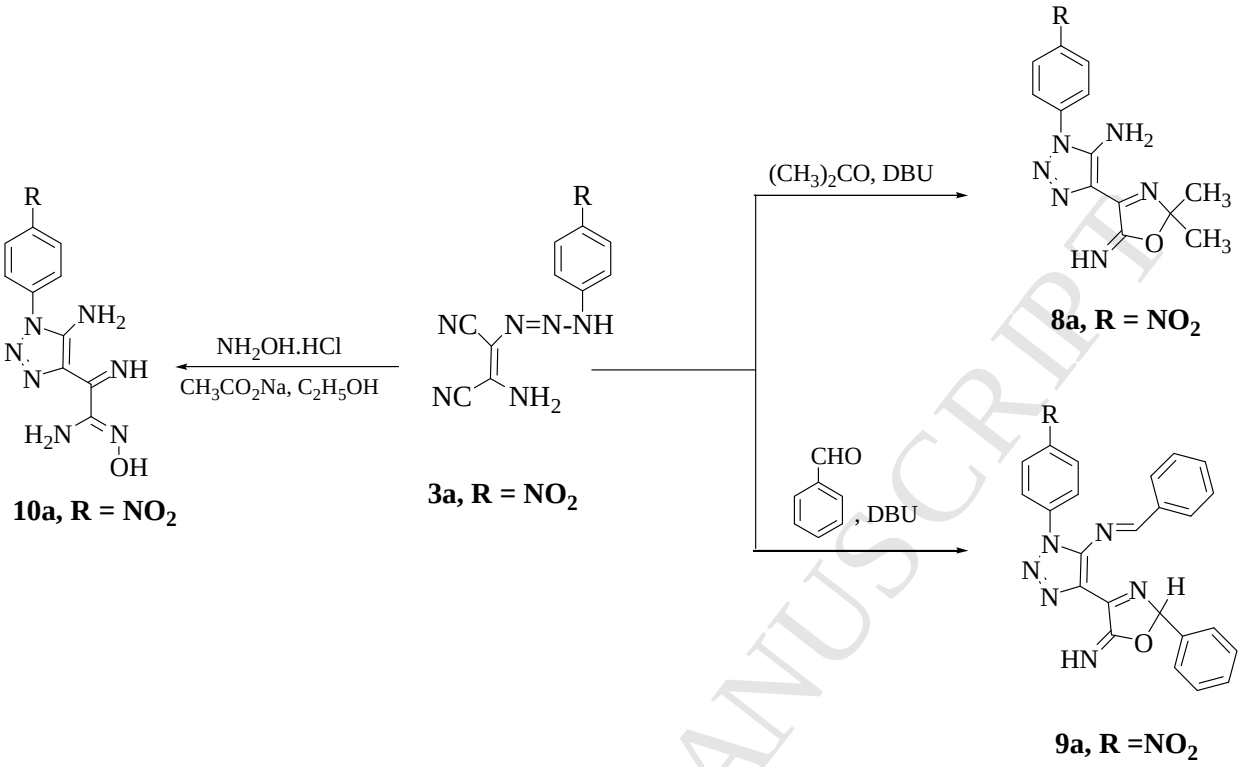


Fig. 1: X-ray crystal structure of triazole **8b.**

Comparison of both ^{1}H/^{13}C NMR spectra of **8a** with **8b** confirmed the structure assigned to **8a**. Apparently, triazole **4a** is an intermediate formed during the reaction of maleonitrile derivative **3a** with acetone and DBU as a catalyst.



10a, R = NO_2

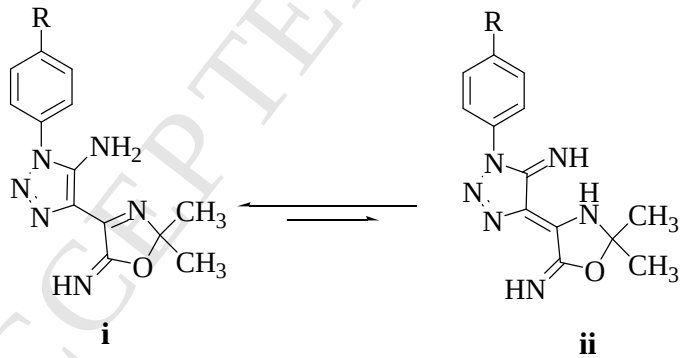
3a, R = NO_2

8a, R = NO_2

9a, R =NO_2

Scheme 2

Further, tautomers (**i**, **ii**) of both novel triazoles **8a** and **8b** were detected in their ^{1}H NMR spectra.



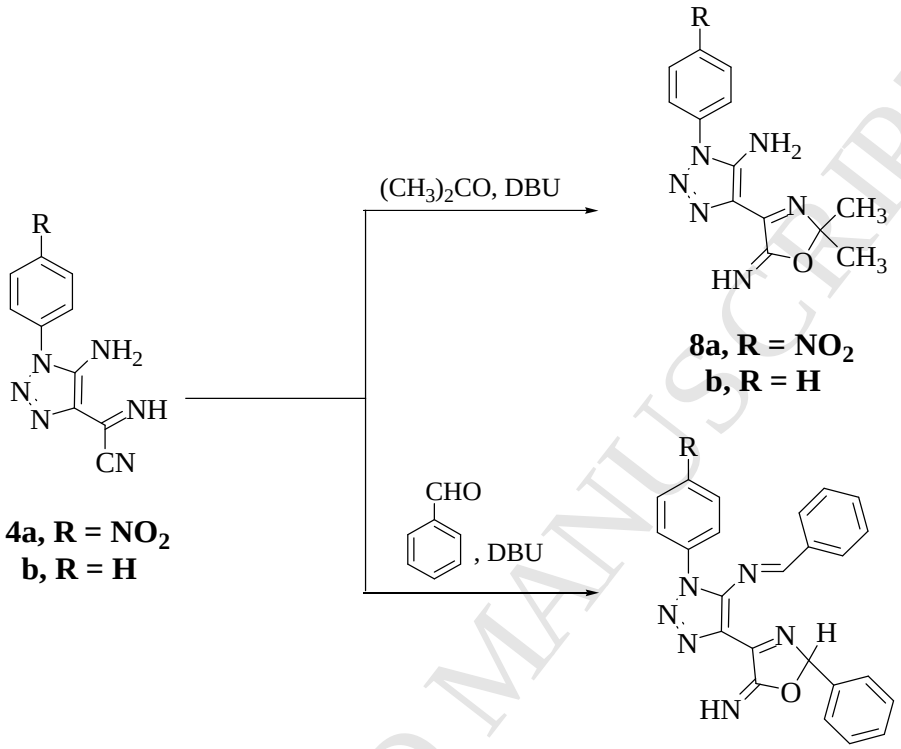
i **ii**

8a, R = NO_2
b, R = H

Scheme 3

This observation was generalised by using benzaldehyde in the presence of a catalytic amount of DBU at room temperature. Yellow solids were collected from both reactants (**3a** and a brown

solid that contained **4b** as a minor product). All of the spectra revealed the presence of two extra phenyl groups. The compounds were identified as triazoles **9a** and **9b**. (**Schemes 2** and **4**).



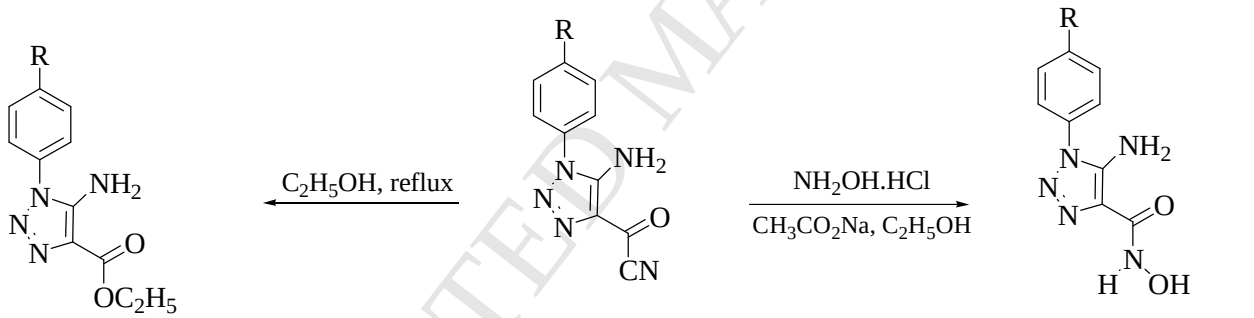
Scheme 4

Table 2: Conditions for the reactions of triazoles with carbonyl compounds

Entry	Triazole	Carbonyl compound	Reaction Conditions	Product/ yield (%)
1	**3a**	**acetone**	excess acetone and 0.25 ml DBU, rt.	**8a (43)**
2	**3a**	**benzaldehyde**	excess benzaldehyde and 0.25 ml DBU, rt	**9a (30)**
3	**4b**	**acetone**	excess acetone and 0.25 ml DBU, rt	**8b (55)**
4	**4b**	**benzaldehyde**	excess benzaldehyde and 0.25 ml DBU, rt	**9b (36)**

Because the isolated products **3a** and **5b–d** contain functional groups that can be transformed into other reactive functions, the reactions of **3a** and **5b–d** with hydroxylamine hydrochloride were also investigated. The conditions adopted for these reactions are identical to those described in our previous paper.[32,33] Hydroxylamine hydrochloride and sodium acetate were added to a suspension of **3a** and **5b**–**d** in ethanol, and the mixture was stirred at room temperature until

completion of the reaction, as determined by TLC using EtOAc:hexane 2:1. A white solid was formed from the reaction of **3a** with hydroxylamine hydrochloride and sodium acetate. Upon recrystallisation in hot ethanol, only **10a** was obtained, as in **Scheme 2**. However, the original collected product showed traces of the elimination product, which could not be isolated. Besides, reaction of **5b–d** with hydroxylamine hydrochloride and sodium acetate in ethanol afforded **11b–d**. All of the products were detected in the filtrate and collected after evaporation of the solvent followed by recrystallisation in hot ethanol. The X-ray crystal structure shown in **Fig. 2** confirmed the proposed structure of **11b**.[48] The filtered solids formed from the reaction mixture contained traces of nucleophilic addition products on the cyano group, as evidenced by the ^{1}H NMR spectra obtained. Unfortunately, attempts to separate the products failed. Competition between nucleophilic addition and nucleophilic substitution of the cyano function had been previously observed in the reaction of 6-cyanopurines with secondary amines and reported by our group.[34]



12b, R = H

5b, R = H
c, R = OCH_3
d, R = CH_3

11b, R = H
c, R = OCH_3
d, R = CH_3

Table 3: Conditions used for the reaction of triazoles **3a** and **5b-d** with $NH_2OH.HCl$

Entry	Triazole	Solvent	Reaction condition	Product	Yield
1	**3a**	EtOH	$NH_2OH.HCl$, CH_3CO_2Na, rt	**10a**	68%
2	**5b**	EtOH	$NH_2OH.HCl$, CH_3CO_2Na, rt	**11b**	42%
3	**5c**	EtOH	$NH_2OH.HCl$, CH_3CO_2Na, rt	**11c**	35%
4	**5d**	EtOH	$NH_2OH.HCl$, CH_3CO_2Na, rt	**11d**	27%

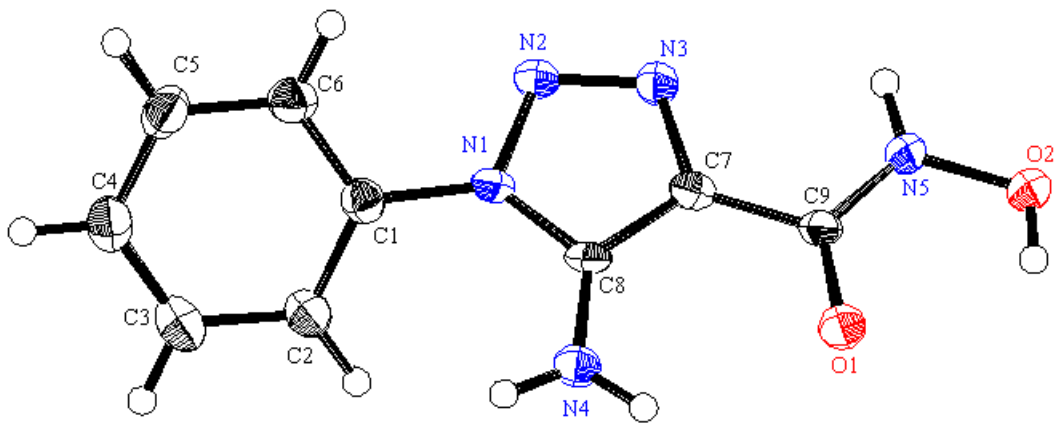


Fig. 2: X-ray crystal structure of compound **11b.**

Recrystallisation of **5b** twice in hot ethanol afforded crystals suitable for X-ray analysis. These crystals were identified as ethyl 5-amino-1-phenyl-1*H*-1,2,3-triazole-4-carboxylate **12b** shown in **Fig. 3**.[49] Acceleration of the nucleophilic displacement of the cyano function by the ethoxy group is clearly due to further heating.

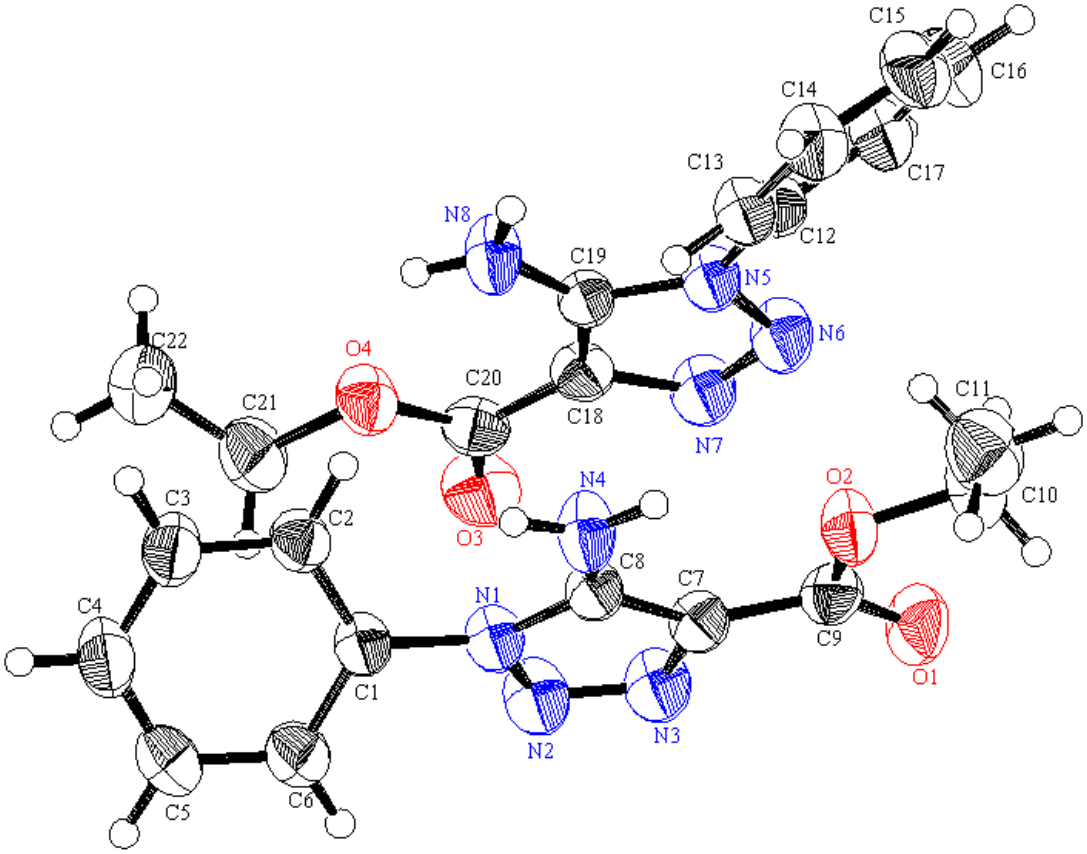


Fig. 3: X-ray crystal structure of compound **12b.**

CONCLUSION

In summary, this paper describes a method for synthesising multifunctional trisubstituted triazoles and a triazene maleonitrile derivative from the reaction of DAMN with phenyl/substituted phenyl diazonium chlorides. The proposed method has several notable advantages compared with previously reported procedures: it is mild, economical and, most importantly, azide-free. In addition, the triazoles and triazene maleonitrile derivative obtained proved to be potentially useful precursors for other triazole derivatives. The compounds formed herein could have various important applications, and the findings confirm that DAMN is a rich and inexpensive source of potentially active heterocyclic compounds.

EXPERIMENTAL

General

Diazonium salts **2** were prepared according to literature procedures.[31a] Melting points were determined with a Sanyo (Gallaenkamp) instrument. Infrared spectra were recorded using KBr pellets and a Jasco FT-IR 6300 instrument, and ν_{max} was recorded in cm^{-1}. ^{1}H and ^{13}C-NMR spectra were determined by using a Bruker DPX instrument at 400 MHz for ^{1}H-NMR and 100 MHz for ^{13}C-NMR and DMSO-d_6 as a solvent with TMS as an internal standard. Chemical shifts are reported in δ (ppm). Mass spectra were measured using GCMS DFS Thermo spectrometer, with the EI (70 EV) mode. X-ray crystal structure determined by using Single Crystal X-ray Diffractometer Rigaku Rapid II and Bruker X8 Prospector.

Single crystal analysis

All single crystal data collections were made on diffractometer using filtered Mo-Kα radiation. The structure was solved by direct methods and expanded using Fourier techniques. Non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined. All calculations were performed using the CrystalStructure crystallographic software package and refinement of crystal data was performed (Acta Cryst. A64, 112-122).

*Preparation of 5-(5-imino-2,2-dimethyl-2,5-dihydrooxazol-4-yl)-3-aryl-3*H*-1,2,3-triazol-4*-amine ***3a*** *and 2-(5-amino-1-4-aryl/substituted aryl-1*H*-1,2,3-triazol-4-yl)-2-oxoacetonitrile* ***5b-e***

Freshly prepared diazonium salts **2a–e** were added to a solution of DAMN **1** (2.00 g, 18.5 mmol) in ethanol (75.0 mL) at room temperature and stirred for 3 h. The solids formed were filtered, washed with distilled water followed by ethanol and then dried.

*2-(5-Amino-1-(4-nitrophenyl)-1*H*-1,2,3-(triazol-4-yl)-2-iminoacetonitrile* (**3a**): light yellow amorphous solid (2.09 g, 8.13 mmol, 44%), m.p. 186-189^{o}C [Found accurate mass: 257.0654; m/z (EI) (M^{+}) 257, 100%; $C_{10}H_7N_7O_2$ requires: 257.0655; M 257]; δ_H 400 MHz (DMSO-d_6, TMS) 7.39 (d, 2H, *J* = 9.2 Hz, ArH), 7.81 (s, 2H, NH_2), 8.22 (d, 2H, *J* = 9.2 Hz, ArH), 12.89 (s, 1H, NH); δ_C 100 MHz (DMSO-d_6, TMS) 146.7, 141.7, 125.9, 125.8, 114.1, 113.9, 113.8, 105.3; ν_{max}: (KBr) 3402, 3299, 3228, 3193, 1623, 1595, 1581, 1527, 1500, 1487, 1382, 1330 cm^{-1}.

*2-(5-Amino-1-phenyl-1*H*-1,2,3-triazol-4-yl)-2-oxoacetonitrile* (**5b**): light yellow fine needles (0.58 g, 2.72 mmol, 15%), m.p. 230-232 ^{o}C [Found accurate mass: 213.0645; m/z (EI) (M^{+}) 213, 35%, $C_{10}H_7N_5O$ requires: 213.0645; M 213]; δ_H 400 MHz (DMSO-*d*$_6$, TMS) 7.64-7.57 (m, 5H, ArH), 7.82 (s, 2H, NH_2); δ_C 100 MHz (DMSO-*d*$_6$, TMS) 156.7, 147.3 133.4, 130.0, 129.9, 128.8, 125.3, 113.8; ν_{max}: (KBr) 3438, 3340, 2235, 1645, 1595, 1552, 1515, 1458, 1402, 1350 cm^{-1}.

*2-(5-Amino-1-(4-methoxyphenyl)-1*H*-1,2,3-(triazol-4-yl)-2-oxoacetonitrile* (**5c**): off-white crystalline powder (0.4 g, 1.64 mmol, 9%), m.p. 222-225 ^{o}C [Found accurate mass: 243.0749; m/z (EI) (M^{+}) 243, 100%; $C_{11}H_9N_5O_2$ requires: 243.0750; M 243]; δ_H 400 MHz (DMSO-*d*$_6$, TMS) 3.85 (s, 3H, OCH_3), 7.14 (d, 2H, *J* = 8.8 Hz, ArH), 7.47 (d, 2H, *J* = 9.2 Hz, ArH), 7.70 (s, 2H, NH_2); δ_C 100 MHz (DMSO-*d*$_6$, TMS) 160.3, 156.6, 147.9, 128.7, 127.2, 126.0, 115.0, 113.8, 55.7; ν_{max}:(KBr) 3440, 3344, 2233, 1658, 1645, 1610, 1589, 1554, 1523, 1454, 1440, 1404, 1342 cm^{-1}.

*2-(5-Amino-1-p-tolyl-1*H*-1,2,3-(triazol-4-yl)-2-oxoacetonitrile* (**5d**): off-white needles (0.88 g, 3.87 mmol, 21%), m.p. 250-255 ^{o}C [Found accurate mass: 227.0801; m/z (EI) (M^{+}) 227, 85%; $C_{11}H_9N_5O$ requires: 227.0801; M 227]; δ_H 400 MHz (DMSO-*d*$_6$, TMS) 2.42 (s, 3H, CH_3), 7.47-7.42 (m, 4H, ArH), 7.73 (s, 2H, NH_2); δ_C 100 MHz (DMSO-*d*$_6$, TMS) 156.9, 147.4, 140.0, 130.9, 130.4, 128.9, 125.2, 113.8, 20.9; ν_{max}: (KBr) 3438, 3340, 1658, 1645, 1589, 1552, 1527, 1454, 1500, 1404, 1342 cm^{-1}.

*2-(5-Amino-1-(4-chlorophenyl)-1*H*-1,2,3-(triazol-4-yl)-2-oxoacetonitrile* (**5e**): colourless amorphous solid (1.09 g, 4.41 mmol, 24%), m.p. 221-225 ^{o}C [Found accurate mass: 247.0255; m/z (EI) (M^{+}) 246.9, 44%; $C_{10}H_6N_5OCl$ requires: 247.0255; M 247]; δ_H 400 MHz (DMSO-*d*$_6$, TMS) 7.60 (d, 2H, *J* = 8.8 Hz, ArH), 7.68 (d, 2H, *J* = 8.8 Hz, ArH), 7.87 (s, 2H, NH_2); δ_C 100 MHz (DMSO-*d*$_6$, TMS) 156.8, 147.6, 134.8, 132.3, 130.1, 128.9, 127.5, 113.8; ν_{max}: (KBr) 3436, 3341, 3228, 3100, 3059, 2990, 2783, 2581, 2520, 2293, 2236, 1891 cm^{-1}.

*Preparation of 5-Amino-1-(4-nitrophenyl)-1*H*-1,2,3-triazole-4-carbimidoyl cyanide* ***4a***

A catalytic amount of DBU (2 drops) was added to a suspension of **3a** (0.257 g, 1.0 mmol) in 10.0 ml of ethanol. The mixture was stirred at room temperature for 2 h, the solid obtained was filtered.

*5-Amino-1-(4-nitrophenyl)-1*H-*1,2,3-triazole-4-carbimidoyl cyanide* (**4a**)*:* off-white crystalline powder (0.173 g, 0.67 mmol, 67.3%), mp 157-160 ^{0}C [Found accurate mass: 257.0655; m/z (EI), (M^+) 257.1 15%, $C_{10}H_7O_2N_7$ requires: 257.0655; M 257]; δ_H 400MHz (DMSO-d_6,TMS) 7.31 (s, 2H, NH_2), 7.95 (d, 2H, *J* = 8.8 Hz, ArH), 8.46 (d, 2H, *J* = 8.8 Hz, ArH), 2.27 (s, 1H, NH); ν_{max} (KBr) 3529, 3419, 3321, 3267, 3103, 3079, 2857, 1923, 1787, 1639, 1590, 1557 cm^{-1}

*Preparation of 2-(5-amino-1-phenyl-1*H-*1,2,3-triazol-4-yl)-2-iminoacetonitrile **4b***

Sodium acetate was stirred into an ethanolic solution of DAMN **1**. Phenyl diazonium chloride **2b** was added to the resulting solution with some crushed ice and stirring was continued for 3 h. A light brown solid containing **4b** as a minor product was obtained. This product was filtered and vacuum dried.

*Preparation of 5-(5-imino-2,2-dimethyl-2,5-dihydrooxazol-4-yl)-3-phenyl-3*H-*1,2,3-triazol-4-*amine ***8a*** *and 5-(5-imino-2,2-dimethyl-2,5-dihydrooxazol-4-yl)-3-phenyl-3*H-*1,2,3-triazol-4-amine **8b**.*

Compounds **3a**, **4a** and **4b** (0.25 g) were individually suspended in a large excess of acetone. While stirring, DBU (0.25 mmol) was added dropwise to each of the solutions at room temperature, and stirring was continued for 24 h. The product was filtered off and recrystallised from acetone.

*5-(5-Imino-2,2-dimethyl-2,5-dihydrooxazol-4-yl)-3-(4-nitrophenyl)-3*H-*1,2,3-triazol-4-amine* (**8a**): off-white crystals (0.13 g, 0.41 mmol, 43%), m.p. 197-200^{o}C [Found accurate mass: 315.1075; m/z (EI) (M^+) 314.9 100% $C_{13}H_{13}N_7O_3$requires: 315.1074; M 315]; δ_H 400 MHz (DMSO-d_6,TMS) 1.59 (s, 6H, $2CH_3$), 7.07 (s, 2H, NH_2), 7.97 (d, 2H, *J* = 8.8 Hz, ArH), 8.49 (d, 2H, *J* = 8.8 Hz, ArH), 8.79 (s, 1H, NH); δ_C 100 MHz (DMSO-d_6, TMS) 165.1, 147.9, 147.3, 145.0, 139.5, 125.3, 120.2, 108.9, 106.9, 26.7; ν_{max}: (KBr) 3399, 3367, 3295, 3272, 3222, 2991, 2938, 2911, 2856, 2761, 2450, 1677, 1645 cm^{-1}.

*Tautomer triazole of **8a ii***

δ_H 400 MHz (DMSO-*d*$_6$, TMS) 1.59 (s, 6H, 2CH_3), 7.94 (d, 2H, *J* = 8.8 Hz, ArH), 8.15 (s, 2H, 2NH), 8.47 (d, 2H, *J* = 8.8 Hz, ArH), 9.15 (s, 1H, NH).

*5-(5-Imino-2,2-dimethyl-2,5-dihydrooxazol-4-yl)-3-phenyl-3*H*-1,2,3-triazol-4-amine* (**8b i**): off-white crystals (0.17 g, 0.62 mmol, 54.8%), m.p. 178-182^{o}C [Found accurate mass: 270. 1223; m/z (EI) (M^+) 270 82% $C_{13}H_{14}N_6O$ requires: 270.1223; M 270]; δ_H 400 MHz (DMSO-*d*$_6$, TMS) 1.58 (s, 6H, 2CH_3), 6.78 (s, 2H, NH_2), 7.66-7.58 (m, 5H, ArH), 8.81 (s, 1H NH); δ_C 100 MHz (DMSO-*d*$_6$, TMS) 165.7, 163.17, 152.97, 148.5, 145.5, 145.2, 135.2, 134.8, 130.4, 130.3, 130.0, 129.73, 125.1, 125.0, 120.4, 120.3, 109.2, 107.3, 27.2; ν_{max}: (KBr) 3411, 3284, 3224, 3157, 3062, 3008, 2987, 2939, 2912, 2850, 2754, 2671, 2127, 1676, 1643, 1618, 1596, 1575, 1523 cm^{-1}.

*Tautomer of triazole **8b ii***

δ_H 400 MHz (DMSO-*d*$_6$, TMS): 1.58 (s, 6H, 2CH_3), 7.66-7.58 (m, 5H, ArH), 7.83 (s, 2H, 2NH), 9.09 (s, 1H, NH).

*Preparation of (*E*)-*N*-benzylidene-5-(5-imino-2-phenyl-2,5-dihydrooxazol-4-yl)-3-(4-nitrophenyl)-3*H*-1,2,3-triazol-4-amine **9a***

DBU (0.25 mmol) was added to a stirred suspension of **3a** in a large excess of benzaldehyde and stirred for 24 h at room temperature. The product was filtered and recrystallised from ethanol.

*(*E*)-*N*-Benzylidene-5-(5-imino-2-phenyl-2,5-dihydrooxazol-4-yl)-3-(4-nitrophenyl)-3*H*-1,2,3-triazol-4-amine* (**9a**): light yellow fine needles **9a** (0.129 g, 0.28 mmol, 30%) m.p. 296-299 ^{o}C [Found accurate mass: 451.1387; m/z (EI) (M^+) 450.8 10% $C_{24}H_{17}N_7O_3$ requires: 451.1387; M 451]; δ_H 400 MHz (DMSO-*d*$_6$, TMS) 7.22 (s, 2H, 2CH), 7.58-7.56 (m, 3H, ArH), 7.63-7.62 (m, 3H, ArH), 7.95-7.93 (m, 2H, ArH), 8.07-8.04 (m, 2H, ArH), 8.23-8.20 (m, 2H, ArH), 8.52-8.49 (m, 2H, ArH), 8.90 (s, 1H, NH) δ_C 100 MHz (DMSO-*d*$_6$, TMS) 158.1, 154.81, 147.3, 145.8, 141.9, 140.8, 136.2, 132.4, 131.8, 129.7, 128.9, 127.7, 127.0, 126.8, 125.7, 125.5, 125.0, 121.8; ν_{max}: (KBr) 3421, 3281, 3161, 3060, 2921, 2852, 1622, 1597, 1573, 1543, 1520, 1486 cm^{-1}.

*Preparation of (*E*)*-N-*Benzylidene-5-(5-imino-2-phenyl-2,5-dihydro oxazol-4-yl)-3-phenyl-3*H-*1,2,3-triazol-4-amine* ***9b***

A catalytic amount of DBU (0.25 mmol) was added to a stirred suspension of triazole **4b** in an excess of benzaldehyde, and stirring was continued for 24 h. A small amount of the product formed. Upon evaporation of the filtrate, trituration with methanol and recrystallisation from methanol, a large amount of the product was obtained as a fine powder.

*(*E*)*-N-*Benzylidene-5-(5-imino-2-phenyl-2,5-dihydro oxazol-4-yl)-3-phenyl-3*H-*1,2,3-triazol-4-amine* (**9b**): light yellow fine needles (0.17 g, 0.41 mmol, 36%), m.p. 203-207 ^{o}C [Found accurate mass: 406 1536; m/z (EI) (M^{+}) 406 95% $C_{24}H_{18}N_6O_1$ requires: 406.1536; M 406]; δ_H 400 MHz (DMSO-d_6, TMS) 6.99 (s, 2H, 2CH), 7.60-7.54 (m, 4H, ArH), 7.65-7.61 (m, 3H, ArH), 7.72-7.67 (m, 4H, ArH), 7.94-7.92 (m, 2H, ArH), 8.22-8.20 (m, 2H, ArH), 8.87 (s, 1H, NH); δ_C 100 MHz (DMSO-d_6, TMS)* 157.6, 153.9, 145.0, 141.2, 135.7, 135.2, 131.8, 131.3, 129.8, 129.2, 129.2, 129.0, 128.4, 127.7, 126.5, 126.4, 124.2, 120.7; ν_{max}: (KBr) 3423, 3315, 3284, 3184, 3058, 3031, 2968, 2923, 2418, 2366, 2337, 2229, 1697, 1627, 1606, 1568 cm^{-1}.

* Column chromatography (EtOAc:hexane)

*Preparation of (*Z*)-2-(5-Amino-1-(4-nitrophenyl)-1*H-*1,2,3-(triazol-4-yl)-*N*'-hydroxy-2-iminoacetamidine* ***10a***

Hydroxylamine hydrochloride (5.0 mmol) and sodium acetate (3.7 mmol) were added to a suspension of **3a** (1.0 mmol) in ethanol. The mixture was stirred overnight at room temperature, and the solids formed were collected by filtration and crystallised from ethanol.

*(*Z*)-2-(5-Amino-1-(4-nitrophenyl)-1*H-*1,2,3-(triazol-4-yl)-*N*'-hydroxy-2-iminoacetamidine* (**10a**): yellow amorphous solid (0.12 g, 0.44 mmol, 68%), m.p. 205-208 ^{o}C [Found accurate mass: 290.0872; m/z (EI) (M^{+}) 288 100%; $C_{10}H_{10}N_8O_3$ requires: 290.0870; M 290]; δ_H 400 MHz (DMSO-d_6, TMS) 5.41 (s, 2H, NH_2), 5.79 (s, 2H NH_2) 7.93 (d, 2H, ArH, J = 9.2 Hz), 8.42 (d, 2H, ArH, J = 8.8 Hz), 9.97 (s, 1H, NH), 11.90 (s, 1H, OH); δ_C 100 MHz (DMSO-d_6, TMS) 147.4, 146.7, 140.9, 140.4, 125.2, 124.2, 124.0, 121.6, ν_{max}: (KBr) 3461, 3401, 3383, 3358, 3107, 3068, 2920, 2853, 1658, 1624, 1593 cm^{-1}.

Preparation of 5-Amino-N-*hydroxy-1-aryl-1*H-*1,2,3-triazole-4-carboxamides* ***11b-d***

Hydroxylamine hydrochloride (5.0 mmol) and sodium acetate (3.7 mmol) were added to a suspension of **5b–d** (1.0 mmol) in ethanol, and stirring was continued overnight at room temperature. A yellow oil was obtained by concentrating the filtrate. Trituration using DCM yielded a powder, which was further crystallised from ethanol.

5-Amino-N-*hydroxy-1-phenyl-1*H-*1,2,3-triazole-4-carboxamide* (**11b**): light yellow crystalline powder (0.11 g, 0.5 mmol, 42%), m.p. 175-179 ^{o}C [Found accurate mass: 219.0750; m/z (EI) (M^{+}) 219.1, 45%; $C_9H_9N_5O_2$ requires: 219.0750; M 219]; δ_H 400 MHz (DMSO-d_6, TMS) 6.34 (s, 2H, NH_2), 7.64-7.54 (m, 5H, ArH), 8.86 (s, 1H, NH), 11.01 (s, 1H, OH); δ_C 100 MHz (DMSO-d_6, TMS) 160.6, 144.5, 134.8, 129.8, 129.1, 124.1, 120.0; ν_{max}: (KBr) 3496, 3415, 3377, 3321, 3242, 3072, 1660, 1631, 1610 cm^{-1}.

5-Amino-N-*hydroxy-1-(4-methoxyphenyl)-1*H-*1,2,3-triazole-4-carboxamide* (**11c**): light brown crystals (0.05 g, 0.20 mmol, 35%), m.p. 203-207 ^{o}C [Found accurate mass: 249.0857; m/z (EI) (M^{+}) 249 15%; $C_{10}H_{11}N_5O_3$ requires: 249.0856; M 249]; δ_H 400 MHz (DMSO-d_6, TMS) 3.84 (s, 3H, OCH_3), 6.21 (s, 2H, NH_2), 7.13 (d, 2H, J = 8.8 Hz, ArH), 7.48 (d, 2H, J = 8.8 Hz, ArH), 8.84 (s, 1H, NH), 10.97 (s, 1H, OH); δ_C 100 MHz (DMSO-d_6, TMS) 160.6, 159.6, 144.6, 127.5, 126.0, 119.8, 114.8, 55.6; ν_{max}: (KBr) 3429, 3337, 3198, 3108, 3062, 2970, 2928, 2846, 2591, 2551, 2484, 2045, 1888, 1627, 1588, 1570 cm^{-1}.

5-Amino-N-*hydroxy-1-p-tolyl-1*H-*1,2,3-triazole-4-carboxamide* (**11d**): yellow solid (0.11 g, 0.47 mmol, 27%), m.p. 155-160 ^{o}C [Found accurate mass: 233.0905; m/z (EI) (M^{+}) 233 15%; $C_{10}H_{11}N_5O_2$ requires:233.0907; M 233]; δ_H 400 MHz (DMSO-d_6, TMS) 2.40 (s, 3H, OCH_3), 6.27 (s, 2H, NH_2), 7.40-7.48 (m, 4H, ArH), 8.85 (s, 1H, NH), 11.00 (s, 1H, OH); δ_C 100 MHz (DMSO-d_6, TMS) 160.6, 144.5, 138.7, 132.3, 130.1, 124.0, 119.9, 20.7; ν_{max}: (KBr) 3433, 3340, 3201, 2922, 1656, 1622, 1587, 1560, 1521, 1492 cm^{-1}

*Preparation of Ethyl-5-amino-1-phenyl-1*H-*1,2,3-triazole-4-carboxylate* ***12b***

Crystallisation of **5b** in ethanol twice afforded **12b** as off-white crystals.

*Ethyl-5-amino-1-phenyl-1*H-*1,2,3-triazole-4-carboxylate* (**12b**): off-white crystals (0.11 g, 0.50 mmol, 50%), m.p. 111-115 ^{o}C [Found accurate mass: 232.0954; m/z (EI) (M^{+}) 232.60% $C_{11}H_{12}N_4O_2$ requires: 232.0954; M 232]; δ_H 400 MHz (DMSO-d_6, TMS) 1.33-1.3 (m, 3H, CH_3), 4.34-4.28 (m, 2H, CH_2), 6.54 (s, 2H, NH_2), 7.64-7.56 (m, 5H, ArH); δ_C 100 MHz (DMSO-d_6, TMS) 161.8, 146.2, 134.5, 129.8, 129.3, 124.5, 119.1, 59.7, 14.4; ν_{max}: (KBr) 3456, 3382, 3286, 3236, 3168, 3066, 2999, 2977, 2929, 2900, 2869, 1714, 1618, 1579, 1564 cm^{-1}.

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47. Crystal data for compound **8b**: (ref. CCDC 881281) can be obtained on request from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EW, UK. CCDC.

48. Crystal data for compound **11b**: (ref. CCDC 911674) can be obtained on request from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EW, UK. CCDC.

49. Crystal data for compound **12b**: (ref. CCDC 886296) can be obtained on request from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EW, UK. CCDC.