Synthesis and oxidative cyclization of 2-arylhydrazono-2-cyanoacetamides to 5-amino-2-aryl-2H-[1,2,3]triazole-4-carbonitrile

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Abstract

A general and convenient method for the synthesis of 2-arylhydrazono-2-cyanoacetamides, containing either a cytosine or tryptamine moiety, or other secondary and primary amines was elaborated. A series of 5-amino-2-aryl-2H-[1,2,3]-triazole-4-carbonitriles was successfully prepared by oxidation of these amidines with copper acetate in pyridine. The screening of the biological activity of the synthesized triazoles and amidines have shown that, some of these compounds possess fungicidal activity at concentrations of 50 µg/mL against some fungi tested.

Keywords: Amidines, cytosine, tryptamine, oxydation, 1,2,3-triazole, fungicide activity

Introduction

Amidines, that can be considered as nitrogen analogs of carboxylic acids, are a structural part of numerous compounds of biological interest.¹ They were found to possess anti-degenerative,² anticancer,³ anti-platelet,⁴ and antimicrobial⁵ activity. A number of synthetic inhibitors of serine proteases, NOS (nitric oxide synthase) and integrin antagonists have an amidino moiety in the structure.⁶ Amidines are convenient building blocks in organic synthesis; mainly for the synthesis of heterocyclic compounds.⁷ An interesting approach to biologically active compounds concerns the synthesis of compounds with fragments of natural compounds. In this respect the amidines are excellent candidates for the synthesis of such type of compounds because the amines that are mainly used for their synthesis are widespread in nature (aminoacids, peptides, alkaloids).

This paper presents details on the synthesis of 2-arylhydrazonoacetamides with various substituents at the amidine moiety and the study of their oxidative cyclization to 5-amino-2-aryl-2H-[1,2,3]-triazoles, including those containing the fragments of piperazine, tryptamine and the natural alkaloid cytosine. The latter were prepared for fungicidal studies in experiments *in vitro*.

Results and Discussion

There are many synthetic approaches to amidines known from the literature. They are mainly based either on addition of amines and ammonia to nitriles⁸ or on the substitution reactions of imidoyl chlorides, imidates and thioimidates with amines.¹ The course of the reactions of the first group is mainly governed by the electrophilicity of the cyano group and the nucleophilicity of the amines and often requires the use of catalysts (Lewis acid at high temperature, CuCl₂ with aluminum amide, or the presence of lanthanide triflate).⁹

There are very few examples of the synthesis of 2-arylhydrazonoacetamidines by reaction of 2-arylhydrazonomalononitriles with morpholine, piperidine and dimethylamine described in the literature.⁸ It was not clear from this report whether this reaction had generality, whether primary amines and ammonia could be used in this reaction, and whether various aryl substituted malononitriles reacted with amines. Therefore, the scope of this reaction remained to be determined.

To find a general method for the synthesis of 2-arylhydrazonoacetamidines we have studied the reaction of 2-arylhydrazonomalononitriles **1a-h** with ammonia, primary and secondary amines (Scheme 1).

- 1 Ar = 4-MeOC₆H₄ (**a**), C₆H₅ (**b**), 4-ClC₆H₄ (**c**), 4-FC₆H₄ (**d**), 3,5-F₂C₆H₃ (**e**), 2,4-Cl₂C₆H₃ (**f**), 4-EtO₂CC₆H₄ (**g**), 4-NO₂C₆H₄ (**h**)
- 2 NR¹R² = NH₂ (**a**), NHMe (**b**), NH-c-C₆H₁₁ (**c**), Pyrrolidin-1-yl (**d**), Piperidin-1-yl (**e**), Morpholin-4-yl (**f**)
- 3 NR¹R² = NH₂, Ar = 4-MeOC₆H₄ (**a**), C₆H₅ (**b**), 4-ClC₆H₄ (**c**)
- 4 NR¹R² = NHMe, Ar = 4-MeOC₆H₄ (**a**), C₆H₅ (**b**), 4-ClC₆H₄ (**c**), 4-NO₂C₆H₄ (**d**)
- 5 NR¹R² = NH-c-C₆H₁₁, Ar = 4-MeOC₆H₄ (**a**), C₆H₅ (**b**), 4-ClC₆H₄ (**c**), 4-NO₂C₆H₄ (**d**)
- 6 NR¹R² = Pyrrolidin-1-yl, Ar = 4-MeOC₆H₄ (**a**), 4-FC₆H₄ (**b**), 3,5-F₂C₆H₃ (**c**), 4-NO₂C₆H₄ (**d**)
- 7 NR¹R² = Piperidin-1-yl, Ar = 4-MeOC₆H₄ (**a**), 4-FC₆H₄ (**b**), 3,5-F₂C₆H₃ (**c**)
- 8 NR¹R² = Morpholin-4-yl, Ar = 4-FC₆H₄ (**a**), 3,5-F₂C₆H₃ (**b**)

Scheme 1

We have found that the optimal conditions for the reaction include the use of ethanol at 70 °C. Effective stirring was found to be an important factor to obtain good yields of the products. The use of this protocol allowed us to prepare a large series of 2-arylhydrazonoacetamidines **3-8** in good yields (Scheme 1). The structures of amidines **3-8** were proved by NMR and mass-spectra. The mass-spectra of the prepared compounds contain the peaks corresponding to their molecular weights.

In principle 2-arylhydrazonoacetamidines can exist in three tautomeric forms **A-C** (Scheme 2). It is interesting to note that a single set of signals corresponding to all proton-containing groups was registered in the NMR spectra of **3-8**.

Scheme 2

There are no NH proton signals in the ¹H NMR spectra of compounds **3-8** that would correspond to the hydrazono group. The signals of the amino groups of the amidine fragment are shown as a broad four proton singlet for compounds **3** at 6.65 – 7.18 ppm; as a one proton singlet and a two proton singlet for compounds **4,5** at 7.15 – 7.42 ppm; and as a two proton singlet for compounds **6-8** at 6.58-6.97 ppm. IR spectra of compounds **3-8** show a few broad bands between 3200-3450 cm⁻¹ confirming the presence of amino groups.

Figure 1 X-Ray of 3-Amino-2-(4-methoxyphenylazo)-3-piperidin-1-yl-acrylonitrile (**7a**).

The study of single crystals of 3-amino-4-methoxyphenylazo-3-piperidin-1-yl-acrylonitrile **7a** obtained from EtOH by X-ray analysis (Figure 1) and NMR data showed that for compounds **3-8** preferred form is the form of isomer **C**. Furthermore, this compound exists in the form of the *E,E*-isomer, probably because of intramolecular hydrogen bonds as it is shown in Figure 1. It is worth noting that the conjugated C=C and N=N bonds are coplanar with a deviation of less than 3°. It should be noted that the replacement of one of the cyano groups in the malononitriles **1** by a carbamoyl function drastically decreases the reactivity of the second cyano group and 2-arylhydrazono-2-cyanoacetamides do not react with amines.

We have expanded this method to prepare amidines **10-12** bearing fragments of natural compounds, in a yield of 50-88% by reaction of the malononitrile derivatives **1a-h** with tryptamine, cytosine and piperazine (Scheme 3).

Scheme 3

Indeed, a large series of 2-arylhydrazonoacetamides **3-8**, **10-12** was synthesized. It was found that the scope of this reaction is quite broad; ammonia and any primary and secondary amines react with 2-arylmalononitriles to form 2-arylhydrazonoacetamidines.

Because of the fact that 1,2,3-triazole derivatives are shown to be interesting objects for testing of biological activity¹⁰ and 4-cyano-1,2,3-triazoles may be excellent precursor for the different heterocyclic derivatives, we made attempts to devise a general method for the synthesis of 2*H*-1,2,3-triazoles by oxidative cyclization of 2-arylhydrazonoacetamidines. One of the purposes of this study was to prepare triazoles containing the tryptamine and cytosine moiety.

The oxidative cyclization of 2-arylhydrazonoacetamidines **4-7** and **10-12** was carried out by a modified protocol⁸ with copper acetate in pyridine at 60 °C under vigorous stirring to form triazoles **13-22** in good yield (Scheme 4).

^1H and ^{13}C NMR spectra of the prepared compounds correspond to the proposed structures. In contrast to the starting materials **4-7**, **10-12**, the ^1H NMR spectra of the compounds **13-22** do not contain the primary amino group proton signals. Furthermore, mass-spectra of these compounds have molecular weights peaks that are for two units less than those of the starting amidines.

Scheme 4

The main feature of the IR spectra of **13,14,17** is the presence of a single intense band at $3360\text{-}3380\text{ cm}^{-1}$ corresponding to the NH group. Indeed the spectral data proved the involvement of primary amino groups of compounds **4,5,10** in the process of oxidative cyclization and formation of rather the structures **13,14,17** than **23**.

1,2,3-Triazoles have found many applications in the pharmaceutical and agricultural industries.¹⁰ Fungicides containing triazole moieties prevent disease and are used to increase the yield.^{10c}

A number of new compounds were tested for fungicide activity in comparison with the starting amidines using the fungi growth inhibition method (Table 1).¹¹

Table 1 revealed that the nature of the substituent on the aromatic ring and the type of *tert*-cycloalkylamino group may have considerable impact on the antifungal activities of the target compounds. Of particular importance, a piperidino or cytisine group generally enhances the antifungal activity (amidine **7b**, **11e-f** and triazole **16c**, **18b-f**). The activity of **18f** was even more than 90% against *Sclerotinia sclerotiorum* (**K**) and *Rhizoctonia solani* Kuhn (**L**), therefore it is suitable for further structure modification to obtain compounds with high fungicidal activity. The introduction of one or two fluorine atoms onto the triazole aromatic ring imparts appreciable antifungal activity (**18d** and **18e**; **18c** and **18f**). On the other hand the introduction of two fluorine atoms on the aromatic nucleus of the amidine group decreases the antifungal activity of these compounds (**6b** and **6c**; **7b** and **7c**; **8a** and **8b**).

All the target compounds were found to be inactive against *Cercospora rachidicola*. All compounds synthesized had no systemic acquired resistance (data not shown).

Conclusions

In conclusion, a series of new arylhydrazonoacetamides were synthesized and transformed to 2-aryl-2H-1,2,3-triazole-5-amine by oxidative heterocyclization. It has been shown that this method allows to introduce the fragments of the natural products (tryptamine) or alkaloids (cytisine) into the structure of hydrazonoamidines and triazoles. Indeed new general methods for the synthesis of 2-

arylhydrazonoacetamidines and of 2-aryl-2*H*-1,2,3-triazole-5-amines have been elaborated. The target compounds were screened for antifungal activity and some compounds exhibited an inhibitory effect against some fungi tested at concentration of 50 µg/mL. The biological effect is sensitive to structural variations of the amidine and triazole fragments, and some structures deserve further derivatisation for fungicide development.

Table 1. Results of *in vitro* fungicide activity determination

Compd. No.	Fungi growth inhibition, %											
	A	B	C	D	E	F	G	H	I	J	K	L
6b	27.3	46.7	0	11.1	4.8	70.7	70.7	36.4	14.3	13.6	-	-
6c	18.2	0	0	0	0	36.6	51.6	36.4	0	13.6	-	-
7b	27.3	46.7	0	11.1	4.8	61.0	59.4	31.4	14.3	22.7	-	-
7c	9.1	26.7	0	0	0	12.2	53.1	36.4	28.6	13.6	-	-
8a	27.3	46.7	6.7	0	0	68.3	56.3	36.4	0	22.7	-	-
8b	9.1	26.7	0	11.1	4.8	9.8	56.3	31.8	14.3	13.6	-	-
10d	45.5	46.7	0	33.3	19	56.1	64.1	45.5	14.3	27.3	-	-
10e	27.3	20.0	40	33.3	4.8	41.5	51.6	45.5	14.3	18.2	-	-
11e	18.2	40	0	11.1	9.5	63.4	35.6	40.9	0	13.6	-	-
11f	45.5	73.3	6.7	22.1	33.3	61.0	59.4	50.0	28.6	31.4	-	-
15e	18.2	20	0	22.2	4.8	24.4	43.8	40.9	0	13.6	-	-
16c	36.4	20	6.7	44.4	23.8	70.7	67.2	68.2	0	40.9	-	-
17f	45.5	26.7	0	33.3	9.5	36.6	40.6	59.1	14.3	27.3	-	-
18b	-	37.1	-	28.0	-	5.9	-	-	-	-	51.9	55.6
18c	-	40.0	-	36.0	-	0	-	-	-	-	63.0	46.7
18d	-	54.3	-	16.0	-	0	-	-	-	-	22.2	24.4
18e	-	65.7	-	56.0	-	17.6	-	-	-	-	88.9	68.9
18f	45.5	57.6	0	60.2	42.9	71.7	65.6	45.5	28.6	54.5	92.6	95.6

A –*Cercospora beticola*; **B** –*Fusarium oxysporum* f. *cucumerinum*; **C** –*Cercospora rachidicola*; **D** –*Alternaria solani*; **E** –*Gibberella zeae*; **F** –*Physalospora piricola*; **G** –*Pellicularia sasakii*; **H** –*Colletotrichum lagenarium*; **I** –*Verticillium dahliae*; **J** –*Phytophthora infestans*; **K** –*Sclerotinia sclerotiorum*; **L** –*Rhizoctonia solani* Kuhn.

Experimental Section

General Procedures. Melting points were measured with a SNP Stuart melting points apparatus and are uncorrected. Infrared spectra were recorded on a Specord IR-75 in potassium bromide pellets. Mass spectra were obtained by using electron impact ionization techniques on a Varian MAT 311A spectrometer (ionizing voltage of 70eV). ¹H and ¹³C NMR spectra were recorded on a «Bruker WP-250» (250 MHz for ¹H) and Bruker DRX-400 (400 MHz for ¹H and 100 MHz for ¹³C). The solvent for the NMR was DMSO-*d*₆. Chemical shifts (δ) are reported in ppm relative to TMS. Crystallographic data for the structure reported in this paper were measured with an Xcalibur 3 CCD (graphite monochromator, MoKa) and have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 677318. All reactions were monitored by thin layer chromatography, carried out on silica gel Sorbfil UV-254 sheets. Yields refer to chromatographically and spectroscopically pure material. All chemicals were used as supplied by Sigma-Aldrich and Acros. Pyridine and ethanol were distilled prior to use. 2-Arylhyaizonomalononitriles **1** were prepared according to the procedure in the literature.¹²

General procedure for the synthesis of arylhydrazonoacetamidine 3-8, 10-12

A mixture of 0.01 mol hydrazone **1** and 1.3 mol of the corresponding amine in 50 mL ethanol was stirred and was heated at 70 °C for about 10 h (TLC). Then, the reaction mixture was poured onto crushed ice. The product which separated was collected by filtration and was crystallized from ethanol.

3,3-Diamino-2-(4-methoxyphenylazo)-acrylonitrile (3a). Yellow solid (1.52 g, 70%); mp 242-243 °C; IR (KBr): $\nu_{\max}$ 3450, 3420, 3350, 3250, 3200 (NH), 3000, 2930, 2900, 2830 (CH), 2180 (CN) cm^{-1} ; ^1H NMR (250 MHz): δ 3.78 (s, 3H, OMe), 6.65-6.85 (m, 6H, $2\text{NH}_2 + \text{H-Ar}$), 7.47 (d, 2H, H-Ar, $J = 8.8$ Hz); MS: m/z (%) 217 (M^+ , 62.5%); *Anal.* Calcd. for $\text{C}_{10}\text{H}_{11}\text{N}_5\text{O}$: C, 55.29; H, 5.10; N, 32.24. Found: C, 55.51; H, 5.23; N, 32.45.

3,3-Diamino-2-phenylazo-acrylonitrile (3b). Yellow solid (1.20 g, 64%); mp 239-241 °C; IR (KBr): $\nu_{\max}$ 3420, 3410, 3350, 3250, 3200 (NH), 2180 (CN) cm^{-1} ; ^1H NMR (250 MHz): δ 6.97 (br s, 4H, 2NH_2), 7.06 (t, 1H, H-Ar, $J = 7.4$ Hz), 7.24 (t, 2H, H-Ar, $J = 7.3$ Hz), 7.49 (d, 2H, H-Ar, $J = 7.4$ Hz); MS: m/z (%) 187 (M^+ , 31.6%); *Anal.* Calcd. for $\text{C}_9\text{H}_9\text{N}_5$: C, 57.74; H, 4.85; N, 37.41. Found: C, 57.53; H, 4.71; N, 37.63.

3,3-Diamino-2-(4-chlorophenylazo)-acrylonitrile (3c). Yellow solid, (1.35 g, 61%); mp 249-251 °C; IR (KBr): $\nu_{\max}$ 3420, 3410, 3350, 3250, 3200 (NH), 2180 (CN) cm^{-1} ; ^1H NMR (400 MHz): δ 7.18 (br s, 4H, 2NH_2), 7.29 and 7.57 (AA'XX', 4H, H-Ar, $J = 8.8$ Hz); ^{13}C NMR (100 MHz): δ 91.4, 115.4, 121.9 (2C), 128.5 (2C), 129.1, 152.3, 161.3; MS: m/z (%) 221 (M^+ , 39.5%); *Anal.* Calcd. for $\text{C}_9\text{H}_8\text{ClN}_5$: C, 48.77; H, 3.64; N, 31.60. Found: C, 48.89; H, 3.81; N, 31.45.

3-Amino-2-(4-methoxyphenylazo)-3-methylaminoacrylonitrile (4a). Yellow crystals (2.08 g, 90%); mp 313-315 °C; IR (KBr): $\nu_{\max}$ 3440, 3315, 3260, 3175, 3100 (NH), 2950, 2930, 2910 2825 (CH), 2180 (CN) cm^{-1} ; ^1H NMR (250 MHz): δ 2.93 (d, 3H, Me, $J = 4.8$ Hz), 3.76 (s, 3H, OMe), 7.15 (br s, 2H, NH_2), 7.35-7.45 (m, 1H, NH), 6.80 and 7.45 (AA'XX', 4H, H-Ar, $J = 8.8$ Hz); MS: m/z (%) 231 (M^+ , 67.6%); *Anal.* Calcd. for $\text{C}_{11}\text{H}_{13}\text{N}_5\text{O}$: C, 57.13; H, 5.67; N, 30.28. Found: C, 57.45; H, 5.75; N, 30.45.

3-Amino-3-methylamino-2-phenylazoacrylonitrile (4b). Yellow crystals, (1.33 g, 66%); mp 225-227 °C; IR (KBr): $\nu_{\max}$ 3430, 3330, 3260 (NH), 2180 (CN) cm^{-1} ; ^1H NMR (250 MHz): δ 2.92 (d, 3H, Me, $J = 4.5$ Hz), 7.03 (t, 1H, H-Ar, $J = 7.3$ Hz), 7.3-7.4 (m, 3H, H-Ar+NH), 7.49 (d, 2H, H-Ar, $J = 8.0$ Hz), 7.56 (br s, 2H, NH_2); MS: m/z (%) 201 (M^+ , 41.6%); *Anal.* Calcd. for $\text{C}_{10}\text{H}_{11}\text{N}_5$: C, 59.69; H, 5.51; N, 34.80. Found: C, 59.41; H, 5.83; N, 35.03.

3-Amino-2-(4-chlorophenylazo)-3-methylaminoacrylonitrile (4c). Yellow crystals (2.02 g, 86%); mp 219-220 °C; ^1H NMR (400 MHz): δ 2.90 (d, 3H, Me, $J = 4.5$ Hz), 7.32 and 7.57 (AA'XX', 4H, H-Ar, $J = 9.0$ Hz), 7.60 (br s, 2H, NH_2), 7.84 (q, 1H, NH, $J = 4.5$ Hz); ^{13}C NMR (100 MHz): δ 28.6, 91.5, 115.6, 121.8 (2C), 128.4 (2C), 128.6, 152.5, 160.0; MS: m/z (%) 235 (M^+ , 35.3%); *Anal.* Calcd. for $\text{C}_{10}\text{H}_{10}\text{ClN}_5$: C, 50.96; H, 4.28; N, 29.72. Found: C, 50.71; H, 4.36; N, 28.03.

3-Amino-3-methylamino-2-(4-nitrophenylazo)-acrylonitrile (4d). Yellow crystals (2.10 g, 85%); mp 290-291 °C; ^1H NMR (400 MHz): δ 2.94 (d, 3H, Me, $J = 4.5$ Hz), 7.68 and 8.12 (AA'XX', 4H, H-Ar, $J = 9.2$ Hz), 8.00 (br s, 2H, NH_2), 8.15 (q, 1H, NH, $J = 4.5$ Hz); ^{13}C NMR (100 MHz): δ 28.9, 95.5, 114.5, 120.1 (2C), 124.7 (2C), 142.7, 159.1, 159.5; *Anal.* Calcd. for $\text{C}_{10}\text{H}_{10}\text{N}_6\text{O}$: C, 48.78; H, 4.09; N, 34.13. Found: C, 48.55; H, 4.26; N, 34.33.

3-Amino-3-cyclohexylamino-2-(4-methoxyphenylazo)-acrylonitrile (5a). Yellow crystals (2.48 g, 83%); mp 173-174 °C; IR (KBr) $\nu_{\max}$ 3430, 3330, 3210, 3160 (NH), 2940, 2860, 2830 (CH), 2180 (CN) cm^{-1} ; ^1H NMR (250 MHz): δ 1.20-2.0 (m, 10H, 5CH_2), 3.60-3.75 (m, 1H, CH), 3.77 (s, 3H, OMe), 6.75-6.80 (m, 1H, NH), 7.25 (br s, 2H, NH_2), 6.82 and 7.40 (AA'XX', 4H, H-Ar, $J = 8.7$ Hz); MS: m/z (%) 299 (M^+ , 49.1%); *Anal.* Calcd. for $\text{C}_{16}\text{H}_{21}\text{N}_5\text{O}$: C, 64.19; H, 7.07; N, 23.39. Found: C, 64.41; H, 7.23; N, 23.54.

3-Amino-3-cyclohexylamino-2-phenylazo-acrylonitrile (5b). Yellow crystals (2.25 g, 84%); mp 181-182 °C; ^1H NMR (250 MHz): δ 1.02-2.04 (m, 10H, 5CH_2), 3.83-4.09 (m, 1H, CH), 7.17 (t, 1H, H-Ar, $J = 7.3$ Hz), 7.37 (t, 2H, H-Ar, $J = 7.2$ Hz), 7.74 (d, 2H, H-Ar, $J = 7.3$ Hz), 9.15 (d, 1H, NH, $J = 8.5$ Hz), 9.6 (br s, 2H, NH_2); MS: m/z (%) 269 (M^+ , 35.9); *Anal.* Calcd. for $\text{C}_{15}\text{H}_{19}\text{N}_5$: C, 66.89; H, 7.11; N, 26.00. Found: C, 66.59; H, 6.89; N, 26.23.

3-Amino-2-(4-chlorophenylazo)-3-cyclohexylaminoacrylonitrile (5c). Yellow crystals (1.90 g, 63%); mp 185-186 °C; ^1H NMR (250 MHz): δ 1.10-2.00 (m, 10H, 5CH_2), 3.55-3.75 (m, 1H, CH), 6.97 (d, 1H, NH, $J = 9.0$ Hz), 7.42 (br s, 2H, NH_2), 7.24 and 7.46 (AA'XX', 4H, H-Ar, $J = 8.6$ Hz); MS: m/z (%) 303 (M^+ , 53.7%); *Anal.* Calcd. for $\text{C}_{15}\text{H}_{18}\text{ClN}_5$: C, 59.31; H, 5.97; N, 23.05. Found: C, 59.55; H, 6.13; N, 23.33.

3-Amino-3-cyclohexylamino-2-(4-nitrophenylazo)-acrylonitrile (5d). Yellow crystals (2.15 g, 68%); mp 260-261 °C; ^1H NMR (400 MHz): δ 1.20-1.50 (m, 5H, CH_2), 1.55-1.65 (m, 1H, CH_2), 1.70-1.80 (m, 2H, CH_2), 1.80-1.90 (m, 2H, CH_2), 3.60-3.70 (m, 1H, CH), 7.66 and 8.12 (AA'XX', 4H, H-Ar, $J = 9.0$ Hz), 7.82 (d, 1H, NH, $J = 9.0$ Hz), 7.99 (s, 2H, NH_2); ^{13}C NMR (100 MHz): δ 24.6, 24.8 (2C), 31.7 (2C), 59.7, 95.9, 114.6, 120.2 (2C), 124.7 (2C), 142.7, 157.7, 159.0; *Anal.* Calcd. for $\text{C}_{15}\text{H}_{18}\text{N}_6\text{O}_2$: C, 57.31; H, 5.77; N, 26.73. Found: C, 57.38; H, 5.91; N, 27.03.

3-Amino-2-(4-methoxyphenylazo)-3-pyrrolidin-1-yl-acrylonitrile (6a). Yellow crystals (2.27 g, 84 %); mp 195-196 °C; IR (KBr): $\nu_{\max}$ 3450, 3340, 3190 (NH), 2970, 2940, 2880, 2840 (CH), 2180 (CN) cm^{-1} ; ^1H NMR (400 MHz): δ 1.90-1.95 (m, 4H, 2CH₂), 3.61-3.65 (m, 4H, 2CH₂), 3.76 (s, 3H, OMe), 7.12 (br s, 2H, NH₂), 6.89 and 7.44 (AA'XX', 4H, H-Ar, J = 9.0 Hz); ^{13}C NMR (100 MHz): δ 24.8 (2C), 49.5 (2C), 55.2, 91.5, 113.9 (2C), 117.5, 121.5 (2C), 147.7, 157.4, 158.3; MS: m/z (%) 271 (M^+ , 59.2%); *Anal.* Calcd. for C₁₄H₁₇N₅O: C, 61.98; H, 6.32; N, 25.81. Found: C, 61.74; H, 6.03; N, 26.06.

3-Amino-2-(4-fluorophenylazo)-3-pyrrolidin-1-yl-acrylonitrile (6b). Yellow crystals (2.02 g, 78%); mp 190-191 °C; ^1H NMR (250 MHz): δ 1.95-2.05 (m, 4H, 2CH₂), 3.60-3.78 (m, 4H, 2CH₂), 6.9-7.1 (m, 4H, H-Ar+NH₂), 7.42-7.55 (m, 2H, H-Ar); *Anal.* Calcd. for C₁₃H₁₄FN₅: C, 60.22; H, 5.44; N, 27.01. Found: C, 59.85; H, 5.25; N, 27.36.

3-Amino-2-(3,5-difluorophenylazo)-3-pyrrolidin-1-yl-acrylonitrile (6c). Yellow crystals (2.5 g, 85%); mp 240-241 °C; IR (KBr): $\nu_{\max}$ 3420, 3400, 3300 (NH), 2970, 2950, 2920, 2870 (CH), 2190 (CN) cm^{-1} ; ^1H NMR (250 MHz): δ 1.90-2.10 (m, 4H, 2CH₂), 3.60-3.80 (m, 4H, 2CH₂), 6.59 (tt, 1H, H-Ar, J = 8.9, 2.1 Hz), 7.0-7.15 (m, 2H, H-Ar), 7.31 (br s, 2H, NH₂); *Anal.* Calcd. for C₁₃H₁₃F₂N₅: C, 56.31; H, 4.73; N, 25.26. Found: C, 56.16; H, 4.95; N, 25.52.

3-Amino-2-(4-nitrophenylazo)-3-pyrrolidin-1-yl-acrylonitrile (6d). Yellow crystals (2.4 g, 85%); mp 259-260 °C; IR (KBr) $\nu_{\max}$ 3420, 3400, 3300 (NH), 2970, 2950, 2920, 2870 (CH), 2190 (CN) cm^{-1} ; ^1H NMR (250 MHz): δ 1.95-2.10 (m, 4H, 2CH₂), 3.65-3.75 (m, 4H, 2CH₂), 7.54 (br s, 2H, NH₂), 7.57 and 8.10 (AA'XX', 4H, H-Ar, J = 9.2 Hz); ^{13}C NMR: (100 MHz): δ 24.9 (2C), 50.5 (2C), 96.8, 115.7, 120.1 (2C), 124.7 (2C), 142.8, 157.6, 159.0; *Anal.* Calcd. for C₁₃H₁₄N₆O₂: C, 54.54; H, 4.93; N, 29.35. Found: C, 54.35; H, 5.17; N, 29.61.

Amino-2-(4-methoxyphenylazo)-3-piperidin-1-yl-acrylonitrile (7a). Yellow crystals (1.85 g, 65%); mp 134-136 °C; IR (KBr): $\nu_{\max}$ 3415, 3315, 3205, 3160 (NH), 2940, 2860, 2840 (CH), 2180 (CN) cm^{-1} ; ^1H NMR (250 MHz): δ 1.70 (br s, 6H, 3CH₂), 3.57 (br s, 4H, 2CH₂), 3.78 (s, 3H, OMe), 7.18 (br s, 2H, NH₂), 6.83 and 7.43 (AA'XX', 4H, H-Ar, J = 9.2 Hz); MS: m/z (%) 285 (M^+ , 56.9%); *Anal.* Calcd. for C₁₅H₁₉N₅O: C, 63.14; H, 6.71; N, 24.54. Found: C, 62.88; H, 6.89; N, 24.68.

3-Amino-2-(4-fluorophenylazo)-3-piperidin-1-yl-acrylonitrile (7b). Yellow crystals (1.70 g, 62%); mp 200-201 °C; ^1H NMR (250 MHz): δ 1.70 (br s, 6H, 3CH₂), 3.59 (br s, 4H, 2CH₂), 7.02 (t, 2H, H-Ar, J = 8.9 Hz), 7.32 (br s, 2H, NH₂), 7.46 (dd, 2H, H-Ar, J = 9.0, 5.0 Hz); *Anal.* Calcd. for C₁₄H₁₆FN₅: C, 61.52; H, 5.90; N, 25.62. Found: C, 61.29; H, 5.76; N, 25.90.

3-Amino-2-(3,5-difluorophenylazo)-3-piperidin-1-yl-acrylonitrile (7c). Yellow crystals (1.60 g, 55%); mp 220-221 °C; IR (KBr): $\nu_{\max}$ 3410, 3310, 3210 (NH), 2960, 2940, 2920, 2865 (CH), 2180 (CN) cm^{-1} ; ^1H NMR (250 MHz): δ = 1.71 (br s, 6H, 3CH₂), 3.61 (br s, 4H, 2CH₂), 6.60 (tt, 1H, H-Ar, J = 8.9, 2.2 Hz), 7.05-7.10 (m, 2H, H-Ar), 7.65 (br s, 2H, NH₂); *Anal.* Calcd. for C₁₄H₁₅F₂N₅: C, 57.72; H, 5.19; N, 24.04. Found: C, 57.53; H, 5.27; N, 24.37.

3-Amino-2-(4-fluorophenylazo)-3-morpholin-4-yl-acrylonitrile (8a). Yellow crystals (1.93 g, 70%); mp 198-200 °C; ^1H NMR (250 MHz): δ 3.55-3.75 (m, 8H, 4CH₂), 7.04 (br s, 2H, NH₂), 7.25 (t, 2H, H-Ar, J = 8.5 Hz), 7.40-7.50 (m, 4H, H-Ar+NH₂); *Anal.* Calcd. for C₁₃H₁₄FN₅O: C, 56.72; H, 5.13; N, 25.44. Found: C, 56.95; H, 5.32; N, 25.64.

3-Amino-2-(3,5-difluorophenylazo)-3-morpholin-4-yl-acrylonitrile (8b). Yellow crystals (1.90 g, 65%); mp 119-220 °C; IR (KBr): $\nu_{\max}$ 3410, 3300, 3200 (NH), 2980, 2920, 2860 (CH), 2190 (CN) cm^{-1} ; ^1H NMR (250 MHz): δ 3.60-3.80 (m, 8H, 4CH₂), 6.63 (tt, 1H, H-Ar, J = 9.0, 2.3 Hz), 7.05-7.15 (m, 2H, H-Ar), 7.81 (br s, 2H, NH₂); *Anal.* Calcd. for C₁₃H₁₃F₂N₅O: C, 53.24; H, 4.47; N, 23.88. Found: C, 52.95; H, 4.63; N, 24.12.

3-Amino-3-[2-(1H-indol-3-yl)-ethylamino]-2-(4-methoxyphenylazo)-acrylonitrile (10a). Yellow crystals (3.15 g, 87%); mp 161-162 °C; IR (KBr): $\nu_{\max}$ 3440, 3310, 3240 (NH), CH 2910, 2865, 2840, CN 2180 cm^{-1} ; ^1H NMR (250 MHz): δ 3.06 (t, 2H, CH₂, J = 7.2 Hz), 3.61 (dt, 2H, CH₂, J = 6.5, 7.2 Hz), 3.77 (s, 3H, OMe), 6.81 (d, 2H, H-Ar, J = 9.3 Hz), 6.99 (t, 2H, H-Ind, J = 7.8 Hz), 7.06 (s, 1H, H-Ind), 7.23 (m, 3H, NH+NH₂), 7.34 (m, 3H, H-Ar+H-Ind), 7.57 (d, 1H, H-Ind, J = 7.5 Hz), 10.7 (s, 1H, NH); MS: m/z (%) 360 (M^+ , 41.15 %); *Anal.* Calcd. for C₂₀H₂₀N₆O: C, 66.65; H, 5.59; N, 23.32. Found: C, 66.38; H, 5.78; N, 23.53.

3-Amino-2-(4-chlorophenylazo)-3-[2-(1H-indol-3-yl)-ethylamino]-acrylonitrile (10b). Yellow crystals (3.1 g, 87%); mp 176-178 °C; IR (KBr): $\nu_{\max}$ 3440, 3310, 3240 (NH), 2910, 2865, 2840 (CH), 2180 (CN) cm^{-1} ; ^1H NMR (400 MHz): δ 3.02 (t, 2H, CH₂, J = 7.6 Hz), 3.62 (br s, 2H, CH₂), 6.99 (t, 1H, H-Ind, J = 6.8 Hz), 7.03 (t, 1H, H-Ind, J = 7.8 Hz), 7.16 (s, 1H, H-Ind), 7.24 (d, 2H, H-Ar, J = 8.0 Hz), 7.33-7.38 (3H, m, H-Ar+H-Ind), 7.56 (d, 1H, H-Ind, J = 7.3 Hz), 7.68-7.73 (m, 3H, NH+NH₂), 10.9 (s, 1H, NH); MS: m/z (%) 364 (M^+ , 17.6 %); *Anal.* Calcd. for C₁₉H₁₇ClN₆: C, 62.55; H, 4.70; N, 23.03. Found: C, 62.31; H, 4.87; N, 23.31.

4-{2-Amino-1-cyano-2-[2-(1H-indol-3-yl)-ethylamino]-vinylazo}-benzoic acid ethyl ester (10c). Colorless crystals (3.00 g, 80%); mp 215-216 °C; IR (KBr): $\nu_{\max}$ 3440, 3310, 3240 (NH), 2910, 2865, 2840 (CH), 2180 (CN)

cm⁻¹; ¹H NMR (400 MHz): δ 1.31 (t, 3H, CH₃, J = 7.2 Hz), 3.06 (t, 2H, CH₂, J = 7.6 Hz), 3.61 (dt, 2H, CH₂, J = 6.5, 7.6 Hz), 4.28 (q, 2H, CH₂, J = 7.2 Hz), 6.99 (t, 2H, H-Ind, J = 7.8 Hz), 7.06 (t, 2H, H-Ind, J = 8.0 Hz), 7.24 (s, 1H, H-Ind), 7.36 (d, 1H, H-Ind, J = 8.4 Hz), 7.54 and 7.89 (AA'XX', 4H, H-Ar, J = 8.8 Hz), 7.62 (d, 1H, H-Ind, J = 8.0 Hz), 7.70-7.90 (brs, 3H, NH₂+NH) 10.7 (s, 1H, NH); ¹³C (100 MHz): δ 14.2, 24.4, 42.0, 60.3, 93.4, 110.8, 111.4, 115.1 (2C), 118.3, 118.4, 120.0 (2C), 121.0, 123.1, 125.1, 127.1, 130.0, 136.2, 157.2, 159.0, 165.7; MS: *m/z* (%) 402 (M⁺, 34.2%); *Anal.* Calcd. for C₂₂H₂₂N₆O₂: C, 65.66; H, 5.51; N, 20.88. Found: C, 65.41; H, 5.43; N, 20.67.

3-Amino-2-(4-fluorophenylazo)-3-[2-(1*H*-indol-3-yl)-ethylamino]-acrylonitrile (10d). Yellow crystals (2.78 g, 80%); mp 218-220 °C; ¹H NMR (400 MHz): δ 3.02 (t, 2H, CH₂, J = 7.6 Hz), 3.62 (br s, 2H, CH₂), 6.8-7.2 (m, 4H, H-Ar+H-Ind), 7.2 (s, 1H, H-Ind), 7.36 (d, 1H, H-Ind, J = 7.5 Hz), 7.4-7.7 (m 6H, H-Ar+H-Ind+NH+NH₂), 10.89 (s, 1H, NH); ¹³C (100 MHz): δ 24.6, 42.0, 90.9, 110.9, 111.4, 115.2 (d, 2C, ²J_{CF} = 22.2 Hz), 115.9 118.4, 121.0, 121.6 (d, 2C, ³J_{CF} = 7.9 Hz), 123.1, 127.0, 136.2, 150.4, 159.3, 160.0 (d, ¹J_{CF} = 240 Hz); *Anal.* Calcd. for C₁₉H₁₇FN₆: C, 65.51; H, 4.92; N, 24.12. Found: C, 65.32; H, 4.71; N, 24.35.

3-Amino-2-(3,5-difluorophenylazo)-3-[2-(1*H*-indol-3-yl)-ethylamino]-acrylonitrile (10e). Yellow crystals (1.8 g, 50%); mp 210-212 °C; ¹H NMR (400 MHz): δ 3.08 (t, 2H, CH₂, J = 7.0 Hz), 3.72 (br s, 2H, CH₂), 6.72 (t, 1H, H-Ar, J = 7.0 Hz), 6.80-7.2 (m, 5H, H-Ind+H-Ar+NH₂), 7.32 (d, 1H, H-Ind, J = 8.0 Hz), 7.50-7.70 (m, 3H, H-Ind+H-Ar), 7.8 (t, 1H, NH, J = 6.9 Hz), 10.7 (brs, 1H, NH); ¹³C (100 MHz): δ 24.4, 42.1, 92.6, 99.3 (t, ²J_{CF} = 27.2 Hz), 102.9 (d, 2C, ²J_{CF} = 25.5 Hz), 110.9, 111.4, 115.1, 118.3, 118.4, 121.0, 123.0, 127.1, 136.2, 156.8 (t, ³J_{CF} = 9.6 Hz), 158.9, 163.0 (dd, 2C, ¹J_{CF} = 242.3, ³J_{CF} = 15.0 Hz); *Anal.* Calcd. for C₁₉H₁₆F₂N₆: C, 62.29; H, 4.40; N, 22.94. Found: C, 62.05; H, 4.53; N, 23.14.

3-Amino-2-(4-nitrophenylazo)-3-[2-(1*H*-indol-3-yl)-ethylamino]-acrylonitrile (10f). Yellow crystals (3.1 g, 63%); mp 308-310 °C; ¹H NMR (400 MHz): δ 3.03 (t, 2H, CH₂, J = 7.2 Hz), 3.66 (t, 2H, CH₂), 6.98 (t, 1H, H-Ind, J = 6.8 Hz), 7.08 (t, 1H, H-Ind, J = 7.2 Hz), 7.24 (s, 1H, H-Ind), 7.36 (d, 2H, H-Ar, J = 8.0 Hz), 7.33-7.38 (3H, m, H-Ar+H-Ind), 7.56 (d, 1H, H-Ind, J = 7.3 Hz), 7.68-7.73 (m, 3H, NH+NH₂), 10.9 (s, 1H, NH); ¹³C (100 MHz): δ 24.2, 42.1, 95.7, 110.7, 111.4, 114.5, 118.3 (2C), 120.1 (2C), 121.0, 123.2, 124.7 (2C), 127.0, 136.2, 142.7, 158.6, 159.0; *Anal.* Calcd. for C₁₉H₁₇ClN₆: C, 62.55; H, 4.70; N, 23.03. Found: C, 62.31; H, 4.87; N, 23.31.

3-Amino-2-(4-methoxyphenylazo)-3-(8-oxo-1,5,6,8-tetrahydro-2*H*,4*H*-1,5-methano-pyrido[1,2-*a*][1,5]diazocin-3-yl)-acrylonitrile (11a). Yellow crystals (2.93 g, 75%); mp 183-185 °C; ¹H NMR (250 MHz): δ 1.99 and 2.07 (AA'BB', 2H, CH₂, J = 12.8 Hz), 2.58 (br s, 1H, CH), 3.23 (br s, 1H, CH), 3.39 (d, 1H, CH, J = 13.1 Hz), 3.54 (d, 1H, CH, J = 13.1 Hz), 3.68-3.72 (m, 1H, CH), 3.76 (s, 3H, OMe), 4.02 (d, 1H, CH, J = 13.2 Hz), 4.30 (d, 1H, CH, J = 13.8 Hz), 4.42 (d, 1H, CH, J = 15.3 Hz), 6.12 (d, 1H, H-Ar, J = 6.5 Hz), 6.20 (d, 1H, H-Ar, J = 9.0 Hz), 7.23 (br s, 2H, NH₂), 7.26 (dd, 1H, H-Ar, J = 9.0, 6.5 Hz), 6.84 and 7.42 (AA'XX', 4H, H-Ar, J = 9.0 Hz); ¹³C (100 MHz): δ 24.94, 27.0, 33.9, 47.8, 53.0, 55.2, 55.4, 92.1, 104.8, 113.9 (2C), 116.2, 117.1, 121.8 (2C), 139.0, 147.4, 149.4, 157.8, 162.38, 162.7; MS: *m/z* (%) 390 (M⁺, 7.5%); *Anal.* Calcd. for C₂₁H₂₂N₆O₂: C, 64.60; H, 5.68; N, 21.52. Found: C, 64.43; H, 5.47; N, 21.63.

3-Amino-3-(8-oxo-1,5,6,8-tetrahydro-2*H*,4*H*-1,5-methano-pyrido[1,2-*a*][1,5]diazocin-3-yl)-2-phenylazo-acrylonitrile (11b). Colorless crystals (3.13 g, 87%); mp 163-165 °C; ¹H NMR (250 MHz): δ 1.97 and 2.03 (AA'BB', 2H, CH₂, J = 12.5 Hz), 2.61 (br s, 1H, CH), 3.24 (s, 1H, CH), 3.40 (d, 1H, CH, J = 13.6 Hz), 3.55 (d, 1H, CH, J = 12.8 Hz), 3.70 (dd, 1H, CH, J = 15.8, 6.3 Hz), 4.0-4.08 (m, 1H, CH), 4.33 (d, 1H, CH, J = 13.2 Hz), 4.43 (d, 1H, CH, J = 16.1 Hz), 6.12 (d, 1H, H-Ar, J = 7.0 Hz), 6.22 (d, 1H, H-Ar, J = 8.8 Hz), 7.05 (t, 1H, H-Ar, J = 7.0 Hz), 7.25-7.20 (m, 3H, H-Ar), 7.27 (d, 2H, H-Ar, J = 8.5 Hz), 7.30 (br s, 2H, NH₂); MS: (%) *m/z* 360 (M⁺, 9.6%); *Anal.* Calcd. for C₂₀H₂₀N₆O: C, 66.65; H, 5.59; N, 23.32. Found: C, 66.89; H, 5.71; N, 23.12.

4-[2-Amino-1-cyano-2-(8-oxo-1,5,6,8-tetrahydro-2*H*,4*H*-1,5-methano-pyrido[1,2-*a*][1,5]diazocin-3-yl)-vinylazo]-benzoic acid ethyl ester (11c). Yellow crystals 3.00 g (70%); mp 245-246 °C; ¹H NMR (250 MHz): δ 1.13 (t 3H, Me, J = 7.1 Hz), 1.96 and 2.05 (AA'BB', 2H, CH₂, J = 12.8 Hz), 2.60 (br s, 1H, CH), 3.30 (d, 1H, CH, J = 8.3 Hz), 3.43 (d, 1H, CH, J = 13.2 Hz), 3.58 (dd, 1H, CH, J = 10.7), 3.69 (dd, 1H, CH, J = 15.4, 15.2 Hz), 4.0 (d, 1H, CH, J = 13.2 Hz), 4.26-4.31 (m, 3H, CH), 4.37 (d, 1H, CH, J = 15.4 Hz), 6.19 (1H, d, H-Ar, J = 7.0 Hz), 6.24 (d, 1H, H-Ar, J = 9.0 Hz), 7.32 (dd, H-Ar, J = 9.0, 7.0 Hz), 7.50 and 7.88 (AA'XX', 4H, H-Ar, J = 8.7 Hz), 7.79 (br s, 2H, NH₂); MS: *m/z* 432 (M⁺, 15.3%); ¹³C NMR (100 MHz): δ 14.2, 24.8, 27.0, 33.9, 47.7, 53.0, 55.5, 60.3, 94.4, 104.8, 116.0, 116.3, 120.2 (2C), 125.7, 130.0 (2C), 139.0, 149.0, 156.9, 162.1, 162.5, 165.6; MS: *m/z* (%) 432 (M⁺, 13.2); *Anal.* Calcd. for C₂₃H₂₄N₆O₃: C, 63.88; H, 5.59; N, 19.43. Found: C, 63.86; H, 5.70; N, 19.61.

3-Amino-2-(4-chlorophenylazo)-3-(8-oxo-1,5,6,8-tetrahydro-2*H*,4*H*-1,5-methano-pyrido[1,2-*a*][1,5]diazocin-3-yl)-acrylonitrile (11d). Yellow crystals (3.7 g, 93%); mp 170-171 °C; ¹H NMR (400 MHz): δ 2.00 and 2.11 (AB, 2H, CH₂, J = 15.0 Hz), 2.61 (s, 1H, CH), 3.24 (s, 1H, CH), 3.41 (d, 1H, CH, J = 15.0 Hz), 3.56 (dd, 1H, CH, J = 13.0, 12.7 Hz), 3.69 (dd, 1H, CH, J = 15.5, 14.3 Hz), 4.02 (m, 1H, CH), 4.31 (d, 1H, CH, J = 13.5 Hz), 4.42 (d, 1H,

CH, $J = 15.7$ Hz), 6.12 (dd, 1H, CH, $J = 6.5, 1.0$ Hz), 6.21 (1H, dd, CH, $J = 9.0, 1.0$ Hz), 7.25 (dd, 1H, CH, $J = 9.0, 6.5$ Hz), 7.25 and 7.43 (AA'XX', 4H, H-Ar, $J = 8.8$ Hz), 7.41 (s, 2H, NH₂); *Anal.* Calcd. for C₂₀H₁₉ClN₆O: C, 60.84; H, 4.85; N, 21.28. Found: C, 60.78; H, 5.15; N, 21.40.

3-Amino-2-(4-fluorophenylazo)-3-(8-oxo-1,5,6,8-tetrahydro-2H,4H-1,5-methano-pyrido[1,2-a][1,5]diazocin-3-yl)-acrylonitrile (11e). Yellow crystals (3.33 g, 88%); mp 173-175 °C; ¹H NMR (250 MHz): δ 1.99 and 2.10 (AA'BB', 2H, CH₂, $J = 14.1$ Hz), 2.49 (br s, 1H, CH), 3.26 (br s, 1H, CH), 3.34-3.60 (m, 2H, CH), 3.70 (dd, 1H, CH, $J = 16.0, 6.5$ Hz), 3.97-4.10 (m, 1H, CH), 4.31 (d, 1H, CH, $J = 13.2$ Hz), 4.42 (d, 1H, CH, $J = 15.8$ Hz), 6.12 (d, 1H, H-Ar, $J = 7.0$ Hz), 6.22 (d, 1H, H-Ar, $J = 9.0$ Hz), 6.96-7.09 (m, 2H, H-Ar), 7.26 (dd, 1H, H-Ar, $J = 9.0, 7.0$ Hz), 7.33 (brs, 2H, NH₂), 7.42-7.52 (m, 2H, H-Ar); ¹³C NMR (100 MHz): δ 24.8, 26.9, 33.9, 47.7, 52.9, 55.4, 92.6, 104.8, 115.3 (d, 2C, ²J_{CF} = 22.2 Hz), 116.2, 116.6, 122.0 (d, 2C, ³J_{CF} = 8.1 Hz), 139.0, 149.2, 150.1, 160.3 (d, ¹J_{CF} = 241 Hz), 162.1, 162.7; MS: m/z (%) 378 (M⁺, 9.4%); *Anal.* Calcd. for C₂₀H₁₉FN₆O: C, 63.48; H, 5.06; N, 22.21. Found: C, 63.69; H, 5.21; N, 22.12.

3-Amino-2-(2,4-dichlorophenylazo)-3-(8-oxo-1,5,6,8-tetrahydro-2H,4H-1,5-methano-pyrido[1,2-a][1,5]diazocin-3-yl)-acrylonitrile (11f). Yellow crystals (3.52 g, 82%); mp 223-224 °C; ¹H NMR (250 MHz): δ 2.04 and 2.17 (AA'BB', 2H, CH₂, $J = 12.5$ Hz), 2.62 (br s, 1H, CH), 3.26 (br s, 1H, CH), 3.4-3.5 (m, 1H, CH), 3.57 (d, 1H, CH, $J = 11.5$ Hz), 3.68 (dd, 1H, CH, $J = 15.5, 6.3$ Hz), 4.0-4.1 (m, 1H, CH), 4.34 (d, 1H, H-Ar, $J = 13.8$ Hz), 4.43 (d, 1H, CH, $J = 15.8$ Hz), 6.13 (d, 1H, H-Ar, $J = 6.8$ Hz), 6.23 (d, 1H, H-Ar, $J = 8.0$ Hz), 7.15-7.3 (m, 2H, H-Ar), 7.34 (d, 1H, H-Ar, $J = 2.0$ Hz), 7.49 (d, 1H, H-Ar, $J = 8.5$ Hz), 7.6 (br s, 1H, NH₂); MS: m/z (%) 428 (M⁺, 9.5%); *Anal.* Calcd. for C₂₀H₁₈Cl₂N₆O: C, 55.96; H, 4.23; N, 19.58. Found: C, 56.16; H, 4.45; N, 19.39.

3-Amino-2-(3,5-difluorophenylazo)-3-(8-oxo-1,5,6,8-tetrahydro-2H,4H-1,5-methano-pyrido[1,2-a][1,5]diazocin-3-yl)-acrylonitrile (11g). Yellow crystals (2.45 g, 62%); mp 257-258 °C; ¹H NMR (250 MHz): δ 2.05 and 2.11 (AA'BB', 2H, CH₂, $J = 12.5$ Hz), 2.66 (br s, 1H, CH), 3.30 (d, 1H, CH, $J = 13.8$ Hz), 3.45 (d, 1H, CH, $J = 14.5$ Hz), 3.78 (dd, 1H, CH, $J = 17.0, 5.0$ Hz), 3.9-4.2 (m, 3H, CH), 6.4-7.1 (m, 2H, H-Ar), 7.12 (t, 1H, H-Ar, $J = 9.3$ Hz), 7.27 (t, 1H, H-Ar, $J = 7.5$ Hz), 7.49 (d, 2H, H-Ar, $J = 6.3$ Hz); MS: m/z (%) 396 (M⁺, 12.6%); *Anal.* Calcd. for C₂₀H₁₈F₂N₆O: C, 60.60; H, 4.58; N, 21.20. Found: C, 60.86; H, 4.70; N, 21.43.

3-Amino-2-(4-chlorophenylazo)-3-[4-(3-chlorophenyl)-piperazin-1-yl]-acrylonitrile (12a). Colorless crystals (2.60 g, 65 %); mp 154-155 °C; ¹H NMR (250 MHz): δ 3.20-3.50 (m, 4H, CH₂), 3.60-3.95 (m, 4H, CH₂), 6.74 (dd, 1H, H-Ar, $J = 7.4, 1.4$ Hz), 6.85 (dd, 1H, H-Ar, $J = 8.8, 2.0$ Hz), 6.85-6.90 (m, 1H, H-Ar), 7.18 (dd, 1H, H-Ar, $J = 8.5, 1.9$ Hz), 7.27 and 7.50 (AA'XX', 4H, H-Ar, $J = 8.8$ Hz), 7.60 (br s, 2H, NH₂); MS: m/z (%) 401 (M⁺, 13.5%); *Anal.* Calcd. for C₁₉H₁₈Cl₂N₆: C, 56.87; H, 4.52; N, 20.94. Found: C, 56.62; H, 4.43; N, 20.51.

3-Amino-2-(4-chlorophenylazo)-3-[4-(3-methoxyphenyl)-piperazin-1-yl]-acrylonitrile (12b). Yellow crystals (3.05 g, 77 %); mp 178-179 °C; ¹H NMR (250 MHz): δ 3.08-3.28 (m, 4H, 2CH₂), 3.66-3.88 (m, 4H, 2CH₂), 3.71 (s, 3H, OMe), 6.85-6.90 (m, 1H, H-Ar), 6.78 (d, 2H, H-Ar, $J = 8.8$ Hz), 7.16 (d, 1H, H-Ar, $J = 8.9$ Hz), 7.27 and 7.50 (AA'XX', 4H, H-Ar, $J = 8.5$ Hz), 7.56 (br s, 2H, NH₂); MS: m/z (%) 396 (M⁺, 18.3%); *Anal.* Calcd. for C₂₀H₂₁ClN₆O: C, 60.53; H, 5.33; N, 21.18. Found: C, 60.22; H, 5.49; N, 21.41.

3-Amino-2-(4-chlorophenylazo)-3-(4-pyridin-2-yl-piperazin-1-yl)-acrylonitrile (12c). Yellow crystals (2.17 g, 59%); mp 169-171 °C; ¹H NMR (250 MHz): δ 3.35 (br s, 4H, 2CH₂), 3.63 (br s, 4H, 2CH₂), 6.69 (t, 1H, H-Pyr, $J = 4.9$ Hz), 6.85 (d, 1H, H-Pyr, $J = 8.6$ Hz), 7.28 (br s, 2H, NH₂), 7.34 (t, 1H, H-Pyr, $J = 8.4$ Hz), 7.51 and 7.90 (AA'XX', 4H, H-Ar, $J = 8.8$ Hz), 7.57 (t, 1H, H-Pyr, $J = 4.9$ Hz); MS: m/z (%) 367 (M⁺, 23.5%); *Anal.* Calcd. for C₁₈H₁₈ClN₇: C, 58.78; H, 4.93; N, 26.65. Found: C, 58.51; H, 4.71; N, 26.82.

3-Amino-2-(4-chlorophenylazo)-3-(4-pyrimidin-2-yl-piperazin-1-yl)-acrylonitrile (12d). Yellow crystals (2.32 g, 63%); mp 169-171 °C; ¹H NMR (250 MHz): δ 3.50-3.59 (m, 4H, 2CH₂), 3.80-3.95 (m, 4H, 2CH₂), 6.55 (t, 1H, H-Pyrim, $J = 4.3$ Hz), 7.50 and 7.85 (AA'XX', 4H, H-Ar, $J = 9.3$ Hz), 8.20 (d, 2H, H-Pyrim, $J = 4.3$ Hz), 7.22 (brs, 2H, NH₂); MS: m/z (%) 368 (M⁺, 16.5%); *Anal.* Calcd. for C₁₇H₁₇ClN₈: C, 55.36; H, 4.65; N, 30.38. Found: C, 55.58; H, 4.80; N, 30.57.

General procedure of synthesis of 5-amino-2-aryl-2H-[1,2,3]triazole-4-carbonitrile 13-22. To solution of 0.005 mol amidine **3-8, 10-12** in 50 ml pyridine was added 1.3 g (0.011 mol) Cu(OAc)₂. The contents were stirred and were heated at 60 °C about 5-6 hours. Then, the reaction mixture was cooled and diluted with water. The precipitate was collected by filtration and crystallized from ethanol.

2-(4-Methoxyphenyl)-5-methylamino-2H-[1,2,3]triazole-4-carbonitrile (13a). Grey solid (0.80 g, 70%); mp 168-169 °C; IR (KBr): $\nu_{\max}$ 3380 (NH), 3000, 2950, 2920, 2840, 2810 (CH), 2230 (CN) cm⁻¹; ¹H NMR (250 MHz): δ 2.89 (d, 3H, NHMe, $J = 5.0$ Hz), 3.83 (s, 3H, OMe), 6.68 (q, 1H, NH, $J = 5.0$ Hz), 6.99 and 7.83 (AA'XX', H-Ar, 4H, $J = 8.9$ Hz); MS: m/z (%) 229 (M⁺, 100%); *Anal.* Calcd. for C₁₁H₁₁N₅O: C, 57.63; H, 4.84; N, 30.55. Found: C, 57.49; H, 4.75; N, 30.37.

5-Methylamino-2-phenyl-2H-[1,2,3]triazole-4-carbonitrile (13b). Grey solid (0.58 g 57%); mp 130-131 °C; IR (KBr): $\nu_{\max}$ 3380 (NH), 2950, 2910, 2880, 2810 (CH), 2240 (CN) cm^{-1} ; ^1H NMR (250 MHz): δ 2.91 (d, 3H, NHMe, $J = 4.6$ Hz), 6.76 (q, 1H, NH, $J = 4.6$ Hz), 7.36 (t, 1H, H-Ar, $J = 7.3$ Hz), 7.49 (t, 2H, H-Ar, $J = 7.3$ Hz), 7.93 (d, 2H, H-Ar, $J = 7.7$ Hz); ^{13}C NMR (100 MHz): δ 29.9, 106.4, 112.5, 118.3(2C), 128.2, 129.7 (2C), 138.4, 157.6; MS: m/z (%) 199 (M^+ , 100 %); *Anal.* Calcd. for $\text{C}_{10}\text{H}_9\text{N}_5$: C, 60.29; H, 4.55; N, 35.15. Found: C, 60.49; H, 4.38; N, 35.35.

5-Methylamino-2-(4-nitrophenyl)-2H-[1,2,3]triazole-4-carbonitrile (13c). Brown solid (1.16 g, 95%); mp 189-90 °C; ^1H NMR (250 MHz): δ = 2.9 (d, 3H, Me, $J = 3.5$ Hz), 7.2 (br, 1H, NH), 8.1 and 8.3 (AA'XX', H-Ar, 4H, $J = 8.9$ Hz); *Anal.* Calcd. for $\text{C}_{10}\text{H}_8\text{N}_6\text{O}_2$: C, 49.18; H, 3.30; N, 34.41. Found: C, 49.33; H, 3.48; N, 34.68.

5-Cyclohexylamino-2-(4-methoxyphenyl)-2H-[1,2,3]triazole-4-carbonitrile (14a). Grey solid (1.25 g, 84%); mp 153-155 °C; IR (KBr): $\nu_{\max}$ 3350 (NH), 2930, 2850 (CH), 2230 (CN) cm^{-1} ; ^1H NMR (250 MHz): δ 0.99-2.11 (m, 10H, 5CH₂), 3.57-3.30 (m, 1H, CH), 3.83 (s, 3H, OMe), 6.44-6.67 (d, 1H, NH, $J = 6.2$ Hz), 7.00 and 7.81 (AA'XX', 4H, H-Ar, $J = 9.3$ Hz); ^{13}C NMR (100 MHz): δ 24.5 (2C), 25.3, 32.2 (2C), 52.34, 55.5, 105.5, 113.0, 114.7 (2C), 120.0 (2C), 132.1, 156.0, 159.0; MS: m/z (%) 297 (M^+ , 100%); *Anal.* Calcd. for $\text{C}_{16}\text{H}_{19}\text{N}_5\text{O}$: C, 64.63; H, 6.44; N, 23.55. Found: C, 64.41; H, 6.28; N, 23.67.

5-Cyclohexylamino-2-phenyl-2H-[1,2,3]triazole-4-carbonitrile (14b). Grey solid (0.99 g, 84%); mp 171-173 °C; IR (KBr): $\nu_{\max}$ 3350 (NH), 2930, 2850 (CH), 2230 (CN) cm^{-1} ; ^1H NMR (250 MHz): δ 1.20-1.45 (m, 5H, CH), 1.85-1.60 (m, 3H, CH₂), 1.90-2.15 (m, 2H, CH₂), 3.56-3.34 (m, 1H, CH), 6.67 (d, 1H, NH, $J = 8.0$ Hz), 7.29-7.46 (m, 1H, H-Ar), 7.90 (d, 2H, H-Ar, $J = 7.9$ Hz), 7.50 (t, 2H, H-Ar, $J = 7.5$ Hz); ^{13}C NMR (400 MHz): δ 24.6 (2C), 25.3, 32.2 (2C), 52.4, 106.5, 112.8, 118.3 (2C), 128.2, 129.7 (2C), 138.4, 156.0; MS: m/z (%) 267 (M^+ , 53.8%); *Anal.* Calcd. for $\text{C}_{15}\text{H}_{17}\text{N}_5$: C, 67.39; H, 6.41; N, 26.20. Found: C, 67.61; H, 6.28; N, 26.45.

2-(4-Methoxyphenyl)-5-pyrrolidin-1-yl-2H-[1,2,3]triazole-4-carbonitrile (15a). Grey solid (1.25 g, 89%); mp 126-127 °C; IR (KBr): $\nu_{\max}$ 3380 (NH), 2980, 2940, 2880, 2840, (CH), 2220 (CN) cm^{-1} ; ^1H NMR (400 MHz): δ 1.94-1.99 (m, 4H, 2CH₂), 3.47-3.52 (m, 4H, 2CH₂), 3.81 (s, 3H, OMe), 7.11 and 7.85 (AA'XX', 4H, H-Ar, $J = 9.3$ Hz); ^{13}C NMR (100 MHz): δ 24.8 (2C), 48.2 (2C), 55.5, 104.8, 113.9, 114.8 (2C), 120.1 (2C), 132.0, 155.7, 159.2; MS: m/z (%) 269 (M^+ , 100%); *Anal.* Calcd. for $\text{C}_{14}\text{H}_{15}\text{N}_5\text{O}$: C, 62.44; H, 5.61; N, 26.00. Found: C, 62.31; H, 5.48; N, 26.31.

2-Phenyl-5-pyrrolidin-1-yl-2H-[1,2,3]triazole-4-carbonitrile (15b). Grey solid (1.15 g, 95%); mp 102-103 °C; IR (KBr): $\nu_{\max}$ 3380 (NH), 2980, 2940, 2880 (CH), 2230 (CN) cm^{-1} ; ^1H NMR (250 MHz): δ 1.93-2.14 (m, 4H, 2CH₂), 3.36-3.68 (m, 4H, 2CH₂), 7.39 (t, 1H, H-Ar, $J = 7.5$ Hz), 7.51 (t, 2H, H-Ar, $J = 7.5$ Hz), 7.93 (d, 2H, H-Ar, $J = 6.5$ Hz); ^{13}C NMR (100 MHz): δ 25.0 (2C), 48.2 (2C), 105.7, 113.7, 118.4(2C), 128.4, 129.7, 138.3, 161.9 (2C); MS: m/z (%) 239 (M^+ , 100%); *Anal.* Calcd. for $\text{C}_{13}\text{H}_{13}\text{N}_5$: C, 65.26; H, 5.48; N, 29.27. Found: C, 65.01; H, 5.25; N, 29.42.

2-(4-Chlorophenyl)-5-pyrrolidin-1-yl-2H-[1,2,3]triazole-4-carbonitrile (15c). Grey solid (2.15 g, 78%); mp 132-133 °C; ^1H NMR (250 MHz): δ 1.95-2.10 (m, 4H, 2CH₂), 3.45-3.60 (m, 4H, 2CH₂), 7.51 and 7.91 (AA'XX', 4H, H-Ar, $J = 8.8$ Hz); MS: m/z (%) 273 (M^+ , 100%); *Anal.* Calcd. for $\text{C}_{13}\text{H}_{12}\text{ClN}_5$: C, 57.04; H, 4.42; N, 25.59. Found: C, 56.81; H, 4.20; N, 25.82.

2-(4-Fluorophenyl)-5-pyrrolidin-1-yl-2H-[1,2,3]triazole-4-carbonitrile (15d) White solid (1.0 g, 77%); mp 120-121 °C; ^1H NMR (250 MHz): δ 2.05 (br s, 4H, 2CH₂), 3.54 (br s, 4H, 2CH₂), 7.29 (m, 2H, H-Ar), 7.92 (m, 2H, H-Ar); *Anal.* Calcd. for $\text{C}_{13}\text{H}_{12}\text{FN}_5$: C, 60.69; H, 4.70; N, 27.22. Found: C, 60.93; H, 4.550; N, 26.96.

2-(3,5-Difluorophenyl)-5-pyrrolidin-1-yl-2H-[1,2,3]triazole-4-carbonitrile (15e). Grey-green solid (1.38 g, 100%); mp 160-162 °C; ^1H NMR (250 MHz): δ 1.85 (br s, 4H, 2CH₂), 3.54 (brs, 4H, 2CH₂), 7.0-7.25 (m, 1H, H-Ar), 7.45-7.6 (m, 2H, H-Ar); *Anal.* Calcd. for $\text{C}_{13}\text{H}_{11}\text{F}_2\text{N}_5$: C, 56.73; H, 4.03; N, 25.44. Found: C, 56.53; H, 4.20; N, 25.62.

2-(4-Methoxyphenyl)-5-piperidin-1-yl-2H-[1,2,3]triazole-4-carbonitrile (16a). Grey solid (1.36 g, 96%); mp 96-97 °C; ^1H NMR (250 MHz): δ 1.67 (br s, 4H, 3CH₂), 1.90-2.10 (m, 2H, CH₂), 3.40-3.52 (m, 4H, 2CH₂), 3.84 (s, 3H, Me), 7.01 and 7.83 (AA'XX', 4H, H-Ar, $J = 9.3$ Hz); ^{13}C NMR (100 MHz): δ 23.3, 24.3 (2C), 48.0 (2C), 55.5, 106.1, 113.7, 114.7 (2C), 120.1 (2C), 131.9, 157.9, 159.3; MS: m/z (%) 283 (M^+ , 100%); *Anal.* Calcd. for $\text{C}_{15}\text{H}_{17}\text{N}_5\text{O}$: C, 63.59; H, 6.05; N, 24.72. Found: C, 63.73; H, 5.83; N, 24.21.

2-(4-Chlorophenyl)-5-piperidin-1-yl-2H-[1,2,3]triazole-4-carbonitrile (16b). Grey solid (1.00 g, 78%); mp 84-85 °C; ^1H NMR (250 MHz): δ 1.68 (br s, 6H, 3CH₂), 3.40-3.50 (br s, 4H, 2CH₂), 7.52 and 7.91 (AA'XX', 4H, H-Ar, $J = 8.3$ Hz); ^{13}C NMR (100 MHz): δ 23.3, 24.3 (2C), 47.9 (2C), 107.4, 113.4, 120.1 (2C), 129.7 (2C), 132.8, 136.9, 157.8; MS: m/z (%) 287 (M^+ , 36%); *Anal.* Calcd. for $\text{C}_{14}\text{H}_{14}\text{ClN}_5$: C, 58.44; H, 4.90; N, 24.34. Found: C, 58.63; H, 4.72; N, 24.65.

2-(4-Fluorophenyl)-5-piperidin-1-yl-2H-[1,2,3]triazole-4-carbonitrile (16c). Violet solid (0.72 g, 50%); mp 121-122 °C; ¹H NMR (250 MHz): δ 1.61 (br s, 6H, 3CH₂), 3.50 (br s, 4H, 2CH₂), 7.25-7.35 (m, 2H, H-Ar), 7.8-8.05 (m, 2H, H-Ar); MS: *m/z* (%) 271 (M⁺, 36%); *Anal.* Calcd. for C₁₄H₁₄FN₅: C, 61.98; H, 5.20; N, 25.81. Found: C, 61.67; H, 4.96; N, 26.05. 271

2-(3,5-Difluorophenyl)-5-piperidin-1-yl-2H-[1,2,3]triazole-4-carbonitrile (16d). Grey solid (1.4 g, 97%); mp 130-131 °C; ¹H NMR (250 MHz): δ 1.63 (br s, 6H, 3CH₂), 3.49 (br s, 4H, 2CH₂), 7.35 (t, 1H, H-Ar, J = 8.9 Hz), 7.57 (d, 2H, H-Ar, J = 6.0 Hz); MS: *m/z* (%) 289 (M⁺, 36%); *Anal.* Calcd. for C₁₄H₁₃F₂N₅: C, 58.13; H, 4.53; N, 24.21. Found: C, 58.36; H, 4.65; N, 24.45.

5-[2-(1H-Indol-3-yl)-ethylamino]-2-(4-methoxyphenyl)-2H-[1,2,3]triazole-4-carbonitrile (17a). Grey solid (1.54 g, 86%); mp 96-98 °C; IR (KBr): ν_{max} 3400, 3360, (NH), 2960, 2930, 2860, 2840 (CH), 2230 (CN) cm⁻¹; ¹H NMR (250 MHz): δ 3.04 (br s, 2H, CH₂), 3.55 (br s, 2H, CH₂), 3.83 (s, 3H, OMe), 6.80-7.19 (m, 5H, H-Ind+H-Ar+NH), 7.32 (d, 2H, H-Ind, J = 7.0 Hz), 7.58 (d, 1H, H-Ind, J = 6.3 Hz), 7.83 (d, 2H, H-Ar, J = 7.8 Hz), 10.60 (br s, 1H, NH); ¹³C NMR (100 MHz): δ 24.8, 44.3, 55.5, 111.4, 111.6, 112.8 (2C), 114.7 (2C), 118.2 (2C), 119.9, 120.9 (2C), 122.8, 127.2, 132.1, 136.2, 156.9, 159.0; MS: *m/z* (%) 358 (M⁺, 10.5%); *Anal.* Calcd. for C₂₀H₁₈N₆O: C, 67.03; H, 5.06; N, 23.45. Found: C, 67.31; H, 5.18; N, 23.58.

4-{4-Cyano-5-[2-(1H-indol-3-yl)-ethylamino]-[1,2,3]triazol-2-yl}-benzoic acid ethyl ester (17b). Grey solid (1.24 g, 62%); mp 221-222 °C; ¹H NMR (400 MHz): δ 1.37 (t, 3H, Me, J = 7.2 Hz), 3.03 (t, 2H, CH₂, J = 6.8 Hz), 3.65 (dt, 2H, CH₂, J = 6.5, 6.8 Hz), 4.30 (q, 2H, CH₂, J = 7.2 Hz), 6.95 (t, 1H, H-Ind J = 6.8 Hz), 7.04 (t, 1H, H-Ind, J = 7.0 Hz), 7.12-7.16 (m, 1H, H-Ind), 7.33 (d, 1H, H-Ind, J = 8.3 Hz), 7.5-7.7 (m, 2H, NH+H-Ind), 7.45 and 7.87 (AA'XX', H-Ar, 4H, J = 8.5 Hz), 10.60 (br s, 1H, NH); MS: *m/z* (%) 400 (M⁺, 15.5%); *Anal.* Calcd. for C₂₂H₂₀N₆O₂: C, 65.99; H, 5.03; N, 20.99. Found: C, 65.68; H, 5.25; N, 21.28.

2-(4-Fluorophenyl)-5-[2-(1H-Indol-3-yl)-ethylamino]-2H-[1,2,3]triazole-4-carbonitrile (17c). Grey solid (1.2 g, 70%); mp 220-221 °C; ¹H NMR (400 MHz): δ 3.0 (br s, 2H, CH₂), 3.5 (br s, 2H, CH₂), 7.0-7.15 (m, 2H, H-Ind+H-Ar), 7.2 (s, 1H, H-Ind), 7.25-7.65 (m, 4H, H-Ar+H-Ind), 7.60-7.63 (m, 1H, H-Ind), 7.90-7.97 (m, 2H, H-Ind+NH), 10.8 (br s, 1H, NH); *Anal.* Calcd. for C₁₉H₁₅FN₆: C, 65.89; H, 4.37; N, 24.26. Found: C, 65.68; H, 4.55; N, 24.47.

2-(3,5-Difluorophenyl)-5-[2-(1H-Indol-3-yl)-ethylamino]-2H-[1,2,3]triazole-4-carbonitrile (17d). Brown solid (1.70 g, 96%); mp 139-141 °C; ¹H NMR (400 MHz): δ 3.09 (t, 2H, CH₂, J = 7.0 Hz), 3.76 (br s, 2H, CH₂), 6.59 (br, 1H, H-Ar), 6.90-7.1 (m, 3H, H-Ind+H-Ar), 7.18 (brs, 1H, H-Ind), 7.30-7.60 (m, 4H, H-Ind+H-Ar+NH), 10.7 (brs, 1H, NH); *Anal.* Calcd. for C₁₉H₁₄F₂N₆: C, 62.63; H, 3.87; N, 23.07. Found: C, 62.41; H, 4.01; N, 23.32.

2-(4-Methoxyphenyl)-5-(8-oxo-1,5,6,8-tetrahydro-2H,4H-1,5-methano-pyrido[1,2-a][1,5]diazocin-3-yl)-2H-[1,2,3]triazole-4-carbonitrile (18a). Yellow crystals (2.93g, 75%); mp 148-150 °C; ¹H NMR (250 MHz): δ 2.03 (br s, 2H, CH₂), 2.65 (br s, 1H, CH), 3.26 (br s, 1H, CH), 3.39 (d, 2H, CH, J = 13.0 Hz), 3.80 (br s, 1H, CH), 3.82 (s, 3H, OMe), 3.90-4.15 (m, 3H, CH₂), 6.15 (d, 2H, H-Ar, J = 6.8 Hz), 6.98 and 7.75 (AA'XX', 4H, H-Ar, J = 8.3 Hz), 7.23 (t, 1H, H-Ar, J = 6.5 Hz); MS: *m/z* (%) 388 (M⁺, 7.5%); *Anal.* Calcd. for C₂₁H₂₀N₆O₂: C, 64.94; H, 5.19; N, 21.64. Found: C, 64.67; H, 5.28; N, 21.63.

5-(8-Oxo-1,5,6,8-tetrahydro-2H,4H-1,5-methano-pyrido[1,2-a][1,5]diazocin-3-yl)-2-phenyl-2H-[1,2,3]triazole-4-carbonitrile (18b). Grey solid (1.31 g, 67%); mp 172-3 °C; ¹H NMR (400 MHz): δ 2.04 (s, 2H, CH₂), 2.66 (s, 1H, CH), 3.32 (m, 3H, CH), 3.78 (dd, 1H, CH, J = 15.0, 14.0 Hz), 4.1 (m, 3H, CH), 6.16 (d, 2H, H-Ar, J = 7.5 Hz), 7.27 (dd, 1H, CH J = 7.5, 8.0 Hz), 7.51 and 7.87 (AA'XX', 4H, H-Ar, J = 8.5 Hz); *Anal.* Calcd. for C₂₀H₁₈N₆O: C, 67.03; H, 5.06; N, 23.45. Found: C, 67.33; H, 4.83; N, 23.57.

2-(4-Fluorophenyl)-5-(8-oxo-1,5,6,8-tetrahydro-2H,4H-1,5-methano-pyrido[1,2-a][1,5]diazocin-3-yl)-2H-[1,2,3]triazole-4-carbonitrile (18d). Grey solid (1.35 g, 72%); mp 107-109 °C; ¹H NMR (250 MHz): δ 2.04 (br s, 2H, CH₂), 2.65 (br s, 1H, CH), 3.25-3.40 (m, 3H, CH), 3.90 (d, 1H, CH, J = 15.5, 6.3 Hz), 3.85-4.05 (m, 2H, CH), 4.11 (d, 1H, CH, J = 13.0 Hz), 6.16 (d, 2H, H-Ar, J = 7.0 Hz), 7.24-7.31 (m, 3H, H-Ar), 7.87-7.93 (m, 2H, H-Ar); ¹³C NMR (100 MHz): δ 24.3, 26.4, 33.3, 48.9, 53.4, 54.5, 104.6, 107.0, 113.0, 115.9, 116.5 (d, 2C, J = 23.4 Hz), 120.9 (d, 2C, J = 8.9 Hz), 134.6, 138.9, 149.9, 157.7, 161.6 (d, J = 244.8 Hz), 162.0; MS: *m/z* (%) 376 (M⁺, 25); *Anal.* Calcd. for C₂₀H₁₇FN₆O: C, 63.82; H, 4.55; N, 22.33. Found: C, 63.57; H, 4.28; N, 22.21.

2-(2,4-Dichlorophenyl)-5-(8-oxo-1,5,6,8-tetrahydro-2H,4H-1,5-methano-pyrido[1,2-a][1,5]diazocin-3-yl)-2H-[1,2,3]triazole-4-carbonitrile (18e). Grey solid (1.62 g, 76%); mp 138-139 °C; ¹H NMR (250 MHz): δ 2.04 (br s, 2H, CH), 2.63 (br s, 1H, CH), 3.3-3.45 (m, 3H, CH), 3.65-3.72 (m, 1H, CH), 3.9-4.2 (m, 3H, CH), 6.14 (d, 2H, H-Ar, J = 7.0 Hz), 7.26 (t, 1H, HAr, J = 7.0 Hz), 7.53 (d, 1H, H-Ar, J = 8.0 Hz), 7.60-7.75 (m, 2H, H-Ar); MS: *m/z* (%) 427 (M⁺, 26.4%); *Anal.* Calcd. for C₂₀H₁₆Cl₂N₆O: C, 56.22; H, 3.77; N, 19.67. Found: C, 56.47; H, 3.58; N, 19.43.

2-(3,5-Difluorophenyl)-5-(8-oxo-1,5,6,8-tetrahydro-2H,4H-1,5-methanopyrido[1,2-a][1,5]diazocin-3-yl)-2H-[1,2,3]triazole-4-carbonitrile (18f). Grey solid (1.35 g, 72%); mp 107-109 °C; ¹H NMR (250 MHz): δ 2.04 (br s, 2H, CH₂), 2.65 (br s, 1H, CH), 3.25-3.40 (m, 3H, CH), 3.90 (d, 1H, CH, J = 15.5, 6.3 Hz), 3.85-4.05 (m, 2H, CH), 4.11 (d, 1H, CH, J = 13.0 Hz), 6.16 (d, 2H, H-Ar, J = 7.0 Hz), 7.24-7.31 (m, 3H, H-Ar), 7.87-7.93 (m, 2H, H-Ar); ¹³C NMR (100 MHz): δ 24.3, 26.4, 33.3, 48.9, 53.4, 54.5, 102.6 (d, 2C J = 20.9 Hz), 103.9 (t, J = 24.8 Hz), 104.6, 108.3, 113.0, 115.9, 138.9, 139.6 (t, 2C, J = 13.3 Hz), 149.9, 157.7, 161.6 (d, J=244.8 Hz), 162.0; MS: *m/z* (%) 394 (M⁺, 25%); *Anal.* Calcd. for C₂₀H₁₆F₂N₆O: C, 60.91; H, 4.09; N, 21.31. Found: C, 60.73; H, 4.28; N, 21.07.

2-(4-Chlorophenyl)-5-[4-(3-chlorophenyl)-piperazin-1-yl]-2H-[1,2,3]triazole-4-carbonitrile (19). Grey solid (1.30 g, 65%); mp 154-155 °C; ¹H NMR (250 MHz): δ 3.19-3.43 (m, 4H, 2CH₂), 3.43-3.65 (m, 4H, 2CH₂), 6.78 (d, 1H, H-Ar, J = 7.8 Hz), 6.90 (d, 1H, H-Ar, J = 8.2 Hz), 6.90-7.0 (m, 1H, H-Ar), 7.19 (dd, 1H, H-Ar, J = 8.0, 1.9 Hz), 7.54 and 7.95 (AA'XX', 4H, H-Ar, J = 8.3 Hz) 7; MS: *m/z* (%) 399 (M⁺, 23%); *Anal.* Calcd. for C₁₉H₁₆Cl₂N₆: C, 57.16; H, 4.04; N, 21.05. Found: C, 57.38; H, 4.25; N, 21.36.

2-(4-Chlorophenyl)-5-[4-(3-methoxyphenyl)-piperazin-1-yl]-2H-[1,2,3]triazole-4-carbonitrile (20). Grey solid (0.91 g, 55%); mp 170-171 °C; ¹H NMR (250 MHz): δ 3.31-3.35 (m, 4H, 2CH₂), 3.63-3.67 (m, 4H, 2CH₂), 3.75 (s, 3H, OMe), 6.36 (dd, 1H, H-Ar, J = 7.8, 2.1 Hz), 6.47-6.50 (m, 1H, H-Ar), 6.55 (dd, 1H, H-Ar, J = 8.3, 1.8 Hz), 7.10 (dd, 1H, H-Ar, J = 8.3, 1.8 Hz), 7.54 and 7.96 (AA'XX', 4H, H-Ar, J = 8.5 Hz); MS: *m/z* (%) 394 (M⁺, 45%); *Anal.* Calcd. for C₂₀H₁₉ClN₆O: C, 60.84; H, 4.85; N, 21.28. Found: C, 60.57; H, 4.95; N, 21.47.

2-(4-Chlorophenyl)-5-(4-pyridin-2-yl-piperazin-1-yl)-2H-[1,2,3]triazole-4-carbonitrile 21. Grey solid (1.50 g, 90%); mp 146-148 °C; ¹H NMR (250 MHz): δ 3.58-3.61 (m, 4H, 2CH₂), 3.69-3.72 (m, 4H, 2CH₂), 6.69 (t, 1H, H-Pyr, J = 4.9 Hz), 6.92 (d, 1H, H-Pyr, J = 5.0 Hz), 7.58 (t, 1H, H-Ar, J = 7.4 Hz), 7.65 and 7.98 (AA'XX', 4H, H-Ar, J = 9.0 Hz), 7.57 (t, 1H, H-Pyr, J = 4.9 Hz); ¹³C NMR (100 MHz): δ 43.7 (2C), 46.7 (2C), 107.4, 107.8, 113.3, 113.5, 118.6 (2C), 128.7, 129.8 (2C), 137.6, 138.2, 147.6, 157.8, 158.7; MS: *m/z* (%) 365 (M⁺, 35%); *Anal.* Calcd. for C₁₈H₁₆ClN₇: C, 59.10; H, 4.41; N, 26.80. Found: C, 59.35; H, 4.65; N, 26.57.

2-(4-Chlorophenyl)-5-(4-pyrimidin-2-yl-piperazin-1-yl)-2H-[1,2,3]triazole-4-carbonitrile 22. Grey solid (1.55 g, 85%); mp 116-117 °C; ¹H NMR (250 MHz): δ 3.52-3.61 (m, 4H, 2CH₂), 3.95-3.99 (m, 4H, 2CH₂), 6.61 (t, 1H, H-Pyrim, J = 4.3 Hz), 7.54 and 7.95 (AA'XX', 4H, H-Ar, J = 8.8 Hz), 8.33 (d, 2H, H-Pyrim, J = 4.3 Hz); MS: *m/z* (%) 366 (M⁺, 54.5%); *Anal.* Calcd. for C₁₇H₁₅ClN₈: C, 55.67; H, 4.12; N, 30.55. Found: C, 55.45; H, 4.25; N, 30.27.

Fungicide Screening Method. Using the fungi growth inhibition method for fungicide activity determination.¹¹ A solution of the compound in a concentration of 500 mg/mL was dissolved in water assisted by DMF (0.1mL) and then 50 µg/mL of the compound was placed on an agar plate, the fungi were inoculated and cultured in the culture tank at 24 °C-26 °C. The diameter of the fungi spread was measured two days later, and the growth inhibition was calculated by comparison to the corresponding control.

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