Utility of Cyano Acid Hydrazide in Heterocyclic Chemistry: A New Route for the Synthesis of New 1,2,4-Triazolo[1,5-a]pyridines and 1,2,4-Triazolo[1,5-a]isoquinolines

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1,2,4-Triazolo[1,5-a]pyridines, 1,2,4-Triazolo[1,5-a]isoquinolines

Cyano acid hydrazide **1** was condensed with cyclohexanone in refluxing ethanolic piperidine to yield the hydrazone **4**. Compound **4** reacts with arylidines **5a–i** to yield the 1,2,4-triazolo[1,5-a]pyridines **7a–i**. Compound **4** also reacts with mixtures of aliphatic aldehydes and different active methylene reagents to yield 1,2,4-triazolo[1,5-a]pyridines **8a–d**. Similarly reaction of **4** with arylazomalononitrile to yield the triazolopyridines **10a–d**. Reaction of **4** with aromatic aldehydes gives **12a–e**. Compound **8a** reacts with elemental sulfur to yield the thieno-1,2,4-triazolopyridine **13**. This underwent cycloaddition with acrylonitrile, ω-nitrostyrene, chalcone, N-phenylmalemide, dimethylacetylenedicarboxylate and tetracyanoethylene yielding the isoquinolines **15–18**. All new compounds have been characterized by their IR, ^{1}H NMR and mass spectra.

Introduction

Polyfunctionally substituted heteroaromatics are interesting as potential biodegradable agrochemicals [1,2] intermediates in dye industry [3,4] and as pharmaceuticals [5,6]. In spite of enormous number of papers published every year describing synthesis of such compunds, general inexpensive routes are rather limited. In recent years we were involved in programme directed at developing efficient synthesis of polyfunctionally heteroaromatics from simple and inexpensive starting materials [7–10]. In previous publications we have shown that **1** is an excellent adduct for the synthesis of heterocyclic systems [11]. In conjunction with this work we report here the results of our further investigation on cyano acid hydrazide **1**.

Results and Discussion

It has been found that condensation of **1** with cyclohexanone in refluxing ethanolic piperidine yields the hydrazone **4** or **3**. The possibility that the ketone has condensed with the active methylene function in **1** was excluded based on spectral data IR, ^{1}H NMR and MS. The IR spectrum of the reaction product reveals the absence of an NH_2 group and the ^{1}H NMR spectrum exhibits a signal at δ 2.8 ppm for a CH_2 moiety. Compound **4** reacts with arylidinemalononitrile **5a–d**, arylidinecyanoacetate **5e,f** and arylidinecyanothioacetamide **5g–i** to yield product of addition and hydrogen elimination which may be formulated as the oxidized adduct **6** or the 1,2,4-triazolopyridines **7a–i**. Structures **7a–i** were considered to be the only reaction products based on spectroscopic data. Thus no NH_2 signal can be detected in the IR spectrum of **7a** whereas the ^{1}H NMR spectrum of **7a** shows two signals at δ 2.9 ppm and δ 3.2 ppm for two NH groups.

Recently we have shown that mixture of aliphatic aldehyde and malononitrile can be used as synthetic equivalents to alkylidinemalononitrile [12]. Thus compound **4** reacts with mixtures of acetaldehyde/malononitrile, acetaldehyde/ethyl cyanoacetate as well as with mixtures of formaldehyde/malononitrile and formaldehyde/ethyl cyanoacetate to yield the 1,2,4-triazolo[1,5-a]pyridines **8a–d**. The arylazomalononitriles **9a–d** reacts with compound **4** to yield the 1,2,4-triazolo[1,5-a]pyridines **10a–d**.

Attempts were made to cendense **4** with aromatic aldehydes to form **11**. However under a variety of conditions only **12a–e** were formed. The structure of compounds **12a–e** were confirmed by spectroscopic data (IR, ^{1}H NMR and MS). It is interesting to report that compound **12** cannot be

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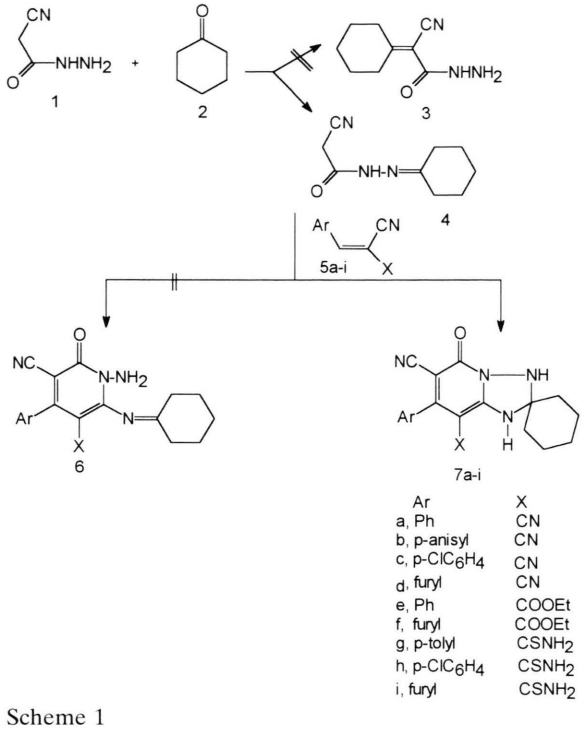
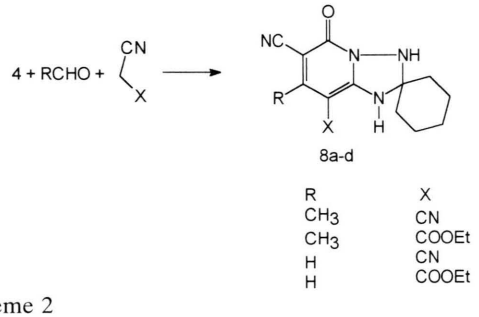
readily obtained by direct condensation of cyclohexanonehydrazone and aromatic aldehyde or by condensation of arylhydrazone with cyclohexanone.

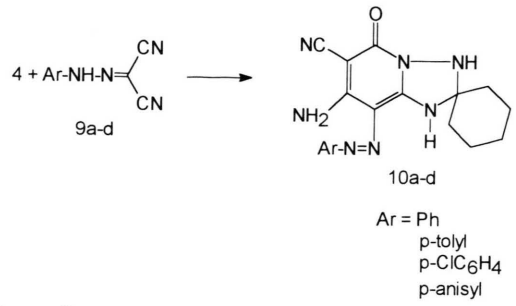


Scheme 1

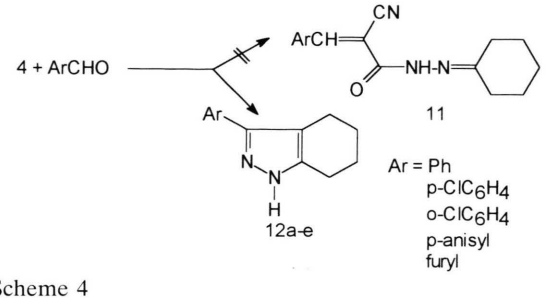


Scheme 2

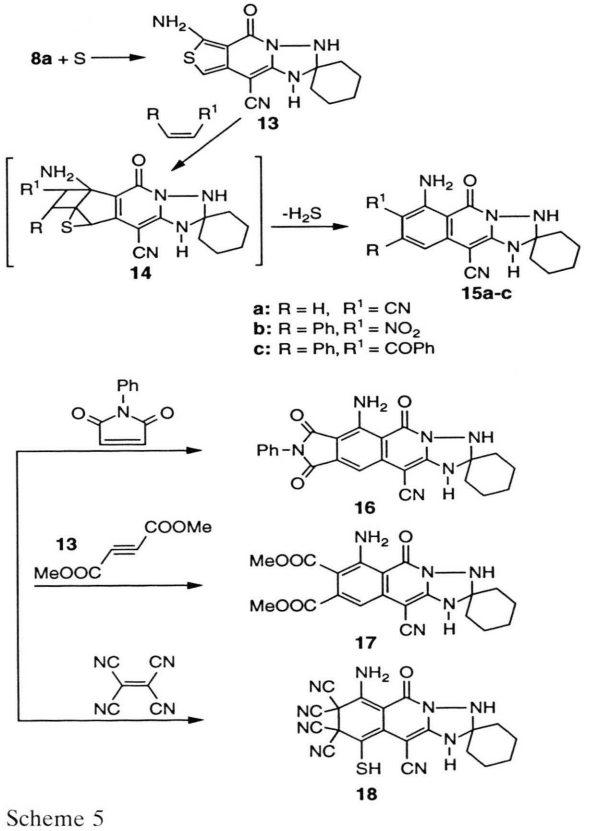
In the last few years a new synthesis of benzoazines utilizing alkylazinylcarbonitriles as starting materials has been reported [7, 13]. We have found that compound **8a** reacts with elemental sulfur in ethanolic triethylamine to yield thieno-1,2,4-triazolopyridine **13**. This underwent, cycloaddition with acrylonitrile, ω-nitrostyrene, chalcone, N-phenylmalemide, dimethylacetylenedicarboxylate and tetracyanoethylene yielding the isoquinolines **15a–c** and **16–18**. All new compounds have been



Scheme 3



Scheme 4



Scheme 5

characterized by their IR, ^{1}H NMR and mass spectra. Comound **15a** was produced either from reaction of **13** with acrylonitrile or from the reaction of **8a** with formaldehyde and malononitrile.

Experimental

All melting points are uncorrected. IR spectra were recorded on a Shimadzu 470 spectrophotometer, ^{1}H NMR spectra were measured with a Varian Em-390 spectrometer. Microanalyses were performed by the microanalytical data unit at Cairo University. Mass spectra were recorded with a mass spectrometer MS 30 MS 9 (AEI) at 70 ev.

Preparation of N-cyclohexanomethylidine-2-cyanoacetohydrazide (**4**)

To a solution of **1** (0.01 mol) in 30 ml ethanol, cyclohexanone **2** (0.01 mol) was added. The reaction mixture was treated with few drops of piperidine and refluxed for 3 h. The solid product was collected by filtration and recrystallized from ethanol as colourless crystals from ethanol (85%); m.p. 160 °C; IR: 3300–3220 cm^{-1} (NH); 2200 cm^{-1} (CN); 1670 cm^{-1} (CO); ^{1}H NMR: δ 1.2–1.4 (m, 10H, cyclohexyl-H); 2.8 (s, 2H, CH_2); 11.4 (s, 1H, NH); MS: *m/z* 179 (M^+).

$C_9H_{13}N_3O$

Calcd	C 60.32	H 7.31	N 23.45%,
Found	C 60.5	H 7.4	N 23.6%.

General procedure for the preparation of **7a–i**

To a solution of **4** (0.01 mol) in ethanol (50 ml), the appropriate arylidines reagent (0.01 mol) were added. The reaction mixture was treated with few drops of piperdine, then refluxed for 3 h. The solid product was collected by filtration and recrystallized from the proper solvent.

5-Oxo-1H-2,3-dihydro-7-phenyl-2-sprio[cyclohexan-1,2,4-triazolo[1,5-a]pyridine]-6,8-dicarbonitriles (**7a**)

Compound **7a** was obtained as green crystals from ethanol (69%); m.p. 310 °C; IR: 3420–3300 cm^{-1} (2NH); 2225, 2220 cm^{-1} (2CN); 1650 cm^{-1} (CO); ^{1}H NMR: δ 1.2–1.4 (m, 10H, cyclohexyl-H); 2.9 (s, 1H, NH); 3.2 (s, 1H, NH); 7.0–7.6 (m, 5H, aromatic CH); MS: *m/z* 331 (M^+).

$C_{19}H_{17}N_5O$ (331.38)

Calcd	C 68.87	H 5.17	N 21.13%,
Found	C 68.9	H 5.4	N 21.3%.

5-Oxo-1H-2,3-dihydro-7-p-anisyl-2-spiro[cyclohexan-1,2,4-triazolo[1,5-a]pyridine]-6,8-dicarbonitriles (**7b**)

Compound **7b** was obtained as colourless crystals from ethanol (73%); m.p. 265 °C; IR: 3410–3320 cm^{-1} (2NH); 2222, 2220 cm^{-1} (2CN); 1650 cm^{-1} (CO); ^{1}H NMR: δ 1.2–1.4 (m, 10H, cyclohexyl-H); 3.8 (s, 3H, OCH_3); 5.7 (s, 1H, NH); 7.0–7.6 (m, 4H, aromatic H); 8.4 (s, 1H, NH); MS: *m/z* 361 (M^+).

$C_{20}H_{19}N_5O_2$ (361.40)

Calcd	C 66.47	H 5.30	N 15.38%,
Found	C 66.6	H 5.4	N 19.5%.

5-Oxo-1H-2,3-dihydro-7-(p-Cl-phenyl)-2-spiro[cyclohexan-1,2,4-triazolo[1,5-a]pyridine]-6,8-dicarbonitriles (**7c**)

Compound **7c** was obtained as colourless crystals from ethanol (69%); m.p. 120 °C; IR: 3420–3300 cm^{-1} (2NH); 2225, 2220 cm^{-1} (2CN); 1650 cm^{-1} (CO); ^{1}H NMR: δ 1.2–1.4 (m, 10H, cyclohexyl-H); 7.2–7.6 (m, 4H, aromatic H); 11.3 (s, 2H, 2NH); MS: *m/z* 265 (M^+).

$C_{19}H_{16}N_5OCl$ (265.82)

Calcd	C 62.38	H 4.41	N 19.14	Cl 9.96%,
Found	C 62.5	H 4.6	N 19.3	Cl 9.6%.

5-Oxo-1H-2,3-dihydro-7-furyl-2-spiro[cyclohexan-1,2,4-triazolo[1,5-a]pyridine]-6,8-dicarbonitriles (**7d**)

Compound **7a** was obtained as brown crystals from ethanol (69%); m.p. 280 °C; IR: 3420–3300 cm^{-1} (2NH); 2224, 2220 cm^{-1} (2CN); 1650 cm^{-1} (CO); ^{1}H NMR: (insoluble); MS: *m/z* 321 (M^+).

$C_{17}H_{15}N_5O_2$ (321.34)

Calcd	C 63.54	H 4.71	N 21.79%,
Found	C 63.8	H 4.9	N 21.9%.

Ethyl-6-cyano-7-phenyl-5-oxo-1H-2,3-dihydro-2-spiro[cyclohexan-1,2,4-triazolo[1,5-a]pyridine]-8-carboxylate (**7e**)

Compound **7e** was obtained as orange crystals from diethyl ether (65%); m.p. 110 °C; IR: 3390–3350 cm^{-1} (2NH), 2200cm^{-1} (CN); 1720 cm^{-1} (CO ester); 1650 cm^{-1} (CO); ^{1}H NMR: δ 1.2–1.4 (m, 10H, cyclohexyl-H); 1.7 (t, 3H, CH_3); 3.2 (s, 2H, 2NH); 4.2 (q, 2H, CH_2); 7.20–7.7 (m, 5H, aromatic CH); MS: *m/z* 378 (M^+).

$C_{21}H_{22}N_4O_3$ (378.43)

Calcd	C 66.65	H 5.86	N 14.81%,
Found	C 66.8	H 6.0	N 15.0%.

Ethyl-6-cyano-7-furyl-5-oxo-1H-2,3-dihydro-2-spiro[cyclohexan-1,2,4-triazolo[1,5-a]pyridine]-8-carboxylate (**7f**)

Compound **7f** was obtained as red crystals from ethanol (65%); m.p. 280 °C; IR: 3400–3350 cm^{-1} (2NH), 2200 cm^{-1} (CN); 1730 cm^{-1} (CO ester); 1650 cm^{-1} (CO); ^1H NMR: (insoluble); MS: *m/z* 368 (M^+).

$C_{19}H_{20}N_4O_4$ (368.39)

Calcd	C 61.95	H 5.47	N 15.71%,
Found	C 62.2	H 5.6	N 15.4%.

6-Cyano-7-(p-tolyl)-5-oxo-1H-2,3-dihydro-2-spiro[cyclohexan-1,2,4-triazolo[1,5-a]pyridine]-8-thiocarboxamide (**7g**)

Compound **7g** was obtained as gray crystals from ethanol (70%); m.p. 180 °C; IR: 3400–3350 cm^{-1} (NH_2); 3350–3100 cm^{-1} (2NH); 2200 cm^{-1} (CN); 1650 cm^{-1} (CO); ^1H NMR: δ 1.3–1.5 (m, 10H, cyclohexyl-H); 2.0 (s, 3H, CH_3); 3.1 (s, 2H, 2NH); 7.2–7.7 (m, 4H, aromatic CH); MS: *m/z* 379 (M^+).

$C_{20}H_{21}N_5OS$ (379.48)

Calcd	C 63.3	H 5.58	N 18.46	S 8.45%,
Found	C 63.5	H 5.8	N 18.5	S 8.6%.

6-Cyano-7-(p-Cl-phenyl)-5-oxo-1H-2,3-dihydro-2-spiro[cyclohexan-1,2,4-trizolo[1,5-a]pyridine]-8-thiocarboxamide (**7h**)

Compound **7h** was obtained as yellow crystals from diethyl ether (74%); m.p. 130 °C; IR: 3400–3370 cm^{-1} (NH_2); 3370–3100 cm^{-1} (2NH), 2200 cm^{-1} (CN); 1650 cm^{-1} (CO); MS: *m/z* 399 (M^+).

$C_{19}H_{18}N_5OSCl$ (399.90)

Calcd	C 57.07	H 4.54	N 17.51	S 8.02%,
Found	C 57.3	H 4.7	N 17.8	S 8.3%.

6-Cyano-7-furyl-5-oxo-1H-2,3-dihydro-2-spiro[cyclohexan-1,2,4-triazolo[1,5-a]pyridine]-8-thiocarboxamide (**7i**)

Compound **7i** was obtained as gray crystals from ethanol (70%); m.p. 278 °C; IR: 3400–3300 cm^{-1} (NH_2); 3300–3100 cm^{-1} (2NH), 2200 cm^{-1} (CN); 1650 cm^{-1} (CO); MS: *m/z* 355 (M^+).

$C_{17}H_{17}N_5O_2S$ (355.41)

Calcd	C 57.45	H 4.82	N 19.7	S 9.02%,
Found	C 57.5	H 4.8	N 19.9	S 9.3%.

General procedure for the preparation of **8a–d**

To a solution of 4 (0.01 mol) in ethanol (50 ml), the appropriate aliphatic aldehyde and the appropriate active methylene reagent (0.01 mol) were added. The reaction mixture was treated with few drops of piperidine, then refluxed for 3 h. The solid product was collected by filtration and recrystallized from the proper solvent.

7-Methyl-5-oxo-1H-2,3-dihydro-2-spiro-[cyclohexan-1,2,4-triazolo[1,5-a]pyridine]-6,8-dicarbonitriles (**8a**)

Compound **8a** was obtained as colourless crystals from DMF/ethanol (80%); m.p. 310 °C; IR: 3361–3316 cm^{-1} (2NH); 2225 cm^{-1} (CN); ^1H NMR: δ 1.0–1.4 (m, 10H, cyclohexyl-H); 1.8 (s, 3H, CH_3); 3.2 (s, 2H, 2NH); MS: *m/z* 269 (M^+).

$C_{14}H_{15}N_5O$ (269.31)

Calcd	C 62.44	H 5.61	N 26.01%,
Found	C 62.6	H 5.8	N 26.3%.

Ethyl-6-cyano-7-methyl-5-oxo-1H-2,3-dihydro-2-spiro[cyclohexan-1,2,4-triazolo[1,5-a]pyridine]-8-carboxylate (**8b**)

Compound **8b** was obtained as buff crystals from ethanol (75%); m.p. 200 °C; IR: 3422, 3330 cm^{-1} (2NH); 2210 cm^{-1} (CN); 1717 cm^{-1} (CO ester); 1653 cm^{-1} (CO); ^1H NMR δ 1.0–1.3 (m, 13H, CH_3, cyclohexyl-H); 1.6 (t, 3H, CH_3); 3.2 (s, 2H, 2NH); 4.2 (q, 2H, CH_2); MS: *m/z* 316 (M^+).

$C_{16}H_{20}N_4O_3$ (316.16)

Calcd	C 60.75	H 6.37	N 17.71%,
Found	C 60.9	H 6.8	N 17.9%.

5-Oxo-1H-2,3,7-trihydro-2-spiro[cyclohexan-1,2,4-triazolo[1,5-a]pyridine]-6,8-dicarbonitriles (**8c**)

Compound **8c** was obtained as yellow crystals from DMF/ethanol (73%); m.p. 320 °C; IR: 3360–3330 cm^{-1} (2NH); 2222, 2220 cm^{-1} (2CN); 1650 cm^{-1} (CO); MS: *m/z* 255 (M^+).

$C_{13}H_{13}N_5O$ (255.28)

Calcd	C 61.17	H 5.13	N 27.43%,
Found	C 61.4	H 5.3	N 27.6%.

Ethyl-6-cyano-5-oxo-1H-2,3,7-trihydro-2-spiro-[cyclohexan-1,2,4-triazolo[1,5-a]pyridine]-8-carboxylate (**8d**)

Compound **8d** was obtained as red crystals from ethanol (78%); m.p. 165 °C; IR: 3329–3320 cm^{-1} (2NH); 2221 cm^{-1} (CN); 1739 cm^{-1} (CO ester); 1645 cm^{-1} (CO); ^1H NMR: δ 1.0–1.3 (m, 10H, cyclohexyl-H); 1.5 (t, 3H, CH_3); 3.0 (s, 2H, 2NH); 4.2 (q, 2H, CH_2); 8.0 (s, 1H, pyridine-H); MS: *m/z* 302 (M^+).

$C_{15}H_{18}N_4O_3$ (302.33)

Calcd	C 59.59	H 6.0	N 18.53%,
Found	C 59.7	H 6.1	N 18.7%.

General procedure for the preparation of **10a–d**

To a solution of **4** (0.05 mol) in ethanol (50 ml), arylazomalononitrile **9a–d** (0.05 mol) and piperidine (2 drops) were added. The reaction mixture was heated under reflux for 3 h then left to stand. The solid product was collected by filtration and recrystallized from the proper solvent.

7-Amino-5-oxo-8-phenylazo-1H-2,3-dihydro-2-spiro[cyclohexan-1,2,4-triazolo[1,5-a]pyridine]-6-carbonitrile (**10a**)

Compound **10a** was obtained as brown crystals from ethanol (80%); m.p. 260 °C; IR: 3390–3350 cm^{-1} (NH_2); 3340–3300 cm^{-1} (2NH); 2215 cm^{-1} (CN); 1653 cm^{-1} (CO); ^1H NMR: δ 1.0–1.3 (m, 10H, cyclohexyl-H); 3.3 (s, 2H, 2NH); 7.0–7.7 (m, 7H, aromatic CH and NH_2); MS: *m/z* 349 (M^+).

$C_{18}H_{19}N_7O$ (349.40)

Calcd	C 61.88	H 5.48	N 28.06%,
Found	C 62.0	H 5.6	N 28.3%.

7-Amino-5-oxo-8-p-tolylazo-1H-2,3-dihydro-2-spiro[cyclohexan-1,2,4-triazolo[1,5-a]pyridine]-6-carbonitrile (**10b**)

Compound **10b** was obtained as brown crystals from ethanol (80%); m.p. 250 °C; IR: 3400–3370 cm^{-1} (NH_2); 3370–3310 cm^{-1} (2NH); 2200 cm^{-1} (CN); 1650 cm^{-1} (CO); ^1H NMR: δ 1.0–1.3 (m, 10H, cyclohexyl-H); 3.0 (s, 2H, 2NH); 3.4 (s, 3H, CH_3); 7.0–7.9 (m, 7H, aromatic CH and NH_2); MS: *m/z* 363 (M^+).

$C_{19}H_{21}N_7O$ (362.42)

Calcd	C 62.79	H 5.82	N 26.98%,
Found	C 62.9	H 6.0	N 27.3%.

7-Amino-5-oxo-8-(p-Cl-phenylazo)-1H-2,3-dihydro-2-spiro[cyclohexan-1,2,4-triazolo-[1,5-a]pyridine]-6-carbonitrile (**10c**)

Compound **10c** was obtained as brown crystals from ethanol (78%); m.p. 262 °C; IR: 3400–3340 cm^{-1} (NH_2); 3340–3300 cm^{-1} (2NH); 2210 cm^{-1} (CN); 1655 cm^{-1} (CO); ^1H NMR: δ 1.0–1.3 (m, 10H, cyclohexyl-H); 3.2 (s, 2H, 2NH); 7.0–7.5 (m, 6H, aromatic CH and NH_2); MS: *m/z* 383 (M^+).

$C_{18}H_{18}N_7OCl$ (383.84)

Calcd	C 56.32	H 4.73	N 25.54%,
Found	C 56.6	H 4.9	N 25.7%.

7-Amino-5-oxo-8-p-anisylazo-1H-2,3-dihydro-2-spiro[cyclohexan-1,2,4-triazolo[1,5-a]pyridine]-6-carbonitrile (**10d**)

Compound **10d** was obtained as brown crystals from ethanol (74%); m.p. 255 °C; IR: 3400–3350 cm^{-1} NH_2; 3350–3320 cm^{-1} (2NH); 2220 cm^{-1} (CN); 1650 cm^{-1} (CO); ^1H NMR δ 1.0–1.3 (m, 10H, cyclohexyl-H); 3.9 (s, 3H, OCH_3); 6,.4 (s, 1H, NH); 6.8 (br, 2H, NH_2); 7.0–8.0 (m, 4H, aromatic CH); 8.0 (s, 1H, NH); MS: *m/z* 379 (M^+).

$C_{19}H_{21}N_7O_2$ (379.42)

Calcd	C 60.5	H 5.58	N 25.84%,
Found	C 60.7	H 6.0	N 26.0%.

General procedure for the preparation of 3-arylcyclohexano[c]-1H-pyrazole (**12a–e**)

A mixture of 2 (0.01 mol) and benzaldehyde (0.01 mol) in ethanol (30 ml) was treated with a little amount of triethylamine, then refluxed for 3 h. The reaction mixture left to stand and the solid product was collected by filtration and recrystallized from the proper solvent.

3-Phenylcyclohexano[c]-1H-pyrazole (**12a**)

Compound **12a** was obtained as orange crystals from ethanol (77%); m.p. 150 °C; IR: 3400–3300 cm^{-1} (NH); 3050 cm^{-1} (aliphatic CH); 1600–1590 cm^{-1} (aromatic CH); ^1H NMR: δ 1.4–1.8 (m, 8H, cyclohexyl-H); 7.2–7.6 (m, 5H, aromatic CH); 8.9 (s, 1H, NH); MS: *m/z* 198 (M^+).

$C_{13}H_{14}N_2$ (198.27)

Calcd	C 78.75	H 7.12	N 14.13%,
Found	C 78.9	H 7.4	N 14.3%.

3-(p-Cl-Phenyl)cyclohexano[c]-1H-pyrazole (**12b**)

Compound **12b** was obtained as yellow crystals from ethanol (75%); m.p. 190 °C; IR: 3400–3100 cm^{-1} (NH); 3030 cm^{-1} (aliphtic CH); 1600–1590 cm^{-1} (aromatic CH); ^1H NMR: δ 1.3–1.9 (m, 8H, cyclohexyl-H); 7.2–7.6 (m, 4H, aromatic H); 8.8 (s, 1H, NH); MS: *m/z* 232 (M^+).

$C_{13}H_{13}N_2Cl$ (232.71)

Calcd	C 67.1	H 5.63	N 12.04	Cl 15.23%,
Found	C 67.3	H 5.8	N 12.3	Cl 15.3%.

3-(o-Cl-Phenyl)cyclohexano[c]-1H-pyrazole (**12c**)

Compund **12c** was obtained as orange crystals from ethanol (75%); m.p. 200 °C; IR: 3390–3290 cm^{-1} (NH); 3060 cm^{-1} (aliphatic CH); 1600–1590 cm^{-1} (aromatic CH); ^1H NMR: δ 1.2–1.6 (m, 8H,

cyclohexyl-H); 7.2–7.6 (m, 4H, aromatic H); 9.0 (s, 1H, NH); MS: *m/z* 232 (M^+).

$C_{13}H_{13}N_2Cl$ (232.71)

Calcd	C 67.1	H 5.63	N 12.04	Cl 15.24%,
Found	C 67.4	H 5.8	N 12.2	Cl 15.3%.

3-p-Anisylcyclohexano[c]-1H-pyrazole (**12d**)

Compound **12d** was obtained as yellow crystals from ethanol (78%); m.p. 188 °C; IR: 3380–3280 cm^{-1} (NH); 3040 cm^{-1} (aliphatic CH); 1600–1590 cm^{-1} (aromatic CH); ^1H NMR: δ 1.3–1.7 (m, 8H, cyclohexyl-H); 3.8 (s, 3H, OCH_3); 7.0–7.6 (m, 5H, aromatic CH and NH); MS: *m/z* 228 (M^+).

$C_{14}H_{16}N_2O$ (228.29)

Calcd	C 73.66	H 7.06	N 12.27%,
Found	C 73.8	H 7.3	N 13.3%.

3-Furylcyclohexano[c]-1H-pyrazole (**12e**)

Compound **12e** was obtained as brown crystals dioxane (82%); m.p. 300 °C; IR: 3400–3310 cm^{-1} (NH); 3050 cm^{-1} (CH); 1600–1590 cm^{-1} (aromatic CH); ^1H NMR: δ 1.4–1.8 (m, 8H, cyclohexyl-H); 2.8 (s, 1H, NH); 6.5–7.0 (m, 3H, furyl CH); MS: *m/z* 188 (M^+).

$C_{11}H_{12}N_2O$ (188.23)

Calcd	C 70.19	H 6.43	N 14.88%,
Found	C 70.3	H 6.8	N 15.0%.

6-Amino-5-oxo-1H-2,3-dihydrothieno[3,4-c]-2-spiro[cyclohexan-1,2,4-triazolo[1,5-a]pyridine]-9-carbonitrile (**13**)

A mixture of **8a** (0.01 mol) and elemental sulfur (0.01 mol) in 50 ml ethanol was treated with a little amount of triethylamine, then refluxed for 3 h. The solid product formed was collected by filtration and recrystallized from ethanol as green crystals (70%); m.p. 290 °C; IR: 3450–3380 cm^{-1} (NH_2); 3350–3300 cm^{-1} (2NH); 2200 cm^{-1} (CN); 1655 cm^{-1} (CO); MS: *m/z* 301 (M^+).

$C_{14}H_{15}N_5OS$ (301.37)

Calcd	C 55.8	H 5.02	N 23.24	S 10.64%,
Found	C 55.9	H 5.2	N 23.5	S 10.8%.

General procedure for the preparation of compounds **15a–c** *and* **16–18**

To a solution of **13** (0.01 mol) in dry pyridine, the appropriate dienophils were added. The reaction mixture was refluxed for 3 h. Then poured on ice-cold water and neutralized with dilute HCl. The solid product was collected by filtration and recrystallized from the proper solvent.

6-Amino-4-oxo-1H-2,3-dihydro-2-spiro-[cyclohexan-1,2,4-triazolo[1,5-a]isoquinoline]-7,10-dicarbonitriles (**15a**)

Compound **15a** was obtained as orange crystals from ethanol (69%); m.p. 315 °C; IR: 3440–3350 cm^{-1} (NH_2); 3317–3191 cm^{-1} (2NH); 2222 cm^{-1} (2CN); 1650 cm^{-1} (CO); ^1H NMR: δ 1.4–1.8 (m, 10H, cyclohexyl-H); 2.8 (s, 2H, 2NH); 7.8–8.0 (m, 4H, aromatic CH and NH_2).

$C_{17}H_{16}N_6O$ (320.35)

Calcd	C 63.74	H 5.03	N 26.23%,
Found	C 63.9	H 5.3	N 26.4%.

6-Amino-7-nitro-8-phenyl-4-oxo-1H-2,3-dihydro-2-spiro[cyclohexan-1,2,4-triazolo[1,5-a]-isoquinoline]-10-carbonitrile (**15b**)

Compound **15b** was obtained as gray crystals from dioxane (60%); m.p. 250 °C; IR: 3390–3350 cm^{-1} (NH_2); 3300–3200 cm^{-1} (2NH); 2200 cm^{-1} (CN); 1645 cm^{-1} (CO); MS: *m/z* 416 (M^+).

$C_{22}H_{20}N_6O_3$ (416.44)

Calcd	C 63.45	H 4.84	N 20.18%,
Found	C 63.6	H 5.0	N 20.3%.

6-Amino-7-benzoyl-8-phenyl-4-oxo-1H-2,3-dihydro-2-spiro[cyclohexan-1,2,4-triazolo-[1,5-a]isoquinoline]-10-carbonitrile (**15c**)

Compound **12c** was obtained as yellow crystals from DMF/ethanol (70%); m.p. 310 °C; IR: 3430 cm^{-1} (NH_2); 3300–3200 cm^{-1} (2NH); 2200 cm^{-1} (CN); 1665 and 1650 cm^{-1} (2CO); ^1H NMR: δ 1.4–1.8 (m, 10H, cyclohexyl-H); 2.8 (s, 2H, 2NH); 7.2–8.2 (m, 13H, aromatic CH and NH_2); MS: *m/z* 427 (M^+).

$C_{25}H_{25}N_5O_2$ (427.51)

Calcd	C 70.24	H 5.89	N 16.38%,
Found	C 70.4	H 5.9	N 16.5%.

6-Amino-8-phenyl-5,7,9-trioxo-1H-2,3-dihydro-2-spiro[cyclohexan-1,2,4-triazolo-[1,5-a]isoquinoline]-11-carbonitrile (**16**)

Compound **16** was obtained as gray crystals from ethanol (66%); m.p. 270 °C; IR: 3400–3370 cm^{-1} (NH_2); 3300–3200 cm^{-1} (2NH); 2200 cm^{-1} (CN); 1660 and 1650 cm^{-1} (CO);^1H NMR: δ 1.4–1.8 (m, 10H, cyclohexyl-H); 3.0 (s, 2H, 2NH); 7.2–8.2 (m, 8H, aromatic CH and NH_2); MS: *m/z* 440 (M^+).

$C_{24}H_{20}N_6O_3$ (440.46)

Calcd	C 65.45	H 4.58	N 19.08%,
Found	C 65.7	H 4.8	N 19.3%.

Methyl-6-amino-10-cyano-5-oxo-1H-2,3-dihydro-2-spiro[cyclohexan-1,2,4-triazolo[1,5-a]-isoquinoline]-7,8-dicarboxlyte (**17**)

Compound **17** was obtained as gray crystals from DMF/ethanol (73%); m.p. 310 °C IR: 3400–3350 cm^{-1} (NH_2); 3350–3220 cm^{-1} (2NH); 2200 cm^{-1} (CN); 1680 and 1650 cm^{-1} (2CO); ^1H NMR: δ 3.7 (s, 6H, $2CH_3$); 4.0–4.5 (m, 10H, cyclohexyl-H); 8.2 (m, 3H, aromatic CH and NH_2); 8.7 (s, 2H, 2NH); MS: *m/z* 411 (M^+).

$C_{20}H_{21}N_5O_5$ (411.42)

Calcd	C 58.39	H 5.4	N 17.02%,	
Found	C 58.6	H 5.4	N 17.3%.	

6-Amino-5-oxo-10-mercapto-1H-2,3-dihydro-2-spiro[cyclohexan-1,2,4-triazolo[1,5-a]-isoquinoline]-7,8,10-pentacarbonitriles (**18**)

Compound **18** was obtained as gray crystals from DMF/ethanol (66%); m.p. 320 °C; IR: 3410–3330 cm^{-1} (NH_2); 3320–3200 cm^{-1} (2NH); 2200 cm^{-1} (CN); 1650 cm^{-1} (CO); ^1H NMR: (insoluble); MS: *m/z* 429 (M^+).

$C_{20}H_{15}N_9OS$ (429.46)

Calcd	C 55.94	H 3.52	N 29.35	S 7.47%,
Found	C 56.2	H 3.8	N 29.5	S 7.5%.

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