# Functionally substituted arylhydrazones as building blocks in heterocyclic synthesis: routes to pyridazines and pyridazinoquinazolines

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**Abstract**

The arylhydrazones **2a-c** were prepared via coupling acetoacetic acid with aromatic diazonium salts. These arylhydrazones condensed with ethyl cyanoacetate and malononitrile to yield the acyclic product **4** which cyclised only after long reflux into the pyridazines **5** or 6,11-dihydropyridazino[1,6-*a*]quinazoline-4-carbonitrile **6** depending on the nature of substituent on the aryl moiety. Compound **2b** and **2c** reacted with α,β-unsaturatednitriles **7** to yield the pyridazinoquinazoline **13** and **16** respectively.

**Keywords**: Azaenamines, pyridazines, pyridazinoquinazolines

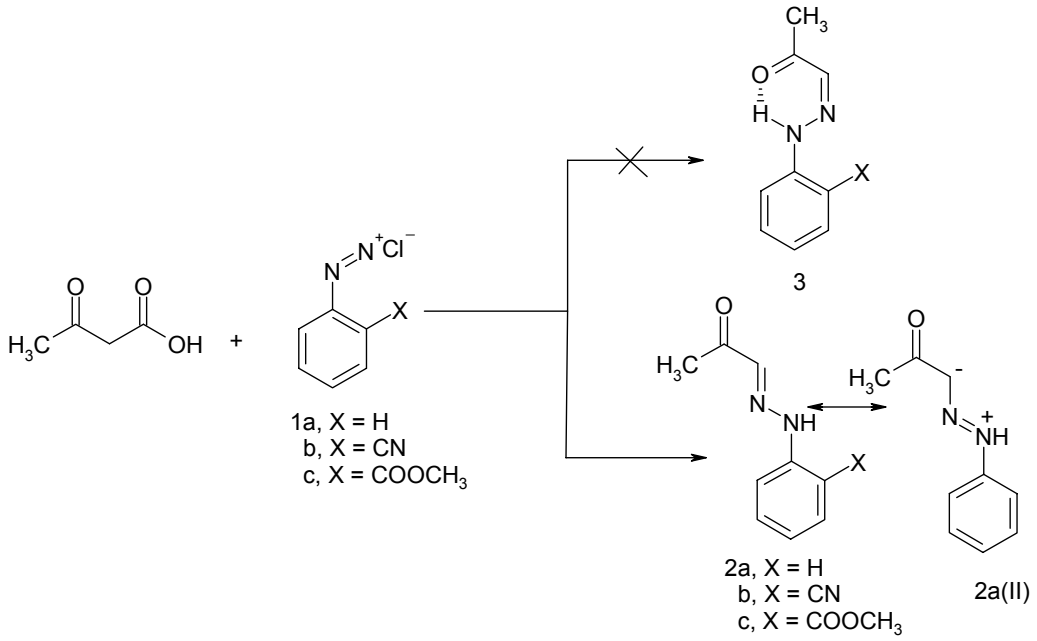
## Introduction

The chemistry and pharmacology of pyridazines has recently received considerable interest. This can be readily realized from vast number of papers and patents dealing with synthesis [1-5], chemistry [6-8], and biological activities of pyridazine derivatives [9,10]. In the last few years we have been involved in a programme aimed at developing efficient syntheses of pyridazines and fused pyridazines [11-14] utilizing functionally substituted arylhydrazones precursors. In conjunction of this work we report here routes to pyridazinones, and pyridazinoquinazolines utilizing the readily obtainable **2a-c** as starting materials.

## Results and Discussion

Coupling acetoacetic acid with the diazonium salts **1a-c** has afforded the corresponding pyruvaldehyde arylhydrazones **2a-c** in 74-90.8 % yields. Although it seemed logical to assign to syn structure **3** for these compounds based on observed low field NH signal that is attributable to

deshielding by hydrogen bonding, X-ray crystal structure of **2a** (figure 1) indicated that it exists in the antiform **2a**. The low field hydrazone NH at δ 12 ppm is not thus due to deshielding by hydrogene bonding as has been claimed earlier but most likely resulted from delocalization of nitrogen lone pair (C.f. Scheme 1 structure **2a(II)**). Although, possible hydrogen bonding of hydrazone NH with DMSO cannot be overlooked.




**Scheme 1**

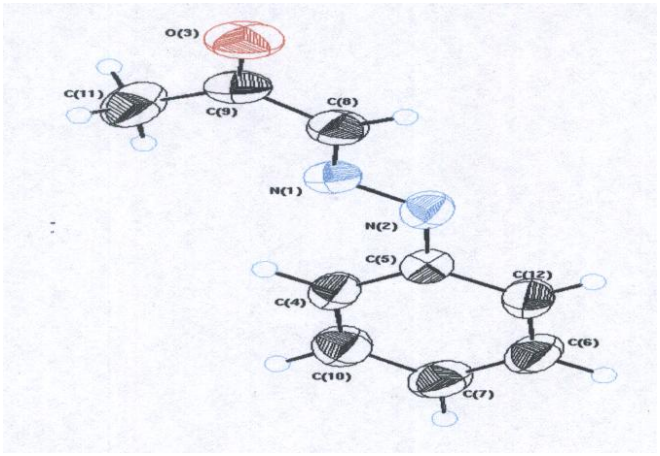
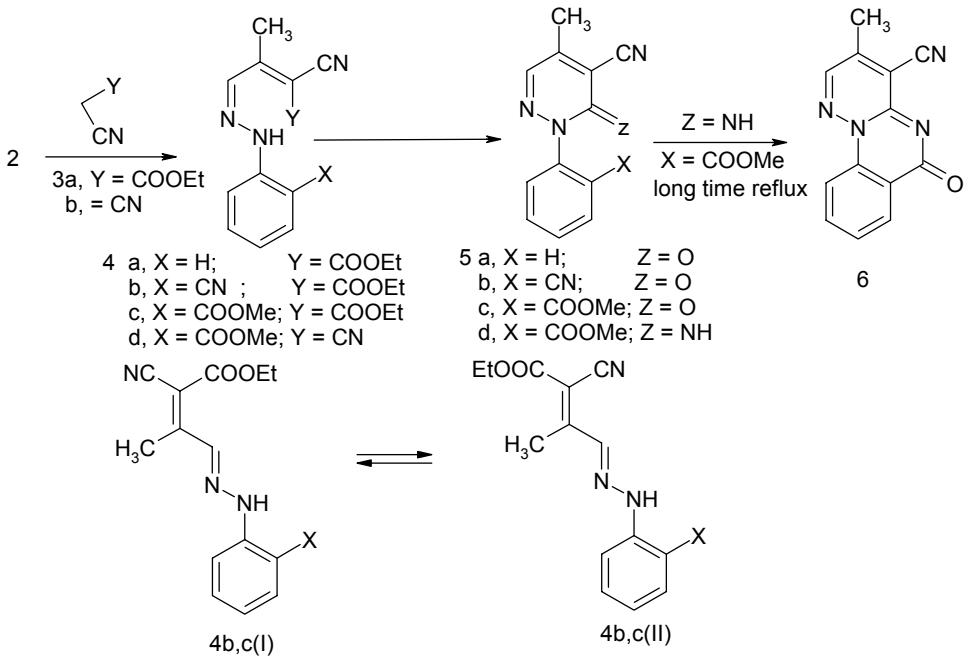



**Figure 1**. X-ray structure of compound 2a

**Table 1.** Selected bond lengths and bond angles for compound 2a

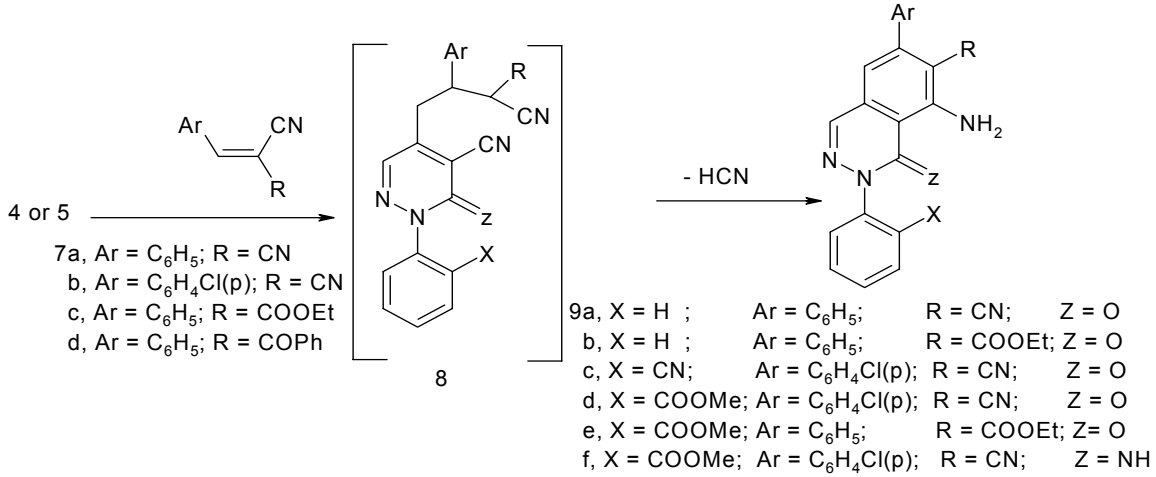
| Bond | Bond length | Bond | Bond angle |
|---|---|---|---|
| N1-N2 | 1.335 | N2-N1-C8 | 117.8 |
| N1C8 | 1.285 | N1-N2-C5 | 121.6 |
| N2-C5 | 1.395 | N2-C5-C4 | 122.4 |
| C8-C9 | 1.450 | O3-C9-C8 | 118.9 |

Compound **2b** condensed with ethyl cyanoacetate **3a** to yield the acyclic condensation product **4b** which cyclised into pyridazine **5b** only on long reflux in acetic acid. This is in contrast to the behavior of **2a**, where the acyclic intermediate **4a** could never be isolated, on reacting it with **3a** [15]. In contrast to the behavior of **2a,b**, compound **2c** condenses with ethyl cyanoacetate to yield acyclic product **4c,** which failed to cyclise into pyridazine **5c** under a variety of conditions. The difference in behavior between **2a,b** and **2c** toward ethyl cyanacetate is believed to result from interaction with the ester function and hydrazone nitrogen which is involved in hydrogen bonding with ester function. $^1$H NMR indicates that **4b,c** exist as a mixture of cis and trans forms **I** and **II**. Thus two overlapping triplets for $CH_3$ ester and two overlapping quartets for $CH_2$ were observed. Aromatic protons revealed expected pattern. Azomethine CH appeared as two signals and it is difficult to assign which CH for which isomer as complex factors are involved in this situation. Compound **2c** also condensed with malononitrile **3b** to yield the acyclic product **4d** which then cyclises into pyridazinooquinazoline derivative **6** via intermediacy of **5d**.



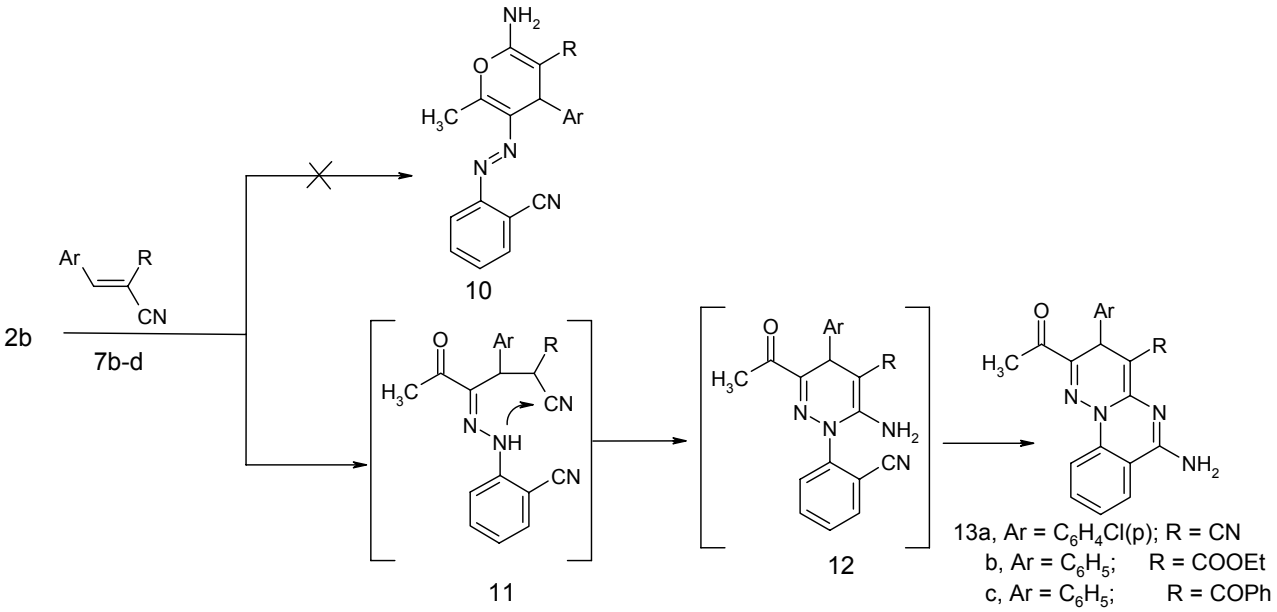

**Scheme 2**

Compounds **5a,b** react readily with α-substituted cinnamonitriles **7a-c** to yield acyclic intermediate **8** that readily cyclized into phthalazine derivatives **9a-c** via hydrogen cyanide elimination. These same products were obtained from reaction of compounds **4b-d** with α-substituted cinnamonitriles. It is believed that compounds **4** are initially cyclised into pyridazines **5** under reaction conditions which then reacts with α-cinnamonitriles to give the targeted molecule. (C.f. scheme 3)



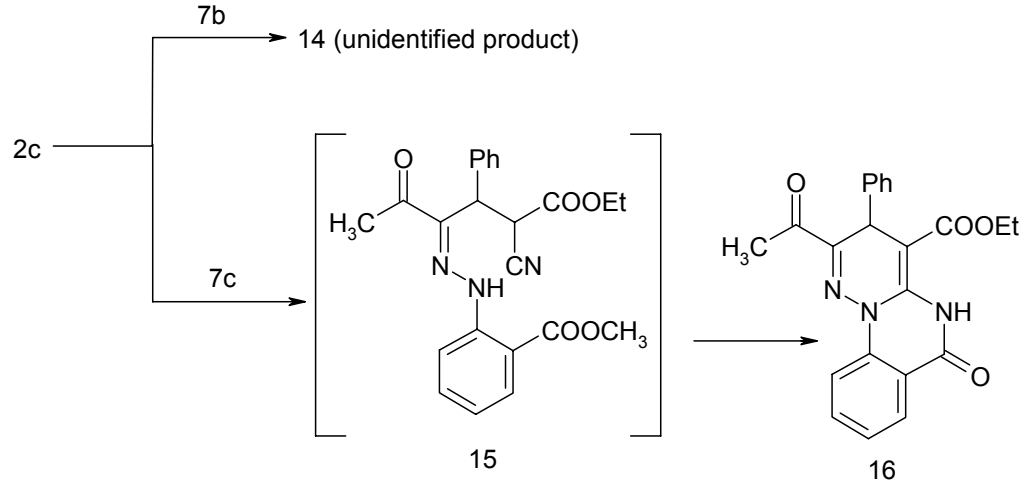

**Scheme 3**

It has recently been shown that aldehydehydrazone CH is electron rich and reacts with electrophiles [16-18]. Although it was proposed that presence of electron donating substituents at hydrazone nitrogen is necessary to maintain reactivity, we could show very recently that aryl hydrazones are also sufficiently reactive toward electrophiles under relatively mild conditions [18]. The reactivity of **2a** toward α,β-unsaturated nitriles has recently been utilized by us to construct a new synthetic approach for 1,4-dihydro-6-aminopyridazines[13]. In the present work we would like to show that even **2b,c** with electron attracting substituents on aryl moiety are also reactive toward electrophiles. Thus reacting **2b** with p-chlorobezylidnemalononitrile **7b**, ethyl benzylidenecyanoacetat **7c**, and 2-benzoyl-3-phenylacrylonitrile **7d** has resulted in formation of 1:1 adduct that can in theory be assigned structures **10-13**. Structure **13a** was readily established based on $^{13}$C NMR that revealed presence of methyl signal at δ 25.21ppm and only one cyano carbon at δ 112.08 ppm. The structures of **13b,c** were elucidated based on IR and NMR where IR spectra revealed the absence of CN signals We believe that initially **11** is formed and cyclized into **12** which then cyclized into **13**. (C.f. Scheme 4).




**Scheme 4**

In contrast to this **2c** reacted with **7b** to yield a product **14** that could not be identified. On the other hand, the reaction of **2c** with **7c** results in the formation of product of cyclization with methanol elimination to give compound **16**. The structure of **16** was elucidated based on IR which indicated the absence of CN band, $^{1}$H NMR which indicated the absence of $OCH_3$ signal, and $^{13}$C NMR spectra which indicated the absence of any CN and $OCH_3$ bands and signals. (C.f. scheme 5).




**Scheme 5**

## Conclusions

We could show that Pyruvaldehyde-1-arylhydrazones **2a-c** are valuable precursors to polyfunctionally substituted pyridazines, and pyridazinoquinazoline, moreover we could clearly show that hydrazone CH in **2** is activated toward electrophiles and thus can undergo Michael addition to α-substituted cinnamonitriles under mild conditions.

## Experimental Section

**General Procedures.** All melting points were determined on a Stuart melting point apparatus and are uncorrected. The $^{1}$H and $^{13}$CNMR spectra (300 MHz) were recorded on Varian Gemini NMR spectrometer. Chemical shifts (δ) are given from TMS (0 ppm) as internal standard for $^{1}$H-NMR and $^{13}$C-NMR. Mass spectra were measured on a Shimadzu GMMS -QP-1000 EX mass spectrometer at 70 eV. The elemental analyses were performed at the micro analytical center, Cairo University. The IR spectra were recorded in KBr using a FTIR unit Bruker-vector 22 spectrophotometer. The crystal structure was determined by the X-ray unit at the National Research Center, Dokki, Cairo.

**Crystallographic analysis for compound 2a**. The crystals were mounted on a glass fiber. All measurements were performed on an ENRAF NONIUNS FR 590. The data were collected at temperature 20 ± 1 $^{o}$C using the ω scanning technique to a maximum of 20 of 27.12$^{o}$. The temperature was solved by direct method using SIR 92 and full-matrix least squares. Nonhydrogen atoms were refined anisotropically. Hydrogen atoms were located geometrically and were refined isotropically.

**Crystal data.** $C_9H_{10}N_2O$, M = 162.19, monoclinic, *a* = 5.4337 (2), *b*= 10.1221 (5), c= 16.1178 (10) Å, α = γ = 90.00$^{o}$, β = 10.(18) *10$^{1o}$ space group: $P2_1/c$. Z =4, $D_x$ = 1.236 Mg m$^{-3}$, reflection 871 measured, $\theta_{max}$ = 25.03$^{o}$ , ωR factor = 0.108

**General procedures for preparation of arylhydrazonopropan-2-one (2)** [ref. 19]A mixture of KOH (3.5 g) in 100 ml of water, and 6.5 ml of ethyl acetoacetate was allowed to stir at room temperature for 24 hours. This solution is then cooled at 0 $^{o}$C temperature and then acidified with 4.5 ml of Conc..HCl in 15 ml of ice water. The resulting solution is the treated with aryldiazonium chloride (prepared from the corresponding aromatic amine (0.05 mol) and the appropriate quantities of both HCl and sodium nitrite). The mixture is made basic by addition of 8.0 g of sodium acetate. The solid product, so formed was collected by filtration.

**(Phenyl-hydrazono)-propan-2-one (2a).** [ref. 19] Yield 1.2 g (74 %) as a solid, which was recrystallized from toluene to give yellow crystals (m.p 148-150) $^{o}$C [lit. m.p. = 148 $^{o}$C]; *Anal*. Calcd. for $C_9H_{10}N_2O$ (162.19): C, 66.65; H, 6.21; N, 17.27. Found: C, 66.43; H, 6.05; N, 17.15. IR (KBr, cm$^{-1}$): 3249.6 (NH), 1649.58 (CO); $^{1}$H MNR (300 MHz, DMSO-d6): δ, ppm: 2.32 (s, 3H, $CH_3$), 6.93 (s, 1H, vinyl-H), 6.95-7.339 (m, 5H, Ph-H), 11.33 (s, 1H, NH).;MS (EI): m/z (%) = 162 ($M^+$).

**2-[*N*"-(2-Oxo-propylidene)-hydrazino]-benzonitrile (2b).** Yield 1.4 g (74.8%) as a solid, which was recrystallized from from ethanol as white solid (m.p: 122-124 $^{o}$C). *Anal*. Calcd. for $C_{10}H_9N_3O$ (187.20): C, 64.16; H, 4.97; N, 22.45. Found: C, 64.45; H, 4.92; N, 22.67. IR (KBr, $cm^{-1}$): 3256.8 (NH), 2222 (CN), 1675 (CO). $^1$H MNR (300 MHz, DMSO-d6): δ, ppm 2.36 (s, 3H, $CH_3$), 7.05-7.11 (m, 1H, Ar-H5), 7.37 (d, 1H, Ar-H6), 7.47 (s, 1H, vinyl-H), 7.59 (m, 1H, Ar-H4), 7.68 (d, 1H, Ar-H3), 11.51 (s, 1H, NH); MS (EI): m/z (%) = 187 ($M^+$).

**2-[*N*"-(2-Oxo-propylidene)-hydrazino]-benzoic acid methyl ester (2c).** Yield 2 g (90.8%) as a solid, which was recrystallized from from ethanol as white solid (m.p: 99-101$^{o}$C). *Anal.* Calcd. for $C_{11}H_{12}N_2O_3$ (220.23): C, 59.99; H, 5.49; N, 12.72. Found: C, 60.20; H, 5.67; N, 12.59. IR (KBr, $cm^{-1}$): 3248.3 (NH), 1677.7, 1593 (CO). $^1$H MNR (300 MHz, DMSO-d6): δ, ppm, δ =2.35 (s, 3H, $CH_3$), 3.87 (s, 3H, $OCH_3$), 7.00-7.06 (m, 1H, Ar-H5), 7.6 (s, 1H, vinyl-H), 7.60-7.63 (m, 1H, Ar-H4), 7.76 (d, 1H, Ar-H3), 7.89 (d, 1H, Ar-H6) 11.37 (s, 1H, NH). MS (EI): m/z (%) = 220 ($M^+$)

**General method for preparation of 4b and 4c.** A mixture of 2b or 2c (0.01 mol), ethyl cyanoacetate (0.01 mol), and ammonium acetate (2g) in acetic acid (20 ml) was heated at 200 $^{o}$C for 5 min, then left to cool and poured onto water. The solid product obtained was crystallized from ethanol.

**2-Cyano-4-[(2-cyano-phenyl)-hydrazono]-3-methyl-but-2-enoic acid ethyl ester (4b).** Yield 2.5 g (88.65%)( m.p:128-130 $^{o}$C). *Anal*. Calcd. for $C_{15}H_{14}N_4O_2$ (282.30): C, 63.82; H, 5.00; N, 19.85. Found: C, 63.72; H, 4.83; N, 19.62. IR (KBr, $cm^{-1}$): 3245.2 (NH), 2228.5 (CN), 1722.5 (CO) $^1$H MNR (300 MHz, DMSO-d6): δ, ppm 1.28 (2 t, 3H,$CH_3$, $J$ = 7.2 Hz), 2.57 (s, 3H, $CH_3$), 4.27 (2 q, 2H, $CH_2$, $J$ = 7.2 Hz), 7.08-7.71 (m, 4H, Ar-H), 8.44 (s, 0.48 H, vinyl -H), 9.11(s, 0.52 H, vinyl-H), 11.99 (s, 1H, NH). MS (EI): m/z (%) = 282 ($M^+$).

**2-[*N*"-(3-cyano-3-ethoxycarbonyl-2-methyl-allylidene)-hydrazino]-benzoic acid methyl ester (4c).** Yield 2.72 g (86.26%) (m.p: 142-144 $^{o}$C). *Anal.* Calcd. for $C_{16}H_{17}N_3O_4$ (315.33): C, 60.94; H, 5.43; N, 13.33. Found: C, 60.82; H, 5.62; N, 13.61. IR (KBr, $cm^{-1}$): 3446.8 (NH), 2211.1 (CN), 1718 , 1681 (CO). $^1$H MNR (300 MHz, DMSO-d6): δ, ppm 1.29 (2 t, 3H, $CH_3$, $J$ = 7.2 Hz), 2.57 (s, 3H, $CH_3$), 3.89 (s, 3H, $OCH_3$), 4.25(2 q, 2H, $CH_2$, $J$ = 7.2 Hz), 7.03-7.89 (m, 4H, Ar-H), 8.42 (s, 0.47 H, vinyl-H), 9.00 (s, 0.53, vinyl-H), 11.75 (s, 1H, NH). MS (EI): m/z (%) = 315 ($M^+$).

**Preparation of 2-[N"-(3,3-dicyano-2-methyl-allylidene)-hydrazino]-benzoic acid methyl ester (4d).** A mixture of 2c (10 mmol), and malononitrile was refluxed in ethanol (20 ml) in presence of piperidine for 5 min. The solvent was evaporated under vacuum and the crude product was collected and crystallized from ethanol / Dioxan.

Yield 2.32 g (86.48%); m.p: 212-214 $^{o}$C. *Anal.* Calcd. for $C_{14}H_{12}N_4O_2$ (268.28): C, 62.68; H, 4.51; N, 20.88. Found: C, 62.42; H, 4.72; N, 20.61. IR (KBr, $cm^{-1}$): 3231.4 (NH), 2218.9 (CN), 1691.9 (CO). $^1$H MNR (300 MHz, DMSO-d6): δ, ppm 2.48(s, 3H, $CH_3$), 3.89(s, 3H, $OCH_3$), 7.10-7.90 (m, 4H, Ar-H), 8.40 (s, 1H, vinyl-H), 11.85 (s, 1H, NH) $^{13}$C MNR (300 MHz, DMSO-d6): δ, ppm 16.88 ($CH_3$), 52.34 ($OCH_3$), 79.87 (C-CN), 112.67, 113.76 (CN), 113.96, 115.49,

122.05, 130.84, 134.54, 135.44 (CH-Ar), 143.66 (CH-vinyl), 166.79 (C-$CH_3$), 168.07 ($COOCH_3$). MS (EI): m/z (%) = 268 ($M^+$).

**General method for preparation of 5a,b.** A mixture of each of 2a or 2b (0.01 mol), ethyl cyanoacetate (0.01 mol), and ammonium acetate (2g) in acetic acid (20 ml) was heated under reflux for 3 hours, then left to cool and poured onto water. The solid product obtained was crystallized from ethanol.

**4-Methyl-6-oxo-1-phenyl-1,6-dihydropyridazine-5-carbonitrile (5a).** Yield 1.82 g (86.16%) (m.p: 158-160 $^oC$) . *Anal.* Calcd. for $C_{12}H_9N_3O$ (211.23): C, 68.24; H, 4.29; N, 19.89. Found: C, 68.16; H, 4.14; N, 20.01. IR (KBr, $cm^{-1}$): 2233 (CN), 1659.4 (CO). $^1H$ MNR (300 MHz, DMSO-d6): δ, ppm 2.47 (s, 3H, $CH_3$), 7.54 - 7.55 (m. 5H, Ar-H), 8.25 (s, 1H, pyridazine-H). $^{13}C$ MNR (300 MHz, DMSO-d6): δ, ppm 19.12 ($CH_3$), 114.06 (C-CN), 114.48 (CN), 126.59, 126.83, 129.77, 129.88 (CH-Ar), 139.91 (CH-pyridazine), 141.60 (C-$CH_3$), 157.08 (CO). MS (EI): m/z (%) = 211 ($M^+$).

**1-(2-Cyano-phenyl)-4-methyl-6-oxo-1,6-dihydropyridazine-5-carbonitrile (5b).** Yield 2.0 g (84.47%) (m.p: 170-172$^oC$). *Anal.* Calcd. for $C_{13}H_8N_4O$ (236.23): C, 66.10; H, 3.41; N, 23.72. Found: C, 66.26; H, 3.54; N, 23.85. IR (KBr, $cm^{-1}$): 2232.8 (CN), 1665.8 (CO). $^1H$ MNR (300 MHz, DMSO-d6): δ, ppm 2.52 (s, 3H, $CH_3$), 7.71-7.76 (m, 2H, Ar-H3,4), 7.93 (m, 1H, Ar-H5), 8.09 (d, 1H, Ar-H6), 8.34 (s, 1H, pyrimidine-H). MS (EI): m/z (%) = 236 ($M^+$)..

**Preparation of 3-methyl-6-oxo-6,11-dihydropyridazino[1,6-a]quinazoline-4-carbonitrile (6)**

A mixture of 2c (10 mmol), and malononitrile was refluxed in ethanol (20 ml) in presence of piperidine for 30 min. The solvent was evaporated under vacuum and the crude product was collected and crystallized from Dioxan.

Yield 2.1 g (88.9%) (m.p: 280-282 $^oC$). *Anal.* Calcd. for $C_{13}H_8N_4O$ (236.23): C, 66.10; H, 3.41; N, 23.72. Found: C, 66.23; H, 3.52; N, 23.61. IR (KBr, $cm^{-1}$): 2234.9 (CN), 1655 (CO). $^1H$ MNR (300 MHz, DMSO-d6): δ, ppm 2.61 (s, 3H, $CH_3$), 7.72-8.39 (m, 4H, Ar-H), 8.78 (s, 1H, pyridazine-H). MS (EI): m/z (%) = 236 ($M^+$).

**General procedure for preparation of phthalazines 9a-f. Methode A**. A mixture of 4 (or 5) (10 mmol), and benzylidene derivatives 7 was refluxed in ethanol (20 ml) in presence of piperidine for 2 h. The solvent was evaporated under vacuum and the crude product was collected and crystallized from ethanol.

**Methode B.** A mixture of 4 (or 5) (10 mmol), and benzylidene derivatives 7 (10 mmol) in pyridine (2 ml) was irradiated in microwave oven for two minutes, then poured onto water and acidified with dilute hydrochloric acid. The solid product obtained was crystallized from ethanol.

**5-amino-4-oxo-3,4-dihydro-phthalazine-6-carbonitrile (9a).** Yield 3.20 g (80.40%); m.p: 288-290 $^oC$. *Anal.* Calcd. for $C_{21}H_{14}N_4O$ (338.37): C, 74.54; H, 4.17; N, 16.56. Found: C, 74.62; H, 4.24; N, 16.71. IR (KBr, $cm^{-1}$): 3453.4, 3300.4 ($NH_2$), 2207.1 (CN), 1657.2 (CO). $^1H$ MNR (300 MHz, $CDCl_3$): δ, ppm 6.92 (s, 1H, Ar-H),7.28 (br s, 2H, $NH_2$),7.43-7.64 (m, 10H, Ar-H) 8.17 (s, 1H, pyridazine-H). $^{13}C$ MNR (300 MHz, $CDCl_3$): δ, ppm 96.48 (C-CN), 110.48 (CN), 113.85, 117, 126.4, 128.91, 129.06, 129.36, 129.05, 129.56, 130.23, 134.25, 138.17, 139.25, 141.69 (CH-Ar), 151.51(C-$NH_2$), 154.21(CH-pyridazine), 161.02 (CO). MS (EI): m/z (%) = 338 ($M^+$).

**5-Amino-4-oxo-3,7-diphenyl-3,4-dihydro-phthalazine-6-carboxylic acid ethyl ester (9b).** Yield 33.2 g (86.1%) (m.p: 112-114 $^{o}$C). *Anal.* Calcd. for $C_{23}H_{19}N_3O_3$ (385.43): C, 71.68; H, 4.97; N, 10.90. Found: C, 71.62; H, 4.92; N, 10.81. IR (KBr, cm$^{-1}$): 3432.3, 3293.6 ($NH_2$), 1688.1, 1640.6 (CO). $^1$H MNR (300 MHz, DMSO-d6): δ, ppm 0.77 (t, 3H, $CH_3$, $J$ = 7.2 Hz), 3.96 (q, 2H, $CH_2$, $J$ = 7.2 Hz), 6.97 (s, 1H, Ar-H), 7.32-7.62 (m, 10H, Ar-H), 7.84 (br s, 2H, $NH_2$), 8.34 (s, 1H, pyridazine-H). $^{13}$C MNR (300 MHz, DMSO-d6): δ, ppm 13.11 ($CH_3$), 60.69 ($CH_2$), 113.7(C-COOEt), 125.73, 126.19, 127.64, 127.88, 128.33, 128.55, 128.64, 132.17, 139.19, 140.95, 141.66 (CH-Ar), 148.12 (C-Ph), 149.75 (C-$NH_2$), 160.63 (CH-pyridazine, 167.42 (CO). MS (EI): m/z (%) = 385 ($M^+$).

**5-amino-7-(4-chloro-phenyl)-3-(2-cyano-phenyl)-4-oxo-3,4-dihydro-phthalazine-6-carbonitrile (9c).** Yield 3.20 g (80.4%); m.p: 288-290 $^{o}$C. *Anal.* Calcd. for $C_{22}H_{12}ClN_5O$ (397.83): C, 66.42; H, 3.04; N, 17.60. Found: C, 66.53; H, 3.16; N, 17.63. IR (KBr, cm$^{-1}$): 3471.9, 3332.1 ($NH_2$), 2208.8 (CN), 1656.1 (CO). $^1$H MNR (300 MHz, DMSO-d6): δ, ppm 7.18 (s, 1H, Ar-H), 7.63-7.95 (m, 8H, Ar-H), 8.07 (s, 2H, $NH_2$), 8.52 (s, 1H, pyridazine-H). MS (EI): m/z (%) = 397 ($M^+$).

**2-[8-Amino-6-(4-chloro-phenyl)-7-cyano-1-oxo-1H-phthalazin-2-yl]-benzoic acid methyl ester (9d).** Yield 3.52 g (81.7%) (m.p: 295-297 $^{o}$C). *Anal*. Calcd. for $C_{23}H_{15}ClN_4O_3$ (430.85): C, 64.12; H, 3.51; N, 13. Found: C, 64.25; H, 3.42; N, 12.92. IR (KBr, cm$^{-1}$): 3437.7, 3356.2 ($NH_2$), 2213.9 (CN), 1686.8, 1651.3 (CO). $^1$H MNR (300 MHz, DMSO-d6): δ, ppm 3.87 (s, 3H, $CH_3$), 6.73 (br s, 2H, $NH_2$), 6.90-7.87 (m, 9H, Ar-H), 8.31 (s, 1H, pyridazine-H). MS (EI): m/z (%) = 430 ($M^+$).

**5-Amino-3-(2-methoxycarbonyl-phenyl) -4-oxo-7-phenyl-3,4-dihydro-phthalazin-6-carboxylic acid ethyl ester (9e).** Yield 3.51 g (79.15%) (m.p: 158-160 $^{o}$C). *Anal.* Calcd. for $C_{25}H_{21}N_3O_5$ (443.46): C, 67.71; H, 4.77; N, 9.48. Found: C, 67.63; H, 4.62; N, 9.32. IR (KBr, cm$^{-1}$): 3459.8, 3310.1($NH_2$), 1728, 1691.5, 1641.5 (CO). $^1$H MNR (300 MHz, DMSO-d6): δ, ppm 0.75 (t, 3H, $CH_3$, $J$ = 7.2 Hz), 3.66(s, 3H, $CH_3$), 3.95 (q, 2H, $CH_2$, $J$ = 7.2 Hz), 7.01 (s, 1H, Ar-H), 7.34 (br s, 2H, $NH_2$), 7.43-7.97(m, 9H, Ar-H), 8.36(s, 1H, pyridazine-H). MS (EI): m/z (%) = 443 ($M^+$).

**2-[8-Amino-6-(4-chloro-phenyl)-7-cyano-1-imino-1H-phthalazin-2-yl]-benzoic acid methyl ester (9f).** Yield 3.31 g (77%) (m.p: 320 $^{o}$C). *Anal*. Calcd. for $C_{23}H_{16}ClN_5O_2$ (429.87): C, 64.27; H, 3.75; N, 16.29. Found: C, 64.44; H, 3.86; N, 16.25. IR (KBr, cm$^{-1}$): 3432.3 (NH), 3353, 3246.3 ($NH_2$), 2212.9 (CN), 1685.5 (CO). $^1$H MNR (300 MHz, DMSO-d6): δ, ppm 3.88 (s, 3H, $CH_3$), 6.74 (m, 11H, Ar-H and $NH_2$), 8.32 (s, 1H, pyridazine-H), 11.41 (s, 1H, NH); MS (EI) m/z (%) = 429 ($M^+$).

**General procedures for preparation of triaza-phenanthrenes 13a-c and 16. Methode A.** A mixture of azaenamine 2b or 2c (10 mmol), and benzylidene derivatives 6a-c was refluxed in pyridine (20 ml) for 2 h. , then poured onto water and acidified with dilute hydrochloric acid. The solid product obtained was crystallized from ethanol.

**Methode B.** A solution of each of 2b or 2c (10 mmol) was treated with the benzylidene 7a-c (10

mmol) in pyridine (2 ml) was irradiated in microwave oven for two minutes, then poured onto water and acidified with dilute hydrochloric acid. The solid product obtained was crystallized from ethanol.

**2-Acety;-6-amino-3-(4-chlorophenyl)-3,11-dihydro-pyridazino[1,6-a]quinazoline-4-carbonitrile (13a).** Yield 3.15 g (83.82%); m.p: 230-232 $^{o}$C. *Anal.* Calcd. for $C_{20}H_{14}ClN_5O$ (375.82): C, 63.92; H, 3.75; N, 18.63. Found: C, 63.63; H, 3.69; N,3.84. IR (KBr, $cm^{-1}$): 3435.8, 3425.1 ($NH_2$), 2223 (CN), 1687 (CO). $^1$H MNR (300 MHz, DMSO-d6): δ, ppm 2.47 (s, 3H, $CH_3$), 4.9 (s, 1H, pyridazine-H), 7.18(s, 2H, $NH_2$), 7.29-8.15 (m, 8H, Ar-H) ). $^{13}$C MNR (300 MHz, DMSO-d6): δ, ppm 25.21 ($CH_3$), 37.28(CH pyridazine), 67.65(C-CN), 112.08(CN), 114.44, 120.48, 124.15, 124.72, 128.89, 129.25, 132.12, 134.43, 139.94, 141.37 (CH-Ar), 144.68(C-$COCH_3$), 147.30 (C6-pyridazine), 156.39(C- $NH_2$), 195.72 (CO). MS (EI): m/z (%) = 375 ($M^+$).

**Ethyl-2-Acety-6-amino-3-phenyl-3,11-dihydro-pyridazino[1,6-a]quinazoline-4-carboxylate (13b).** Yield 3.15 g (83.82%) (m.p: 194-196 $^{o}$C). *Anal.* Calcd. for $C_{22}H_{20}N_4O_3$ (388.43): C,68.03; H, 5.19; N, 14.42. Found: C, 68.22; H, 5.23; N,14.36. IR (KBr, $cm^{-1}$): 3490.9, 3375.2 ($NH_2$), 1681.8 (CO). $^1$H MNR (300 MHz, DMSO-d6): δ, ppm 1.19 (t, 3H, $CH_3$, $J$ = 6.9 Hz), 2.53 (s, 3H, $CH_3$), 4.06(q, 2H, $CH_2$, $J$ = 6.9 Hz), 5.34 (s, 1H, pyridazine-H), 7.06 (s, 2H, $NH_2$), 7.20-8.06 (m, 9H, Ar-H). MS (EI): m/z (%) = 388 ($M^+$).

**2-Acety;-6-amino-4-benzoyl-3-phenyl-3,11-dihydro-pyridazino[1,6-a]quinazoline (13c)** Yield 3.12 g (74.20%) (m.p: 222-224 $^{o}$C). *Anal.* Calcd. for $C_{26}H_{20}N_4O_2$ (420.47): C,74.27; H, 4.79; N, 13.32. Found: C, 74.15; H, 4.83; N,13.26. IR (KBr, $cm^{-1}$): 3444.9, 3332.9 ($NH_2$), 1686.6, 1637.7 (CO). $^1$H MNR (300 MHz, DMSO-d6): δ, ppm 2.60 (s, 3H, $CH_3$), 5.37 (s, 1H, pyridazine-H), 7.10 (s, 2H, $NH_2$)7.15-8.04 (m, 14H, Ar-H); MS (EI): m/z (%) = 420 ($M^+$).**3-Ethyl-2-Acety-6-oxo-3-phenyl-3,5,6,11-tetrahydro-pyridazino[1,6-a]quinazoline-4-carboxylate (16).** Yield 3.12 g (80.12%) (m.p: 206-208 $^{o}$C). *Anal.* Calcd. for $C_{22}H_{19}N_3O_4$ (389.41): C,67.86; H, 4.92; N, 10.79. Found: C, 67.78; H, 4.83; N,10.67. IR (KBr, $cm^{-1}$): 3432 (NH), 1718, 1695.5, 1639 (CO). $^1$H MNR (300 MHz, DMSO-d6): δ, ppm 1.15 (t, 3H, $CH_3$, $J$ = 7.2 Hz), 2.48 (s, 3H, $CH_3$), 4.09 (q, 2H, $CH_2$, $J$ = 7.2 Hz), 5.14 (s, 1H, pyridazine-H), 7.18 (s, 2H, $NH_2$), 7.24-8.01 (m, 9H, Ar-H), 11.66 (s, 1H, NH). MS (EI): m/z (%) = 389 ($M^+$).

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