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PYRIDAZINE DERIVATIVES AND RELATED COMPOUNDS PART 10.[1] REACTIONS OF 3-DIAZOPYRAZOLO[3,4-*c*]PYRIDAZINE WITH REACTIVE METHYLENE COMPOUNDS AND OTHER GROUPS

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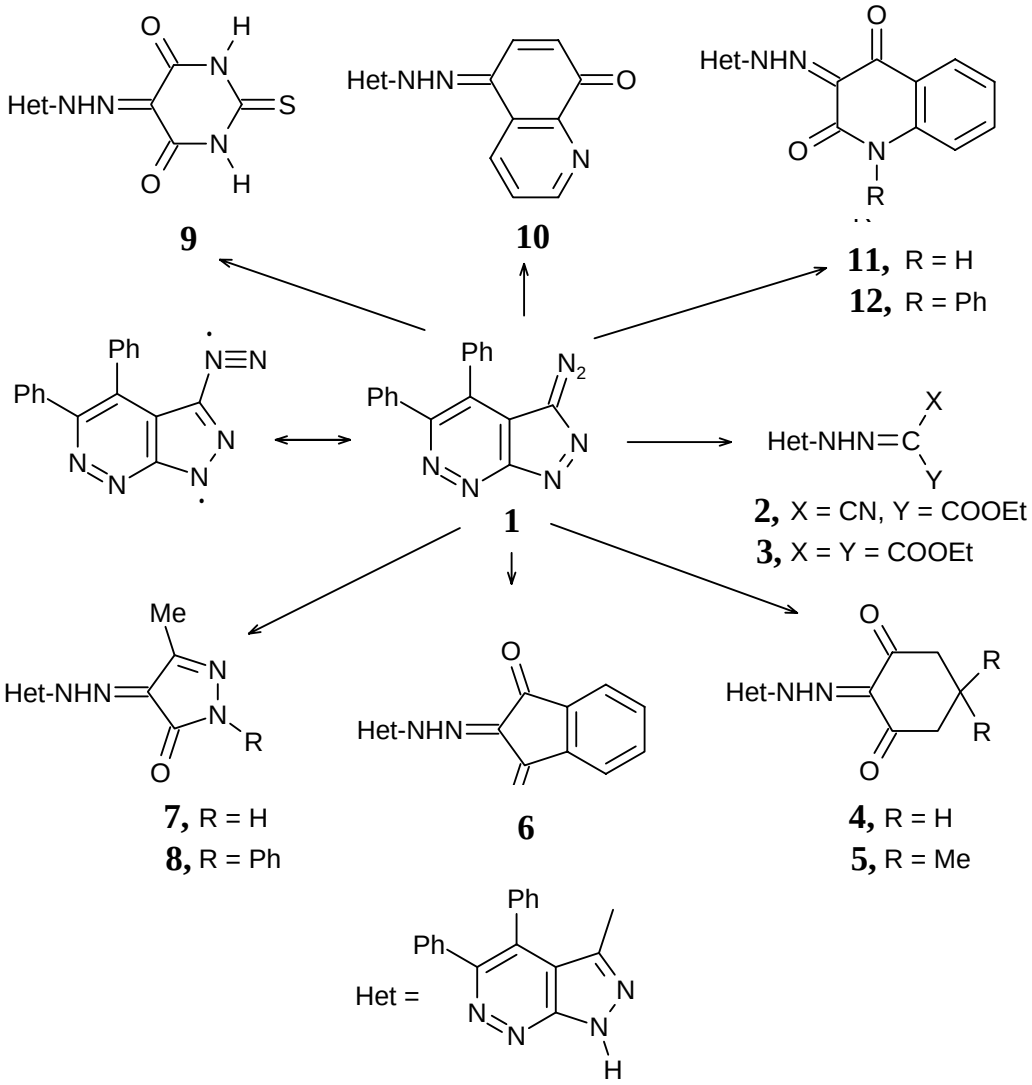
Abstract – 3-Diazopyrazolo[3,4-*c*]pyridazine was synthesized and its transformations were investigated. With reactive methylene compounds the corresponding hydrazones and condensed 1,2,4-triazines were formed. With aromatic amines and naphthols the diazo compound was converted into arylazo derivatives. The diazo compound underwent cycloaddition, reacting as a 1,4-dipole to yield cycloaddition products.

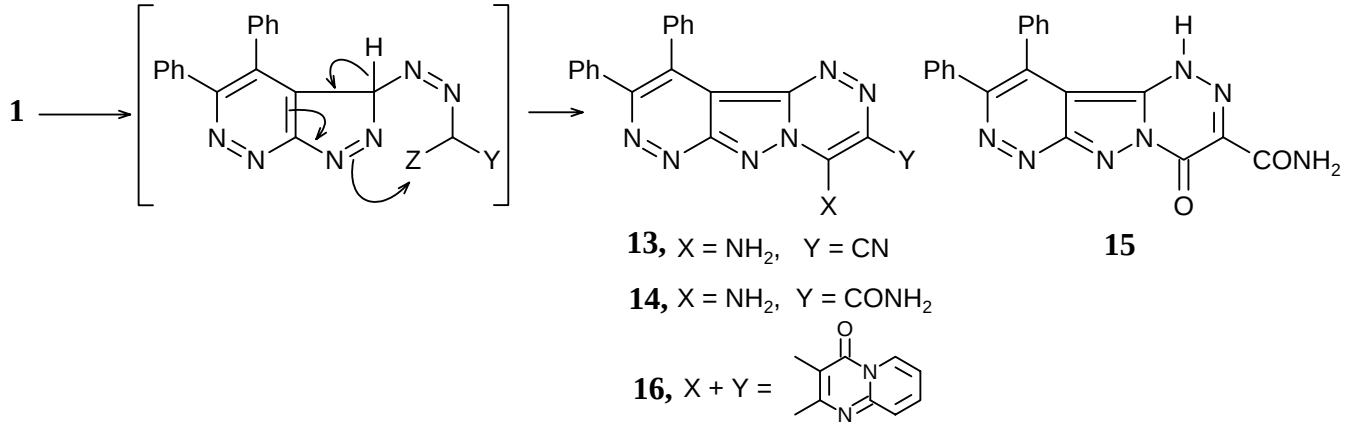
Heterocyclic diazo compounds represent an interesting class of reactive substrates and their stability depends mainly on charge delocalization through the heterocyclic ring. Moreover, several heterocyclic diazo compounds possess a biological activity.[2] In view of these facts and our interest in the synthetic potential of fused pyridazine systems, we reported the synthesis of naphtho[2,1-c]pyridazino[3`,4`:3,4]pyrazolo[5,1-*c*]-1,2,4-triazine and pyridazino[3`,4`:3,4]pyrazolo[5,1-*c*]-1,2,4-triazine derivatives based on coupling reaction of 3-diazo-4,5-diphenylpyrazolo[3,4-*c*]pyridazine (**1**) with β–naphthol and with ethyl acetoacetate respectively.[3] In continuation of this work, we report here the results of our further investigation on the reaction of compound (**1**) with further active methylene compounds and cycloaddition reactions.

The reaction of **1** with ethyl cyanoacetate, diethyl malonate, cyclohexane-1,3-dione, dimedone, 1,3-indandione, 3-methyl-5-pyrazolone, 1-phenyl-3-methyl-5-pyrazolone, thiobarbituric acid, 8-hydroxyquinoline, 4-hydroxycarbostyrile and 4-hydroxy-1-phenyl-2-quinolone, formed easily the corresponding hydrazone compounds (**2-12**). For all compounds of this type several tautomeric forms can be written. For example, compounds of the types (**2**) and (**3**) can be regarded as azo compounds or as hydrazones, and the carbonyl part can be written in the keto or enolized form. The end of the reaction was judged by the disappearance of the diazo compound according to TLC analysis. The reaction time varied from a few minutes to several hours. The reaction products were isolated in high yield and gave satisfactory elemental analysis. The spectroscopic properties of the products were in excellent agreement with the proposed structures.

On the other hand, malononitrile, cyanoacetamide, malonamide and malonyl-α-aminopyridine[4] afforded

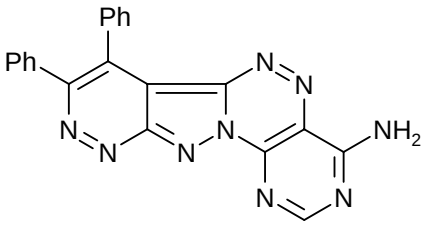


pyridazino[3`,4`:3,4]pyrazolo[5,1-*c*]-1,2,4-triazine derivatives (**13-16**). The assignment of the cyclic compounds involves the initial formation of acyclic hydrazones which undergo immediate intramolecular nucleophilic attack of pyrazole ring 2-nitrogen to the cyano group or amide carbonyl group.



The *o*-aminonitrile (**13**) was converted into compound (**17**) in boiling formamide.[5]

The reaction of the *o*-aminonitrile (**13**) with phenyl isocyanate yielded the thiourea derivative (**18**). With view of studying some of the reactions of the hydrazone (**2**), that was allowed to react with hydrazine



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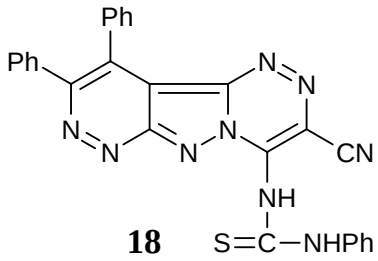

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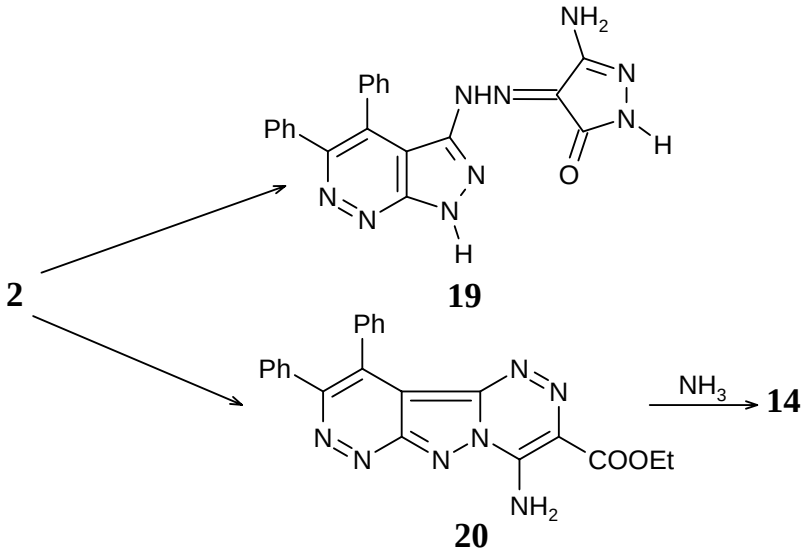
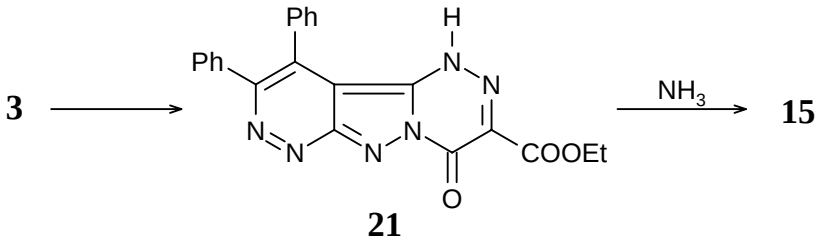
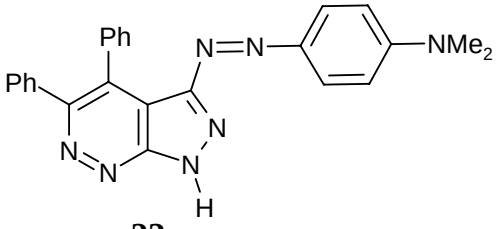
hydrate produced aminopyrazolone derivative (**19**), and the hydrazone (**2**) was also readily cyclized in concentrated sulfuric acid at 70° to give the ester (**20**), whose reaction with alcoholic ammonia afforded the amide (**14**).



Thermal cyclization of compound (**3**) was unsuccessful, but its refluxing in glacial acetic acid provided the ester (**21**), whose reaction with alcoholic ammonia afforded the amide (**15**).



Azo coupling of **1** also took place with *N*,*N*-dimethylaniline, β-naphthylamine, naphthol-AS and with naphthol-AS-LC to give the C-azo products (**22-25**).



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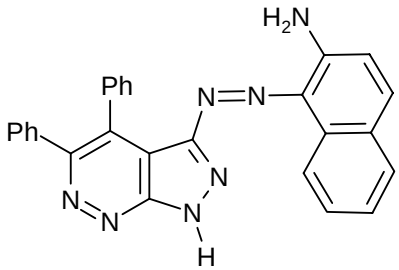

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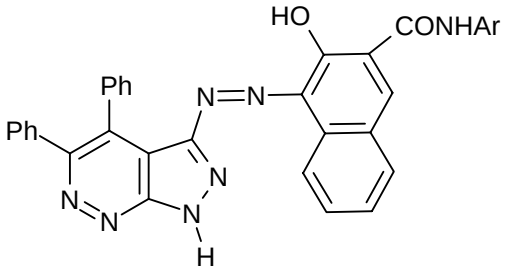
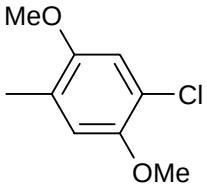


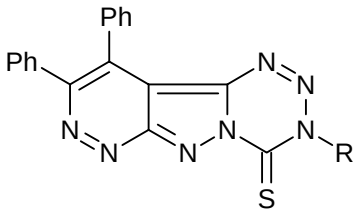
24, Ar = Ph

25, Ar =



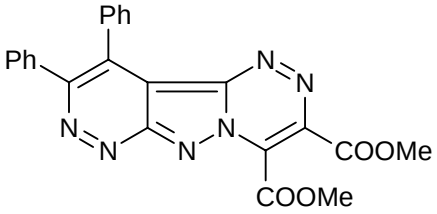
Compound (**1**), because of charge polarization and potential bifunctional reactivity, reacts with dipolarophiles to give cycloaddition products. Compound (**1**) reacts with phenyl isothiocyanate as well as ethoxycarbonylisothiocyanate in boiling dichloromethane to give cyclic tetrazine derivatives (**26**) and (**27**). These reactions were regarded as a [4+2] cycloaddition of the diazo derivative to isothiocyanates.

The cycloaddition reaction of diazo compound (**1**) with dimethyl acetylenedicarboxylate at room temperature afforded dimethyl 9,10-diphenylpyridazino[3`,4`:3,4]pyrazolo[5,1-*c*]-1,2,4-triazine-3,4-di-carboxylate (**28**).



26, R = Ph

27, R = COOEt



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EXPERIMENTAL

All the melting points are uncorrected. The IR spectra of the compounds were recorded on a Perkin Elmer spectrophotometer model 1310, ^{1}H-NMR spectra on a Perkin Elmer R12B spectrometer and chemical shifts (δ) are in ppm relative to internal tetramethylsilane and mass spectra were recorded on a Shimadzu GCMS-GB 1000 PX (70 eV).

Compound (**1**) was prepared in 96% yield as yellow crystals (mp 110°C) by diazotization of 3-amino-4,5-diphenyl-1*H*-pyrazolo[3,4-*c*]pyridazine with sodium nitrite in glacial acetic acid at rt.[3] Its IR spectrum revealed an absorption band at 2119 cm^{-1} typical for diazo compounds,[6] MS spectrum: m/z: 298 (M^{+}, 8.5%), 271 (51.4%), 242 (100%), 214 (66.3%).

General Procedure for the Preparation of Coupling Products from 3-Diazo-4,5-diphenylpyrazolo-[3,4-*c*]pyridazine (1) and Active Methylene Compounds.

A solution of compound (**1**) (0.6 g, 2 mmol) in ethanol or in glacial acetic acid (20 mL) was treated with the corresponding active methylene compound (2 mmol). The reaction mixture was refluxed for few minutes to several hours. The separated product was filtered off and recrystallized. In this manner the following compounds were prepared.

Ethyl 2-cyano-2-(4,5-diphenyl-1*H*-pyrazolo[3,4-*c*]pyridazin-3-ylhydrazono) acetate (2).

Light brown crystals, 72% yield, mp 247-248°C (ethanol); MS: m/z 411 (M^+, 100%), 338 (52%), 284 (66.6%), 214 (42.1%), 127 (34%), 77 (84.3%). IR: 3218-3160 (NH), 2225 (CN), 1720 (C=O), 1620 (C=N) and 1550 cm^{-1} (C=C); ^{1}H-NMR (DMSO-d_6): 14.5 (s, 1H, NH), 12.4 (s, 1H, NH), 7.8-7.2 (m, 10H, 2Ph), 4.6-4.4 (q, J = 6.4 Hz, 2H, $C\underline{H}_2CH_3$) and 1.3 (t, J = 6.4 Hz, 3H, $CH_2C\underline{H}_3$). Anal. Calcd for $C_{22}H_{17}N_7O_2$: C, 64.22; H, 4.17; N, 23.83. Found: C, 64.20; H, 4.10; N, 23.70.

Diethyl 4,5-diphenyl-1*H*-pyrazolo[3,4-*c*]pyridazin-3-ylhydrazonomalonate (3).

White crystals, 60% yield, mp 144-145°C (ethanol); IR: 3420, 3300 (NH), 1700 (C=O), 1655 (C=N) and 1515 cm^{-1} (C=C), ^{1}H-NMR (DMSO-d_6): 14.3 (s, 1H, NH), 12.4 (s, 1H, NH), 7.6-7.3 (m, 10H, 2Ph), 4.6-4.0 (m, 4H, 2 $C\underline{H}_2CH_3$) and 1.5-1.3 (m, 6H, 2 $CH_2C\underline{H}_3$). MS: m/z 458 (M^+, 14.79%), 385 (100%), 330 (13.83%), 271 (48.34%). Anal. Calcd for $C_{24}H_{22}N_6O_4$: C, 62,87; H, 4.84; N, 18.33. Found: C, 62.70; H, 4.70; N, 18.20

2-(4,5-Diphenyl-1*H*-pyrazolo[3,4-*c*]pyridazin-3-ylhydrazono)-1,3-cyclohexanedione (4).

Brown crystals, 54% yield, mp > 300°C (ethanol); IR: 3500, 3470 (NH), 1695 (C=O), 1625 (C=N) and 1550 cm^{-1} (C=C); ^{1}H-NMR (DMSO-d_6): 7.6-7.2 (m, 10H, 2Ph), 3.9-3.6 (m, 2H, 4`-$CH_2$), 3.1-2.8 (m, 2H, 5`-CH_2) and 2.6-2.2 (m, 2H, 6`-CH_2). Anal. Calcd for $C_{23}H_{18}N_6O_2$: C, 67,30; H, 4.42; N, 20.48. Found: C, 67.20; H, 4.30; N, 20.30.

5,5-Dimethyl-2-(4,5-diphenyl-1*H*-pyrazolo[3,4-*c*]pyridazin-3-ylhydrazono)-1,3-cyclohexanedione (5).

Yellow crystals, 28% yield, mp 187-188°C (ethanol); IR: 3550, 3470 (NH), 1710, 1700 (C=O), 1650 (C=N) and 1530 cm^{-1} (C=C); ^{1}H-NMR ($CDCl_3$): 7.6-7.2 (m, 10H, 2Ph), 3.65 (s, 2H, 4`-$CH_2$), 2.85 (s, 2H, 6`-CH_2) and 1.25 (s, 6H, $2CH_3$). Anal. Calcd for $C_{25}H_{22}N_6O_2$: C, 68.47; H, 5.06; N, 19.17. Found: C, 68.40; H, 4.90; N, 19.00.

2-(4,5-Diphenyl-1*H*-pyrazolo[3,4-*c*]pyridazin-3-ylhydrazono)-1,3-indanedione (6).

Orange crystals, 64% yield, mp 267-268°C (ethanol); IR: 3300 (NH), 1695, 1667 (C=O), 1655 (C=N) and 1515 cm^{-1} (C=C), ^{1}H-NMR ($CDCl_3$): 13.9 (s, 1H, NH), 12.8 (br s, 1H, NH) and 7.8-7.2 (m, 14H, aromatic protons). Anal. Calcd for $C_{26}H_{16}N_6O_2$: C, 70,26; H, 3.63; N, 18.91. Found: C, 70.10; H, 3.50; N, 18.80.

3-Methyl-4-(4,5-diphenyl-1*H*-pyrazolo[3,4-*c*]pyridazin-3-ylhydrazono)-2-pyrazolin-5-one (7).

Yellow crystals, 75% yield, mp > 300°C (ethanol); IR: 3170 (NH), 1670 (C=O), 1625 (C=N) and 1530 cm^{-1} (C=C); ^{1}H-NMR (DMSO-d_6): 9.9 (d, J=5.3 Hz, 1H, NH hydrazone), 8.6 (br, 1H, NH pyrazolo), 8.2 (br, 1H, NH pyrazolone), 7.8-7.6 (m, 10H, 2Ph) and 2.8 (s, 3H, CH_3). Anal. Calcd for $C_{21}H_{16}N_8O$: C, 63,62; H, 4.07; N, 28.27. Found: C, 63.50; H, 3.90; N, 28.10.

3-Methyl-1-phenyl-4-(4,5-diphenyl-1*H*-pyrazolo[3,4-*c*]pyridazin-3-ylhydrazono)-2-pyrazolin-5-one (8).

Orange crystals, 88% yield, mp 298-299°C (ethanol); IR: 3175 (NH), 1675 (C=O), 1630 (C=N) and 1525 cm^{-1} (C=C); ^{1}H-NMR (DMSO-d_6): 9.9 (d, J=5.2 Hz,1H, NH hydrazone), 8.6 (br, 1H, NH pyrazolo), 7.8-7.6 (m, 15H, 3Ph) and 2.8 (s, 3H, CH_3). Anal. Calcd for $C_{27}H_{20}N_8O$: C, 68,63; H, 4.27; N, 23.72. Found: C, 68.50; H, 4.10; N, 23.60.

5-(4,5-Diphenyl-1*H*-pyrazolo[3,4-*c*]pyridazin-3-ylhydrazono)-2-thioxohexahydropyrimidine-4,6-dione (9).

Yellow crystals, 90% yield, mp 290-291^{o}C (ethanol); IR: 3310 (NH), 1695, 1690 (C=O), 1650 (C=N) and 1535 cm^{-1} (C=C); ^{1}H-NMR (DMSO-d_6): 14.5 (s, 1H, NH), 13.5 (s, 1H, NH) and 7.6 - 7.0 (m, 10H, 2Ph). Anal. Calcd for $C_{21}H_{14}N_8O_2S$: C, 57,00; H, 3.19; N, 25.33. Found: C, 56.90; H, 3.00; N, 25.20.

5-(4,5-Diphenyl-1*H*-pyrazolo[3,4-*c*]pyridazin-3-ylhydrazono)quinolin-8(5*H*)-one (10).

White crystals, 80% yield, mp 177-178^{o}C (ethanol), IR: 3310 (NH), 1695 (C=O), 1655 (C=N) and 1510 cm^{-1} (C=C), ^{1}H-NMR ($CDCl_3$): 7.8-7.2 (m, 15H, 2Ph and quinoline protons). Anal. Calcd for $C_{26}H_{17}N_7O$: C, 70,42; H, 3.86; N, 22.11. Found: C, 70.30; H, 3.70; N, 22.00.

3-(4,5-Diphenyl-1*H*-pyrazolo[3,4-*c*]pyridazin-3-ylhydrazono)quinoline-2,4-(1*H*,3*H*)-dione (11).

Orange crystals, 63% yield, mp 289-290^{o}C (ethanol); IR: 3340 (NH), 1670 (C=O), 1656 (C=N) and 1530 cm^{-1} (C=C); ^{1}H-NMR (DMSO-d_6): 14.8 (br, 1H, NH) and 8.1-7.0 (m, 14H, aromatic phenyl groups). Anal. Calcd for $C_{26}H_{17}N_7O_2$: C, 67,96; H, 3.73; N, 21.34. Found: C, 67.80; H, 3.60; N, 21.20.

3-(4,5-Diphenyl-1*H*-pyrazolo[3,4-*c*]pyridazin-3-ylhydrazono)-1-phenylquinoline-2,4-(1*H*,3*H*)-dione (12).

Orange crystals, 55% yield, mp 284-285^{o}C (ethanol); IR: 3400 (NH), 1690 (C=O), 1650 (C=N) and 1530 cm^{-1} (C=C); ^{1}H-NMR (DMSO-d_6): 8.2 - 6.9 (m, 15H, 3Ph) and 6.6 - 6.2 (m, 4H, aromatic ring). Anal. Calcd for $C_{32}H_{21}N_7O_2$: C, 71,76; H, 3.95; N, 18.31. Found: C, 71.60; H, 3.80; N, 18.20.

4-Amino-9,10-diphenylpyridazino[3`,4`:3,4]pyrazolo[5,1-*c*]-1,2,4-triazine-3-carbonitrile (13).

Red crystals, 81% yield, mp > 300^{o}C (1-butanol); IR: 3320, 3300 (NH_2), 2220 (CN), 1660 (C=N) and 1530 cm^{-1} (C=C), ^{1}H-NMR (DMSO-d_6): 7.6-7.1 (m, 10H, 2Ph) and 5.95 (s, 2H, NH_2 disappeared by addition of D_2O). Anal. Calcd for $C_{20}H_{12}N_8$: C, 65,92; H, 3.32; N, 30.75. Found: C, 65.80; H, 3.20; N, 30.60.

4-Amino-9,10-diphenylpyridazino[3`,4`:3,4]pyrazolo[5,1-*c*]-1,2,4-triazine-3-carboxamide (14).

Yellow crystals, 52% yield, mp > 300^{o}C (ethanol); IR: 3400, 3300, 3200 (NH_2), 1680 (C=O), 1590 (C=N) and 1510 cm^{-1} (C=C); ^{1}H-NMR (DMSO-d_6): 7.5 - 7.3 (m, 10H, 2 Ph) and 3.6 (s, 4H, 4NH). Anal. Calcd for $C_{20}H_{14}N_8O$: C, 62,82; H, 3.69; N, 29.30. Found: C, 62.70; H, 3.60; N, 29.20.

9,10-Diphenyl-1,4-dihydro-4-oxopyridazino[3`,4`:3,4]pyrazolo[5,1-*c*]-1,2,4-triazine-3-carboxamide (15).

Orange crystals, 62% yield, mp 201-202^{o}C (1-butanol); IR: 3200 (NH_2), 1686 (C=O), 1630 (C=N) and 1520 cm^{-1} (C=C), ^{1}H-NMR (DMSO-d_6): 11.88 (br s, 1H, NH), 7.6-7.0 (m, 10H, 2Ph) and 6.9 (br s, 2H, NH_2). Anal. Calcd for $C_{20}H_{13}N_7O_2$: C, 62,66; H, 3.42; N, 25.58. Found: C, 62.50; H, 3.30; N, 25.40.

10,11-Diphenylpyridazino[3`,4`:3,4]pyrazolo[5,1-*c*]pyrido[1`,2`:1,2]pyrimido[4,5-*e*]-1,2,4-triazin-14-one (16).

Orange crystals, 60% yield, mp > 300^{o}C (acetic acid); IR: 1665 (C=O), 1655 (C=N) and 1560 cm^{-1}

(C=C); ^{1}H-NMR (CF_3COOD): 8.8 - 8.6 (m, 4H, aromatic H) and 8.2 - 7.4 (m, 10H, 2Ph). Anal. Calcd for $C_{25}H_{14}N_8O$: C, 67.86; H, 3.19; N, 25.33. Found : C, 67.70; H, 3.00; N, 25.20.

12-Amino-8,9-diphenylpyridazino[3`,4`:3,4]pyrazolo[5,1-*c*]pyrimido[4,5-*e*]-1,2,4-triazine (17).

The aminonitrile (**13**) (1.0 g, 2.7 mmol) was boiled in formamide (10 mL) for 1 h and the mixture was diluted with water to precipitate crystals. The solid product was collected and recrystallized from dimethylformamide, (0.6 g, 56%), mp > 300^{o}C; IR: 3340, 3325 (NH_2), 1655 (C=N) and 1530 cm^{-1} (C=C), ^{1}H-NMR (DMSO-d_6): 8.13 (s, 2H, NH_2 exchangeable with D_2O), 7.61-7.20 (m, 10H, 2Ph) and 6.8 (s, 1H, H-2). Anal. Calcd for $C_{21}H_{13}N_9$: C, 64.44; H, 3.35; N, 32.21. Found: C, 64.20; H, 3.20; N, 32.10.

9,10-Diphenyl-4-(*N*-phenylthiocarbamoylamino)pyridazino[3`,4`:3,4]pyrazolo[5,1-*c*]-1,2,4-triazine-3-carbonitrile (18).

A mixture of the o-aminonitrile (**13**) (0.73 g, 2 mmol) and phenylisothiocyanate (0.27 g, 2 mmol) in 1-butanol (20 mL) was refluxed for 5 h. The yellow solid separated on cooling was filtered and recrystallized from 1-butanol, (0.88 g, 88%), mp 242-243^{o}C; IR: 3450, 3150 (NH), 1680 (C=S) and 1525 cm^{-1} (C=C); ^{1}H-NMR (DMSO-d_6): 13.0 (s, 1H, NH), 12.7 (s, 1H, NH) and 7.5-7.3 (m, 15H, 3Ph). Anal. Calcd for $C_{27}H_{17}N_9S$: C, 64.91; H, 3.43; N, 25.23. Found: C, 69.90; H, 3.40; N, 25.20.

3-Amino-4-(4,5-diphenyl-1*H*-pyrazolo[3,4-*c*]pyridazin-3-ylhydrazono)-2-pyrazolin-5-one ((19).

To a solution of acyclic hydrazone (**2**) (0.82 g, 2 mmol) in ethanol (20 mL), hydrazine hydrate (85%, 1 mL, 20 mmol) was added. The reaction mixture was refluxed for 3 h. Upon cooling a brown precipitate product was filtered and recrystallized from ethanol, (0.7 g, 80%), mp > 300^{o}C; IR: 3355, 3280, 3210, 3140 (NH), 1680 (C=O), 1620 (C=N) and 1570 cm^{-1} (C=C); ^{1}H-NMR (DMSO-d_6): 7.8 - 7.2 (m, 10H, 2Ph) and 3.4 (br s, 2H, NH_2). Anal. Calcd for $C_{20}H_{15}N_9O$: C, 60.44; H, 3.80; N, 31.72. Found: C, 60.30; H, 3.70; N, 31.60.

Ethyl 4-amino-9,10-diphenylpyridazino[3`,4`:3,4]pyrazolo[5,1-*c*]-1,2,4-triazine-3-carboxylate (20).

Heating acyclic hydrazone (**2**) (1 g, 2.44 mmol) in conc. sulfuric acid (5 mL) at 70^o for 10 min. The reaction mixture after cooling was poured onto water (100 mL). The solid precipitated filtered, recrystallized from ethanol, (0.7 g, 78%), mp > 300^{o}C; IR: 3340, 3210 (NH_2), 1670 (C=O), 1625 (C=N) and 1510 cm^{-1} (C=C); ^{1}H-NMR (DMSO-d_6): 9.8 (s, 2H, NH_2), 7.7-7.2 (m, 10H, 2Ph), 4.6-4.4 (q, *J*=6.5 Hz, 2H, C<u>H</u>$_2$CH$_3$) and 1.3 (t, *J*=6.5 Hz, 3H, CH$_2$C<u>H</u>$_3$). Anal. Calcd for $C_{22}H_{17}N_7O_2$: C, 64.22; H, 4.17; N, 23.83. Found: C, 64.00; H, 4.00; N, 23.70.

Ethyl 9,10-diphenyl-1,4-dihydro-4-oxopyridazino[3`,4`:3,4]pyrazolo[5,1-*c*]-1,2,4-triazine-3-carboxylate (21).

Compound (**3**) (1 g, 2.18 mmol) was dissolved in glacial acetic acid (20 mL), and heated under reflux for 3 h. The solvent was evaporated to one-third of its original volume, and after cooling the product separated was filtered off and recrystallized from ethanol, (0.75 g, 83%), mp 291-292^{o}C; IR: 3200 (NH), 1739, 1690 (C=O), 1620 (C=N), and 1515 cm^{-1} (C=C), ^{1}H-NMR (DMSO-d_6): 11.7 (br s, 1H, NH), 7.67-

7.40 (m, 10H, 2Ph), 4.5-4.3 (q, *J*=6.0 Hz, 2H, $C\underline{H}_2CH_3$) and 1.3 (t, *J*=6.0 Hz, 3H, $CH_2C\underline{H}_3$). Anal. Calcd for $C_{22}H_{16}N_6O_3$: C, 64.07; H, 3.91; N, 20.38. Found: C, 63.90; H, 3.70; N, 20.10.

Reaction of o-aminoester (20) and ester (21) with ammonia.

A solution of compound (**20**) or (**21**) (0.5 g) in absolute ethanol (50 mL) was saturated at 0° with dry ammonia gas and left at rt for 24 h. The mixture was filtered to remove insoluble solid and the filtrate was evaporated to afford the o-aminocarboxamide (**14**) (0.35 g, 76%) or carboxamide (**15**) (0.3 g, 65%) respectively.

4,5-Diphenyl-3-[4-(*N*,*N*-dimethylanilin-1-yl)azo]-1*H*-pyrazolo[3,4-*c*]pyridazine (22).

To a solution of compound (**1**) (0.6 g, 2 mmol) in ethanol (20 mL), was added at rt *N*,*N*-dimethylaniline (0.25 g, 2 mmol) in ethanol (20 mL). A brown crystals deposit. The separated product was filtered and recrystallized from ethanol (0.49, 58%), mp 266 – 268°C; IR: 1655 (C=N) and 1535 cm^{-1} (C=C), ^{1}H-NMR ($CDCl_3$):12.1 (br s, 1H, NH), 7.8-7.4 (m, 2H, aryl), 7.6-7.5 (m, 2H, aryl), 7.4-7.0 (m, 10H, 2Ph) and 3.25 (s, 6H, NMe_2). Anal. Calcd for $C_{25}H_{21}N_7$: C, 71.58; H, 5.05; N, 23.37. Found: C, 71.40; H, 4.90; N, 23.20.

4,5-Diphenyl-3-[(2-naphthylamin-1-yl)azo]-1*H*-pyrazolo[3,4-*c*]pyridazine (23).

A mixture of compound (**1)** (0.6 g, 2 mmol) and β-naphthylamine (0.29 g, 2 mmol) in ethanol (30 mL) containing sodium acetate (0.4 g) was refluxed for 30 min. Brown crystals deposit during the refluxing time. The separated product was collected and recrystallized from ethanol (0.72 g, 81%), mp 266-267^{o}C; IR: 3320, 3300 (NH_2), 1660 (C=N) and 1530 cm^{-1} (C=C), ^{1}H-NMR (DMSO-d_6): 13.1 (br s, 1H, NH), 8.1 (s, 2H, NH_2) and 7.8-7.6 (m, 16H, aromatic protons). Anal. Calcd for $C_{27}H_{19}N_7$: C, 73.45; H, 4.34; N, 22.21. Found: C, 73.30; H, 4.20; N, 22.10.

Reaction of compound (1) with naphthol-AS and naphthol-AS-LC.

To a solution of compound (**1**) (0.6 g, 2 mmol) in ethanol (30 mL). Was added naphthol AS (0.53 g, 2 mmol) or naphthol-AS-LC (0.72 g, 2 mmol) in water (10 mL) containing sodium hydroxide (0.1 g, 2.5 mmol). The reaction mixture was stirred at rt for 30 min. After acidification with 50% hydrochloric acid, a red compound was separated, filtered and recrystallized from ethanol, (**24**, 1.1 g, 97%), mp 190-191^{o}C; IR: 3400 br (OH), 1660 (C=O), 1650 (C=N) and 1535 cm^{-1} (C=C), ^{1}H-NMR (DMSO-d_6): 12.6 (br s, 1H, NH), 10.6 (s, 1H, CONH), 10.3 (s, 1H, OH) and 7.8-7.2 (m, 20H, aromatic protons). Anal. Calcd for $C_{34}H_{23}N_7O_2$: C, 72.71; H, 4.13; N, 17.46. Found: C, 72.60; H, 4.00; N, 17.30 and (**25**, 1.2 g, 90%), mp 119-120^{o}C; IR: 1650 (C=O), 1640 (C=N) and 1530 cm^{-1} (C=C), ^{1}H-NMR (DMSO-d_6): 13.1 (br s, 1H, NH), 10.6 (s, 1H, CONH), 10.4 (s, 1H, OH), 7.6-7.1 (m, 17H, aromatic protons), 3.61 (s, 3H, OMe-2`) and 3.4 (s, 3H, OMe-5`). Anal. Calcd for $C_{36}H_{26}N_7O_4Cl$: C, 65.90; H, 3.99; N, 14.94. Found: C, 65.70; H, 3.80; N, 14.70 respectively.

3,9,10-Triphenylpyridazino[3`,4`:3,4]pyrazolo[5,1-*d*]-1,2,3,5-tetrazine-4-thione (26).

Phenyl isothiocyanate (0.27 g, 2 mmol) in dichloroethane (10 mL) was added dropwise to compound (**1**) (0.6 g, 2 mmol) in dichloroethane (40 mL) at rt. The reaction mixture was refluxed 2 h. A yellow crystals deposit on cooling was filtered and recrystallized from dichloroethane, (0.35 g, 40%), mp 152-153^{o}C; IR: 1660 (C=N), 1270 (C=S) and 1550 cm^{-1} (C=C), ^{1}H-NMR (DMSO-d_6): 7.8-7.6 (m, 5H, NPh) and 7.5-7.1 (m, 10H, 2Ph). Anal. Calcd for $C_{24}H_{15}N_7S$: C, 66.49; H, 3.49; N, 22.62. Found: C, 66.40; H, 3.30; N, 22.50.

3-Ethoxycarbonyl-9,10-diphenylpyridazino[3`,4`:3,4]pyrazolo[5,1-*d*]-1,2,3,5-tetrazine-4-thione (27). To a solution of compound (**1**) (0.6 g, 2 mmol) in dichloroethane (40 mL). Was added ethoxycarbonyl-isothiocyante (0.27 g, 2 mmol) in dichloroethane (10 mL). The reaction mixture was refluxed for 2 h. Brown crystals deposit on cooling, filtered and recrystallized from dichloroethane, (0.58 g, 67%), mp 233 - 234^{o}C; IR: 1700 (C=O), 1660 (C=N), 1275 (C=S) and 1540 cm^{-1} (C=C); ^{1}H-NMR (DMSO-d_6): 7.8-7.5 (m, 10H, 2Ph), 4.6-4.4 (q, *J*=7.2 Hz, 2H, C$\underline{H_2}$CH$_3$) and 1.3 (t, *J*=7.2 Hz, 3H, CH$_2$C$\underline{H_3}$). Anal. Calcd for $C_{21}H_{15}N_7O_2S$: C, 58.73; H, 3.52; N, 22.83. Found: C, 58.60; H, 3.40; N, 22.70.

Dimethyl 9,10-diphenylpyridazino[3`,4`:3,4]pyrazolo[5,1-*c*]-1,2,4-triazine-3,4-dicarboxylate (28). A solution of **1** (0.6 g, 2 mmol) in acetonitrile (30 mL) was treated with dimethyl acetylenedicarboxylate (0.29 g, 2 mmol), and the reaction mixture was stirred at rt for 48 h. The solvent was evaporated to one-third of its original volume, and after addition of petroleum ether the product separated (0.53, 70%), mp 190-191^{o}C (ethanol-water); IR: 1710, 1705 (C=O), 1630 (C=N), and 1520 cm^{-1} (C=C), ^{1}H-NMR (DMSO-d_6): 7.54-7.10 (m, 10H, 2Ph), 3.69 (s, 3H, COOMe-3) and 3.6 (s, 3H, COOMe-4). Anal. Calcd for $C_{23}H_{16}N_6O_4$: C, 62.72; H, 3.66; N, 19.08. Found: C, 62.50; H, 3.50; N, 18.80.

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