Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Design and Synthesis of Some New Pyrazolo[1,5-a]pyrimidines, Pyrazolo[5,1-c]triazines, Pyrazolo[3,4-d]pyridazines, and Isoxazolo[3,4-d]pyridazines Containing the Pyrazole Moiety

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Accepted author version posted online: 22 Feb 2012.Version of record first published: 21 Feb 2013.

To cite this article: Abdou O. Abdelhamid , Abdelgawad A. Fahmi & Karema N. M. Halim (2013): Design and Synthesis of Some New Pyrazolo[1,5-a]pyrimidines, Pyrazolo[5,1-c]triazines, Pyrazolo[3,4-d]pyridazines, and Isoxazolo[3,4-d]pyridazines Containing the Pyrazole Moiety, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 43:8, 1101-1126

To link to this article: http://dx.doi.org/10.1080/00397911.2011.616639

Synthetic Communications®, 43: 1101–1126, 2013

ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397911.2011.616639

DESIGN AND SYNTHESIS OF SOME NEW PYRAZOLO[1,5-*a*]PYRIMIDINES, PYRAZOLO [5,1-*c*]TRIAZINES, PYRAZOLO[3,4-*d*]PYRIDAZINES, AND ISOXAZOLO[3,4-*d*]PYRIDAZINES CONTAINING THE PYRAZOLE MOIETY

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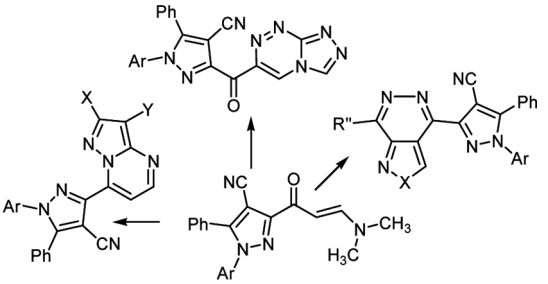
GRAPHICAL ABSTRACT



Abstract *Pyrazolo[1,5-*a*]pyrimidines, pyrazolo[5,1-*c*]triazines, [1,2,4]triazolo [4,3-*a*]pyrimidine, [1,2,4]triazolo[3,4-*c*][1,2,4]triazine, pyrazolo[3,4-*d*]pyridazines, and isoxazolo[3,4-*d*]pyridazines were prypared from 3-(3-(dimethylamino)acryloyl)-1-aryl-5-diphenyl-1*H*-pyrazole-5-carbonitrile with each of hydrazonoyl halides, hydroximoyl chlorides, heterocyclic amines, and diazotized heterocyclic amines. All the newly synthesized compounds were confirmed by elemental analyses, spectral data, and alternative synthetic routes whenever possible.*

Keywords Isoxazolo[3,4-*d*]pyridazines; pyrazolo[1,5-*a*]pyrimidines; pyrazolo[3,4-*d*]pyridazines; pyrazolo[5,1-*c*]triazines

INTRODUCTION

Some pyrazole derivatives possess biological and pharmacological activities[1–9] and also find application in dyes.[10,11] Robins et al. reported that certain 3-substituted pyrazolo[1,5-*a*]pyrimidines inhibit the metabolism schistosomiasis in snails.[12,13] Also, pyrazolopyrimidine systems are reported as inhibitors for the synthesis of DNA and RNA in the cells of some types of cancer[14] and viruses.[15]

Received June 23, 2011.

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In addition, a large number of thiazole derivatives have been found to exhibit pharmacological activity.[16–21] In view of this we become interested in the synthesis of some new pyrazoles, pyrazolo[1,5-*a*]pyrimidines, pyrazolo[5,1-*c*]triazines, pyrazolo[3,4-*d*]pyridazines, and isoxazolo[3,4-*d*]pyridazines. This work is an extension of an ongoing research program devoted to the synthesis and characterization of different heterocyclic ring systems endowed with potential biological activities.[22–28]

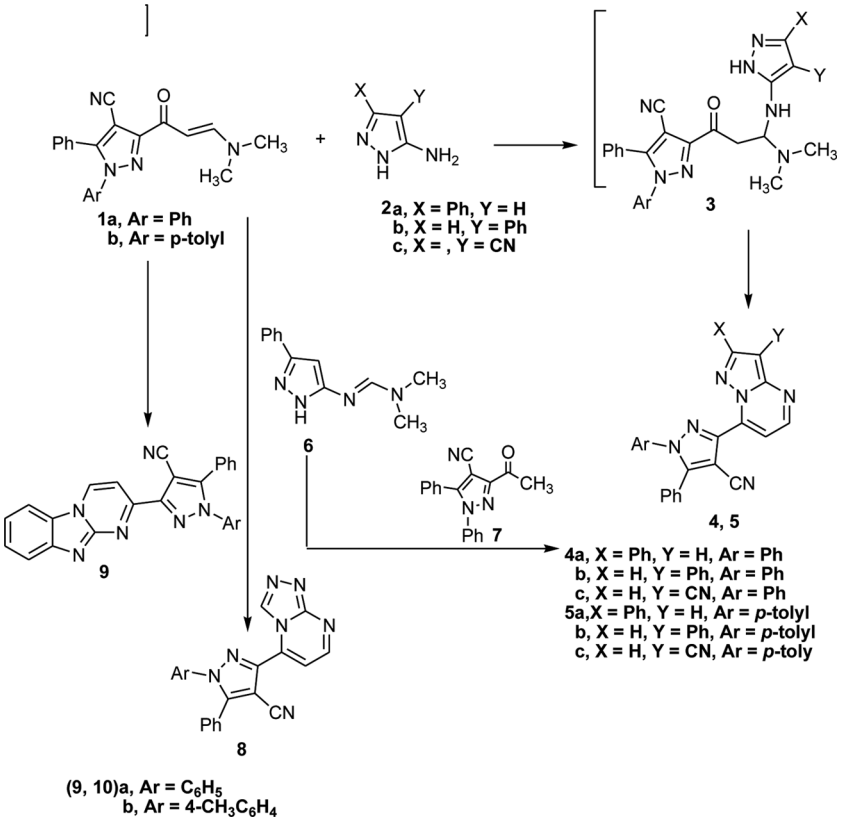
RESULTS AND DISCUSSION

Treatment of 3-((*E*)-3-(dimethylamino)acryloyl)-1,5-diphenyl-1H-pyrazole-4-carbonitrile **1a** with 3-amino-5-phenylpyrazole **2a** in acetic acid containing ammonium acetate by boiling under reflux gave 1,5-diphenyl-3-(2-phenylpyrazolo[1,5-*a*]pyrimidin-7-yl)-1*H*-pyrazole-4-carbonitrile **4a**. The structure **4a** was established by elemental analysis, spectral data, and alternative synthesis [^{1}H NMR $\delta = 6.55$ (s, 1H, pyrazole H-4), 7.26–7.80 (m, 12 H, ArH's), 8.23 (d, 2H, $J = 6$ Hz), 8.34 (d, 2H, $J = 6$ Hz), 9.29 (d, 1H)]. The formation of compound **4** is assumed to take place via an initial Michael addition of the exocyclic amino group in compound **2** to the activated double bond in **1a** to give the acyclic nonisolable intermediate **3**, which undergoes cyclization and aromatization via loss of both dimethylamine and water molecules, producing the final isolable product **4a**. Although the endocyclic imino group in compound **2a** is the most nucleophilic center, nevertheless, it is the most sterically hindered site,[29] as shown in Scheme 1. Thus, treatment of *N,N*-dimethyl-*N*′-(3-phenyl-1*H*-pyrazol-5-yl)formamidine **6** with 3-acetyl-1,5-diphenyl-1*H*-pyrazole-4-carbonitrile **7** in ethanol under reflux gives a product identical in all aspects (mp, mixed mp, and spectra) with **4a** (Scheme 1). Analogously, **1a** and **1b** reacted with the appropriate aminopyrazoles **2b** and **c**, 3-aminotraiazole, and 2-aminobenzimidazole to afford pyrazolo[1,5-*a*]pyrimidines **4b**, **4c**, **5a–c**, [1,2,4]triazolo[4,3-*a*]pyrimidine **8a** and **8b**, and benzo[4,5]imidazo[1,2-*a*]pyrimidine **9a** and **9b**, respectively.

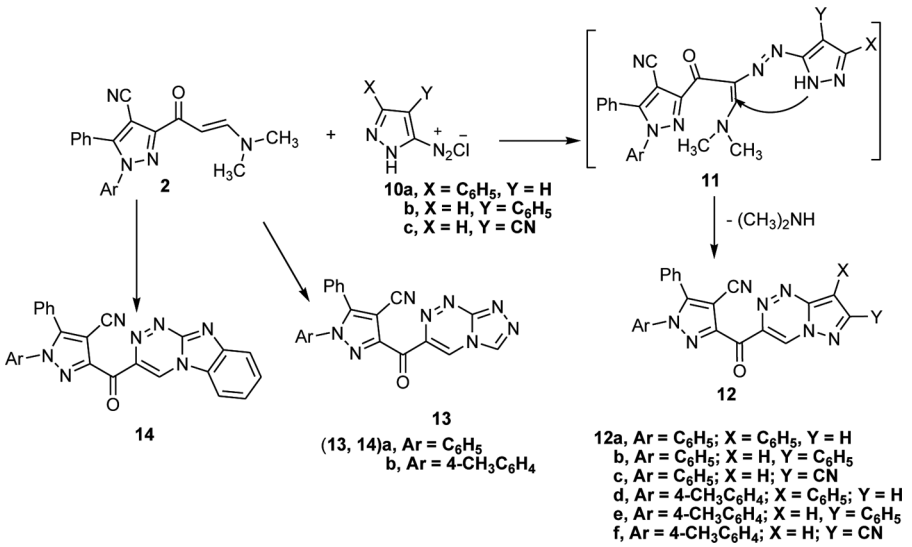
On the other hand, treatment of **2** with diazotized 3-amino-5-phenylpyrazole **10a** in an ethanolic sodium acetate solution gave 1,5-diphenyl-3-(8-phenyl-pyrazolo[5,1-*c*][1,2,4]triazine-3-carbonyl)-1*H*-pyrazole-4-carbonitrile **12a** (Scheme 2). Structure **12a** was elucidated by elemental analysis and spectral data. The formation of **12a** was formed via coupling diazonium chloride **10a** to **2** to form the intermediate **11**, which converted to the final product **6** through elimination of dimethylamine.

Analogously, treatment of the appropriate diazonium salt **10a–c**, triazole-3-diazonium nitrate, or benzimidazole-2-diazonium sulfate with each of **2a** and **2b** in ethanolic sodium acetate afforded pyrazolo[5,1-*c*][1,2,4]triazines **12b–g**, [1,2,4]triazolo[3,4-*c*][1,2,4]triazine **13a** and **b** and benzo[4,5]imidazo[2,1-*c*][1,2,4]triazine **14a** and **b**, respectively (Scheme 2).

Also, treatment of **2a** with benzenediazonium chloride in ethanol containing sodium acetate as a buffer solution yielded 3-[3-oxo-2-(phenyl-hydrazono)-propionyl]-1,5-diphenyl-1*H*-pyrazole-4-carbonitrile **15a**. Structure **15a** was confirmed by elemental analysis, spectral data, and chemical transformation. ^{1}H NMR spectrum of **15a** showed signals at $\delta = 6.65$–8.27 (m, 15 H, ArH's), 9.98 (s, 1H, -CHO), and 14.39



Scheme 1. Pyrazolo[1,5-*a*]pyrimidines, triazolo[4,3-*a*]pyrimidine, and benzo[4,5]imidazo[1,2-*a*]pyrimidine derivatives.



Scheme 2. Pyrazolo[5,1-*c*]triazine, triazolo[3,4-*c*]triazine, and benzo[4,5]imidazo[2,1-*c*]triazine derivatives.

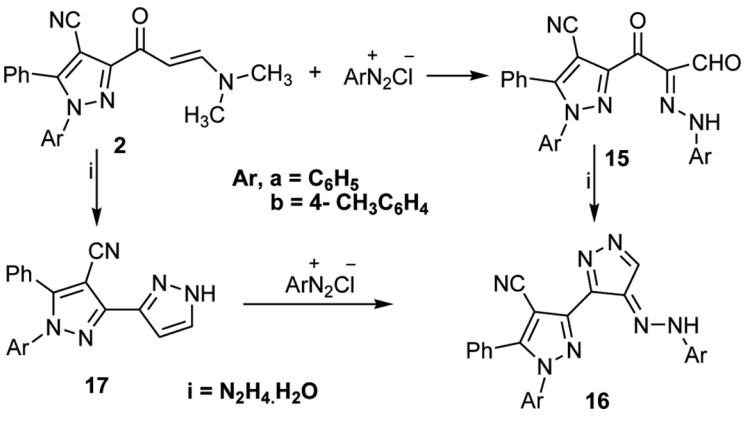
(s, br., 1H, NH). Thus, **15a** was reacted with hydrazine hydrate in boiling ethanol under reflux to give 1,5-diphenyl-4′-(phenyl-hydrazono)-1*H*,4′*H*-[3,3′]bipyrazolyl-4-carbonitrile **16a** (Scheme 3). Also, **2a** reacted with hydrazine hydrate to give 1,5-diphenyl-3-(1*H*-pyrazol-3-yl)-1*H*-pyrazole-4-carbonitrile **17a**. Compound **17a** was reacted with benzenediazonium chloride in ethanolic sodium acetate solution to afford a product identical in all respects (mp, mixed mp, and spectra) with **17a**.

Treatment of *C*-ethoxycarbonyl-*N*-phenylhydrazonoyl chloride (**18a**) with **2a** and triethylamine in boiling benzene under reflux afforded ethyl 4-(4-cyano-1,5-diphenyl-1*H*-pyrazole-3-carbonyl)-1-phenyl-1*H*-pyrazole-3-carboxylate (**22a**) (Scheme 4). ^{1}H NMR spectrum of **22a** showed signals at $\delta = 1.13$ (t, 3H, $J = 7$ Hz, $CH_2\underline{CH_3}$), 4.18 (q, 2H, $J = 7$ Hz, $\underline{CH_2}CH_3$), 7.44–7.88 (m, 15H, ArHs), and 8.44 (s, 1H, pyrazole H-5). Similarly, the appropriate hydrazonoyl halides **18a–e** reacted with each of **2a** and **2b** to give pyrazole derivatives **22b–e** and **23a–e**.

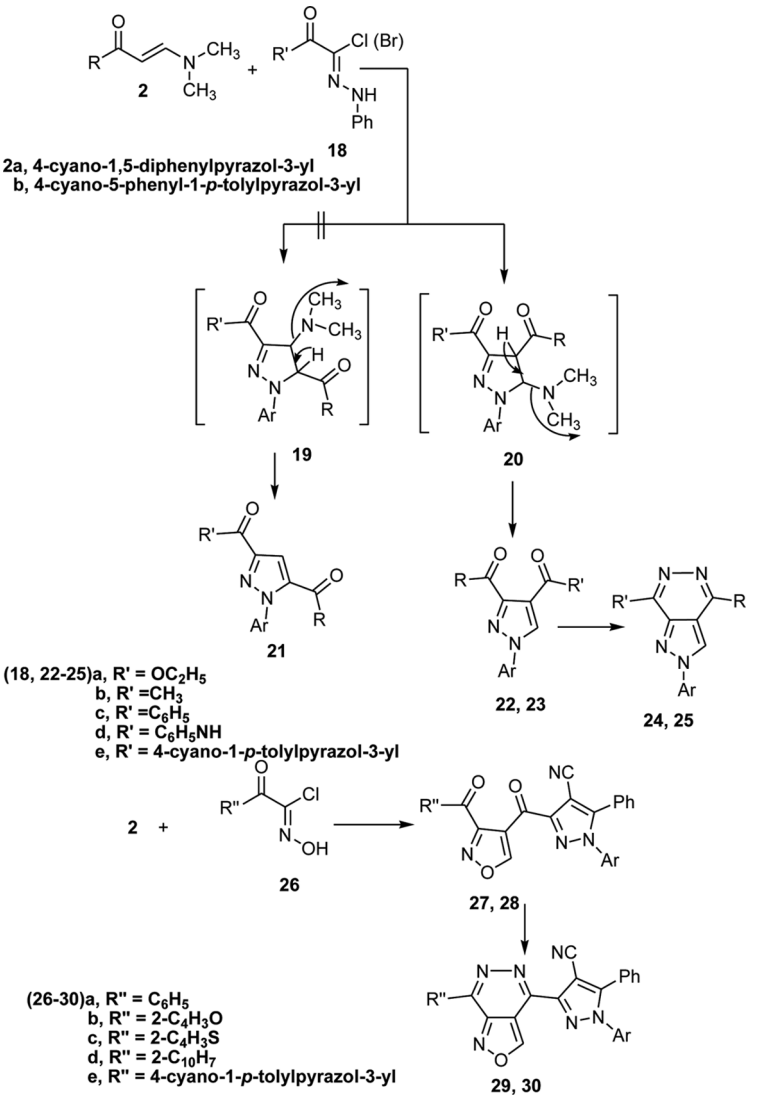
Compound **22a** with hydrazine hydrate in boiling ethanol afforded one isolable product according to thin-layer chromatography (TLC), formulated as 3-(7-oxo-2-phenyl-6,7-dihydro-2*H*-pyrazolo[3,4-*d*]pyridazin-4-yl)-1,5-diphenyl-1*H*- pyrazole-4-carbonitrile (**24a**). Structure of **24a** was elucidated by elemental analysis, spectral data, and alternative synthesis. ^{1}H NMR spectrum of **24a** showed signals at $\delta = 7.23$–8.41 (m, 15 H, ArHs), 8.52 (s, 1H, pyrazole H-5), and 12.12 (s, br., 1H, NH). Thus, treatment of either **22a** (or **22b)** and **23a** (or **23 g**) with boiling hydrazine hydrate in ethanol gave a product identical in all aspects (mp, mixed mp, and spectra) with **24a** and **25a**, respectively.

Also, pyrazolo[3,4-*d*]pyridazines **24b**,**c**,**e** and **25a–d** were obtained from the appropriate pyrazoles **22b**,**c**,**e** and **23a–c**,**e** with hydrazine hydrate (Scheme 4).

Treatment of the appropriate hydroximoyl chlorides **26a–e** with each of **2a** and **2b** in toluene at room temperature in the presence of triethylamine (or boiling without triethylamine) gave 4,5-diacylisoxazoles **27a–e** and **28a–e**, respectively. Compounds **27a–e** and **28a–e** were converted to isoxazolo[3,4-*d*] pyridazines **29a–e** and **30a–e**, respectively (Scheme 4).



Scheme 3. Pyrazoles **16** and **17**.



Scheme 4. Pyrazolo[3,4-*d*]pyridazines and isoxazolo[3,4-*d*]pyrimidines.

EXPERIMENTAL

All melting points were determined on an electrothermal apparatus and are uncorrected. Infrared (IR) spectra were recorded (KBr discs) on a Shimadzu Fourier Transform (FT)–IR 8201 PC spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ and $(CD_3)_2SO$ solutions on a Varian Gemini 300-MHz spectrometer and chemical shifts are expressed in δ units using tetramethylsilane (TMS) as an internal reference. Elemental analyses were carried out at the Microanalytical Center of the Cairo University.

3-(3-(Dimethylamino)acryloyl)-1,5-diphenyl-1H-Pyrazole-4-carbonitrile (1a) and 3-(3-(Dimethylamino)acryloyl)-5-phenyl-1-p-Tolyl-1H-Pyrazole-4-carbonitrile (1b)

Equimolar amounts of each 3-acetyl-1,5-diphenyl-1*H*-pyrazole-4-carbonitrile and 3-acetyl-5-phenyl-1-*p*-tolyl-1*H*-pyrazole-4-carbonitrile and dimethylformamide-dimethylacetal (50 mmol each) were refluxed in dry xylene (40 mL) for 4 h. The hot solution was evaporated to its half volume and then cooled. The resulting solid was collected and crystallized to give **1a** and **1b**.

3-((E)-3-(Dimethylamino)acryloyl)-1,5-diphenyl-1H-pyrazole-4-carbonitrile (1a). Pale brown crystals from EtOH, yield (81%), mp: 236–238 °C; IR (KBr): 3059, 2952 (CH), 2228 (CN), 1641 (CO, conjugated), 1563 (C=C); ^{1}H NMR ($CDCl_3$): $\delta = 2.97$ (s, 3H, CH_3), 3.18 (s, 3H, CH_3), 6.15 (d, 1H, $J = 12$ Hz, CH=CH), 7.27–7.42 (m, 10H, ArH's), and 7.94 (d, 1H, $J = 12$ Hz, CH=CH); ^{13}C NMR ($CDCl_3$): $\delta = 41.2$ (NCH_3), 88.1, 93.5, 117.6 (CN), 129.3, 129.5, 129.7, 129.8, 130.2, 130.3, 143.5, 143.6, 152.2, 159.4, 184.2; MS: $m/z = 344$ (M + 1, 1.9%), 343 (M^+, 10.14%), 342 (M − 1, 34.88%), 326 (27.88%), 325 (100%), 300 (10.64%), 272 (21.53%), 103 (6.09), 94 (10.08%). Anal. calcd. for $C_{21}H_{18}N_4O$ (342.39): C, 73.67; H, 5.30; N, 16.36. Found: C, 73.82; H, 5.15; N, 16.57%.

3-((E)-3-(Dimethylamino)acryloyl)-5-phenyl-1-p-tolyl-1H-pyrazole-4-carbonitrile (1b). Pale brown crystals from EtOH, yield (82%), mp: 224–226 °C; IR (KBr): 3060, 2952 (CH), 2225 (CN), 1639 (CO, conjugated), 1562 (C=C), 1350 (CH_3); ^{1}H NMR [$(CD_3)_2SO$]: $\delta = 2.37$ (s, 3H, CH_3), 2.88 (s, 3H, CH_3), 3. 17 (s, 3H, CH_3), 5.80–5.84 (d, 1H, $J = 12$ Hz, CH=CH), 7.24–7.46 (m, 9H, ArH's) and 7.81–7.85 (d, 1H, $J = 12$ Hz, CH=CH); ^{13}C NMR [$(CD_3)_2SO$]: $\delta = 20.6$ (CH_3), 41.3 (NCH_3), 88.3, 93.7, 117.2 (CN), 125.3, 129.2, 130.7, 132.3, 136.6, 137.5, 143.6, 152.2, 159.4, 184.4; MS: $m/z = 356$ (M^+, 100%), 314 (4.49%), 287 (32.91%), 257 (13.53%), 242 (7.68%), 230 (7.64), 178 (12.27%), 167 (4.29%), 163 (12.87%), 154 (21.45%), 141 (10.99%), 127 (13.00%), 114 (9.53%), 104 (10.46%), 98 (75.99%), 84 (21.27%), 76 (16.06%), 69 (49.94%), 65 (23.88%), 54 (50.74%). Anal. calcd. for $C_{22}H_{20}N_4O$ (356.42): C, 74.14; H, 5.66; N, 15.72. Found: C, 74.25; H, 5.75; N, 15.92%.

Pyrazolo[1,5-a]pyrimidine 4a–c, 5a–c, 1,2,4-triazolo[4,3-a]pyrimidine 8a and b, and 4a-hydropyrimidino[1,2-a]benzimidazoles 9a and 9b

A mixture of the appropriate 3-amino-5-phenylpyrazole, 3-amino-4-phenylpyrazole, 3-amino-4-cyanopyrazole, 3-aminotriazole, or 2-aminobenzimidazole (5 mmol); 3-(3-(dimethylamino)acryloyl)-1,5-diphenyl-1*H*-pyrazole-4-carbonitrile (**1a**) or 3-(3-(dimethylamino)acryloyl)-5-phenyl-1-*p*-tolyl-1*H*-pyrazole-4-carbonitrile (**1b**) (5 mmol); and ammonium acetate (0.37 g, 5 mmol) in acetic acid (20 mL) was refluxed for 4 h. The resulting solid that formed was collected and recrystallized from the proper solvent to give **4a**–**c**, **5a**–**c**, **8a**, **8b**, **9a**, and **9b**, respectively.

1,5-Diphenyl-3-(2-phenylpyrazolo[1,5-a]pyrimidin-7-yl)-1H-pyrazole-4-carbonitrile (4a). Pale yellow crystals from diluted AcOH, yield (87%), mp: 187–189 °C; IR (KBr): 3043 (CH, aromatic), 2229 (CN), 1612 (C=N), and 1585

(C=C); ^{1}H NMR ($CDCl_3$): δ = 7.09–8.52 (m, 17H, ArH's) and 9.11 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$): δ = 96.8 (pyrazole C-4), 102.2, 111.1, 121.6 (CN), 124.1, 127.5, 128.1, 128.6, 129.4, 129.5, 130.3, 130.4, 131.2, 131.3, 131.5, 133.6, 133.7, 141.2, 151.4, 152.6, 153.1, 155.6; MS: m/z = 439 (M + 1, 13.2%), 438 (M^+, 19.5%), 307 (5.7%), 229 (9.2%), 219 (4.6%), 195 (5.7%), 165 (10.9), 151 (5.7%), 118 (5.2%), 104 (8%), 103 (6.9%), 102 (8.6%), 11 (9.8%), 91 (7.5%), 90 (6.9%), 89 (10.3%), 77 (100%), 63 (11.5%), and 51 (57.5%). Anal. calcd. for $C_{28}H_{18}N_6$ (438.48): C, 79.76; H, 4.18; N, 11.63. Found: C, 79.72; H, 4.22; N, 11.65%.

1,5-Diphenyl-3-(3-phenylpyrazolo[1,5-a]pyrimidin-7-yl)-1H-pyrazole-4-carbonitrile (4b). Pale brown crystals from AcOH, yield (87%), mp: 202–204 °C; IR (KBr): 3043 (CH, aromatic), 2228 (CN), 1610 (C=N) and 1587 (C=C); ^{1}H NMR ($CDCl_3$): δ = 7.09–8.41 (m, 17H, ArH's) and 9.10 (s, 1H, ArH);^{13}C NMR ($CDCl_3$): δ = 108.2, 108.1, 110.6, 122.1 (CN), 124.3, 126.1, 126.4, 128.2, 129.3, 129.4, 129.6, 130.2, 130.4, 131.3, 131.5, 133.5, 141.2, 148.4, 151.2, 153.3, 154.8 (pyrazole C-3); MS: m/z = 439 (M + 1, 13.2%), 438 (M^+, 19.5%), 307 (5.7%), 229 (9.2%), 219 (4.6%), 195 (5.7%), 165 (10.9), 151 (5.7%), 118 (5.2%), 104 (8%), 103 (6.9%), 102 (8.6%), 11 (9.8%), 91 (7.5%), 90 (6.9%), 89 (10.3%), 77 (100%), 63 (11.5%), and 51 (57.5%). Anal. calcd. for $C_{28}H_{18}N_6$ (438.48): C, 79.76; H, 4.18; N, 11.63. Found: C, 79.72; H, 4.22; N, 11.65%.

7-(4-Cyano-1,5-diphenyl-1H-pyrazol-3-yl)pyrazolo[1,5-a]pyrimidine-3-carbonitrile (4c). Pale cream crystals from EtOH, yield (86%), mp: 208–210 °C; IR (KBr): 3062 (CH, aromatic), 2227 (CN), 1613 (C=N) and 1565 (C=C); ^{1}H NMR ($CDCl_3$): δ = 7.27–8.05 (m, 7H, ArH's), 8.32 (m, 4H, ArH's), 8.42 (s, 1H, pyrazole H-5), 9.04 (s, 1H, pyrimidine H-4); ^{13}C NMR ($CDCl_3$): δ = 81.2, 102.1, 110.7, 112.1, 120.0 (CN), 122.2 (CN), 1233.8, 127.8, 129.2, 129.3, 130.2, 130.3, 131.1, 131.3, 131.4, 141.2, 151.4, 153.4, 156.4, 158.7 (pyrazole C-3); MS: m/z = 389 (M + 2, 5.3%), 388 (M + 1, 16%), 387 (55%), 396 (M − 1, 100%), 385 (54%), 325 (5.3%), 213 (7.4%), 197 (6.4%), 178 (8.5%), 167 (10.6%), 150 (11.7%), 143 (10.6%), 142 (16%), 127 (9.6%), 124 (10.6%), 97 (10.6%), 77 (75.5%), 64 (12.8%). Anal. calcd. for $C_{23}H_{13}N_7$ (387.4): C, 71.31; H, 3.38; N, 25.31. Found: C, 71.12; H, 4.11; N, 25.55%.

5-Phenyl-3-(2-phenylpyrazolo[1,5-*a*]pyrimidin-7-yl)-1-*p*-tolyl-1*H*-pyrazole-4-carbonitrile (4d). Pale cream crystals from diluted AcOH, yield (87.7%), mp: 194–196 °C; IR (KBr): 3043 (CH, aromatic), 2226 (CN), 1622 (C=N), and 1600 (C=C); ^{1}H NMR ($CDCl_3$): δ = 2.36 (s, 3H, CH_3), 6.41 (s, 1H, pyrazole H-4), 7.21–8.02 (m, 13H, ArH's), 8.31 (d, 2H, J = 8 Hz, ArH's) and 9.11 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$): δ = 19.8 (CH_3), 97.2 (pyrazole c-4), 102.1, 110.8, 122.2 (CN), 124.2, 127.3, 128.2, 128.5, 130.3, 131.1, 131.2, 131.3, 131.4, 133.2, 136.3, 141.2, 151.2, 152.3, 153.1, 155.4; MS: m/z = 454 (M + 2, 5.9%), 452 (M^+, 100%), 425 (34.1%), 218 (25.3%), 203 (15.9%), 193 (34.1%), (13%), 177 (13%), 166 (28.7%), 151 (7.5%), 142 (19.8%), 140 (23.9%), 127 (16.7%), 115 (46.7%), 103 (33%), 914 (50%), 89 (33.2%), 77 (35.1%), 65 (34%). Anal. calcd. for $C_{29}H_{20}N_6$ (452.51): C, 76.97; H, 4.45; N, 18.57. Found: C, 77.10; H, 4.32; N, 18.65%.

5-Phenyl-3-(3-phenylpyrazolo[1,5-*a*]pyrimidin-7-yl)-1-*p*-tolyl-1*H*-pyrazole-4-carbonitrile (4e). Dark yellow crystals from AcOH, yield (87%), mp: 202–204 °C;

IR (KBr): 3045 (CH, aromatic), 2225 (CN), 1625 (C=N), and 1600 (C = C); ^{1}H NMR ($CDCl_3$): $\delta = 2.34$ (s, 3H, CH_3), 6.93 (d, 2H, $J = 8$ Hz, ArH), 7.23–8.22 (m, 14H, ArH's), and 9.11 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$): $\delta = 20.1$ (CH_3), 102.1, 108.4, 110.7, 122.1 (CN), 124.4, 126.3, 126.4, 128.2, 129.5, 130.4, 131.2, 131.3, 131.4, 133.3, 136.5, 141.3, 148.2, 151.2, 153.6, 154.4 (pyrazolo C-3). Anal. calcd. for $C_{29}H_{20}N_6$ (452.51): C, 76.97; H, 4.45; N, 18.57. Found: C, 76.80; H, 4.12; N, 18.85%.

7-(4-Cyano-5-phenyl-1-*p*-tolyl-1*H*-pyrazol-3-yl)pyrazolo[1,5-*a*]pyrimidine-3-carbonitrile (4f). Pale yellow crystals from EtOH, yield (86%), mp 238–240 °C; IR (KBr): 3136 (CH, aromatic), 2230 (CN), 1616 (C=N), 1562 (C=C) and 1323 (CH_3); ^{1}H NMR [$(CD_3)_2SO$]: $\delta = 2.36$ (s, 3H, CH_3), 7.23–8.42 (m, 11H, ArH's), and 9.51 (s, 1H, ArH); ^{13}C NMR [$(CD_3)_2SO$]: $\delta = 20.4$ (CH_3), 81.5, 102.4, 111.1, 112.4 (CN), 122.2 (CN), 124.5, 128.3, 129.5, 130.3, 1311.2, 131.4, 131.8, 136.3, 141.2, 151, 153.1, 156.3, 158.5 (pyrazole C-3); MS: $m/z = 401$ (M^+, 100%), 373 (2.5%), 228 (4.5%), 202 (9.6%), 192 (13.6%), 139 (4.6%), 104 (4.4%), 101 (7.1%), 90 (37.4), 77 (15.1%), 64 (33.4). Anal. calcd. for $C_{24}H_{15}N_7$ (401.42): C, 71.81; H, 3.77; N, 24.42. Found: C, 71.85; H, 3.52; N, 24.65%.

3-([1,2,4]Triazolo[1,5-a]pyrimidin-7-yl)-1,5-diphenyl-1H-pyrazole-4-carbonitrile (8a). Yellow crystals from diluted AcOH, yield (85%), mp: 295–297 °C; IR (KBr): 3062 (CH, aromatic), 2225 (CN), 1623 (C=N) and 1586 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: $\delta = 7.27$–8.02 (m, 7H, ArH's), 8.29 (s, 1H, triazole H-3), 9.72 (d, 1H, $J = 4$ Hz, pyrimidine H-4); ^{13}C NMR [$(CD_3)_2SO$]: $\delta = 102.1$ (pyrazole C-4), 110.2, 117.8 (CN), 124.4, 128.5, 129.8, 129.9, 130.2, 130.7, 131.2, 134.4, 136.8, 141.1, 145.2 (triazole C-5), 149.3, 151.2, 157.8; MS: $m/z = 389$ (M + 2, 5.3%), 388 (M + 1, 16%), 387 (55%), 396 (M − 1, 100%), 385 (54%), 325 (5.3%), 213 (7.4%), 197 (6.4%), 178 (8.5%), 167 (10.6%), 150 (11.7%), 143 (10.6%), 142 (16%), 127 (9.6%), 124 (10.6%), 97 (10.6%), 77 (75.5%), 64 (12.8%). Anal. calcd. for $C_{21}H_{13}N_7$(387.4): C, 69.41; H, 3.61; N, 26.98. Found: C, 69.42; H, 3.72; N, 26.75%.

3-([1,2,4]Triazolo[4,3-a]pyrimidin-5-yl)-5-phenyl-1-p-tolyl-1H-pyrazole-4-carbonitrile (8b). Colorless crystals from diluted AcOH, yield (85%), mp 264–266 °C; IR (KBr): 3085 (CH, aromatic), 2233 (CN), 1658 (C=N) and 1589 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: $\delta = 2.28$ (s, 3H, CH_3), 7.27–7.30 (m, 3H, ArH's), 7.67–7.73 (m, 3H, ArH's), 7.87 (d, 2H, $J = 8$ Hz, ArH,s), 8.312 (d, 2H, $J = 8$ Hz), 9.39 (s, 1H, ArH), 9.72 (s, 1H, ArH); ^{13}C NMR [$(CD_3)_2SO$]: $\delta = 20.1$ (CH_3), 101.2, 111.1, 117.8 (CN), 124.4, 128.4, 128.4, 129.5, 130.2, 131.3, 131.9, 143.5, 136.9, 141.2, 145.4 (triazole C-5), 149.2, 151.5, 158.2; MS: $m/z = 387$ (M + 1, 12.2%), 377 (M^+, 100%), 301 (12.7%), 287 (14.30%), 257 (4.9%), 165 (7%), 149 (11.9), 146 (11.5%), 127 (7.2%), 114 (12.5%), 92 (17.5%), 79 (10.4%), 78 (9.1%), 77 (76.5%), 68 (19.8%), 65 (100%). Anal. calcd. for $C_{22}H_{15}N_7$(377.4): C, 70.01; H, 4.01; N, 25.98. Found: C, 69.85; H, 3.92; N, 26.10%.

3-Benzo[4,5]imidazo[1,2-a]pyrimidin-4-yl-1,5-diphenyl-1H-pyrazole-4-carbonitrile (9a). Yellow crystals from dioxane, yield (86.9%), mp >300 °C; IR (KBr): 3085 (CH, aromatic), 2230 (CN), 1658 (C=N) and 1589 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: $\delta = 7.27$–7.50 (m, 6H, ArH's), 7.67 (d, 2H, $J = 8$ Hz, ArH's), 7.87–8.12

(m, 5H, ArH's), 8.31 (d, 2H, $J = 8$ Hz, ArH's), 9.39 (s, 1H, ArH); ^{13}C NMR [$(CD_3)_2SO$]: $\delta = 101.8$, 110.9, 115.2, 117.2 (CN), 119.5, 122.2, 124.3, 124.5, 128.6, 129.2, 129.5, 130.3, 130.5, 137.1, 137.4, 141.2, 147.4, 149.3, 155.8, 158.2; MS: $m/z = 413$ (M + 1, 2.2%), 412 (M^+, 0.9%), 319 (2.5%), 244 (11.45%), 180 (24.99%), 141 (10.40%), 114 (11.06), 103 (11.7%), 91 (10.5%), 90 (18.65%), 77 (100%), 65 (8.9%), 64 (11.28%). Anal. calcd. for $C_{26}H_{16}N_6$(412.45): C, 75.71; H, 3.91; N, 20.38. Found: C, 75.85; H, 3.90; N, 20.10%.

3-Benzo[4,5]imidazo[1,2-*a*]pyrimidin-4-yl-5-phenyl-1-*p*-tolyl-1*H*-pyrazole-4-carbonitrile (9b). Pale yellow crystals from diluted dimethylformamide (DMF), yield (87%), mp 276–278 °C; IR (KBr): 3085 (CH, aromatic), 2230 (CN), 1658 (C=N) and 1589 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: $\delta = 2.34$ (s, 3H, CH_3), 7.21–7.32 (m, 5H, ArH's), 7.67–7.83 (m, 6H, ArH's), 8.10 (d, 1H, $J = 8$ Hz, ArH,s), 8.31 (d, 2H, $J = 8$ Hz), 9.35 (s, 1H, ArH); ^{13}C NMR [$(CD_3)_2SO$]: $\delta = 20.8$ (CH_3), 101.9, 110.3, 115.2, 117.6 (CN), 119.1, 122.4, 124.6, 124.7, 128.4, 129.4, 132.5, 137.4, 141.3, 147.2, 149.4, 155.2, 157.8; MS: $m/z = 427$ (M + 1, 1.31%), 301 (26.56%), 286 (34.66%), 244 (6.91%), 194 (19.5%), 165 (8.53%), 140 (10.6), 127 (10.35%), 114 (15.09%), 104 (25.53%), 103 (32.85%), 91 (100%), 89 (49.53%), 77 (96.06%), 65 (83.80%), 63 (40.89%). Anal. calcd. for $C_{27}H_{18}N_6$(426.47): C, 76.04; H, 4.25; N, 19.71. Found: C, 76.15; H, 3.95; N, 19.55%.

(Pyrazolo[5,1-*c*][1,2,4]triazin-3-yl)methanone 12a–e, ([1,2,4]Triazolo[3,4-*c*][1,2,4]triazin-6-yl)(1*H*-pyrazol-3-yl)methanone 13a and b, Benzo[4,5]imidazo[2,1-*c*][1,2,4]triazin-3-yl-(1*H*-pyrazol-3-yl)-methanone 14a and b, 1*H*-Pyrazol-3-yl)-4*H*-pyrazol-4-ylidene)hydrazine 16, and 3-(1*H*-Pyrazol-3-yl)-1*H*-pyrazole 17

A solution of the appropriate diazonium salt of heterocyclic amines [(3-amino-5-phenylpyrazole (**3a**), 3-amino-4-phenylpyrazole (**3b**), 3-amino-4-cyano-pyrazole (**3c**), 3-amino-1,2,4-triazole (**3d**), and 2-amino-benzimidazole (**3e**)] (5 mmol) was added to a mixture of sodium salt of 5-hydroxy-1-naphtho[2,1-*b*]furan-2-ylpropenone (**2**) (5 mmol), sodium acetate (0.65 g, 5 mmol) in ethanol (30 mL) at 0–5 °C while stirring. The resulting solid that formed after 3 h was collected, washed with water, and recrystallized to give **12a**–**c**, **13a**–**c**, **14a**, **14b**, **16**, and **17**, respectively

1,5-Diphenyl-3-(7-phenyl-pyrazolo[5,1-c][1,2,4]triazine-4-carbonyl)-1H-pyrazole-4-carbonitrile (12a). Brown crystals from EtOH, yield (93%), mp: 214–216 °C; IR (KBr): 3057 (CH, aromatic), 2227 (CN), 1642 (C=O) and 1567 (C=C); ^{1}H NMR ($CDCl_3$): $\delta = 6.67$ (s, 1H, pyrazole H-4), 7.27–8.05 (m, 13H, ArH's), 8.42 (d, 2H, $J = 8$ Hz, ArH's), 9.72 (d, 1H, $J = 8$ Hz, ArH); ^{13}C NMR ($CDCl_3$): $\delta = 88.1$, 103.2, 117.6 (CN), 125.6, 126.8, 129.1, 129.2, 129.4, 131.3, 131.7, 133.4, 138.8, 143.2, 145.2, 151.7, 152.4, 153.2, 153.5, 181.2 (CO); MS: $m/z = 467$ (M^+, 5.3%), 439 (6.0%), 296 (4.27%), 272 (27.45.3%), 244 (5.4%), 216 (16.4%), 180 (15.5%), 141 (70.6%), 101 (19.7%), 88 (28.6%), 76 (56%). Anal. calcd. for $C_{28}H_{17}N_7O$ (467.48): 71.94; H, 3.67; N, 20.97. Found: C, 72.12; H, 3.78; N, 20.85%.

1,5-Diphenyl-3-(8-phenyl-pyrazolo[5,1-c][1,2,4]triazine-4-carbonyl)-1H-pyrazole-4-carbonitrile (12b). Dark brown from EtOH, yield (93%), mp: 242–244 °C; IR (KBr): 3058 (CH, aromatic), 2233 (CN), 1654 (C=O) and 1596 (C=C); ^{1}H NMR ($CDCl_3$): 7.27–8.05 (m, 13H, ArH's), 8.42 (d, 3H, $J = 8$ Hz, ArH's), 9.72 (d, 1H, $J = 8$ Hz, ArH); ^{13}C NMR ($CDCl_3$): $\delta = 103.0$, 118.1 (CN), 128.1, 128.3, 129.2, 129.4, 129. 6, 131.6, 134.3, 139.2, 143.2, 145.4, 151.2, 152.3, 153.4, 154.6, 181.2 (CO); MS: $m/z = 467$ (M^+, 100%), 439 (5.99%), 272 (27.54%), 269 (15.27%), 244 (5.26%), 223 (10.69%), 216 (16.05%), 190 (15.65%), 177 (5.26%), 152 (10.16%), 141 (70.53%), 127 (8.87%), 104 (7.10%), 101 (19.66%), 88 (29.90%). Anal. calcd. for $C_{28}H_{17}N_7O$ (467.48): C, 71.94; H, 3.67; N, 20.97. Found: C, 72.12; H, 3.78; N, 20.85%.

4-(4-Cyano-1,5-diphenyl-1H-pyrazole-3-carbonyl)-pyrazolo[5,1-c][1,2,4] triazine-8-carbonitrile (12c). Yellowish green crystals from diluted AcOH, yield (95%), mp: 218–220 °C; IR (KBr): 3070 (CH, aromatic), 2237 (CN), 1664 (C=O) and 1596 (C=C); ^{1}H NMR ($CDCl_3$): 7.27–8.05 (m, 7H, ArH's), 8.22 (d, 2H, $J = 8$ Hz, ArH's), 8.42 (d, 2H, $J = 8$ Hz, ArH's), 9.72 (d, 1H, $J = 8$ Hz, ArH); ^{13}C NMR ($CDCl_3$): $\delta = 88.2$, 98.2, 117.3 (CN), 122.1 (CN), 129.1, 129.2, 129.5, 129.7, 129.9, 131.2, 131.6, 136.2, 143.1, 145.3, 151.2, 151.4, 152.3, 180.9 (CO); MS: $m/z = 400$ (0.86%), 325 (19.85%), 315 (4.73%), 287 (7.33%), 272 (12.09%), 245 (11.33%), 180 (11.35%), 167 (14.75%), 149 (32.74%), 141 (5.92%), 114 (6.96%), 98 (33.98%), 78 (10.88%), 77 (100%), 70 (69.51%), 65 (21.48%). Anal. calcd. for $C_{23}H_{12}N_8O$ (416.39): C, 66.34; H, 2.90; N, 26.91. Found: C, 66.12; H, 2.78; N, 26.65%.

5-Phenyl-3-(7-phenyl-pyrazolo[5,1-c][1,2,4]triazine-4-carbonyl)-1-p-tolyl-1H-pyrazole-4-carbonitrile (12d). Brown crystals from EtOH, yield (93%), mp: 198–200 °C; IR (KBr): 3055 (CH, aromatic), 2233 (CN), 1684 (C=O) and 1595 (C=C), 1350 (CH_3); ^{1}H NMR [$(CD_3)_2SO$]: 2.37 (s, 3H, CH_3), 7.17–7.81 (m, 10H, ArH's), 8.16 (d, 2H, $J = 8$ Hz, ArH's), 8.42 (d, 2H, $J = 8$ Hz, ArH's), 9.02 (s, 1H, ArH), 9.85 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$): $\delta = 20.1$ (CH_3), 87.9, 103.2, 117.6 (CN), 125.2, 125.4, 126.2, 129.4, 129.7, 130.9, 131.6, 132.3, 133.8, 136.7, 137.5, 139.4, 145.4, 151.2, 152.4, 153.1, 153.4 (pyrazole C-4), 181.2 (CO). Anal. calcd. for $C_{29}H_{19}N_7O$ (481.51): C, 72.34; H, 3.98; N, 20.36. Found: C, 72.12; H, 3.78; N, 20.55%.

5-Phenyl-3-(7-phenyl-pyrazolo[5,1-c][1,2,4]triazine-3-carbonyl)-1-p-tolyl-1H-pyrazole-4-carbonitrile (12e). Pale brown crystals from EtOH, yield (93%), mp 262–264 °C; IR (KBr): 3055 (CH, aromatic), 2237 (CN), 1658 (CO), 1608 (C=N) and 1595 (C=C), 1350 (CH_3); ^{1}H NMR [$(CD_3)_2SO$]: 2.36 (s, 3H, CH_3), 7.12–7.79 (m, 10H, ArH's), 8.16 (d, 2H, $J = 8$ Hz, ArH's), 8.42 (d, 2H, $J = 8$ Hz, ArH's), 9.02 (s, 1H, ArH), 9.85 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$): $\delta = 20.0$ (CH_3), 88.2, 101.2 (pyrszole C-3), 117.6 (CN), 125.3, 128.4, 129.3, 129.6, 130.4, 131.2, 132.5, 134.5, 136.6, 137.82, 139.4, 145.5, 151.2, 152.4, 153.3, 154.6, 181.1 (CO); MS: $m/z = 482$ (M + 1, 30.7%), 481 (100%), 480 (M − 1, 87.2%), 286 (28.4%), 285 (17.6%), 223 (16.8%), 194 (11.2%), 155 (13.9%), 142 (12.2%), 140 (13.0%), 128 (12.6%), 115 (18.7%), 114 (12.5%), 102 (20.2%), 91 (30.0%), 89 (14.8%), 77

(24.6%), 65 (33.2%). Anal. calcd. for $C_{29}H_{19}N_7O$ (481.51): C, 72.34; H, 3.98; N, 20.36. Found: C, 72.25; H, 3.74; N, 20.47%.

4-(4-Cyano-5-phenyl-1-p-tolyl-1H-pyrazole-3-carbonyl)-pyrazolo[5,1-c][1,2,4]-triazine-8-carbonitrile (12f). Yellow crystals from EtOH, yield (95%), mp 204–206 °C; IR (KBr): 3070 (CH, aromatic), 2237 (CN), 1664 (C=O) and 1596 (C=C); ^{1}H NMR ($CDCl_3$): 2.41 (s, 3H, CH_3), 7.27–7.34 (m, 3H, ArH's), 7.70–7.82 (m, 2H, ArH's), 8.22–8.45 (m, 2H, ArH's), 8.72 (s, 1H, ArH), 8.85 (d, 2H, $J = 8$ Hz, Hz, ArH), 10.82 (s, 1H, ArH); ^{13}C NMR: 20.2 (CH_3), 88.1, 97.9 (pyrazole C-3), 117.6 (CN), 120.4 (CN), 125.4, 129.4, 129.6, 132.2, 137.1, 137.4, 145.2, 151.4, 151.5, 152.2, 181.2 (CO); MS: $m/z = 343$ (100%), 328 (3.59%), 310 (11.35%), 272 (49.42%), 243 (12.66%), 230 (6.17%), 179 (24.96%), 171 (8.66%), 156 (32.74%), 141 (18.54%), 127 (6.43%), 114 (11.13%), 97 (61.14%), 84 (13.72%), 77 (45.49%), 64 (32.52%), 54 (37.17%), 51 (17.77). Anal. calcd. for $C_{24}H_{14}N_8O$ (430.42): C, 66.97; H, 3.28; N, 26.03. Found: C, 67.12; H, 3.18; N, 26.25%.

1,5-Diphenyl-3-([1,2,4]triazolo[3,4-c][1,2,4]triazine-5-carbonyl)-1H-pyrazole-4-carbonitrile (13a). Yellowish green crystals from diluted AcOH, yield (92%), mp: 192–194 °C; IR (KBr): 3062 (CH, aromatic), 2233 (CN), 1659 (C=O), and 1593 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: 7.27–7.7.64 (m, 6H, ArH's), 7.95 (d, 2H, $J = 8$ Hz, ArH's), 8.45 (s, 1H, ArH), 8.65 (d, 2H, $J = 8$ Hz, ArH), 9.82 (s, 1H, ArH); ^{13}C NMR: 87.9, 117.6 (CN), 129.2, 129.3, 129.6, 129.9, 13.2, 131.5, 139.5 (triazole C-5), 143.4, 144.5, 145.5, 150.8, 152.2, 156.3, 178.4 (CO); MS: $m/z = 365$ (M-N_2, 1.91%), 287 (4.19%), 272 (13.07%), 259 (6.15%), 245 (27.15%), 149 (10.50%), 104 (28.20%), 104 (40.23%), 91 (37.09%), 77 (100%), 65 48.24%), 50 (79.19%). Anal. calcd. for $C_{21}H_{12}N_8O$ (392.11): C, 64.28; H, 3.08; N, 28.56. Found: C, 64.15; H, 3.28; N, 28.69%.

5-Phenyl-1-p-tolyl-3-([1,2,4]triazolo[3,4-c][1,2,4]triazine-5-carbonyl)-1H-pyrazole-4-carbonitrile (13b). Yellowish green crystals from diluted AcOH, yield (92.5%), mp 250–252 °C; IR (KBr): 3062 (CH, aromatic), 2237 (CN), 1660 (C=O), 1635 (C=N), and 1380 (CH_3); ^{1}H NMR [$(CD_3)_2SO$]: 2.41 (s, 3H, CH_3), 7.27–7.34 (m, 3H, ArH's), 7.70–7.79 (m, 2H, ArH's), 8.20–8.28 (m, 2H, ArH's), 8.45 (s, 1H, ArH), 8.65 (d, 2H, $J = 8$ Hz, ArH), 9.82 (s, 1H, ArH); ^{13}C NMR: 20.1 (CH_3), 87.9, 117.6 (CN), 125.4, 129.4, 129.6, 130.4, 132.3, 136.7, 137.6, 139.4 (triazole C-5), 144.4, 145.6, 156.4, 178.4 (CO); MS: $m/z = 407$ (M + 1, 2.03%), 406 (M^+, 10.86%), 258 (12.49%), 243 (10.71%), 230 (4.33%), 215 (4.65%), 180 (8.12%), 147 (28.20%), 119 (39.48%), 103 (47.27%), 92 (12.73%), 91 (50.10%), 97 (4.32%), 74 (12.80%), 67 (10.61%), 64 (100%), 54 (7.65%), 54 (13.95), 53 (60.06%), 50 (62.87%). Anal. calcd. for $C_{22}H_{14}N_8O$ (406.4): C, 65.02; H, 3.47; N, 27.57.03. Found: C, 65.12; H, 3.68; N, 27.75%.

3-(Benzo[4,5]imidazo[2,1-c][1,2,4]triazine-4-carbonyl)-1,5-diphenyl-1H-pyrazole-4-carbonitrile (14a). Pale cream crystals from diluted AcOH, yield (92.8%), mp >300 °C; IR (KBr): 3062 (CH, aromatic), 2233 (CN), 1654 (C=O), and 1593 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: 7.27–7.85 (m, 8H, ArH's), 8.15–8.35 (m, 2H, ArH's), 8.42–8.65 (m, 2H, ArH's), 8.65 (d, 1H, $J = 8$ Hz, ArH), 8.65 (d, 1H, $J = 8$ Hz, Hz, ArH), 9.27 (s, 1H, ArH); ^{13}C NMR: 87.9, 113.2, 117.5 (CN), 118.5, 124.4, 124.5, 129.3, 129.6, 129.7, 129.9, 130.7, 131.3, 131.6, 143.3, 144.2, 144.4, 146.3, 148.2, 152.3,

155.4, 178.8 (CO); MS: $m/z = 413$ (M-N_2, 0.67%), 342 (3.75%), 326 (12.87%), 259 (5.15%), 167 (8.25%), 149 (32.21%), 141 (5.69%), 114 (4.76%), 98 (67.07%), 81 (42.17%), 79 (23.02%), 77 (97.19%), 69 (48.95%). Anal. calcd. for $C_{26}H_{15}N_7O$ (441.44): C, 70.74; H, 3.42; N, 22.21. Found: C, C, 70.87 H, 3.25; N, 22.00%.

3-(Benzo[4,5]imidazo[2,1-c][1,2,4]triazine-4-carbonyl)-5-phenyl-1-p-tolyl-1H-pyrazole-4-carbonitrile (14b). Pale cream crystals from diluted AcOH, yield (93%), mp 194–196 °C; IR (KBr): 3047 (CH, aromatic), 2233 (CN), 1654 (C=O), 1624 (C=N), and 1380 (CH_3); ^{1}H NMR [$(CD_3)_2SO$]: $\delta = 2.38$ (s, 3H, CH_3), 7.27–7.75 (m, 7H, ArH's), 8.10–7.14 (m, 2H, ArH's), 8.20–8.23 (m, 2H, ArH's), 8.65 (d, 1H, $J = 8$ Hz, ArH), 8.72 (d, 1H, $J = 8$ Hz, ArH), 9.18 (s, 1H, ArH); ^{13}C NMR [$(CD_3)_2SO$]: $\delta = 20.1$ (CH_3), 88.1, 113.2, 117.5 (CN), 118.2, 124.3, 124.5, 129.2, 129.4, 129.8, 130.7, 132.2, 136.7, 137.6, 144.6, 144.7, 145.9, 148.4, 152.2, 179.1 (CO); MS: $m/z = 456$ (M^+, 011%), 356 (16.17%), 340 (60.78%), 301 (12.09%), 286 (20.97%), 273 (12.06%), 258 (28.36%), 243 (15.36%), 231 (6.74%), 215 (8.34%), 194 (21.76%), 165 (7.91%), 152 (14.87%), 140 (18.92%), 127 (31.24%), 114 (26.17%), 100 (13.79%), 98 (88.09%), 91 (73.86%), 88 (31.33%), 76 (72.94%), 69 (49.98%), 54 (100%), 50 (40.1%). Anal. calcd. for $C_{27}H_{17}N_7O$ (455.47): C, 71.20; H, 3.76; N, 21.53. Found: C, 71.00; H, 3.57; N, 21.35%.

3-[3-Oxo-2-(phenylhydrazono)propanoyl]-1,5-diphenyl-1H-pyrazole-4-carbonitrile (15a). Yellow crystals from diluted AcOH, yield (96%), mp 210–212 °C; IR (KBr): 3047 (CH), 2870, 2785 (CH, Fermi resonance), 2229 (CN), 1640 (CO), 1562 (C=C), and 1380 (CH_3); ^{1}H NMR [$(CD_3)_2SO$]: 6.89–8.51 (m, 15H, ArH's), 9.75 (s, 1H, C<u>H</u>O), 14.89 (s, br., 1H, NH); MS: $m/z = 420$ ($M + 1$, 0.1%), 343 (20.36%), 326 (56.41%), 259 (6.68%), 152 (6.50%), 140 (8.22%), 103 (6.69%), 98 (67.48%), 81 (18.55%), 77 (54.37%), 70 (33.26%), 68 (18.02%), 54 (100%). Anal. calcd. for $C_{25}H_{17}N_5O_2$ (419.43): C, 71.59; H, 4.09; N, 16.70. Found: C, 71.65; H, 4.18; N, 16.85%.

3-[3-Oxo-2-(p-tolylhydrazono)propanoyl]-1,5-diphenyl-1H-pyrazole-4-carbonitrile (15b). Brown crystals from EtOH, yield (96%), mp 220–222 °C; IR (KBr): 3047 (CH), 2816, 2765 (CH, Fermi resonance), 2229 (CN), 1640 (CO), 1562 (C=C), and 1353 (CH_3); ^{1}H NMR [$(CD_3)_2SO$]: 2.32 (s, 3H, $CH_3C_6H_4$), 7.26–8.34 (m, 14H, ArH's), 9.75 (s, 1H, C<u>H</u>O), 14.89 (s, br., 1H, NH); MS: $m/z = 433$ (M^+, 0.07%), 343 (28.50%), 329 (12.17%), 325 (75.95%), 272 (10.49%), 259 (13.02%), 141 (13.77%), 98 (48.05%), 77 (54.48%), 69 (49.42%), 54 (100%). Anal. calcd. for $C_{26}H_{19}N_5O_2$ (433.46): C, 72.04; H, 4.42; N, 16.16. Found: C, 72.13; H, 4.57; N, 16.34%.

3-[3-Oxo-2-(phenylhydrazono)propanoyl]-1-p-tolyl-5-phenyl-1H-pyrazole-4-carbonitrile (15c). Brown crystals from EtOH, yield (96%), mp: 212–214 °C; IR (KBr): 3047 (CH), 2804, 2754 (CH, Fermi resonance), 2225 (CN), 1640 (CO), 1566 (C=C), and 1350 (CH_3); ^{1}H NMR [$(CD_3)_2SO$]: 2.38 (s, 3H, $CH_3C_6H_4$), 7.26–8.34 (m, 14H, ArH's), 9.75 (s, 1H, C<u>H</u>O), 14.89 (s, br., 1H, NH); MS: $m/z = 433$ (M^+, 0.19%), 357 (37.80%), 340 (100%), 287 (11.33%), 98 (32.91%), 91 (12.94%), 77 (5.99%), 69 (24.96%), 65 (12.46%), 55 (31.15%). Anal. calcd. for $C_{26}H_{19}N_5O_2$ (433.46): C, 72.04; H, 4.42; N, 16.16. Found: C, 72.08; H, 4.48; N, 16.38%.

3-[3-Oxo-2-(p-tolylhydrazono)propanoyl]-1-p-tolyl-5-phenyl-1H-pyrazole-4-carbonitrile (15d). Red crystals from EtOH, yield (96%), mp: 202–204 °C; IR (KBr): 3047 (CH), 2804, 2754 (CH, Fermi resonance), 2230 (CN), 1640 (CO), 1566 (C=C), and 1353 (CH_3); ^{1}H NMR [$(CD_3)_2SO$]: 2.38 (s, 3H, $CH_3C_6H_4$), 2.40 (s, 3H, $CH_3C_6H_4$), 7.26–8.34 (m, 13H, ArH's), 9.75 (s, 1H, C<u>H</u>O), 14.89 (s, br., 1H, NH); MS: $m/z = 447$ (M^+, 0.19%), 357 (37.55%), 340 (100%), 287 (10.04%), 273(9.52%), 98 (43.41%), 91 (14.61%), 84 (9.05%), 81 (9.44%), 76 (7.85%), 69 (32.50%), 65 (13.71%), 54 (45.10%). Anal. calcd. for $C_{27}H_{21}N_5O_2$ (447.49): C, 72.47; H, 4.73; N, 15.65. Found: C, 72.52; H, 4.94; N, 15.72%.

Synthesis of Pyrazoles 17a and b

A mixture of the appropriate **1a** and **1b** (5 mmol) and hydrazine hydrate (0.5 mL, 10 mmol) in ethanol (15 mL) was refluxed for 2 h. The resulting solid was collected and recrystallized from ethanol to give **17a** and **17b**.

1,5-Diphenyl-3-(4H-pyrazol-3-yl)-1H-pyrazole-4-carbonitrile (17a). Brown crystals from EtOH, yield (81%), mp 236–238 °C; IR (KBr): 3047 (CH), 2230 (CN), 1640 (CO), 1566 (C=C), and 1353 (CH_3); ^{1}H NMR [$(CD_3)_2SO$]: 6.45 (s, 1H, pyrazple H-4), 7.26–8.33 (m, 11H, ArH's and pyrazole H-5), 11.89 (s, br., 1H, NH). Anal. calcd. for $C_{19}H_{13}N_5$ (311.34): C, 73.30; H, 4.21; N, 22.49. Found: C, 73.45; H, 4.33; N, 22.4962%.

5-Phenyl-3-(4H-pyrazol-3-yl)-1-p-tolyl-1H-pyrazole-4-carbonitrile (17b). Colorless crystals from EtOH, yield (80%), mp 278–280 °C; IR (KBr): 3047 (CH), 2804, 2754 (CH, Fermi resonance), 2230 (CN), 1640 (CO), 1566 (C=C), and 1353 (CH_3); ^{1}H NMR [$(CD_3)_2SO$]: 2.38 (s, 3H, $CH_3C_6H_4$), 6.44 (s, 1H, pyrazple H-4), 7.21–8.25 (m, 10H, ArH's and pyrazole H-5), 11.89 (s, br., 1H, NH). Anal. calcd. for $C_{20}H_{15}N_5$ (325.37): C, 73.83; H, 4.65; N, 21.52. Found: C, 73.75; H, 4.54; N, 21.74%.

Synthesis of Pyrazoles 16a–d

A mixture of the appropriate **15a**–**d** and hydrazine hydrate (5 mmol), (0.5 g, 0.5 mL, 10 mmol) in ethanol (15 mL) was refluxed for 2 h. The resulting solid was collected and recrystallized to give **16a**–**d**, respectively.

Alternative method. A solution of the appropriate arendiazonium chloride (5 mmol) was added to a mixture of the appropriate **15a** and **b** (5 mmol) and sodium acetate (0.65 g, 5 mmol) in ethanol (30 mL) at 0–5 °C while stirring. The resulting solid that formed after 3 h was collected, washed with water, and recrystallized from the proper solvent to give a product identical in all aspects (mp, mixed mp, and spectra) with the corresponding **16a**–**d**.

4,5-Dimethyl-1-phenyl-1H,4'h-3,3'-bipyrazol-4'-one phenylhydrazone (16a). Dark red crystals from EtOH, yield (88%), mp 256–258 °C; IR (KBr): 3282 (NH), 3070 (CH), 2218 (CN), 1589 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: 7.18–8.01 (m, 15H, ArH's), 8.54 (s, 1H, pyrazole H-5), 10.89 (s, br., 1H, NH); MS: $m/z = 414$ ($M - 1$, 0.01%), 311 (100%), 282 (10.34%), 77 (19.76%), 51 (17.12%). Anal. calcd.

for $C_{25}H_{17}N_7$ (415.45): C, 72.28; H, 4.12; N, 23.60. Found: C, 72.35; H, 4.31; N, 23.72%.

4,5-Dimethyl-1-phenyl-1H,4′H-3,3′-bipyrazol-4′-one(4-methylphenyl) hydrazone (16b). Light pink crystals from diluted AcOH, yield (89%), mp 260–226 °C; IR (KBr): 3283 (NH), 3066 (CH), 2218 (CN), 1589 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: 2.38 (s, 3H, $CH_3C_6H_4$), 7.26–8.34 (m, 14H, ArH's), 8.75 (s, 1H, pyrazole H-5), 10.89 (s, br., 1H, NH); MS: $m/z = 429$ (M − 1, 0.05%), 311 (100%), 282 (18.18%), 255 (13.00), 228 (6.09%), 216 (7.27%), 190 (8.72%), 178 (10.91%), 151 (12.8%), 126 (13.39%), 134 (7.77%), 100 (9.63%), 94 (6.63%), 88 (6.45%), 76 (70.93%), 66 (11.31%), 63 (15.84%), 51 (70.65%). Anal. calcd. for $C_{26}H_{19}N_7$ (429.48): C, 72.71; H, 4.46; N, 22.83. Found: C, 72.92; H, 4.64; N, 22.77%.

4,5-Dimethyl-1-(4-methylphenyl)-1H,4′H-3,3′-bipyrazol-4′-one phenyl-hydrazone (16c). Yellow crystals from EtOH, yield (88%), mp 262–264 °C; IR (KBr): 3294 (NH), 3043 (CH), 2221 (CN), 1577 (C=C), ^{1}H NMR [$(CD_3)_2SO$]: 2.38 (s, 3H, $CH_3C_6H_4$), 7.15–8.22 (m, 14H, ArH's), 8.55 (s, 1H, pyrazole H-5), 10.89 (s, br., 1H, NH); MS: $m/z = 430$ (M + 1, 0.06%), 326 (67.28%), 281 (6.79%), 255 (7.14), 228 (10.30%), 215 (10.38%), 204 (9.15%), 189 (8.85%), 177 (13.25%), 167 (12.46%), 151 (28.88%), 126 (24.97%), 103 (17.33%), 100 (21.29%), 93 (17.60%), 91 (43.56%), 88 (38.91%), 78 (70.65%), 66 (23.52%), 65 (100%), 53 (9.307%), 52 (20.30%), 50 (62.87%). Anal. calcd. for $C_{26}H_{19}N_7$ (429.48): C, 72.71; H, 4.46; N, 22.83. Found: C, 72.94; H, 4.58; N, 22.98%.

4,5-Dimethyl-1-phenyl-1H,4′H-3,3′-bipyrazol-4′-one (4-methylphenyl)-hydrazone (16d). Brown crystals from EtOH, yield (89%), mp 264–266 °C; IR (KBr): 3290 (NH), 3143 (CH), 2221 (CN), 1577 (C=C), ^{1}H NMR [$(CD_3)_2SO$]: 2.38 (s, 3H, $CH_3C_6H_4$), 2.40 (s, 3H, 4-$CH_3C_6H_4$), 7.27–8.15 (m, 13H, ArH's), 8.47 (s, 1H, pyrazole H-5), 10.75 (s, br., 1H, NH). Anal. calcd. for $C_{27}H_{21}N_7$ (443.5): C, 73.12; H, 4.77; N, 22.11. Found: C, 73.27; H, 4.85; N, 22.46%.

5-Phenyl-3-(1-phenyl-1H-pyrazole-4-carbonyl)-1-p-tolyl-1H-pyrazole-4-carbonitrile 22 and 23

Equimolar amounts of each of 3-(3-(dimethylamino)acryloyl)-1,5-diphenyl-1*H*-pyrazole-4-carbonitrile (**1a**) or 3-(3-(dimethylamino)acryloyl)-5-phenyl-1-*p*-tolyl-1*H*-pyrazole-4-carbonitrile (**1b**) and the appropriate hydrazonoyl halides **18a**–**e** (5 mmol) were refluxed in dry toluene (20 mL) containing triethylamine (0.75 mL) for 3 h. The hot solution was filtered off, and the filtrate was evaporated and triturated with petroleum ether (40–60 °C). The resulting solid was collected and recrystallized from ethanol to give **22a**–**e** and **23a**–**e**.

Ethyl 4-(4-cyano-1,5-diphenyl-1H-pyrazole-3-carbonyl)-1-phenyl-1H-pyrazole-3-carboxylate (22a). Pale yellow crystals from EtOH, yield (85%), mp 190–192 °C; IR (KBr): 3060, 2981 (CH), 2232 (CN), 1731 (C=O), 1649 (C=N), 1591 (C=C), 1437 (CH_2) and 138 (CH_3); ^{1}H NMR [$(CD_3)_2SO$]: δ = 1.10 (t, 3H, $J = 7.5$ Hz, $CH_2\underline{CH_3}$), 4.15 (q, 2H, $J = 7.5$ Hz, $\underline{CH_2}CH_3$), 7.37–7.75 (m, 13H, ArH's), 7.82–7.96 (m, 2H, ArH's), 9.31 (s, 1H, pyrazole C-5); ^{13}C NMR [$(CD_3)_2SO$]: δ = 14.5 (CH_3), 60.6 (CH_2), 94.8, 117.6 (CN), 120.1, 123.1, 127.3, 129.2, 129.3, 129.4, 129.8,

130.8, 131.2, 132.8, 140.7, 142.6, 144.6, 147.8, 152.4, 160.4 (CO), 178.7 (CO); MS: $m/z = 489$ (M + 2, 1.8%), 488 (M + 1,16.7.5%), 487 (M^+, 24.1%), 442 (29.8%), 272 (12.4%), 215 (19.9%), 180 (15.8%), 141 (16.3%), 104 (48.2%), 77 (100%), 65 (4.1%). Anal. calcd. for $C_{29}H_{21}N_5O_3$ (487.51): C, 71.45; H, 4.34; N, 14.37. Found: C, 71.20; H, 4.57; N, 14.35%.

3-(3-Acetyl-1-phenyl-1H-pyrazole-4-carbonyl)-1,5-diphenyl-1H-pyrazole-4-carbonitrile (22b). Pale cream crystals from diluted AcOH, yield (84%), mp 198–200 °C; IR (KBr): 3062, 2914 (CH), 2229 (CN), 1700, 1656 (2 C=O), 1594 (C=C), and 1350 (CH_3); ^{1}H NMR [$(CD_3)_2SO$]: δ = 2.61 (s, 3H, CH_3), 7.35–7.63 (m, 13H, ArH's), 7.95–7.99 (d, 2H, $J = 8$ Hz), ArH's), 9.25 (s, 1H, pyrazole C-5); ^{13}C NMR [$(CD_3)_2SO$]: δ = 27.1 (CH_3), 94.5, 117.6 (CN), 119.8, 127.1, 127.3, 128.7, 129.4, 129.5, 129.9, 131.2, 132.6, 142.3, 144.5, 146.3, 149.6, 150.4, 152.6, 180.1 (CO), 194.8 (CO); MS: $m/z = 459$ (M + 2, 5.2%), 458 (M + 1, 11.0%), 457 (M^+, 23.5)%, 456 (M − 1, 13.5%), 442 (36.5%), 325 (12.9%), 272 (13.9%), 213 (14.8%), 171 (40.0%), 141 (14.2%), 104 (20.0%), 77 (100%), 51 (29.0%). Anal. calcd. for $C_{28}H_{19}N_5O_2$ (457.48): C, 73.51; H, 4.19; N, 15.31. Found: C, 73.35; H, 4.31; N, 15.48%.

3-(3-Benzoyl-1-phenyl-1H-pyrazole-4-carbonyl)-1,5-diphenyl-1H-pyrazole-4-carbonitrile (22c). Brown crystals from AcOH, yield (80%), mp 219–221 °C; IR (KBr): 3061 (CH), 2230 (CN), 1654 (C=O), 1592 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: δ = 7.16–7.60 (m, 18H, ArH's), 7.96–7.98 (d, 2H,, $J = 8$ Hz), ArH's), 9.44 (s, 1H, pyrazole C-5); ^{13}C NMR [$(CD_3)_2SO$]: δ = 94.5, 117.6 (CN), 119.8, 125.2, 127.6, 127.9, 129.2, 129.3, 129.6, 130.2, 130.6, 131.2, 132.4, 138.2, 141.5, 144.7, 145.4, 150.2, 152.1, 153.4, 178.6 (CO), 187.3 (CO); MS: $m/z = 521$(M + 2, 2.3%), 520 (M + 1, 13.2%), 519 (M^+, 29)%, 490 (4.7%), 442 (12.4%), 275 (112.9%), 275 (11.9%), 180 (7.9%), 106 (6.2%), 105 (82.7%), 104 (10.0%), 77 (100%), 51 (23.2%). Anal. calcd. for C_{28} $C_{33}H_{21}N_5O_2$ (519.55): C, 76.29; H, 4.07; N, 13.48. Found: C, 76.08; H, 4.12; N, 13.61%.

4-(4-Cyano-1,5-diphenyl-1H-pyrazole-3-carbonyl)-3-carbamoyl-1-phenyl-1H-pyrazole (22d). Brown crystals from AcOH, yield (86%), mp: 198–200 °C; IR (KBr): 3260 (NH), 3025 (CH), 2230 (CN), 1679 (C=O), 1639 (C=N), 16.1 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: δ = 7.12–7.72 (m, 18H, ArH's), 9.35 (s, 1H, pyrazole C-5), 10.72 (s, br., 1H, NH); ^{13}C NMR [$(CD_3)_2SO$]: δ = 94.5, 117.6 (CN), 119.8, 120.7, 124.4, 127.5, 129.3, 129.4, 129.6, 129.9, 130.2, 131.4, 132.7, 140.4, 140.8, 143.2, 134.5, 145.6, 148.3, 152.4, 157.7 (CO), 178.2 (CO). Anal. calcd. for C_{28} $C_{33}H_{22}N_6O_2$ (534.57): C, 74.14; H, 4.15; N, 15.72. Found: C, 74.00; H, 3.95; N, 15.57%.

3-({4-[(4-Cyano-1,5-diphenylpyrazol-3-yl)carbonyl]1-phenylpyrazole-3-yl}-carbonyl}-1-(4-methylphenyl)-5-phenylpyrazole-4-carbonitrile (22e). Pale cream crystals from diluted AcOH, yield (84.7%), mp 250–252 °C; IR (KBr): 3061, 2919 (CH), 2234 (CN), 1681 (C=O), 1646 (C=N), 1596 (C=C), 1379 (CH_3); ^{1}H NMR [$(CD_3)_2SO$]: δ = 2.27 (s, 3H, CH_3), 7.09–8.03 (m, 24H, ArH's), 9.74 (s, 1H, pyrazole C-5); ^{13}C NMR [$(CD_3)_2SO$]: δ = 20.1 (CH_3), 91.6, 94.5, 117.6 (CN), 119.8, 124.2, 125.3, 127.6, 128.4, 129.2, 129.4, 129.8, 130.2, 131.4, 132.2, 132.7, 136.6, 137.5, 142.5, 144.6, 144.8, 148.2, 150.3, 152.1, 154.3, 174.5 (CO),

178.6 (CO); MS: $m/z = 700$ (M^+, 0.59%), 676 0.69%), 580 (0.71%), 325 (4.38%), 286 (6.61%), 180 (3.77%), 167 (14.13%), 149 (40.14%), 111 (10.79%), 92 (11.64%), 84 (18.16%), 77 (37.98%), 77 (100%), 57 (52.79%), 50 (18.33%). Anal. calcd. for $C_{44}H_{28}N_8O_2$ (700.75): C, 75.42; H, 4.03; N, 15.99. Found: C, 75.21; H, 3.83; N, 16.19%.

Ethyl 4-(4-cyano-5-phenyl-1-p-tolyl-1H-pyrazole-3-carbonyl)-1-phenyl-1H-pyrazole-3-carboxylate (23a). Yellow crystals from diluted AcOH, yield (85%), mp 210–212 °C; IR (KBr): 3039, 2920 (CH), 2233 (CN), 1708 (C=O), 1658 (CO, conjugated), 1596 (C=C), 1413 (CH_2), 1379 (CH_3); ^{1}H NMR [$(CD_3)_2SO$]: 1.16 (t, 3H, $J = 7.5$ Hz, $CH_2\underline{CH_3}$), 2.34 (s, 3H, CH_3), 4.14 (q, 2H, $J = 7.5$ Hz, $\underline{CH_2}CH_3$), 7.28–8.41 (m, 12H, ArH's), 8.52 (d, 1H, $J = 8$ Hz, ArH's), 8.48 (s, 1H, pyrazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: $\delta = 14.4$ (CH_3), 20.1 (CH_3), 60.4 (CH_2), 94.5, 117.6 (CN), 119.8, 123.1, 125.4, 127.3, 129.4, 129.5, 130.3, 132.1, 132.7, 136.6, 138.7, 140.6, 142.8, 147.7, 152.5, 160.4 (CO), 180.1 (CO); MS: $m/z = 504$ (M + 2, 1.18)%, 503 (M + 1, 4.34%), 202 (M^+, 14.56%), 429 (4.31%), 301 (5.47%), 257 (5.35%), 244 (7.15%), 243 (10.65%), 215 (15.45%), 149 (17.19%), 142 (11.05%), 103 (62.03%), 91 (42.21%), 77 (100%), 65 (24.65%), 57 (21.75%). Anal. calcd. for $C_{30}H_{23}N_5O_3$ (501.54): C, 71.84; H, 4.62; N, 13.96. Found: C, 72.00; H, 4.81; N, 14.15%.

3-(3-Acetyl-1-phenyl-1H-pyrazole-4-carbonyl)-5-phenyl-1-p-tolyl-1H-pyrazole-4-carbonitrile (23b). Pale gray crystals from diluted AcOH, yield (85%), mp 188–190 °C; IR (KBr): 3052, 2920 (CH), 2233 (CN), 1708 (C=O), 1658 (C=N), 1596 (C=C), 1379 (CH_3); ^{1}H NMR [$(CD_3)_2SO$]: $\delta = 2.36$ (s, 3H, CH_3), 2.62 (s, 3H, CH_3), 7.28–8.41 (m, 12H, ArH's), 8.52 (d, 1H, $J = 8$ Hz, ArH's), 8.49 (s, 1H, pyrazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: $\delta = 20.1$ (CH_3), 27.5 (CH_3), 94.5, 117.6 (CN), 119.8, 125.5, 127.3, 128.8, 129.2, 129.4, 130.7, 132.2, 123.4, 136.6, 138.5, 142.5, 146.7, 149.4, 150.7, 152.2, 180.3 (CO), 194.8 (CO); MS: $m/z = 472$ (M^+, 100%), 457 (96.57%), 443 (35.03%), 428 (11.85%), 418 (8.36%), 401 (25.55%), 367 (6.39%), 356 (13.88%), 339 (43.25%), 301 (17.23%), 286 (19.61%), 273 (9.68%), 258 (22.56%), 243 (16.99%), 230 (13.47%), 213 (32.80%), 171 (61.22%), 155 (15.76%), 141 (13.50%), 114 (16.06%), 103 (40.68%), 90 (52.98%), 76 (53.70%), 64 (30.69%). Anal. calcd. for $C_{29}H_{21}N_5O_2$ (471.51): C, 73.87; H, 4.49; N, 14.85 Found: C, 73.68; H, 4.54; N, 15.11%.

3-(3-Benzoyl-1-phenyl-1H-pyrazole-4-carbonyl)-5-phenyl-1-p-tolyl-1H-pyrazole-4-carbonitrile (23c). Pale cream crystals from diluted AcOH, yield (80%), mp 185–187 °C; IR (KBr): 3058 (CH), 2233 (CN), 1658 (C=O), 1600 (C=C), 1384 (CH_3); ^{1}H NMR [$(CD_3)_2SO$]: $\delta = 2.36$ (s, 3H, CH_3), 7.28–8.41 (m, 19H, ArH's), 8.49 (s, 1H, pyrazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: (=20.0 (CH_3), 94.5, 117.6 (CN), 119.8, 125.3, 127.7, 129.3, 129.6, 130.2, 132.3, 132.7, 136.4, 138.2, 138.6, 141.6, 145.7, 150.4, 152.7, 153.6, 178.2 (CO), 187.4 (CO); MS: $m/z = 534$ (M + 1, 28.29%), 472 (44.46%), 457 (65.55%), 443 (18.66%), 415 (11.00%), 400 (4.95%), 214 (43.43%), 178 (10.27%), 154 (33.79%), 141 (17.37%), 115 (18.76%), 104 (87.95%), 90 (64.43%), 77 (100%), 65 (26.02%). Anal. calcd. for $C_{34}H_{23}N_5O_2$ (533.58): C, 76.53; H, 4.34; N, 13.13. Found: C, 76.35; H, 4.45; N, 13.27%.

4-(4-Cyano-5-phenyl-1-p-tolyl-1H-pyrazole-3-carbonyl)-3-carbamoyl-1-phenyl-1H-pyrazole (23d). Brown crystals from diluted AcOH, yield (87%), mp 132–134 °C; IR (KBr): 3475 (NH), 3042 (CH), 2231 (CN), 1676 (C=O), 1624 (C=N), 1601 (C=C), 1368 (CH_3); ^{1}H NMR (CD_3Cl): $\delta = 2.39$ (s, 3H, CH_3), 7.14–7.92 (m, 19H, ArH's), 9.27 (s, 1H, pyrazole H-5), 11.58 (s, br., 1H, NH); ^{13}C NMR [$(CD_3)_2SO$]: (=20.1 (CH_3), 94.5, 117.6 (CN), 119.8, 120.8, 124.5, 125.7, 127.6, 129.4, 129.7, 130.4, 130.5, 132.4, 132.8, 136.7, 138.5, 140.3, 140.6, 143.5, 145.6, 148.2, 152.1, 157.7 (CO), 177.9 (CO); MS: $m/z = 549$ (M + 1, 5%), 548 (M^+, 18.5%), 274 (17.4%), 193 (13.5%), 104 (12.4%), 89 (7.9%), 77 (26%), 76 (14%), 65 (22.5%). Anal. calcd. for $C_{34}H_{24}N_6O_2$ (548.59): C, 74.44; H, 4.41; N, 15.32. Found: C, 74.65; H, 4.31; N, 15.48%.

3-[(4-{[4-Cyano-1-(4-methylphenyl)-5-phenylpyrazol-3-yl]carbonyl}-1-phenyl-pyrazol-3-yl)carbonyl]-1-(4-methylphenyl)-5-phenylpyrazole-4-carbonitrile (23e). Pale brown crystals from AcOH, yield (85%), mp 256–258 °C; IR (KBr): 3055 (CH), 2233 (CN), 1678 (C=O), 1639 (C=N), 1600 (C=C), 1380 (CH_3); ^{1}H NMR [$(CD_3)_2SO$]: $\delta = 2.39$ (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 7.14–7.92 (m, 23H, ArH's), 9.27 (s, 1H, pyrazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: (=20.1 (CH_3), 91.7, 94.5, 117.6 (CN), 120.1, 124.2, 125.4, 127.4, 128.2, 129.4, 130.7, 132.3, 132.8, 136.6, 138.7, 142.4, 144.6, 148.3, 150.2, 152.2, 154.8, 174.5 (CO), 178.1 (CO); MS: $m/z = 715$ (M + 1, 0.81%), 714 (M^+, 0.80%), 456 (4.60%), 286 (11.07%), 258 (11.22%), 243 (15.13%), 231 (8.52%), 195 (7.09%), 171 (4.52%), 155 (14.24%), 104 (36.75%), 91 (58.81%), 77 (100%), 65 (36.95%). Anal. calcd. for $C_{45}H_{30}N_8O_2$ (714.77): C, 75.62; H, 4.23; N, 15.68. Found: C, 75.80; H, 4.35; N, 15.87%.

3-(Isoxazole-4-carbonyl)-5-phenyl-1-p-tolyl-1H-pyrazole-4-carbonitrile 27 and 28

Method A. Triethylamine (0.5 g, (0.75 ml, 5 mmol) was added dropwise to an equimolar amount of **1a** (or **1b**) and the appropriate hydroximoyl chloride **26a–d** (5 mmol, each) in dry toluene (20 ml) while stirring. The reaction mixture was stirred for 6 h, the solvent was evaporated and then it was triturated with petroleum ether (40–60 °C). The resulting solid was collected and crystallized to give **27a–e** and **28a–d** respectively.

Method B. Equimolar amount of **1a** (or **1b**) and the appropriate hydroximoyl chloride **26a–d** (5 mmol, each) in dry toluene (20 ml) were heated under reflux for 18 h. The reaction mixture was filtered off, the solvent was evaporated, and the filtrate was triturated with petroleum ether (40–60 °C). The resulting solid was collected and crystallized to give products identical in all aspects (mp, mixed mp, and spectra) with **27a–e** and **28a–d**, respectively.

3-(3-Benzoyl-isoxazole-4-carbonyl)-1,5-diphenyl-1H-pyrazole-4-carbonitrile (27a). Brown crystals from diluted AcOH, yield (84%), mp 178–180 °C; IR (KBr): 3062, 2918 (CH), 2233 (CN), 1681 (C=O), 1658 (C=N), 1593 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: $\delta = 7.14$–7.71 (m, 9H, ArH's), 8.26 (d, 2H, $J = 8$ Hz), 8.52 (d, 4H, $J = 8$ Hz), 8.95 (s, 1H, isoxazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: (=94.5, 117.6 (CN), 118.8, 128.5, 129.4, 129.6, 130.2, 130.5, 132.9, 137.2, 142.4, 144.6, 152.2,

162.2, 179.6 (CO), 187.4 (CO), 191.8 isoxazole C-5); MS: $m/z = 445$ (M + 1, 0.44%), 444 (M^+,1.63%), 339 (0.75%), 311 (2.94%), 287 (0.96%), 272 (4.41%), 180 (2.03%), 105 (100%), 77 (51.36%), 51 (19.27%). Anal. calcd. for $C_{27}H_{16}N_4O_3$ (444.44): C, 72.97; H, 3.63; N, 12.61. Found: C, 73.12; H, 3.75; N, 12.45%.

3-[3-(Furan-2-carbonyl)-isoxazole-4-carbonyl]-1,5-diphenyl-1H-pyrazole-4-carbonitrile (27b). Gray crystals from AcOH, yield (84%), mp 178–180 °C; IR (KBr): 3015, 2923 (CH), 2237 (CN), 1658 (C=O), 1558 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: δ = 6.63 (d, 1H, $J = 6$ Hz, furan H-4), 7.14–7.28 (m, 7H, ArH's), 8.01 (d, 1H, $J = 6$ Hz, furan H-5), 8.26 (d, 2H, $J = 8$ Hz), 8.52 (d, 2H, $J = 8$ Hz), 8.95 (s, 1H, isoxazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: (=94.5, 109.8, 114.5, 117.6 (CN), 129.3, 129.5, 129.7, 129.9, 130.7, 131.3, 132.7, 137.5, 144.8, 145.7, 151.2, 151.4, 152.4, 160.2 (CO), 180.0 (CO), 183.8 (isoxazole C-5); MS: $m/z = 435$ (M + 2, 0.44%), 434 (M + 1, 2.02%), 405 (M^+, 5.13%), 272 (1.49%), 244 (0.52%), 180 (0.59%), 95 (100%), 77 (13.74%), 51 (7.29%). Anal. calcd. for $C_{25}H_{14}N_4O_4$ (434.4): C, 69.12; H, 3.25; N, 12.90. Found: C, 69.00; H, 3.41; N, 13.15%.

1,5-Diphenyl-3-[3-(thienyl-2-carbonyl)-isoxazole-4-carbonyl]-1H-pyrazole-4-carbonitrile (27c). Beige crystals from diluted AcOH, yield (84%), mp: 156–158 °C; IR (KBr): 3097, 2923 (CH), 2233 (CN), 1658 (C=O), 1596 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: δ = 7.14–7.98 (m, 11H, ArH's), 8.24 (d, 2H, $J = 8$ Hz), 8.94 (s, 1H, isoxazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: (= 94.5, 114.5, 117.6 (CN), 125.3, 129.3, 129.5, 130.8, 131.3, 132.2, 132.7, 142.1, 144.7, 147.8, 151.5, 152.4, 166.9, 179.7 (CO), 179.9 (CO), 183.7 (isoxazole C-5); MS: $m/z = 452$ (M + 2, 0.47%), 451 (M + 1, 1.58%), 450 (M^+, 5.30%), 339 (0.57%), 272 (1.41%), 141 (1.65%), 111 (100%), 77 (16.47%), 51 (7.85%). Anal. calcd. for $C_{25}H_{14}N_4O_3S$ (450.47): C, 66.66; H, 3.13; N, 12.44; S, 7.12. Found: C, 66.84; H, 3.00; N, 12.60; S, 7.32%.

3-[3-(Naphthalene-2-carbonyl)-isoxazole-4-carbonyl]-1,5-diphenyl-1H-pyrazole-4-carbonitrile (27d). Brown crystals from AcOH, yield (85%), mp 208–210 °C; IR (KBr): 3068, 2916 (CH), 2233 (CN), 1639 (C=O), 1562 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: δ = 7.14–8.12 (m, 13H, ArH's), 8.42 (d, 2H, $J = 8$ Hz), 8.57 (d, 1H, $J = 8$ Hz), 8.94 (s, 1H, isoxazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: (=94.5, 117.6 (CN), 119.1, 126.4, 127.8, 128.3, 128.7, 129.3, 129.5, 129.7, 129.8, 129.9, 130.7, 131.2, 131.3, 132.6, 133.2, 133.1, 133.3, 142.2, 144.7, 152.2, 161.9, 179.5 (CO), 187.3 (CO), 191.8 (isoxazole C-5); MS: $m/z = 496$ (M + 2, 0.02%), 495 (M + 1, 0.07%), 494 (M^+, 0.17%), 325 (100%), 272 (9.74%), 180 (5.20%), 98 (16.10%), 77 (6.58%), 55 (10.74%). Anal. calcd. for $C_{31}H_{18}N_4O_3$ (494.5): C, 75.29; H, 3.67; N, 11.33. Found: C, 75.31; H, 3.75; N, 11.46%.

5-[(3-{[4-Cyano-1-(4-methylphenyl)-5-phenylpyrazol-3-yl]carbonyl}isoxazol-4-yl)carbonyl]- 2,3-diphenyl-5-hydropyrazole-4-carbonitrile (27e). Pale cream crystals from diluted AcOH, yield (88%), mp 168–170 °C; IR (KBr): 3060, 2922 (CH), 2235 (CN), 1697 (C=O), 1557 (C=N), 1540 (C=C), 1385 (CH_3); ^{1}H NMR [$(CD_3)_2SO$]: δ = 2.41 (s, 3H, CH_3), 7.14–7.79 (m, 11H, ArH's), 8.142 (d, 2H, $J = 8$ Hz), 8.40 (d, 2H, $J = 8$ Hz), 8.51 (d, 4H, $J = 8$ Hz), 8.94 (s, 1H, isoxazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: (=20.1 (CH_3), 91.6, 94.5, 117.6 (CN), 117.9 (CN), 125.6, 129.3, 129.5,129.9, 130.9, 132.4, 132.6, 137.5, 144.7, 147.2, 151.5, 152.2, 159.7, 174.6 (CO), 179.8 (CO), 193.2 (isoxazole C-5); MS: $m/z = 624$ (M − 1,

0.02%), 337 (73.087%), 329 (30.12%), 303 (49.82%), 286 (7.77%), 273 (100%), 260 (31.43%), 246 (10.67%), 189 (14.63%), 154 (34.85%), 141 (43.12%), 104 (37.66.%), 90 (44.28%), 76 (64.80%), 50 (33.48%). Anal. calcd. for $C_{38}H_{23}N_7O_3$(625.63): C, 72.95; H, 3.71; N, 15.67. Found: C, 73.15; H, 3.50; N, 15.79%.

3-(3-Benzoyl-isoxazole-4-carbonyl)-5-phenyl-1-p-tolyl-1H-pyrazole-4-carbonitrile (28a). Yellow crystals from diluted AcOH, yield (84%), mp 210–212 °C; IR (KBr): 3056, 2918 (CH), 2233 (CN), 1659 (C=O), 1565 (C=C), 1385; ^{1}H NMR [$(CD_3)_2SO$]: $\delta = 2.33$ (s, 3H, CH_3), 7.21–7.93 (m, 14H, ArH's), 9.48 (s, 1H, isoxazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: (=20.1 (CH_3), 94.5, 117.6 (CN), 118.5, 125.6, 128.5, 129.3, 129.7, 131.1, 132.2, 132.8, 136.7, 138.8, 142.4, 152.5, 161.7, 179.5 (CO), 187.3 (CO), 192.0 (isoxazole C-5); MS: $m/z = 459$ (M + 1, 1.39%), 458 (M^+, 4.15%), 339 (12.74%), 300 (17.78%), 286 (15.63%), 273 (4.45%), 194 (4.75%), 105 (100%), 91 (14.56%), 77 (45.32%), 51 (17.77%). Anal. calcd. for $C_{28}H_{18}N_4O_3$(458.47): C, 73.35; H, 3.96; N, 12.22. Found: C, 73.53; H, 4.15; N, 12.35%.

3-{[3-(2-Furoyl)isoxazol-4-yl]carbonyl}-1-(4-methylphenyl)-5-phenyl-1H-pyrazole-4-carbonitrile (28b). Yellow crystals from diluted DMF, yield (84%), mp 188–190 °C; IR (KBr): 2925 (CH), 2230 (CN), 1670 (C=O), 1562 (C=C), 1385; ^{1}H NMR [$(CD_3)_2SO$]: $\delta = 2.33$ (s, 3H, CH_3), 6.32 (s, 1H, furan H-3), 7.21–7.93 (m, 12H, ArH's), 9.23(s, 1H, isoxazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: (=20.1 (CH_3), 94.5, 109.8, 114.5, 117.6 (CN), 125.4, 129.3, 129.5, 130.7, 132.1, 132.7, 136.5, 137.4, 138.8, 146.1, 151.2, 152.1, 160.2, 179 (CO), 180 (CO), 183.3 (isoxazole C-5); MS: $m/z = 448$ (M^+, 4.2%), 447 (4.2%), 325 (7.9%), 301 (7.4%), 286 (11.6%), 121 (10.6%), 112 (21.7%), 95 (100%), 84 (25.9%), 93 (12.7%), 91 (12.2%), (77 (6.9%), 65 (18.0%). Anal. calcd. for $C_{26}H_{16}N_4O_4$ (448.43): C, 69.64; H, 3.60; N, 12.49. Found: C, 69.45; H, 3.72; N, 12.57%.

5-Phenyl-3-[3-(thienyl-2-carbonyl)-isoxazole-4-carbonyl]-1-p-tolyl-1H-pyrazole-4-carbonitrile (28c). Pale cream crystals from diluted AcOH, yield (85%), mp 174–176 °C; IR (KBr): 3058, 2920 (CH), 2237 (CN), 1705 (C=O), 1658 (C=N), 1516 (C=C), 1384 (CH_3); ^{1}H NMR [$(CD_3)_2SO$]: $\delta = 2.34$ (s, 3H, CH_3), 7.14–7.18 (m, 10H, ArH's), 8.26 (d, 2H, $J = 8$ Hz), 8.52 (d, 2H, $J = 8$ Hz), 8.95 (s, 1H, isoxazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: (=20.1 (CH_3), 94.5, 109.8, 114.5, 117.6 (CN), 125.0, 125.5, 129.4, 129.7, 130.1, 132.0, 132.4, 132.8, 136.4, 138.7, 142.2, 147.8, 151.6, 152.2, 166.9, 179.8 (CO), 180.0 (CO), 183.2 (isoxazole C-5); MS: $m/z = 456$ (M + 2, 0.66%), 465 (M + 1, 1.52%), 464 (M^+, 5.36%), 354 (0.71%), 325 (2.71%), 301 (4.37%), 286 (10.02%), 272 (0.69%), 258 (1.41%) 243 (1.48%), 180 (2.48%), 111 (100%), 91 (9.46%), 77 (8.36%), 51 (5.11%). Anal. calcd. for $C_{26}H_{16}N_4O_3S$ (464.09): C, 67.23; H, 3.47; N, 12.06; S, 6.90. Found: C, 67.10; H, 3.62; N, 11.89; S, 7.15%.

3-[3-(Naphthalene-2-carbonyl)-isoxazole-4-carbonyl]-5-phenyl-1-p-tolyl-1H-pyrazole-4-carbonitrile (28d). Pale cream crystals from diluted AcOH, yield (86%), mp 204–206 °C; IR (KBr): 3055, 2920 (CH), 2233 (CN), 1666 (C=O), 1627 (C=N), 1566 (C=C), 1353 (CH_3); ^{1}H NMR [$(CD_3)_2SO$]: $\delta = 2.34$ (s, 3H, CH_3), 7.14–7.29 (m, 14H, ArH's), 8.52 (d, 2H, $J = 8$ Hz), 8.95 (s, 1H, isoxazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: (=20.1 (CH_3), 94.5, 109.8, 114.5, 117.6 (CN), 125.5, 126.4, 127.8, 129.4, 129.7, 130.2, 131.4, 131.6, 132.4, 133.2, 134.2, 142.2, 152.4, 162.0, 179.0,

(CO), 187 (CO), 191.8 (isoxazole C-5); MS: $m/z = 510$ (M + 2, 0.63%), 509 (M + 1, 2.63%), 508 (M^+, 7.29%), 325 (10.94%), 172 (28.87%), 155 (100%), 128 (13.25%), 127 (95.07%), 115 (3.88%), 101 (7.19%), 89 (3.20%), 77 (15.19%), 65 (10.60%). Anal. calcd. for $C_{32}H_{20}N_4O_3$ (508.53): C, 75.58; H, 3.96; N, 11.02. Found: C, 75.77; H, 4.11; N, 11.15%.

5-[(3-{[4-Cyano-1-(4-methylphenyl)-5-phenylpyrazol-3-yl]carbonyl} isoxazol-4-yl)carbonyl]-2-(4-methylphenyl)-3-phenyl-5-hydropyrazole-4-carbonitrile (28e). Pale cream crystals from diluted AcOH, yield (88%), mp 174–176 °C; IR (KBr): 3053, 2921 (CH), 2235 (CN), 1385 (CH_3); ^{1}H NMR [$(CD_3)_2SO$]: δ = 2.34 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 7.14–7.95 (m, 14H, ArH's), 8.12 (d, 4H, $J = 8$ Hz), 8.45(d, 4H, $J = 8$ Hz), 8.78 (s, 1H, isoxazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: (=20.1 (CH_3), 94.5, 109.8, 114.5, 117.2 (CN), 117.8 (CN), 125.5, 129.4, 129.7, 130.7, 132.2, 132.7, 136.8, 137.2, 138.2, 147.4, 151.4, 152.2, 159.8, 174.5 (CO), 179.7 (CO), 183.4 (isoxazole C-5); MS: $m/z = 638$ (M − 1, 1.25%), 601 (1.27%), 584 (1.1%), 286 (3.04%), 284 (5.2%), 243 (2.05%), 202 (3.55%), 167 (5.73%), 160 (5.05%), 149 (22.23%), 125 (19.45%), 103 (10.53%), 91 (39.33%), 81 (10.2%), 78 (17.00%), 77 (100%), 65 (52.98%). Anal. calcd. for $C_{39}H_{25}N_7O_3$ (639.66): C, 73.23; H, 3.94; N, 15.33. Found: C, 73.31; H, 4.12; N, 15.51%.

3-(2-P-Tolyl-2h-pyrazolo[3,4-d]pyridazin-4-yl)-1H-pyrazole-4-carbonitrile 24, 25 and 3-(7-Phenyl-isoxazolo[3,4-d]pyridazin-4-yl)-1-p-tolyl-1H-pyrazole-4-carbonitrile 29, 30

Equimolar amounts of each of the appropriate pyrazoles (**22a**–**e**, and **23a**–**e**), isoxazoles (**27a**–**e** and **28a**–**e**), 5 mmol), and hydrazine hydrate (1 ml, 99%) in ethanol (20 ml) were boiled under reflux for 2 h. The resulting solid was collected and crystallized to give pyrazolo[3,4-*d*]pyridazines (**24a**–**e** and **25a**–**e**) and isoxazolo[3,4-*d*]pyridazines (**29a**–**e** and **30a**–**e**), respectively.

3-(6,7-Dihydro-7-oxo-2-phenyl-2h-pyrazolo[3,4-d]pyridazin-4-yl)-1-phenyl-1H-pyrazole-4-carbonitrile (24a). Cololess crystals from AcOH, yield (84%), mp 322–324 °C; IR (KBr): 3381 (NH), 3059, (CH), 2230 (CN), 1684 (CO), 1591 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: δ = 7.48–8.08 (m, 14H, ArH's), 9.21 (s, 1H, pyrazole H-5), 12.93 (s, br., 1H, NH); ^{13}C NMR [$(CD_3)_2SO$]: (=104.5, 117.6 (CN), 120.5, 124.2 (pyrazole C-5), 125.6, 127.2, 128.4, 129.5, 129.9, 131.4, 131.6, 138.6, 139.6, 146.4, 148.2, 149.7, 154.2, 155.0 (CO); MS: $m/z = 454$ (M − 1, 4.3%), 453 (61.7%), 452 (95.7%), 425 (12.8%), 285 (10.8%), 227 (23.7%), 207 (12.8%), 138 (8.5%), 137 (12.8%), 138 (10.6%), 127 (12.8%), 104 (38.3%), 103 (17%), 102 (19.1%), 93 (10.6^), 92 (10.6%), 90 (8.5%), 89 (27.7%), 77 (100%), 65 (25.5%). Anal. calcd. for $C_{27}H_{17}N_7O$ (455.15): C, 71.20; H, 3.76; N, 21.53. Found: C, 71.35; H, 3.57; N, 21.72%.

3-(7-Methyl-2-phenyl-2h-pyrazolo[3,4-d]pyridazin-4-yl)-1,5-diphenyl-1H-pyrazole-4-carbonitrile (24b). Pale cream crystals from AcOH, yield (89%), mp 288–290 °C; IR (KBr): 3061, 2989 (CH), 2223 (CN), 1590 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: δ = 2.93 (s, 3H, CH_3), 7.48–8.18 (m, 15H, ArH's), 9.41 (s, 1H, pyrazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: (=17.2 (CH_3), 104.5, 117.6 (CN), 122.5 (pyrazole C-5), 124.2, 126.6, 128.2, 129.7, 129.8, 131.2, 131.3, 139.3, 139.8, 143.2, 149.7, 151.6, 156.8,

168.1; MS: $m/z = 455$ (M + 2, 4.5%), 454 (M + 2, 15.9%), 453 (M^+, 54.9%), 452 (M − 1, 87.3%), 321 (2.6%), 226 (4.9%), 190 (5.2%), 180 (6.4%), 115 (5.2%), 104 (7.9%), 77 (100%), 76 (20.6%), 64 (6.9%). Anal. calcd. for $C_{28}H_{19}N_7$ (453.5): C, 74.16; H, 4.22; N, 21.62. Found: C, 74.34; H, 4.40; N, 21.81%.

1,5-Diphenyl-3-(2,7-diphenyl-2H-pyrazolo[3,4-d]pyridazin-4-yl)-1H-pyrazole-4-carbonitrile (24c). Pale yellow crystals from AcOH, yield (90%), mp 300–302 °C; IR (KBr): 3057 (CH), 2225 (CN), 1635 (C=N), 1595 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: δ = 7.52–8.82 (m, 15H, ArH's), 9.53 (s, 1H, pyrazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: (=104.5, 117.6 (CN), 120.5, 123.9, 124.0 (pyrazole C-5), 126.2, 127.2, 128.3, 129.1, 129.8, 131.0, 131.2, 131.4, 131.7, 136.2, 139.6, 139.7, 140.4, 149.8, 151.8, 156.0, 157.9; MS: $m/z = 517$ (M + 2, 3.12%), 5.16 (M + 2, 8.77%), 515 (M^+, 22.02%), 300 (6.3%), 284 (30.87%), 257 (6.44%), 243 (10.82%), 184 (16.60%), 167 (7.67%), 140 (7.84%), 104 (38.53%), 77 (100%), 76 (20.6%), 65 (30.00%). Anal. calcd. for $C_{33}H_{21}N_7$ (515.57): C, 76.88; H, 4.11; N, 19.02. Found: C, 77.00; H, 4.25; N, 19.23%.

3-(4-(4-Cyano-1,5-diphenyl-1H-pyrazol-3-yl)-2-phenyl-2H-pyrazolo[3,4-d]pyridazin-7-yl)-5-phenyl-1-p-tolyl-1H-pyrazole-4-carbonitrile (24d). Yellow crystals from AcOH, yield (92%), mp >340 °C; IR (KBr): 3054 (CH), 2227 (CN), 1590 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: δ = 2.34 (s, 3H, CH_3), 7.26–8.15 (m, 24H, ArH's), 9.55 (s, 1H, pyrazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: (=21 (CH_3), 96.5, 104.5, 117.6 (CN), 120.1, 122.2, 124.1, 127.2, 127.7 (CN), 128.3, 130.8, 131.2, 131.6, 133.2, 136.8, 139.4, 140.7, 141.6, 146.2, 147.1, 149.7, 151.7, 166.1, 166.6; MS: $m/z = 696$ (M^+, 1.23%), 630 (1.53%), 572 (4.10%), 534 (3.19%), 439 (1.72%), 270 (7.62%), 167 (7.53%), 149 (21.87%), 135 (13.46%), 111 (7.06%), 97 (25.74%), 77 (100%), 69 (51.09%). Anal. calcd. for $C_{44}H_{28}N_{10}$ (696.76): C, 75.85; H, 4.05; N, 20.10. Found: C, 76.00; H, 3.85; N, 20.32%.

3-(6,7-Dihydro-7-oxo-2-p-tolyl-2h-pyrazolo[3,4-d]pyridazin-4-yl)-1,5-diphenyl-1H-pyrazole-4-carbonitrile (25a). Colorless crystals from dioxane, yield (85%), mp 272–274 °C; IR (KBr): 3425 (OH), 3062 (CH), 2233 (CN), 1728 (CO), 1658 (C=N), 1600 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: δ = 2.32 (s, 3H, CH_3), 7.26–8.09 (m, 14H, ArH's), 8.95 (s, 1H, pyrazole H-5), 12.21 (s, br., 1H, NH);^{13}C NMR [$(CD_3)_2SO$]: δ = 20.2 (CH_3), 104.2, 117.6 (CN), 120.4, 124.1, 125.7 (pyrazole C-5), 127.2, 128.4, 129.1, 129.5, 129.8, 131.3, 131.6, 139.0, 139.8, 146.3, 148.1, 149.4, 145.2 (CO), 154.8; MS: $m/z = 471$ (M + 2, 2.04%), 470 (M + 1, 2.07%), 469 (M^+, 16.58%), 380 (3.13%), 270 (3.25%), 243 (2.04%), 218 (2.17%), 165 (3.45%), 154 (2.49%), 127 (4.04%), 104 (14.86%), 92 (19.18%), 91 (19.79%), 78 (10.59%), 77 (100%), 65 (17.76%). Anal. calcd. for $C_{28}H19\,N_7O$ (469.5): C, 71.63; H, 4.08; N, 20.88. Found: C, 71.75; H, 3.89; N, 21.00%.

3-(7-Methyl-2-p-tolyl-2H-pyrazolo[3,4-d]pyridazin-4-yl)-1,5-diphenyl-1H-pyrazole-4-carbonitrile (25b). Pale cream crystals from diluted AcOH, yield (89%), mp 218–220 °C; IR (KBr): 3043 (CH), 2235 (CN), 1643 (C=N), 1593 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: δ = 2.32 (s, 3H, CH_3), 2.61 (s, 3H, CH_3), 7.24–8.14 (m, 14H, ArH's), 8.92 (s, 1H, pyrazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: δ = 17.1 (CH_3), 20.2 (CH_3), 104.2, 117.6 (CN), 121.1, 122.8 (pyrazole C-5), 123.7, 126.8, 128.4, 129.4, 129.8, 131.2, 131.4, 131.7, 139.4, 139.7, 143.2, 149.6, 151.7, 156.8, 168.1; MS: $m/z = 467$

(M^+, 100%), 325 (13.14%), 333 (4.25%), 242 (8.46%), 230 (7.82%), 226 (5.74%), 219 (10.17%), 178 (10.09%), 151 (10.19%), 140 (11.75%), 127 (10.81%), 105 (9.97%), 90 (41.27%), 91 (19.79%), 78 (10.59%), 77 (49.45%), 65 (25.39%). Anal. calcd. for $C_{29}H_{21}N_7$ (467.52): C, 74.50; H, 4.53; N, 20.97. Found: C, 74.34; H, 4.35; N, 21.15%.

1,5-Diphenyl-3-(7-phenyl-2-p-tolyl-2H-pyrazolo[3,4-d]pyridazin-4-yl)-1H-pyrazole-4-carbonitrile (25c). Yellow crystals from diluted AcOH, yield (90%), mp 252–254 °C; IR (KBr): 3058 (CH), 2229 (CN), 1593 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: $\delta = 2.32$ (s, 3H, CH_3), 7.24–8.24 (m, 20H, ArH's), 8.95 (s, 1H, pyrazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: $\delta = 20.1$ (CH3), 104.2, 117.6 (CN), 123.8, 123.9 (pyrazole C-5), 127.6, 128.2, 128.8, 129.3, 129.9, 131.0, 131.2, 131.3, 131.6, 136.2, 139.5, 139.8, 140.5, 149.8, 151.5, 156.7, 157.8; MS: $m/z = 529$ (M^+, 0.34%), 310 (65.23%), 296 (84.69%), 284 (9.82%), 269 (45.46%), 254 (32.53%), 241 (17.80%), 231 (11.79%), 228 (18.44%), 221 (17.75%), 196 (7.12%), 177 (32.30%), 165 (14.05%), 162 (52.45%), 155 (58.13%), 148 (28.88%), 90 (100%), 76 (39.48%), 65 (51.97%). Anal. calcd. for $C_{34}H_{23}N_7$ (529.59): C, 77.11; H, 4.38; N, 18.51. Found: C, 77.25; H, 4.42; N, 18.35%.

3-(4-(4-Cyano-5-phenyl-1-p-tolyl-1H-pyrazol-3-yl)-2-p-tolyl-2h-pyrazolo[3,4-d]pyridazin-7-yl)-1,5-diphenyl-1H-pyrazole-4-carbonitrile (25d). Yellow crystals from diluted AcOH, yield (92%), mp >330 °C; IR (KBr): 3033 (CH), 2229 (CN), 1598 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: $\delta = 2.32$ (s, 6H, $2CH_3$), 7.24–8.31 (m, 23H, ArH's), 8.85 (s, 1H, pyrazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: $\delta = 20.1$ (CH_3), 95.3, 104.2, 117.6 (CN), 119.1 (pyrazole), 122.2, 124.8, 126.1, 126.7, 127.1, 127.7 (CN), 128.3, 129.4, 130.9, 131.4, 131.6, 133.2, 136.7, 139.9, 140.7, 141.4, 146.2, 147.1, 149.6, 151.7, 166.2, 166.8; MS: $m/z = 711$ (M^+, 2.37%), 570 (6.14%), 300 (5.81%), 285 (4.25%), 259 (13.68%), 241 (5.54%), 219 (4.88%), 194 (4.22%), 180 (10.05%), 191 (4.39%), 177 (3.58%), 166 (6.30%), 154 (3.01%), 150 (4.10%), 147 (10.21%), 127 (8.46%), 114 (9.46%), 104 (25.98%), 91 (43.81%), 77 (100%), 65 (43.62%). Anal. calcd. for $C_{45}H_{30}N_{10}$(710.79): C, 76.04; H, 4.25; N, 19.71. Found: C, 75.85; H, 4.12; N, 19.94%.

1,5-Diphenyl-3-(7-phenylisoxazolo[4,3-d]pyridazin-4-yl)-1H-pyrazole-4-carbonitrile (29a). Colorless crystals from EtOH, yield (89%), mp 248–250 °C; IR (KBr): 3058 (CH), 2233 (CN), 1596 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: $\delta = 7.24$–8.31 (m, 15H, ArH's), 8.65 (s, 1H, oxazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: $\delta = 104.2$, 113.6, 119.0 (CN), 123.8, 128.2, 128.7, 129.3, 129.8, 131.2, 131.3, 131.5, 131.7, 136.3, 141.7, 148.2, 149.6, 150.4 (oxazole C-5), 153.2, 156.2, 158.6; MS: $m/z = 442$ ($M + 1$, 11.36%), 441 (M^+, 32.29%), 338 (10.01%), 310 (5.99%), 272 (11.69%), 180 (19.40%), 172 (30.21%), 155 (22.20%), 141 (13.80%), 127 (37.98%), 115 (22.05%), 105 (18.37%), 77 (100%), 65 (11.24%). Anal. calcd. for $C_{27}H_{16}N_6O$ (440.46): C, 73.63; H, 3.66; N, 19.08. Found: C, 73.82; H, 3.45; N, 19.12%.

3-(7-(Furan-2-yl)isoxazolo[4,3-d]pyridazin-4-yl)-1,5-diphenyl-1H-pyrazole-4-carbonitrile (29b). Brown crystals from diluted AcOH yield (89%), mp 280–282 °C; IR (KBr): 3028 (CH), 2229 (CN), 1593 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: $\delta = 6.68$ (d, 1H, $J = 8$ Hz, furan H-3), 7.24–8.31 (m, 12H, ArH's), 8.65 (s, 1H, oxazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: $\delta = 104.2$, 112.2, 113.4, 116.5, 118.6 (CN), 123.9, 128.6, 129.6, 129.9, 131.2, 131.6, 131.8, 141.3, 148.4, 149.2 (oxazole C-5),

149.7, 150.6, 153.4, 153.8, 157.6, 158.5; MS: $m/z = 432$ (M + 2, 1.66%), 431 (M + 1, 6.01%), 430 (M^+, 30.93%), 338 (3.74%), 310 (3.01%), 272 (7.53%), 244 (3.73%), 180 (25.30%), 141 (9.46%), 123 (4.12%), 104 (14.03%), 77 (100%), 65 (4.54%). Anal. calcd. for $C_{25}H_{14}N_6O_2$(430.42): C, 69.76; H, 3.28; N, 19.53. Found: C, 69.65; H, 3.18; N, 19.75%.

1,5-Diphenyl-3-(7-(thien-2-yl)isoxazolo[4,3-d]pyridazin-4-yl)-1H-pyrazole-4-carbonitrile (29c). Yellow crystals from diluted AcOH yield (89%), mp 284–286 °C; IR (KBr): 3066 (CH), 2233 (CN), 1600 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: δ = 7.24–8.41 (m, 13H, ArH's), 8.85 (s, 1H, isoxazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: δ = 104.2, 111.6, 116.1, 118.7 (CN), 125.8, 129.7, 129.9. 131.2, 131.4, 131.7, 140.4, 141.6, 147.7 (oxazole C-5), 149.7, 149.9, 150.8, 154.5, 154.7, 156.5. 167.2; MS: $m/z = 448$ (M + 1, 4.10%), 446 (M^+, 38.72%), 338 (3.74%), 391 (5.84%), 310 (5.84%), 272 (8.75%), 180 (27.59%), 141 (13.43%), 123 (15.19%), 110 (10.19%), 104 (9.89%), 77 (100%), 65 (5.99%). Anal. calcd. for $C_{25}H_{14}N_6OS$ (446.48): C, 67.25; H, 3.16; N, 18.82; S, 7.18. Found: C, 67.37; H, 3.04; N, 18.98; S, 7.33%.

3-(7-(Naphthalen-2-yl)isoxazolo[4,3-d]pyridazin-4-yl)-1,5-diphenyl-1H-pyrazole-4-carbonitrile (29d). Pale yellow crystals from diluted AcOH yield (90%), mp 258–260 °C; IR (KBr): 3058 (CH), 2225 (CN), 1593 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: δ = 7.28–8.33 (m, 16H, ArH's), 8.83 (s, 1H, ArH), 8.85 (s, 1H, isoxazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: δ = 104.2, 118.6 (CN), 123.1, 125.4, 125.7, 126.4, 126.6, 127.4, 128.7, 129.7, 129.9, 131.1, 131.2, 131.3, 131.4, 131.45, 140.0, 141.4, 149.2, 149.7, 153.1, 154.5, 157.8, 163.0; MS: $m/z = 490$ (M^+, 1.10%), 489 (M − 1, 1.0%), 311 (3.74%), 255 (5.84%), 77 (45.36%). Anal. calcd. for $C_{31}H_{18}N_6O$ (490.51): C, 75.91; H, 3.70; N, 17.13. Found: C, 76.11; H, 3.85; N, 17.26%.

3-(4-(4-Cyano-1,5-diphenyl-1H-pyrazol-3-yl)isoxazolo[4,3-d]pyridazin-7-yl)-5-phenyl-1-p-tolyl-1H-pyrazole-4-carbonitrile (29e). Pale cream crystals from diluted AcOH yield (92%), mp 242–244 °C; IR (KBr): 3060 (CH), 2235 (CN), 1597 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: δ = 2.32 (s, 3H, CH_3), 7.24–8.33 (m, 19H, ArH's), 8.85 (s, 1H, isoxazole H-5);^{13}C NMR [$(CD_3)_2SO$]: δ = 20.1 (CH_3), 95.4, 104.2, 110.7, 118.6 (CN), 123.7, 127.8, 128.3, 129.8, 130.8, 131.4, 131.8, 133.2, 136.8, 141.4, 142.8, 146.3 (isoxazole C-5, 147.5, 149.3, 154.6, 1.65.7, 167.8. Anal. calcd. for $C_{38}H_{23}N_9O$ (621.65): C, 73.42; H, 3.73; N, 20.28. Found: C, 73.24; H, 3.85; N, 20.42%.

5-Phenyl-3-(7-phenylisoxazolo[4,3-d]pyridazin-4-yl)-1-p-tolyl-1H-pyrazole-4-carbonitrile (30a). Colorless crystals from diluted AcOH yield (89%), mp 270–272 °C; IR (KBr): 3044 (CH), 2225 (CN), 1617 (C=N), 1576 (C=C); ^{1}H NMR [$(CD_3)_2SO$]: δ = 2.34 (s, 3H, CH_3), 7.19–8.14 (m, 14H, ArH's), 8.84 (s, 1H, isoxazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: δ = 20.1 (CH_3), 104.2, 113.4, 118.6 (CN), 124.5, 128.3, 128.4, 129.9, 131.1, 131.6, 133.6, 136.2, 136.4, 142.5, 148.4, 149.3, 150.5 (isoxazole C-5), 152.9, 156.8, 158.5. Anal. calcd. for $C_{28}H_{18}N_6O$ (454.48): C, 74.00; H, 3.99; N, 18.49. Found: C, 74.15; H, 4.18; N, 18.67%.

3-[7-(2-Furyl)isoxazolo[3,4-d]pyridazin-4-yl]-1-(4-methylphenyl)-5-phenyl-1H-pyrazole-4-carbonitrile (30b). Deep brown from diluted AcOH yield (89%), mp 242–244 °C; IR (KBr): 3066 (CH), 2233 (CN), 1600 (C=C); ^{1}H NMR

[$(CD_3)_2SO$]: δ = 2.34 (s, 3H, $CH_3C_6H_4$), 6.92–8.23 (m, 12H, ArH's), 8.93 (s, 1H, isoxazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: δ = 20.1 (CH_3), 104.2, 112.1, 113.4, 116.8, 117.8 (CN), 124.2, 128.6, 129.8, 131.4, 131.5, 133.0, 136.7, 142.1, 148.2, 149.8 (isoxazole C-5), 150.4, 153.5, 153.8, 156.8, 158.2; MS: $m/z = 446$ (0.44%), 310 (79.38%), 296 (100%), 284 (11.96%), 291 (53.33%), 268 (52.26%), 255 (34.69%), 228 (20.76%), 215 (18.35%), 203 (25.10%), 193 (31.06%), 189 (16.10%), 194 (11.84%), 177 (35.26%), 167 (18.29%), 165 (14.52%), 151 (25.14%), 140 (44.05%), 134 (19.04%), 114 (33.09%), 131 (15.78%), 100 (30.71%), 91 (72.61%), 88 (31.98%), 76 (48.90%), 65 (59.48%). Anal. calcd. for $C_{26}H_{16}N_6O_2$ (444.44): C, 70.26; H, 3.63; N, 18.91. Found: C, 70.45; H, 3.72; N, 19.07%.

5-Phenyl-3-(7-(thien-2-yl)isoxazolo[4,3-d]pyridazin-4-yl)-1-p-tolyl-1H-pyrazole-4-carbonitrile (30c). Brown crystals from EtOH yield (89%), mp 238–240 °C; IR (KBr): 3066 (CH), 2233 (CN), 1600 (C=C); ^1H NMR [$(CD_3)_2SO$]: δ = 2.34 (s, 3H, CH_3), 7.24–8.41 (m, 12H, ArH's), 8.85 (s, 1H, isoxazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: δ = 20.1 (CH_3), 113.4, 118.8 (CN), 124.2, 127.4, 128.3, 129.8, 131.6, 131.7, 132.5, 123.7, 133.2, 136.1, 139.4, 142.2, 148.3, 149.2 (isoxazole C-5), 149.9, 158.5, 160.4, 162.8; MS: $m/z = 462$ (M + 2, 16.39%), 461 (M + 1, 8.88%), 460 (M^+, 16.39%), 448 (20.45%), 477 (5.63%), 405 (7.25%), 390 (5.09%), 352 (12.13%), 315 (17.84%), 286 (15.91%), 231 (11.31%), 194 (37.18%), 155 (10.95%), 128 (15.81%), 123 (26.57%), 121 (30.89%), 111 (23.92%), 110 (17.92%), 104 (22.91%), 96 (23.00%), 91 (100%), 77 (56.98%), 65 (77.35%). Anal. calcd. for $C_{26}H_{16}N_6OS$ (460.11): C, 67.81; H, 3.50; N, 18.25; S, 6.96. Found: C, 67.71; H, 3.68; N, 18.12; S, 7.15%.

3-(7-(Naphthalen-2-yl)isoxazolo[4,3-d]pyridazin-4-yl)-5-phenyl-1-p-tolyl-1H-pyrazole-4-carbonitrile (30d). Colorless crystals from diluted AcOH yield (87%), mp: 278–280 °C; IR (KBr): 3047 (CH), 2225 (CN), 1577 (C=C); ^1H NMR [$(CD_3)_2SO$]: δ = 2.34 (s, 3H, CH_3), 7.24–8.41 (m, 16H, ArH's), 8.85 (s, 1H, isoxazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: δ = 20.1 (CH_3), 113.4, 118.8 (CN), 123.2, 124.4, 125.3, 127.2, 127.4, 128.2, 129.8, 130.5, 131.4, 131.6, 131.7, 133.4, 136.6, 142.4, 148.0, 149.5, 150.6 (isoxazole C-5), 152.9, 156.6, 158.4. Anal. calcd. for $C_{32}H_{20}N_6O$ (504.54): C, 76.18; H, 4.00; N, 16.66. Found: C, 76.24; H, 4.11; N, 16.82%.

3-(4-(4-Cyano-5-phenyl-1-p-tolyl-1H-pyrazol-3-yl)isoxazolo[4,3-d]pyridazin-7-yl)-5-phenyl-1-p-tolyl-1H-pyrazole-4-carbonitrile (30e). Pale cream crystals from diluted AcOH yield (92%), mp 258–260 °C; IR (KBr): 3047 (CH), 2226 (CN), 1625 (1577 (C=C); ^1H NMR [$(CD_3)_2SO$]: δ = 2.34 (s, 3H, CH_3), 7.24–8.41 (m, 16H, ArH's), 8.85 (s, 1H, oxazole H-5); ^{13}C NMR [$(CD_3)_2SO$]: δ = 20.1 (2 CH_3), 95.6, 104.3, 110.6, 113.4, 118.8 (CN), 124.2, 127.4, 128.3, 129.6, 130.8, 131.6, 133.2, 136.4, 141.2, 142.4, 142.8, 146.6 (isoxazole C-5), 147.2, 148.7, 149.7, 154.3, 165.2, 167.5. Anal. calcd. for $C_{39}H_{25}N_9O$ (635.68): C, 73.69; H, 3.96; N, 19.83. Found: C, 73.69; H, 3.96; N, 19.83%.

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