Synthesis of Novel Pyrazolo[3,4-*d*]pyridazine, Pyrido[1,2-*a*]benzimidazole, Pyrimido[1,2-*a*]benzimidazole and Triazolo[4,3-*a*]Pyrimidine Derivatives

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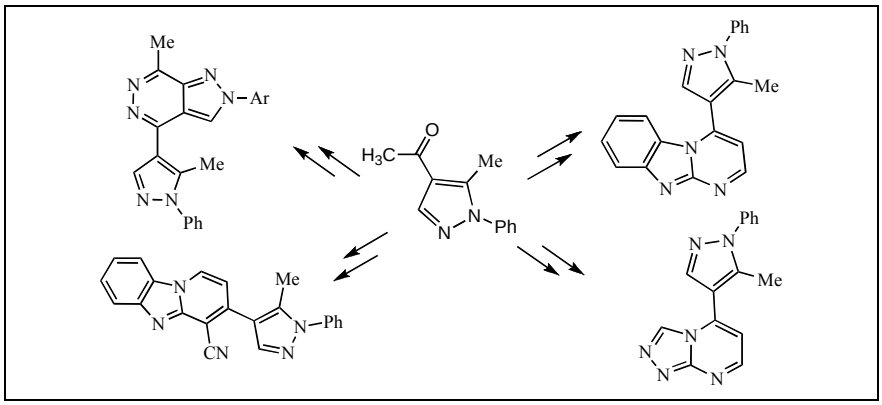

4-Acetyl-5-methyl-1-phenyl-1*H*-pyrazole reacts with dimethylformamide dimethylacetal (DMF-DMA) to afford the corresponding (*E*)1-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)-3-(*N*,*N*-dimethylamino)-2-propen-1-one. The latter product undergoes regioselective 1,3-dipolar cycloaddition with nitrilimines and nitrile oxides to afford the novel 3-aroyl-4-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)carbonyl-1-phenylpyrazole and 3-aroyl-4-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)carbonyl isoxazole derivatives, respectively. It reacts also with 1*H*-benzimidazole-2-acetonitrile, 2-aminobenzimidazole and 3-amino-1,2,4-triazole to afford the novel pyrido[1,2-*a*]benzimidazole, pyrimido[1,2-*a*]benzimidazole and the triazolo[4,3-*a*]pyrimidine derivatives, respectively. The reaction of 3-aroyl-4-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl) carbonyl-1-phenylpyrazole derivatives with hydrazine hydrate led to a new pyrazolo[3,4-*d*]pyridazine derivatives.

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INTRODUCTION

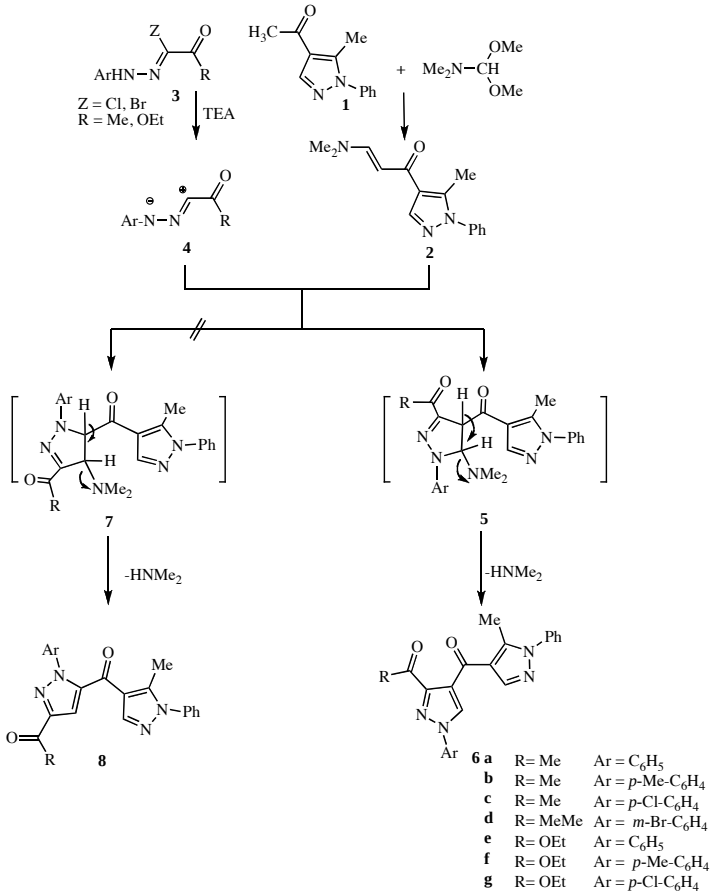
Enaminone derivatives are highly reactive intermediates and are extensively used for the synthesis of a wide variety of heterocyclic systems [1-3]. On the other hand, a great deal of interest has been focused on the synthesis of functionalized pyrazole derivatives due to their synthetic and biological potentialities [4-6]. In continuation of our interest in the synthesis of heterocycles containing a pyrazole moiety for biological screening [7,8], we report here on the synthesis of 1-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)-3-(*N*,*N*-dimethylamino)-2-propen-1-one (**2**) and its utility in 1,3-dipolar cycloaddition reactions with nitrilimines **4a-g** and nitrile oxides **11a-c**. The behavior of compound **2** toward some nitrogen nucleophiles was also investigated.

RESULTS AND DISCUSSION

Treatment of 4-acetyl-5-methyl-1-phenyl-1*H*-pyrazole (**1**) with dimethylformamide dimethylacetal (DMF-DMA) afforded a single product identified as (*E*)-1-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)-3-(*N,N*-dimethylamino)-2-propen-1-one (**2**) in a high yield. The ^{1}H nmr spectrum of the latter product displayed a singlet signal at δ 2.98 due to *N,N*-dimethyl protons, a singlet signal at δ 2.59 due to methyl group, two doublets at δ 5.51 and 7.69 (J = 12.3 Hz) due to olefinic protons, a singlet signal at δ 7.91 due to pyrazole-5-CH protons, in addition to an aromatic multiplets in the region δ 7.25-7.45. The value of the coupling constant (J = 12.3 Hz) for the ethylenic protons indicates that the enaminone **2** exists exclusively in the *E*-configuration.

The regioselectivity in 1,3-dipolar cycloaddition of nitrilimines **4a-g** with the enaminone **2** was investigated, for example, reaction of the enaminone **2** with the nitrilimines **4a** (generated *in situ* by the action of triethylamine on the hydrazonoyl chloride **3a**) afforded a single product (as examined by TLC and ^{1}H nmr spectroscopy) for which the two regioisomeric cycloadducts **5a** and **7a** seemed possible (Scheme 1). However, the regioisomer **6a** was assigned for the reaction product on the basis of its ^{1}H nmr spectrum and its chemical transformation outlined in Scheme 2. The ^{1}H nmr spectrum of the isolated product revealed four singlets at δ 2.46, 2.59, 8.00 and 8.97 due to acetyl-CH_3, pyrazole ring-methyl protons, pyrazole-3-CH proton and

Scheme 1

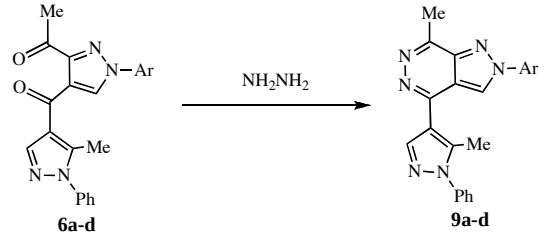


pyrazole-5-CH proton, respectively, in addition to an aromatic multiplet in the region δ 7.45-7.62. Its ir spectrum showed two carbonyl absorption bands at 1690 and 1635 cm^{-1}. The formation of the pyrazole **6a** is assumed to take place *via* a regioselective 1,3-cycloaddition of the nitrilimine intermediate **4a** to the activated double bond of the enaminone **2** to form the non-isolable intermediate **5a**, followed by elimination of dimethylamine under the reaction conditions.

A further confirmation of the structure of compound **6a** comes from its reaction with hydrazine to afford the corresponding 4-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)-7-methyl-2-phenylpyrazolo[3,4-*d*]pyridazine (**9a**) (Scheme 2).

Prompted by the forgoing results and in order to generalize this reaction, the enaminone **2** was allowed to react with the nitrilimines **4b-g** under the same experimental conditions, which afforded the corresponding pyrazole derivatives **6b-g** (Scheme 1). The products **6b-d** underwent cyclocondensation upon treatment with hydrazine hydrate to give the corresponding pyrazolo[3,4-*d*]pyridazine derivatives **9a-d** (Scheme 2). The structures of the products **6b-d** and **9b-d**

Scheme 2

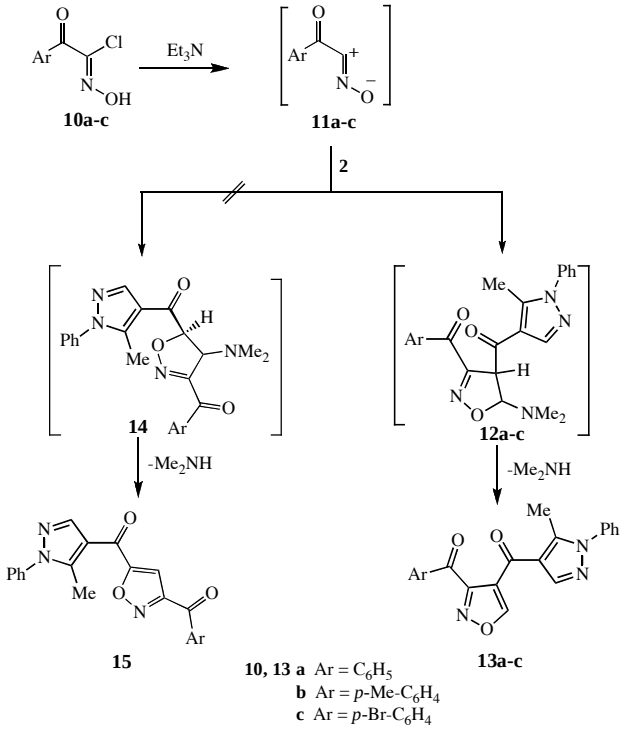


were established on the basis of their elemental analyses and spectral data (see Experimental part).

Similarly, the enaminone **2** reacts with nitrileoxides **11a-c** [liberated, *in situ*, from hydroximoyl chlorides **10a-c**] to afford the corresponding isoxazole derivatives **13a-c** *via* the elimination of dimethylamine molecule from the non-isolable intermediates **12**. The other possible regioisomeric structure **15** was easily ruled out on the basis of the spectral data of the isolated products. The ^1H

nmr spectrum of compound **13a** as a typical example of the prepared series, revealed a singlet signal corresponding to the isoxazole H-5 proton at δ 10.02 which is in complete agreement with the proposed structure.

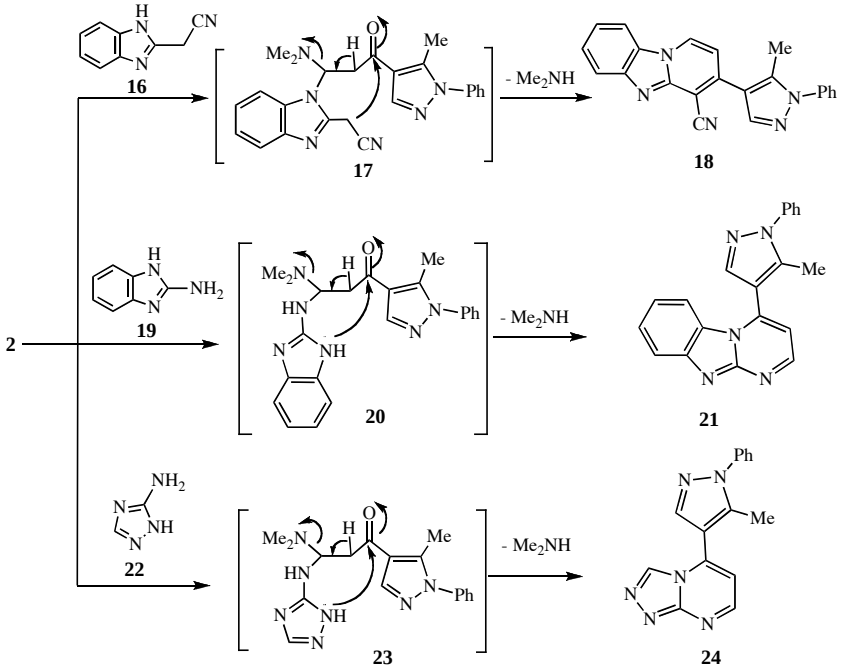
Scheme 3



Next, the behavior of the enaminone **2** toward some nitrogen nucleophiles was also explored. Thus, heating equimolar amounts of compound **2** with 1*H*-benzimidazol-2-ylacetonitrile (**16**) in the presence of a catalytic amount of piperidine, resulted in the formation of a single product (as examined by TLC). The structure of the isolated product was identified as 3-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)-benzo[4,5]imidazo[1,2-*a*]pyridine-4-carbonitrile (**18**). The IR spectrum of compound **18** revealed a characteristic nitrile absorption band at 2191 cm^{-1}, whereas its ^1H nmr spectrum displayed two singlets at δ 2.24 and 8.05 due to CH_3 and pyrazole-3-CH protons, respectively, two doublets at δ 7.04 and 8.32 due to two pyridine protons, in addition to an aromatic multiplet in the region δ 7.02-7.71.

Compound **2** reacted also with 2-aminobenzimidazole (**19**) under the same experimental conditions and gave one isolable product identified as 4-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)-benzo[4,5]imidazo[1,2-*a*]pyrimidine (**21**) (Scheme 4). The IR spectrum of the reaction product revealed no bands due to amino or carbonyl functions. Meover, its ^1H nmr spectrum revealed singlet signal at δ 2.28 due to CH_3, two doublets at δ 7.07 (J = 4.20 Hz) and 8.85 (J = 4.20 Hz) due two pyrimidine-CH protons, and a singlet at δ 8.11 due to pyrazole-3-CH, in addition to an aromatic multiplet in region δ 7.28-7.91. The formation of compound **21** is assumed to take place *via* the addition of the exocyclic amino group in 2-aminobenzimidazole (**19**) to the activated double bond in the enaminone **2** to give the acyclic non-isolable intermediate **20**, which undergoes intramolecular cyclization and subsequent aromatization

Scheme 4



via the loss of dimethylamine and water molecules to afford the final product **21** as depicted in Scheme 4.

The enaminone **2** reacted also with 3-amino-1,2,4-triazole (**22**) and afforded a high yield of 5-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)-[1,2,4]triazolo[4,3-*a*]pyrimidine (**24**) which was assigned based on its elemental analysis and spectral data. A plausible mechanism for the formation of compound **24** is outlined in Scheme 4. The latter product is assumed to be formed *via* an initial addition of an amino group of 3-amino-1,2,4-triazole to the activated double bond in the enaminone **2** followed by elimination of dimethylamine and water molecules from the non-isolable intermediate **23** to afford the final product **24**.

EXPERIMENTAL

All melting points were measured on a Gallenkamp melting point apparatus. The infrared spectra were recorded in potassium bromide disks on a pye Unicam SP 3300 and Shimadzu FTIR 8101 PC infrared spectrophotometers. The nmr spectra were recorded on a Varian Mercury VX-300 nmr spectrometer. ^{1}H spectra were run at 300 MHz and ^{13}C spectra were run at 75.46 MHz in deuterated chloroform ($CDCl_3$) or dimethylsulphoxide (DMSO-d_6). Chemical shifts were related to that of the solvent. Mass spectra were recorded on a Shimadzu GCMS-QP 1000 EX mass spectrometer at 70 eV. Elemental analyses were carried out at the Microanalytical Center of Cairo University, Giza, Egypt.

The hydrazonoyl halides **3a-g** [9-13], hydroximoyl chlorides **10a-c** [14-16], 4-acetyl-5-methyl-1- phenyl-1*H*-pyrazole (**1**) [17] and 1*H*-benzimidazol-2-ylacetonitrile (**16**) [18], were prepared according to procedures reported in the literature

1-(5-Methyl-1-phenyl-1*H*-pyrazol-4-yl)-3-(*N,N*-dimethyl-amino)-2-propen-1-one (2). A mixture of 4-Acetyl-methyl-1-phenylpyrazole (**1**) (4.0 g, 20 mmol) and dimethylformamide-dimethylacetal (*DMF-DMA*) (2.66 mL, 20 mmol) in dry xylene (20 mL) was refluxed for 8 hours then left to cool to room temperature. The reddish-brown precipitated product was collected by filtration, washed with light petroleum ether (40-60°C), and dried. Recrystallization from benzene afforded 4.64 g (91%) of the enaminone **2**, mp. 159-160°C; ir (KBr) ν_{max}/cm^{-1}: 1644 (conjugated C=O), 1598 (C=N); ^{1}H nmr ($CDCl_3$): δ 2.59 (s, 3H), 2.98 (s, 6H), 5.51 (d, 1H, *J* = 12.3 Hz), 7.25-7.45 (m, 5H, ArH's), 7.69 (d, 1H, *J* = 12.3 Hz), 7.91 (s, 1H); ^{13}C nmr: δ 11.98, 28.74, 93.73, 122.26, 125.25, 128.16, 129.33, 138.90, 140.71, 142.23, 152.48, 182.29; MS (*m/z*): 255 (M^+); Found: C, 70.61; H, 6.79; N, 16.43%. $C_{15}H_{17}N_3O$ requires C, 70.56; H, 6.71; N, 16.46%.

3-Aroyl-4-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)carbonyl-1-phenylpyrazoles 6a-g and 3-Aroyl-4-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)carbonyl isoxazoles 13a-c. General Procedure: To a stirred solution of the appropriate hydrazonoyl halide **3** or hydroximoyl chloride **10** (2 mmol) and the enaminone **2** (0.51 g, 2 mmol) in dry benzene (20 mL) was added triethylamine (0.2 mL) portionwise over a period of 30 minutes, and the mixture was stirred at room temperature for 24 hours. The precipitated triethylamine hydrochloride was filtered off, and the filtrate was evaporated under reduced pressure. The residue was triturated with ethanol. The solid product, so formed in each case, was collected by filtration, washed with water, and dried. Recrystallization from ethanol afforded the corresponding pyrazole or isoxazole derivatives **6a-g** and **11a-c**, respectively.

3-Acetyl-4-(5-methyl-1-phenyl-1*H*-pyrazol-4-carbonyl)-1-phenylpyrazole (6a). Yield (74%); mp. 178-179°C; ir (KBr) ν_{max}/cm^{-1}: 1690 (C=O), 1635 (C=O), 1598 (C=N); ^{1}H nmr ($CDCl_3$): δ 2.46 (s, 3H, CH_3CO), 2.59 (s, 3H, CH_3), 7.45-7.62 (m, 10H, ArH's), 8.00 (s, 1H, pyrazole-3-CH), 8.97 (s, 1H, pyrazole-5-CH); ^{13}C nmr δ 12.13, 27.58, 27.48, 119.01, 120.06, 123.42, 124.08, 126.37, 129.41, 130.09, 135.54, 136.60, 138.96, 142.33, 143.48, 149.57, 182.56, 192.01; MS (*m/z*): 370 (M^+); Found: C, 71.39; H, 4.81; N, 15.16%. $C_{22}H_{18}N_4O_2$ requires C, 71.34; H, 4.90; N, 15.13%

3-Acetyl-4-(5-methyl-1-phenyl-1*H*-pyrazol-4-carbonyl)-1-(4-methylphenyl)pyrazole (6b). Yield (74%); mp. 160-161°C; ir (KBr) ν_{max}/cm^{-1}: 1688 (C=O), 1636 (C=O), 1597 (C=N); ^{1}H nmr ($CDCl_3$): δ 2.25 (s, 3H, CH_3) , 2.46 (s, 3H, CH_3CO), 2.59 (s, 3H, CH_3), 7.25-7.62 (m, 9H, ArH's), 8.00 (s, 1H, pyrazole-3-CH), 8.97 (s, 1H, pyrazole-5-CH); ^{13}C nmr: δ 12.21, 20.58, 27.58, 119.51, 121.06, 124.42, 125.37, 128.80, 129.41, 130.09, 130.76, 136.54, 137.50, 138.26, 143.03, 143.28, 149.54, 182.91, 193.06; MS (*m/z*): 384 (M^+);Found: C, 71.94; H, 5.31; N, 14.66%. $C_{23}H_{20}N_4O_2$ requires C, 71.86; H, 5.24; N, 14.57%.

3-Acetyl-4-(5-methyl-1-phenyl-1*H*-pyrazol-4-carbonyl)-1-(4-chlorophenyl)pyrazole (6c). Yield (75%); mp. 197-198°C; ir (KBr) ν_{max}/cm^{-1}: 1691 (C=O), 1634 (C=O), 1595 (C=N); ^{1}H nmr ($CDCl_3$): δ 2.46 (s, 3H, CH_3CO), 2.59 (s, 3H, CH_3), 7.26-7.65 (m, 9H, ArH's), 8.02 (s, 1H, pyrazole-3-CH), 8.97 (s, 1H, pyrazole-5-CH); ^{13}C nmr: δ 12.22 27.63, 101.39, 120.96, 121.32, 124.62, 125.38, 128.83, 129.48, 129.68, 131.80, 137.59, 138.23, 143.08, 143.38, 149.95, 182.69, 193.03; MS (*m/z*): 404 (M^+); Found: C, 65.31; H, 4.45; Cl, 8.83; N, 13.93%. $C_{22}H_{17}ClN_4O_2$ requires C, 65.27; H, 4.43; Cl, 8.76; N, 13.84%.

3-Acetyl-4-(5-methyl-1-phenyl-1*H*-pyrazol-4-carbonyl)-1-(3-bromophenyl)pyrazole (6d). Yield (81%); mp. 202-203°C; ir (KBr) ν_{max}/cm^{-1}: 1691 (C=O), 1634 (C=O), 1595 (C=N); ^{1}H nmr: ($CDCl_3$) δ 2.46 (s, 3H, CH_3CO), 2.59 (s, 3H, CH_3), 7.26-7.87 (m, 9H, ArH's), 7.98 (s, 1H, pyrazole-3-CH), 8.97 (s, 1H, pyrazole-5-CH); ^{13}C nmr δ 12.12, 27.61, 118.49, 120.80, 122.09, 122.33, 124.47, 125.27, 128.73, 130.53, 131.53, 131.30, 131.57, 138.13, 139.83, 143.00, 143.32, 150.03, 182.43, 192.98; Found: C, 58.88; H, 3.87; Br, 17.81; N, 12.55%. $C_{22}H_{17}BrN_4O_2$ requires C, 58.81; H, 3.81; Br, 17.78; N, 12.47%.

Ethyl-4-(5-methyl-1-phenyl-1*H*-pyrazol-4-carbonyl)-1-phenylpyrazole-3-carboxylate (6e). Yield (72%); mp. 165-166°C; ir (KBr) ν_{max}/cm^{-1}: 1716 (C=O), 1634 (C=O), 1597(C=N); ^{1}H nmr ($CDCl_3$): δ 1.25 (t, 3H, *J* = 6.9Hz CH_3), 2.56 (s, 3H, CH_3), 4.29 (q, 2H, *J* = 6.9Hz CH_2), 7.44-7.98 (m, 10H, ArH's), 8.10 (s, 1H, pyrazole-3-CH), 9.02 (s, 1H, pyrazole-5-CH); ^{13}C nmr: δ 12.16, 13.83, 61.11, 100.64, 119.76, 120.87, 125.08, 125.38, 127.97, 128.86, 129.45, 129.70, 130.85, 138.25, 138.73, 142.65, 143.50, 161.69, 181.72; MS (*m/z*): 400 (M^+); Found: C, 68.96; H, 5.04; N, 13.97%. $C_{23}H_{20}N_4O_3$ requires C, 68.99; H, 5.03; N, 13.99%.

Ethyl-4-(5-methyl-1-phenyl-1*H*-pyrazol-4-carbonyl)-1-(4-methylphenyl)-pyrazole-3-carboxylate (6f). Yield (74%); mp. 162-163°C; ir (KBr) ν_{max}/cm^{-1}: 1716 (C=O), 1634 (C=O), 1595 (C=N); ^{1}H nmr ($CDCl_3$): δ 1.21(t, 3H, *J* = 7.2 Hz CH_3), 2.26 (s, 3H, CH_3), 2.55 (s, 3H, CH_3), 4.27 (q, 2H, *J* = 7.2 Hz CH_2), 7.34-7.93 (m, 9H, ArH's), 8.10 (s, 1H, pyrazole-3-CH), 9.01 (s, 1H, pyrazole-5-CH); ^{13}C nmr: δ 12.16, 13.83, 20.75, 61.07, 100.19, 119.64, 124.98, 125.37, 128.86, 129.45, 130.06, 130.64, 136.52, 137.54, 138.25, 140.60, 142.62, 143.48,161.72, 181.75; MS

(*m/z*): 414 (M^+); Found: C, 69.61; H, 5.21; N, 13.45%. $C_{24}H_{22}N_4O_3$ requires C, 69.55; H, 5.35; N, 13.52%.

Ethyl-4-(5-methyl-1-phenyl-1*H*-pyrazol-4-carbonyl)-1-(4-chlorophenyl)pyrazole-3-carboxylate (6g). Yield (78%); mp. 195-196°C; ir (KBr) ν_{max}/cm^{-1}: 1718 (C=O), 1630 (C=O), 1595 (C=N); ^1H nmr ($CDCl_3$): δ 1.19 (t, 3H, *J* = 7.2 Hz CH_3), 2.56 (s, 3H, CH_3), 4.27 (q, 2H, *J* = 7.2 Hz CH_2), 7.36-7.97 (m, 9H, ArH's), 8.10 (s, 1H, pyrazole-3-CH), 9.04 (s, 1H, pyrazole-5-CH); ^{13}C nmr: δ 12.17, 13.83, 61.17, 100.46, 120.77, 121.45, 125.17, 125.38, 128.86, 129.44, 129.62, 131.08, 137.55, 138.23, 142.69, 143.56, 145.97, 161.58, 181.53; MS (*m/z*): 434 (M^+); Found: C, 63.49; H, 4.43; Cl, 8.13;N, 12.91%. $C_{23}H_{19}ClN_4O_3$ requires C, 63.52; H, 4.40; Cl, 8.15; N, 12.88%.

4-(5-Methyl-1-phenyl-1*H*-pyrazol-4-carbonyl)-3-benzoyl-isoxazole (13a). Yield (60%); mp. 219-220°C; ir (KBr) ν_{max}/cm^{-1}: 1690 (C=O), 1636 (C=O), 1589 (C=N); ^1H nmr ($CDCl_3$): δ 2.59 (s, 3H, CH_3), 7.52-7.95 (m, 10H, ArH's), 8.05 (s, 1H, pyrazole-3-CH), 10.02 (s, 1H, isoxazole-5-CH); Found: C, 70.56; H, 4.22; N, 11.79%. $C_{21}H_{15}N_3O_3$ requires C, 70.58; H, 4.23; N, 11.76%.

4-(5-Methyl-1-phenyl-1*H*-pyrazol-4-carbonyl)-3-(4-methyl-benzoyl)isoxazole (13b). Yield (58%); mp. 214-215°C; ir (KBr) ν_{max}/cm^{-1}: 1687 (C=O), 1636 (C=O), 1589 (C=N); ^1H nmr ($CDCl_3$): δ 2.21 (s, 3H, CH_3), 2.59 (s, 3H, CH_3), 7.49-7.96 (m, 9H, ArH's), 8.02 (s, 1H, pyrazole-3-CH), 10.02 (s, 1H, isoxazole-5-CH); MS (*m/z*): 371 (M^+); Found: C, 71.13; H, 4.66; N, 11.34%. $C_{22}H_{17}N_3O_3$ requires C, 71.15; H, 4.61; N, 11.31%.

4-(5-Methyl-1-phenyl-1*H*-pyrazol-4-carbonyl)-3-(4-bromo-benzoyl)isoxazole (13c). Yield (64%); mp. 259-260°C; ir (KBr) ν_{max}/cm^{-1}: 1689 (C=O), 1634 (C=O), 1589 (C=N); ^1H nmr ($CDCl_3$): δ 2.59 (s, 3H, CH_3), 7.49-7.91 (m, 9H, ArH's), 8.05 (s, 1H, pyrazole-3-CH), 10.04 (s, 1H, isoxazole-5-CH); Found: C, 57.87; H, 3.25; Br, 18.30; N, 9.67%. $C_{21}H_{14}BrN_3O_3$ requires C, 57.82; H, 3.23; Br, 18.32; N, 9.63%.

Reaction of 6a-d with Hydrazine. General Procedure: A mixture of the appropriate pyrazole **6a-d** (1 mmol) and hydrazine hydrate (80%), 0.2 mL) in absolute ethanol (20 mL) was refluxed for 1 hour then left to cool to room temperature. The orange-yellow precipitated product was collected by filtration, washed with ethanol and dried. Recrystallization from dimethylformamid (DMF) afforded the pyrazolo[3,4-*d*]pyridazine derivatives **9a-d**.

4-(5-Methyl-1-phenyl-1*H*-pyrazol-4-yl)-7-methyl-2-phenyl-pyrazolo[3,4-*d*]pyridazine (9a). Yield (91%); mp. 231-232°C; ir (KBr) ν_{max}/cm^{-1}: 1597 (C=N); ^1H nmr (DMSO-d_6): δ 2.24 (s, 3H, CH_3), 2.63 (s, 3H, CH_3), 7.45-7.75 (m, 10H, ArH's), 8.13 (s, 1H, pyrazole-3-CH), 8.95 (s, 1H, pyrazole-5-CH); ^{13}C nmr: δ 12.98, 18.05, 115.46, 116.77, 121.32, 124.59, 125.34, 128.32, 129.17, 129.32, 129.79, 138.91, 139.09, 139.27, 140.52, 143.58, 149.12, 149.91; MS (*m/z*): 366 (M^+); Found: C, 72.19; H, 4.85; N, 22.86%. $C_{22}H_{18}N_6$ requires C, 72.11; H, 4.95; N, 22.94%.

4-(5-Methyl-1-phenyl-1*H*-pyrazol-4-yl)-7-methyl-2-(4-methylphenyl)pyrazolo[3,4-*d*]pyridazine (9b). Yield (96%); mp. 219-220°C; ir (KBr) ν_{max}/cm^{-1}: 1590 (C=N); ^1H nmr (DMSO-d_6): δ 2.19 (s, 3H, CH_3), 2.22 (s, 3H, CH_3), 2.59 (s, 3H, CH_3), 7.25-7.73 (m, 9H, ArH's), 8.11(s, 1H, pyrazole-3-CH), 8.95 (s, 1H, pyrazole-5-CH); MS (*m/z*): 380 (M^+); Found: C, 72.51; H, 5.23; N, 21.90%. $C_{23}H_{20}N_6$ requires C, 72.61; H, 5.30; N, 22.09%.

4-(5-Methyl-1-phenyl-1*H*-pyrazol-4-yl)-2-(4-chlorophenyl)-7-methyl-pyrazolo[3,4-*d*]pyridazine (9c). Yield (86%); mp. 263-264°C; ir (KBr) ν_{max}/cm^{-1}: 1587 (C=N); ^1H nmr (DMSO-d_6): δ 2.25 (s, 3H, CH_3), 2.59 (s, 3H, CH_3), 7.29-7.73 (m, 9H, ArH's), 8.02(s, 1H, pyrazole-3-CH), 9.01 (s, 1H, pyrazole-5-CH); MS (*m/z*): 400 (M^+); Found: C, 65.85; H, 4.19; Cl, 8.73 N, 20.50%. $C_{22}H_{17}ClN_6$ requires C, 65.92; H, 4.27; Cl, 8.84, N, 20.69%.

4-(5-Methyl-1-phenyl-1*H*-pyrazol-4-yl)-2-(3-bromophenyl)-7-methyl-pyrazolo[3,4-*d*]pyridazine (9d). Yield (92%); mp. > 300°C; ir (KBr) ν_{max}/cm^{-1}: 1589 (C=N); ^1H nmr (DMSO-d_6): δ 2.26 (s, 3H, CH_3), 2.61 (s, 3H, CH_3), 7.26-7.87 (m, 9H, ArH's), 8.00(s, 1H, pyrazole-3-CH), 8.95 (s, 1H, pyrazole-5-CH); MS (*m/z*): 445 (M^+); Found: C, 59.27; H, 3.77; Br, 17.89; N, 18.79%. $C_{22}H_{17}BrN_6$ requires C, 59.34; H, 3.85; Br, 17.94; N, 18.87%.

3-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)-benzo[4,5]imidazo-[1,2-*a*]pyridine-4-carbonitrile (18), 4-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)-benzo[4,5]imidazo[1,2-*a*]pyrimidine (21) and 5-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)-[1,2,4]triazolo[4,3-*a*]-pyrimidine (24). General Procedure: To a mixture of the enaminone **2** (0.51g, 2 mmol) and 1*H*-benzimidazol-2-yleacetonitrile (**16**), 2-aminobenzimidazole (**19**), or 3-amino-1,2,4-triazole (**22**) (2 mmol) in absolute ethanol (20 mL) was added piperidine (0.3 mL). The mixture was refluxed for 12 hours then left to cool to room temperature. The precipitated product was collected by filtration, washed with ethanol, and dried. Recrystallization from DMF afforded the corresponding benzo[4,5]imidazo[1,2-*a*]pyridine, benzo[4,5]imidazo[1,2-*a*]pyrimidine and the triazolo[4,3-*a*]pyrimidine derivatives **18, 21,** and **24,** respectively**.**

3-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)-benzo[4,5]imidazo-[1,2-*a*]pyridine-4-carbonitrile (18). Yield (86%); mp. 209-210°C; ir (KBr) ν_{max}/cm^{-1}: 2191 (C≡N), 1633 (C=N); ^1H nmr (DMSO-d_6): δ 2.24 (s, 3H, CH_3), 7.04 (d, 1H, pyridine-CH, *J* = 7.2 Hz), 7.20-7.71 (m, 9H, ArH's), 8.05 (s, 1H, pyrazole-3-CH), 8.32 (d, 1H, pyridine-CH, *J* = 7.2 Hz); ^{13}C nmr: δ 11.12, 99.38, 113.30, 115.90, 119.73, 121.91, 125.03, 125.42, 126.27, 129.41, 129.47, 137.76, 138.89, 138.95, 139.11, 139.55, 144.36, 146.82; MS (*m/z*): 349 (M^+);Found: C, 75.57; H, 4.29; N, 19.85%. $C_{22}H_{15}N_5$ requires C, 75.63; H, 4.33; N, 20.04%.

4-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)-benzo[4,5]imidazo-[1,2-*a*]pyrimidine (21). Yield (88%); mp. 196-197°C; ir (KBr) ν_{max}/cm^{-1}: 1600 (C=N); ^1H nmr (DMSO-d_6): δ 2.28 (s, 3H, CH_3), 7.07 (d, 1H, *J* = 4.2 Hz pyrimidine-3-CH), 7.28-7.91 (m, 9H, ArH's), 8.11 (s, 1H, pyrazole-3-CH), 8.85 (d, 1H, *J* = 4.2 Hz pyrimidine-2-CH); MS (*m/z*): 325 (M^+); Found: C, 73.90; H, 4.58; N, 21.46%. $C_{20}H_{15}N_5$ requires C, 73.83; H, 4.65; N, 21.52%.

5-(5-methyl-1-phenyl-1*H*-pyrazol-4-yl)-[1,2,4]triazolo[4,3-*a*]pyrimidine (24). Yield (94%); mp. 179-180°C; ir (KBr) ν_{max}/cm^{-1}: 1611 (C=N); ^1H nmr (DMSO-d_6): δ 2.56 (s, 3H, CH_3), 7.45 (d, 1H, *J*= 4.8 Hz pyrimidine-3-CH), 7.52-7.62 (m, 5H, ArH's,), 8.59 (s, 1H, pyrazole-3-CH), 8.72 (s, 1H, triazole), 8.88 (d, 1H, *J*= 4.8 Hz pyrimidine-2-CH); ^{13}C nmr δ 12.75, 108.25, 110.61, 125.36, 128.69, 128.96, 129.09, 129.38, 138.44, 140.77, 141.33, 154.53, 155.23; MS (*m/z*): 276 (M^+); Found: C, 65.14; H, 4.42; N, 30.31%. $C_{15}H_{12}N_6$ requires C, 65.21; H, 4.38; N, 30.42%.

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