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Novel Regiospecific Method for Synthesis of 2-(3,5-Diaryl-4,5-dihydro-1*H*-pyrazol-1-yl)-4,6-diarylpyrimidines

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Abstract: The facile, regiospecific, one-pot synthesis of 2-(3,5-diaryl-4,5-dihydro-1*H*-pyrazol-1-yl)-4,6-diarylpyrimidines derivatives has been described, involving a [3 + 2] and [3 + 3] cyclocondensation between the α,β-unsaturated ketones and aminoguanidine bicarbonate.

Keywords: aminoguanidine bicarbonate, 2-(pyrazol-1-yl)pyrimidines, α,β-unsaturated ketones

INTRODUCTION

The structurally novel 2-(1H-pyrazol-1-yl)-pyrimidine derivatives have been reported to have interesting bioactive profiles.[1–4] For example, 4-methoxy-2-(5-methoxy-3-methyl-1H-pyrazol-1-yl)-6-methylpyrimidine (epirizole) is a nonsteroidal anti-inflammatory and analgesic agent therapeutically used in Japan.[5] Many analogs of 2-(1H-pyrazol-1-yl)-pyrimidine show potent inhibition of HCl-ethanol-induced and water-immersion stress-induced ulcers in rats.[6] Moreover, 2-(3,4,-diethyl-1-pyrazolyl)-pyrimidine and 2-(4,5-dihydro-4-methyl-3-arylpyrazol-1-yl)-4,6-dimethylpyrimidines were found to possess herbicidal and fungicidal activity.[3,7] It is pertinent to mention that 1-(pyrimidin-2-yl)-3-pyrazolin-5-one derivatives such as 2-(4,5-

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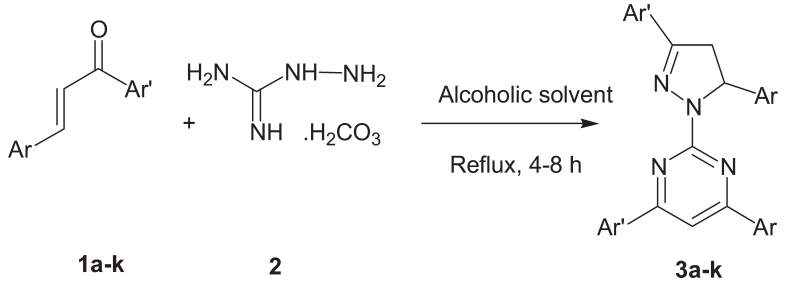
dimethyl-pyrazol-1-yl)-4-thioxo-6-methyl-4H-pyrimidine are associated with cardiotonic activity with an ED_{50} value close to that of milrinone.[8]

Although the 2-(1H-pyrazol-1-yl)-pyrimidine core seems important for imparting several biological properties, the scope in designing simple and efficient synthetic routes still exists. The first synthesis of 2-(pyrazol-1-yl)pyrimidine was reported in 1963.[9] Later, many routes were described, but all of them are fraught with difficulties and modest yields.[10–13] A one-step method was reported in which cyclocondensation of 4-alkoxy-1,1,1-trifluoro-3-alken-2-one and aminoguanidine bicarbonate was carried out wherein 5-hydroxy-substituted 2-(5-hydroxy-4,5-dihydro-1*H*-pyrazol-1-yl) pyrimidine derivatives were formed.[14]

The present work reports a regiospecific one-pot synthesis involving a [3 + 2] and [3 + 3] cyclocondensation between α,β-unsaturated aromatic ketones and aminoguanidine bicarbonate to obtain several novel 2-(3,5-diaryl-4,5-dihydro-1*H*-pyrazol-1-yl)-4,6-diarylpyrimidine derivatives in a regiospecific manner.[15,16]

The α,β-unsaturated ketones (**1a**–**k**) were prepared according to literature methods.[17–19] The advantage of using substituted α,β-unsaturated aromatic ketones was that a wide variety of end products can be synthesized, as variations can be made at both the aromatic rings of the ketones. Subsequent condensation reactions of alcoholic solutions of α,β-unsaturated ketones (**1a**–**k**) with aminoguanidine bicarbonate (**2**) gave 2-(3,5-diaryl-4,5-dihydro-1*H*-pyrazol-1-yl)-4,6-diarylpyrimidine derivatives (**3a**–**k**) (Scheme 1). Initially, experiments with a variety of solvents including N,N-dimethyl formamide (DMF), dimethyl sulfoxide (DMSO), and acetonitrile did not yield the product. Alcoholic solvents were found to be suitable, with ethanol giving optimum yield. Other salts of aminoguanidine including HCl and H_2SO_4 salts also did not give the final products in a one-pot scheme, indicating that the slow release of free base from the H_2CO_3 salt was required for the reaction. Addition of a catalyst like Lewis acid did not yield product, whereas addition of sodium acetate resulted in no substantial improvement of yields. Thus condensation of alcoholic solutions of α,β-unsaturated ketones (**1a**–**k**) with aminoguanidine



Scheme 1.

bicarbonate (**2**) in a simple one-pot reaction gave 2-(3,5-diaryl-4,5-dihydro-1*H*-pyrazol-1-yl)-4,6-diarylpyrimidine derivatives (**3a**–**k**) (Scheme 1).

The versatility of this methodology was expanded with a number of α,β-unsaturated ketones (**1a**–**k**) being used to prepare 2-(3,5-diaryl-4,5-dihydro-1*H*-pyrazol-1-yl)-4,6-diarylpyrimidines (**3a**–**k**) (Table 1).

Although we have not yet established the mechanism of the cyclocondensation reaction between α,β-unsaturated ketones and aminoguanidine bicarbonate in an experimental manner, a possible explanation is proposed in Scheme 2. It involves either a [3 + 2] or [3 + 3] cyclocondensation to give intermediate **I** or **II**, respectively, which again undergoes [3 + 3] or [3 + 2] cyclocondensation, leading to 4,5-dihydropyrimidine-pyrazoline (**III**). Under alkaline conditions, the 4,5-dihydropyrimidine-pyrazoline undergoes aromatization to form the final product, **3** (Scheme 2).

In conclusion, this regiospecific method of synthesis of 2-(3,5-diaryl-4,5-dihydro-1*H*-pyrazol-1-yl)-4,6-diarylpyrimidines in one pot is simple and novel.

EXPERIMENTAL

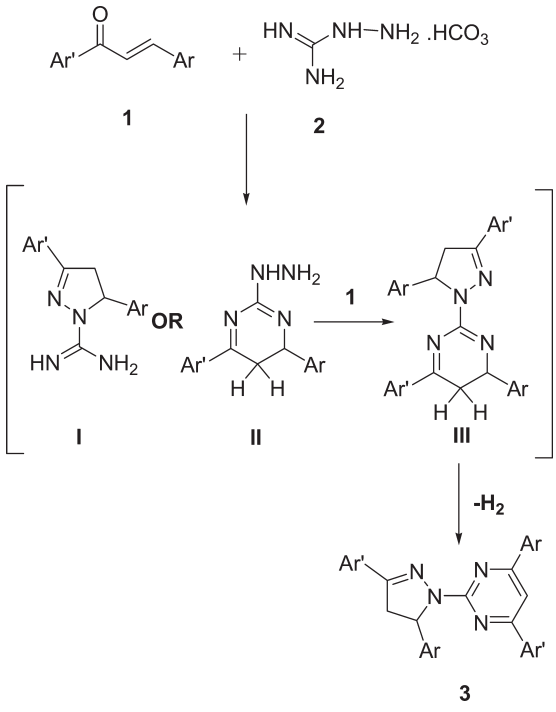
The reagents and solvents were obtained from commercial sources. The melting points of the compounds synthesized were uncorrected and were recorded by the open glass capillary method on an Oswald Precision melting-point apparatus. All the NMR spectra were recorded on a Jeol

Table 1. Yields and melting points of synthesized 2-(3,5-diaryl-4,5-dihydro-1*H*-pyrazol-1-yl)-4,6-diarylpyrimidines (**3a**–**k**)

Compound[a]	Ar	Ar′	Yield (%)[b]	M.P. (°C)
3a	Phenyl	4-Bromophenyl	45	226–228
3b	4-Methoxyphenyl	4-Bromophenyl	40	234–236
3c	Phenyl	4-Chlorophenyl	45	235–238
3d	4-Methoxyphenyl	4-Chlorophenyl	42	254–255
3e	3,4-Dimethoxy phenyl	4-Chlorophenyl	47	240–242
3f	Phenyl	4-Fluorophenyl	55	225–228
3g	4-Methoxyphenyl	4-Fluorophenyl	46	214–216
3h	3,4-Dimethoxy phenyl	4-Fluorophenyl	42	207–209
3i	Phenyl	4-Methoxyphenyl	32	230–232
3j	4-Methoxyphenyl	4-Methoxyphenyl	33	239–241
3k	4-Chlorophenyl	4-Methoxyphenyl	48	242–244

[a]All the synthesized 2-(3,5-diaryl-4,5-dihydro-1*H*-pyrazol-1-yl)-4,6-diarylpyrimidines were characterized spectroscopically (IR, ^{1}H NMR, ^{13}C NMR, MS, and elemental analysis).

[b]Yields indicate isolated yields after column chromatography.



Scheme 2. Proposed reaction mechanism of synthesis of 2-(3,5-diaryl-4,5-dihydro-1*H*-pyrazol-1-yl)-4,6-diarylpyrimidines (**3**).

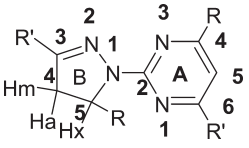
FT-NMR (^{1}H NMR and ^{13}C NMR at 300 MHz) in 5-mm sample tubes in $CDCl_3$ using TMS as internal reference. IR spectra were recorded on a Perkin-Elmer Fourier transform infrared spectrometer or Buck Scientific infrared spectroscopy M500 spectrophotometer using KBr-based pellets. The CHN analysis was recorded on a Perkin-Elmer series 2–2400. Analytical thin-layer chromatography (TLC) was carried out on precoated plates SiO_2 (silica gel 60, F 254, Merck). SiO_2 (Silica gel 60–80 mesh, Merck) was used for column chromatography. Commercial reagents and solvents were used without further purification unless stated. All the products gave melting points and spectral (IR, ^{1}H NMR, ^{13}C NMR, MS, and elemental analysis) data consistent with the assigned structures.

General Procedure for the Synthesis of 2-(3,5-Diaryl-4, 5-dihydro-1*H*-pyrazol-1-yl)-4,6-diarylpyrimidines (3a–k)

A mixture of **1a–k** (5 mmol) and aminoguanidine bicarbonate, **2** (3 mmol), contained in a 50-ml, round-bottom flask was suspended in 30 ml of ethanol, and the mixture was refluxed with stirring. The reaction was

monitored by TLC and continued until the α,β-unsaturated ketone was completely consumed or did not react further. The solvent was evaporated, and the residue thus obtained was suspended in dichloromethane. The insoluble part was filtered off, and the solvent was evaporated under vacuum. The product thus obtained contained impurities (base spot) and some amount of the starting material, and hence it was purified by silica-gel column chromatography to obtain pyrazolyl-pyrimidine (**3a**–**k**) as the major isolable product. The synthesized compounds were characterized using IR, ^{1}H NMR, ^{13}C NMR, and MS spectroscopy and elemental analysis.

Spectral Data of 2-(3,5-Diaryl-4, 5-dihydro-1*H*-pyrazol-1-yl)-4,6-diarylpyrimidines



4-(4-Bromophenyl)-2-[3-(4-bromophenyl)-5-phenyl-4,5-dihydro-1*H*-pyrazol-1-yl]- 6-phenylpyrimidine (**3a**)

Yield 45%; yellow solid; mp 226–228°C. IR (KBr): 3071.7, 2936.8, 1590.7, 1529.2, 1472.2, 808.0 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.23–3.15 (dd, $^{2}J_{HH}$ = 17.4 Hz, $^{3}J_{HH}$ = 6.0 Hz, 1H, pyrazoline H-4 *trans*), 385–3.75 (dd, $^{2}J_{HH}$ = 17.2 Hz, $^{3}J_{HH}$ = 12.3 Hz, 1H, pyrazoline H-4 *cis*), 5.83–5.77 (dd, $^{3}J_{HH}$ = 12.3 Hz, $^{3}J_{HH}$ = 6.0 Hz, 1H, pyrazoline H-5), 7.17 (s, 1H, pyrimidine H-5), 7.91–7.24 (m, 18H, Ar); ^{13}C NMR (300 MHz, $CDCl_3$): δ = 42.39 (C4-pyrazoline), 63.10 (C5-pyrazoline), 103.54 (C5-pyrimidine), 127.29, 127.36, 128.07, 128.51, 128.63, 128.78, 129.01, 130.02, 130.63, 131.73, 131.79, 131.94, 132.11, 136.61, 137.51 (Ar), 150.89 (C3-pyrazoline), 158.92, 164.48, 165.02 (C4-pyrimidine, C2-pyrimidine, C6-pyrimidine); MS (ES + 4.27e4): m/z (%) 608.32, 610.31 (100) [M^+, 612.31. Anal. calcd. for $C_{31}H_{22}Br_2N_4$ (610.34): C, 61.10; H, 3.63; N, 9.18. Found: C, 61.00; H, 3.72; N, 9.20.

4-(4-Bromophenyl)-2-[3-(4-bromophenyl)-5-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazol-1-yl]-6-(4-methoxyphenyl)-pyrimidine (**3b**)

Yield 40%; yellow solid; mp 234–236°C. IR (KBr): 2978.3, 2916.0, 2853.8, 1586.3, 1539.2, 1243.9, 1005.2, 818 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.31–3.26 (dd, $^{2}J_{HH}$ = 17.2 Hz, $^{3}J_{HH}$ =5.5 Hz, 1H, pyrazoline H-4 *trans*), 3.88–3.73 (m, 7H, OCH_3 pyrazoline H-4 *cis*), 5.88–5.83 (dd, $^{3}J_{HH}$ = 11.9 Hz, $^{3}J_{HH}$ = 5.5 Hz, 1H, pyrazoline H-5), 7.26 (s, 1H, pyrimidine H-5), 8.03–6.85 (m, 16H, Ar); ^{13}C NMR (300 MHz, $CDCl_3$): δ = 42.62

(C4-pyrazoline), 55.28, 55.43, (OCH_3), 62.76 (C5-pyrazoline), 103.54 (C5-pyrimidine), 113.95, 114.03, 114.46, 119.90, 120.38, 127.78, 128.58, 128.82, 130.66, 135.47, 136.23, 136.62, 137.53, 159.03, 164.48 (Ar), 150.81 (C3-pyrazoline), 151.44, 156.54, 165.02 (C4-pyrimidine, C2-pyrimidine, C6-pyrimidine). Anal. calcd. for $C_{31}H_{22}Br_2N_4O_2$ (670.39): C, 59.12; H, 3.91; N, 8.36. Found: C, 59.09; H, 3.83; N, 8.30.

4-(4-Chlorophenyl)-2-[3-(4-chlorophenyl)-5-phenyl-4,5-dihydro-1*H*-pyrazol-1-yl]-6-phenyl pyrimidine (**3c**)

Yield 45%; yellow solid; mp 235–238°C. IR (KBr): 3033, 2932, 1572, 1530, 1476, 1563 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.22–3.15 (dd, $^2J_{HH}$ = 17.1 Hz, $^3J_{HH}$ =5.7 Hz, 1H, pyrazoline H-4 *trans*), 3.84–3.75 (dd, $^2J_{HH}$ =17.1 Hz, $^3J_{HH}$ =12.1 Hz, 1H, pyrazoline H-4 *cis*), 5.83–5.77 (dd, $^3J_{HH}$ = 12.1 Hz, $^3J_{HH}$ = 5.5 Hz, 1H, pyrazoline H-5), 7.27 (s, 1H, pyrimidine H-5), 7.90–7.19 (m, 18H, Ar); ^{13}C NMR (300 MHz, $CDCl_3$): δ = 42.45 (C4-pyrazoline), 63.10 (C5-pyrazoline), 104.09 (C5-pyrimidine), 127.27 127.82, 128.07, 128.51, 128.55, 128.63, 128.78, 129.21, 131.19, 131.78, 131.79, 131.94, 132.11, 136.60, 137.40, 137.51, (Ar), 150.86 (C3-pyrazoline), 158.84, 164.48, 165.32 (C4-pyrimidine, C2-pyrimidine, C6-pyrimidine). Anal. calcd. for $C_{31}H_{22}Cl_2N_4$ (521.44): C, 73.01; H, 4.25; N, 10.74. Found: C, 73.00; H, 4.29; N, 10.70.

4-(4-Chlorophenyl)-2-[3-(4-chlorophenyl)-5-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazol-1-yl]-6-(4-methoxyphenyl)-pyrimidine (**3d**)

Yield 42%; yellow solid; mp 254–255°C. IR (KBr): 3016, 2955, 1533, 1475, 820 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.27–3.19 (dd, $^2J_{HH}$ = 17.1 Hz, $^3J_{HH}$ = 5.4 Hz, 1H, pyrazoline H-4 *trans*), 3.87–3.76 (m, 7H, OCH_3, pyrazoline H-4 *cis*), 5.87–5.81 (dd, $^3J_{HH}$ = 12.0 Hz, $^3J_{HH}$ = 5.4 Hz, 1H, pyrazoline H-5), 7.25 (s, 1H, pyrimidine H-5), 8.01–6.84 (m, 16H, Ar); ^{13}C NMR (300 MHz, $CDCl_3$): δ = 42.44 (C4-pyrazoline), 56.02, 56.54, (OCH_3) 63.07 (C5-pyrazoline), 104.00 (C5-pyrimidine), 117.82, 120.38, 125.85, 127.27, 127.84, 128.55, 128.62, 128.77, 130.62, 150.81, 135.43, 136.14, 136.02, 137.53, 143.41, 159.19, 164.39 (Ar), 150.81 (C3-pyrazoline), 151.19, 158.93, 165.92 (C4-pyrimidine, C2-pyrimidine, C6-pyrimidine). Anal. calcd. for $C_{33}H_{26}Cl_2N_4O_2$ (581.50): C, 68.16; H, 4.51; N, 9.64. Found: C, 68.10; H, 4.45; N, 9.62.

4-(4-Chlorophenyl)-2-[3-(4-chororophenyl)-5-(3,4-dimethoxyphenyl)-4,5-dihydro-1*H*-pyrazol-1-yl]-6-(3,4-dimethoxyphenyl) pyrimidine (**3e**)

Yield 47%; yellow solid; mp 240–242°C. IR (KBr): 3027, 3025, 2936, 1575, 1566, 1531 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.28–3.21 (dd, $^2J_{HH}$ = 17.3 Hz, $^3J_{HH}$ = 6.0 Hz, 1H, pyrazoline H-4 *trans*), 3.95–3.80

(m, 13H, OCH_3, pyrazoline H-4 *cis*), 5.88–5.82 (dd, $^3J_{HH} = 12.5$ Hz, $^3J_{HH} = 6.0$ Hz, 1H, pyrazoline H-5), 7.26 (s, 1H, pyrimidine H-5), 8.01–6.80 (m, 14H, Ar); ^{13}C NMR (300 MHz, $CDCl_3$): 42.62 (C4-pyrazoline), 53.63, 55.28, 55.40, 56.02, (OCH_3), 62.76 (C5-pyrazoline), 103.54 (C5-pyrimidine), 110.27, 110.84, 111.35, 117.82, 120.38, 127.78, 128.58, 128.82, 149.42, 130.37, 130.66, 135.47, 136.23, 136.58, 149.18 (Ar), 150.81 (C3-pyrazoline), 151.44, 156.54, 159.03 (C4-pyrimidine, C2-pyrimidine, C6-pyrimidine); MS (ES + 1.85e3): m/z (%) 641 (100) $[M]^+$, 643.29. Anal. calcd. for $C_{35}H_{30}Cl_2N_4O_4$ (641.54): C, 65.53; H, 4.71; N, 8.73. Found: C, 65.36; H, 4.66; N, 8.69.

4-(4-Fluorophenyl)-2-[3-(4-fluorophenyl)-5-phenyl-4,5-dihydro-1*H*-pyrazol-1-yl]-6-phenylpyrimidine (**3f**)

Yield 55%; pale yellow solid; mp 225–228°C. IR (KBr): 3050.9, 2926.4, 1568.4, 1508.5, 1472.2, 1352 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm)= 3.31–3.23 (dd, $^2J_{HH} = 17.3$ Hz, $^3J_{HH} = 5.7$ Hz, 1H, pyrazoline H-4 *trans*), 3.92–3.82 (dd, $^2J_{HH} = 17.1$ Hz, $^3J_{HH} = 12.0$ Hz, 1H, pyrazoline H-4 *cis*), 5.89–5.84 (dd, $^3J_{HH} = 11.5$ Hz, $^3J_{HH} = 5.4$ Hz, 1H, pyrazoline H-5), 7.24 (s, 1H, pyrimidine H-5), 8.00–7.24 (m, 18H, Ar); ^{13}C NMR (300 MHz, $CDCl_3$): $\delta = 42.60$ (C4-pyrazoline), 63.07 (C5-pyrazoline), 104.00 (C5-pyrimidine), 114.03 114.46, 119.90, 125.85, 127.27, 127.84, 128.55, 128.65, 128.77, 130.62, 135.43, 136.14, 136.62, 137.53, 159.03, 164.39 (Ar), 150.81 (C3-pyrazoline), 156.54, 158.93, 165.39 (C4-pyrimidine, C2-pyrimidine, C6-pyrimidine). Anal. calcd. for $C_{31}H_{22}F_2N_4$ (488.52): C, 76.21; H, 4.54; N, 11.47. Found: C, 76.21; H, 4.47; N, 11.35.

4-(4-Fluorophenyl)-2-[3-(4-fluorophenyl)-5-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazol-1-yl]-6-(4-methoxyphenyl) pyrimidine (**3g**)

Yield 46%; pale yellow solid; mp 214–216°C. IR (KBr): 3070.9, 2935.6, 1585.2, 1508, 1476.7, 1413.1 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm)= 3.28–3.20 (dd, $^2J_{HH}$= 17.1 Hz, $^3J_{HH} = 5.4$ Hz, 1H, pyrazoline H-4 *trans*), 3.87–3.75 (m, 7H, OCH_3, pyrazoline H-4 *cis*), 5.86–5.80 (dd, $^3J_{HH} = 12.0$ Hz, $^3J_{HH} = 5.4$ Hz, 1H, pyrazoline H-5), 7.25 (s, 1H, pyrimidine H-5), 8.03–6.83 (m, 16H, Ar); ^{13}C NMR (300 MHz, $CDCl_3$): δ= 42.30 (C4-pyrazoline), 56.02, 56.07 (OCH_3), 62.52 (C5-pyrazoline), 103.24 (C5-pyrimidine), 111.34, 117.92, 120.29, 126.59, 127.22, 129.22, 129.30, 129.51, 130.84, 132.39, 135.14, 136.79, 148.10, 149.12, 158.70, 165.03 (Ar), 151.19 (C3-pyrazoline), 151.83, 159.19, 165.07 (C4-pyrimidine, C2-pyrimidine, C6-pyrimidine); MS (ES + 1.85e3): m/z (%) 549.31 (100) $[M + H]^+$, 550.31. Anal. calcd. for $C_{33}H_{26}F_2N_4O_2$ (548.58): C, 72.25; H, 4.78; N, 10.21. Found: C, 72.30; H, 4.74; N, 10.18.

4-(3,4-Dimethoxyphenyl)-2-[5-(3,4-dimethoxyphenyl)-3-(4-fluorophenyl)-4,5-dihydro-1*H*-pyrazol-1-yl]-6-(4-fluorophenyl)pyrimidine (**3h**)

Yield 42%; pale yellow solid; mp 207–209°C. IR (KBr): 3058.9, 2967.9, 1570, 1529.2, 1472, 1399.5 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ (ppm)= 3.28–3.20 (dd, $^2J_{HH} = 17.4$ Hz, $^3J_{HH} = 6.3$ Hz, 1H, pyrazoline H-4 *trans*), 3.95–3.80 (m, 13H, OCH_3, pyrazoline H-4 *cis*), 5.88–5.82 (dd, $^3J_{HH} = 12.6$ Hz, $^3J_{HH} = 6.3$ Hz, 1H, pyrazoline H-5), 7.26 (s, 1H, pyrimidine H-5), 8.01–6.80 (m, 14H, Ar); ^{13}C NMR (300 MHz, $CDCl_3$): $\delta = 42.81$ (C4-pyrazoline), 53.63, 55.28, 56.02, 56.07, (OCH_3) 62.52 (C5-pyrazoline), 103.24 (C5-pyrimidine), 117.92, 120.29, 126.59, 127.22, 129.22, 129.30, 129.51, 130.84, 135.14, 136.79, 139.66, 140.64, 148.10, 149.12, 149.32, 165.00 (Ar), 151.19 (C3-pyrazoline), 151.83, 159.19, 165.37 (C4-pyrimidine, C2-pyrimidine, C6-pyrimidine). Anal. calcd. for $C_{35}H_{30}F_2N_4O_4$ (608.63): C, 69.07; H, 4.97; N, 9.21. Found: C, 69.10; H, 4.87; N, 9.16.

4-(4-Methoxyphenyl)-2-[3-(4-methoxyphenyl)-5-phenyl-4,5-dihydro-1*H*-pyrazol-1-yl]-6-phenylpyrimidine (**3i**)

Yield 32%; yellow solid; mp 230–232°C. IR (KBr): 3061.3, 2926.4, 1581.1, 1529.2, 1467, 1342 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.28–3.20 (dd, $^2J_{HH} = 17.4$ Hz, $^3J_{HH} = 5.4$ Hz, 1H, pyrazoline H-4 *trans*), 3.87–3.75 (m, 7H, OCH_3, pyrazoline H-4 *cis*), 5.86–5.80 (dd, $^3J_{HH} = 12.0$ Hz, $^3J_{HH} = 5.1$ Hz, 1H, pyrazoline H-5), 7.22 (s, 1H, pyrimidine H-5), 8.03–6.83 (m, 16H, Ar); ^{13}C NMR (300 MHz, $CDCl_3$): $\delta = 42.60$ (C4-pyrazoline), 55.28, 55.40, (OCH_3), 62.26 (C5-pyrazoline), 103.33 (C5-pyrimidine), 114.03, 114.46, 119.90, 126.64, 127.22, 127.29, 128.47, 128.56, 128.82, 129.41, 130.31, 132.39, 136.02, 138.01, 158.77, 160.07, (Ar-C), 151.63 (C3-pyrazoline), 151.83, 161.69, 165.37 (C4-pyrimidine, C2-pyrimidine, C6-pyrimidine). Anal. calcd. for $C_{33}H_{28}N_4O_2$ (512.60): C, 77.32; H, 5.51; N, 10.93, Found: C, 77.21; H, 5.60; N, 10.83.

2-[3,5-Bis-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazol-1-yl]-4,6-bis-(4-methoxy-phenyl) pyrimidine (**3j**)

Yield 33%; yellow solid; mp 239–241°C. IR (KBr): 3009.4, 2905.7, 2833.0, 1565.6, 1534.4, 1477.4, 1238.7, 1031.1 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) = 3.29–3.22 (dd, $^2J_{HH} = 17.4$ Hz, $^3J_{HH} = 5.7$ Hz, 1H, pyrazoline H-4 *trans*), 3.94–3.80 (m, 13H, OCH_3, pyrazoline H-4 *cis*), 5.86–5.80 (dd, $^3J_{HH} = 12.2$ Hz, $^3J_{HH} = 5.7$ Hz, 1H, pyrazoline H-5), 7.22(s, 1H, pyrimidine H-5), 7.97–6.79 (m, 16H, Ar); ^{13}C NMR (300 MHz, $CDCl_3$): $\delta = 42.66$ (C4-pyrazoline), 55.28, 55.38, 56.02, 56.07, (OCH_3) 62.14 (C5-pyrazoline), 102.89 (C5-pyrimidine), 113.90, 113.98, 126.62, 127.18, 127.22, 128.79, 129.18, 129.26, 129.63, 130.45, 135.20, 136.21, 139.53, 140.51, 159.05,

164.92, (Ar-C), 151.61 (C3-pyrazoline), 158.71, 161.59, 165.24 (C4-pyrimidine, C2-pyrimidine, C6-pyrimidine). Anal. calcd. for $C_{35}H_{32}N_4O_4$ (572.65): C, 73.41; H, 5.63; N, 9.78. Found: C, 73.35; H, 5.69; N, 9.74.

4-(4-Chlorophenyl)-2-[5-(4-chlorophenyl)-3-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazol-1-yl]-6-(4-methoxyphenyl)-pyrimidine (**3k**)

Yield 48%; yellow solid; mp 242–244°C. IR (KBr): 3016, 2955, 1533, 1475, 820 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ (ppm)= 3.31–3.23 (dd, $^3J_{HH} = 17.3$ Hz, $^3J_{HH} = 5.4$ Hz, 1H, pyrazoline H-4 *trans*), 3.88–3.73 (m, 7H, OCH_3, pyrazoline H-4 *cis*), 5.89–5.83 (dd, $^3J_{HH} = 12.0$ Hz, $^3J_{HH} = 5.4$ Hz, 1H, pyrazoline H-5), 7.26 (s, 1H, pyrimidine H-5), 8.04–6.85 (m, 16H, Ar); ^{13}C NMR (300 MHz, $CDCl_3$): $\delta = 42.44$ (C4-pyrazoline), 56.02, 56.54, (OCH_3), 63.11 (C5-pyrazoline), 104.00 (C5-pyrimidine), 117.82, 120.38, 125.92, 127.29, 127.81, 128.66, 128.64, 128.77, 130.65, 135.43, 136.14, 136.02, 137.53, 143.41, 159.19, 164.26, (Ar-C), 150.80 (C3-pyrazoline), 151.19, 158.93, 165.90 (C4-pyrimidine, C2-pyrimidine, C6-pyrimidine). Anal. calcd. for $C_{33}H_{26}Cl_2N_4O_2$ (581.49): C, 68.16; H, 4.51; N, 9.64. Found: C, 68.12; H, 4.41; N, 9.52.

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