SYNTHESIS AND SPECTRAL ANALYSIS OF AN ARRAY OF NOVEL 4-(4-MORPHOLINOPHENYL)-6-ARYL-PYRIMIDIN-2-AMINES

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ABSTRACT

An array of newly synthesized novel 4-(4-morpholinophenyl)-6-arylpyrimidin-2-amines **(20-28)** are synthesized from the respective (E)-1-4-morpholinophenyl)-3-aryl-prop-2-en-1-ones **(11-19)** by the treatment of guanidine nitrate in refluxing ethanol catalyzed by lithium hydroxide and characterized by melting point, elemental analysis, MS, FT-IR, one-dimensional NMR (^{1}H & ^{13}C) spectroscopic data.

Keywords: 1-(4-morpholinophenyl) ethanone; (E)-1-4-morpholinophenyl)-3-aryl-prop-2-en-1-ones; 4-(4-morpholinophenyl)-6-arylpyrimidin-2-amines; Guanidine nitrate; Synthesis.

INTRODUCTION

Pyrimidines are the basic nucleus in nucleic acids and have been associated with a number of biological activities. Some notable biological activity of pyrimidine derivatives include adenosine receptor antagonists [1], kinase inhibitors [2], analgesic [3], anti-inflammatory [3], inhibitors of cyclin-Dependent kinases 1 and 2 [4], calcium channel antagonist [5], antihistaminic [6], antitubercular [7] activities. Substituted aminopyrimidine nuclei are common in marketed drugs such as anti-atherosclerotic aronixil, anti-histaminic thonzylamine, anti-anxielytic buspirone, anti-psoriatic enazadrem, and other medicinally relevant compounds.

Morpholine is a simple heterocyclic compound with a great industrial importance. It is used as anticorrosive agent and as chemical intermediate: catalyst, solvent, antioxidant, in the production of various pharmaceuticals and pesticides. 4-Phenyl morpholine derivatives [8] are reported to possess antimicrobial, anti-inflammatory and central nervous system activities. Linezolide (commercially available antimicrobial) also possess a 4-phenyl-morpholine substituent. They are reported to exert a number of important physiological activities such as antidiabetic [9], antiemetic [10], platelet aggregation inhibitors, antihyperlipoproteinemics [9], bronchodilators, growth stimulats [11] and antidepressants [12]. These were also used in the treatment of inflammatory diseases, pain, migraine and asthma [13].

Recently, we exploited the synthesis of 6-aryl-1,2,4,5-tetrazinane-3-thiones [14], fused indazoles [15], 3,4-dihydropyrimidin-2(1*H*)-ones/thiones [16], pyrimidine and 2,6-diarylpiperidin-4-one derivatives [17-19] with a view to incorporate various other bioactive heterocyclic nucleus such as 1,2,3-selenadiazoles, 1,2,3-thiadiazoles, diazepans intact for evaluation of associated antibacterial and antifungal activities. In view of the above and as part of the ongoing research on antimicrobials [17], we planned to synthesize a system, which comprises both N-functionalized morpholine and 2-amino-4,6-diarylpyrimidine components together to give a compact structure like title 4-(4-morpholinophenyl)-6-arylpyrimidin-2-amines.

EXPERIMENTAL

Performing TLC assessed the reactions and the purity of the products. All the reported melting points were taken in open capillaries and were uncorrected. IR spectra were recorded in KBr (pellet forms) on a Nicolet-Avatar–330 FT-IR spectrophotometer and note worthy absorption values (cm^{-1}) alone are listed. ^{1}H and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz respectively on Bruker AMX 400 NMR spectrometer using DMSO-*d* as solvent. The ESI +ve MS spectra were recorded on a Bruker Daltonics LC-MS spectrometer. Satisfactory microanalysis was obtained on Carlo Erba 1106 CHN analyzer.

General procedure for the synthesis of (E)-1-4-morpholinophenyl)-3-aryl-prop-2-en-1-ones (11-19)

To an ethanolic solution of 1-(4-morpholinophenyl) ethanone (0.001 mol) and substituted benzaldehyde (0.001 mol), aqueous sodium hydroxide (0.005 mol) was added drop wise with stirring on a mechanical stirrer for 10 minutes and stirring was continued for 2-6 h. After completion of reaction, the crude product isolated by suction was washed with water, dried and recrystallized from ethanol.

(E)-1-(4-morpholinophenyl)-3-phenyl-prop-2-en-1-one (11)

Reaction time: 4 h; IR (KBr) ν (cm^{-1}): 3007, 2962, 2924, 2852, 1646, 1606, 1190, 769; ^{1}H NMR (δ ppm): 3.33-3.36 (t, 4H, N(CH_2)$_2$, *J*=4.7Hz), 3.87-3.89 (t, 4H, O(CH_2)$_2$, *J*=4.7Hz), 6.93-6.95 (d, 1H, H_2, *J*=8.9Hz); 7.38-7.82 (m, 10H, H_{arom}); 8.01-8.03 (d, 1H, H_3, *J*=8.9Hz); ^{13}C NMR (δ ppm): 47.7 N(CH_2), 66.5 O(CH_2), 122.3 C-2, 143.2 C-3, 113.6, 128.8-130.3 –C_{arom}, 128.2, 135.4, 154.1 *ipso*-C, 188.1 C-1.

(E)-1-(4-morpholinophenyl)-3-*p*-tolyl-prop-2-en-1-one (12)

Reaction time: 5 h; IR (KBr) ν (cm^{-1}): 3012, 2923, 2924, 2851, 1645, 1600, 1194, 810; ^{1}H NMR (δ ppm): 1.57 (*s*, 3H, CH_3 at phenyl ring), 3.32-3.35 (t, 4H, N(CH_2)$_2$, *J*=4.8Hz), 3.86-3.89 (t, 4H, O(CH_2)$_2$, *J*=4.8Hz), 6.92-6.94 (d, 1H, H_2, *J*=8.8Hz); 7.21-7.80 (m, 9H, H_{arom}); 8.00-8.02 (d, 1H, H_3, *J*=8.8Hz); ^{13}C NMR (δ ppm): 21.0 CH_3 at phenyl ring, 47.7 N(CH_2), 66.5 O(CH_2), 121.2 C-2, 143.3 C-3, 113.5, 129.3-130.5 –C_{arom}, 128.2,132.7,140.5,154.1 *ipso*-C, 188.2 C-1.

(E)- 3-(4-chlorophenyl)-1-(4-morpholinophenyl)prop-2-en-1-one (13)

Reaction time: 5 h; IR (KBr) ν (cm^{-1}): 3087, 2967, 2920, 2859, 1597, 1654, 1202, 817; ^{1}H NMR (δ ppm): 3.34-3.37 (t, 4H, N(CH_2)$_2$, *J*=4.7Hz), 3.89-3.91 (t, 4H, O(CH_2)$_2$, *J*=4.8Hz), 6.97-6.99 (d, 1H, H_2, *J*=8.8Hz); 7.35-7.76 (m, 9H, H_{arom}); 8.00-8.02 (d, 1H, H_3, *J*=8.9Hz); ^{13}C NMR (δ ppm): 47.6 N(CH_2), 66.5 O(CH_2), 121.2 C-2, 141.8 C-3, 113.5, 129.4-130.6 –C_{arom}, 129.1,133.8,135.0,154.0 *ipso*-C, 192.2 C-1.

(E)- 3-(4-methoxyphenyl)-1-(4-morpholinophenyl)prop-2-en-1-one (14)

Reaction time: 4 h; IR (KBr) ν (cm^{-1}): 3010, 2961, 2918, 2841, 1645, 1601, 1225; ^{1}H NMR (δ ppm): 3.32-3.35 (t, 4H, N(CH_2)$_2$, *J*=4.8Hz), 3.87-3.90 (t, 4H, O(CH_2)$_2$, *J*=4.8Hz), 3.86 (*s*, 3H, OCH_3 at phenyl ring), 7.59-7.61 (d, 1H, H_2, *J*=8.6Hz); 6.92-7.46 & 7.75-7.79 (m, 9H, H_{arom}); 8.00-8.02 (d, 1H, H_3, *J*=8.7Hz); ^{13}C NMR (δ ppm): 47.6 N(CH_2), 55.3 OCH_3 at phenyl ring, 66.5 O(CH_2), 119.6 C-2, 143.1 C-3, 113.5, 129.2-130.4 –C_{arom}, 127.9,129.9, 153.9, 161.3 *ipso*-C, 187.8 C-1.

(E)- 3-(4-fluorophenyl)-1-(4-morpholinophenyl)prop-2-en-1-one (15)

Reaction time: 4 h; IR (KBr) ν (cm^{-1}): 3009, 2969, 2919, 2849, 1650, 1602, 1227; ^{1}H NMR (δ ppm): 3.33-3.36 (t, 4H, N(CH_2)$_2$, *J*=4.7Hz), 3.87-3.89 (t, 4H, O(CH_2)$_2$, *J*=4.8Hz), 6.93-6.95 (d, 1H, H_2, *J*=8.9Hz); 7.08-7.78 (m, 9H, H_{arom}); 8.00-8.02 (d, 1H, H_3, *J*=8.9Hz); ^{13}C NMR (δ ppm): 47.5 N(CH_2), 66.5 O(CH_2), 121.6 C-2, 141.9 C-3, 113.4, 115.8, 130.1,131.5 –C_{arom}, 128.8, 130.6, 154.1, 162.5 *ipso*-C, 187.8 C-1.

(E)- 3-(4-bromophenyl)-1-(4-morpholinophenyl)prop-2-en-1-one (16)

Reaction time: 2 h; IR (KBr) ν (cm^{-1}): 3001, 2960, 2923, 2845, 1657, 1612, 1227; ^{1}H NMR (δ ppm): 3.32-3.35 (t, 4H, N(CH_2)$_2$, *J*=4.5Hz), 3.86-3.87 (t, 4H, O(CH_2)$_2$, *J*=4.6Hz), 6.94-6.96 (d, 1H, H_2, *J*=8.8Hz); 7.18-7.82 (m, 9H, H_{arom}); 8.01-8.03 (d, 1H, H_3, *J*=8.6Hz); ^{13}C NMR (δ ppm): 47.9 N(CH_2), 65.6 O(CH_2), 121.8 C-2, 142.3 C-3, 113.8, 115.1, 130.7,131.7 –C_{arom}, 128.5, 131.2, 154.7, 162.7 *ipso*-C, 188.8 C-1.

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(E)-1-(4-morpholinophenyl)-3-(3-nitrophenyl)prop-2-en-1-one (17)

Reaction time: 6 h; IR (KBr) ν (cm^{-1}): 3087, 2966, 2923, 2862, 1651, 1608, 1224; ^{1}H NMR (δ ppm): 3.36-3.38 (t, 4H, $N(CH_2)_2$, *J*=4.5Hz), 3.88-3.90 (t, 4H, $O(CH_2)_2$, *J*=4.6Hz), 6.95-6.97 (d, 1H, H_2, *J*=8.9Hz); 7.27-7.91 & 8.23-8.25 (m, 9H, H_{arom}); 8.03-8.05 (d, 1H, H_3, *J*=8.9Hz); ^{13}C NMR (δ ppm): 47.3 $N(CH_2)$, 66.9 $O(CH_2)$, 122.0 C-2, 140.1 C-3, 113.3, 124.2-134.2 $–C_{arom}$, 128.9, 137.1, 148.7, 154.3 *ipso*-C, 187.8 C-1.

(E)-1-(4-morpholinophenyl)-3-(3-chlorophenyl)prop-2-en-1-one (18)

Reaction time: 6 h; IR (KBr) ν (cm^{-1}): 3093, 2969, 2928, 2857, 1593, 1652, 1212, 830; ^{1}H NMR (δ ppm): 3.33-3.36 (t, 4H, $N(CH_2)_2$, *J*=4.6Hz), 3.89-3.91 (t, 4H, $O(CH_2)_2$, *J*=4.6Hz), 6.96-6.98 (d, 1H, H_2, *J*=8.9Hz); 7.33-7.81 (m, 9H, H_{arom}); 7.98-8.00 (d, 1H, H_3, *J*=8.7Hz); ^{13}C NMR (δ ppm): 47.8 $N(CH_2)$, 66.4 $O(CH_2)$, 121.2 C-2, 141.6 C-3, 113.3, 128.8-130.1 $–C_{arom}$, 129.3,133.7,145.2,154.1 *ipso*-C, 192.3 C-1.

(E)-1-(4-morpholinophenyl)-3-(3-fluorophenyl)prop-2-en-1-one (19)

Reaction time: 5 h; IR (KBr) ν (cm^{-1}): 3018, 2974, 2924, 2843, 1649, 1605, 1226; ^{1}H NMR (δ ppm): 3.33-3.36 (t, 4H, $N(CH_2)_2$, *J*=4.8Hz), 3.86-3.88 (t, 4H, $O(CH_2)_2$, *J*=4.7Hz), 6.92-6.94 (d, 1H, H_2, *J*=8.8Hz); 7.18-7.68 (m, 9H, H_{arom}); 7.92-7.94 (d, 1H, H_3, *J*=8.7Hz); ^{13}C NMR (δ ppm): 47.5 $N(CH_2)$, 66.6 $O(CH_2)$, 121.3 C-2, 141.8 C-3, 113.4, 125.3-130.1 $–C_{arom}$, 128.6, 130.5, 154.3, 162.7 *ipso*-C, 187.5 C-1.

General method for the synthesis of 4-(4-morpholinophenyl)-6-aryl-pyrimidin-2-amines (20-28)

A mixture of (*E*)-1-(4-morpholinophenyl)-3-aryl-prop-2-en-1-ones **(11-19)** (0.001 mol) and guanidine nitrate (0.001 mol) in ethanol (50 ml) was refluxed, while a solution of lithium hydroxide (0.005 mol) in water (10 ml) was added portion wise for 1 h. Re-fluxing was continued for further 4 h and the mixture was poured into ice cold water. The formed solid was separated by filtration, and purified by column chromatography using silica gel (100-200 mesh), with ethyl acetate -Petroleum ether (bp40-60) in the ratio (2:8) as eluent.

4-(4-morpholinophenyl)-6-phenylpyrimidin-2-amine (20) IR (KBr) (cm^{-1}): 3355, 3459, 3060, 2961, 2920, 1661, 1599, 1229, 928, 824, 776, 697, 634; ^{1}H NMR (δ ppm): 3.33-3.38 (t, 4H, $N(CH_2)_2$, *J*=4.7Hz), 3.88-3.89 (t, 4H, $O(CH_2)_2$, *J*=4.8Hz), 5.23 (s, 2H, NH_2), 7.38-7.85 (m, 10H, H_{arom}), the signal for H-5 proton may be merged with the aromatic protons; ^{13}C NMR (δ ppm): 46.3 $N(CH_2)$, 67.3 $O(CH_2)$, 103.4 C-5, 163.8 C-2, 164.7 C-6, 165.0 C-4, 127.0-131.5 $–C_{arom}$, 142.1, 153.9, *ipso*-C.

4-(4-morpholinophenyl)-6-p-tolylpyrimidin-2-amine (21) IR (KBr) (cm^{-1}): 3432, 3200, 2967, 2923, 1625, 1599, 1229, 928, 815, 645; ^{1}H NMR (δ ppm): 2.31 (s, 3H, CH_3), 3.34-3.38 (t, 4H, $N(CH_2)_2$, *J*=4.8Hz), 3.86-3.89 (t, 4H, $O(CH_2)_2$, *J*=4.8Hz), 5.25 (s, 2H, NH_2), 7.20-8.12 (m, 9H, H_{arom}), the signal for H-5 proton may be merged with the aromatic protons; ^{13}C NMR (δ ppm): 25.4 CH_3, 46.7 $N(CH_2)$, 67.5 $O(CH_2)$, 104.1 C-5, 163.8 C-2, 164.1 C-6, 164.3 C-4, 126.0-131.4 $–C_{arom}$, 143.8, 152.4, *ipso*-C.

4-(4-chlorophenyl)-6-(4-morpholinophenyl)pyrimidin-2-amine (22) IR (KBr) (cm^{-1}): 3396, 3217, 3027, 2962, 2920, 1656, 1229, 930, 819, 684; ^{1}H NMR (δ ppm): 3.35-3.39 (t, 4H, $N(CH_2)_2$, *J*=4.7Hz), 3.89-3.91 (t, 4H, $O(CH_2)_2$, *J*=4.7Hz), 5.28 (s, 2H, NH_2), 7.26-7.85 (m, 9H, H_{arom}), the signal for H-5 proton may be merged with the aromatic protons; ^{13}C NMR (δ ppm): 47.6 $N(CH_2)$, 66.5 $O(CH_2)$, 104.5 C-5, 163.8 C-2, 164.1 C-6, 164.7 C-4, 127.0-139.1 $–C_{arom}$, 141.5, 152.5, *ipso*-C.

4-(4-methoxyphenyl)-6-(4-morpholinophenyl)pyrimidin-2-amine (23) IR (KBr) (cm^{-1}): 3447, 3200, 2972, 2922, 1659, 1600, 1243, 929, 821, 607; ^{1}H NMR (δ ppm): 3.32-3.35 (t, 4H, $N(CH_2)_2$, *J*=4.6Hz), 3.86 (s, 3H, OCH_3), 3.87-3.90 (t, 4H, $O(CH_2)_2$, *J*=4.8Hz), 5.26 (s, 2H, NH_2), 7.18-7.82 (m, 9H, H_{arom}), the signal for H-5 proton may be merged with the aromatic protons; ^{13}C NMR (δ ppm): 46.7 $N(CH_2)$, 55.0 OCH_3, 67.3 $O(CH_2)$, 103.9 C-5, 163.7 C-2, 164.7 C-6, 165.0 C-4, 127.5-142.1 $–C_{arom}$, 153.8, 154.2 *ipso*-C.

4-(4-fluorophenyl)-6-(4-morpholinophenyl)pyrimidin-2-amine (24) IR (KBr) (cm^{-1}): 3434, 3200, 2967, 2923, 1624, 1599, 1226, 928, 815, 645; ^{1}H NMR (δ ppm): 3.34-3.36 (t, 4H, $N(CH_2)_2$, *J*=4.7Hz), 3.87-3.88 (t, 4H, $O(CH_2)_2$, *J*=4.8Hz), 5.29 (s, 2H, NH_2), 7.30-8.03 (m, 9H, H_{arom}), the signal for H-5 proton may be merged with the aromatic protons; ^{13}C NMR (δ ppm): 46.6 $N(CH_2)$, 67.3 $O(CH_2)$, 103.5 C-5, 163.8 C-2, 164.2 C-6, 164.4 C-4, 126.5-140.0 $–C_{arom}$, 140.6, 154.0 *ipso*-C.

4-(4-bromophenyl)-6-(4-morpholinophenyl)pyrimidin-2-amine (25) IR (KBr) (cm^{-1}): 3398, 3219, 3029, 2965, 2922, 1659, 1231, 934, 821, 687; ^{1}H NMR (δ ppm): 3.36-3.39 (t, 4H, $N(CH_2)_2$, *J*=4.8Hz), 3.87-3.91 (t, 4H, $O(CH_2)_2$, *J*=4.8Hz), 5.29 (s, 2H, NH_2), 7.29-7.87 (m, 9H, H_{arom}), the signal for H-5 proton may be merged with the aromatic protons; ^{13}C NMR (δ ppm): 47.8 $N(CH_2)$, 66.6 $O(CH_2)$, 104.8 C-5, 163.9 C-2, 164.3 C-6, 164.8 C-4, 127.5-139.7 $–C_{arom}$, 152.6, 141.6 *ipso*-C.

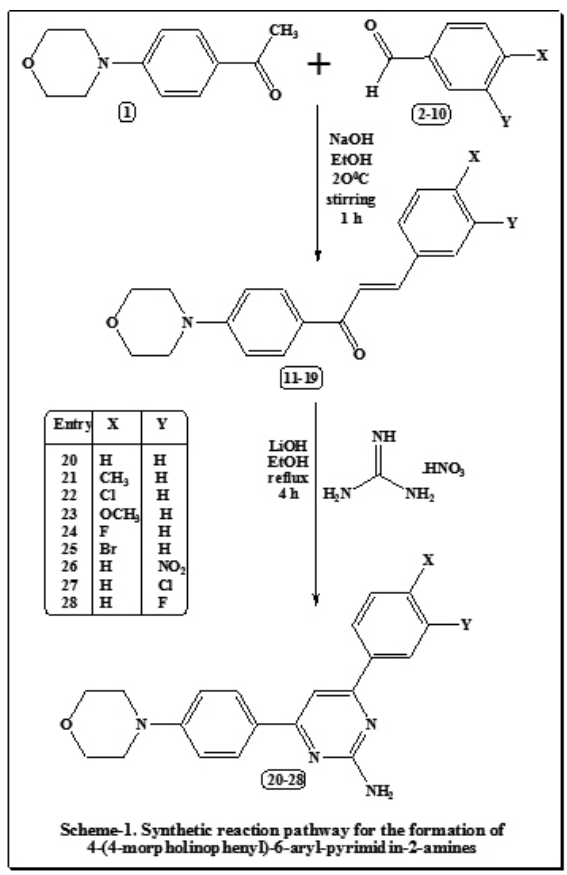
4-(4-morpholinophenyl)-6-(3-nitrophenyl)pyrimidin-2-amine (26) IR (KBr) (cm^{-1}): 3400, 3200, 3060, 2961, 2920, 1661, 1566, 1229, 928, 824, 776, 697; ^{1}H NMR (δ ppm): 3.36-3.39 (t, 4H, $N(CH_2)_2$, *J*=4.6Hz), 3.88-3.92 (t, 4H, $O(CH_2)_2$, *J*=4.6Hz), 5.28 (s, 2H, NH_2), 7.27-8.28 (m, 9H, H_{arom}), the signal for H-5 proton may be merged with the aromatic protons; ^{13}C NMR (δ ppm): 47.3 $N(CH_2)$, 67.6 $O(CH_2)$, 104.4 C-5, 163.8 C-2, 164.2 C-6, 164.4 C-4, 125.2-131.5 $–C_{arom}$, 146.7, 153.9 *ipso*-C.

4-(3-chlorophenyl)-6-(4-morpholinophenyl)pyrimidin-2-amine (27) IR (KBr) (cm^{-1}): 3398, 3219, 3028, 2963, 2923, 1655, 1228, 929, 817, 686; ^{1}H NMR (δ ppm): 3.36-3.38 (t, 4H, $N(CH_2)_2$, *J*=4.6Hz), 3.88-3.90 (t, 4H, $O(CH_2)_2$, *J*=4.7Hz), 5.29 (s, 2H, NH_2), 7.16-7.74 (m, 9H, H_{arom}), the signal for H-5 proton may be merged with the aromatic protons; ^{13}C NMR (δ ppm): 47.7 $N(CH_2)$, 66.6 $O(CH_2)$, 104.4 C-5, 163.6 C-2, 164.3 C-6, 164.8 C-4, 126.2-138.8 $–C_{arom}$, 146.5, 152.3, *ipso*-C.

4-(3-fluorophenyl)-6-(4-morpholinophenyl)pyrimidin-2-amine (28) IR (KBr) (cm^{-1}): 3437, 3204, 2965, 2928, 1623, 1597, 1225, 921, 811, 649; ^{1}H NMR (δ ppm): 3.33-3.35 (t, 4H, $N(CH_2)_2$, *J*=4.7Hz), 3.87-3.88 (t, 4H, $O(CH_2)_2$, *J*=4.8Hz), 5.27 (s, 2H, NH_2), 7.28-8.05 (m, 9H, H_{arom}), the signal for H-5 proton may be merged with the aromatic protons; ^{13}C NMR (δ ppm): 46.8 $N(CH_2)$, 67.4 $O(CH_2)$, 103.7 C-5, 163.9 C-2, 164.4 C-6, 164.5 C-4, 125.9-140.3 $–C_{arom}$, 146.6, 154.2 *ipso*-C.

RESULTS AND DISCUSSION

(E)-1-(4-morpholinophenyl)-3-aryl-prop-2-en-1-ones **(11-19)** are synthesized by the condensation of commercially available 1-(4-morpholinophenyl) ethanone and substituted benzaldehyde in the presence of sodium hydroxide in ethanol at 20^{0}C for 1 h. Treatment of compounds **(11-19)** with guanidine nitrate in the presence of lithium hydroxide in refluxing ethanol for 4 h yields the respective 4-(4-morpholinophenyl)-6-aryl-pyrimidin-2-amines **(20-28)**. The schematic representation and the analytical data of compounds **(20-28)** are given in **Scheme-1** and **Table-1**, respectively. The importance of the title compounds is due to their potential broad-spectrum microbial activity [17]. The structure of the newly synthesized compounds **(20-28)** is confirmed by melting point, elemental analysis, MS, FT-IR, one-dimensional NMR (^{1}H & ^{13}C) spectroscopic data.



Scheme-1. Synthetic reaction pathway for the formation of 4-(4-morpholinophenyl)-6-aryl-pyrimidin-2-amines

Table 1. Physical and analytical data of (E)-1-4-morpholinophenyl)-3-aryl-prop-2-en-1-ones **(11-19)** and 4-(4-morpholinophenyl)-6-arylpyrimidin-2-amines **(20-28).**

Entry				m.p° C	Elemental analysis (%)			m/z
	X	Y	Yield (%)		C Found (calculated)	H Found (calculated)	N Found (calculated)	$(M+1)^{+\cdot}$
11	H	H	95	149	77.78 (77.81)	6.46 (6.48)	4.76 (4.77)	294 $C_{19}H_{19}NO_2$
12	CH_3	H	92	179	78.15 (78.17)	6.81 (6.84)	4.54 (4.56)	308 $C_{20}H_{21}NO_2$
13	Cl	H	90	143	69.70 (69.72)	5.47 (5.50)	4.26 (4.28)	328 $C_{19}H_{18}NO_2Cl$
14	OCH_3	H	90	111	74.29 (74.30)	6.48 (6.50)	4.31 (4.33)	324 $C_{20}H_{21}NO_3$
15	F	H	95	160	73.29 (73.31)	5.76 (5.78)	4.48 (4.50)	312 $C_{19}H_{18}NO_2F$
16	Br	H	85	145	61.27 (61.30)	4.83 (4.87)	3.74 (3.76)	372 $C_{19}H_{18}BrNO_2$
17	H	NO_2	87	135	67.43 (67.45)	5.29 (5.32)	8.26 (8.28)	339 $C_{19}H_{18}N_2O_4$
18	H	Cl	90	138	69.69 (69.72)	5.48 (5.50)	4.25 (4.28)	328 $C_{19}H_{18}NO_2Cl$
19	H	F	90	154	73.28 (73.31)	5.74 (5.78)	4.47 (4.50)	312 $C_{19}H_{18}NO_2F$
20	H	H	80	118	72.05 (72.09)	6.28 (6.30)	16.77 (16.80)	333 $C_{20}H_{21}N_4O$
21	CH_3	H	85	73	72.61 (72.64)	6.59 (6.62)	16.10 (16.12)	347 $C_{21}H_{23}N_4O$
22	Cl	H	78	123	65.31 (65.33)	5.41 (5.44)	15.20 (15.23)	367 $C_{20}H_{20}N_4OCl$
23	OCH_3	H	80	91	69.41 (69.44)	6.31 (6.33)	15.38 (15.41)	363 $C_{21}H_{23}N_4O_2$
24	F	H	90	87	68.38 (68.40)	5.66 (5.69)	15.91 (15.94)	351 $C_{20}H_{20}N_4OF$
25	Br	H	90	93	58.36 (58.40)	4.64 (4.66)	13.59 (13.62)	411 $C_{20}H_{19}BrN_4O$
26	H	NO_2	85	176	65.92 (65.96)	5.47 (5.49)	15.35 (15.38)	364 $C_{20}H_{20}N_5O_3$
27	H	Cl	80	135	65.30 (65.33)	5.42 (5.44)	15.20 (15.23)	367 $C_{20}H_{20}N_4OCl$
28	H	F	78	96	68.37 (68.40)	5.68 (5.69)	15.92 (15.94)	351 $C_{20}H_{20}N_4OF$

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