A Facile Microwave-Assisted "One-Pot" Synthesis of Piperazino Pyrimidinyl Acetamides, a Class of Hybrid Bis Heterocycles and Their Structural Elucidation Using NMR Spectral Techniques

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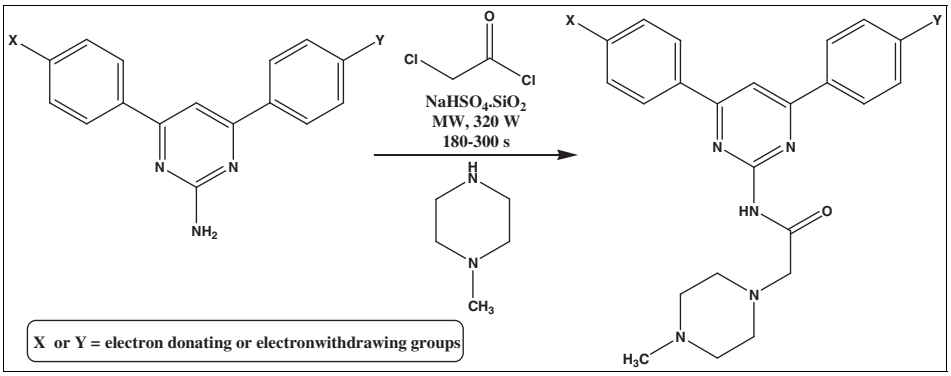

An array of novel piperazino pyrimidinyl acetamides, a class of hybrid bis heterocycles are synthesized in "*one-pot*" by microwave irradiation method catalyzed by heterogeneous $NaHSO_4.SiO_2$ catalyst in dry media and are characterized by melting point, elemental analysis, MS, FT-IR, one-dimensional NMR (^1H and ^{13}C) and two-dimensional ^1H-^1H COSY and ^1H-^{13}C HSQC spectral data.

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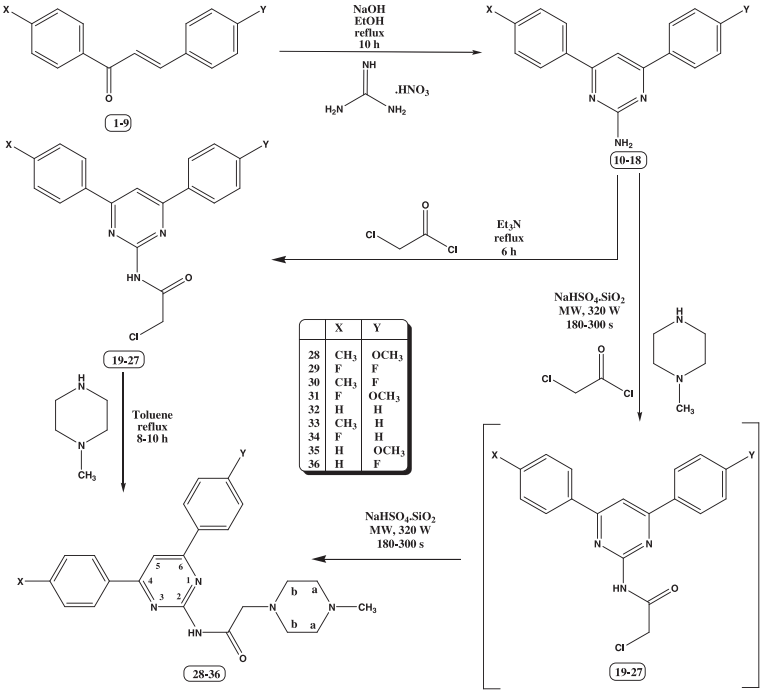
INTRODUCTION

In recent decades, green chemistry has become a major driving force for organic chemists to develop environmentally benign synthetic routes to a variety of compounds [1]. For example, the possibility of performing multicomponent reactions under solvent-free conditions to enhance the reaction efficiency from both economic and ecological points of view have given to this kind of procedures a remarkable synthetic value and received a great attention. The huge interest for such multicomponent reactions during the last years have been oriented toward developing combinatorial chemistry procedures, because of their high efficiency and convenience of these reactions in comparison with multistage procedures [2–5].

Molecules with pyrimidine nucleus were of great interest due to their presence in a wide variety of drugs and biological activities [6–11]. The biological significance of *N*-methylpiperazine nucleus has led us to the synthesis of substituted piperazine derivatives [12–15]. Substituted piperazines, key intermediates in the synthesis of quinolone type antibacterial drugs were used in the synthesis of norfloxacin, ciprofloxacin, norfloxacin, ofloxacin, amifloxacin, fleroxacin, and difloxacin [16]. Furthermore, acetamide derivatives may serve as simple peptide models and they were well known for their curative values since the amide group is an important pharmacophore. Antibiotics such as penicillins and cephalosporins have an amide group.

Silica gel-supported sodium hydrogen sulfate ($NaHSO_4.SiO_2$), a nontoxic and inexpensive catalyst, have been used for one-pot conversion of ketones to amides, [17] synthesis of imines, [18] one-pot synthesis of 1,2,3-selenadiazoles [19], 1,2,4-triazolidin-3-thiones [20], Knoevenagel condensation [21], and morpholino pyrimidinyl acetamides [22]. ^1H NMR and ^{13}C NMR spectral techniques was a versatile tool for the structural elucidation of most of the organic compounds [23–25]. Recently, we have reported quite a few pyrimidine derivatives namely 2-morpholino-*N*-(4,6-diarylpyrimidin-2-yl)acetamides;4-(4-morpholinophenyl)-6-arylpyrimidin-2-amines; 2-phenyl-3-(4,6-diarylpyrimidin-2-yl)thiazolidin-4-ones as potent antibacterial and antifungal agents [26–29]. Moreover, 3-(4′-(4″-fluorophenyl)-6′-phenylpyrimidin-2′-yl)-2-phenylthiazolidin-4-one was used as *in vivo* modulation of

Scheme 1. Reuse studies of heterogeneous $NaHSO_4.SiO_2$ catalyst for the synthesis of **28**, **30**, and **34** under microwave irradiation.



biomarkers of chemoprevention in the 7,12-dimethylbenz[a] anthracene (DMBA) induced hamster buccal pouch carcinogenesis [30]. These biological activities are highly desirable and have been the goal of our current research program [30–33]. These observations prompted us to extend our research in this area to synthesize this biologically active new series of hybrid pyrimidine based novel bis heterocyclic derivatives with the hope to develop some promising antimicrobial and anticancer agents and the work are all under progress. Owing to our interest on the spectral and biological studies of structurally diverse heterocycles, herein we report the "one-pot" synthesis of novel piperazino pyrimidinyl acetamides, a class of hybrid bis heterocycles catalyzed by $NaHSO_4.SiO_2$ under microwave irradiation and their structural elucidation were carried out using various spectral assignments.

RESULTS AND DISCUSSION

The conventional approach for the synthesis of 2-(4-methylpiperazin-1-yl)-*N*-(4,6-diarylpyrimidin-2-yl)acetamides 28-36 was as follows: *E*-1,3-diarylprop-2-en-1-ones 1-9 were synthesized by the Claisen-Schmidt condensation of equimolar quantities of appropriate acetophenone and appropriate benzaldehyde in the presence of sodium hydroxide. Treatment of 1-9 with guanidine nitrate in the presence

Table 1

Physical and analytical data of **28–36**.

Compounds	X	Y	Reaction time Δ (h)/ MW (s)	Yield (%) Δ/MW	m.p. (°C)	Elemental analysis (%) C found (calculated)	H found (calculated)	N found (calculated)	*m/z* $(M+H)^{+\cdot}$ molecular formula
28	CH_3	OCH_3	8/240	60/92	62	69.51 (69.58)	6.69 (6.77)	16.14 (16.23)	432; $C_{25}H_{29}N_5O_2$
29	F	F	8/180	48/85	71	65.16 (65.24)	5.41 (5.47)	16.48 (16.54)	424; $C_{23}H_{23}F_2N_5O$
30	CH_3	F	9/240	52/80	81	68.66 (68.72)	6.14 (6.25)	16.61 (16.69)	420; $C_{24}H_{26}FN_5O$
31	F	OCH_3	8/240	56/88	60	66.11 (66.19)	5.96 (6.02)	15.98 (16.08)	436; $C_{24}H_{26}FN_5O_2$
32	H	H	10/300	48/86	80	71.19 (71.29)	6.38 (6.50)	17.95 (18.07)	388; $C_{23}H_{25}N_5O$
33	CH_3	H	9/240	52/81	68	71.76 (71.79)	6.66 (6.78)	17.31 (17.44)	402; $C_{24}H_{27}N_5O$
34	F	H	8/180	56/90	50	68.06 (68.13)	5.88 (5.97)	17.18 (17.27)	406; $C_{23}H_{24}FN_5O$
35	H	OCH_3	10/300	54/82	53	69.00 (69.04)	6.48 (6.52)	16.68 (16.77)	418; $C_{24}H_{27}N_5O_2$
36	H	F	8/180	46/88	76	68.08 (68.13)	5.84 (5.97)	17.22 (17.27)	406; $C_{23}H_{24}FN_5O$

Table 2

FT-IR absorption frequencies (cm^{-1}) for selected functional groups of compounds **28–36**.

Compounds	Amide NH stretching	Aromatic CH stretching	Aliphatic CH stretching	Amide C═O stretching	C═C stretching	C—N stretching	Aromatic ring stretching
28	3323	3199, 3066, 2998	2956, 2919, 2849	1676	1574	1362, 1251	813, 768, 679
29	3332	3207, 3069	2952, 2919, 2850	1664	1540	1362, 1227	827, 772, 642
30	3329	3196, 3063	2919, 2850	1680	1573	1360, 1226	815, 768, 664
31	3322	3198, 3066	2959, 2919	1676	1573	1362, 1254	821, 747, 672
32	3315	3191, 3057	2918, 2851	1676	1557	1359, 1227	807, 760, 692
33	3318	3193, 3059, 3028	2919, 2850	1680	1569	1360, 1231	813, 770, 694
34	3321	3196, 3061	2963, 2919	1672	1573	1360, 1228	806, 770, 695
35	3325	3199, 3058	2959, 2849	1687	1569	1361, 1256	804, 771, 692
36	3340	3196, 3061	2959, 2919, 2850	1682	1601	1361, 1225	819, 769, 693

of ethanolic sodium hydroxide yielded 2-amino-4,6-diarylpyrimidines 10-18. Compounds 10-18 were converted to respective 2-chloro-N-(4,6-diarylpyrimidin-2-yl)acetamides 19-27 using triethyl amine as catalyst and toluene as solvent. Further reaction of 19-27 with *N*-methylpiperazine in the presence of triethyl amine as catalyst and hazardous toluene as solvent yielded the target molecules 28-36. There were some problems associated with above synthesis, such as severe conditions, very low yields for the reaction, difficulty in separating the products from the system and longer reaction times. In the present "one-pot" procedure, treatment of various substituted 0.005 mol of 2-amino-4,6-diarylpyrimidines 10-18 were treated with 0.005 mol of chloro acetyl chloride along with a catalytic amount of $NaHSO_4.SiO_2$ (20 mg) and irradiated in a microwave oven for 60 s, followed by the addition of 0.005 mol of *N*-methylpiperazine and then irradiated to afford the corresponding 2-(4-methylpiperazin-1-yl)-*N*-(4,6-diarylpyrimidin-2-yl)acetamides 28-36 (Scheme 1 and Table 1) in high yields in dry media under MW irradiation. The reaction was monitored by using TLC method. $NaHSO_4.SiO_2$ catalyst was shown to be one of the most efficient MW absorber with a very high specificity to MW heating. It was able to reach a temperature of 110°C after 3 min of irradiation in a domestic oven (320 W). Mere 20 mg of $NaHSO_4.SiO_2$ catalyst to 0.005 moles of substrates was the most acceptable ratio in terms of efficiency and safety; a power level of 320 W was the most suitable one. The structures of all the newly synthesized compounds 28-36 were discussed with the help of m.p.s, elemental analysis, FT-IR, MS, ^1H, ^{13}C, ^1H-^1H COSY, and ^1H-^{13}C HSQC spectral data.

To determine the structure of the synthesized compounds, *N*-(4-(4-methylphenyl)-6-(4-methoxyphenyl)pyrimidin-2-yl)-2-(4-methylpiperazin-1-yl)acetamide 28 was taken as the model compound. FT-IR spectrum of 28 showed characteristic absorption frequency (Table 2) observed at 3323 cm^{-1} was due to N—H stretching vibration of the amide group. The absorption frequencies at 3199, 3066, and 2998 cm^{-1} were assigned to aromatic C—H stretching vibration. The absorption frequencies at 2956, 2919, and 2849 cm^{-1} were assigned to aliphatic C—H stretching vibration. The band at 1676 cm^{-1} was due to the presence of amide C═O stretching frequency. The absorption bands at 1362, 1251 cm^{-1} were consistent with C—N stretching vibration. The absorption band at 1574 cm^{-1} was due to C═C stretching vibration. In addition, compound 28 displayed characteristic absorption bands (cm^{-1}) at 813, 768, and 679 cm^{-1} were due to aromatic ring stretching; this gives positive evidence for the formation of compound 28. Mass spectrum of compound 28

Table 3

Proton NMR chemical shifts (δ, ppm) of compounds **28–36**.

	Piperazine moiety		Acetamide moiety		Pyrimidine moiety		
Compounds	N—CH_3 (singlet)	Methylene H_a and H_b (broad signal)	CH_2 (singlet)	NH (broad singlet)	H-5 (singlet)	Ar-protons (multiplet)	Others (singlet)
28	2.19	2.97	3.85	10.11	6.58	7.11–8.33	2.36 CH_3, 3.82 OCH_3
29	2.21	2.99	3.82	10.21	6.63	7.17–8.44	–
30	2.27	3.01	3.81	10.94	6.69	7.15–8.29	2.37 CH_3
31	2.20	3.02	3.85	10.89	6.63	7.10–8.42	3.85 OCH_3
32	2.19	2.99	3.85	10.15	6.62	7.49–8.34	–
33	2.28	3.07	3.83	10.93	6.67	7.26–8.34	2.37 CH_3
34	2.26	3.06	3.85	10.98	6.61	7.25–8.44	–
35	2.07	2.98	3.86	10.13	6.72	7.43–8.22	3.83 OCH_3
36	2.17	2.93	3.84	10.16	6.72	7.28–8.32	–

Table 4
Carbon NMR chemical shifts (δ, ppm) of compounds **28–36**.

Compounds	Piperazine moiety			Acetamide moiety		Pyrimidine moiety						
	N—CH_3	Methylene C-a	Methylene C-b	vCH_2	C=O	C-2	C-4	C-5	C-6	Aromatic Carbons	*Ipso* carbons	Others
28	45.43	60.15	52.22	66.88	170.19	163.84	164.25	100.68	164.42	113.56–131.17	133.55, 134.66, 140.02, 157.49	20.90 CH_3, 55.28 OCH_3
29	45.66	59.31	52.53	66.46	170.62	163.78	165.12	101.37	165.44	114.15–130.38	131.45, 133.70, 162.35, 162.48	–
30	44.64	59.15	52.42	66.87	168.51	163.55	163.87	101.24	164.81	115.30–129.88	133.82, 134.44, 140.22, 162.32	20.90 CH_3
31	45.29	60.07	53.08	65.98	169.88	163.71	164.24	101.76	164.48	113.88–128.48	129.10, 129.74, 157.51, 161.88	55.40 OCH_3
32	44.84	59.68	52.98	66.92	171.81	163.98	163.98	101.81	164.84	126.92–130.36	137.32	–
33	44.70	60.46	52.49	65.32	169.28	163.93	164.69	101.46	165.06	126.86–130.30	137.37, 140.16, 141.28	20.97 CH_3
34	45.15	59.92	52.48	66.13	170.10	164.10	165.29	101.49	165.29	115.70–132.62	136.07, 137.25, 157.62	–
35	45.61	60.20	52.25	66.38	169.75	163.87	164.52	101.03	164.76	113.90–131.03	132.32, 137.45, 161.85	55.25 OCH_3
36	45.47	59.29	51.65	65.92	170.56	163.93	164.42	101.60	164.92	114.71–133.32	136.55, 137.27, 157.58	–

showed molecular ion peak at *m/z* 432 ($M^{+\bullet}$+1) which was consistent with the proposed molecular formula of 28. Elemental analysis have been carried out for the representative compound 28, C_{cal} 69.58, C_{obs} 69.51; H_{cal} 6.77, H_{obs} 6.69; N_{cal} 16.23, N_{obs} 16.14 were consistent with the proposed molecular formula ($C_{25}H_{29}N_5O_2$) of 28.

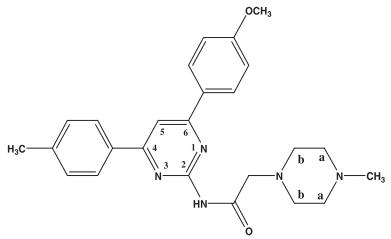
The assignments of ^{1}H NMR signals of 28 have been done based on total widths and spin multiplicities. A singlet observed at 3.85 ppm for two protons was assigned to methylene protons of acetamide moiety (Table 3). The amide proton resonated at 10.11 ppm. An intense unresolved broad signal and a very sharp singlet in the aliphatic region 2.97 and 2.19 ppm with eight and three protons integral, respectively were observed. These signals were due to ring methylene protons of *N*-methylpiperazine and methyl protons of *N*-methyl piperazine moiety, respectively. The H-5 proton of pyrimidine moiety was observed as a singlet at 6.58 ppm. The aromatic protons resonated in the region 7.11–8.33 ppm. Besides these signals, two singlets observed at 2.36 and 3.82 ppm each corresponding to three protons were due to methyl and methoxy protons attached to *para* position of phenyl rings at positions 4 and 6 of pyrimidine moiety.

Among various ^{13}C carbon resonances, (Table 4) the amide carbonyl carbon of 28 resonated at 170.19 ppm. The methylene carbon attached to amide carbonyl carbon resonated at 66.88 ppm. The ^{13}C resonance at 163.84 ppm was assigned to the amide group bearing carbon C-2 of pyrimidine moiety. The ^{13}C resonance observed at 164.25/164.42 and 100.68 ppm was due to the C-4/6 and C-5 carbons of pyrimidine moiety, respectively. There were two ^{13}C resonances observed at 60.15 and 52.22 ppm for the methylene carbons of piperazine moiety viz., C-a and C-b unlike their corresponding protons. The upfield signal was assigned to C-b carbons while the downfield signal to C-a carbons because the former carbons were present at γ-position with respect to the amide carbonyl group thereby experiencing its electronic effect. The methyl carbon of *N*-methyl piperazine moiety resonated at 45.43 ppm. The remaining ^{13}C signals at 133.55, 134.66, 140.02, 157.49 ppm were due to *ipso* carbons. The aromatic carbons were observed at 113.55–131.17 ppm. Moreover, two carbon resonances observed at 20.90 and 55.28 ppm were due to methyl and methoxy carbons attached to *para* position of phenyl rings at positions 4 and 6 of pyrimidine moiety. All the above mentioned assignments were further confirmed by ^{1}H-^{1}H COSY and ^{1}H-^{13}C HSQC spectra.

In the ^{1}H-^{1}H COSY spectrum of 28, the proton signal at 2.97 ppm showed cross peak with the signal at 2.97 ppm and *vice-versa* (Table 5). This mutual correlation clearly revealed that these two signals were due to methylene protons H_a and H_b of piperazine ring, respectively. As the nitrogen of piperazine moiety was having almost similar chemical environment on either side, its ring methylene

Table 5

5^1H-^{1}H COSY correlations for **28**.



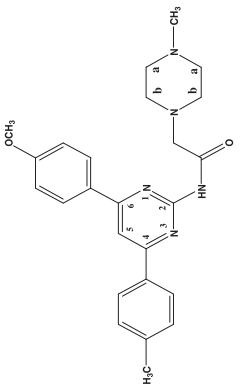
			Piperazine moiety			Acetamide moiety	Pyrimidine moiety				
			N—CH_3	Methylene H_a	Methylene H_b	CH_2	NH	H-5	Ar-CH_3	Ar-OCH_3	Aromatic protons
		ppm	2.19	2.97	2.97	3.85	10.11	6.58	2.36	3.82	7.11–8.33
		Protons									
Piperazine moiety	N—CH_3	2.19									
	Methylene H_a	2.97			coupled						
	Methylene H_b	2.97		coupled							
Acetamide moiety	CH_2	3.85									
Pyrimidine moiety	NH	10.11									
	H-5	6.58									
	Ar-CH_3	2.36									
	Ar-OCH_3	3.82									
	Aromatic protons	7.11–8.33									coupled

protons become equivalent and therefore the signal was assigned to ring methylene protons of *N*-methyl piperazine moiety. Moreover, irrespective of the restricted rotation of the N—CO bond, the rotation about N—C bond of the piperazinoacetyl moiety was very fast and prevents the spin-spin coupling of all the methylene protons of piperazine moiety. Owing to this, their resonances were observed as an intense unresolved broad signal. All these observations strongly confirm the nucleophilic substitution of piperazine moiety in place of chlorine. Also, the cross peaks observed around 7.11–8.33 ppm were due to aromatic protons attached to positions 4 and 6 of pyrimidine moiety.

It is seen that the proton signal at 10.11ppm has no HSQC correlation (Table 6) with any carbon signal. Thus, it was obvious that this signal was due to NH proton attached to pyrimidine moiety. Also the carbon signals at 170.19, 163.84, 164.25, and 164.42 ppm show no correlations with any proton signals. Obviously, these signals were due to different carbons namely amide carbonyl, C-2, C-4, and C-6 of pyrimidine moiety, respectively. The ^{13}C resonance observed at 133.55, 134.66, 140.02, 157.49 ppm also did not show any correlation with proton signals and were due to *ipso* carbons. A singlet at 2.19 ppm showed cross peaks with the ^{13}C signal at 45.43 ppm. Hence the singlet at 2.19 ppm should be due to the *N*-methyl protons and the carbon resonance observed at 45.43 ppm was due to *N*-methyl carbons of piperazine moiety. The ^{13}C signals observed at 60.15 and 52.22 ppm correlated with the broad signal at 2.97 ppm, which were due to the H_a and H_b protons of piperazine ring methyl protons, respectively. Obviously, the carbon signal at 66.88 ppm showed cross peak with the singlet proton signal at 3.85 ppm. From the cross peak it was observed that the carbon signal observed at 66.88 ppm and proton signal observed at 3.85 ppm were due to methylene carbon and protons of acetamide moiety, respectively. A singlet observed at 6.58 ppm showed cross peak with the ^{13}C signal at 100.68 ppm. Hence the singlet observed at 6.58 ppm should be due to H-5 proton of pyrimidine moiety and the carbon signal observed at 100.68 ppm was due to C-5 carbon of pyrimidine moiety. Besides these, two singlets observed at 2.36 and 3.82 ppm showed cross peaks with the carbon signals at 20.90 and 55.28 ppm, respectively due to ring methyl and methoxy protons and carbons, respectively. Moreover, a multiplet observed at 7.11–8.33 ppm showed correlation with carbon signals around 113.56–131.17 ppm due to aromatic protons and carbons, respectively. Therefore with reference to ^{1}H-^{1}H COSY and ^{1}H-^{13}C HSQC correlations in compound 28 the tentative assignments made for piperazine, acetamide, and pyrimidine moieties of 28 protons and carbons were confirmed. Based on ^{1}H-^{1}H COSY and ^{1}H-^{13}C HSQC correlations of 28, the ^{1}H and ^{13}C chemical shifts of 28 were assigned unambiguously.

The conversion of 10-18 into 28-36 by this method was believed to be followed *via* the 2-chloro-*N*-(4,6-diarylpyrimidin-2-yl)acetamides derivative 19-27. In the first step, 2-amino-4,6-diarylpyrimidines 10-18 were converted to their respective intermediate acetamides 19-27 and rapidly rearranged to give 28-36 in the second step. The attempt to isolate the respective intermediate acetamides 19-27 from the reaction mixture was unsuccessful. The formations of 28-36 *via* the intermediate acetamides were confirmed by the same kind of reactions carried

Table 6
6^1H-^{13}C HSQC correlations for **28.**



		ppm	Piperazine moiety N—CH_3 45.43	Piperazine moiety Methylene C_a 60.15	Piperazine moiety Methylene C_b 52.22	Acetamide moiety CH_2 66.88	Acetamide moiety C=O 170.19	Pyrimidine moiety C-5 100.68	Pyrimidine moiety Ar-CH_3 20.90	Pyrimidine moiety Ar-OCH_3 55.28	Pyrimidine moiety Ar-Carbons 113.56–131.17	Pyrimidine moiety *Ipso* carbons 133.55, 134.66, 140.02, 157.49, 163.84, 164.2 5, 164.42
Piperazine moiety	N—CH_3	2.19	Bonded									
	Methylene H_a	2.97		Bonded								
	Methylene H_b	2.97			Bonded							
Acetamide moiety	CH_2	3.85				Bonded						
Pyrimidine moiety	NH	10.11					Bonded					
	H-5	6.58						Bonded				
	Ar-CH_3	2.36							Bonded			
	Ar-OCH_3	3.82								Bonded		
	Aromatic protons	7.11–8.33									Bonded	

out using $NaHSO_4.SiO_2$ catalyst and 2-chloro-*N*-(4,6-diarylpyrimidin-2-yl)acetamides derivatives 19-27 and under microwave irradiation for 120-180 s. The products formed from the above two methods were found to be the same.

A major role was played by $NaHSO_4.SiO_2$ heterogeneous catalyst, which could be recovered and reused (Fig. 1) by simple washing with ethanol after each use and activated in an oven at 110°C for 1 h prior to use, rendering thus the process more economic and green. To perform the reuse studies of $NaHSO_4.SiO_2$ catalyst, reuse studies of catalyst were carried out for the synthesis of 28, 30, and 34 from the respective aminopyrimidine 10, 12, and 16. In total, seven successive reuse runs were possible. However, there was a decrease in the reaction yield was noted after four runs, since recycling leads to loss of efficiency of the catalyst owing to the absorption of organics. Organics on the solid surface result in the reduction of number of active centers. Organic species could be removed at higher temperature reactivating the catalyst. All these constitute a green and efficient alternative to the classical method using benzene as solvent and triethyl amine as catalyst [26].

EXPERIMENTAL

General. Performing TLC assessed the reactions and the purity of the products. All the reported melting points were taken in open capillaries and were uncorrected. BIOTAGE Initiator microwave synthesizer, Sweden a scientific microwave oven was used for the irradiation. IR spectra were recorded in KBr (pellet forms) on a Thermo Nicolet-Avatar–330 FT-IR spectrophotometer (Thermo Fisher Scientific, Waltham, MA) and note worthy absorption values (cm^{-1}) alone were listed. ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively on Bruker AMX 400 NMR spectrometer (Bruker Biospin International, Ag, Aegeristrasse, Switzerland) using *DMSO-d_6* as solvent. ^1H-^1H COSY and ^1H-^{13}C HSQC NMR spectra were recorded on Bruker DRX 500 NMR spectrometer (Bruker Biospin International, Ag, Aegeristrasse, Switzerland) using *DMSO-d_6* as solvent. The ESI +ve MS spectra were recorded on a Varian Saturn 2200 MS spectrometer (Varian, Palo Alto, US). Satisfactory microanalyses were obtained on Carlo Erba 1106 CHN analyzer (Thermo Fisher Scientific, Waltham, MA). By adopting the literature precedent 1,3-diarylprop-2-en-1-ones 1-9 [34], 2-amino-4,6-diarylpyrimidines 10-18 [26] and 2-chloro-*N*-(4,6-diarylpyrimidin-2-yl)acetamides 19-27 [26] were synthesized.

General method for the "one-pot" microwave-assisted synthesis of piperazino pyrimidinyl acetamides catalyzed by $NaHSO_4.SiO_2$ 28–36. A mixture of 4,6-diarylpyrimidin-2-amines 10-18 (0.005 mol), chloroacetyl chloride (0.005 mol) and $NaHSO_4.SiO_2$ (20 mg) was added in an alumina bath and mixed properly with the aid of glass rod (10 s) and then irradiated in a microwave oven for 60 s, and *N*-methylpiperazine (0.005 mol) was added and irradiation is continued up to 180–300 s at 320 W (monitored by TLC). After completion of the reaction, the reaction mixture was extracted with dichloromethane (3 × 5 mL). The catalyst and other solid wastes were removed by filtration. The combined organic layer

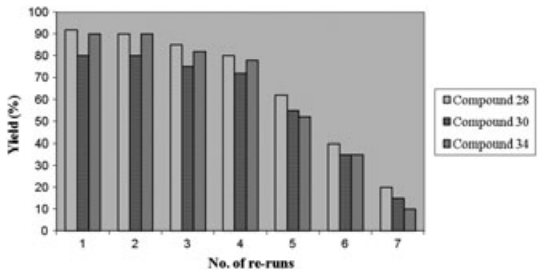


Figure 1. A facile microwave assisted synthesis of hybrid 2-(4-methylpiperazin-1-yl)-*N*-(4,6-diarylpyrimidin-2-yl)acetamides.

was washed with water three times and then dried over anhydrous $MgSO_4$. The organic layer was concentrated *in vacuo* to furnish the products, which were purified by column chromatography using silica gel (100–200 mesh), with toluene:ethyl acetate (2:8) as eluent.

CONCLUSION

In conclusion, we have developed an efficient, environmentally friendly, one-pot microwave-assisted synthesis of a new series of novel piperazino pyrimidinyl acetamides by the reaction of 4,6-diarylpyrimidin-2-amines and chloroacetyl chloride with *N*-methylpiperazine in the presence of heterogeneous $NaHSO_4.SiO_2$ catalyst under microwave irradiation in dry media. The structural elucidations of the synthesized compounds were confirmed unambiguously by elemental analysis, FT-IR, MS, ^1H, ^{13}C, ^1H-^1H COSY, and ^1H-^{13}C HSQC spectral data. The advantages of this environmentally benign and safe protocol include a simple reaction set-up, high product yields, short reaction times and the elimination of solvents.

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