Research Article

ZnO Catalyzed Efficient Synthesis of Some New 2-Substituted-4,6-diarylpyrimidines

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A simple and efficient protocol is developed for the synthesis of 2-substituted-4,6-diarylpyrimidines from one-pot three-component reaction of 4'-hydroxy-3',5'-dinitro substituted chalcones, S-benzylthiuronium chloride (SBT), and heterocyclic secondary amines (morpholine/pyrrolidine/piperidine) in the presence of 15 mol% of ZnO as a heterogeneous catalyst. The present methodology offers several advantages such as being a simple procedure as well as providing excellent yields, and short reaction time. The catalyst is inexpensive, stable, and can be easily recycled and reused for several cycles with consistent activity.

1. Introduction

Since many decades, bioactive heterocyclic compounds are one of the main topics of interest for the medicinal chemists as it displays a number of pharmacological activities. Nitrogen, sulphur, and oxygen containing five- and six-membered heterocyclic compounds have occupied enormous significance in the field of medicinal chemistry. The multicomponent reactions (MCRs) have emerged as an efficient and powerful tool in modern synthetic organic chemistry allowing the facile creation of several new bonds in a one-pot reaction. Therefore, in the last decade, research in academia and industry has increasingly emphasized the use of MCRs as well as domino reaction sequences for a broad range of products [1, 2]. Due to the atom economy, convergent character, and simplicity of one-pot procedures, multicomponent condensation reactions (MCRs) have an advantageous position among other reactions. The discovery and development of novel MCRs is receiving a growing interest from industrial chemistry research groups and represents a new challenge for organic chemists and to the basic understanding of organic chemistry itself [3].

Recently, intensive studies have been focused on the development of catalytic systems owing to their importance in synthetic organic chemistry. One of the most attractive

synthetic strategies favoured by organic chemists is the use of heterogeneous catalyst in increasing the efficiency of a wide range of organic synthesis. Heterogeneous catalysis is being used in the fine chemical industries because of the need for more environmental friendly production technology. This tendency is assisted by the availability of catalytic materials and modern techniques of creating and investigating specific active sites on catalyst surfaces [4, 5]. Metal oxides exhibit both Lewis acid and Lewis base character at their surface [6].

The basic skeleton of chalcones possesses an α , β -unsaturated carbonyl group, used as the starting material for the synthesis of variously substituted different sized heterocycles of physiological importance like antiviral [7], antimalarial [8–10], antileishmanial [11, 12], antioxidant [13], anticancer [14, 15], and antimicrobial [16]. Pyrimidines and its derivatives are known as an important class of heterocyclic compounds in the pharmaceutical industry as well as in synthetic Chemistry [17]. On the other hand, the pyrimidines unit is a privileged heterocyclic motif that forms the core of a large family of nucleic acids and natural products with strong bioactivity profiles and significant structural properties [18].

Keeping in view of diverse biological activities of pyrimidines, it was thought to construct a novel system which may combine these bioactive rings together in a single

molecular framework to see the additive effects towards their biological activities. Hence, as a part of our ongoing program to develop efficient and robust methods for the preparation of biologically relevant compounds [19], we have developed a facile and efficient catalytic approach for the multicomponent one-pot synthesis of novel 2-substituted-4,6-diarylpyrimidines (Scheme 1).

S-benzylthiuronium chloride (SBT) [20] and dicyandiamide (DDA) [21] have emerged from our laboratory team as versatile reagents for the continued synthesis of 2, 4, 6-tri substituted pyrimidines from α , β -unsaturated ketones and heterocyclic secondary amines. Consequently, facile synthesis of substituted pyrimidines was carried out using SBT, α , β -unsaturated ketones and organic bases under microwave irradiation with [22] or without [23] solvents.

To the best of our knowledge, there is no report available in the literature describing the use of ZnO as a catalyst for the synthesis of pyrimidine derivatives. ZnO is very reactive because it offers higher surface area and low coordinating sites. The surface area of the catalyst increases tremendously when size decreases and is responsible for the higher catalytic activity [24]. The effectiveness of the process was studied by comparing the results obtained with and without catalyst under normal conditions. Herein, we wish to report a novel synthesis of 4,6-diaryl-2-(4-morpholinyl/1-pyrrolidinyl/1-piperidinyl)-pyrimidines using ZnO as an efficient, nontoxic, reusable, and commercially available catalyst.

2. Results and Discussion

As a part of our ongoing research interest aimed at developing new synthetic strategies for the bioactive heterocyclic framework, the reaction of chalcones, S-benzylthiuronium chloride, and heterocyclic secondary amines was examined in the presence of catalytic amount (15 mol%) of ZnO under stirring condition at 100°C for 6 hour to give 2-substituted-4,6-diarylpyrimidine derivatives up to quantitative yields. A conceivable mechanism for the formation of the product would be as follows: the ZnO particle facilitates the Michael addition type coupling through Lewis acid sites (Zn^{2+}) coordinated to the enone functionality. On the other hand, ZnO particles can activate SBT so that deprotonation of the N-H bond occurs in the presence of Lewis basic sites (O^{2-}). As a result, the formation of 4,6-diaryl-2-benzylthiopyrimidines proceeds by activation of reactants through both Lewis acids and basic sites of ZnO catalyst and then nucleophilic substitution occurs by heterocyclic secondary amines and afforded 4,6-diaryl-2-(4-morpholinyl/1-pyrrolidinyl/1-piperidinyl)-pyrimidines. The catalyst could be recovered easily by solvent extraction of the product from the reaction mixture. For this, ethyl acetate was used; the aqueous layer containing the ZnO particles could be used for the next cycle.

The reaction was optimized for various reaction parameters such as temperature, solvent, and catalyst loading. The chalcones remain unconsumed when the reaction was done at room temperature. The effect of temperature on the yield of product was monitored from 60 to 120°C (Table 1, entry

TABLE 1: Effect of temperature for the synthesis of 2-substituted-4,6-diarylpyrimidine^a.

Entry	Temperature (°C)	Yield (%)
1	Room temp	Nil
2	60	30
3	80	60
4	100	90
5	120	90

^a Reaction conditions: chalcone (0.002 mol), SBT (0.0022 mol), heterocyclic secondary amine (0.0024 mol), and ZnO catalyst (15 mol%) in DMF (10 mL) at 100°C temperature for 6 h.

TABLE 2: Effect of solvent for the synthesis of 2-substituted-4,6-diarylpyrimidine^a.

Entry	Solvent	Yield (%)
1	None	20
2	H ₂ O	30
3	NMP	68
4	DMSO	75
5	DMF	90

^a Reaction conditions: chalcone (0.002 mol), SBT (0.0022 mol), heterocyclic secondary amine (0.0024 mol), and ZnO catalyst (15 mol%) in DMF (10 mL) at 100°C temperature for 6 h.

TABLE 3: Effect of catalyst loading for the synthesis of 2-substituted-4,6-diarylpyrimidine^a.

Entry	Catalyst (mol%)	Yield (%)
1	5	45
2	10	60
3	15	90
4	20	90

^a Reaction conditions: chalcone (0.002 mol), SBT (0.0022 mol), heterocyclic secondary amine (0.0024 mol), and ZnO catalyst in DMF (10 mL) at 100°C temperature for 6 h.

3b). However, no further increase in the yield was obtained by increasing the temperature from 100 to 120°C. Hence 100°C was chosen as optimum reaction temperature.

An attempt to catalyze the reaction in the absence of solvent resulted in very low yields (Table 2, entry 3b). Among the various solvents studied, DMF was found to be the best solvent giving maximum yield of desired product.

Catalyst concentration was optimized by varying its concentration from 5 to 20 mol% (Table 3, entry 3b). Increase in the product yield was observed from 5 to 20 mol% of catalyst amount. Hence 15 mol% was considered as an optimum catalyst concentration. The transformations of the reacting species were also confirmed by the spectroscopic studies. In FTIR, the disappearance of band at 1680–1710 cm^{-1} was due to the carbonyl group of chalcone, the appearance of band at 1595–1630 cm^{-1} due to cyclization, and in ¹H NMR the appearance of multiplet at δ 3.40–3.90 for the $-\text{CH}_2-\text{N}-\text{CH}_2-$ of morpholine/pyrrolidine/piperidine.

SCHEME 1: Synthesis of the title compounds.

FIGURE 1: Recyclability of ZnO catalyst.

Reusability is one of the important properties of this catalyst. In this study, the catalyst was recovered by filtration from the reaction mixture and reused during three consecutive runs without any apparent loss of activity for the same reaction Figure 1. In order to confirm the effective involvement of ZnO catalyst during transformation, we also performed the experiment under conventional heating without using catalyst [25].

3. Conclusion

We have developed a simple, economic, eco-friendly and highly efficient synthetic strategy for exclusive synthesis of 2-substituted-4,6-diarylpyrimidines using inexpensive, recyclable, and commercially available catalyst. On the other hand, ZnO is remarkably easier to use, nonhazardous, inexpensive, and works under mild conditions.

4. Experimental Section

4.1. General. The reaction mixtures were stirred magnetically. Chemicals were purchased from Sigma-Aldrich, Merck, and used without further purification. ¹H- and ¹³C NMR spectra were recorded using (CDCl₃) on 400 MHz ¹H NMR spectrometer Bruker AV III. The chemical shifts are denoted in δ units (ppm) relative to TMS (δ = 0.00) for protons ¹H: s (singlet), t (triplet), and m (multiplet). Melting points (°C) were measured in open glass capillaries using a Veego (VMP-MP) melting point apparatus and are uncorrected. Infrared spectra (ν, cm⁻¹) were recorded on a Perkin-Elmer spectrophotometer model RX I. Elemental analyses (C, H, N) were in full agreement with the proposed structures within ±0.5% of the theoretical values on a Carlo Erba 1108 analyzer. Monitoring the reactions and checking the purity of the final products were carried out by thin layer chromatography (TLC) using silica gel precoated aluminum sheets (Merck, 60–120 mesh) and visualization with ultraviolet light (UV) at 365 nm and 254 nm.

4.1.1. Procedure for the Synthesis of 4,6-Diaryl-2-(4-morpholinyl/1-pyrrolidinyl/1-piperidinyl) Pyrimidines. The starting compounds (chalcones) were prepared by the Claisen-Schmidt condensation [16]. A mixture of substituted chalcone (0.002 mol), SBT (0.0022 mol), heterocyclic secondary amine (0.0024 mol), and ZnO (15 mol%) in DMF (10 mL) was taken in a 100 mL round bottomed flask and heated at 100°C temperature for 6 h under vigorous stirring. After completion of the reaction as indicated by TLC [Benzene: Ethylacetate, 9:1v/v], reaction mixture was cooled at room temperature and filtered to separate the catalyst. Removal of the excess of solvent under reduced pressure gave crude solid which on recrystallization afforded the title products.

4.1.2. Spectral Analysis of 4,6-Diaryl-2-(4-morpholinyl)-pyrimidines 3a–g. (3a). Yield 86%, mp 105–107°C. IR (KBr): ν 3460, 3115, 1598, 1481, 1253 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 3.45–3.65 (m, 4H, –CH₂–N–CH₂–), 3.70–3.90 (m, 4H, –CH₂–O–CH₂–), 6.80–7.30 (m, 5H, Ar-H), 7.70 (s, 1H), 8.48–8.62 (m, 2H), 12.05 (s, 1H, Ar-OH) ppm. ¹³C NMR (400 MHz, CDCl₃): δ 47.52, 69.51, 123.80, 126.45, 128.65, 130.23, 143.46, 148.53, 150.50, 155.90 ppm. MS *m/z* 423 (M⁺). Anal. calcd for C₂₀H₁₇N₅O₆: C 56.74; H 4.05; N 16.54. Found: C 56.70, H 3.99, N 16.49.

(3b). Yield 90%, mp 165–167°C. IR (KBr): ν 3469, 3125, 1600, 1478, 1252, 861 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 3.50–3.70 (m, 4H, –CH₂–N–CH₂–), 3.75–3.90 (m, 4H, –CH₂–O–CH₂–), 6.80–7.15 (m, 4H, Ar-H), 7.80 (s, 1H), 8.25–8.55 (m, 2H), 12.00 (s, 1H, Ar-OH) ppm. ¹³C NMR (400 MHz, CDCl₃): δ 47.45, 68.60, 123.85, 125.80, 128.80, 130.23, 142.45, 148.50, 151.12, 155.90, 159.53 ppm. MS *m/z* 502 (M⁺). Anal. calcd For C₂₀H₁₆BrN₅O₆: C 47.83; H 3.21; N 13.94. Found: C 47.81, H 3.18, N 13.92.

(3c). Yield 89%, mp 100–102°C. IR (KBr): ν 3462, 3116, 1595, 1475, 1250, 863 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 3.55–3.70 (m, 4H, –CH₂–N–CH₂–), 3.60–3.88 (m, 4H, –CH₂–O–CH₂–), 6.88–7.45 (m, 4H, Ar-H), 7.78 (s, 1H), 8.45–8.63 (m, 2H), 12.10 (s, 1H, Ar-OH) ppm. ¹³C NMR (400 MHz, CDCl₃): δ 47.42, 68.90, 124.81, 126.15, 127.80, 131.25, 141.15, 148.20, 152.10, 155.35, 158.50 ppm. MS *m/z* 502 (M⁺). Anal. calcd For C₂₀H₁₆BrN₅O₆: C 47.83; H 3.21; N 13.94. Found: C 47.85, H 3.17, N 13.90.

(3d). Yield 88%, mp 160–162°C. IR (KBr): ν 3465, 3115, 1598, 1471, 1253, 810 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 3.45–3.75 (m, 4H, –CH₂–N–CH₂–), 3.65–3.90 (m, 4H, –CH₂–O–CH₂–), 6.80–7.20 (m, 4H, Ar-H), 7.75 (s, 1H), 8.40–8.60 (m, 2H), 11.90 (s, 1H, Ar-OH) ppm. ¹³C NMR (400 MHz, CDCl₃): δ 47.45, 68.60, 123.85, 125.80, 128.80, 130.23, 142.45, 148.50, 151.12, 155.90, 159.53 ppm. MS *m/z* 457 (M⁺). Anal. calcd For C₂₀H₁₆ClN₅O₆: C 52.47; H 3.52; N 15.30. Found: C 52.43, H 3.51, N 15.28.

(3e). Yield 86%, mp 97–99°C. IR (KBr): ν 3473, 3118, 1593, 1480, 1256, 821 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 3.50–3.65 (m, 4H, –CH₂–N–CH₂–), 3.70–3.92 (m, 4H, –CH₂–O–CH₂–), 6.85–7.25 (m, 4H, Ar-H), 7.70 (s, 1H), 8.45–8.62 (m, 2H), 9.80 (s, 1H, Ar-OH), 12.00 (s, 1H, Ar-OH) ppm. ¹³C NMR (400 MHz, CDCl₃): δ 47.05, 68.15, 124.80, 125.95, 129.15, 131.45, 144.23, 148.15, 150.36, 155.90, 159.95 ppm. MS *m/z* 439 (M⁺). Anal. calcd For C₂₀H₁₇N₅O₇: C 54.67; H 3.90; N 15.94. Found: C 54.55, H 3.81, N 15.78.

(3f). Yield 89%, mp 136–138°C. IR (KBr): ν 3468, 3111, 1605, 1479, 1258, 818 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 3.50–3.78 (m, 4H, –CH₂–N–CH₂–), 3.70–3.95 (m, 4H, –CH₂–O–CH₂–), 6.65–7.05 (m, 4H, Ar-H), 7.55 (s, 1H), 8.42–8.61 (m, 2H), 12.10 (s, 1H, Ar-OH) ppm. ¹³C NMR (400 MHz, CDCl₃): δ 47.05, 68.95, 123.48, 126.95, 128.35, 131.55, 144.25, 148.86, 150.85, 156.25, 159.25 ppm. MS *m/z* 457 (M⁺). Anal. calcd For C₂₀H₁₆ClN₅O₆: C 52.47; H 3.52; N 15.30. Found: C 52.41, H 3.49, N 15.29.

(3g). Yield 90%, mp 125–127°C. IR (KBr): ν 3460, 3114, 1600, 1472, 1258, 820 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 3.55–3.78 (m, 4H, –CH₂–N–CH₂–), 3.72–3.95 (m, 4H,

–CH₂–O–CH₂–), 6.65–7.08 (m, 4H, Ar-H), 7.58 (s, 1H), 8.42–8.61 (m, 2H), 12.08 (s, 1H, Ar-OH) ppm. ¹³C NMR (400 MHz, CDCl₃): δ 47.05, 68.95, 124.48, 125.95, 127.35, 131.55, 145.25, 147.52, 150.85, 156.65, 159.25 ppm. MS *m/z* 457 (M⁺). Anal. calcd For C₂₀H₁₆ClN₅O₆: C 52.47; H 3.52; N 15.30. Found: C 52.40, H 3.45, N 15.23.

4.1.3. Spectral Analysis of 4,6-Diaryl-2-(1-pyrrolidinyl)-pyrimidines 4a–g. (4a). Yield 88%, mp 81–83°C. IR (KBr): ν 3462, 3115, 1598, 1475, 1266 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 1.70–1.90 (m, 4H, –CH₂–CH₂–), 3.72–3.90 (m, 4H, –CH₂–N–CH₂–), 6.80–7.20 (m, 4H, Ar-H), 7.35 (s, 1H), 8.41–8.63 (m, 2H), 11.80 (s, 1H, Ar-OH) ppm. ¹³C NMR (400 MHz, CDCl₃): δ 25.23, 27.68, 47.80, 123.15, 126.26, 128.30, 130.13, 143.50, 148.45, 155.30 ppm. MS *m/z* 407 (M⁺). Anal. calcd for C₂₀H₁₇N₅O₅: C 58.97; H 4.21; N 17.19. Found: C 58.93, H 4.18, N 17.15.

(4b). Yield 89%, mp 150–152°C. IR (KBr): ν 3460, 3112, 1595, 1477, 1258, 868 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 1.70–1.93 (m, 4H, –CH₂–CH₂–), 3.61–3.79 (m, 4H, –CH₂–N–CH₂–), 6.90–7.25 (m, 4H, Ar-H), 7.61 (s, 1H), 8.41–8.62 (m, 2H), 12.01 (s, 1H, Ar-OH) ppm. ¹³C NMR (400 MHz, CDCl₃): δ 25.25, 27.96, 46.45, 124.45, 126.85, 129.80, 130.50, 142.50, 147.22, 148.87, 155.58, MS *m/z* 486 (M⁺). Anal. calcd For C₂₀H₁₆BrN₅O₅: C 49.40; H 3.32; N 14.40. Found: C 49.38, H 3.28, N 14.35.

(4c). Yield 86%, mp 161–162°C. IR (KBr): ν 3468, 3121, 1603, 1478, 1265, 865 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 1.71–1.98 (m, 4H, –CH₂–CH₂–), 3.52–3.75 (m, 4H, –CH₂–N–CH₂–), 6.90–7.35 (m, 4H, Ar-H), 7.70 (s, 1H), 8.40–8.60 (m, 2H), 11.95 (s, 1H, Ar-OH) ppm. ¹³C NMR (400 MHz, CDCl₃): δ 25.56, 27.25, 47.00, 124.56, 126.12, 129.11, 130.50, 141.00, 146.00, 148.56, 155.01. ppm. MS *m/z* 486 (M⁺). Anal. calcd For C₂₀H₁₆BrN₅O₅: C 49.40; H 3.32; N 14.40. Found: C 49.37, H 3.31, N 14.37.

(4d). Yield 86%, mp 175–176°C. IR (KBr): ν 3470, 3120, 1596, 1481, 1261, 815 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 1.70–1.90 (m, 4H, –CH₂–CH₂–), 3.52–3.70 (m, 4H, –CH₂–N–CH₂–), 7.00–7.35 (m, 4H, Ar-H), 7.70 (s, 1H), 8.35–8.55 (m, 2H), 12.00 (s, 1H, Ar-OH) ppm. ¹³C NMR (400 MHz, CDCl₃): δ 25.05, 27.89, 47.78, 125.05, 126.56, 129.55, 130.02, 140.15, 146.85, 147.95, 155.85, 159.36 ppm. MS *m/z* 441 (M⁺). Anal. calcd For C₂₀H₁₆ClN₅O₅: C 54.37; H 3.65; N 15.85. Found: C 54.35, H 3.60, N 15.81.

(4e). Yield 90%, mp 78–80°C. IR (KBr): ν 3455, 3110, 1600, 1475, 1258, 818 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 1.70–1.92 (m, 4H, –CH₂–CH₂–), 3.55–3.73 (m, 4H, –CH₂–N–CH₂–), 6.85–7.25 (m, 4H, Ar-H), 7.75 (s, 1H), 8.41–8.60 (m, 2H), 9.56 (s, 1H, Ar-OH), 12.01 (s, 1H, Ar-OH) ppm. ¹³C NMR (400 MHz, CDCl₃): δ 25.05, 27.80, 47.06, 124.00, 126.45, 128.05, 130.54, 139.25, 146.02, 147.30, 156.26, 159.80 ppm. MS *m/z* 423 (M⁺). Anal. calcd For C₂₀H₁₇N₅O₆: C 56.74; H 4.05; N 16.54. Found: C 56.65, H 3.92, N 16.42.

(4f). Yield 88%, mp 125–127°C. IR (KBr): ν 3470, 3135, 1615, 1469, 1245, 819 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 1.65–1.88 (m, 4H, –CH₂–CH₂–), 3.58–3.78 (m, 4H, –CH₂–N–CH₂–), 6.85–7.20 (m, 4H, Ar-H), 7.65 (s, 1H), 8.35–8.55

(m, 2H), 12.00 (s, 1H, Ar-OH) ppm. ^{13}C NMR (400 MHz, CDCl_3): δ 25.05, 27.80, 47.12, 124.45, 126.85, 127.00, 129.50, 141.00, 146.01, 147.86, 156.14, 159.15 ppm. MS m/z 441 (M^+). Anal. calcd For $\text{C}_{20}\text{H}_{16}\text{ClN}_5\text{O}_5$: C 54.37; H 3.65; N 15.85. Found: C 54.34, H 3.63, N 15.81.

(4g). Yield 90%, mp 102–104°C. IR (KBr): ν 3475, 3131, 1612, 1470, 1248, 822 cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 1.68–1.86 (m, 4H, $-\text{CH}_2-\text{CH}_2-$), 3.58–3.80 (m, 4H, $-\text{CH}_2-\text{N}-\text{CH}_2-$), 6.82–7.20 (m, 4H, Ar-H), 7.65 (s, 1H), 8.33–8.52 (m, 2H), 12.02 (s, 1H, Ar-OH) ppm. ^{13}C NMR (400 MHz, CDCl_3): δ 25.08, 27.82, 47.12, 123.45, 125.80, 127.05, 129.55, 141.06, 147.05, 147.86, 156.20, 159.10 ppm. MS m/z 441 (M^+). Anal. calcd For $\text{C}_{20}\text{H}_{16}\text{ClN}_5\text{O}_5$: C 54.37; H 3.65; N 15.85. Found: C 54.30, H 3.60, N 15.80.

4.1.4. Spectral Analysis of 4,6-Diaryl-2-(1-piperidinyl)-pyrimidines 5a–g. (5a). Yield 89%, mp 116–118°C. IR (KBr): ν 3460, 3119, 1599, 1479, 1259 cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 1.40–1.62 (m, 6H, $-(\text{CH}_2)_2-$), 3.40–3.71 (m, 4H, $-\text{CH}_2-\text{N}-\text{CH}_2-$), 3.79 (s, 3H, Ar-OCH₃), 6.90–7.20 (m, 4H, Ar-H), 7.65 (s, 1H), 8.35–8.60 (m, 2H), 11.25 (s, 1H, Ar-OH) ppm. ^{13}C NMR (400 MHz, CDCl_3): δ 25.20, 27.35, 47.55, 123.75, 128.54, 130.55, 143.85, 148.75, 150.45, 155.90 ppm. MS m/z 421 (M^+). Anal. calcd for $\text{C}_{21}\text{H}_{19}\text{N}_5\text{O}_5$: C 59.84; H 4.54; N 16.62. Found: C 59.80, H 4.49, N 16.68.

(5b). Yield 86%, mp 171–173°C. IR (KBr): ν 3465, 3111, 1605, 1481, 1261, 855 cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 1.30–1.58 (m, 6H, $-(\text{CH}_2)_3-$), 3.45–3.72 (m, 4H, $-\text{CH}_2-\text{N}-\text{CH}_2-$), 6.60–7.00 (m, 4H, Ar-H), 7.65 (s, 1H), 8.30–8.55 (m, 2H), 11.90 (s, 1H, Ar-OH) ppm. ^{13}C NMR (400 MHz, CDCl_3): δ 25.42, 27.40, 47.75, 124.00, 129.15, 130.05, 143.15, 148.00, 148.85, 150.04, 155.00 ppm. MS m/z 400 (M^+). Anal. calcd For $\text{C}_{21}\text{H}_{18}\text{BrN}_5\text{O}_5$: C 50.41; H 3.63; N 14.00. Found: C 50.38, H 3.61, N 13.98.

(5c). Yield 89%, mp 152–1154°C. IR (KBr): ν 3460, 3115, 1610, 1490, 1255, 861 cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 1.30–1.50 (m, 6H, $-(\text{CH}_2)_2-$), 4.40–4.71 (m, 4H, $-\text{CH}_2-\text{N}-\text{CH}_2-$), 6.90–7.35 (m, 4H, Ar-H), 7.70 (s, 1H), 8.45–8.62 (m, 2H), 11.65 (s, 1H, Ar-OH) ppm. ^{13}C NMR (400 MHz, CDCl_3): δ 25.45, 27.40, 47.80, 124.65, 129.00, 129.95, 143.58, 147.05, 148.95, 151.15, 155.65 ppm. MS m/z 400 (M^+). Anal. calcd For $\text{C}_{21}\text{H}_{18}\text{BrN}_5\text{O}_5$: C 50.41; H 3.63; N 14.00. Found: C 50.37, H 3.65, N 14.02.

(5d). Yield 87%, mp 201–203°C. IR (KBr): ν 3469, 3118, 1603, 1479, 1253, 802 cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 1.40–1.65 (m, 6H, $-(\text{CH}_2)_2-$), 3.42–3.65 (m, 4H, $-\text{CH}_2-\text{N}-\text{CH}_2-$), 6.95–7.35 (m, 4H, Ar-H), 7.66 (s, 1H), 8.42–8.65 (m, 2H), 12.00 (s, 1H, Ar-OH) ppm. ^{13}C NMR (400 MHz, CDCl_3): δ 25.55, 27.05, 47.80, 124.15, 129.45, 130.02, 143.15, 147.00, 148.23, 151.01, 156.35 ppm. MS m/z 455 (M^+). Anal. calcd For $\text{C}_{21}\text{H}_{18}\text{ClN}_5\text{O}_5$: C 55.33; H 3.98; N 15.36. Found: C 55.31, H 3.95, N 15.33.

(5e). Yield 87%, mp 100–102°C. IR (KBr): ν 3468, 3121, 1596, 1471, 1261, 820 cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 1.48–1.68 (m, 6H, $-(\text{CH}_2)_3-$), 3.48–3.71 (m, 4H, $-\text{CH}_2-\text{N}-\text{CH}_2-$), 6.92–7.25 (m, 4H, Ar-H), 7.65 (s, 1H), 8.42–8.60 (m, 2H), 8.56 (s, 1H, Ar-OH), 12.10 (s, 1H, Ar-OH) ppm. ^{13}C NMR (400 MHz, CDCl_3): δ 25.50, 27.23,

47.56, 124.15, 130.01, 131.55, 143.50, 147.48, 148.01, 150.45, 156.85, 159.50 ppm. MS m/z 437 (M^+). Anal. calcd For $\text{C}_{21}\text{H}_{19}\text{N}_5\text{O}_6$: C 57.66; H 4.38; N 16.01. Found: C 57.51, H 4.25, N 15.92.

(5f). Yield 86%, mp 201–203°C. IR (KBr): ν 3464, 3118, 1601, 1468, 1258, 809 cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 1.35–1.53 (m, 6H, $-(\text{CH}_2)_3-$), 3.48–3.70 (m, 4H, $-\text{CH}_2-\text{N}-\text{CH}_2-$), 6.80–7.30 (m, 4H, Ar-H), 7.60 (s, 1H), 8.35–8.58 (m, 2H), 12.00 (s, 1H, Ar-OH) ppm. ^{13}C NMR (400 MHz, CDCl_3): δ 25.21, 27.23, 47.15, 124.56, 130.00, 131.35, 141.52, 146.14, 148.45, 151.56, 156.42, 159.23 ppm. MS m/z 455 (M^+). Anal. calcd For $\text{C}_{21}\text{H}_{18}\text{ClN}_5\text{O}_5$: C 55.33; H 3.98; N 15.36. Found: C 55.31, H 3.95, N 15.30.

(5g). Yield 88%, mp 160–162°C. IR (KBr): ν 3466, 3120, 16012, 1465, 1258, 810 cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 1.35–1.55 (m, 6H, $-(\text{CH}_2)_3-$), 3.45–3.71 (m, 4H, $-\text{CH}_2-\text{N}-\text{CH}_2-$), 6.78–7.32 (m, 4H, Ar-H), 7.65 (s, 1H), 8.35–8.58 (m, 2H), 12.02 (s, 1H, Ar-OH) ppm. ^{13}C NMR (400 MHz, CDCl_3): δ 25.21, 27.25, 47.20, 123.50, 131.02, 132.30, 140.51, 145.18, 147.41, 150.55, 157.40, 160.20 ppm. MS m/z 455 (M^+). Anal. calcd For $\text{C}_{21}\text{H}_{18}\text{ClN}_5\text{O}_5$: C 55.33; H 3.98; N 15.36. Found: C 55.28, H 3.92, N 15.25.

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References

- [1] A. Domling and I. Ugi, "Multicomponent reactions with isocyanides," *Angewandte Chemie International Edition*, vol. 39, pp. 3168–3210, 2000.
- [2] L. Yu, B. Chen, and X. Huang, "Multicomponent reactions of allenes, diaryl diselenides, and nucleophiles in the presence of iodosobenzene diacetate: direct synthesis of 3-functionalized-2-arylselenenyl substituted allyl derivatives," *Tetrahedron Letters*, vol. 48, no. 6, pp. 925–927, 2007.
- [3] J. Zhu and H. Bienayme, *Multicomponent Reactions Wiley-VCH*, 2005.
- [4] R. A. Sheldon and J. Dakka, "Heterogeneous catalytic oxidations in the manufacture of fine chemicals," *Catalysis Today*, vol. 19, no. 2, pp. 215–246, 1994.
- [5] R. A. Sheldon and R. S. Downing, "Heterogeneous catalytic transformations for environmentally friendly production," *Applied Catalysis A*, vol. 189, no. 2, pp. 163–183, 1999.
- [6] K. Tanabe, *Solid Acids and Bases*, Academic Press, New York, NY, USA, 1970.
- [7] J. C. Trivedi, J. B. Bariwal, K. D. Upadhyay et al., "Improved and rapid synthesis of new coumarinyl chalcone derivatives and their antiviral activity," *Tetrahedron Letters*, vol. 48, no. 48, pp. 8472–8474, 2007.
- [8] M. Chen, S. B. Christensen, L. Zhai et al., "The novel oxygenated chalcone, 2,4-dimethoxy-4'-butoxychalcone, exhibits potent activity against human malaria parasite *Plasmodium falciparum* in vitro and rodent parasites *Plasmodium berghei*

- and *Plasmodium yoelii* in vivo," *Journal of Infectious Diseases*, vol. 176, no. 5, pp. 1327–1333, 1997.
- [9] T. Narender, K. Shweta, R. M. Tanvir, S. K. Srinivasa, and S. K. Puri, "Prenylated chalcones isolated from *Crotalaria* genus inhibits in vitro growth of the human malaria parasite *Plasmodium falciparum*," *Bioorganic and Medicinal Chemistry Letters*, vol. 15, no. 10, pp. 2453–2455, 2005.
  - [10] X. Wu, P. Wilairat, and M. L. Go, "Antimalarial activity of ferrocenyl chalcones," *Bioorganic and Medicinal Chemistry Letters*, vol. 12, no. 17, pp. 2299–2302, 2002.
  - [11] M. Liu, P. Wilairat, S. L. Croft, A. L. C. Tan, and M. L. Go, "Structure-activity relationships of antileishmanial and antimalarial chalcones," *Bioorganic and Medicinal Chemistry*, vol. 11, no. 13, pp. 2729–2738, 2003.
  - [12] S. F. Nielsen, S. B. Christensen, G. Cruciani, A. Kharazmi, and T. Liljefors, "Antileishmanial chalcones: statistical design, synthesis, and three-dimensional quantitative structure-activity relationship analysis," *Journal of Medicinal Chemistry*, vol. 41, no. 24, pp. 4819–4832, 1998.
  - [13] S. A. Indiyah, H. Timmerman, M. Samhoedi, S. Sastrohamidjojo, and H. Van Der Goot, "Synthesis of benzylideneacetophenones and their inhibition of lipid peroxidation," *European Journal of Medicinal Chemistry*, vol. 35, no. 4, pp. 449–457, 2000.
  - [14] C. L. Ye, J. W. Liu, D. Z. Wei, Y. H. Lu, and F. Qian, "In vitro anti-tumor activity of 2', 4'-dihydroxy-6'-methoxy-3',5'-dimethylchalcone against six established human cancer cell lines," *Pharmacological Research*, vol. 50, no. 5, pp. 505–510, 2004.
  - [15] K. L. Ameta, N. S. Rathore, and B. Kumar, "Synthesis and in vitro anti breast cancer activity of some novel 1, 5-benzothiazepine derivatives," *Journal of Serbian Chemical Society*, vol. 77, no. 6, pp. 725–731, 2012.
  - [16] K. L. Ameta, B. Kumar, and N. S. Rathore, "Microwave induced improved synthesis of some novel substituted 1, 3-diarylpropenones and their antimicrobial activity," *E-Journal of Chemistry*, vol. 8, no. 2, pp. 665–671, 2011.
  - [17] M. L. Irene, "Pyrimidine as constituent of natural biologically active compounds," *Chemistry and Biodiversity*, vol. 2, no. 1, pp. 1–50, 2005.
  - [18] T. A. Naik and K. H. Chikhaliya, "Studies on synthesis of pyrimidine derivatives and their pharmacological evaluation," *European Journal of Chemistry*, vol. 4, no. 1, pp. 60–66, 2007.
  - [19] K. L. Ameta, N. S. Rathore, and B. Kumar, "Synthesis of some novel chalcones and their facile one-pot conversion to 2-aminobenzene-1, 3-dicarbonitriles using malononitrile," *Analele Universitatii Bucuresti Chimie*, vol. 20, no. 1, pp. 15–24, 2011.
  - [20] P. Sharma, K. F. Hussain, S. Sukhwal, S. Kothari, M. Singhal, and B. L. Verma, "A convenient one-pot synthesis of 2-substituted-4,6-diaryl pyrimidines," *Indian Journal of Chemistry B*, vol. 38, no. 8, pp. 966–968, 1999.
  - [21] S. Kothari, R. Vyas, and B. L. Verma, "A facile one pot conversion of 3',5'-dibromo-4'-hydroxy substituted chalcones to pyrimidine derivatives and their antibacterial and herbicidal activity," *Indian Journal of Heterocyclic Chemistry*, vol. 8, no. 4, pp. 285–288, 1999.
  - [22] U. S. Gahlot, S. S. Rao, S. S. Dulawat, K. L. Ameta, and B. L. Verma, "A facile one-pot microwave assisted conversion of 3'-5'-dibromo/diiodo-4'-hydroxy substituted chalcones to 2-substituted-4,6-diaryl pyrimidines using S-benzylisothiouronium chloride (SBT) and their antibacterial activities," *Afinidad*, vol. 60, no. 508, pp. 558–562, 2003.
  - [23] M. Kidwai, S. Rastogi, and S. Saxena, "Base catalysed pyrimidine synthesis using microwave," *Bulletin of the Korean Chemical Society*, vol. 24, no. 11, pp. 1575–1578, 2003.
  - [24] P. Shiv, M. V. S. Sharma, A. K. Suryanarayana, A. S. Nigam, A. S. Chauhan, and L. N. S. Tomar, "[PANI/ZnO] composite: catalyst for solvent-free selective oxidation of sulfides," *Catalysis Communications*, vol. 10, no. 6, pp. 905–912, 2009.
  - [25] K. L. Ameta, B. Kumar, and N. S. Rathore, "Facile synthesis of some novel 2-substituted-4, 6-diarylpyrimidines using 4'-hydroxy-3', 5'-dinitrochalcones and S-benzylthiouronium chloride," *Organic Communication*, vol. 5, pp. 1–11, 2012.