Eco-Friendly Synthesis and Reactions of Some α, β-Unsaturated Ketones

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Abstract: Effective implementation of ultrasound irradiation for the rapid synthesis of series of chalcones $\mathbf{I_{a-f}}$ via the condensation of aryl ketone and aryl aldehyde in alkaline ethanol. Also, pyridine $\mathbf{4_{a-c}}$, pyrimidine thione $\mathbf{5_{a-d}}$ and diazepine $\mathbf{6_{a,b}}$ derivatives were achieved by Michael addition of compounds containing either active methylene groups or active hydrogen atoms. Moreover, reaction of 2-thione pyrimidine derivative $\mathbf{5_{b-c}}$ with chloroacetic acid afforded thiazolopyrimidine derivatives $\mathbf{7_{a-c}}$. Condensation of $\mathbf{5}_{\mathbf{b-c}}$ with 3-bromopropionic acid gave pyrimido [2,1-b] [1,3] thiazin-4-one derivatives $\mathbf{8_{a-c}}$. The structure of the synthesized compounds were mainly confirmed on the basis spectroscopic methods.

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1-Introduction

Chalcones or 1,3-diaryl-2-propen-l-ones are very important chemical precursors for the preparation a wide variety of heterocyclic systems, such as pyridines, pyrimidines, diazepines, and flavone have been synthesized from chalcones [1-3].

Chalcones and its derivatives have attracted considerable attention due to their diverse pharmacological and biological importance [4-8]. The Micheal reaction is a classical and most efficient methods for formation carbon-carbon bond-forming reaction [9-11]. Generally, Michael addition are carried out in an appropriate solvent in the presence of a strong base. Because of the presence of the strong base, side reactions such rearrangements, multiple condensations and retro-Michael addition are common [12].

Ultrasound-assisted organic synthesis (UAOS) is a green synthetic technique. Compared with classical heating methods, this approach is more suitable, efficient and can controlled easily. It was reported that a large number of organic reactions could be facilitated by ultrasound irradiation with excellent yields, simple experimental procedure, and shorten reaction time [13-18]. Considering the significance of all above discussed aspect and as a part of continuing studies on green synthesis of some heterocyclic rings [19-20]. Herein we wish to report the present study on the synthesis and reactions of chalcones with different reagents utilizing ultrasound irradiation as a green energy source in order to synthesize some pyridine, pyrimidine, diazepine, thiazolopyrimidine and thiazinopyrimidine derivatives with expected biological activity.

2- Experimental

All chemicals were used without any further purification. Melting point are uncorrected. IR spectra were recorded in potassium bromide on Perkin-Elmer 380 and 387 spectrometer. The ^{1}HNMR and ^{13}CNMR spectra were run on a Joel-JNM EX-100 and JNM EX-300 in DMSO-d_6 or $CDCl_3$. Using TMS as internal standard. Chemical shifts (δ) are in ppm relative to TMS. Mass spectra were carried on Shimadzu GCMSQP 5050 spectrometer at 70eV. Sonication was performed in ultrasonic cleaner with a frequency of 35 kHz and a nominal power 200 W. Progress of the reactions was monitored by TLC.

General Procedure for Preparation 1,3-Diaryl-2-propen-l-one $\mathbf{l_{a-f}}$

A mixture of aryl ketone$\mathbf{1_{a-f}}$ (1mmol), aryl aldehyde $\mathbf{2_{a-f}}$ (1mmol), MeOH (10mL) and 2N KOH (4mL) were taken into conical flask. The mixture was irradiated by an ultrasonic generated in water bath at 25^{o}C for 20 min. The solid product left in refrigerator over nigh, diluted with water and neutralized with 2N HCl (4mL), filtered washed with water, dried, and crystallized from the proper solvent.

The authenticity of the products $\mathbf{3_{a-f}}$ was determined by comparing their melting points with literature [21,23] as well as the spectra data of IR and ^{1}HNMR.

1,3-Diphenyl-2-propen-l-one $\mathbf{l_a}$: 90%, m.p.55-56^{o}C (EtOH), IR (cm^{-1}), 1670, 1590, ^{1}HNMR (300 MHz, DMSO-d_6): 7.35 (d, 1H, J = 15.30 Hz, CO - CH =), 7.60 (d, 1H, J = 15.30 Hz, = CH-Ar), 6.90 – 8.20 (m, 10H, Ar-H).

1-phenyl-3-(2-thienyl)-2-propen-l-one 1_b; 86%, m.p. 60-62 ^{o}C (MeOH); IR (cm^{-1}). 1660, 1589 ^{1}HNMR (300 MHz, $CDCl_3$) 7.20 (d, 1H, J = 15.21 Hz,

CO - CH =), 7. 70 (d, 1H, J = 15.40 Hz, = CH-Ar), 7.2- 7. 60 (m, 8H, Ar-H& thiophene - H).

1-(4-bromophenyl)--3- phenyl 2-propen-l-one 1_c: 87% m.p.104- 106°C (EtOH); IR (cm^{-1}), 1670, 1570; ^{1}HNMR (300 MHz, DMSO-d_6): 7.35 (d, 1H, J = 15.30 Hz, CO - CH =), 7. 70 (d, 1H, J = 15.30 Hz, = CH-Ar), 7.10- 8.0 (m, 9H, Ar-H).

1-(4-chlorophenyl)-3-(2-thienyl)-2-propen-l-one1_d: 87%, 117-118°C (AcOH); IR (cm^{-1}) 1660, 1580; ^{1}HNMR (300 MHz, $CDCl_3$): 7.30 (d, 1H, J = 15.4 Hz, CO - CH =), 7. 75 (d, 1H, J = 15.6 Hz, = CH-Ar), 7.11- 7.70 (m, 7H, Ar – H& thiophene - H).

1,3-Di (2-thienyl) -2-propen-l-one l_e: 86%, m.p 98-100°C (EtOH): IR (cm^{-1}), 1660, 1570, ^{1}HNMR (300 MHz, DMSO-d_6): 7.30 (d, 1H, J =15.60 Hz, CO - CH =), 7.78 (d, 1H, J = 15.60, = CH-Ar), 7.01 - 7.70 (m, 6H, thiophene - H).

1-(4-chlorophenyl)-3-(2-furanyl)-propen-2-one l_f: 86%, m.p 80-82°C (EtOH); IR (cm^{-1}): 1650, 1585; ^{1}HNMR (300 MHz, $CDCl_3$): 7.32 (d, 1H, J 15.81 Hz, CO - CH =), 7.78 (d, 1H, J = 15.77, = CH-Ar), 7.11-7.80 (m, 7H, Ar-H & furan-H).

General Procedure for Preparation 2-Amino-3-cyano-4, 6-diaryl- pyridines 4_{a-c}

Method A: A mixture of chalcone $\mathbf{l}_{a-c}$ (1 mmol), malonitrile (1 mmol) and ammonium acetate (1.5g) in (15 mL) water was subjected to ultrasound irradiation in ultrasonic bath at 30°C for 20 min. the mixture was cooled and poured on to ice-cold water, then filtered and recrystallized from ethanol.

Method B: A mixture of aromatic ketone$\mathbf{1}_{a-c}$ (1 mmol), aromatic aldehyde$\mathbf{2}_{a-c}$ (1 mmol), malonitrile (1 mmol) and ammonium acetate (1.5 mmol) in (10 mL) water was subjected to ultrasound irradiation in ultrasonic bath at 30°C for 25 min. reaction mixture was cooled, diluted with water (10 mL), filtered, and recrystallized from ethanol.

2-Amino-3-cyano-4,6-(diphenyl)-pyridine 4_a: 85[A]%, m.p.187-188 ^{0}C (28); (IR, cm^{-1}): 3350, 3310, 2220; ^{1}HNMR (300 MHz, DMSO-d_6); 6.91 (s, 1H, pyridine-H), 7.20- 8.00 (m, 10H, Ar-H), 8.4 (br.s, 2H, NH_2); ^{13}CNMR (100MHz, DMSO-d_6): 109.12 (C≡N); 115.6, 116.11, 128.2, 128.6, 129.70,130.00,132.34, 157.11,158.00 (Aromatic Carbons); MS: (m/z) 271 [M^+] For $C_{18}H_{13}N_3$.

2-Amino-3-cyano-4-(2-thienyl)-6-phenyl-pyridine 4_b: 88% [A], m.p. 128-130^0 C (IR, cm^{-1}): 3350, 3310, 2220; ^{1}H NMR (300 MHz, DMSO-d_6); 7.1 (s, 1H, pyridine-H), 7.20- 8.00 (m, 8H, Ar-H& thiophene - H), 8.16 (br.s, 2H, NH_2); ^{13}CNMR (100MHz, DMSO-d_6): 109.19 (C ≡N), 115.11, 118.1, 123.20, 127.32, 127.38, 128.24, 129.55, 129.70, 130.00, 132.34, 147.11, 159.00 (Aromatic Carbons). MS: (m/z) 277 [M^+] For $C_{16}H_{11}N_3S$.).

2-Amino-3-cyano-4-phenyl-6-(bromophenyl) pyridine 4_c: 85%[A], m.p: 218-220°C, IR (cm^{-1}), br. 3400, 2190; ^{1}H NMR (300 MHz, $CDCl_3$): 6.90 (s, 1H, pyridine-H), 7.2-7.90 (m; 9H, Ar-H), 8.5 (br. s, 2H, NH_2); ^{13}C NMR (100MHz, $CDCl_3$): 109.12 (C ≡ N), 115.11, 120.30, 123.32, 123.50, 127.11, 127.20, 128.32, 129.45, 129.50, 136.14, 140.32 151.12 (Aromatic Carbons). MS: (m/z) 349.9 [M^+] For $C18H12BrN_3$.

General procedure for the preparation of pyrimidin-2-thione derivatives5_{a-d}

Method A: A mixture of chalcones $\mathbf{3}_{a-d}$ (1 mmol), thiourea (1.2 mmol) and potassium hydroxide (0.5g) in ethanol (15 mL) was subjected to ultrasound irradiation in ultrasonic bath at 30°C for 30 min. The reaction mixture was poured on cold water and stirred for 30 min, and the precipitate was filtered washed with water until free from alkali and recrystallized from the proper solvent.

Method B: A mixture of aromatic ketone $\mathbf{1}_{a-d}$ (1 mmol), aromatic aldehyde $\mathbf{2}_{a-d}$ **(**1 mmol), thiourea (1.2mmol), and potassium hydroxide (0.5g) in ethanol (15 mL) was subjected to ultrasound irradiation in ultrasonic bath at 30°C for 30 min, The reaction mixture was poured on cold water and stirred for 30 min, and the precipitate was filtered washed with water until free from alkali and recrystallized from the proper solvent.

4,6-Diphenyl-3,4-dihydro pyrimidin-2-(1H) thione 5a: 84 % [A], m.p 184°C (28) (EtOH), ^{1}H-NMR (300 MHz, $CDCl_3$):4.86(d, 1H, J=5.40Hz, Ar_2-CH), 5.40 (d, 1H, d, J=5.40, Ar_1-C=CH), 6.97-7.50 (m,10H,Ar-H), 8.90 (br,s,2H,NH_2); ^{13}CNMR (100MHz, $CDCl_3$): 55.62 (C-4) 112.6, 120.9, 123.3, 127.6, 128.80, 129.3, 130.5, 133.92, 139.5, 154.53 (Olefinic & Aromatic Carbons), 177.31(C=S); MS: (m/z) 266[M^+] For $C_{16}H_{14}N_2S$.

4--phenyl-6-(2-Thienyl)--3,4-dihydro-pyrimidine- 2(1H) thione 5_b:84 % [A], m.p.120 °C [22] (EtOH); ^{1}H-NMR (300 MHz, $CDCl_3$): 4.75 (1H, d, J = 15.5 Hz, Ar_2- CH),5.40 (1H, d, J =15.43 Hz, Ar_1-C= CH), 6.81-7.70(m,8H,Ar-H & thiophene-H) 8.40 (br,s,1H,NH), 8.60 (br.s,1H,NH), ^{13}CNMR (100MHz, $CDCl_3$): 55.7(C-4),112.4, 120.2, 124.77, 127.85, 129.20, 129.61, 132.5, 134.1, 147.05, 153.30 (Olefinic & Aromatic Carbons), 175.3, (C = S); MS: (m/z) 272 [M^+] For $C_{14}H_{12}N_2S_2$

4-(4-Bromophenyl)-6-phenyl-3,4-dihydro-pyrimidine-2(1H) thione 5_c:85%, 89-90 °C (AcOH), IR 3330, 3227, 1206;, ^{1}H NMR[1] (300MHz, DMSO – d_6): 4.63 (d, 1H, J = 15.20 Hz, Ar_2- CH), 5.25(d, 1H, J = 15.20, Ar_1-C= CH), 7.0 – 8.11 (m,9H, Ar-H), 8.94 (br.s,1H, NH), 9.18(br.s,1H, NH); ^{13}CNMR (100MHz, DMSO – d_6): 55.93 (C-4); 115.31, 118.22, 127.00, 127.21, 130.35, 132.61,132.88, 136.32, 146.22, 155.20 (Olefinic & Aromatic Carbons), 175.04 (C = S); MS: (m/z) 344.9 [M^+] For $C_{16}H_{13}BrN_2S$.

4-(2-Chlorophenyl)-6-(2-Thienyl)-3,4-dihydro-pyrimidine-2(1H) thione 5_d:83% [A], 132-134°C [22] (EtOH); IR 3330, 3227, 1206;, ^{1}H NMR[1] (300MHz, DMSO – d_6): 4.51 (d, 1H, J = 15.20, Ar_2-CH), 5.45(d, 1H, J = 15.20, Ar_1-C= CH), 7.0- 7.8(m, 7H, Ar-H & thiophene -H); 8.1(s,1H, NH), 8.6(s,1H, NH); ^{13}CNMR (100MHz, DMSO - d_6): 56.83 (C-4); 112.31, 118.20, 126.66, 127.81, 127.90, 130.50, 130.56 134.61, 146.22, 155.20 (Olefinic & Aromatic Carbons), 175.04 (C = S);MS: (m/z) 306.5 [M^+] For $C_{14}H_{11}ClN_2S_2$.

General Procedure for the Preparation of 2,4-diaryl-2,3-dihydro-1H-benzo [b] [1,5]diazepine $6_{a,b}$

A mixture of Chalcone $1_{a,b}$ (1 mmol),*o*-phenylenediamine (1.5 mmol) in dry methanol (10 mL) and acetic acid (2 mL), was subject to ultrasound irradiation in ultrasonic bath at 30°C. for 30 min. The reaction mixture was cooled, poured on iced-cold water and stirred for 20 min. The solid filtered, washed with water and recrystallized from ethanol.

2,4-Diphenyl-2,3-Dihydro-1H-benzo [b] [1,5] diazepine 6_a: 85%, m.p 130-131°C;IR (cm^{-1}): 3350, 1600, ^{1}H NMR (300 MHz, $CDCl_3$): 3.20(dd, 1H, J = 12.9 Hz, J = 8.65Hz, = C – CH_2); 3.79 (dd, 1H, J = 12.9Hz, J = 4.1Hz, = C – CH_2), 5.12 (br.s, 1H, NH), 5.30 (dd, 1H, J = 8.65 Hz, J = 4.20. Hz, N – CH-Ar_2), 7.12 - 8.05 (m, 14H, Ar-H); ^{13}C NMR (100MHz, $CDCl_3$): 34.8 (C-3), 68.1 (C -2), 166.8 (C -4), 120.30, 122.52, 125.91, 126.21, 127.14, 128.33, 129.30, 129.91, 130.05, 132.23, 133.13, 133.60, 139.11 (Aromatic Carbons); MS: (m/z) 298 [M^+] For $C_{21}H_{18}N_2$.

2-(2-Theinyl)-4-Phenyl-2,3-Dihydro-1H-benzo [b] [1, 5] diazepine 6_b: 87%,m.p. 150-152 °C,IR (cm^{-1}): 3370, 1600^{1}HNMR (300 MHz, DMSO-d_6), 3.10 (d, 1H, J = 12.31 Hz, J = 8. 23, = C - CH_2), 3.57 (dd, 1H, J =12.31Hz, J = 3.79, = C- CH_2), 5.36 (dd, 1H, J = 8.20, J = 3.75, N – CH-Ar_2); 4.20 (br.s, 1H, NH), 7.01-8.45 (m, 12H, Ar-H);^{13}C NMR (100 MHz, DMSO-d_6): 34.97 (C- 3), 67.75 (C -2), 167.11 (C - 4), 118.93, 120.25, 120.34, 124.30, 127.33, 127.96, 128.5, 129.31, 129.34, 130.52, 138.49, 138.90, 139.1, 139.56, 142.15 (Aromatic Carbons); MS: (m/z) 304 [M^+] For $C_{19}H_{16}N_2S$.

General Procedure for the Preparation of 2,3-dihydro 5,7-diaryl-thiazolo [3,2-a] pyrimidin-2-one derivatives 7_{a-c}:

A mixture of 5_{b-c} (1mmol) and chloroacetic acid (1mmol), anhydrous sodium acetate (4mmol) in glacial acetic acid (20 mL) was subjected to ultrasound irradiation in ultrasonic bath at 50°C for 35 min. The mixture was cooled and poured onto ice-water, then filtered and recrystallized from the proper solvent.

2,3-Dihydro-5-(2-thienyl)-7-phenyl-thiazolo [3,2-a] pyrimidin-2-one 7_a: 83%; 84-86°C [22], (MeOH); IR (cm^{-1}) 1720, 1633; ^{1}H NMR (300 MHz, DMSO - d_6): 3.61 (s, 2H, - CH_2) 5.71 (d, 1H, J = 6.85 Hz, = HC – CH- Ar_2), 6.45 (d,1H, J = 6.75, - C = CH Ar_1), 7.1 - 8.30 (m, 8H, Ar-H & thiophene-H); ^{13}CNMR (100 MHz, DMSO-d_6): 32.40 (C -2), 59.31 (C- 5), 122.40, 124.30, 127.2, 127.41, 128.09, 129.59, 130.61, 132.33, 142.50, 151.20, 167.11 (Olefinic & aromatic carbons), 175.30 (C = O).); MS: (m/z) 304 [M^+] For $C_{16}H_{12}N_2OS_2$.

2,3-Dihydro-5-phenyl-7-(4-bromophenyl)-thiazolo [3,2-a] pyrimidin-2-one 7_b: 81%, 130-132°C (EtOH); IR (cm^{-1}): 1710, 1630; ^{1}HNMR (300 MHz, DMSO-d_6): 3.21 (s, 2H, - CH_2) 5.71 (d, 1H, J = 6.85 Hz, = HC – CH), 6.45 (d,1H, J = 6.45, - C = CH), 7.1 - 8.30 (m, 9H, Ar-H); ^{13}CNMR (100 MHz, DMSO-d_6): 32.70 (C - 2), 59.33 (C -5), 121.43, 124.1, 127.13, 128.80, 129.50, 130.80, 132.10, 133.50, 143.60, 155.80, 167.1 (Olefinic & Aromatic Carbons), 177.04 (C = O); MS: (m/z) 384.9 [M^+] For $C_{18}H_{13}BrN_2OS_2$.

2,3-Dihydro-5-(2-thienyl)-7-(4-chlorophenyl)-thiazolo [3, 2-a] pyrimidin-2-one 7_c: 80%, m.p: 120-122 °C [22], (MeOH); IR (cm^{-1}): 1710, 1620; ^{1}HNMR (300 MHz, DMSO-d_6): 3.11 (s, 2H, CH_2), 5.43 (d, 1H, J = 5.81 Hz, = CH – CH), 6.20 (d, 1H, J = 5.8 Hz, C = CH); 7.0 – 7.99 (m, 7H, Ar-H & thiophene-H); ^{13}CNMR (100 MHz, DMSO-d_6): 31.70 (C-2), 58.99 (C-5), 120, 125.30, 127.10, 127.05, 129.90, 130.80, 132.50, 138.11, 144.50, 155.77, 167.30 (Olefinic & Aromatic Carbons), 177.90 (C = O); MS: (m/z) 346.5 [M^+] For $C_{16}H_{11}ClN_2OS_2$.

General Procedure for the Preparation of 2,3-dihydro-6,8-diaryl-pyrimido [2,1-b] [1,3] thiazin-4-one derivatives 8_{a-c}

A mixture of 5_{a-c} (1 mmol), 3-bromo propionic acid (1mmol), anhydrous sodium acetate (4 mmol), in glacial acetic acid (20mL) was subjected to ultrasound irradiation in ultrasonic bath at 50°C for 30 min. The mixture was cooled and poured onto ice-water, then filtered and recrystallized from the proper solvent.

2,3-Dihydro-6-(2-thienyl)-8-(phenyl)pyrimido [2,1-b] [1,3]thiazin-4-one 8a:83%, m.p:72°C [22], (MeOH); IR (cm^{-1}):1740, 2980; ^{1}HNMR 2.3-3.9(m,4H,CH_2,thiazine -H), 5.3 (d, J = 6.11 Hz, HC - Ar_2), 6.2 (d, 1H, J = 6.11Hz, HC =C-Ar_1), 7.1 – 8.3 (m, 8H, Ar-H & thiophene-H);^{13}C NMR: 21.85 (C - 3), 36.50 (C - 2), 56.13 (C- 6), 112.80, 117.28, 122.50, 126.8, 127.60, 129.50, 129.60, 132.80, 136.73, 144.10, 152.88 (Olefinic & Aromatic Carbons), 170.10 (C = O); MS: (m/z) 326 [M^+] For C17 H14 N2O S2.

2,3-Dihydro-6-phenyl-8-(4-bromophenyl) pyrimido [2,1-b] [1,3] thiazin-4-one 8b: 85%, m.p:100-102°C (AcOH); IR (cm^{-1}), 1680, 2279, ^{1}HNMR (300 MHz, $CDCl_3$): 2.1-3.7 (m, 4H, 2CH_2, thiazine-H), 5. 00 (d, 1H, J = 5.40 Hz, HC - Ar_2), 6.1

(d, 1H, J = 5.05 Hz, HC =C-Ar_1), 7.0 – 8.3 (m, 9H, Ar-H);^{13}CNMR: 21.85 (C-3), 35.80 (C-2), 55.80 (C-6), 112.70, 114.90, 117.50,125.30, 127.3, 129.30, 130.11, 132.1, 136.55,143.98, 152.80 (Olefinic & Aromatic carbons),173.22 (C = O), MS: (: (m/z) 398.9 [M^+] For $C_{19}H_{15}BrN_2OS$.

2,3-Dihydro-6-(2-thienyl)-8-(4-chlorophenyl) pyrimido [2,1-b] [1,3] thiazin-4-one 8b: 85%, m.p:150-152^{o}C [22], (AcOH); IR (cm^{-1}), 1670, 2279, ^{1}HNMR (300 MHz, $CDCl_3$): 2,4-3.7 (m, 4H, $2CH_2$, thiazine-H), 5.6 (d, 1H, J = 5.40 Hz, HC - Ar_2),6.1 (d, 1H, J = 5.64 Hz, HC =C-Ar_1), 7.0 – 8.1 (m, 7H, Ar-H & thiophene-H);^{13}CNMR: 21.85 (C-3), 35.80 (C-2), 55.80 (C-6), 112.70, 114.90, 117.50,125.30, 127.3, 129.30, 130.11, 132.1, 136.55,143.98, 152.80 (Olefinic & Aromatic Carbons),173.22 (C = O), MS: (m/z) 360.5 [M^+] For $C_{17}H_{13}ClN_2OS_2$.

3-Result and Discussion

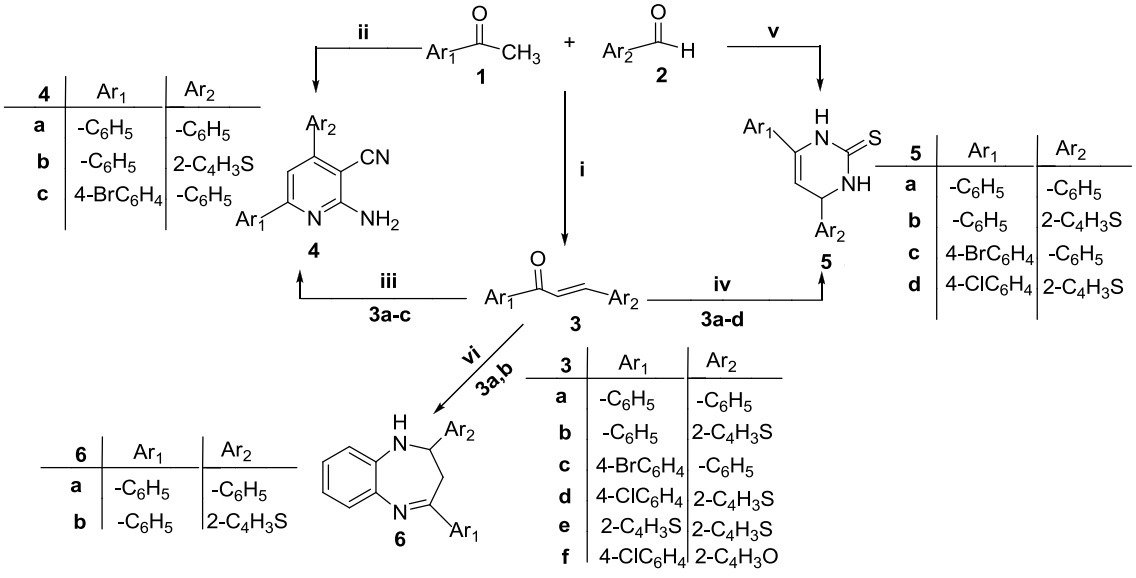
In a continuation of our interest on the synthesis heterocycles using green methods, The present paper describes the synthesis and reactions of chalcones under ultrasonic irradiation. The synthesis of chalcones 3_{a-f} were achieved via the condensation of aromatic ketones $\mathbf{l_{a-f}}$ with various aromatic aldehydes $\mathbf{2_{a-f}}$ catalyzed by KOH under ultrasound irradiation [24, 25] (Scheme 1).

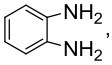
In order to get the optimum conditions in terms of yield and reaction time the impact of several different reaction parameters were studied on the condensation of benzaldehyde and acetophenone as a model reaction. It was found that prolonged reaction time led to increase in polymerization of product and reduced the product yield. Also, it was found that the yield in methanol was higher than other solvents at the same temperature and time [25] (Table 1).

Table1. Effect of different solvent on the reaction of acetophenone with benzaldehyde at different temperature and time.

Compd. No.	Solvent	T (^{o}C)	t (min)	Yield %
1	MeOH	25	20	86
2	MeOH	25	40	85
3	MeOH	25	120	75
4	MeOH	30	20	88
5	MeOH	40	20	87
6	EtOH	25	20	79
7	EtOH	25	40	60
8	EtOH	30	20	80
9	EtOH	40	20	73
10	CH_3CN	25	20	10
11	CH_3CN	25	40	14

Based on the optimized reaction conditions determined above, we carried out the Claisen-Schmidt condensation between aromatic ketone with aromatic aldehydes, under sono-activation at room temperature for 20 min to synthesize the corresponding chalcones 1_{a-f} (Scheme 1).



(i): KOH, MeOH, u.s. (25^{o}C) for 20 min; **(ii):** $CH_2(CN)_2$, $AcONH_4$, H_2O, u. s. (30^{o}C) for 20 min; **(iii):** $AcONH_4$, H_2O, u. s. (30^{o}C) for 25 min; **(iv):** $(NH_2)_2C=S$, KOH, EtOH, (30^{o}C) for 30 min; **(v):** $(NH_2)_2C=S$, KOH, EtOH, (30^{o}C) for 30 min; **(vi):**  , EtOH, (30^{o}C) for 30 min

Scheme 1: Synthesis of compounds 3-6.

Two simple methods are used for synthesis amino-cynopyrimdine derivatives **4**$_{a-c}$ in good yields, under ultrasound irradiation. While one way involved chalcone **3**$_{a-c}$ and malonitrile in the presence of ammonium acetate in water at 30^{o}C for 25min., the other employed one pot three component reaction of **l**$_{a-c}$, aromatic aldehydes **2**$_{a-c}$ and malonitrile at 30^{o}C for 20 min. (scheme 1).

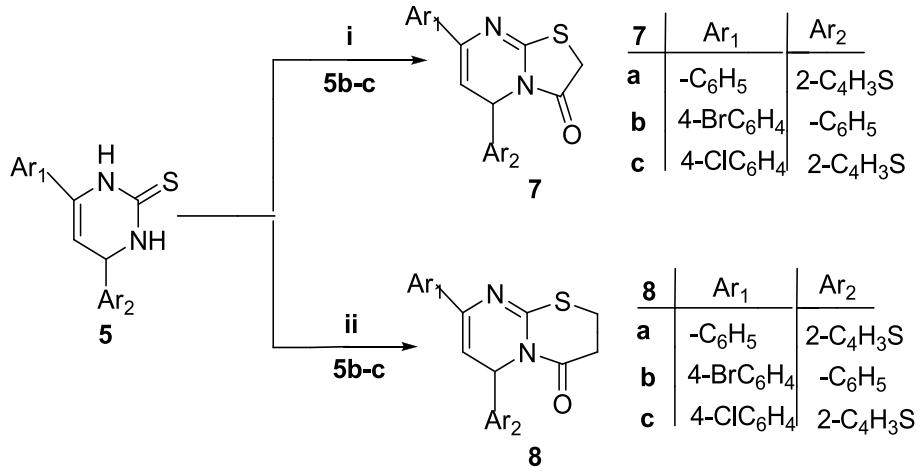
Compounds **4**$_{a-c}$ were confirmed by spectral data. The IR spectrum of **4**$_{a}$ showed a C ≡ N stretching peak at 2220 cm^{-1}. The ^{1}HNMR spectrum displayed abroad singlet at δ8.4 ppm for NH_2. The ^{13}C NMR spectrum showed a line at δ109.12ppm for C ≡ N in addition to absorption of the other sp^3 and sp^2 carbons of molecules (See Experimental).

Pyrimidine 2-thione derivatives **5**$_{a-d}$ were obtained by the reaction of chalcones 3 $_{a-d}$ with thiourea in the presence of potassium hydroxide in ethanol at 30^{o}C for 30 min. The one-pot synthesis of products **5** $_{a-d}$ has been carried via reaction of aromatic ketones **1**$_{a-d}$ with aromatic aldehydes **2** $_{a-d}$ and thiourea at the same conditions (Scheme 1). The structure of compounds **5**$_{a-c}$ were characterized by IR, ^{1}HNMR, ^{13}C NMR and MS.

The ^{1}H-NMR spectrum of compound 5$_{a}$ contained two doublet each integrated for two protons, at 4.86ppm (1H, Ar_2-CH) and at 5.40ppm (1H, Ar_1-C=CH) as well as br. signal at 8.90 ppm for 2NH, beside other protons of the compounds (See Experimental).

The common strategy for the preparation of 1,5-benzodiazepine moiety **6** is cyclo-condesation of *o*-phenylenediamine derivatives with carbonyl compounds [29]. Using the same reaction conditions compounds **3**$_{a,b}$were reacted with *o*-phenylenediamine under ultrasonic irradiation to afford the corresponding 2,4-diaryl benzo [b] [1,4] diazepine derivatives in yields ranging from 85-87% [29-31] (Scheme 1).

The IR spectrum of **6**$_{b}$ showed the absence of the peak of C=O and the appearance of NH stretching at 3370 cm^{-1}. The ^{13}C NMR spectrum of showed absorption at δ 34.97 ppm for (C - 3), at δ 67.75ppm for (C-2) and at δ167.11 ppm for (C-4), beside the other lines of sp^3 and sp^2 carbons of the molecules (See Experimental).



(i): CH_2COOH, $AcONH_4$, AcOH, u. s. (50^{o}C) for 35 min;
(ii): $BrCH_2CH_2COOH$, $AcONH_4$, AcOH, u. s. (50^{o}C) for 30 min

Scheme 2: Synthesis of compounds 7 & 8.

Furthermore, treatment of the thiopyrimidine derivatives**5**$_{b-d}$ with choloroacetic acid in glacial acetic acid in presence of excess anhydrous sodium acetate under ultrasonic irradiation afforded the thiazolopyrimidine derivatives 7$_{a-c}$ in good yields. (Scheme 2).

The chemical structures were proved by IR, ^{1}H-NMR, ^{13}C NMR and MS.

The IR spectrum of 7$_{a}$ showed the disappearance of NH and C = S stretching bands and the appearance of C = O stretching band at1720 cm^{-1}. The ^{13}C NMR spectrum of showed a lines at 32.40 and 59.31 ppm for (C- 2) and (C- 5) respectively, and at 175.30 ppm for C = O in addition to absorption of the other sp^3 and sp^2 carbons of the molecules (See Experimental).

Finally, compounds 5$_{b-d}$ were reacted with 3--bromopropionic acid catalyzed by glacial acetic acid

in the presence of excess anhydrous sodium acetate under ultrasonic irradiation at 50°C within 30 min to give pyrimido [2,1-b] thiazino derivatives $\mathbf{8_{a-c}}$.

The structure of $\mathbf{8_{a-c}}$ were supported by Spectral data. Thus, the IR spectrum of $\mathbf{8_b}$ showed a C = O stretching peak at 1680 cm^{-1}. The ^{1}H-NMR, spectrum of showed a multiplet at δ2.1-3.7 ppm for the two methylene groups at position 2 and 3 beside the other aliphatic and aromatic protons of the molecule (See Experimental).

4-Conclusion

In conclusion, we have developed an efficient procedure for synthesis chalcones and some of its derivatives under ultrasonic irradiation in excellent yield. There are several advantages to the current methodology, including shorten reaction time, milder conditions, and higher yields.

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