





Ultrasound-Assisted One Pot Synthesis of Novel 5-(1-(Substituted phenyl)-4,5-diphenyl-1H-imidazol-2-yl)-4-methylthiazole ⁺

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- + Presented at the 22nd International Electronic Conference on Synthetic Organic Chemistry, 15 November– 15 December 2018; Available Online: https://sciforum.net/conference/ecsoc-22.

Published: 14 November 2018

Abstract: This work reports synthesis of ten novel derivatives of 5-(1-(substituted phenyl)-4,5-diphenyl-1H-imidazol-2-yl)-4-methylthiazole **5**(**a**–**o**). The reaction of benzil, primary aryl amines, 4-methylthiazole-5-carbaldehyde and ammonium acetate was carried out in one pot in the presence of eco-friendly catalyst Ceric ammonium nitrate in solvent ethanol to give final compounds. The structures of the synthesized compounds were confirmed by spectral characterization such as IR, ¹H-NMR, ¹³C-NMR and mass spectral studies.

Keywords: imidazole; green chemistry; ultrasound; CAN; multicomponent reaction

1. Introduction

Imidazole is a privileged fragment in modern medicinal chemistry considering its broad spectrum and affinity towards various biological targets, especially as an antifungal agent [1,2].

The synthesis of organic molecules through multicomponent reactions (MCRs) is a fascinating area of research [3–9], because they are the significant basis of automated and high throughput synthesis, molecular diversity and empowering rapid generation of organic molecules. MCRs are distinct as reactions that materialize in one reaction vessel (one pot) having more than two starting reactants to form a single product [10,11]. MCRs on numerous occasions are an effective alternative to multistep sequential synthesis for instance, they show a high degree of atom efficiency as the maximum if not all of the atoms of the starting reactants are transformed in to the product [12,13]. They are convergent as a number of starting reactants combine in one step reaction to form the target molecules, they are having a higher degree of efficiency since the product formation takes place in one-step, in place of multiple sequential steps, bond formation between several atoms other than hydrogen atoms takes place in one synthetic step, therefore they display extremely high bond-forming-index (BFI) [14–18].There is still a need of general awareness among synthetic chemists that MCRs are undeniably able to deal with delicate chemical problems in an environmentally friendly manner. This work thus aims to explore the scope and opportunities which the utilization of MCRs can bring to eco-friendly green synthesis and process design.

The shortcomings associated with existing methods of organic synthesis reported for the imidazole derivatives, by a conventional method like stirring at room temperature, and by refluxing,

required several hours for the completion of reaction with a much lower amount of product yield and higher consumption of solvents, time and electricity. Green chemistry is a new branch of chemistry which has become a major motivation for organic chemists and druggists to develop environmentally gentle path for the synthesis of organic compounds of biological importance.

The use of ultrasound to promote chemical reactions is called sono-chemistry. Ultrasonicassisted organic synthesis (UAOS) is a green synthetic approach and it is a powerful technique to support an increase in reaction rate [19–21]. It can also be considered as important tool for conservation of energy and minimization of waste as compared to the conventional techniques [22,23]. This research work is introducing ultrasound- promoted synthesis of thiazolinedin-4-one derivative from the readily available starting materials under mild and selective conditions.

In this research work we are reporting the synthesis of 5-(1-(substituted phenyl)-4,5-diphenyl-1H-imidazol-2-yl)-4-methylthiazole **5**(**a**–**o**) derivatives in excellent yield using eco- friendly, prompt and suitable ultrasound-assisted green chemistry protocol.

2. Results and Discussion

Chemistry

Herein, we are reporting the synthesis 5-(1-(substituted phenyl)-4,5-diphenyl-1H-imidazol-2-yl)-4-methylthiazole **5**(**a**–**o**) as illustrated in Figure 1.



Figure 1. One pot synthesis of 5-(1-(substituted phenyl)-4,5-diphenyl-1H-imidazol-2-yl)-4-methylthiazole **5**(**a**-**o**).

A mixture of benzil (0.01 mol), 4-methylthiazole-5-carbaldehyde (0.01 mol), primary aryl amines (0.01 mol), ammonium acetate (0.01 mol) and cerric ammonium nitrate (15 mol %) as an eco-friendly catalyst was dissolved in solvent ethanol (5 mL) was subjected to ultra-sonication at room temperature. The obtained products 5(a-j) were recrystallized from ethanol and were obtained in better yields. Synthesis by a conventional method like reflexing required 3–4 h for the completion of reaction; whereas by using green chemistry tool like ultra-sonication the time of synthesis was reduced to 25 min to 35 min. The physical characterization is as shown in Table 1.

The synthesis of all derivatives of 5-(1-(substituted phenyl)-4,5-diphenyl-1H-imidazol-2-yl)-4methylthiazole 5(a-o) was carried out by refluxing and ultrasonic irradiation methods for comparison of conventional and modern green chemistry tool using ultra-sonication. The time required for completion of reaction with yield in percent is mentioned in Table 2.

Synthesis of 5-(1-(substituted phenyl)-4,5-diphenyl-1H-imidazol-2-yl)-4-methylthiazole **5**(**a**–**o**) derivatives was carried out by green protocol in excellent yield with 87% to 90% by one pot, four component reaction of benzil, 4-methylthiazole-5-carbaldehyde, primary aryl amines, and ammonium acetate in presence catalyst cerric ammonium nitrate in benign solvent ethanol by eco-friendly, rapid and suitable ultrasound-promoted green chemistry protocol. The structures of the synthesized compounds 5(**a**–**o**) were confirmed on the basis of their respective spectral data like IR, mass, ¹H-NMR, ¹³C-NMR spectra and elemental analysis.

Compound	Ar	Mol. Formula	Mol. Weight	% Yield	M.P. (°C)
5a	Phenyl	C25H19N3S	393.50	88	202-204
5b	4-Chlorophenyl	C25H18ClN3S	427.95	89	252-254
5c	4-Bromophenyl	C25H18BrN3S	472.40	90	254-256
5d	4-Nitrophenyl	$C_{25}H_{18}N_4O_2S$	438.50	89	225-228
5e	2-Methylphenyl	C26H21N3S	407.53	87	214-216
5f	4-Methylphenyl	C26H21N3S	407.53	88	210-212
5g	2-Methoxyphenyl	$C_{26}H_{21}N_3OS$	423.53	89	228-230
5h	4-Methoxyphenyl	$C_{26}H_{21}N_3OS$	423.53	89	232-234
5i	2,4 -Dichlorophenyl	$C_{25}H_{17}Cl_2N_3S$	462.39	89	256-258
5j	2,4-Dimethylphenyl	C27H23N3S	421.56	90	200-202
5k	2,4-Dinitrophenyl	$C_{25}H_{17}N_5O_4S$	483.50	87	218-220
51	4-Chloro-2-nitrophenyl	$C_{25}H_{17}ClN_4O_2S$	472.95	86	232-234
5m	2,6-Dichloro-4-nitrophenyl	$C_{25}H_{16}Cl_2N_4O_2S$	507.39	88	234-236
5n	Benzyl	C26H21N3S	407.53	90	220-222
50	Naphthalen-1-yl	C29H21N3S	443.56	87	210-212

Table 1. Physical characterization of 5-(1-(substituted phenyl)-4,5-diphenyl-1H-imidazol-2-yl)-4-methylthiazole **5**(**a**–**o**).

Table 2. Comparison of reaction kinetics of conventional refluxing and ultrasonic irradiation methods for the synthesized compounds **5**(**a**–**o**).

Entry	Conventional Refluxing		Ultrasonic Irradiation		
	Time (min)	Yield (%)	Time (min)	Yield (%)	
5a	240.00	72	30	88	
5b	180.00	62	25	89	
5c	230.00	74	25	90	
5d	240.00	71	30	89	
5e	230.00	73	30	87	
5f	200.00	65	30	88	
5g	230.00	67	35	89	
5h	190.00	68	35	89	
5i	220.00	66	30	89	
5j	240.00	69	25	90	
5k	240.00	71	35	87	
51	195.00	77	35	86	
5m	200.00	78	35	88	
5n	225.00	69	30	90	
50	235.00	65	35	87	

3. Materials and Methods

General Information

All the reactions were performed in oven-dried glass wares. All the chemicals used for synthesis were procured from Merck (Mumbai, Maharashtra, India), Sigma (Mumbai), HiMedia (Mumbai) or Qualigens (Mumbai) and used without further purification. The ultrasound sonicator (Sonics Vibracell, Model No. VCX 500, Newtown, CT, USA) equipped with solid synthetic probe, 13 mm in tip diameter, operating at 20 kHz with a maximum power output of 500 W, was used for synthesis of final title compounds. The progress of each reaction was monitored by ascending thin layer chromatography (TLC) using pre-coated silica gel F254 aluminum TLC sheets (Merck) and the spots were visualized by UV light and iodine vapors. Elemental analyses (C, H, and N) was done with a FLASHEA 112 Shimadzu'analyzer (Mumbai) and all analyses were consistent (within 0.4%) with

theoretical values. Infrared (IR) spectra were recorded on a PS 4000 FTIR (JASCO, Tokyo, Japan) using KBr pellets. ¹H and ¹³C-NMR spectra were recorded on a Avance 400 spectrometer (Bruker, Billerica, MA, USA) fitted with an Aspect 3000 computer and all the chemical shifts (ppm) were referred to internal TMS for ¹H and DMSO-*d*₆ for ¹³C-NMR. ¹H-NMR data are reported in the order of chemical shift, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; br, broad; br s, broad singlet; m, multiplet and/or multiple resonance) and number of protons. A Micro TOF-Q-II (Bruker Daltonics, Billerica, MA, USA with electron spray ionization (ESI) was used to obtain the HRMS data.

4. Experimental Section

General procedure for the synthesis of 5-(1-(substituted phenyl)-4,5-diphenyl-1H-imidazol-2-yl)-4-methylthiazole **5**(**a**-**o**).

In a borosil beaker, a mixture of benzil (0.01 mol), 4-methylthiazole-5-carbaldehyde (0.01 mol), primary aryl amines (0.01 mol), ammonium acetate (0.01 mol) and Ceric ammonium nitrate (15 mol %) as an eco-friendly catalyst was dissolved in solvent ethanol (5 m1) and the beaker was kept in an acoustic chamber. The solid probe of ultrasound was lowered down in the beaker so as to immersed in the solvent and subjected to ultra-sonication at room temperature for 25 min to 35 min. The completion of reaction was monitored by TLC. After completion of reaction, the mixture poured into ice-water mixture. The solid precipitate product was filtered dried. The crude product was purified by recrystallization from ethanol. Solvent system chosen determination was n-hexane: ethyl acetate (4:1). The products were obtained in good yield (88% 92%). The physical characterization data of the synthesized compounds 5-(1-(substituted phenyl)-4,5-diphenyl-1H-imidazol-2-yl)-4-methylthiazole 5(a–o) is as shown in Table 1.

Structures of the synthesized derivatives **5**(**a**–**o**) were confirmed by spectral studies as reported below:

4-Methyl-5-(1,4,5-triphenyl-1H-imidazol-2-yl) thiazole 5a:

IR (KBr) ν_{max} (cm⁻¹): 3155 CH stretching, 1601 C=C stretching, 1580 C=N stretching; ¹H-NMR(DMSO-*d*₆), δ ppm: 3.12 (s, 3H, –CH₃ of thiazole ring), 7.51–7.85 (m, 5H, 5H, 5H of aromatic rings), 8.99 (s, 1H of thiazole ring); ¹³C-NMR(DMSO-*d*₆), δ ppm: 12.6, 114.5, 122.4(2), 127.6(4), 128.9(4), 129.1(4), 129.8(2), 131.5, 133.9, 138.3(2), 142.6, 150.7 and 152.4; MS (ESI) *m*/*z*: 395.13 [M + 2]⁺; Molecular Formula: C₂₅H₁₉N₃S; Elemental Analysis: Calculated (C, H, N, S) 76.31, 4.87, 10.68, 8.15. Found: 75.69, 5.01, 11.23, 9.75.

5-(1-(4-Chlorophenyl)-4,5-diphenyl-1H-imidazol-2-yl)-4-methylthiazole **5b**:

IR (KBr) v_{max} (cm⁻¹): 3150 CH stretching, 1600 C=C stretching, 1580 C=N stretching, 699 C–Cl stretching; ¹H-NMR(DMSO-*d*₆), δ ppm: 3.10 (s,3H, –CH₃ of thiazole ring), 6.65–8.10 (m, 4H, 5H, 5H of aromatic rings), 8.85 (s, 1H of thiazole ring); ¹³C-NMR(DMSO-*d*₆), δ ppm: 11.93, 111.63, 125.31(2), 127.81(4), 128.5, 128.12, 128.71, 129.18, 129.65, 129.74, 129.87, 130.93(2), 131.43, 133.28(2), 136.34, 138.90(2), 145.55, and 161.36; MS (ESI) *m/z*: 431.72 [M + 4]+; Molecular Formula: C₂₅H₁₈ClN₃S; Elemental Analysis: Calculated (C, H, Cl, N, S) 70.16, 4.24, 8.28, 9.82, 7.49. Found: 71.21, 5.47, 7.98, 10.01, 8.12.

5-(1-(4-Bromophenyl)-4,5-diphenyl-1H-imidazol-2-yl)-4-methylthiazole 5c:

IR (KBr) ν_{max} (cm⁻¹): 3100 CH stretching, 1607 C=C stretching, 1580 C=N stretching, 680 C–Br stretching; ¹H-NMR(DMSO-*d*₆), δ ppm: 3.15 (s, 3H,–CH₃ of thiazole ring), 7.52–7.84 (m, 4H, 5H, 5H of aromatic rings), 8.94 (s, 1H of thiazole ring); ¹³C-NMR(DMSO-*d*₆), δ ppm: 13.2, 115.2, 122.1, 125.2(2), 127.3(4), 128.5(3), 129.1(4), 130.7, 132.9(2), 133.2, 137.4, 139.2, 143.5, 151.7 and 152.5; MS (ESI) *m/z*: 476.04 [M + 4]⁺; Molecular Formula: C₂₅H₁₈BrN₃S; Elemental Analysis: Calculated (C, H, Br, N, S) 63.56, 3.84, 16.91, 8.90, 6.79. Found: 62.93, 3.55, 17.44, 9.14, 7.78.

4-Methyl-5-(1-(4-nitrophenyl)-4,5-diphenyl-1H-imidazol-2-yl) thiazole 5d:

IR (KBr) ν_{max} (cm⁻¹): 3102 CH stretching, 1605 C=C stretching, 1581 C=N stretching; ¹H-NMR(DMSO-*d*₆), δ ppm: 2.99 (s, 3H, –CH₃ of thiazole ring), 7.55–8.68 (m, 4H, 5H, 5H of aromatic rings), 8.98 (s, 1H of thiazole ring); ¹³C-NMR(DMSO-*d*₆), δ ppm: 12.9, 113.8, 121.9(2), 123.5(2), 126.7(4), 127.9(2), 128.8(4),

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130.5, 133.4, 138.6(2), 142.8, 145.2, 147.7, 149.9 and 153.1; MS (ESI) *m*/*z*: 440.12 [M + 2]⁺; Molecular Formula: C₂₅H₁₈N₄O₂S; Elemental Analysis: Calculated (C, H, N, S) 68.48, 4.14, 12.78, 7.31. Found: 69.17, 5.52, 13.44, 8.75.

5-(4,5-Diphenyl-1-o-tolyl-1H-imidazol-2-yl)-4-methylthiazole **5e**:

IR (KBr) ν_{max} (cm⁻¹): 3100 CH stretching, 1602 C=C stretching, 1580 C=N stretching; ¹H-NMR(DMSO-*d*₆), δ ppm: 2.03 (s, 3H,–CH₃ of aromatic ring), 2.98 (s, 3H,–CH₃ of thiazole ring), 7.53–7.87 (m, 4H, 5H, 5H of aromatic rings), 8.93 (s, 1H of thiazole ring); ¹³C-NMR(DMSO-*d*₆), δ ppm: 13.2, 17.5, 113.7, 121.0, 125.6(2), 126.7(4), 127.9(2), 130.2(4), 131.8, 132.7(2), 134.0, 138.8, 139.2, 139.7, 143.3, 151.1 and 153.6; MS (ESI) *m*/*z*: 409.15 [M + 2]⁺; Molecular Formula: C₂₆H₂₁N₃S; Elemental Analysis: Calculated (C, H, N, S) 76.63, 5.19, 10.31, 7.87. Found: 77.32, 6.45, 11.24, 8.12.

5-(4,5-Diphenyl-1-p-tolyl-1H-imidazol-2-yl)-4-methylthiazole **5f**:

IR (KBr) v_{max} (cm⁻¹): 3100 CH stretching, 1604 C=C stretching, 1581 C=N stretching; ¹H-NMR(DMSO-*d*₆), δ ppm: 2.54 (s, 3H,–CH₃ of aromatic ring), 2.88 (s, 3H,–CH₃ of thiazole ring), 7.56–7.89 (m, 4H, 5H, 5H of aromatic rings), 8.87 (s, 1H of thiazole ring); ¹³C-NMR(DMSO-*d*₆), δ ppm: 13.4, 22.3, 115.1, 124.5(2), 126.9(4), 128.3(2), 129.6(4), 130.4(2), 131.7, 134.2, 136.3, 137.4, 138.5(2), 143.6, 151.8 and 153.2; MS (ESI) *m*/*z*: 409.15 [M + 2]⁺; Molecular Formula: C₂₆H₂₁N₃S; Elemental Analysis: Calculated (C, H, N, S) 76.63, 5.19, 10.31, 7.87. Found: 77.24, 6.02, 11.14, 8.36.

5-(1-(2-Methoxyphenyl)-4,5-diphenyl-1H-imidazol-2-yl)-4-methylthiazole 5g:

IR (KBr) ν_{max} (cm⁻¹): 3101 CH stretching, 1600 C=C stretching, 1565 C=N stretching; ¹H-NMR(DMSO-*d*₆), δ ppm: 3.07 (s, 3H,–CH₃ of thiazole ring), 4.11 (s, 3H, –OCH₃), 7.53–7.80 (m, 4H, 5H, 5H of aromatic rings), 8.88 (s, 1H of thiazole ring); ¹³C-NMR(DMSO-*d*₆), δ ppm: 13.5, 56.8, 113.5, 115.9, 118.7, 122.9, 125.7, 128.5(4), 128.9(2), 129.5(5), 131.2, 133.8, 138.4(2), 143.2, 151.6, 153.2 and 158.1; MS (ESI) *m*/*z*: 425.14 [M + 2]⁺; Molecular Formula: C₂₆H₂₁N₃OS; Elemental Analysis: Calculated (C, H, N, S) 73.73, 5.00, 9.92, 7.57. Found: 74.55, 6.12, 10.22, 8.14.

5-(1-(4-Methoxyphenyl)-4,5-diphenyl-1H-imidazol-2-yl)-4-methylthiazole **5h**:

IR (KBr) v_{max} (cm⁻¹): 3107 CH stretching, 1605 C=C stretching, 1580 C=N stretching; ¹H-NMR(DMSO-*d*₆), δ ppm: 2.95 (s, 3H,–CH₃ of thiazole ring), 3.68 (s, 3H, –OCH₃), 6.64–7.94 (m, 4H, 5H, 5H of aromatic rings), 7.95 (s, 1H of thiazole ring); ¹³C-NMR(DMSO-*d*₆), δ ppm: 13.33, 55.39, 111.63, 114.33(2), 125.33(2), 126.60(2), 128.07, 128.12, 128.71, 129.18, 129.65, 129.74, 129.87, 130.93(4), 131.43(2), 136.34, 145.55, 161.15 and 161.36; MS (ESI) *m/z*: 425.72 [M + 2]⁺; Molecular Formula: C₂₆H₂₁N₃OS; Elemental Analysis: Calculated (C, H, N, S) 73.73, 5.00, 9.92, 7.57. Found: 74.85, 6.14, 10.34, 8.12.

5-(1-(2,4-Dichlorophenyl)-4,5-diphenyl-1H-imidazol-2-yl)-4-methylthiazole 5i:

IR (KBr) v_{max} (cm⁻¹): 3158 CH stretching, 1606 C=C stretching, 1587 C=N stretching, 701 C–Cl stretching; ¹H-NMR(DMSO-*d*₆), δ ppm: 3.19 (s, 3H,–CH₃ of thiazole ring), 7.45–7.81 (m, 3H, 5H, 5H of aromatic rings), 8.91 (s, 1H of thiazole ring); ¹³C-NMR(DMSO-*d*₆), δ ppm: 13.8, 113.4, 15.2, 126.8(4), 127.5, 128.9(2), 129.7(4), 131.5, 132.1, 134.6, 136.2(2), 138.1(2), 139.2, 141.5, 151.4 and 153.7; MS (ESI) *m*/*z*: 468.05 [M + 6]⁺; Molecular Formula: C₂₅H₁₇C₁₂N₃S; Elemental Analysis: Calculated (C, H, Cl, N, S) 64.94, 3.71, 15.33, 9.09, 6.93. Found: 65.11, 4.58, 16.47, 10.25, 7.12.

5-(1-(2,4-Dimethylphenyl)-4,5-diphenyl-1H-imidazol-2-yl)-4-methylthiazole **5***j*:

IR (KBr) ν_{max} (cm⁻¹): 3161 CH stretching, 1612 C=C stretching, 1589 C=N stretching; ¹H-NMR(DMSO-*d*₆), δ ppm: 1.99 (s, 3H,–CH₃ of Ar. ring), 2.54 (s, 3H,–CH₃ of Ar. ring), 3.11 (s, 3H,–CH₃ of thiazole ring), 7.58–7.87 (m, 3H, 5H, 5H of aromatic rings), 8.87 (s, 1H of thiazole ring); ¹³C-NMR(DMSO-*d*₆), δ ppm: 11.9, 20.6, 23.8, 115.1, 126.7(4), 128.2(2), 129.8(4), 131.2, 132.4(2), 133.3, 134.9, 136.2, 138.3(2), 139.4, 143.5, 144.1, 151.9 and 153.5; MS (ESI) *m/z*: 423.16 [M + 2]+; Molecular Formula: C₂₇H₂₃N₃S; Elemental Analysis: Calculated (C, H, N, S) 76.93, 5.50, 9.97, 7.61. Found: 77.14, 6.98, 10.54, 8.57.

5-(1-(2,4-Dinitrophenyl)-4,5-diphenyl-1H-imidazol-2-yl)-4-methylthiazole **5k**:

IR (KBr) ν_{max} (cm⁻¹): 3112 CH stretching, 1614 C=C stretching, 1592 C=N stretching; ¹H-NMR(DMSO-*d*₆), δ ppm: 3.07 (s, 3H,–CH₃ of thiazole ring), 7.58–8.99 (m, 3H, 5H, 5H of aromatic rings), 9.08 (s, 1H of thiazole ring); ¹³C-NMR(DMSO-*d*₆), δ ppm: 13.4, 113.7, 121.2, 126.8(4), 128.7(2), 130.1(4), 130.8, 131.5(2), 133.7(2), 138.6(2), 142.9, 145.2, 149.3, 151.9 and 153.4; MS (ESI) *m*/*z*: 485.10 [M + 2]⁺; Molecular Formula: C₂₅H₁₇N₅O₄S; Elemental Analysis: Calculated (C, H, N, S) 62.10, 3.54, 14.48, 6.63. Found: 63.02, 4.21, 15.18, 7.98.

5-(1-(4-Chloro-2-nitrophenyl)-4,5-diphenyl-1H-imidazol-2-yl)-4-methylthiazole 51:

IR (KBr) ν_{max} (cm⁻¹): 3145 CH stretching, 1609 C=C stretching, 1586 C=N stretching, 705 C–Cl stretching; ¹H-NMR(DMSO-*d*₆), δ ppm: 2.95 (s, 3H,–CH₃ of thiazole ring), 7.51–8.68 (3H, 5H, 5H of aromatic rings), 8.89 (s, 1H of thiazole ring); ¹³C-NMR(DMSO-*d*₆), δ ppm: 12.9, 114.5, 123.6, 125.7(2), 126.5(4), 127.9(2), 128.7(4), 130.4, 134.2(2), 135.6, 138.4(2), 141.6, 143.5, 151.8 and 153.1; MS (ESI) *m*/*z*: 476.07 [M + 4]⁺; Molecular Formula: C₂₅H₁₇ClN₄O₂S; Elemental Analysis: Calculated (C, H, Cl, N, S) 63.49, 3.62, 7.50, 11.85, 6.78. Found: 64.57, 4.45, 8.71, 12.44, 7.54.

5-(1-(2,6-Dichloro-4-nitrophenyl)-4,5-diphenyl-1H-imidazol-2-yl)-4-methylthiazole 5m:

IR (KBr) v_{max} (cm⁻¹): 3156 CH stretching, 1604 C=C stretching, 1585 C=N stretching, 698 C–Cl stretching; ¹H-NMR(DMSO-*d*₆), δ ppm: 3.11 (s, 3H,–CH₃ of thiazole ring), 7.37–8.19 (m, 2H, 5H, 5H of aromatic rings), 8.95 (s, 1H of thiazole ring); ¹³C-NMR(DMSO-*d*₆), δ ppm: 13.1, 115.4, 124.3(2), 128.2(4), 129.4(2), 130.1(4), 132.8, 134.5, 138.2(2), 138.6(2), 141.5, 143.8, 148.4, 151.7 and 153.9; MS (ESI) *m*/*z*: 513.04 [M + 6]⁺; Molecular Formula: C₂₅H₁₆Cl₂N₄O₂S; Elemental Analysis: Calculated (C, H, Cl, N, S) 59.18, 3.18, 13.97, 11.04, 6.32. Found: 60.11, 4.54, 14.21, 12.75, 7.30.

5-(1-Benzyl-4,5-diphenyl-1H-imidazol-2-yl)-4-methylthiazole 5n:

IR (KBr) ν_{max} (cm⁻¹): 3158 CH stretching, 1607 C=C stretching, 1587 C=N stretching; ¹H-NMR(DMSO-*d*₆), δ ppm: 3.04 (s, 3H,–CH₃ of thiazole ring), 5.87 (s, 2H, –CH2 of benzyl ring), 7.52–7.83 (m, 5H, 5H, 5H of aromatic rings), 8.99 (s, 1H of thiazole ring); ¹³C-NMR(DMSO-*d*₆), δ ppm: 13.5, 48.2, 115.4, 125.3, 127.1(4), 127.8(2), 128.5(4), 129.7(4), 130.2, 133.3, 138.4, 139.2, 142.3, 145.9, 151.4 and 153.7; MS (ESI) *m*/*z*: 408.15 [M + 2]⁺; Molecular Formula: C₂₆H₂₁N₃S; Elemental Analysis: Calculated (C, H, N, S) 76.63, 5.19, 10.31, 7.87. Found: 77.24, 6.35, 11.23, 8.28.

4-Methyl-5-(1-(naphthalen-1-yl)-4,5-diphenyl-1H-imidazol-2-yl) thiazole 50:

IR (KBr) v_{max} (cm⁻¹): 3151 CH stretching, 1609 C=C stretching, 1588 C=N stretching; ¹H-NMR(DMSO-*d*₆), δ ppm: 3.02 (s, 3H,–CH₃ of thiazole ring), 7.58–8.15 (m, 5H, 5H, 7H of aromatic rings), 8.89 (s, 1H of thiazole ring); ¹³C-NMR(DMSO-*d*₆), δ ppm: 13.6, 115.3, 124.8, 126.1(2), 126.5, 127.3, 127.5(3), 127.9(2), 128.5(4), 129.6(4), 130.3, 131.2, 133.4, 135.6, 138.1, 138.9, 143.2, 151.6 and 153.4; MS (ESI) *m*/*z*: 444.15 [M + 2]⁺; Molecular Formula: C₂₉H₂₁N₃S; Elemental Analysis: Calculated (C, H, N, S) 78.53, 4.77, 9.47, 7.23. Found: 79.31, 5.47, 10.25, 8.45.

5. Conclusions

In conclusion, a novel series of 5-(1-(substituted phenyl)-4,5-diphenyl-1H-imidazol-2-yl)-4methylthiazole **5(a–o)** was obtained using green synthetic tool like ultra-sonication. The use of green method i.e., use of ultra-sonication as a green synthetic strategy shows certain benefits over conventional refluxing as follows: (1) reactions required much less time for completion and were carried at room temperature (2) rate of reaction enhanced (3) the use of a significantly lower amount of solvent ethanol (5) ecofriendly, as the reactions are carried out in closed acoustic chamber (6) a shortened and clean work-up procedure. The potential of 5-(1-(substituted phenyl)-4,5-diphenyl-1Himidazol-2-yl)-4-methylthiazole can be developed as an antimicrobial agent and can be expected to act as an excellent scaffold for lead optimization and drug discovery. Acknowledgments: The authors are thankful to the Fatima Rafiq Zakaria Chairman Maulana Azad Educational. Trust, Principal Maulana Azad Postgraduate & Research Centre, Aurangabad and Zahid Zaheer, Principal, Y.B. Chavan College of Pharmacy, Rafiq Zakaria Campus, Aurangabad 431 001 (M.S.), India for providing the laboratory facility. UDN is very much thankful to Babasaheb Ambedkar Research and Training Institute (BARTI), Pune for Financial Support.

References

- 1. Kathiravan, M.K.; Salake, A.B.; Chothe, A.S.; Dudhe, P.B.; Watode, R.P.; Mukta, M.S.; Gadhwe, S. The biology and chemistry of antifungal agents: A review. *Bioorg. Med. Chem.* **2012**, *20*, 5678–5698.
- 2. Zhai, B.; Lin, X.R. Recent Progress on Antifungal Drug Development. Curr. Pharm. Biotechnol. 2011, 12, 1255.
- 3. Akritopoulou-Zanze, I. Isocyanide-based multicomponent reactions in drug discovery. *Curr. Opin. Chem. Biol.* **2008**, *12*, 324–331.
- 4. Moos, W.H.; Hurt, C.R.; Morales, G.A. Combinatorial chemistry: Oh what a decade or two can do. *Mol. Divers.* **2009**, *13*, 241–245.
- 5. Kalinski, C.; Umkehrer, M.; Weber, L.; Kolb, J.; Burdack, C.; Ross, G. On the industrial applications of MCRs: molecular diversity in drug discovery and generic drug synthesis. *Mol. Divers.* **2010**, *14*, 513–522.
- 6. Domling, A.; Wang, W.; Wang, K. Chemistry and biology of multicomponent reactions. *Chem. Rev.* **2012**, *112*, 3083–3135.
- 7. Magedov, I.V.; Kornienko, A. Multicomponent reactions in alkaloid-based drug discovery. *Chem. Heterocycl. Compd.* **2012**, *48*, 33–38.
- 8. Slobbe, P.; Ruijter, E.; Orru, R.V.A.Recent application of multicomponent reaction in medicinal chemistry. *Med. Chem. Commun.* **2012**, *3*, 1189–1218.
- 9. Ruijter, E.; Orru, R.V.A. Multicomponent reactions opportunities for the pharmaceutical industry. *Drug Discov. Today Technol.* **2013**, *10*, 15–20.
- 10. Domling, A. Recent developments in isocyanide based multicomponent reactions in applied chemistry. *Chem. Rev.* **2006**, *106*, 17–89.
- 11. Hulme, C.; Gore, V. Multi-Component Reactions: Emerging Chemistry in Drug Discovery from Xylocain to Crixivan. *Curr. Med. Chem.* **2003**, *10*, 51–80.
- 12. Brauch, S.; Van Berkel, S.S.; Westermann, B. Higher-order multicomponent reactions: beyond four reactants. *Chem. Soc. Rev.* 2013, 42, 4948–4962.
- 13. Zhu, J.; Bienayme, H. Multicomponent Reactions; Wiley-VCH: Weinheim, Germany, 2005.
- 14. Andraos, Unification of Reaction Metrics for Green Chemistry II: Evaluation of Named Organic Reactions and Application to Reaction Discovery. J. Org. Process Res. Dev. 2005, 9, 404–431.
- 15. Da Silva, E.N. Multicomponent reactions as a green approach. Res. J. Chem. Environ. 2007, 11, 90–91.
- 16. Zhu, J.; Wang, Q.; Wang, M.X. *Handbook of Green Chemistry*; Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, Germany, 2010.
- 17. Huang, Y.; Yazbak, A.; Domling, A. *Green Techniques for Organic Synthesis and Medicinal Chemistry*; John Wiley & Sons, Ltd.: Chichester, UK, 2012; pp. 497–522.
- 18. Andraos, J. On the probability that ring-forming multicomponent reaction are intrinsically green: Setting thresholds for intrinsic greennerss based on design strategy and experimental reaction performance. *ACS Sustain. Chem. Eng.* **2013**, *1*, 496–512.
- 19. Lindley, J.; Lorimer, J.P.; Mason, T.J. Enhancement of an Ullmann coupling reaction induced by ultrasound. *Ultrasonics* **1986**, *24*, 292–293.
- 20. Bang, K.; Lee, K.; Park, Y.K.; Lee, P.H. Sonochemical Reformatsky reaction using indium. *Bull. Korean Chem. Soc.* **2002**, *23*, 1272–1276.
- 21. Lee, P.H. Indium and gallium-mediated addition reactions. Bull. Korean Chem. Soc. 2007, 28, 17–28.
- 22. Saleh, T.S.; Abd EL-Rahman, N.M. Ultrasound promoted synthesis of substituted pyrazoles and isoxazoles containing sulphone moiety. *Ultrason Sonochem*. **2009**, *16*, 237–242.
- 23. Nikalje, A.G.; Shaikh, S.I. Ultrasound-promoted synthesis of indole appended Heyerocycles. *World J. Pharmacy Pharm. Sci.* **2014**, *3*, 1282–1302.



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