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One-Pot Synthesis of Thiazoles *via* Hantzsch Thiazole Reaction and Their Antimicrobial Activity

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In this work, substituted 2-bromo-1-phenylethanone compounds (**1a-c**) synthesized by reaction of bromine and various subtituted acetophenone. Compounds (**1a-c**) treated with thiosemicarbazide and several carbonyl species to gave corresponding substituted 4-phenyl-1,3-thiazole derivatives (**2a-c to 6a-c**) *via* multicomponent reaction and Hantzsch thiazole synthesis. All the synthesized compound tested for their antimicrobial activity.

Keywords: Hantzsch thiazole synthesis, Pyrazolone, Thiazolidione, Isatine.

INTRODUCTION

Nitrogen and sulfur containing nucleus have played a crucial part in the history of heterocyclic chemistry and also been used extensively as important synthons in organic synthesis. Owing to the versatile medicinal activities of azoles, a significant amount of research activity has been directed towards this class. Thiazole linked molecule have a broad spectrum of pharmacological activities, such as antiinflammatory [1], antihypertensive properties [2], antibacterial [3], antifungal [4] and as well as being used as cystic fibrosis transmembrane conductance regulator [5] (CFTR). Thiazolidinediones nucleus play important role in antihyperglycemic activity [6], anti-HIV activity [7], antihyperglycemic activity [8] and peroxisome proliferator activated receptors (PPARs) activity [9]. Isatine containing candidates are important classes of nitrogen containing heterocycles and they constitute useful intermediates in organic synthesis [10]. They have been discovered for their applications in dyes, building blocks for the synthesis of organic semiconductors and medicinal functions such as antioxidant properties [11]. The furan derivatives has attracted much attention in recent studies due to their biological evaluation such as neuroprotection [12], oxytocin antagonism [13], antioxidant, anti-inflammatory, antibacterial [14], β-aggregate specific effect for Alzheimer's disease treatment [15], cholinesterase inhibition [16], H-3 receptor antagonism with dyes function improvement [17], anticonvulsant [18], antidepressant [19] and anticancer against different types of carcinoma [20-23]. Pyrazole conjugated moieties have proved for their effective pharmaceutical activities like anti-inflammatory [24], antifungal [25], antibacterial [26,27], anticonvulsant [28-31], antitumor [32] and antitubercular [33] properties.

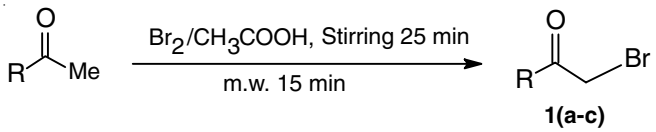
EXPERIMENTAL

All melting points were determined in open capillary tube and are uncorrected. The IR spectra were recorded on Perkin-Elmer-1800 spectrometer. The ^{1}H NMR spectra ($CDCl_3$) were scanned on a DRX-300 (300 MHz) spectrometer using TMS as internal standard and chemical shifts are expressed in δ, ppm. The mass spectra were recorded on Jeol SX-102 (FAB) spectrometer. Microwave induced reaction were carried out in CATA scientific microwave synthesis system (2450 MHz, catalyst system, India). Purity of synthesized compounds was checked by elemental analysis and homogeneity was checked by TLC using silica gel-G, as adsorbent and visualization was accomplished by iodine.

Conventional synthesis of 2-bromo-1-phenyl ethanone (1a): Acetophenone (0.55 mmol) and 100 mL glacial acetic acid taken in beaker. Similarly, bromine (0.125 mmol) and 100 mL glacial acetic acid taken in another beaker and it added drop by drop in the solution of acetophenone and glacial acetic acid with occasionally shaking. Reaction mass stay for 30 min, poured in ice water, isolated the solid and recrystallized from ethanol. Physico-chemical data of the synthesized compounds are given in Table-1.

Microwave assisted synthesis of 2-bromo-1-phenyl-ethanone (1a): Acetophenone (0.55 mmol) and 100 mL glacial acetic acid taken in beaker. Similarly, bromine (0.125 mmol) and 100 mL glacial acetic acid taken in another beaker and it

added drop by drop in the solution of acetophenone and glacial acetic acid with occasionally shaking. Reaction mixture was transferred in an Erlenmeyer flask and irradiated under microwave irradiation for 15 min with a time interval of 35 s, after the completion of reaction indicated by TLC, poured in ice water, isolated the solid and recrystallized from ethanol (**Scheme-I**). Physico-chemical data of the synthesized compounds are given in Table-1. IR (KBr, ν_{max}, cm^{-1}): 3055 (Ar-H str), 2950 (CH_2, str.), 1685 (C=O str.), ^1H NMR ($CDCl_3$) δ: 7.04-8.16 (m, 5H, Ar-H), 3.06 (s, 2H, CH_2); MS: *m/z* 199 $[M]^{+\cdot}$, 119, 103, 77.



1(a-c)

R: **a** = C_6H_5; **b** = *p*-Br-C_6H_4; **c** = *p*-F-C_6H_4

Scheme-I

Similarly compounds **1b-c** were prepared with minor changes in stirring time and work up process.

2-Bromo-1-(4-bromophenyl)ethanone (1b): IR (KBr, ν_{max}, cm^{-1}): 3065 (Ar-H str), 2980 (CH_2, str.), 1690 (C=O str.), ^1H NMR ($CDCl_3$) δ: 7.12-8.23 (m, 4H, Ar-H), 3.14 (s, 1H, CH_2); MS: *m/z* 277$[M]^{+\cdot}$, 198, 182, 156, 76.

2-Bromo-1-(4-fluorophenyl)ethanone (1c): IR (KBr, ν_{max}, cm^{-1}): 3072 (Ar-H str), 2990 (CH_2, str.), 1696 (C=O str.), ^1H NMR ($CDCl_3$) δ: 7.17-8.33 (m, 4H, Ar-H), 3.23 (s, 2H, CH_2); MS: *m/z* 217$[M]^{+\cdot}$, 137, 121, 95, 76.

Conventional synthesis of 2-(5-ethoxy-3-methyl-1H-pyrazol-1-yl)-4-phenyl-1,3-thiazole (2a): Take an equimolar mixture of compound (**1a**) 2-bromo-1-phenylethanone (0.01 mmol), thiosemicarbazide (0.01 mmol) and ethyl aceto acetate (0.01 mmol) in conical flask and add 10 % HBr sol as a catalysis than stirrer at room temperature for about 25 min gave the solid. It was filtered, washed with cold methanol and recrystallized from ethanol. Physico-chemical data of the synthesized compounds are given in Table-1.

Microwave assisted synthesis of 2-(5-ethoxy-3-methyl-1H-pyrazol-1-yl)-4-phenyl-1,3-thiazole (2a): Take an equimolar mixture of compound (**1a**) 2-bromo-1-phenylethanone (0.01 M), thiosemicarbazide (0.01 mmol) and ethyl aceto-acetate (0.01 mmol) and add 10 % HBr sol as a catalysis in Erlenmeyer flask and irradiated under microwave irradiation for 15 min with a time interval of 40 s, after the completion of reaction indicated by TLC, then poured in crushed ice, solid appear which was isolated, washed with cold methanol and recrystallized from ethanol (**Scheme-II**). Physico-chemical data of the synthesized compounds are given in Table-1.

IR (KBr, ν_{max}, cm^{-1}): 3077 (Ar-H, str.), 2973 (CH_2, str.), 1620 (C=N thiazole, str.), 1601(C=N, pyrazole, str.), 1363 (N-N), 1262 (C-O-C, str.); ^1H NMR ($CDCl_3$) δ: 7.43-7.70 (m, 5 H, Ar-H), 7.24 (s, 1H, thiazole), 6.72 (s, 1H, pyrazole), 3.39 (s, 3H, CH_3); MS: *m/z* 285 $[M]^{+\cdot}$, 240, 225, 160, 77.

Similarly compounds **2b-c** were prepared with some changes in reflux time and work up process.

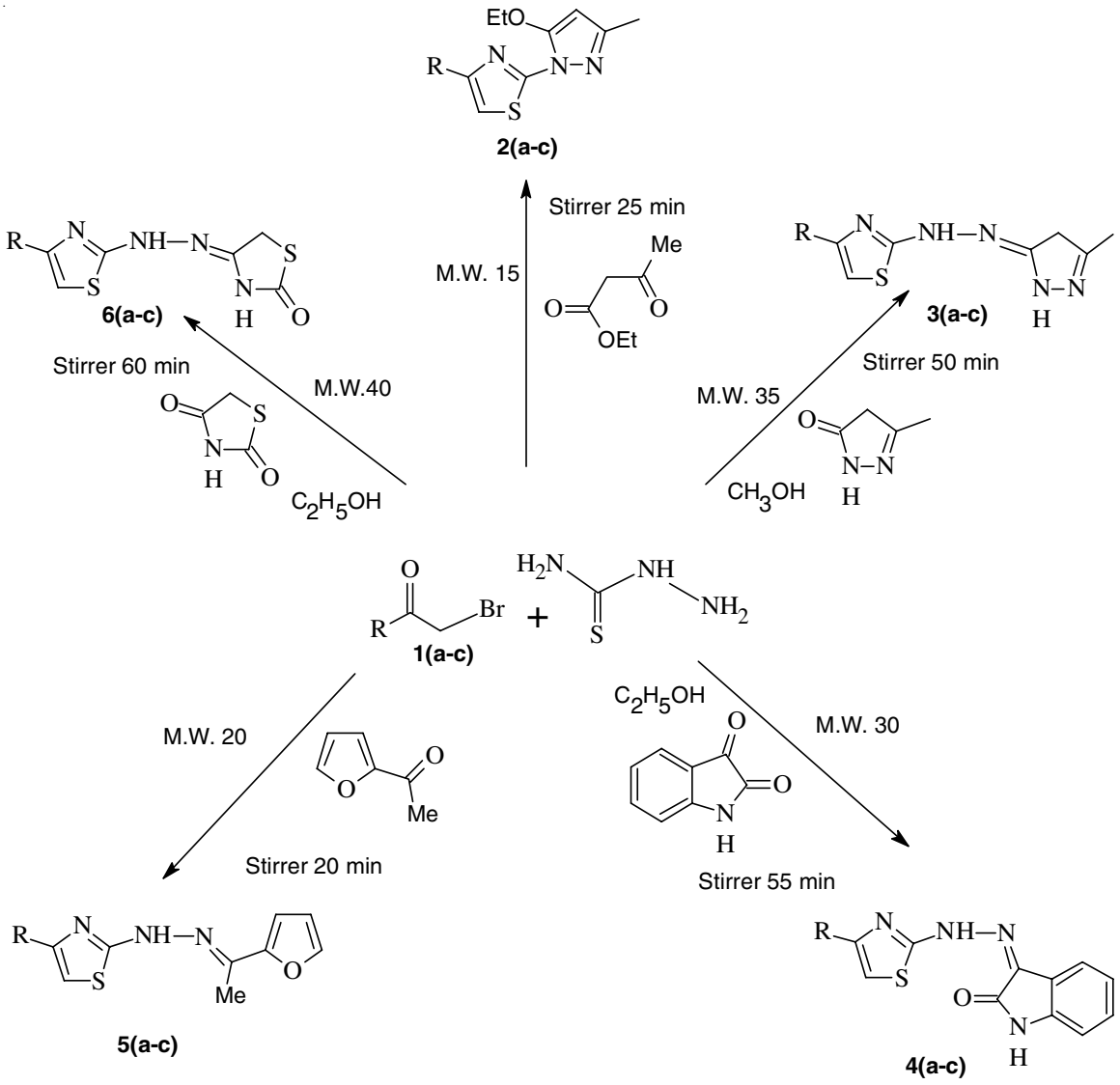
4-(4-Bromophenyl)-2-(5-ethoxy-3-methyl-1H-pyrazol-1-yl)-1,3-thiazole (2b): IR (KBr, ν_{max}, cm^{-1}): 3086 (Ar-H, str.), 2977 (CH_2, str.), 1626 (C=N thiazole, str.), 1607(C=N, pyrazole, str.), 1369 (N-N), 1268 (C-O-C, str.); ^1H NMR ($CDCl_3$) δ: 7.53-7.80 (m, 4H, Ar-H), 7.34 (s, 1H, thiazole), 6.75 (s, 1H, pyrazole), 3.42 (s, 3H, CH_3); MS: *m/z* 365 $[M]^{+\cdot}$, 367, 319, 304, 239, 156, 76.

2-(5-Ethoxy-3-methyl-1H-pyrazol-1-yl)-4-(4-fluorophenyl)-1,3-thiazole (2c): IR (KBr, ν_{max}, cm^{-1}): 3094 (Ar-H, str.), 2985 (CH_2, str.), 1633 (C=N, thiazole, str.), 1615 (C=N, pyrazole, str.), 1376 (N-N, str.), 1277 (C-O-C, str.); ^1H NMR ($CDCl_3$) δ: 7.63-7.91 (m, 4H, Ar-H), 7.39 (s, 1H, thiazole), 6.77 (s, 1H, pyrazole), 3.46 (s, 3H, CH_3); MS: *m/z* 303 $[M]^{+\cdot}$, 258, 243, 178, 95, 76.

Conventional synthesis of 2-[-2-(5-methyl-2,4-dihydro-3H-pyrazol-3-ylidene)hydrazino]-4-phenyl-1,3-thiazole (3a): Take an equimolar mixture of compound (**1a**) 2-bromo-1-phenylethanone (0.01 mmol), thiosemicarbazide (0.01 mmol) and methanolic solution of methyl pyrazole (0.01 mmol) and add 10 % HBr sol as a catalysis in conical flask

TABLE-1
PHYSICAL AND ANALYTICAL DATA OF NEW SYNTHESIZED COMPOUNDS **1a-c** TO **6a-c**

Compd.	m.f.	m.w.	m.p. (°C)	Yield (%): Conven. (M.W.)	Elemental analysis (%): Found (calcd.)			
					C	H	N	S
1a	C_8H_7BrO	199	49	80 (86)	48.25 (48.27)	3.50 (3.54)	-	-
1b	$C_8H_6Br_2O$	277	51	75 (80)	34.60 (34.57)	2.19 (2.18)	-	-
1c	C_8H_6BrFO	217	54	82 (85)	44.25 (44.27)	2.78 (2.79)	-	-
2a	$C_{15}H_{15}N_3OS$	285	248	86 (90)	63.10 (63.13)	5.26 (5.30)	14.70 (14.73)	11.22 (11.24)
2b	$C_{15}H_{14}N_3OSBr$	364	249	84 (89)	44.48 (44.46)	3.88 (3.87)	11.56 (11.54)	8.82 (8.80)
2c	$C_{15}H_{14}N_3OSBrF$	303	253	81 (85)	59.35 (59.39)	4.64 (4.65)	13.83 (13.85)	10.56 (10.57)
3a	$C_{13}H_{13}N_5S$	271	256	76 (80)	57.50 (57.54)	4.82 (4.83)	25.79 (25.81)	11.80 (11.82)
3b	$C_{13}H_{12}N_5SBr$	350	261	87 (90)	44.60 (44.58)	3.46 (3.45)	20.02 (20.00)	9.17 (9.16)
3c	$C_{13}H_{12}N_5SF$	289	263	83 (87)	53.95 (53.97)	4.17 (4.18)	24.19 (24.21)	11.06 (11.08)
4a	$C_{17}H_{12}N_4OS$	320	272	70 (80)	63.70 (63.73)	3.76 (3.78)	17.45 (17.49)	09.99 (10.01)
4b	$C_{17}H_{11}N_4OSBr$	399	275	71 (75)	51.17 (51.14)	2.80 (2.78)	14.05 (14.03)	8.05 (8.03)
4c	$C_{17}H_{11}N_4OSF$	338	277	69 (78)	60.31 (60.34)	3.25 (3.28)	16.53 (16.56)	9.45 (9.48)
5a	$C_{15}H_{13}N_3OS$	283	189	65 (70)	63.55 (63.58)	4.60 (4.62)	14.80 (14.83)	11.29 (11.32)
5b	$C_{15}H_{12}N_3OSBr$	362	192	67 (75)	49.75 (49.73)	3.36 (3.34)	11.63 (11.60)	8.88 (8.85)
5c	$C_{15}H_{12}N_3OSF$	301	194	68 (80)	59.75 (59.79)	4.00 (4.01)	13.91 (13.94)	10.60 (10.64)
6a	$C_{12}H_{10}N_4OS_2$	290	298	78 (85)	49.60 (49.64)	3.45 (3.47)	19.25 (19.30)	22.06 (22.09)
6b	$C_{12}H_9N_4OS_2Br$	369	307	79 (87)	39.05 (39.03)	2.47 (2.46)	15.19 (15.17)	17.40 (17.37)
6c	$C_{12}H_9N_4OS_2F$	308	313	77 (86)	46.70 (46.74)	2.93 (2.94)	18.13 (18.17)	20.76 (20.80)



Scheme-II

and stirrer at room temperature for about 50 min gave the solid. It was filtered, washed with cold methanol and recrystallized from ethanol. Physico-chemical data of the synthesized compounds are given in Table-1.

Microwave assisted synthesis of 2-[-2-(5-methyl-2,4-dihydro-3H-pyrazol-3-ylidene) hydrazino]-4-phenyl-1,3-thiazole (3a): Take an equimolar mixture of compound (**1a)** 2-bromo-1-phenylethanone (0.01 mmol), thiosemicarbazide (0.01 mmol) and methanolic solution of methyl pyrazole (0.01 mmol) and add 10 % HBr sol. as a catalysis in Erlenmeyer flask and irradiated under microwave irradiation for 35 min with a time interval of 45 s, after the completion of reaction indicated by TLC, then poured in crushed ice, solid appear which was isolated, washed with cold methanol and recrystallized from ethanol (**Scheme-II**). Physico-chemical data of the synthesized compounds are given in Table-1.

IR (KBr, ν_{max}, cm^{-1}): 3336 (N-H, ring, str.), 3210 (N-H, str.), 3045 (Ar-H, str.), 2931 (CH_2, str.), 1632 (C=N, thiazole, str.), 1551 (C=N, pyrazole, str.), 1483 (N-N, str.), ^{1}H NMR ($CDCl_3$) δ: 7.21-7.80 (m, 5H, Ar-H), 6.77 (s, 1H, C-H, thiazole ring), 5.30 (s, 1H, N-H), 4.70 (s, 1H, N-H ring) 2.26 (s, 2H, CH_2, ring), 1.24 (s, 3H, CH_3); MS: *m/z* 271 $[M]^{+\cdot}$, 256, 189, 160, 77.

Similarly compounds **3b-c** were prepared with some change in stirring time and work up process.

4-(4-bromophenyl)-2-[-2-(5-methyl-2,4-dihydro-3H-pyrazol-3-ylidene)hydrazino]-1,3-thiazole (3b): IR (KBr, ν_{max}, cm^{-1}): 3341 (N-H, ring, str.), 3217 (N-H, str.), 3046 (Ar-H, str.), 2941 (CH_2, str.), 1640 (C=N, thiazole, str.), 1559 (C=N, pyrazole, str.), 1493 (N-N, str.); ^{1}H NMR ($CDCl_3$) δ: 7.32-8.10 (m, 4H, Ar-H), 6.81 (s, 1H, C-H, thiazole ring), 5.34 (s, 1H, N-H), 4.75 (s, 1H, N-H ring), 3.51 (s, 2H, CH_2, ring), 1.30 (s, 3H, CH_3); MS: *m/z* 351 $[M]^{+\cdot}$, 353, 335, 268, 239, 156, 76.

4-(4-Fluorophenyl)-2-[-2-(5-methyl-2,4-dihydro-3H-pyrazol-3-ylidene)hydrazino]-1,3-thiazole (3c): IR (KBr, ν_{max}, cm^{-1}): 3346 (N-H, ring, str.), 3222 (N-H, str.), 3049 (Ar-H, str.), 2950 (CH_2, str.), 1646 (C=N, thiazole, str.), 1565 (C=N, pyrazole, str.), 1498 (N-N, str.); ^{1}H NMR ($CDCl_3$) δ: 7.34-8.15 (m, 4H, Ar-H), 6.85 (s, 1H, C-H, thiazole ring), 5.38 (s, 1H, N-H), 4.80 (s, 1H, N-H ring), 3.54 (s, 2H, CH_2, ring), 1.34 (s, 3H, CH_3); MS: *m/z* 289 $[M]^{+\cdot}$, 274, 207, 178, 95, 76.

Conventional synthesis of 3-[(4-phenyl-1,3-thiazol-2-yl)hydrazono]-1,3-dihydro-2H-indol-2-one (4a): Take an equimolar mixture of compound (**1a**) 2-bromo-1-phenylethanone (0.01 mmol), thiosemicarbazide (0.01 mmol) and ethanolic solution of isatine (0.01 mmol) and add 10 % HBr sol as a catalysis in conical flask and stirrer at room temperature for about 55 min gave the solid. It was filtered, washed with cold methanol and recrystallized from ethanol. Physico-chemical data of the synthesized compounds are given in Table-1.

Microwave assisted synthesis of 3-[(4-phenyl-1,3-thiazol-2-yl)hydrazono]-1,3-dihydro-2H-indol-2-one (4a): Take an equimolar mixture of compound (**1a**) 2-bromo-1-phenylethanone (0.01 mmol), thiosemicarbazide (0.01 mmol) and ethanolic solution of isatine (0.01 mmol) and add 10 % HBr sol as a catalysis in Erlenmeyer flask and irradiated under microwave irradiation for 30 min with a time interval of 35 s, after the completion of reaction indicated by TLC, than poured in crushed ice, solid appear which was isolated, washed with cold methanol and recrystallized from ethanol (**Scheme-II**). Physico-chemical data of the synthesized compounds are given in Table-1.

IR (KBr, ν_{max}, cm^{-1}): 3403 (N-H, ring, str.), 3315 (N-H, str.), 3162 (Ar-H, str.), 1676 (C=O, str.), 1618 (C=N, ring, str.), 1463 (N-N, str.); ^{1}H NMR ($CDCl_3$) δ: 7.02-8.84 (m, 9H, Ar-H), 6.51 (s, 1H, C-H, thiazole), 4.90 (s, 1H, NH), 3.80 (s, 1H, NH, ring); MS: *m/z* 320 $[M]^{+\cdot}$, 304, 189, 160, 77.

3-{[4-(4-Bromophenyl)-1,3-thiazol-2-yl]hydrazono}-1,3-dihydro-2H-indol-2-one (4b): IR (KBr, ν_{max}, cm^{-1}): 3414 (N-H, ring, str.), 3327 (N-H, str.), 3176 (Ar-H, str.), 1683 (C=O, str.), 1624 (C=N, ring, str.), 1476 (N-N); ^{1}H NMR ($CDCl_3$) δ: 7.11-7.91 (m, 8H, Ar-H), 6.60 (s, 1H, C-H, thiazole), 4.95 (s, 1H, NH), 3.86 (s, 1H, NH, ring); MS: *m/z* 400 $[M]^{+\cdot}$, 402, 383, 268, 239, 156, 76.

3-{[4-(4-Fluorophenyl)-1,3-thiazol-2-yl]hydrazono}-1,3-dihydro-2H-indol-2-one (4c): IR (KBr, ν_{max}, cm^{-1}): 3417 (N-H, ring, str.), 3332 (N-H, str.), 3179 (Ar-H, str.), 1685 (C=O, str.), 1628 (C=N, ring, str.), 1480 (N-N, str.); ^{1}H NMR ($CDCl_3$) δ: 7.14-7.95 (m, 8H, Ar-H), 6.64 (s, 1H, C-H, thiazole), 4.97 (s, 1H, NH), 3.89 (s, 1H, NH, ring); MS: *m/z* 338 $[M]^{+\cdot}$, 322, 207, 178, 95, 76.

Conventional synthesis of 2-[-2-(1-furan-2-ylethylidene)-hydrazino]-4-phenyl-1,3-thiazole (5a): Take an equimolar mixture of compound (**1a**) 2-bromo-1-phenylethanone (0.01 mmol), thiosemicarbazide (0.01 mmol) and acetyl furan (0.01 mmol) and add 10 % HBr sol as a catalysis in conical flask and stirrer at room temperature for about 20 min gave the solid. It was filtered, washed with cold methanol and recrystallized from ethanol. Physico-chemical data of the synthesized compounds are given in Table-1.

Microwave assisted synthesis of 2-[-2-(1-furan-2-ylethylidene)hydrazino]-4-phenyl-1,3-thiazole (5a): Take an equimolar mixture of compound (**1a**) 2-bromo-1-phenylethanone (0.01 mmol), thiosemicarbazide (0.01 mmol) and acetyl furan (0.01 mmol) and add 10 % HBr sol as a catalysis in Erlenmeyer flask and irradiated under microwave irradiation for 20 min with a time interval of 50 s, after the completion of reaction indicated by TLC, than poured in crushed ice, solid appear which was isolated, washed with cold methanol and recrystallized from ethanol (**Scheme-II**). Physico-chemical data of the synthesized compounds are given in Table-1.

IR (KBr, ν_{max}, cm^{-1}): 3431 (N-H, str.), 3131 (Ar-H, str.), 1615 (C=N, str.), 1494 (N-N, str.), 1360 (C=N, ring, str.), 1284 (C-O-C, str.); ^{1}H NMR ($CDCl_3$) δ: 7.15-8.05 (m, 8H, Ar-H), 6.50 (s, 1H, C-H, thiazole), 4.99 (s, 1H, NH), 3.40 (s, 3H, CH_3); MS: *m/z* 283 $[M]^{+\cdot}$, 268, 201, 160, 78.

4-(4-Bromophenyl)-2-[-2-(1-furan-2-ylethylidene)-hydrazino]-1,3-thiazole (5b): IR (KBr, ν_{max}, cm^{-1}): 3441 (N-H, str.), 3138 (Ar-H, str.), 1624 (C=N, str.), 1499 (N-N, str.), 1366 (C=N, ring, str.), 1295 (C-O-C, str.); ^{1}H NMR ($CDCl_3$) δ: 7.20-8.10 (m, 7H, Ar-H), 6.54 (s, 1H, C-H, thiazole), 5.04 (s, 1H, NH), 3.45 (s, 3H, CH_3); MS: *m/z* 363 $[M]^{+\cdot}$, 365, 347, 280, 239, 156, 76.

4-(4-Fluorophenyl)-2-[-2-(1-furan-2-ylethylidene)-hydrazino]-1,3-thiazole (5c): IR (KBr, ν_{max}, cm^{-1}): 3445 (N-H, str.), 3142 (Ar-H, str.), 1630 (C=N, str.), 1510 (N-N, str.), 1371 (C=N, ring, str.), 1301(C-O-C, str.); ^{1}H NMR ($CDCl_3$) δ: 7.22-8.13 (m, 7H, Ar-H), 6.57 (s, 1H, C-H, thiazole), 5.10 (s, 1H, NH), 3.50 (s, 3H, CH_3); MS: *m/z* 301$[M]^{+\cdot}$, 286, 219, 178, 95, 76.

Conventional synthesis of 4-[(4-phenyl-1,3-thiazol-2-yl)hydrazono]-1,3-thiazolidin-2-one (6a): Take an equimolar mixture of compound (**1a**) 2-bromo-1-phenylethanone (0.01 mmol), thiosemicarbazide (0.01 mmol) and ethanolic solution of thiazolidione (0.01 mmol) and add 10 % HBr sol as a catalysis in conical flask and stirrer at room temperature for about 60 min gave the solid. It was filtered, washed with cold methanol and recrystallized from ethanol. Physico-chemical data of the synthesized compounds are given in Table-1.

Microwave assisted synthesis 4-[(4-phenyl-1,3-thiazol-2-yl)hydrazono]-1,3-thiazolidin-2-one (6a): Take an equimolar mixture of compound (**1a**) 2-bromo-1-phenylethanone (0.01 mmol), thiosemicarbazide (0.01 mmol) and ethanolic solution of thiazolidione (0.01 mmol) and add 10 % HBr sol as a catalysis in Erlenmeyer flask and irradiated under microwave irradiation for 40 min with a time interval of 55 s, after the completion of reaction indicated by TLC, than poured in crushed ice, solid appear which was isolated, washed with cold methanol and recrystallized from ethanol (**Scheme-II**). Physico-chemical data of the synthesized compounds are given in Table-1.

IR (KBr, ν_{max}, cm^{-1}): 3336 (N-H, ring, str.), 3212 (N-H, str.), 3103 (Ar-H, str.), 2945 (CH_2, str.), 1633 (C=O, str.), 1553 (C=N, str. ring), 1484 (N-N, str.); ^{1}H NMR ($CDCl_3$) δ: 7.24-7.77 (m, 5H, Ar-H), 6.81 (s, 1H, C=C-H, ring), 5.54 (s, 1H, N-H), 4.80 (s, 1H, N-H, ring), 2.01 (s, 2H, CH_2, ring); MS: *m/z* 290 $[M]^{+\cdot}$, 274, 189, 160, 77.

4-{[4-(4-Bromophenyl)-1,3-thiazol-2-yl]hydrazono}-1,3-thiazolidin-2-one (6b): IR (KBr, ν_{max}, cm^{-1}): 3347 (N-H, ring, str.), 3223 (N-H, str.), 3112 (Ar-H, str.), 2955 (CH_2, str.), 1642 (C=O, str.), 1565 (C=N, str. ring), 1493 (N-N, str.); ^{1}H NMR ($CDCl_3$) δ: 7.34-7.81 (m, 4H, Ar-H), 6.85 (s, 1H, C=C-H, ring), 5.60 (s, 1H, N-H), 4.86 (s, 1H, N-H, ring), 2.05 (s, 2H, CH_2, ring); MS: *m/z* 370$[M]^{+\cdot}$, 372, 353, 268, 239, 156, 76.

4-{[4-(4-Fluorophenyl)-1,3-thiazol-2-yl]hydrazono}-1,3-thiazolidin-2-one (6c): IR (KBr, ν_{max}, cm^{-1}): 3352 (N-H, ring, str.), 3228 (N-H, str.), 3116 (Ar-H, str.), 2965 (CH_2, str.), 1650 (C=O, str.), 1571 (C=N, str. ring), 1497 (N-N, str.); ^{1}H NMR ($CDCl_3$) δ: 7.38-7.86 (m, 4H, Ar-H), 6.89 (s, 1H, C=C-H, ring), 5.68 (s, 1H, N-H), 4.89 (s, 1H, N-H, ring), 2.10 (s, 2H, CH_2, ring); MS: *m/z* 308 $[M]^{+\cdot}$, 292, 207, 178, 95, 76.

TABLE-2
ANTIMICROBIAL ACTIVITY OF SYNTHESIZED COMPOUNDS ON 200 ppm **2a-c** TO **6a-c** [ZONE OF INHIBITION (mm)]

Compd.	Antibacterial activity				Antifungal activity	
	B. subtilis	*E. coli*	*S. typhi*	*P. aeruginosa*	*A. fumigatus*	*C. albicans*
2a	++	++	++	++	+++	++
2b	++	+	++	++	++	++
2c	+	++	+	++	++	+
3a	++	++	+	++	+	++
3b	+	++	++	++++	++	++
3c	++	+	+	++	+	++
4a	++++	++	+	++	+	++
4b	+++	+	++	+	++	++
4c	+	++	+	++	++	+
5a	++	+	+	++	++	+++
5b	+	+	++	+	+	++
5c	++	++	+	+	++	+
6a	+++	+	++	++	++	+++
6b	+	++	++	+++	+++	++++
6c	++	+	+	++	++	+
STD_1	+++	+++	++	+++	--	--
STD_2	--	--	--	--	+++	+++

+ = 10-14 (poor activity), ++ = 15-18 (moderate activity), +++ = 19-22 (good activity), ++++ = 23-26 (strong activity).
Standard: STD_1 = Ciprofloxacin, STD_2 = Flucanazole,

RESULTS AND DISCUSSION

Compound **1a** was achieved by reaction with acetophenone and bromine. The structure of this compound is confirmed by ^{1}H NMR, presence of a singlet at δ 3.02 due to (CH_2) group and IR absorptions at 1685 cm^{-1} due to the C=O group. Compounds **2a-6a** is synthesized by multicomponent reaction *via* Hantzsch thiazole process. In this reaction compound **1a** reacts with thiosemicarbazide and ethyl acetoacetate to give compound **2a** and it confirmed by disappear of C=O group peak at 1685 cm^{-1} and appear of two C=N group peak at 1620 and 1601 cm^{-1}. Similarly, compound **3a** achieved by reaction with compound **1a**, thiosemicarbazide and pyrazolone it exhibit singlet at δ 4.70 due to the N-H group of pyrazole. In another path compound **1a**, thiosemicarbazide and isatin stirrer to give compound **4a** which is confirmed by IR absorptions at 1676 cm^{-1} due to the C=O group and ^{1}H NMR singlet at δ 3.80 due to the N-H group of isatine. In next path compound **1a**, thiosemicarbazide and acetyl furan cyclized and give final compound **5a**, it show sharp singlet at δ 3.40 corresponding to the CH_3 group and IR absorptions at 1284 cm^{-1} due to the C-O-C group of the furan. In last path compound **1a**, treated with thiosemicarbazide and thiazolidione to give compound **6a**, which is confirmed by IR absorptions at 1633 cm^{-1} due to the C=O group and ^{1}H NMR singlet at δ 4.80 due to the N-H group of thiazolodione. All the synthesized compound are tested for their antimicrobial activity.

Biological activity: All the synthesized compounds were tested against four bacterial strains *viz.*, *B. subtilis, S. typhi, P. aeruginosa*, *E. coli* and two fungal strains *A. fumigatus* and *C. albicans* by using cup and well method at 200 ppm concentrations in DMF. It is clear that compounds **4a** exhibit strong activity and **6a** show good activity against *B. subtilis.* Similarly, compound **3b** possesses strong activity and **6b** show good activity against *P. aeruginosa.* Compound **2a** exhibit good activity against *A. fumigatus* and **6b** show strong activity against *C. albicans*. Hence, the conclusion can be drawn that synthesized compounds are better antibacterial and antifungal. The screening have been summarized in Table-2.

Conclusion

In this work, thiazole and their derivatives were synthesized using multicomponent conventional and microwave method. This clearly indicates that synthesis of thiazole derivatives in microwave afforded better yield in short time and eco-friendly route. The multicomponent process also takes less time and give excellent yield compare to another conventional process and this method supported to the development of green chemistry.

Synthesized compounds are tested for antibacterial and antifungal activity. Compound **4a** exhibit strong activity against *B. subtilis* and compound **6a** show moderate to good against both microbial. Compounds **2a** and **5a** show good activity against fungi. All over result is that compound **3b** shows strong activity against *P. aeruginosa* bacterial strains and **6b** exhibit strong activity against *C. albicans* fungal strains as compared to the standard drugs (STD).

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REFERENCES

1. K.R.A. Abdellatif, M.A. Abdelgawad, H.A.H. Elshemy and S.S.R. Alsayed, *Bioorg. Chem.*, **64**, 1 (2016).
2. V.B. Jadhav, M.V. Kulkarni, V.P. Rasal, S.S. Biradar and M.D. Vinay, *J. Med. Chem.*, **43**, 1721 (2008).
3. R. Budriesi, P. Ioan, A. Locatelli, S. Cosconati, A. Leoni, M.P. Ugenti, A. Andreani, R. Di Toro, A. Bedini, S. Spampinato, L. Marinelli, E. Novellino and A. Chiarini, *J. Med. Chem.*, **51**, 1592 (2008).
4. K.F.M. Atta, O.O.M. Farahat, A.Z.A. Ahmed and M.G. Marei, *Molecules*, **16**, 5496 (2011).

5. T. Juspin, M. Laget, T. Terme, N. Azas and P. Vanelle, *Eur. J. Med. Chem.*, **45**, 840 (2010).
6. R. Budriesi, P. Ioan, A. Leoni, N. Pedemonte, A. Locatelli, M. Micucci, A. Chiarini and L.J.V. Galietta, *J. Med. Chem.*, **54**, 3885 (2011).
7. B.C.C. Cantello, M.A. Cawthorne, G.P. Cottam, P.T. Duff, D. Haigh, R.M. Hindley, C.A. Lister, S.A. Smith and P.L. Thurlby, *Med. Chem.*, **37**, 3977 (1994).
8. A. Chimirri, S. Grasso, C. Molica, A.M. Monforte, P. Monforte, M. Zappala, G. Bruno, F. Nicolo, M. Witvrouw, H. Jonckeere, J. Balzarini and E. De Clercq, *Antivir. Chem. Chemother.*, **8**, 363 (1997).
9. B.S. Furniss, A.J. Hannaford, P.W.G. Smith and A.R. Tatchell, Vogel's Textbook of Practical Organic Chemistry, edn 5, p. 807 (1989).
10. J.M. Lehmann, L.B. Moore, T.A. Smith-Oliver, W.O. Wilkison, T.M. Willson and S.A. Kliewer, *J. Biol. Chem.*, **270**, 12953 (1995).
11. U. Sehlstedt, P. Aich, J. Bergman, H. Vallberg, B. Nordén and A. Gräslund, *J. Mol. Biol.*, **278**, 31 (1998).
12. A. Jeney, *Bioorg. Med. Chem.*, **177**, 220 (1960).
13. J.M. Grisar, F.N. Bolkenius, M.A. Petty and J. Verne, *J. Med. Chem.*, **38**, 453 (1995).
14. B. Jójárt, T.A. Martinek and Á. Márki, *J. Comput. Aided Mol. Des.*, **19**, 341 (2005).
15. S.S. Sangapure and R. Basawaraj, *Indian J. Pharm. Sci.*, **66**, 221 (2004).
16. M. Ono, M.P. Kung, C. Hou and H.F. Kung, *Nucl. Med. Biol.*, **29**, 633 (2002).
17. W.M. Luo, Q.S. Yu, M. Zhan, D. Parrish, J.R. Deschamps, S.S. Kulkarni, H.W. Holloway, G.M. Alley, D.K. Lahiri, A. Brossi and N.H. Greig, *J. Med. Chem.*, **48**, 986 (2005).
18. M. Cowart, R. Faghih, M.P. Curtis, G.A. Gfesser, Y.L. Bennani, L.A. Black, L. Pan, K.C. Marsh, J.P. Sullivan, T.A. Esbenshade, G.B. Fox and A.A. Hancock, *J. Med. Chem.*, **48**, 38 (2005).
19. A.F. Abdel-Magid, B.E. Maryanoff, S.J. Mehrman, M.H. Parker and A.B. Reitz, US Patent 276,528 (2006).
20. M.E. Page, J.F. Cryan, A. Sullivan, A. Dalvi, B. Saucy, D.R. Manning and I. Lucki, *J. Pharmacol. Exp. Ther.*, **302**, 1220 (2002).
21. I. Hayakawa, R. Shioya, T. Agatsuma, H. Furukawa, S. Naruto and Y. Sugano, *Bioorg. Med. Lett.*, **14**, 4383 (2004).
22. M.R. Saberi, T.K. Vinh, S.W. Yee, B.J.N. Griffiths, P.J. Evans and C. Simons, *J. Med. Chem.*, **49**, 1016 (2006).
23. S.K. Lee, B. Cui, R.P. Mehta, A.D. Kinghorn and J.M. Pezzuto, *Chem. Biol. Interact.*, **115**, 215 (1998).
24. S. Pautus, S.W. Yee, M. Jayne, M.P. Coogan and C. Simons, *Bioorg. Med. Chem.*, **14**, 3643 (2006).
25. R.H. Udupi, A.S. Kushnoor and A.R. Bhat, *Indian J. Heterocycl. Chem.*, **8**, 63 (1998).
26. S.S. Korgaokar, P.H. Patil, M.J. Shah and H.H. Parekh, *Indian J. Pharm. Sci.*, **58**, 222 (1996).
27. O.O. Ajani, C.A. Obafemi, C.O. Ikpo, K.O. Ogunniran and O.C. Nwinyi, *Chem. Heterocycl. Comp.*, **45**, 1370 (2009).
28. D. Nauduri and G.B. Reddy, *Chem. Pharm. Bull. (Tokyo)*, **46**, 1254 (1998).
29. E. Palaska, M.I. Aytemir, T. Uzbay and D. Erol, *Eur. J. Med. Chem.*, **36**, 539 (2001).
30. O. Ruhogluo, Z. Ozdemir, U. Calis, B. Gumusel and A.A. Bilgin, *Arzneimittelforschung Drug Res.*, **55**, 431 (2005).
31. Y. Rajendra Prasad, A. Lakshmana Rao, L. Prasoona, K. Murali and P. Ravi Kumar, *Bioorg. Med. Chem. Lett.*, **15**, 5030 (2005).
32. Z. Özdemir, H.B. Kandilci, B. Gümüsel, Ü. Calis and A.A. Bilgin, *Eur. J. Med. Chem.*, **42**, 373 (2007).
33. E.C. Taylor and H.H. Patel, *Tetrahedron*, **48**, 8089 (1992).
34. A.A. Santilli, D.H. Kim and F.J. Gregory, *J. Pharm. Sci.*, **64**, 1057 (1975).