SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF THIAZOLE DERIVATIVES CONTAINING TRIAZOLE MOIETY USING LiBr AS A CATALYST

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ABSTRACT

Synthesis of triazole derivatives from 2-mercaptobenzothiazole has been achieved in four steps under microwave irradiation. LiBr potentially replace solvents and corrosive acids in this reaction scheme. The products of triazole derivatives have shown antimicrobial activity.

Keywords: *LiBr, Microwave irradiation, Solvent free condition, Basic alumina*

INTRODUCTION

At the beginning of this century, organic solvent free reactions have attracted considerable interest due to increase of awareness about environmental problems in chemical research and industry [1]. Organic solvent-free reactions have many advantages such as reduced pollution, lower costs and simplicity. Another aspect, which is receiving increasing attention, is the water - accessible Lewis acid catalysts in many chemical transformations [2]. Water, as the reaction medium, is generally considered as inexpensive, safe and environmentally benign alternative to synthetic solvents [3]. This prompted the systemic investigation into the feasibility of organic solvent – less catalyzed reactions under microwave irradiations. Microwave irradiation has been used for variety of applications including synthetic organic chemistry [4]. Benzothiazole derivatives have been studied extensively because of their broad spectrum of biological activities [5-8]. Similarly triazoles display a number of antimicrobial activities like antifungal [9-11], anti-mycobacterial [12], antibacterial [13-15] and varity of industrial applications [16]. Benzothiazole derivatives bearing triazole moiety are widely investigated for their pharmacological properties [17-18]. The Knoevengeal condensation has been a subject of considerable interest and to effect this condensation efficiently, large number of catalyst have been explored e.g. sodium acetate in glacial acetic acid, piperidinium benzoate in refluxing toluene, zeolite, tetrabutylammonium bromide, refluxing reactants in toluene at 110 °C for 3 days, etc. Certainly, these processes are not facile as they require long reaction times, high temperature and products are obtained in low yields. LiBr can potentially replace solvents and conventional corrosive acids in many of their applications [19-24].

EXPERIMENTAL SECTION

Materials

All reagents were obtained commercially and used after purification. Basic alumina, 4-nitrobenzaldehyde and 2-, 3- or 4-chlorobenzaldehyde were obtained from Himedia. 2-, 3- or 4-hydroxybenzaldehydes, benzaldehyde, dichloromethane, hydrazine hydrate and ethylchloroacetate, were obtained from CDH. All other chemicals like lithium bromide and carbon disulphide were obtained from Merck, 2- or 4-methoxybenzaldehyde & 2-mercapto benzothiazole were obtained from SRL and Otto Kemi, respectively.

Instrumentation

All reactions were carried out in a domestic microwave oven (Kenstar, Model No. OM-26 EGO). Melting points are uncorrected and determined in open capillaries. Reactions were monitored by thin layer chromatography using silica gel-G as adsorbent using ethyl acetate: n-hexane (7: 3) as eluent and products were detected by iodine vapors. IR spectra (KBr pellets) were recorded on Perkin-Elmer 1800 (FTIR) spectrometer. ^{1}H NMR spectra (DMSO-d_6) were taken on a Bruker DRX spectrometer (300MHz FT NMR) using TMS as internal standard and chemical shift were expressed in δ. Mass spectra were taken on a Jeol SX-102/PA-6000 (EI) spectrometer and elemental analysis was carried out on C, H, N analyzer (Elemental Vario Carlo Alba 1108). The results were found to be in good agreement with the calculated values (± 0.2%). The starting compounds were prepared according to reported method.

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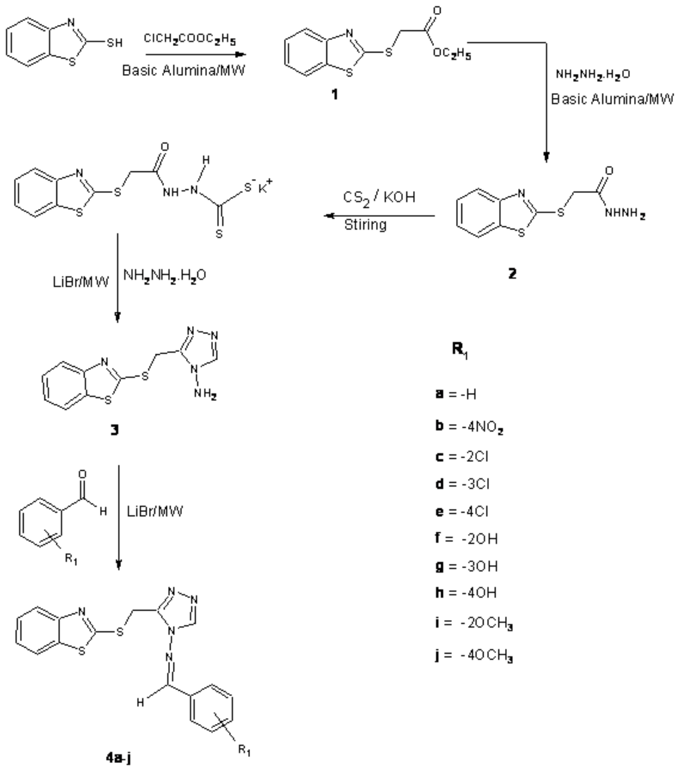

Reaction Scheme

Procedure

Microwave induced synthesis of ethyl (1, 3-benzo thiazol-2-ylsulfanyl) acetate (1)

2-Mercaptobenzothiazole (0.01 mole) and ethyl chloroacetate (0.01 mole) adsorbed over basic alumina were placed in a conical flask and exposed to microwave irradiation at 800 W for 4.0 min. After completion of reaction (monitored by TLC), the reaction mixture was cooled to room temperature. Then dichloromethane (20 mL) was added and the mixture was stirred for 5 min, filtered, evaporated and recrystallized from ethanol to afford compound **1**.

Found: C 52.14, H 4.39, N 5.32, S 25.30% Calc. for $C_{11}H_{11}NS_2O_2$: C 52.19, H 4.30, N 5.38 S 25.39% IR (KBr cm^{-1}) : 3023 (C-H str., Ar-H), 1180 (C-O-C str.), 1221 (C-S str.), 1723 (C=O str.), 1614 (C=N str.), 1601 (C=C str.) and 2915 (CH_3 str.).

^{1}H NMR (DMSO - d_6:δ_H ppm 1.23 (t, 3H, CH_3), 4.13 (q, 2H, CH_2), 2.62 (s, 2H, S-CH_2-) and 6.73-7.87 (m, 4H, Ar-H).

Conventional synthesis of ethyl (1, 3-benzothiazol-2-ylsulfanyl) acetate (1). An equimolar solution of 2-mercaptobenzothiazole (0.01 mole) and ethyl chloroacetate (0.01 mole) in dry acetone 4 mL in the presence of anhydrous K_2CO_3 (1 g) was refluxed on a water bath for 16 h. The solvent was removed by vacuum distillation and the residue was recrystallized from ethanol to afford compound **1**.

Microwave induced synthesis of 2-(1,3-benzo thiazol-2-ylsulfanyl) acetohydrazide (2)

Compound **1** (0.01 mole) and hydrazine hydrate (0.01 mole) adsorbed over basic alumina was placed in a conical flask and exposed to microwave irradiation at 350 W for 3.5 min. After completion of reaction (monitored by TLC), the reaction mixture was cooled to room temperature. Then dichloromethane (20 mL) was added and the mixture was stirred for 5 min, filtered, evaporated and recrystallized from ethanol to afford compound **2**.

Found: C 45.19, H 3.80, N 17.60, S 26.79% Calc. for $C_9H_9N_3OS_2$: C 45.14, H 3.72, N 17.51, S 26.70% IR (KBr cm^{-1}): 3030 (C-H str., Ar-H), 3352, 3378, 3289 (-$NHNH_2$ str.), 1222 (C-S str.), 1602 (C=C str.), 1665 (C=O) and 1615 (C=N str.).

^{1}H NMR (DMSO - d_6:δ_H ppm 2.01 (s, 2H, NH_2), 7.88 (s, 1H, CONH), 2.61 (s, 2H, S-CH_2) and 6.80-7.88 (m, 4H, Ar-H).

Conventional synthesis of 2-(1,3-benzothiazol-2-ylsulfanyl) acetohydrazide (2). Compound **1** (0.01 mole) and hydrazine hydrate (0.01 mole) in ethanol (20 mL) was refluxed about 5 h on a steam bath. After cooling the resulting solid was filtered, dried and recrystallized from ethanol to obtain compound **2**.

Microwave induced synthesis of 3-[(1,3-benzo thiazol-2-ylsulfanyl)methyl]-4H-1,2,4-triazole-4-amine (3)

A mixture of compound **2** (0.01 mole) and CS_2 in ethanol (20 mL) in the presence of KOH (0.5 g) were stirred for 12-15 hr. to obtain potassium salt of phenyl carboxy-hydrazide. Now this potassium salt (0.01 mole), hydrazine hydrate (0.01 mole) and LiBr (10 mole %) were placed in small conical flask and mixed with glass rod at room temperature. The mixture was then exposed to microwave radiations at 720 W for 6.5 min. After completion of reaction (monitored by TLC), the reaction mixture was cooled to room temperature. Water (15 mL) was then added to reaction mixture and stirred for 5 min. The solid thus obtained was filtered, dried and recrystallized from ethanol to afford compound **3**.

Found: C 58.65, H 4.01, N 12.81, S 19.57% Calc. for $C_{10}H_9N_5S_2$: C 58.69, H 3.95, N 12.85, S 19.51% IR (KBr cm^{-1}): 3031 (C-H str., Ar-H), 3376, 3280 (-NH_2 str.), 1220 (C-S str.), 1604 (C=C str.), 1616 (C=N str.), 2559 (S-H str.), 1051 (N-N str.), 1255 (C-N str.) and 2962 (CH_2 str.).

^{1}H NMR (DMSO - d_6:δ_H ppm 2.03 (s, 2H, NH_2), 2.60 (s, 2H, S-CH_2), 2.65 (s, 1H, SH) and 6.78-7.84 (m, 4H, Ar-H).

Conventional synthesis of 3-[(1,3-benzothiazol-2-ylsulfanyl)methyl]-4H-1,2,4-triazole-4-amine (3). Compound **2** (0.01 mole) and hydrazine hydrate (0.01 mole) and 2-3 drops of Conc. HCl in ethanol (25 mL) was refluxed on water bath for about 6 h. The solvent was removed and residue was recrystallized from 1 : 1 ethanol : water to yield compound **3**.

Microwave induced synthesis of 3-[(1,3-benzo thiazol-2-ylsulfanyl)methyl]-N-[(Z)-phenylmethylidene]-4H-1, 2, 4-triazole-4-amine (4a)

Compound **3** (0.01 mole) and benzaldehyde (0.01 mole) and LiBr (10 mole %) were placed in small conical flask and mixed with glass rod at room temperature. The mixture was then exposed to microwave radiations at 840W for 5-6 min. After completion of reaction (monitored by TLC), the reaction mixture was cooled to room temperature. Water (15 mL) was then added to reaction mixture and then stirred for 5 min. The solid thus obtained was filtered, dried and recrystallized from ethanol to afford compound **4a**.

Found : C 53.25, H 3.41, N 48.29, S 25.05% Calc. for $C_{17}H_{13}N_5S_3$: C 53.20, H 3.4, N 48.20, S 25.10% IR (KBr cm^{-1}): 3032 (C-H str., Ar-H), 1224 (C-S str.), 1257 (C-N str.), 1625 (C=N str.), 2960 ($-CH_2$ str.), 3065 (C-H str., Ar-CH), 1052 (N-N str.), 2560 (S-H str.) and 1605 (C=C str.).

^1H NMR (DMSO - d_6:δ_H ppm 4.71 (s, 1H, =CH-Ar), 2.61 (s, 2H, $S-CH_2$), 2.66 (s, 1H, SH) and 7.28 - 7.94 (m, 9H, Ar-H).

Compounds **4b-j** were prepared similarly by treating **3** with various aromatic aldehydes.

3-[(1,3-Benzothiazol-2-ylsulfanyl)methyl]-N-[(Z)-(4-nitro phenyl)methylidene]-4H-1,2,4-triazole-4-amine (4b). Found: C 47.67, H 2.83, N 19.60, S 22.42% Calc. for $C_{17}H_{12}N_6S_3O_2$: C 47.60, H 2.77, N19.67, S 22.49% IR (KBr cm^{-1}): 3033 (C-H str., Ar-H), 1225 (C-S str.), 1255 (C-N str.), 1626 (C=N str.), 2962 ($-CH_2$ str.), 3066 (C-H str., Ar-CH), 1053 (N-N str.), 2561 (S-H str.), 1551, 1412 ($Ar-NO_2$ str.) and 1604 (C=C str.).

^1H NMR (DMSO - d_6:δ_H ppm 4.73 (s, 1H, =CH-Ar), 2.64 (s, 2H, $S-CH_2$), 2.68 (s, 1H, SH) and 7.30 - 7.96 (m, 8H, Ar-H).

3-[(1,3-Benzothiazol-2-ylsulfanyl)methyl]-N-[(Z)-(2-chlo rophenyl)methylidene]-4H-1,2,4-triazole-4-amine (4c). Found: C 48.87, H 2.86, N 16.78, S 23.03% Calc. for $C_{16}H_{12}N_5S_3Cl$: C 48.80, H 2.90, N 16.70, S 23.07% IR (KBr cm^{-1}): 3034 (C-H str., Ar-H), 1226 (C-S str.), 1254 (C-N str.), 1625 (C=N str.), 2964 ($-CH_2$ str.), 3068 (C-H str., Ar-CH), 1057 (N-N str.), 2565 (SH str.), 832 (Ar-Cl str.) and 1607 (C=C str.).

^1H NMR (DMSO - d_6:δ_H ppm 4.77 (s, 1H, =CH-Ar), 2.66(s, 2H, $S-CH_2$), 2.72 (s, 1H, SH) and 7.33 - 7.99 (m, 8H, Ar-H).

3-[(1,3-Benzothiazol-2-ylsulfanyl)methyl]-N-[(Z)(3-chlo rophenyl)methylidene]-4H-1,2,4-triazole-4-amine (4d). Found: C 48.86, H 2.87, N 16.75, S 23.01% Calc. for $C_{16}H_{12}N_5S_3Cl$: C 48.79, H 2.92, N 16.80, S 23.09% IR (KBr cm^{-1}): 3032 (C-H str., Ar-H), 1224 (C-S str.), 1252 (C-N str.), 1623 (C=N str.), 2962 ($-CH_2$ str.), 3064 (C-H str., Ar-CH), 1056 (N-N str.), 2564 (S-H str.), 829 (Ar-Cl str.) and 1605 (C=C str.).

^1H NMR (DMSO - d_6:δ_H ppm 4.76 (s, 1H, =CH-Ar), 2.65 (s, 2H, $S-CH_2$), 2.71 (s, 1H, SH) and 7.32 - 7.98 (m, 8H, Ar-H).

3-[(1,3-Benzothiazol-2-ylsulfanyl)methyl]-N-[(Z)-(4-chlo rophenyl)methylidene]-4H-1,2,4-triazole-4-amine (4e). Found: C 48.88, H 2.90, N 16.76, S 23.00% Calc. for $C_{16}H_{12}N_5S_3Cl$: C 48.81, H 2.81, N16.70, S 23.08% IR (KBr cm^{-1}): 3035 (C-H str., Ar-H), 1227 (C-S str.), 1255 (C-N str.), 1626 (C=N str.), 2965 ($-CH_2$ str.), 3069 (C-H str., Ar-CH), 1058 (N-N str.), 2566 (S-H str.), 833 (Ar-Cl str.) and 1608 (C=C str.).

^1H NMR (DMSO - d_6:δ_H ppm 4.78 (s, 1H, =CH-Ar), 2.67 (s, 2H, $S-CH_2$), 2.73 (s, 1H, SH) and 7.34 - 7.99 (m, 8H, Ar-H).

2-[(Z)-({3-[(1,3-benzothiazol-2-ylsulfanyl)methyl]-4H-1,2,4-triazol-4-yl}imino) methyl]phenol (4f). Found: C 51.13, H 3.29 N 17.55, S 24.06% Calc. for $C_{17}H_{13}N_5S_3O$: C 51.09, H 3.22, N 17.49, S 24.12% IR (KBr cm^{-1}): 3033 (C-H str., Ar-H), 1225 (C-S str.), 1256 (C-N str.), 1626 (C=N str.), 2963 ($-CH_2$ str.), 3063 (C-H str., Ar-CH), 1050 (N-N str.), 2561 (S-H str.), 1605 (C=C str.) and 3591 (O-H str.).

^1H NMR (DMSO - d_6:δ_H ppm4.73 (s, 1H, =CH-Ar), 2.62 (s, 2H, $S-CH_2$), 2.70 (s, 1H, SH), 3.66 (s, 1H, OH) and 7.30 - 7.95 (m, 8H, Ar-H).

3-[(Z)-({3-[(1,3-benzothiazol-2-ylsulfanyl)methyl]-4H-1,2,4-triazol-4-yl}imino) methyl]phenol (4g). Found: C 51.11, H 3.26, N 17.52, S 24.07% Calc. for $C_{17}H_{13}N_5S_3O$: C 51.0, H 3.34, N 17.58, S 24.11% IR (KBr cm^{-1}): 3032 (C-H str., Ar-H), 1224 (C-S str.), 1257 (C-N str.), 1625 (C=N str.), 2962 ($-CH_2$ str.), 1054 (N-N str.), 3070 (C-H str., Ar-CH), 3589 (O-H str.), 2565 (S-H str.) and 1607 (C=C str.).

^1H NMR (DMSO - d_6:δ_H ppm 4.71 (s, 1H, =CH-Ar), 2.65 (s, 2H, $S-CH_2$), 3.63 (s, 1H, OH), 2.67 (s, 1H, SH) and 7.29 - 7.98 (m, 8H, Ar-H).

4-[(Z)-({3-[(1,3-benzothiazol-2-ylsulfanyl)methyl]-4H-1,2,4-triazol-4-yl}imino) methyl]phenol (4h). Found: C 51.12, H 3.27, N 17.56, S 21.09% Calc. for $C_{17}H_{13}N_5S_3O$: C 51.08, H 3.35, N 17.45, S 24.16% IR (KBr cm^{-1}): 3036 (C-H str., Ar-H), 1228 (C-S str.), 1260 (C-N str.), 1628 (C=N str.), 2968 ($-CH_2$ str.), 1052 (N-N str.), 3071 (C-H str., Ar-CH), 3593 (O-H str.), 2567 (S-H str.) and 1608 (C=C str.).

^1H NMR (DMSO - d_6:δ_H ppm 4.76 (s, 1H, =CH-Ar), 2.67 (s, 2H, $S-CH_2$), 3.67 (s, 1H, OH), 2.69 (s, 1H, SH) and 7.32 - 7.99 (m, 8H, Ar-H).

Table 1. Physical data of synthesized compounds
a = Conventional, b = Microwave + Solvent,
c = Microwave + LiBr (solvent free) under microwave irradiation

Compd.	R	Mol. Formula	Mol. Weight	M.P. (°C)	Yield [a] [Time] (h)	Yield [b] [Time] (min)	Yield [c] [Time] (min)
1	-	$C_{11}H_{11}NS_2O_2$	253	58	66 [16]	69 [6]	76 [4]
2	-	$C_9H_9N_3OS_2$	239	192	61 [5]	70 [5]	78 [3.5]
3	-	$C_{10}H_9N_5S_2$	263	153	65 [6]	86 [5]	80 [3]
4a	C_6H_5	$C_{17}H_{13}N_5S_3$	383	168	68 [6]	72 [4.5]	89 [2.5]
4b	$-4NO_2C_6H_4$	$C_{17}H_{12}N_6S_3O_2$	428	160	73 [6]	75 [4.5]	87 [3]
4c	$-2ClC_6H_4$	$C_{16}H_{12}N_5S_3Cl$	418	165	72 [6]	77 [4.5]	85 [3]
4d	$-3ClC_6H_4$	$C_{16}H_{12}N_5S_3Cl$	418	172	70 [6]	76 [4.5]	87 [3]
4e	$-4ClC_6H_4$	$C_{16}H_{12}N_5S_3Cl$	418	180	68 [8]	72 [6]	86 [5]
4f	$-2OHC_6H_4$	$C_{17}H_{13}N_5S_3O$	399	214	69 [8]	72 [5.5]	88 [4]
4g	$-3OHC_6H_4$	$C_{17}H_{13}N_5S_3O$	399	211	65 [8]	70 [6]	85 [5]
4h	$-4OHC_6H_4$	$C_{17}H_{13}N_5S_3O$	399	226	68 [6]	70 [6]	80 [5]
4i	$-2OCH_3C_6H_4$	$C_{18}H_{15}N_5S_3O$	413	219	68 [8]	70 [6]	86 [5]
4j	$-4OCH_3C_6H_4$	$C_{18}H_{15}N_5S_3O$	413	272	79 [3]	82 [6]	90 [5]

3-[(1,3-Benzothiazol-2-ylsulfanyl)methyl]-N-[(Z)-(2-methoxyphenyl)methylidene] -4H-1,2,4-triazole-4-amine (4i). Found: C 52.30, H 3.68, N 16.92, S 23.28% Calc. for $C_{18}H_{15}N_5S_3O$: C 52.21, H 3.60, N 16.99, S 23.20% IR (KBr cm^{-1}): 3035 (C-H str., Ar-H), 1227 (C-S str.), 1261 (C-N str.), 1630 (C=N str.), 2970 ($-CH_2$ str.), 1054 (N-N str.), 3072 (C-H str., Ar-CH), 1107 ($C-O-CH_3$ str.), 2569 (S-H str.), and 1607 (C=C str.).
^{1}H NMR (DMSO - d_6:δ_H ppm 4.75 (s, 1H, =CH-Ar), 2.66 (s, 2H, $S-CH_2$), 3.33 (s, 3H, -OCH3), 2.71 (s, 1H, SH) and 7.33 - 7.97 (m, 8H, Ar-H).

3-[(1,3-Benzothiazol-2-ylsulfanyl)methyl]-N-[(Z)-(4-methoxyphenyl)methylidene] -4H-1,2,4-triazole-4-amine (4j). Found: C 52.29, H 3.69, N 16.91 S 23.29% Calc. for $C_{18}H_{15}N_5S_3O$: C 52.23, H 3.62, N 16.95, S 23.21% IR (KBr cm^{-1}): 3037 (C-H str., Ar-H), 1229 (C-S str.), 1263 (C-N str.), 1632 (C=N str.), 2973 ($-CH_2$ str.), 1056 (N-N str.), 3075 (C-H str., Ar-CH), 1109 ($C-O-CH_3$ str.), 2571 (S-H str.) and 1610 (C=C str.).
^{1}H NMR (DMSO - d_6:δ_H ppm 4.77 (s, 1H, =CH-Ar), 2.68 (s, 2H, $S-CH_2$), 3.35 (s, 3H, -OCH3), 2.73 (s, 1H, SH) and 7.34 - 7.99 (m, 8H, Ar-H).

Conventional synthesis of 5-[(1,3-benzothiazol-2-ylsulfanyl)methyl]-4-[(phenylmethylidene)amino]-4H-1,2,4-triazole-3-thiol (4a)

Compound **4a** (0.01 mole) and benzaldehyde (0.01 mole) and 2-3 drops of glacial acetic acid in ethanol (25 mL) was refluxed on water bath for about 4 hr. The solvent was removed and residue was recrystallized from ethanol to yield compound **4a**. Compounds **4b-j** were prepared similarly by treating **3** with various aromatic aldehydes.

RESULT AND DISCUSSION

2-Mercapto benzothiazole treated with ethyl chloroacetate adsorbed over basic alumina yielded ethyl (1,3-benzothiazol-2-ylsulfanyl)acetate **1**. Its structure was confirmed by the IR bands at 1180 cm^{-1} due to C-O-C and 1723 cm^{-1} due to C=O of ester. It is supported by the presence of quartet and triplet of CH_2CH_3 at δ 1.23 and 4.13 ppm in ^{1}H NMR. The compound **1** was treated with hydrazine hydrate to give 2-(1,3-benzothiazol-2-ylsulfanyl) acetohydrazide **2.** Compound **2** is confirmed by the disappearance of CH_2CH_3 in ^{1}H NMR and appearance of 3352, 3378 of NH_2 and 3289, NH in IR region. Compound **2** was then

Table 2. Antimicrobial activity of some synthesized compounds (500 ppm)

Compd.	Antifungal activity (Activity index)		Antibacterial activity (Activity index)			
	A. fumigatus	*C. albicans*	*E.coli*	*B.subtilis*	*P.aeurogenosa*	*K.pneumoniae*
4a	41	24 (0.61)	27 (0.75)	21 (0.65)	19 (0.47)	24 (0.66)
4b	43	32 (0.82)	32 (0.88)	23 (0.71)	22 (0.55)	26 (0.72)
4c	42	33 (0.84)	30 (0.83)	26 (0.81)	24 (0.60)	28 (0.77)
4f	40	29 (0.74)	29 (0.80)	24 (0.75)	20 (0.50)	25 (0.69)
C_1	Nil	39	-	-	-	-
C_2	-	-	36	32	40	36

[a] Activity index = Inhibition area of the sample / inhibition area of the standard.
Standard: C_1 = Flucanazole , C_2 = Ciprofloxacin

reacted with CS_2 in the presence of KOH to obtain potassium salt of phenyl carboxy-hydrazide. Compound 3-[(1,3-benzothiazol-2-ylsulfanyl)methyl]-4H-1,2,4-triazole-4-amine **3** were synthesized by the treatment of potassium salt of phenyl carboxy-hydrazide with hydrazine hydrate in the presence of catalytic amount of LiBr. It was confirmed by the appearance of a band due to SH group at 2559 cm^{-1} in IR spectra and singlet of SH at δ 2.65 in ^{1}H NMR. The disappearance of singlet of –CONH moiety in ^{1}H NMR and band at 1665 cm^{-1} due to C=O in IR spectra also supports this structure. Compound **4** possesses NH_2 moiety, which undergoes condensation with various aromatic aldehydes in the presence of LiBr to give 5-[(1,3-benzothiazoi-2-ylsulfanyl)methyl]-4-[(substituted phenylmethylidene)amino]-4H-1, 2, 4-triazole-3-thiol **4a-j.** The formation of compounds **4a-j** was confirmed by the disappearance of an intense peak of NH_2 group in compounds **3** due to condensation with substituted benzaldehydes and appearance of a new singlet at 4.71 ppm due to arylidine proton (=CH-Ar) of chalcone moiety.

ANTIMICROBIAL ACTIVITY

Pure culture of pathogenic bacteria and pathogenic fungi used for antimicrobial activity was produced from RNT Medical College and Microbial Research Laboratory, Department of Botany, Mohanlal Sukhadia University, Udaipur. Four compounds were screened *in vitro* for their antibacterial activities against four strains of bacteria (*Escherichia coli, Bacillus subtilis, Klebsiella pneumonia* and *Pseudomonas aeuroginosa*) and two strains of fungi (*Aspergillus fumigates* and *Candida albicans*) using the Cup or Well method.

Growth medium for bacteria

Nutrient agar medium was used to culture bacteria. The composition of nutrient agar medium was as follows: Beef extract: 3 g, Peptone; 5 g, Sodium Chloride: 5 g, Agar-Agar: 1.5 g, Distilled water: 1000 mL.

Growth medium for fungi

Sabourand agar medium was used to culture bacteria. The composition of Sabourand agar medium was as follows: Glucose: 20 g, Peptone; 10 g, Agar-Agar: 1.5 g, Distilled water: 1000 mL

Cup or Well Method

Nutrient agar medium was autoclaved at 15 psi and 121°C for 15 min. Sterilized Petri dishes were placed in laminar flow bench. One end of the lid of each Petri dish was lifted and approximately 15-20 mL of molten agar medium was poured into it and left for solidification. These were then inoculated with 0.2 mL suspension of organism by spread plate method. With the help of sterile borer, four wells were made in the medium and filled with 500 ppm solution of synthesized compounds. Similarly, other wells were made for standard drug. These Petri dishes were sealed with paraffin and incubated at 37 °C in an incubator. The Petri dishes were examined for zone of inhibition after 24-28 h. Same method is used for antifungal activity. Commercial antibacterial ciprofloxacin and antifungal flucanazole were used as standard drugs.

The results have been tabulated in the form of inhibition zones and activity index in Table 2. The results revealed that all tested compounds exhibit moderate to strong activity against both fungi and *E. coli*. Compounds **4a, 4b, 4c** and **4f** shows considerable potency against *A. fumigatus* while against *C. albicans* they are moderately active. Similarly, compounds **4a**, **4b**, **4c** and **4f** are found to show excellent activity against *E. coli* while against *P. aeurogenosa,* they exhibited moderate activity.

CONCLUSION

From the above studies we can advocate this method as facile, efficient and environ-economic for the synthesis of 5-[(1,3-benzothiazol-2-ylsulfanyl)methyl]-4-

[(phenyl substituted)amino]-4H-1, 2, 4-triazole-3-thiol **4a-j** with catalytic amount of LiBr using basic alumina as inorganic solid support.

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