

Solvent Free Synthesis of Methylthio / Methylsulfonyl Chalcones as Potential Anti-Microbial Agents

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Abstract: An attempt was made for a convenient, easy, safer, solvent free and efficient microwave synthesis of a series of methylthio/methylsulfonyl chalcones with potential antibacterial and antifungal activities. Most of prepared compounds showed potential biological activity against different bacterial and fungal strains. The compound **5j** and **5k** displayed most potent activity against different bacterial and fungal strains.

Keywords: Chalcones, Microwave synthesis, Antibacterial, Antifungal

Introduction

Chalcones constitute an important group of natural product and reserve as precursors for the synthesis of different class of flavonoids, flavones, arones *etc.*, which are common substrate in plant¹. Therefore, chalcones (1,3-diaryl-2-propen-1-ones), a biosynthetic product of the shikimate pathway have received a great deal of attention due to their relatively simple structure, key precursor in the synthesis of most biologically important heterocycles and most important their wide variety of pharmacological activities^{2,3} includes anti-bacterial, anti-malarial, anti-tumor, anti-fungal, anti-inflammatory, anti- HIV activities *etc.* Therefore the synthesis of chalcones and their functionalized derivatives are a primary objective for an organic or medicinal chemist. The traditional methods for this synthesis involves the use of strong acid or bases with conventional heating bears health and environmental hurdles such as catalysts recovery, waste disposal problem etc with low yields and longer reaction time. In this prospect, heterogeneous catalysts are considered as an ecofriendly alternative when combined with energy efficient sources like microwave irradiation or ultrasonication. Microwave irradiation becomes very popular techniques not only at laboratory scale (*e.g.*, CEM Microwaves) but also at kilo scale (*e.g.*, Anton paar (Synthos-3000)) due to its unique

advantage of shorter reaction time, cleaner reaction product, higher yield and better selectivity being a valuable alternative to accomplish more efficient synthesis of a variety of organic compounds.

Regarding biologically potent compounds thiomethyl⁴/methoxy⁵/halogeno⁶ group containing chalcones have great potential. In continuation of our ongoing endeavors in the development of different biologically potent chalcones⁷⁻¹² we now report facile non-conventional (MWI) and heterogeneous (Ba(OH)₂-celite) approach for the synthesis of thiomethyl/methylsulfonyl substituted chalcones and their antimicrobial activities. The effect of microwave on percentage yield and reaction time has been studied. It was observed that product was easily obtained by extraction and the catalyst- solid support (Ba(OH)₂-celite) was reused for another reaction only after activation by heating at 100 °C for 2 h. Initially, we synthesized chalcones by conventional manner by using 10% KOH or NaOH solutions and stirring for 10-15 h. However, in these cases longer reaction time, problem in isolation and low yield due to side reaction *i.e.* cannizaro reaction was observed. Where as in solid support with Ba(OH)₂-celite and MWI, the reactions were quite faster and comparatively high yield and recyclability of solvents and solid support was observed. The current method was found to be exclusively convenient, simple workup, less time taking, high yielding, no side reaction, atom efficient, ecofriendly and effective.

Experimental

Reagents and solvents were from commercial suppliers (Sigma-Aldrich, CDH, Thomas-Baker *etc.*) and used as provided, unless indicated otherwise. Melting points were determined in open glass capillaries and are uncorrected. IR spectra were recorded on Perkin-Elmer spectrum GX spectrophotometer on KBr plate. ¹H NMR and ¹³C NMR spectra were recorded on Bruker NMR-400 MHz at 400.1 MHz and 100 MHz on Top Spin 3.0 software, using CDCl₃ and DMSO-d₆ as the solvents. The chemical shifts are expressed in δ ppm. Coupling constants (*J*) are reported in Hertz. Mass spectra were recorded on API-2000 ESI-MS instrument. Mass spectrometry data are reported in the form of *m/z*. Experiments were performed using Whirlpool 27G microwave oven with microwave energy output 900 W and frequency 2450 MHz. The purity of the compounds was checked on MERCK 25 DC-Alufolien Silica Gel 60 F₂₅₄ Aluminium sheets TLC Plates.

Synthesis of (3-chloro-2-methylphenyl)(methyl)sulfane (2)

To a stirred solution of compound **1** (1.0 eq.) an aqueous solution of sodium thiomethoxide (1.5 eq.) was added drop wise at room temperature. Then the reaction mass was stirred at 45-50 °C for 4 h. The progress of reaction was monitored on TLC. After completion of reaction, the reaction mixture was evaporated and crude was purified by crystallization by dichloromethane to afford title compound **2**. ESI-MS *m/z* for C₈H₉ClS calcd. 172.68 found 173.5 (M+1) and 175.5 (M+3).

Synthesis of 1-(2-chloro-3-methyl-4-(methylthio)phenyl)ethanone (3)

To a stirred solution of AlCl₃ (1.3 eq.) in dichloromethane at 10-15 °C acetyl chloride (1.2 eq.) was added drop wise. This mixture was stirred for 0.5 h. then reaction mixture was cooled to 0-5 °C and compound **2** (1.0 eq.) was added slowly in drop wise manner. This reaction mixture was stirred at same temperature for 2. Reaction was quenched by dil. HCl and extracted by dichloromethane. Organic layer was dried over sodium sulphate and evaporated under reduced pressure to get compound **3**. ESI-MS *m/z* for C₁₀H₁₁ClOS calcd. 214.7 found 215.6 (M+1) and 217.6 (M+3).

Synthesis of 1-(2-chloro-3-methyl-4-(methylsulfonyl)phenyl)ethanone (4)

To a stirred solution of compound **3** (1.0 eq.) in acetic acid (5 vol) hydrogen peroxide (3.0 eq.) was added drop wise and stirred at room temperature for 10-12 h. The progress of reaction was monitored on TLC. After completion of reaction, the reaction mixture was quenched with sodium bicarbonate and extracted with ethyl acetate. Organic layer was evaporated and crude was purified by crystallization by dichloromethane/ Methanol to afford title compound **4**. ESI-MS m/z for $C_{10}H_{11}ClO_3S$ calcd. 246.7 found 247.7 (M+1) and 249.7 (M+3).

General Procedure for the synthesis of 5(a-l)

Method A: Conventional

To a solution of substituted acetophenone **3/4** (1 mmol) and aromatic aldehyde **6(a-f)** (1 mmol) dissolved in ethanol/methanol (10 mL) 10% aq. solution of KOH was added. The reaction mixture was stirred at room temperature for 24-36 h. After the completion of the reaction as monitored by TLC, the reaction mixture was treated with ice-cold water/dilute acid to get the precipitate of crude product. The product was filtered, washed with water and recrystallized with ethanol or ethanol-benzene mixture (1:1; v/v) to afford analytical samples of the products.

Method B: Solid phase microwave irradiation (MWI)

To a solution of substituted acetophenone **3/4** (1 mmol) and aromatic aldehyde **6(a-f)** (1 mmol) was mixed properly with catalyst-solid support (5:95% w/w) by proper grinding. The reaction mixture was placed in an alumina bath¹² inside the microwave oven and irradiated intermittently at power level 60% for a period as specified in Table 1. On completion of the reaction (TLC), the mixture was cooled and extracted by diethylether and recrystallized using similar procedure as mentioned in method A.

(E)-1-(2-Chloro-3-methyl-4-(methylthio)phenyl)-3-phenylprop-2-en-1-one (5a)

MWI reaction time = 10 min; Light yellow; M.P. 95-97 °C; Yield 83%; IR (ν_{\max} , KBr); 1647 (CO), 1597 (Ar), 1066 (CH=CH trans) cm^{-1} ; ^1H NMR (DMSO- d_6) δ ; 7.36-7.39 (d, $J=14.8$ Hz, 1H- β), 7.29-7.31 (m, 2H), 7.22-7.26 (d, $J=14.8$ Hz, 1H- α), 7.11-7.31(m, 5H), 2.56 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (DMSO- d_6) δ ; 15.22, 16.93, 122.79 (C- α), 126.63, 126.91, 130.48, 130.66, 132.90, 135.77, 140.41, 142.67, 147.10 (C- β), 153.58, 194.16 (CO); ESI-MS m/z for $C_{17}H_{15}ClOS$ calcd. 302.82 found 303.27 (M+1) and 305.27 (M+3).

(E)-1-(2-Chloro-3-methyl-4-(methylthio)phenyl)-3-(4-methoxyphenyl)prop-2-en-1-one (5b)

MWI reaction time = 8 min; Off white; M.P. 138-140 °C; Yield 84%; IR (ν_{\max} , KBr); 1629 (CO), 1599 (Ar), 1028 (CH=CH trans) cm^{-1} ; ^1H NMR (DMSO- d_6) δ ; 7.70-7.72 (d, 2H), 7.35-7.37 (d, 2H), 7.29-7.33 (d, $J=14.8$ Hz, 1H- β), 7.07-7.10 (d, $J=14.8$ Hz, 1H- α), 6.97-6.99 (d, 2H), 3.81 (s, 3H), 2.55 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (DMSO- d_6) δ ; 15.22, 16.92, 55.87, 114.98, 122.75 (C- α), 124.79, 127.07, 127.29, 130.56, 131.24, 132.91, 135.87, 142.78, 146.38 (C- β), 162.10, 193.62 (CO); ESI-MS m/z for $C_{18}H_{17}ClO_2S$ calcd. 332.84 found 332.40 (M+1) and 334.4 (M+3).

(E)-1-(2-Chloro-3-methyl-4-(methylthio)phenyl)-3-(3,4-dimethoxyphenyl)prop-2-en-1-one (5c)

MWI reaction time = 6 min; Light yellow; M.P. 142-144 °C; Yield 88%; IR (ν_{\max} , KBr); 1640 (CO), 1596 (Ar), 1023 (CH=CH trans) cm^{-1} ; ^1H NMR (DMSO- d_6) δ ; 7.37-7.38 (m, 2H), 7.31-7.35 (d, $J=15.6$ Hz, 1H- β), 7.28-7.30 (m, 2H), 7.12-7.16 (d, $J=15.6$ Hz, 1H- α),

6.99-7.01 (d, $J=8.4$ Hz, 1H), 3.80 (s, 6H), 2.56 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (DMSO- d_6) δ : 15.23, 16.93, 56.09, 56.13, 111.38, 112.08, 122.78 (C- α), 124.11, 125.05, 126.97, 127.40, 128.79, 130.51, 132.89, 135.95, 142.68, 147.04 (C- β), 149.50, 151.97, 193.86 (CO); ESI-MS m/z for : $\text{C}_{19}\text{H}_{19}\text{ClO}_3\text{S}$ calcd. 362.87 found 363.4 (M+1) and 365.4 (M+3).

(E)-1-(2-Chloro-3-methyl-4-(methylthio)phenyl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (5d)

MWI reaction time = 7 min; Light yellow; M.P. 146-148 °C; Yield 91%; IR (ν_{max} , KBr); 1664 (CO), 1607 (Ar), 1065 (CH=CH trans) cm^{-1} ; ^1H NMR (DMSO- d_6) δ : 7.35-7.38 (d, $J=14.8$ Hz, 1H- β), 7.29-7.31 (m, 2H), 7.21-7.25 (d, $J=14.8$ Hz, 1H α), 7.11(s, 2H), 3.81 (s, 6H), 3.70 (s, 3H), 2.56 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (DMSO- d_6) δ : 15.21, 16.90, 56.55, 60.54, 60.59, 106.94, 122.74 (C- α), 126.68, 126.99, 130.52, 130.63, 132.89, 135.75, 140.44, 142.77, 147.04 (C- β), 153.58, 194.06 (CO); ESI-MS m/z for $\text{C}_{20}\text{H}_{21}\text{ClO}_4\text{S}$ calcd. 392.90 found 393.07 (M+1) and 395.07 (M+3).

(E)-1-(2-Chloro-3-methyl-4-(methylthio)phenyl)-3-(2,4-dichlorophenyl)prop-2-en-1-one (5e)

MWI reaction time = 5 min; Yellow; M.P. 130-132 °C; Yield 90%; IR (ν_{max} , KBr); 1664 (CO), 1603 (Ar), 1060 (CH=CH trans) cm^{-1} ; ^1H NMR (DMSO- d_6) δ : 7.29- 8.07 (m, 5H), 7.66-7.70 (d, $J=16$ Hz, 1H- β), 7.37-7.40 (d, $J=16$ Hz, 1H α), 2.56 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (DMSO- d_6) δ : 15.18, 16.87, 122.65 (C- α), 127.57, 128.57, 129.88, 130.03, 130.26, 130.81, 131.40, 133.02, 135.0, 135.46, 136.39, 138.79, 144.01 (C- β), 192.68 (CO); ESI-MS m/z for $\text{C}_{17}\text{H}_{13}\text{Cl}_3\text{OS}$ calcd. 371.71 found 372.96 (M+1) and 374.96 (M+3).

(E)-3-(4-Bromophenyl)-1-(2-chloro-3-methyl-4-(methylthio)phenyl)prop-2-en-1-one(5f)

MWI reaction time = 3 min; Yellow; M.P. 119-121 °C; Yield 87%; IR (ν_{max} , KBr); 1671 (CO), 1601 (Ar), 1059 (CH=CH trans) cm^{-1} ; ^1H NMR (DMSO- d_6) δ : 7.29-7.74 (m, 6H), 7.39-7.43 (d, $J=16$ Hz, 1H- β), 7.26-7.30 (d, $J=16$ Hz, 1H α), 2.56 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (DMSO- d_6) δ : 15.20, 16.90, 122.72 (C- α), 124.81, 127.31, 127.75, 130.67, 131.18, 132.44, 132.97, 133.97, 135.37, 143.36, 144.64 (C- β), 193.44 (CO); ESI-MS m/z for $\text{C}_{17}\text{H}_{14}\text{BrClOS}$ calcd. 381.71 found 383.1 (M+1) and 385.01 (M+3).

(E)-1-(2-Chloro-3-methyl-4-(methylsulfonyl)phenyl)-3-phenylprop-2-en-1-one (5g)

MWI reaction time = 11 min; Light brown; M.P. 122-124 °C; Yield 87 %; IR (ν_{max} , KBr); 1629 (CO), 1599 (Ar), 1028 (CH=CH trans) cm^{-1} ; ^1H NMR (DMSO- d_6) δ : 7.38-7.41 (d, $J=15$ Hz, 1H- β), 7.45-7.47 (m, 2H), 7.25-7.28 (d, $J=15$ Hz, 1H α), 7.15-7.37 (m, 5H), 3.42 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (DMSO- d_6) δ : 15.13, 49.21, 122.93 (C- α), 126.64, 126.95, 130.51, 134.66, 137.91, 139.37, 141.41, 143.71, 148.20(C- β), 155.59, 194.16 (CO); ESI-MS m/z for $\text{C}_{17}\text{H}_{15}\text{ClO}_3\text{S}$ calcd. 334.82 found 333.7 (M+1) and 335.7 (M+3).

(E)-1-(2-Chloro-3-methyl-4-(methylsulfonyl)phenyl)-3-(4-methoxyphenyl)prop-2-en-1-one (5h)

MWI reaction time = 6 min; Light yellow; M.P. 149-151 °C; Yield 80%; IR (ν_{max} , KBr); 1644 (CO), 1597 (Ar), 1045 (CH=CH trans) cm^{-1} ; ^1H NMR (DMSO- d_6) δ : 7.73-7.75 (m, 2H), 7.39-7.41 (d, 2H), 7.32-7.36 (d, $J=15.2$ Hz, 1H- β), 7.09-7.12(d, $J=15.2$ Hz, 1H α), 6.98-6.99 (d, 2H), 3.82 (s, 6H), 3.43 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (DMSO- d_6) δ : 15.07, 49.31, 55.90, 155.2, 122.99(C- α), 126.31, 128.27, 128.59, 131.51, 134.97, 136.37, 138.92, 144.18, 148.3904 (C- β), 162.91, 194.42(CO); ESI-MS m/z for $\text{C}_{18}\text{H}_{17}\text{ClO}_4\text{S}$ calcd. 364.84 found 389.2 (M+Na).

(E)-1-(2-Chloro-3-methyl-4-(methylsulfonyl)phenyl)-3-(3,4-dimethoxyphenyl)prop-2-en-1-one (5i)

MWI reaction time = 4 min; Light pink; M.P. 186-189 °C; Yield 91%; IR (ν_{\max} , KBr); 1639 (CO), 1509 (Ar), 1023 (CH=CH trans) cm^{-1} ; ^1H NMR (DMSO- d_6) δ : 7.44-7.45 (m, 2H), 7.34-7.37 (d, $J=15.4$ Hz, 1H- β), 7.32-7.33 (m, 2H), 7.13-7.16 (d, $J=15.4$ Hz, 1H α), 3.81 (s, 6H), 3.44 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (DMSO- d_6) δ : 15.09, 49.37, 56.02, 56.23, 111.73, 111.99, 122.93 (C- α), 126.41, 127.21, 127.73, 129.04, 129.89, 131.42, 133.45, 139.21, 144.27, 148.53 (C- β), 150.27, 152.49, 194.70 (CO); ESI-MS m/z for $\text{C}_{19}\text{H}_{19}\text{ClO}_5\text{S}$ calcd. 394.87 found 393.07 (M-1).

(E)-1-(2-Chloro-3-methyl-4-(methylsulfonyl)phenyl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (5j)

MWI reaction time = 3.5 min; yellow; M.P. 135-138 °C; Yield 82%; IR (ν_{\max} , KBr); 1640 (CO), 1599 (Ar), 1029 (CH=CH trans) cm^{-1} ; ^1H NMR (DMSO- d_6) δ : 7.37-7.41 (d, $J=15.1$ Hz, 1H- β), 7.35-7.36 (m, 2H), 7.23-7.26 (d, $J=15.1$ Hz, 1H α), 7.17 (s, 2H), 3.73 (s, 3H), 3.85 (s, 6H), 3.70 (s, 3H), 3.44 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (DMSO- d_6) δ : 1511, 49.42, 56.29, 60.61, 60.69, 107.42, 122.98 (C- α), 128.18, 128.71, 131.53, 132.07, 133.91, 138.35, 141.74, 144.37, 148.88 (C- β), 155.31, 194.81 (CO); ESI-MS m/z for $\text{C}_{20}\text{H}_{21}\text{ClO}_6\text{S}$ calcd. 424.90 found 424.3 (M-1).

(E)-1-(2-Chloro-3-methyl-4-(methylsulfonyl)phenyl)-3-(2,4-dichlorophenyl)prop-2-en-1-one (5k)

MWI reaction time = 5.5 min; Light yellow; M.P. 133-135 °C; Yield 86%; IR (ν_{\max} , KBr); 1645 (CO), 1601 (Ar), 1042 (CH=CH trans) cm^{-1} ; ^1H NMR (DMSO- d_6) δ : 7.31-8.13 (m, 5H), 7.67- 7.71- (d, $J=16$ Hz, 1H- β), 7.37-7.41 (d, $J=16$ Hz, 1H α), 3.47 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (DMSO- d_6) δ : 15.03, 49.36, 122.78 (C- α), 128.17, 129.53, 130.09, 130.99, 131.04, 131.83, 133.21, 135.09, 136.17, 136.59, 136.89, 139.99, 145.41 (C- β), 193.19 (CO); ESI-MS m/z for $\text{C}_{17}\text{H}_{13}\text{Cl}_3\text{O}_3\text{S}$ calcd. 403.71 found 404.6 (M+1) and 406.6 (M+3).

(E)-3-(4-bromophenyl)-1-(2-chloro-3-methyl-4-(methylsulfonyl)phenyl)prop-2-en-1-one (5l)

MWI reaction time = 3 min; Light brown; M.P. 108-110 °C; Yield 88%; IR (ν_{\max} , KBr); 1644 (CO), 1604 (Ar), 1044 (CH=CH trans) cm^{-1} ; ^1H NMR (DMSO- d_6) δ : 7.26-7.77 (m, 6H), 7.40-7.44 (d, $J=15.8$ Hz, 1H- β), 7.28-7.31 (d, $J=15.8$ Hz, 1H α), 3.45 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (DMSO- d_6) δ : 15.08, 49.39, 122.93 (C- α), 126.21, 128.97, 129.51, 130.99, 132.47, 133.09, 133.97, 134.59, 136.91, 144.42, 146.03 (C- β), 193.44 (CO); ESI-MS m/z for $\text{C}_{17}\text{H}_{14}\text{BrClO}_3\text{S}$ calcd. 413.71 found 414.07 (M+1) and 415.07 (M+3).

Results and Discussion

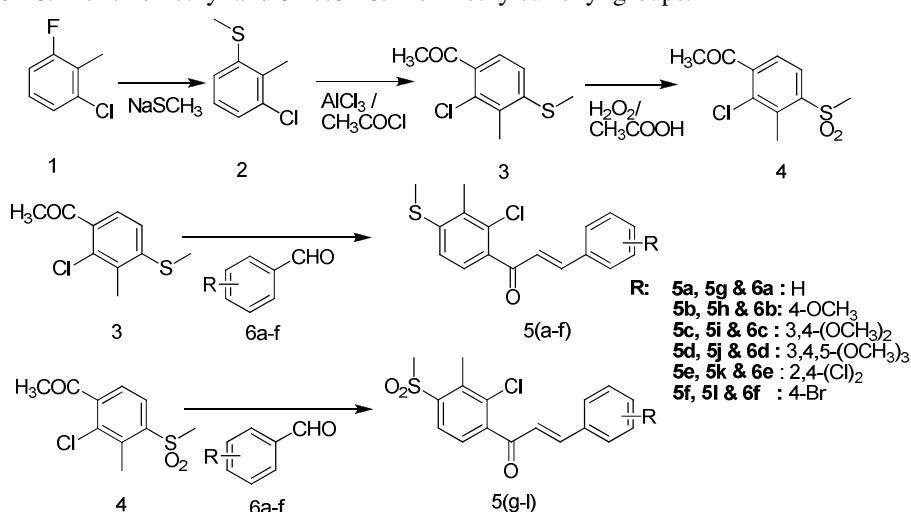
Chemistry

As per the synthetic route given in Scheme 1, the intermediate compounds were synthesized using well established methods in which thiomethyl group was introduced by nucleophilic substitution of fluoro by thiomethyl group. This was acetylated by Friedel-Crafts acylation to get compound **3**. This acetophenone was further oxidized by hydrogen peroxide in acetic acid to achieve final material **4**.

These acetophenone (**3** and **4**) and other different methoxy substituted benzaldehydes (**6a-f**) were condensed on a solid inorganic support (10% $\text{Ba}(\text{OH})_2$ -celite) under microwave irradiation to afford the desired chalcone in 3 to 10 min time. The structures of all synthesized

compounds were established on the basis of their spectral data. In the IR spectra the chalcone had absorption around $1660\text{--}1625\text{ cm}^{-1}$ and near 1000 cm^{-1} indicative of the conjugated carbonyl and --CH=CH-- out of plane trans vibrations. The C=C bond absorptions were seen around $1610\text{--}1550\text{ cm}^{-1}$. The C-Cl and C-S-CH_3 absorption were seen around $804\text{--}807$, $1240\text{--}1280\text{ cm}^{-1}$ respectively. The ^1H NMR doublets at δ 7.35-7.10 and 7.70-7.40 with coupling constant values of $\sim 15\text{ Hz}$ indicated the presence of two ethylenic hydrogens $\text{H-}\alpha$ and $\text{H-}\beta$ respectively as AB pattern in the *E*-configuration. The chemical shift of $\text{H-}\alpha$ proton is of higher field than those of $\text{H-}\beta$ proton in all chalcones. This may be possible due to the polarization of C=C double bond in the system being predominantly caused by the carbonyl group so as to make electron density greatest at the α -position than that of β -position. The methylthio and methyl sulfonyl group was identified by their characteristic δ values near 3.0 δ for methylthio and near 3.5 δ for methyl sulfonyl groups respectively.

^{13}C NMR spectra of synthesized compounds showed three characteristic signals in the region $194\text{--}190\text{ }\delta$, $125\text{--}122\text{ }\delta$ and $149\text{--}144\text{ }\delta$ assigned to α - β -unsaturated carbonyl, ethylenic C_α and C_β respectively along with other signals of aromatic and substituted carbon and δ 15.0-16.2 for thiomethyl and δ 47.8-48.2 for methylsulfonyl groups.



Antimicrobial evaluation

All the representative compounds were screened *in vitro* for their antibacterial activity against *Proteus mirabilis*, *Klebsiella pneumonia*, *Escherichia coli* and *Pseudomonas aeruginosa* by using cup-plate agar diffusion method by measuring the zone of inhibition in mm (Table 1). The test compounds were used at the concentration of $1000\text{ }\mu\text{g/mL}$ in DMSO and streptomycin was used as standard drug with DMSO as control. All the compounds were active against *B. subtilis*. Chalcones having polar hydroxyl and methyl groups along with electron withdrawing nitro groups (**3b** and **3c**) and lipophilic chloro group along with or without polar methoxy (**3m** and **3p**) showed significant activity against *B. subtilis* where as chalcones having lipophilic chloro group along with polar methoxy or dimethylamino groups (**3m** and **3r**) showed significant greatest activity against *E. coli* and was comparable to standard used.

The cup plate method using PDA medium¹⁴ was employed to study antifungal activity of *Candida albicans* and *Aspergillus fumigatus*. Each test compound was dissolved in 5 mL of dimethyl sulfoxide (1000 µg/mL) volume of and 1 mg/mL of each compound were used for testing. Amphotericin-B was used as standard drug (100 µg/mL) and dimethyl sulfoxide as a control. The observed zone of inhibition was measured in mm (Table 1).

In correlating the biological activities of compounds with their structure, it was observed that the most potent antibacterial compounds **5d** and **5j** had methoxy functional groups and most potent antifungal compounds had **5e** and **5k** had chloro functional groups respectively. The notable point is that most of the compounds had methoxy groups which influence their activity compare to methyl and chloro groups. It was also noted that sulfones also enhance antibacterial and fungal activity compare to methylthio group. This may be because the sulfone group supplies its electron more strongly than the methylthio group, as the former group contain two electronegative oxygen atoms.

Table 1. Antimicrobial activity of the synthesized compounds **5a-l**

Compd. No.	Antibacterial activity Zone of inhibition in mm (activity index)				Antifungal activity zone of inhibition in mm (activity index)	
	<i>P. mirabilis</i>	<i>K.pneumonia</i>	<i>E.coli</i>	<i>P.aeruginosa</i>	<i>C.albicans</i>	<i>A.fumigatus</i>
5a	10 (0.59)	9 (0.56)	9 (0.56)	11 (0.61)	15 (0.88)	8 (0.8)
5b	10 (0.59)	11 (0.69)	10 (0.63)	12 (0.56)	17 (1.0)	10 (1.0)
5c	8 (0.47)	7 (0.44)	7 (0.44)	6 (0.33)	12 (0.71)	8 (0.8)
5d	11 (0.65)	13 (0.81)	12 (0.75)	13 (0.72)	13 (0.76)	9 (0.9)
5e	9 (0.53)	9 (0.56)	8 (0.50)	12 (0.56)	18 (1.05)	10 (1.0)
5f	9 (0.53)	11 (0.69)	9 (0.56)	7 (0.39)	16 (0.94)	9 (0.9)
5g	7 (0.41)	8 (0.50)	9 (0.56)	9 (0.5)	14 (0.78)	7 (0.7)
5h	8 (0.47)	10 (0.63)	11 (0.69)	16 (0.89)	19 (1.06)	8 (0.8)
5i	9 (0.53)	9 (0.56)	10 (0.63)	8 (0.44)	14 (0.78)	10 (1.0)
5j	13 (0.76)	14 (0.88)	14 (0.88)	15 (0.83)	15 (0.88)	11 (1.1)
5k	10 (0.59)	11 (0.69)	9 (0.56)	14 (0.78)	20 (1.18)	13 (1.3)
5l	11 (0.65)	10 (0.63)	10 (0.63)	9 (0.5)	13 (0.76)	10 (1.0)
C1	17	16	16	18	17	10

Activity Index = inhibition zone of compound / inhibition zone of standard drug C1 = Ciprofloxacin (for antibacterial activity) and Amphotericin B (for antifungal activity)

Conclusion

In summary we have reported a general and potential route for the synthesis of chalcones using Ba(OH)₂-cilite solid support. Condensation was clean with high yield in a short span of time and further utilization of green chemistry where solvents and solid support both were recycled. Antimicrobial activities showed that many of these newly synthesized chalcones have excellent activities *i.e.* **5d**, **5j**, **5l** against *P. mirabilis*, **5d**, **5j** against *K. pneumonia*, **5j** against *E. coli*, **5d**, **5h**, **5j** and **5l** against *P. aeruginosa*, **5a**, **5b**, **5e**, **5f**, **5h** and **5k** against *C. albicans* and **5b**, **5e**, **5i**, **5j**, **5k**, **5l** against *A. fumigatus*.

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