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α-Tosyloxyacetophenones: As a precursor in ultrasonic assisted multicomponent, diastereoselective synthesis of *trans*-2,3-dihydrofuro[3,2-c] coumarins using [BMIm]OH and their antimicrobial evaluation

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ABSTRACT

*An eco-friendly, facile and efficient approach for the diastereoselective synthesis of differently substituted trans-2,3-dihydrofuro[3,2-c]coumarins is described. The method is based on the use of α-tosyloxyketones as a precursor and ultrasonic irradiation as a source of energy and ionic liquid [BMIm]OH, which functions both as a catalyst and the reaction medium for the synthesis of trans-2,3-dihydrofuro[3,2-c]coumarins. The developed protocol provides a better alternative to the existing methods as it involves utilization of α-tosyloxyacetophenones avoiding the use of α-haloacetophenones.The antifungal and antibacterial evaluation of the title compounds **4a-4l** is also described.*

Keywords: [BMIm]OH,α-Tosyloxyketones, Antifungal, Antibacterial, Ultrasonic irradiation, Furo[3,2-*c*]coumarin

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INTRODUCTION

Dihydrofurans represents an important class of oxygen containing heterocyclic compounds having a wide range of biological activities and form the basic structure of many natural products [1,2]. Due to wide range of biological activities related with this class of compound, development of various new and efficient methods for these compounds has been an area of current interest. Among the various reported procedures for the synthesis of dihydrofuran derivatives, oxidative coupling reactions of alkenes with active methylene compounds involving transition metal salts such us cerium(IV) ammonium nitrate[3,4] and manganese(III) acetate[5,6] and reactions of diazo compounds[7] or iodonium ylides[8] with alkenes employing organocatalyst are the most common. Moreover, 4-hydroxycoumarin is a recurring structural motif in many natural products of medicinal interest[9].

Because of the unique properties, such as low vapour pressure, high chemical and thermal stability, solvating ability, non-flammability, behaviour as acidic or basic catalysts and recyclability associated with room temperature ionic liquids they are widely recognised as green solvents in synthetic organic chemistry. [10,11] Owing to these green credentials, ionic liquids have attracted great interest as environmentally benign reaction media[12] catalysts[13] and reagents [14] besides having many other applications.Also the use of ultrasonic irradiation in chemical reactions as an alternative energy source has proved to be one of the stepping stone towards the green syntheses as it offers advantage of enhanced reactivity, shorter reaction times and higher yields of pure products compared to the traditional heating methods [15, 16].

Keeping in mind the biological importance associated with furo[3,2-*c*]coumarinsand need for the development of greener protocol for their synthesis. We decided to establish a greener protocol for the synthesis along with antifungal and antibacterial evaluation of furo[3,2-*c*]coumarins that was more universal and satisfied the criteria of green chemistry.

EXPERIMENTAL SECTION

Melting points were taken in open capillaries and are uncorrected. IR spectra were recorded on a Perkin-Elmer 1800 Fourier transform (FT)–IR spectrophotometer.^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker 300-MHz instrument using tetramethysilane (TMS) as an internal standard. The chemical shifts are expressed in parts per million (ppm) downfield from an internal tetramethylsilane(TMS) standard. Ultrasonic bath (54 KHz, 300 W, 1Lt Capacity) of Through clean ultrasonic Pvt. Ltd (India) was used for the reactions under ultrasonic irradiation. α-Tosyloxyacetophenones**(2)**, required for the synthesis of targeted compounds were prepared according to the procedure reported in the literature[17].

General procedure for the synthesis of 4a-4l

A mixture of 4-hydroxycoumarin **(1)**(1.0 mmol), α-tosyloxyacetophenone **(2)**(1.0 mmol), benzaldehyde **(3)**(1.0 mmol) and pyridine(1.0 mmol) in water (10 ml) was placed in a 50 ml round bottomed flask. To this was added 40 mol% [BmIm]OH. The reaction mixture was sonicated at 50 ^{o}C for 45-60 min. After completion of the reaction as evident by TLC using (ethyl acetate: petroleum ether; 25:75, v/v), the reaction mixture was allowed to cool to room temperature, water was added to the reaction mixture and the precipitate thus formed was collected by filtration at suction pump and washed with cold ethanol to afford *trans*-2-aryloyl-3-aryl-2,3-dihydrofuro[3,2-*c*]coumarins **(4a-4l)** in high yield.

Characterization data of compound (4a-4l)

Compound 4a: IR (ν_{max}, cm^{-1}): 1716, 1649;^{1}H NMR(δ, ppm): 4.79-4.80 (d, 1H, J = 5.4 Hz), 6.17-6.19 (d, 1H, J = 4.8 Hz), 7.30-7.40 (m, 7H), 7.49-7.51 (d, 2H, J = 7.2 Hz), 7.60-7.66 (m, 1H), 7.81-7.87 (m, 3H);^{13}C NMR: 192.1, 166.4, 159.3, 155.4, 139.6, 134.5, 133.2, 133.0, 129.3, 129.1, 128.2, 127.6, 124.2, 123.2, 117.0, 112.2, 105.4, 92.6, 49.3; Anal Calcd for $C_{24}H_{16}O_4$: C 78.25, H 4.48; Found: C 78.02, H 4.77.

Compound 4b: IR (ν_{max}, cm^{-1}): 1706, 1661; ^{1}H NMR (δ, ppm): 4.83-4.84 (d, 1H, J = 5.1 Hz), 6.12-6.14 (d, 1H, J = 5.1 Hz), 7.30-7.42 (m, 7H), 7.48-7.50 (d, 2H, J = 8.7 Hz), 7.60-7.65 (m, 1H), 7.82-7.88 (m, 3H); ^{13}C NMR: 48.76, 92.37, 104.95, 112.10, 117.10, 123.22, 124.19, 126.16, 128.98, 129.18, 129.44, 129.78, 130.67, 133.03, 134.04, 138.15, 145.74, 155.45, 159.19, 166.50, 191.42; Anal. Calcd for $C_{24}H_{15}O_4Cl$: C 71.56, H 3.73 %; Found C 71.52, H 3.72 %.

Compound 4c: IR (ν_{max}, cm^{-1}): 1722, 1606; ^{1}H NMR (δ, ppm): 3.82 (s, 3H), 4.73 (d, 1H, J = 4.8Hz), 6.15 (d, 1H, J = 4.8Hz), 6.91 (d, 2H, J = 9.0Hz), 7.23 (d, 2H, J = 9.0Hz) , 7.35 (t, 1H, J = 7.2Hz), 7.40 (d, 1H, J = 7.8Hz), 7.51 (t, 2H, J = 7.8Hz), 7.61 (t, 1H, J = 7.8Hz), 7.66 (t, 1H, J = 7.2Hz), 7.85 (d, 1H, J = 7.8Hz), 7.90 (d, 2H, J = 7.8Hz);^{13}C NMR : 192.2, 166.2, 159.4, 155.4, 134.4, 133.2, 132.9, 131.6, 129.1, 129.0, 128.7, 124.1, 123.2, 117.0, 114.7, 112.2, 105.5, 92.8, 55.3, 48.9; Anal Calcd for $C_{25}H_{18}O_5$: C 75.37, H 4.55; Found: C 74.90, H 4.83.

Compound 4d: IR (ν_{max}, cm^{-1}): 1712(s), 1648(s); ^{1}H NMR(δ, ppm): 4.82 (d, 1H, J = 4.8Hz), 6.12 (d, 1H, J = 5.4Hz), 7.25 (d, 2H, J = 9.0Hz), 7.36-7.34 (m, 3H), 7.40 (d, 1H, J = 8.4Hz), 7.52 (t, 2H, J = 7.8Hz), 7.62 (t, 1H, J = 7.2Hz), 7.67 (t, 1H, J = 7.2Hz), 7.83 (d, 1H, J = 7.8Hz), 7.90 (d, 2H, J = 7.8Hz);^{13}C NMR: 191.8, 166.5, 159.2, 155.4, 138.1, 134.6, 134.1, 133.2, 133.1, 129.5, 129.1, 129.0, 124.2, 123.2, 117.1, 112.1, 104.9, 92.4, 48.7; Anal Calcd for $C_{24}H_{15}ClO_4$: C 71.56, H 3.75; Found: C 71.48, H 3.94.

Compound 4e: IR (ν_{max}, cm^{-1}): 1735, 1685; ^{1}H NMR (δ, ppm): 2.45 (s, 3H, CH_3), 4.79-4.81 (d, 1H, J = 4.8 Hz), 6.16-6.18 (d, 1H, J = 4.8 Hz), 7.29-7.41 (m, 9H), 7.55-7.64 (m, 1H), 7.80-7.87 (m, 3H); ^{13}C NMR: 21.82, 49.46, 92.61, 105.37, 115.45, 117.02, 123.38, 127.58, 128.12, 129.26, 130.68, 132.63, 139.68, 153.40, 159.29, 164.98, 191.70; Anal. Calcd for $C_{25}H_{18}O_4$: C 78.53, H 4.71 %; Found C 78.49, H 4.72 %.

Compound 4f: IR (ν_{max}, cm^{-1}): 1744, 1674; ^{1}H NMR (δ, ppm): 2.37 (s, 3H, CH_3), 4.77- 4.79 (d, 1H, J = 4.8 Hz), 6.11-6.13 (d, 1H, J = 4.8 Hz), 7.16-7.42 (m, 8H), 7.60-7.65 (m, 1H), 7.83-7.86 (dd, 1H, J = 0.9 Hz, J′ = 7.8 Hz), 7.94-7.98 (dd, 2H, J = 5.4 Hz, J' = 9.0 Hz); ^{13}C NMR: 21.13, 49.08, 92.65, 105.45, 112.18, 116.16, 116.45, 117.06, 123.12, 124.12, 127.41, 129.71, 129.75, 130.01, 131.79, 131.92, 132.87, 136.46, 138.01, 155.41, 159.20, 164.74, 166.08, 168.15, 190.68; Anal. Calcd for $C_{25}H_{17}O_4F$: C 75.00, H 4.25 %; Found C 74.73, H 4.22 %.

Compound 4g: IR (ν_{max}, cm^{-1}): 1715, 1636; ^{1}H NMR (δ, ppm): 4.82-4.84 (d, 1H, J = 5.1 Hz), 6.11-6.13 (d, 1H, J = 5.1 Hz), 7.28-7.42 (m, 7H), 7.60-7.68 (m, 3H), 7.78-7.85 (m, 3H); ^{13}C NMR: 49.20, 92.57, 105.32, 112.10, 117.10, 123.13, 124.17, 127.54, 128.26, 129.36, 129.91, 130.52, 132.02, 132.41, 132.96, 139.39, 155.42, 159.14, 166.12, 191.22; Anal. Calcd for $C_{24}H_{15}O_4Br$: C 64.45, H 3.36 %. Found C 64.39, H 3.36 %.

Compound 4h: IR (ν_{max}, cm^{-1}): 1715, 1636; ^1H NMR (δ, ppm): 3.92 (s, 3H, OCH_3), 4.81-4.82 (d, 1H, J= 4.8 Hz), 6.14-6.16 (d, 1H, J= 4.8 Hz), 6.96-6.99 (d, 2H, J = 9.0 Hz), 7.32-7.43 (m, 7H), 7.60-7.65 (m, 1H), 7.85-7.91 (m, 3H); ^{13}C NMR: 49.55, 55.61, 92.52, 105.40, 112.26, 114.28, 117.04, 123.21, 124.09, 126.12, 127.59, 128.09, 129.26, 131.46, 132.83, 139.73, 155.42, 159.32, 164.54, 166.42, 190.58; Anal. Calcd for $C_{25}H_{18}O_5$: C 75.37, H 4.52 %; Found C 75.67, H 4.85 %.

Compound 4i: IR (ν_{max}, cm^{-1}): 1712, 1649; ^1H NMR (δ, ppm): 2.36 (s, 3H), 4.74 (d, 1H, J = 4.8Hz), 6.16 (d, 1H, J = 4.8Hz), 7.35 (t, 1H, J = 7.8Hz), 7.40 (d, 1H, J = 8.4Hz), 7.50 (t, 2H, J = 7.8Hz), 7.61 (t, 1H, J = 7.8Hz), 7.66 (t, 1H, J = 7.2Hz), 7.85 (d, 1H, J = 7.8Hz), 7.90 (d, 2H, J = 7.2Hz);^{13}C NMR: 192.2, 166.3, 159.3, 155.4, 137.9, 136.6, 134.4, 133.2, 132.8, 130.0, 129.1, 129.0, 127.4, 124.1, 123.2, 117.0, 112.2, 105.5, 92.7, 49.2, 21.2; Anal Calcd for $C_{25}H_{18}O_4$: C 78.52, H 4.74; Found: C 78.59, H 5.04.

Compound 4j: IR (ν_{max}, cm^{-1}): 1723, 1658; ^1H NMR (δ, ppm): 2.37 (s, 3H, CH_3), 4.76- 4.78 (d, 1H, J = 4.8 Hz), 6.10-6.12 (d, 1H, J = 4.8 Hz), 7.22-7.42 (m, 8H), 7.57-7.65 (m, 1H), 7.83-7.88 (m, 3H); ^{13}C NMR: 21.13, 49.02, 92.66, 105.43, 112.15, 117.06, 123.12, 124.14, 127.41, 129.39, 129.66, 130.02, 130.46, 132.89, 136.40, 138.04, 141.06, 155.40, 159.18, 166.06, 191.10; Anal. Calcd for $C_{25}H_{17}O_4Cl$: C 72.03, H 4.08 %; Found C 72.01, H 4.03 %.

Compound 4k: IR (ν_{max}, cm^{-1}): 1744, 1674; ^1H NMR (δ, ppm): 2.37 (s, 3H, CH_3), 2.46 (s, 3H, CH_3), 4.73-4.75 (d, 1H, J = 4.8 Hz), 6.14-6.16 (d, 1H, J = 4.8 Hz), 7.28-7.42 (m, 8H), 7.59-7.65 (m, 1H), 7.80-7.82 (d, 2H, J = 8.1 Hz), 7.86-7.88 (d, 1H, J = 7.8 Hz); ^{13}C NMR: 21.14, 21.81, 49.26, 92.69, 105.51, 112.29, 117.02, 123.21, 124.07, 127.44, 129.18, 129.91, 130.67, 132.78, 136.68, 137.86, 145.52, 155.41, 159.32, 166.32, 191.78; Anal. Calcd for $C_{26}H_{20}O_4$: C 78.77, H 5.05 %; Found C 78.73, H 5.03 %.

Compound 4l: IR (ν_{max}, cm^{-1}): 1720, 1660; ^1H NMR (δ, ppm): 2.47 (s, 3H, CH_3), 4.80-4.82 (d, 1H, J = 5.1 Hz), 6.10-6.12 (d, 1H, J = 5.1 Hz), 7.25-7.43 (m, 8H), 7.61-7.66 (m, 1H), 7.80-7.86 (m, 3H); ^{13}C NMR: 49.20, 92.59, 105.32, 112.10, 117.09, 123.25, 124.18, 127.54, 128.26, 129.35, 129.41, 129.52, 130.48, 132.15, 132.97, 139.40, 141.10, 155.41, 159.16, 166.14, 191.02; Anal. Calcd for $C_{25}H_{17}O_4Cl$: C 72.03, H 4.08 %; Found C 72.0, H 4.01 %.

Biological activities

Antimicrobial assay

Total six microbial strains were selected on the basis of their clinical importance in causing diseases in humans. Two Gram-positive bacteria (*Staphylococcus aureus* MTCC 96 and *Bacillus subtilis* MTCC 121); two Gram-negative bacteria (*Escherichia coli* MTCC 1652 and *Pseudomonas aeruginosa* MTCC 741) and two fungi, *Aspergillus niger* and *A. flavus*, the ear pathogens isolated from the patients of Kurukshetra [18], were used in the present study for evaluation of antimicrobial activity of the chemical compounds. All the bacterial cultures were procured from Microbial Type Culture Collection (MTCC), IMTECH, Chandigarh. The bacteria were subcultured on Nutrient agar whereas fungi on Sabouraud's dextrose agar.

Antibacterial activity

The antibacterial activity of 12 chemical compounds was evaluated by the agar well diffusion method. All the microbial cultures were adjusted to 0.5 McFarland standard, which is visually comparable to a microbial suspension of approximately 1.5 $\times 10^6$ cfu/mL. 20mL of Mueller Hinton agar medium was poured into each Petri plate and plates were swabbed with 100 µL inocula of the test microorganisms and kept for 15 min for adsorption. Using sterile cork borer of 8mm diameter, wells were bored into the seeded agar plates and these were loaded with a 100 µL volume with concentration of 2.0mg/mL of each compound reconstituted in the dimethylsulphoxide (DMSO). All the plates were incubated at 37^0C for 24 hrs. Antibacterial activity of each compound was evaluated by measuring the zone of growth inhibition against the test organisms with zone reader (HiAntibiotic zone scale). DMSO was used as a negative control whereas Ciprofloxacin was used as positive control. This procedure was performed in three replicate plates for each organism and the mean values of the diameter of inhibition zones ± standard deviations were calculated [19].

Determination of Minimum Inhibitory Concentration (MIC) of chemical compounds

MIC is the lowest concentration of an antimicrobial compound that will inhibit the visible growth of a microorganism after overnight incubation**.** MIC of the various compounds against bacterial strains was tested through a modified agar well diffusion method [19]. In this method, a two fold serial dilution of each chemically synthesized compound was prepared by first reconstituting the compound in DMSO followed by dilution in sterile distilled water to achieve a decreasing concentration range of 512 to 1µg/mL. A 100 µL volume of each dilution was introduced into wells (in triplicate) in the agar plates already seeded with 100µL of standardized inoculum (10^6 cfu/mL) of the test microbial strain. All test plates were incubated aerobically at 37^oC for 24 hrs and observed for the inhibition zones. MIC, taken as the lowest concentration of the chemical compound that completely inhibited the

growth of the microbe, showed by a clear zone of inhibition, was recorded for each test organism. Ciprofloxacin was used as positive control.

Antifungal activity

The antifungal activity of 12 chemical compounds was evaluated by poisoned food technique [20]. The molds were grown on Sabouraud's dextrose agar (SDA) at 25^0C for 7 days and used as inocula. The 15mL of molten SDA (45^0C) was poisoned by the addition of 100 µL volume of each compound having concentration of 2.0mg/ml reconstituted in the DMSO, poured into a sterile Petri plate and allowed it to solidify at room temperature. The solidified poisoned agar plates were inoculated at the center with fungal plugs (8mm diameter) obtained from the colony margins and incubated at 25^0C for 7 days. DMSO was used as the negative control whereas Fluconazole was used as the positive control. The experiments were performed in triplicates. Diameter of fungal colonies was measured and expressed as percent mycelial inhibition.

Percent inhibition of myelial growth = (dc-dt) / dc × 100

dc = average diameter of fungal colony in negative control sets
dt = average diameter fungal colony in experimental sets

RESULTS AND DISCUSSION

We began our study with the optimization of four component reaction of4-hydroxycoumarin **(1)**, α-tosyloxyacetophenone **(2)**, benzaldehyde **(3)** and pyridine. To achieve our aim firstly, 4-hydroxycoumarin **(1)**(1.0 mmol), α-tosyloxyacetophenone **(2)**(1.0 mmol), benzaldehyde **(3)** (1.0 mmol), and pyridine(1.0 mmol)was dissolved in water (10 ml) in a 50 ml round bottomed flask. To this $NaHCO_3$ (30 mol%) was added and the reaction mixture was sonicated at room temperature for 4 hr. the reaction was incomplete even after 4 hr. as evident by TLC using (ethyl acetate: petroleum ether; 25:75, v/v). Usual workup followed by purification afforded the trans-2-benzoyl-3-phenyl-2,3-dihydrofuro[3,2-*c*]coumarin**(4a)** in 35 % yield (Table 1, entry 1).The structures of **4a** were confirmedby the combined use of ^{1}H NMR, IR and ^{13}C NMR spectra and elemental analysis. In ^{1}H NMR of compound **4a**, the two protons at the 2,3-position of the dihydrofuran (DHF) ring display two doublets at δ 4.798–4.814 and δ6.169–6.185 ppm with the vicinal coupling constant J= 4.8 Hz. According to careful analysis and comparison to the previously reported results, it was concluded that the2,3-dihydrofuro[3,2-*c*]coumarins are trans-isomers [21].

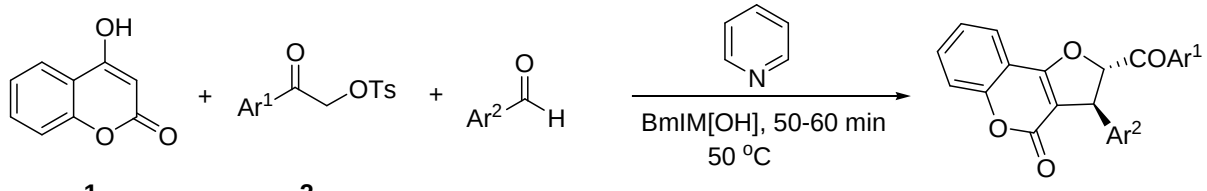
To improve the reaction efficacy it was further investigated using different basic reagents (Table 1, entry 2-5). It was found that using [BmIm]OH (30 mol%) results in the formation of **4a**in 75% yield in 2h (Table 1, entry 6). Inspired by the results obtained using [BmIm]OH as a catalyst in H_2O using ultrasonic irradiation at room temperature. The reaction was further explored by changing amount of catalyst and temperature (Table 1, entry 7-10). The reaction was then explored using different solvents (Table 1, entry 10, 11) but this didn't improve the results. Using [BmIm]OH (40 mol%) as a catalyst in H_2O using ultrasonic irradiation at 50^oC results in the formation of **4a** in 94% yield in 45 min (Table 1, entry 9).

Table 1. Reaction 4-hydroxycoumarin (1), α-tosyloxyacetophenone (2), benzaldehyde (3) and pyridine under various conditions[a]

Entry	Solvent	Catalyst (mol %)	Temp (^{o}C)	Time (min)	Yield (%)
1	H_2O	$NaHCO_3$(30)	35	240	35 [b]
2	H_2O	Piperidine (30)	35	240	40 [b]
3	H_2O	DBU (30)	35	240	50 [b]
4	H_2O	NaOH (30)	35	120	55[b]
5	H_2O	Imidazole (30)	35	120	60[b]
6	H_2O	[BmIm]OH (30)	35	120	75
7	H_2O	[BmIm]OH (40)	35	90	82
8	H_2O	[BmIm]OH (50)	35	90	78
9	H_2O	[BmIm]OH (40)	50	45	94
10	EtOH	[BmIm]OH (40)	50	70	88
11	MeOH	[BmIm]OH (40)	50	75	84

*[a]Reaction was performed using 4-hydroxycoumarin **(1)** (1.0 mmol), α-tosyloxyacetophenone **(2)** (1.0 mmol), benzaldehyde **(3)** (1.0 mmol), and pyridine (1.0 mmol) under ultrasonic irradiation, [b] Incomplete reaction*

To delineate the approach the same reaction was explored further using various substituted α-tosyloxyacetophenones **(2)**, different aromatic aldehydes **(3)**containing both electron donating and electron releasing groups under similar conditions to afford trans-2,3-dihydrofuro-[3,2-*c*]coumarin**(4a-4l)** (Scheme 1) (Table 2).



Scheme 1. Multicomponent, ionic mediated and ultrasound assisted synthesis of *trans*-2,3-dihydrofuro[3,2-*c*]coumarin

Table 2. Physical data of *trans*-2,3-dihydrofuro[3,2-*c*]coumarin(4a-4l)

Product	Ar^1	Ar^2	M.pt (°C) (lit mp°C)[21]	Yield (%)
4a	C_6H_5	C_6H_5	197 (198)	94
4b	4-ClC_6H_4	C_6H_5	221 (220)	88
4c	C_6H_5	4-$OMeC_6H_4$	180 (180)	90
4d	C_6H_5	4-ClC_6H_4	173 (172)	88
4e	4-MeC_6H_4	C_6H_5	227 (226)	90
4f	4-FC_6H_4	4-MeC_6H_4	215 (215)	88
4g	4-BrC_6H_4	C_6H_5	234 (234)	84
4h	4-$OMeC_6H_4$	C_6H_5	220 (220)	90
4i	C_6H_5	4-MeC_6H_4	194 (195)	92
4j	4-ClC_6H_4	4-MeC_6H_4	240 (240)	86
4k	4-MeC_6H_4	4-MeC_6H_4	256 (256)	92
4l	4-MeC_6H_4	4-ClC_6H_4	251 (250)	94

Biological screening

A total of 12 chemical compounds were screened for their antibacterial and antifungal activity. Tested chemical compounds possessed variable antibacterial activity against Gram-positive (*Staphylococcus aureus, Bacillus subtilis*) bacteria and antifungal activity against *Aspergillus niger* and *A. flavus.* However, tested chemical compounds did not exhibit any activity against Gram-negative bacteria. Positive controls produced significantly sized inhibition zones against the tested bacteria and fungi; however, negative control produced no observable inhibitory effect against any of the test organism as shown in Table 1 and 3.

Table 1: Antibacterial activity of chemical compounds through agar well diffusion method

Compound No.	Diameter of growth of inhibition zone (mm)[a]			
	Staphylococcus aureus	***Bacillus subtilis***	***Escherichia coli***	***Pseudomonas aeruginosa***
4a	16.3	17.0	-	-
4b	17.6	**18.6**	-	-
4c	15.0	15.6	-	-
4d	15.3	16.3	-	-
4e	16.3	17.6	-	-
4f	**18.3**	**20.3**	-	-
4g	17.6	**18.6**	-	-
4h	15.3	17.3	-	-
4i	14.6	15.6	-	-
4j	14.3	15.3	-	-
4k	14.6	15.6	-	-
4l	14.6	15.3	-	-
Ciprofloxacin	26.6	24.0	25.0	22.0

- No activity, [a]Values, including diameter of the well (8mm), are means of three replicates

Tested chemical compounds showed zone of inhibition ranging between 14mm and 20mm against the bacteria. On the basis of zone of inhibition produced against the test bacterium, compound number 4f was found to be most effective against *B. subtilis* and *S. aureus*, with zone of inhibition of 20.3mm and 18.3mm, respectively. However other tested compounds showed moderate antibacterial activity (Table 1).

In the whole series, the MIC of chemical compounds ranged between 64 and 256 µg/ml against the tested bacteria. Compound no **4f** was found to be best as they exhibit the lowest MIC of 64µg/ml against *S. aureus* and four compounds namely, **4b,4f, 4g, 4k** showed lowest MIC of 64 µg/ml against *B. subtilis* (Table 2).

Table 2: Minimum inhibitory concentration (MIC) (in µg/ml) of compounds by using modified agar well diffusion method

Compound No.	*Staphylococcus aureus*	*Bacillus subtilis*
4a	128	128
4b	128	**64**
4c	128	128
4d	128	128
4e	128	128
4f	**64**	**64**
4g	128	**64**
4h	128	128
4i	256	128
4j	256	128
4k	256	**64**
4l	256	128
Ciprofloxacin	6.25	6.25

nt- Not tested

Table 3: Antifungal activity of chemical compounds through poisoned food method

Compound No.	Mycelial growth inhibition (%)	
	Aspergillus niger	*Aspergillus flavus*
4a	44.4	48.8
4b	46.6	**51.1**
4c	35.5	37.7
4d	41.1	43.3
4e	43.3	45.5
4f	**51.1**	**53.3**
4g	**53.3**	**57.7**
4h	41.1	43.3
4i	43.3	45.5
4j	38.8	41.1
4k	35.5	37.7
4l	37.7	42.2
Fluconazole	81.1	77.7

CONCLUSION

In summary, we have developed an efficient and green protocol for the synthesis of *trans*-2,3-dihydrofuro[3,2-*c*]coumarins in good yields through a one-pot, three-component, condensation reaction of an 4-hydroxycoumarin **(1)**, α-tosyloxyacetophenone **(2)**, benzaldehyde **(3)**and pyridineusing40 mol% [BmIm]OH as catalyst in aqueous solution. The reaction was performed under ultrasonic irradiation. The use of α-tosyloxyacetophenones over α-haloacetophenones makes this method more convenient in handling. The convenient, greener and efficient characteristics of this protocol make it of prime importance for synthesising such type of furan rings which are then screened for their antifungal activity, antibacterial activity. Amongall the tested chemical compounds, compound no 4f showed good antibacterial and antifungal activity

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