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Original Article

1-(SUBSITUTED)-4, 4, 6-TRIMETHYL-3, 4-DIHYDROPYRIMIDINE-2(*1H*)-THIONE: GREEN SYNTHESIS, ANTIBACTERIAL ACTIVITY AND DNA PHOTOCLEAVAGE ACTIVITY

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ABSTRACT

Objective: 1-(subsituted)-4,4,6-trimethyl-3,4-dihydropyrimidine-2(*1H*)-thione: Green synthesis, antibacterial activity and DNA photocleavage activity.

Methods: In the present study, 1-(subsituted)-4,4,6-trimethyl-3,4-dihydropyrimidine-2(*1H*)-thione has been achieved under mild reaction conditions by employing microwave assisted and grind stone method. All the synthesized compounds were evaluated for their DNA nicking activity. Some of them were selected as to evaluate their antibacterial effect against gram- positive (*Enterococcus*) and gram-negative (*Escherichia coli, Klebsiella pneumoniae and Pseudomonas aeruginosa*) bacteria. The outcome of the study indicating that compounds containing flour, methoxy and chloro substituent were found to exhibit complete DNA cleavage at 40 µg/µl concentration.

Results: The reported compounds synthesized through greener methods such as grindstone and microwave assisted synthesis.

Conclusion: Some of the compounds have exhibited promising antibacterial and DNA Photoclevage activity.

Keywords: 2-Thiopyrimidine, Microwave assisted synthesis, Grindstone method, Antibacterial activity, DNA cleavage activity.

INTRODUCTION

Pyrimidine derivatives are extensively investigated due to their great biological significance and the main constituent of nucleic acids. They found to exhibit remarkable pharmacological activities [1-3] such as anti-cancer [4,5], anti-tumor [6,7], anti-inflammatory [8] and antifungal [9] etc. They are also widely used as agrochemical, pharmaceuticals, dyes [10], organic additives in electroplating of steel [11] and in the polymerization process [12]. A literature survey reveals that DNA is the primary target receptor of most anticancer and antitumor drugs [13-15]. DNA of cancer cells can be damaged as a result of interaction with small molecules, which in turn blocks the cell division and finally cause the death of cancer cells. Thus, it is important to study DNA cleavage under irradiation without any additives such as metal and reducing agents for designing DNA binding drugs or as a site directed photonucleases for accessing structural and genetic information [16].

In addition to the biological significance, it is necessary to develop simple and effective synthetic routes for the organic compounds by using available reagents. Green approaches gaining great interest are grinding stone method [17-23] and microwave assisted synthesis [24-26] as these processes avoid toxic chemicals besides providing shorter reaction time. Today, there is great need to develop safe and environmentally friendly process without using volatile and toxic solvents.

Perusal of literature revealed that 1-(subsituted)-4,4,6-trimethyl-3,4-dihydropyrimidine-2(*1H*)-thione had already been synthesized by conventional method [27-29]. In continuation our ongoing interest towards the developments of greener protocols in organic synthesis and further to evaluate the potential of synthesized heterocycles, it was planned to explore the new and efficient methodology by non-conventional approaches for the synthesis of potent DNA cleaving and antibacterial agents.

MATERIALS AND METHODS

All the chemicals purchased from a common commercial supplier (Hi-media, Loba, S.D. Fine chemicals and Rankem) including solvents which were of LR grade and used as supplied. Double distilled water was used in the present investigation. Melting points were determined using Digital melting point apparatus (Paraffin bath) and are uncorrected. Thin layer chromatography was performed on silica gel G for TLC (Rankem) and the spots were visualized by iodine vapors or by irradiation with UV light (254nm). Microwave assisted synthesis were carried out in an open glass vessel on modified microwave oven model 2001 ETB with rotating tray and a power source 230V, at an output energy of 800W and 2450 MHz frequency. The microwave reactions were performed using on/off cycling to control the temperature. The ^{1}H NMR spectra of the compounds were recorded on Bruker spectrophotometer at 400 MHz instrument, using TMS as internal reference standard in DMSO d_6. Infrared spectra were recorded using the KBr disc on Perkin Elmer RZX FTIR spectrophotometer. The mass spectra were recorded on Q-ToF Micro Waters LC-MS spectrometer.

Chemical synthesis

1. Synthesis of 4-Isothiocynato-4-methylpentan-2-one (1)

Sulphuric acid (1.1mol) was diluted with distilled ice cold water (100 ml) and was added over a period of 25 minutes to mesityl oxide (1 mol) at 15°C. Added ammonium thiocyanate (1.1mol) aqueous solution to the mixture at 21°C in one lot. Separated oily layer after 15 min stirring, washed with aqueous sodium carbonate solution and with distilled water. Finally, the oily layer dried using anhydrous sodium sulphate[27].

2. General procedures for 1-(subsituted)-4,4,6-trimethyl-3,4-dihydropyrimidine-2(*1H*)-thione (3a-m)

Method A

The 4-Isothiocynato-4-methylpentan-2-one (0.01mol) and amine (0.01mol) were dissolved in 10 ml ethanol and added H_2SO_4 in catalytic amount. Then the reaction mixture subjected to refluxing on water bath and reaction progress was monitored by TLC. The content was cooled and solid was filtered, washed with alcohol and crystallized from glacial acetic acid.

Method B

A mixture of 4-Isothiocynato-4-methylpentan-2-one (0.01mol) and amine (0.01mol) was taken in the glass test tube, add only one drop of H_2SO_4 and then subjected to MWI for 50-70 sec. TLC monitoring, sampling at an interval of 10 sec. during course of reaction. On completion of the reaction, 5ml of ethanol was added to the product, filtered solid and crystallized from glacial acetic acid.

Method C

A mixture of 4-Isothiocynato-4-methylpentan-2-one (0.01mol) and amine (0.01mol) was taken in a mortar and add only one drop of conc. H_2SO_4. Grind the reaction mixture with the pestle with the interval heating on water bath for 35-40 min. On completion of the reaction (TLC monitoring), the same work-up procedure was followed as adopted in method B.

1-Phenyl-4,4,6-trimethyl-3,4-dihydropyrimidine-2(*1H*)-thione (3a)

^{1}H NMR (DMSO d_6) δ_H: 1.32 (s, 6H, 4-CH_3), 1.45 (s, 3H, 6-CH_3), 4.83 (s, 1H, 5H), 7.1-7.4 (m, 5H-aromatic), 8.59 (s, 1H, NH). **IR (KBr) cm^{-1}**: 3380 (N-H *str.*), 1540 (C=S *str.*), 3120 (Ar. C-H *str.*). **MS (ES$^+$) *m/z*** [M+1]$^+$ 233.1.

1-(2-Methylphenyl)-4,4,6--trimethyl-3,4-dihydropyrimidine-2(*1H*)-thione (3b)

^{1}H NMR (DMSO d_6) δ_H: 1.32 (s, 6H, 4-CH_3), 1.48 (s, 3H, 6-CH_3), 2.36 (s, 3H, 2-CH_3-benzene), 4.81 (s, 1H, 5H), 7.0-7.22 (m, 4H-aromatic), 8.76 (s, 1H, NH). **IR (KBr) cm^{-1}**: 3410 (N-H *str.*), 1525 (C=S *str.*), 3112 (Ar. C-H *str.*). **MS (ES$^+$) *m/z*** [M+1]$^+$ 247.12.

1-(4-Methylphenyl)-4,4,6-trimethyl-3,4-dihydropyrimidine-2(*1H*)-thione (3c)

^{1}H NMR (DMSO d_6) δ_H: 1.32 (s, 6H, 4-CH_3), 1.45 (s, 3H, 6-CH_3), 2.30 (s, 3H, 4-CH_3-benzene), 4.82 (s, 1H, 5H), 6.90-7.22 (m, 4H-aromatic), 8.62 (s, 1H, NH). **IR (KBr) cm^{-1}**: 3408 (N-H *str.*), 1510 (C=S *str.*), 3123 (Ar. C-H *str.*). **MS (ES$^+$) *m/z*** [M+1]$^+$ 247.12.

1-(4-Methoxyphenyl)-4,4,6-trimethyl-3,4-dihydropyrimidine-2(*1H*)-thione (3d)

^{1}H NMR (DMSO d_6) δ_H: 1.32 (s, 6H, 4-CH_3), 1.48 (s, 3H, 6-CH_3), 3.81 (s, 3H, 4-OCH_3-benzene), 4.81 (s, 1H, 5H), 6.81-7.09 (m, 4H-aromatic), 8.40 (s, 1H, NH). **IR (KBr) cm^{-1}**: 3410 (N-H *str.*), 1545 (C=S *str.*), 3115 (Ar. C-H *str.*). **MS (ES$^+$) *m/z*** [M+1]$^+$ 263.12.

1-(2-Fluorophenyl)-4,4,6--trimethyl-3,4-dihydropyrimidine-2(*1H*)-thione (3e)

^{1}H NMR (DMSO d_6) δ_H: 1.31 (s, 6H, 4-CH_3), 1.46 (s, 3H, 6-CH_3), 4.86 (s, 1H, 5H), 7.09-7.21 (m, 4H-aromatic), 8.75 (s, 1H, NH). **IR (KBr) cm^{-1}**: 3395 (N-H *str.*), 1505 (C=S *str.*), 3124 (Ar. C-H *str.*). **MS (ES$^+$) *m/z*** [M+1]$^+$ 251.10.

1-(4-Fluorophenyl)-4,4,6--trimethyl-3,4-dihydropyrimidine-2(*1H*)-thione (3f)

^{1}H NMR (DMSO d_6) δ_H: 1.32 (s, 6H, 4-CH_3), 1.46 (s, 3H, 6-CH_3), 4.86 (s, 1H, 5H), 7.09-7.20 (m, 4H-aromatic), 8.75 (s, 1H, NH). **IR (KBr) cm^{-1}**: 3398 (N-H *str.*), 1535 (C=S *str.*), 3120 (Ar. C-H *str.*). **MS (ES$^+$) *m/z*** [M+1]$^+$ 251.10.

1-(4-Chlorophenyl)-4,4,6-trimethyl-3,4-dihydropyrimidine-2(*1H*)-thione (3g)

^{1}H NMR (DMSO d_6) δ_H: 1.33 (s, 6H, 4-CH_3), 1.48 (s, 3H, 6-CH_3), 4.84 (s, 1H, 5H), 7.15-7.37 (m, 4H-aromatic), 8.69 (s, 1H, NH). **IR (KBr) cm^{-1}**: 3400 (N-H *str.*), 1555 (C=S *str.*), 3120 (Ar. C-H *str.*). **MS (ES$^+$) *m/z*** [M+1]$^+$ 268.02.

1-(4-Nitrophenyl)-4,4,6-trimethyl-3,4-dihydropyrimidine-2(*1H*)-thione (3h)

^{1}H NMR (DMSO d_6) δ_H: 1.33 (s, 6H, 4-CH_3), 1.46 (s, 3H, 6-CH_3), 4.1(s, 2H, 2-NH_2-benzene) 4.82 (s, 1H, 5H), 7.48 (d, 2H-aromatic, *J*= 8.8 Hz), 8.24 (d, 2H-aromatic, *J*= 7.2 Hz), 8.21 (s, 1H, NH). **IR (KBr) cm^{-1}**: 3425 (N-H *str.*), 1495 (C=S *str.*), 3124 (Ar. C-H *str.*), 1518 (N-O *asym. str.*); 1341 (N-O *sym. str.*). **MS (ES$^+$) *m/z*** [M+1]$^+$ 278.09.

1-(α- Naphthyl)-4,4,6--trimethyl-3,4-dihydropyrimidine-2(*1H*)-thione (3i)

^{1}H NMR (DMSO d_6) δ_H: 1.32 (s, 3H, 4-CH_3), 1.42 (s, 3H, 4-CH_3), 1.48 (s, 3H, 6-CH_3), 4.91 (s, 1H, 5H), 7.31 -7.93 (m, 7H-aromatic), 8.67 (s, 1H, NH). **IR (KBr) cm^{-1}**: 3400 (N-H *str.*), 1525 (C=S *str.*), 3024 (Ar. C-H *str.*). **MS (ES$^+$) *m/z*** [M+1]$^+$ 283.12.

1-Methyl-4,4,6--trimethyl-3,4-dihydropyrimidine-2(*1H*)-thione (3j)

^{1}H NMR (DMSO d_6) δ_H: 1.32 (s, 6H, 4-CH_3), 1.48 (s, 3H, 6-CH_3), 2.48 (s, 3H, 1- CH_3), 4.91 (s, 1H, 5H), 8.61 (s, 1H, NH). **IR (KBr) cm^{-1}**: 3400 (N-H *str.*), 1530 (C=S *str.*). **MS (ES$^+$) *m/z*** [M+1]$^+$171.09.

1-Propyl-4,4,6-trimethyl-3,4-dihydropyrimidine-2(*1H*)-thione (3k)

^{1}H NMR (DMSO d_6) δ_H: 0.88 (m, 3H, 3-propyl), 1.31 (s, 6H, 4-CH_3), 1.45 (s, 3H, 6-CH_3), 1.51(m, 2H, 2-propyl), 3.29 (s, 3H, 1-propyl), 4.93 (s, 1H, 5H), 8.63 (s, 1H, NH). **IR (KBr) cm^{-1}**: 3410 (N-H *str.*), 1495 (C=S *str.*). **MS (ES$^+$) *m/z*** [M+1]$^+$199.12.

1-Butyl-4,4,6-trimethyl-3,4-dihydropyrimidine-2(*1H*)-thione (3l)

^{1}H NMR (DMSO d_6) δ_H: 0.86 (m, 3H, 4-butyl), 1.24 (m, 2H, 3-butyl), 1.31 (s, 6H, 4-CH_3), 1.41 (m, 2H, 2-butyl), 1.45 (s, 3H, 6-CH_3), 3.32 (m, 2H, 1- butyl), 4.93 (s, 1H, 5H), 8.63 (s, 1H, NH). **IR (KBr) cm^{-1}**: 3414 (N-H *str.*), 1540 (C=S *str.*). **MS (ES$^+$) *m/z*** [M+1]$^+$213.14.

1-(β-Phenyethyl)-4,4,6-trimethyl-3,4-dihydropyrimidine-2(*1H*)-thione (3m)

^{1}H NMR (DMSO d_6) δ_H: 1.34 (s, 6H, 4-CH_3), 1.45 (s, 3H, 6-CH_3), 3.69 (m, 2H, 1-methylene), 2.77 (m, 2H, 2-methylene), 4.91 (s, 1H, 5H), 7.03-7.18 (m, 5H, Ar.), 8.79 (s, 1H, NH). **IR (KBr) cm^{-1}**: 3420 (N-H *str.*), 1520 (C=S *str.*), 3023 (Ar. C-H *str.*) **MS (ES$^+$) *m/z*** [M+1]$^+$ 261.14.

DNA photocleavage activity

The cleavage of plasmid DNA was determined by agarose gel electrophoresis. The experiments were performed in a volume of 10 µl containing the plasmid DNA in TE (*Tris* 10mM, EDTA 0.01mM, pH 8.0) buffer in the presence of 40 µg of the synthesized compounds. The samples were taken in polyethylene microcentrifuge tubes, which were then irradiated for 30 min at room temperature in trans-illuminator (8000mW/cm) at 360nm. Further, the samples were incubated at 37°C for one hour. The 6X loading dye containing 0.25% bromophenol blue and 30% glycerol (8 µl) was mixed with irradiated sample. The analysis of samples were carried out on a 0.8% agarose horizontal slab gel in *Tris*-Acetate EDTA buffer (40 mM Tris, 20 mM acetic acid, 1 mM EDTA, pH: 8.0). Untreated plasmid DNA was maintained as a control in each run of gel electrophoresis, which was carried out at 5V/cm for 2.0 h. The gel was stained with ethidium bromide (1 µg/ml) and photographed under UV light [30].

***In vitro* antibacterial activity**

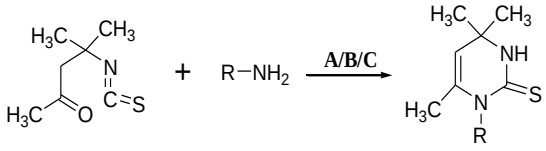
Synthesized compounds have been studied for their antibacterial activity by Agar well diffusion method [31, 32] in DMF (Dimethylformamide) solvent against various pathogenic strains viz. *Enterococcus* (Gram Positive) and *Escherichia coli, Klebsiella pneumoniae and Pseudomonas aeruginosa* (Gram Negative) bacteria. These strains were isolated from the patients in Maharishi Markandeshwar Medical College, Maharishi Markandeshwar University, Mullana, Haryana. 25 ml of nutrient agar medium was poured into each petri plate and the agar plates were swabbed with 100 µl inocula of each test bacterium 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 50 µl volume. Solutions of the test compounds and standards were prepared in DMF at a concentration of 2000 µg/ml. From this stock solution, twofold dilutions of the compounds (2, 4, 8...512 µg/ml)

were inoculated to the corresponding wells. All the plates were further incubated at 37 °C for 24 hrs. The antibacterial activity of each synthesized compound was evaluated by measuring the zone of growth inhibition with zone reader (Hi Antibiotic zone scale) and the MIC was determined as the lowest concentration of the compound tested that was able to inhibit visible growth of bacteria. DMF was used as a negative control, whereas Ampicillin was used as a standard. This procedure was performed in three replicate plates for each organism.

RESULTS AND DISCUSSION

Chemistry

In the present study, synthesis of 1-(subsituted)-4,4,6-trimethyl-3,4-dihydropyrimidine-2(*1H*)-thione (**3a-m**) derivatives through microwave and grind stone approaches was performed and compared with the conventional approach in terms of particular reaction times and yields (**Scheme 1**). The compounds **3a-m** were prepared by reacting equal moles of 4-Isothiocynato-4-methylpentan-2-one (**1)** and substituted amines (**2a-m)** under different reaction conditions in acidic medium (1-2 drops of conc. H_2SO_4), whereas the conventional approach requires longer reaction time under reflux about 3-4 h in ethanol. In an attempt to reduce reaction time and acknowledging the benefits of 'Concept of Green Chemistry', the same reaction was performed using greener approaches due to many advantages like no solvent requirement, easy operation, eco-friendly, less reaction time with better yields of desired products and purity. The results are summarized in **Table 1**. It has been observed that microwave and grind stone approaches required shorter reaction time, i.e. 50-70 sec. and 35-45 min, respectively, for completion of reaction as compared to conventional method. The microwave method requires lesser reaction time and gave better yields in comparison of the other two methods. ^{1}H NMR spectral data confirm the cyclization of **1** with **2a-m** into **3a-m**. The proton of carbon adjacent to keto group (-C**H**-C=O) gave a singlet at δ 2.7 which was disappeared on cyclization, and a signal at δ 4.7-4.93 indicated the formation of (-C=C**H**-) group in the title compounds. The signal of the methyl protons adjacent to keto group (C**H$_3$**-C=O) appeared as singlet at δ 2.20 in **1** but on cyclization these protons appeared at δ 1.4-1.49 which suggested that the environment of these protons has become changed as a result of cyclization. The IR spectral data further strengthen these facts too. The band appeared in final products between 3400-3350 cm^{-1} indicated the presence of (-NH) group in the final product while the disappearance of bands in spectra between 2200-2030 cm^{-1} and 1775-1650 cm^{-1} indicated the absence of isothiocyanate group and keto group, respectively in **3a-m**. Finally the formation of a desired series of **3a-m** compounds was confirmed on the basis of their mass spectra.



1 **2a-m** **3a-m**

A: EtOH, H_2SO_4/3-4 h (reflux); B: H_2SO_4/50-70 sec (MWI); C: H_2SO_4/ 30- 40 min (grind)

Scheme 1: Synthetic diagram of the 1-(subsituted)-4,4,6-trimethyl-3,4-dihydropyrimidine-2(1*H*)-thione derivatives (3a-m).Table 1: Reaction time, yields and melting points of compounds (3a-m)

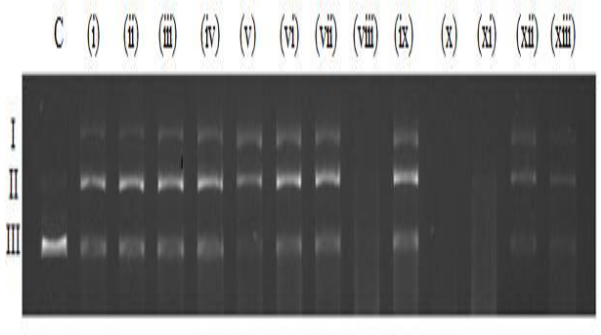
Compounds	R	Method A			Method B			Method C		
		Time (h)	Yield (%)	M.p. (°C)	Times (sec)	Yield (%)	M.p. (°C)	Time (min)	Yield (%)	M.p. (°C)
3a	C_6H_5	3	90	192-194[27]	50	91	192-194	35	90	192-194
3b	2-$CH_3C_6H_4$	3	86	201-203[27]	50	89	200-202	35	87	201-203
3c	4-$CH_3C_6H_4$	3.1	84	191-193[27]	60	85	192-194	40	84	191-193
3d	4-$OCH_3C_6H_4$	3.2	65	188-190[28]	60	70	188-190	40	66	189-191
3e	2-FC_6H_4	3	88	168-170	50	88	169-171	35	89	169-171
3f	4- FC_6H_4	3	89	181-183	50	90	182-184	35	89.5	182-184
3g	4-ClC_6H_4	3.1	89	187-189[29]	50	89	187-189	35	90	187-189
3h	4-$NO_2C_6H_4$	3.2	90	201-203[28]	60	91	200-202	40	90	200-202
3i	$C_{10}H_7$	3.3	90	214-216[29]	70	93	213-215	45	92	214-216
3j	CH_3	3	79	87-89[27]	50	82	86-88	35	82	86-88
3k	C_3H_7	3	73	106-108	50	78	107-109	35	75	105-107
3l	C_4H_9	3	75	113-115[28]	50	79.5	111-113	35	75	111-113
3m	2-$C_6H_5C_2H_4$	3	69	133-135	50	72	134-136	35	72	133-135

DNA photocleavage activity

The molecules possessing the -NH and substituted at 2- position within the same motif were found to exhibit ability to interact with DNA and cleavage DNA significantly [33, 34]. The compounds having thione group showed higher DNA cleaving activity because they have more intersystem crossing efficiency and higher photosensitizing activity [35].

The ability of synthesized compounds to interact with plasmid DNA was examined by agarose gel electrophoresis and results are presented in **Figure 1**. All the solutions were prepared in DMSO. The agarose gel electrophoresis worked on principle that super coiled DNA (III) migrates faster than open circular form (I) (when one strand get nicked), a linear form (II) (both strands cleavage) generated which migrates in between form (I) and (III).

The compounds **3d**, **3f** and **3g** degraded the DNA totally as shown in **Figure 1**. In case of other compounds, all three forms of DNA are well visualized, which suggested that plasmid DNA is converted specifically into an open coil (II) and Linear (I) as well.



C: DNA (control); Lane-(i): DNA + 3j; Lane-(ii): DNA+ 3k; Lane-(iii): DNA+ 3l; Lane-(iv): DNA+ 3m; Lane-(v): DNA+ 3a; Lane-(vi): DNA+ 3b; Lane-(vii): DNA+ 3c; Lane-(viii): DNA+ 3d; Lane-(ix): DNA+ 3e; Lane-(x): DNA+ 3f: Lane-(xi): DNA+ 3g: Lane-(xii): DNA+ 3h: Lane-(xiii): DNA+ 3i.

Fig. 1: Gel electrophoretogram of compounds (3a-m)

***In vitro* antibacterial activity**

The results of antibacterial activity (zone of inhibition and minimum inhibitory concentration) have been summarized in **Table 2** & **3**. The observed minimum inhibitory concentrations (MIC) presented in **Table 3** were in accordance with the results gained in the primary screening. All tested compounds (**3a-d**, **3f-i**), possessed variable antibacterial activity against the Gram-positive bacteria and Gram-negative bacteria. Compounds **3f**, **3h** and **3i** have shown good activity against gram positive, i.e *Enterococcus* (with MIC range 16-32 µg/ml). On the other hand, compounds **3d**, **3f**, **3g**, **3i** and **3h** have also shown good activity against *K. pneumoniae* (with MIC 32-64 µg/ml), *E.coli* (with MIC 32-64 µg/ml), *P. aeruginosa* (with MIC 16-32 µg/ml) respectively.

Table 2: MIC (µg/ml) values of compounds (3a-d, 3f-i) and standard against the respective microorgnisms

Compounds	MIC (µg/ml)			
	E. Coli	*K. pneumoniae*	*P. aeruginosa*	*Enterococcus*
3a	128	128	64	64
3b	128	128	64	128
3c	128	128	64	128
3d	64	32	64	64
3f	32	64	64	16
3g	64	64	64	64
3h	64	64	32	32
3i	64	64	16	32
Std.	02	02	08	02

Table 3: *In vitro* antibacterial activity of (3a-d, 3f-i) by agar well diffusion method

Compounds	Zone of inhibition (mm)			
	E. Coli	*K. pneumoniae*	*P. aeruginosa*	*Enterococcus*
3a	19	17	16	18
3b	19	20	18	19
3c	17	18	16	16
3d	18	18	19	17
3f	20	17	16	19
3g	20	17	19	18
3h	16	18	19	17
3i	16	17	16	18
Std.	24	22	24	21

CONCLUSION

In conclusion, a series of 1-(subsituted)-4,4,6-trimethyl-3,4-dihydropyrimidine-2(*1H*)-thione have been synthesized through conventional and non-conventional greener approaches like microwave and grindstone methods. In general, the compounds **3d, 3f,** and **3g** having *p*-methoxyphenyl, *p*-fluorophenyl, and *p*-chlorophenyl substituent respectively showed prominent DNA photocleavage activity. In additions to this, compounds bearing electron withdrawing groups such as **3d**, **3f**, **3h** and **3i** also exhibited prominent antibacterial activity against both gram positive and gram negative micro-organisms.

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