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Research Article

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An efficient three component one-pot synthesis of some new tetrahydro-indeno-[1,2-*d*]pyrimidinone and dihydro-*1H*-indeno[1,2-*d*]pyrimidine derivatives using Antimony (III) chloride as a catalyst and investigation of their antimicrobial activity

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ABSTRACT

An efficient and convenient procedure has been developed for the synthesis of some new tetrahydro-indeno[1,2-d]pyrimidinone ***4a-h*** *and dihydro-1H-indeno[1,2-d]pyrimidine* ***5a-c*** *derivatives in high yields. Tetrahydro-indeno [1,2-d]pyrimidinone derivatives* ***4a-h*** *have been synthesized by the reaction between corresponding, cyclic ketones* ***1a-c,*** *(thio) urea* ***2a-b*** *and aldehyde* ***3a-f*** *in the presence of Antimony(III)chloride ($SbCl_3$) in refluxing acetonitrile. Dihydro-1H-indeno[1,2-d]pyrimidine derivatives* ***5a-c*** *have been synthesized by the reaction between corresponding tetrahydro-indeno [1,2-d]pyrimidinone* ***4a-h*** *derivatives and alkyl bromide in ethanol. The structures of new compounds have been evaluated on the basis of elemental analysis, FT- IR, ^{1}H NMR and ^{13}C NMR spectral data. They have also been screened for their antimicrobial activities.*

Keywords: Biginelli reaction, pyrimidinone, antimicrobial activity

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INTRODUCTION

In recent years, dihydropyrimidinones (DHPMs) and their derivatives have occupied an important position in natural and synthetic organic chemistry, due to their wide range of biological activities [1], such as antibacterial, antiviral, antihypertensive, antitumor effects and calcium channel blockers. Scaffold decoration of DHPMs is highly important for creating structural diversity to produce “drug-like” molecules for biological screening. The synthesis of DHPMs was first reported by Biginelli in 1893[2] and has been reviewed recently [3]. Improved procedures and new Biginelli-like scaffolds have been reported over the past decade and a variant of the Biginelli condensation has been described for its application to the total synthesis of bioactive guanidine alkaloids [4]. Basically, these methods are all similar in the use of different Lewis acid catalyst as well as protic acid under classical reflux [5]. Other studies have focused on the use of ionic liquids [6], microwave irradiation [7] and combinatorial chemistry [8]. The use of boron compounds [9], TMSCl [10] and heterogeneous catalysts, such as tangstophosphoric acid [11], Zeolite [12], montmorillonite [13], ion-exchange resins [14] and grindstone technique [15] have also been reported. However, to the best of our knowledge, there have been relatively few reports of the synthesis of fused DHPMs from cyclic ketones with high yields using Antimony(III)chloride as a catalyst. More recently, the Biginelli reaction has been employed for the synthesis of DHPMs, which used cyclic ketones instead of open-chain dicarbonyl compounds using Antimony(III)chloride ($SbCl_3$) [16], concentrated HCl [17] and H_2SO_4 [18] as the catalyst. DHPMs derivatives have attracted considerable attention since they exhibit potent antibacterial activity against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* [19] and calcium antagonist activity [20-21].

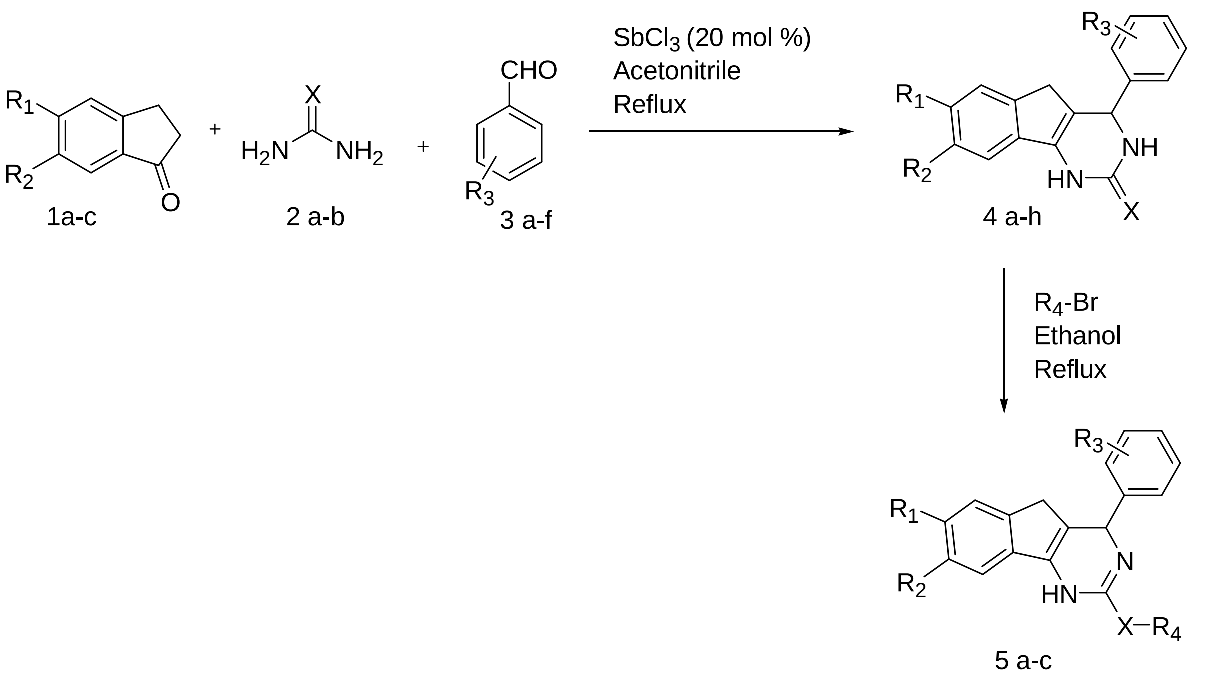
Multicomponent condensation reactions (MCRs) have recently been discovered to be a powerful method for the synthesis of organic compounds, since the products are formed in a single step and diversity can be achieved by simply varying each component [22-26]. The original Biginelli protocol for the preparation of the DHMPs consisted of heating a mixture of the three components (aldehyde , β-keto-ester , and urea) in ethanol containing a catalytic amount of HCl. This procedure leads in one step-one pot to the desired DHPM. The major drawback associated with this protocol is the low yields, particularly for substituted aromatic and aliphatic aldehydes [27].

The advantage of using Antimony(III)chloride ($SbCl_3$) in the synthesis of tetrahydro-indeno[1,2-d]pyrimidinone and dihydro-1H-indeno[1,2-d]pyrimidine derivatives provides better results with more sterically hindered substrates with high yield. $SbCl_3$ is inexpensive, easy to handle on large scale [16]. In view of the above observation, we wish to report herein biologically active heterocyclic systems containing tetrahydro-indeno[1,2-d]pyrimidinone and dihydro-1H-indeno[1,2-d]pyrimidine derivatives. Herein Antimony (III) chloride ($SbCl_3$) catalyst was significantly more effective than other acid catalyst in the Biginelli reaction of cyclic ketones and it provides better results with more sterically hindered substrates with high yields (Scheme-1).

EXPERIMENTAL SECTION

All the reagents were obtained commercially and used without further purification. All melting points were taken in open capillaries and are uncorrected. The monitoring of the progress of all reactions and homogeneity of the synthesized compounds was carried out by TLC. TLC was run using TLC aluminum sheets silica gel $60F_{254}$ (Merck). Elemental analysis (% C, H, N) was carried out by Perkins Elmer 2400 CHN elemental analyzer. IR spectra were recorded on a shimadzu FTIR 8401 spectrophotometer in KBR. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance 400 MHz spectrometer using TMS as internal standard. Mass spectra were scanned on a shimadzu LCMS 2010 spectrometer.

SCHEME-1



General procedure for preparation of 4a-h:
To a mixture of cyclic ketone **1a-c** (1mmol), urea or thiourea **2a-b** (1.5 mmol) and aldehyde **3a-f** (1mmol) in acetonitrile, catalytic amount of Antimony(III)chloride (20 mol %) was added and content was refluxed for 8 hours. After completion of the reaction as monitored by TLC, the reaction mixture is poured into ice-cold water and stirred for 10-15 minutes. The content of the flask were then filtered and washed with cold water (20 ml) to remove excess urea or thiourea. The solid so obtained was the corresponding dihydropyrimidinone (**4a-h**). It was then recrystallized by hot ethanol to get the pure product (Scheme 1).

4-Phenyl-1,3,4,5-tetrahydro-indeno[1,2-d]pyrimidine-2-thione (4a). White solid, (75 %), m.p. 220-223 °C, Anal.Calcd for $C_{17}H_{14}N_2S$: C 73.35, H 5.07, N 10.06% Found: C 73.30, H 5.15, N 10.17%. IR (KBr, cm^{-1}): 3311, 3229 (2NH), 3010, 3024 (ArC-H), 1611 (C=C), 1188 (C=S). ^1H NMR (400 MHz, DMSO-d_6): δ 2.73-2.80 (d, 1H, CH), 3.21-3.29 (d, 1H, CH), 5.58 (s, 1H, CH), 7.10-7.59 (m, 9H, Ar-H), 7.75 (s, 1H, NH), 9.83 (s, 1H, NH), ^{13}C NMR (400 MHz, DMSO-d_6) δ: 26.9 (CH_2), 60.4 (CH), 103.7, 122.1, 123.1, 124.0, 127.4, 128.2, 128.8, 135.2, 135.9, 139.5, 141.7, 142.4 (Ar-C), 179.4 (C=S), MS: (M+1) 279.09.

Table-1: Physical data for the product 4a-h and 5a-c

No.	R_1	R_2	R_3	R_4	X	m.p. °C	Yield %	M.F. (M.Wt.)	Elemental analysis (calcd./ found)		
									%C	%H	%N
4a	H	H	H	-	S	220-223	75	$C_{17}H_{14}N_2S$ 278.37	73.35 73.30	5.07 5.15	10.06 10.17
4b	H	H	H	-	O	256-259	82	$C_{17}H_{14}N_2O$ 262.31	77.84 77.75	5.38 5.25	10.68 10.74
4c	H	NO_2	4-Br	-	S	290-293	85	$C_{17}H_{12}BrN_3O_2S$ 402.27	50.76 50.65	3.01 3.00	10.45 10.52
4d	H	NO_2	4-Cl	-	S	>300	86	$C_{17}H_{12}ClN_3O_2S$ 357.81	57.06 57.14	3.38 3.25	11.74 11.62
4e	OCH_3	OCH_3	H	-	S	>300	80	$C_{19}H_{18}N_2O_2S$ 338.42	67.43 67.36	5.36 5.47	8.28 8.32
4f	OCH_3	OCH_3	4-OCH_3	-	S	>300	90	$C_{20}H_{20}N_2O_3S$ 368.45	65.20 65.34	5.47 5.35	7.60 7.72
4g	OCH_3	OCH_3	2-Cl	-	S	>300	81	$C_{19}H_{17}ClN_2O_2S$ 372.87	61.20 61.34	4.60 4.50	7.51 7.61
4h	OCH_3	OCH_3	3-OCH_3	-	S	>300	79	$C_{20}H_{20}N_2O_3S$ 368.45	65.20 65.11	5.47 5.60	7.60 7.68
5a	H	NO_2	4-Br	C_2H_5	S	>300	86	$C_{19}H_{16}BrN_3O_2S$ 430.32	53.03 53.11	3.75 3.69	9.76 9.88
5b	H	NO_2	4-Br	CH_3	S	>300	84	$C_{18}H_{14}BrN_3O_2S$ 416.26	51.93 52.02	3.39 3.45	10.09 9.98
5c	H	H	H	CP	S	>300	88	$C_{22}H_{22}BrN_2S$ 346.49	76.26 76.39	6.40 6.30	8.08 7.99

4-Phenyl-1,3,4,5-tetrahydro-indeno[1,2-d]pyrimidine-2-one (4b). Off-white solid, (82 %), m.p. 256-259 °C, Anal.Calcd for $C_{17}H_{14}N_2O$: C 77.84, H 5.38, N 10.68% Found: C 77.75, H 5.25, N 10.74%. IR (KBr, cm^{-1}): 3311, 3229 (2NH), 3010, 3024 (ArC-H), 1611 (C=C), 1688 (C=O). ^1H NMR (400 MHz, DMSO-d_6): δ 2.76-2.83 (d, 1H, CH), 3.19-3.26 (d, 1H, CH), 5.50 (s, 1H, CH), 7.0-7.55 (m, 9H, Ar-H), 7.82 (s, 1H, NH), 9.74 (s, 1H, NH), ^{13}C NMR (400 MHz, DMSO-d_6) δ: 28.2 (CH_2), 62.4 (CH), 105.6, 125.1, 126.3, 126.8, 127.0, 127.4, 128.5, 128.8, 129.3, 137.3, 137.5, 141.7 (Ar-C), 162.5 (C=O), MS: (M+1) 263.1.

4-(4-Bromo-phenyl)-8-nitro-1,3,4,5-tetrahydro-indeno[1,2-d]pyrimidine-2-thione (4c). Yellow solid, (85 %), m.p. 290-293 °C, Anal.Calcd for $C_{17}H_{12}BrN_3O_2S$: C 50.76, H 3.01, N 10.45% Found: C 50.65, H 3.00, N 10.52%. IR (KBr, cm^{-1}): 3323, 3260 (2NH), 2951 (ArC-H), 1614 (C=C), 1530, 1350 (N-O), 1183 (C=S), 592 (C-Br). ^1H NMR (400 MHz, DMSO-d_6): δ 2.73-2.8 (d, 1H, CH), 3.21-3.28 (d, 1H, CH), 5.43 (s, 1H, CH), 7.1 (dd, 2H, Ar-H), 7.27 (d, 1H, Ar-H), 7.4 (dd, 2H, Ar-H), 7.7 (s, 1H, NH),7.9 (dd, 1H, Ar-H), 8.1 (dd, 1H, Ar-H), 9.78 (s, 1H, NH), ^{13}C NMR (400 MHz, DMSO-d_6) δ: 27.3 (CH_2), 59.7 (CH), 104.2, 122.1, 122.3, 124.5, 128.2, 128.6, 129.9, 135.4, 139.5, 141.7, 142.1, 146.4 (Ar-C), 175.4 (C=S), MS: (M+1) 403.98.

4-(4-Chloro-phenyl)-8-nitro-1,3,4,5-tetrahydro-indeno[1,2-d]pyrimidine-2-thione (4d). Off-white solid, (86 %), m.p. >300 °C, Anal.Calcd for $C_{17}H_{12}ClN_3O_2S$: C 57.06, H 3.38, N 11.74% Found: C 57.14, H 3.25, N 11.62%. IR (KBr, cm^{-1}): 3310, 3245 (2NH), 2959 (ArC-H), 1618 (C=C), 1527, 1344 (N-O), 1192 (C=S), 755 (C-Cl). ^1H NMR (400 MHz, DMSO-d_6): δ 2.70-2.82 (d, 1H, CH), 3.18-3.26 (d, 1H, CH), 5.39 (s, 1H, CH), 7.14 (dd, 2H, Ar-H), 7.2 (d, 1H, Ar-H), 7.42 (dd, 2H, Ar-H), 7.7 (s, 1H, NH), 7.89 (dd, 1H, Ar-H), 8.14 (dd, 1H, Ar-H), 9.72 (s, 1H, NH), ^{13}C NMR (400 MHz, DMSO-d_6) δ: 27.1 (CH_2), 58.2 (CH), 103.9, 121.1, 121.3, 124.7, 128.6, 128.8, 130.3, 137.4, 139.6, 141.9, 142.3, 145.9 (Ar-C), 177.6 (C=S), MS: (M+1) 358.04.

7,8-Dimethoxy-4-phenyl-1,3,4,5-tetrahydro-indeno[1,2-d]pyrimidine-2-thione (4e). White solid, (80 %), m.p. >300 °C, Anal.Calcd for $C_{19}H_{18}N_2O_2S$: C 67.43, H 5.36, N 8.28% Found: C 67.36, H 5.47, N 8.32%. IR (KBr, cm^{-1}): 3312, 3249 (2NH), 2965 (ArC-H), 1622 (C=C), 1238 & 1046 (OCH_3), 1182 (C=S). ^1H NMR (400 MHz, DMSO-

d$_6$): δ 2.71-2.83 (d, 1H, CH), 3.16-3.26 (d, 1H, CH), 3.90 (s, 6H, OCH_3), 5.38 (s, 1H, CH), 6.89 (s, 1H, Ar-H), 7.09 (s, 1H, Ar-H), 7.23-7.61 (m, 5H, Ar-H), 7.79 (s, 1H, NH), 9.78 (s, 1H, NH), ^{13}C NMR (400 MHz, DMSO-*d*$_6$) δ: 27.8 (CH_2), 56.5 (OCH_3), 60.9 (CH), 103.8, 123.7, 116.4, 125.7, 127.3, 128.4, 128.7, 128.9, 139.6, 141.8, 144.6, 146.4 (Ar-C), 175.9 (C=S), MS: (M+1) 339.11.

7,8-Dimethoxy-4-(4-methoxy-phenyl)-1,3,4,5-tetrahydro-indeno[1,2-d]pyrimidine-2-thione (4f). White solid, (90 %), m.p. >300 °C, Anal.Calcd for $C_{20}H_{20}N_2O_3S$: C 65.20, H 5.47, N 7.60% Found: C 65.34, H 5.35, N 7.72%. IR (KBr, cm^{-1}): 3312, 3249 (2NH), 2965 (ArC-H), 1622 (C=C), 1238 & 1046 (OCH_3), 1182 (C=S). ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 2.71-2.83 (d, 1H, CH), 3.16-3.26 (d, 1H, CH), 3.80 (s, 3H, OCH_3), 3.90 (s, 6H, OCH_3), 5.38 (s, 1H, CH), 6.89 (s, 1H, Ar-H), 7.09 (s, 1H, Ar-H), 7.33-7.62 (m, 4H, Ar-H), 7.79 (s, 1H, NH), 9.78 (s, 1H, NH), ^{13}C NMR (400 MHz, DMSO-*d*$_6$) δ: 27.3 (CH_2), 55.7 (OCH_3), 56.5 (OCH_3), 60.8 (CH), 103.8, 113.4, 114.2, 116.4, 128.6, 128.7, 128.9, 135.6, 141.8, 143.6, 146.4, 159.8 (Ar-C), 175.9 (C=S).

4-(2-Chloro-phenyl)-7,8-dimethoxy-1,3,4,5-tetrahydro-indeno[1,2-d]pyrimidine-2-thione (4g). Off-white solid, (81 %), m.p. >300 °C, Anal.Calcd for $C_{19}H_{17}ClN_2O_2S$: C 61.20, H 4.60, N 7.51% Found: C 61.34, H 4.50, N 7.61%. IR (KBr, cm^{-1}): 3325, 3252 (2NH), 2965 (ArC-H), 1620 (C=C), 1239 & 1056 (OCH_3), 1152 (C=S). ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 2.68-2.79 (d, 1H, CH), 3.11-3.19 (d, 1H, CH), 3.90 (s, 6H, OCH_3), 5.38 (s, 1H, CH), 6.79 (s, 1H, Ar-H), 7.02 (s, 1H, Ar-H), 7.29-7.65 (m, 4H, Ar-H), 7.89 (s, 1H, NH), 9.78 (s, 1H, NH), ^{13}C NMR (400 MHz, DMSO-*d*$_6$) δ: 27.3 (CH_2), 56.3 (OCH_3), 59.8 (CH), 104.4, 114.2, 116.4, 126.5, 127.2, 128.3, 128.7, 128.9, 131.4, 139.6, 141.8, 145.2, 146.9 (Ar-C), 177.9 (C=S).

7,8-Dimethoxy-4-(3-methoxy-phenyl)-1,3,4,5-tetrahydro-indeno[1,2-d]pyrimidine-2-thione (4h). White solid, (79 %), m.p. >300 °C, Anal.Calcd for $C_{20}H_{20}N_2O_3S$: C 65.20, H 5.47, N 7.60% Found: C 65.11, H 5.60, N 7.68%. IR (KBr, cm^{-1}): 3334, 3241 (2NH), 2955 (ArC-H), 1630 (C=C), 1240 & 1037 (OCH_3), 1183 (C=S). ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 2.77-2.8 (d, 1H, CH), 3.11-3.23 (d, 1H, CH), 3.73 (s, 3H, OCH_3), 3.88 (s, 6H, OCH_3), 5.29 (s, 1H, CH), 6.77 (s, 1H, Ar-H), 6.97 (s, 1H, Ar-H), 7.3-7.52 (m, 4H, Ar-H), 7.81 (s, 1H, NH), 9.0 (s, 1H, NH), ^{13}C NMR (400 MHz, DMSO-*d*$_6$) δ: 27.6 (CH_2), 55.7 (OCH_3), 56.4 (OCH_3), 58.8 (CH), 104.2, 113.2, 114.2, 115.4, 120.7, 128.7, 128.9, 129.2, 141.8, 142.3, 146.2, 146.4, 160.8 (Ar-C), 177.1 (C=S).

General procedure for preparation of (5a-c):
To a mixture of corresponding compound **4** (1 mmol) and alkyl bromide (1.5 mmol), ethanol (10ml) was added, content was refluxed for 20 hours. After completion of the reaction as monitored by TLC, the reaction mixture is poured into water and stirred for 10-15 minutes. The content of the flask were then filtered and washed with water (20 ml). The solid so obtained was the corresponding (**5a-c**). It was then recrystallized by hot isopropyl alcohol to get the pure product (Scheme 1).

4-(4-Bromo-phenyl)-2-ethylsulfanyl-8-nitro-4,5-dihydro-1H-indeno[1,2-d]pyrimidine (5a). Off-white solid, (86 %), m.p. >300 °C, Anal.Calcd for $C_{19}H_{16}BrN_3O_2S$: C 53.03, H 3.75, N 9.76% Found: C 53.11, H 3.69, N 9.88%. IR (KBr, cm^{-1}): 3241 (NH), 3015 (ArC-H), 1630 (C=C), 1527 & 1344 (N-O), 580 (C-Br). ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 1.24-1.29 (t, 3H, CH3), 2.98-3.06 (d, 1H, CH), 3.23-3.28 (d, 1H, CH), 3.30-3.37 (q, 2H, CH_2), 6.06 (s, 1H, CH), 7.24-7.75 (m, 7H, Ar-H), 10.65 (s, 1H, NH), ^{13}C NMR (400 MHz, DMSO-*d*$_6$) δ: 15.5 (CH_3), 17.9 (CH_2), 27.9 (CH_2), 58.8 (CH), 103.2, 120.2, 121.3, 122.8, 130.7, 131.7, 131.9, 136.5, 136.9, 141.8, 142.9, 146.2 (Ar-C), 162.1 (C-S), MS: (M+1) 431.01.

4-(4-Bromo-phenyl)-2-methylsulfanyl-8-nitro-4,5-dihydro-1H-indeno[1,2-d]pyrimidine (5b). White solid, (84 %), m.p. >300 °C, Anal.Calcd for $C_{18}H_{14}BrN_3O_2S$: C 51.93, H 3.39, N 10.09% Found: C 52.02, H 3.45, N 9.98%. IR (KBr, cm^{-1}): 3241 (NH), 2955 (ArC-H), 1630 (C=C), 1535 & 1339 (N-O), 578 (C-Br). ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 1.24 (s, 3H, CH_3), 2.98-3.08 (d, 1H, CH), 3.22-3.23 (d, 1H, CH), 5.68 (s, 1H, CH), 7.21-7.73 (m, 7H, Ar-H), 10.65 (s, 1H, NH), ^{13}C NMR (400 MHz, DMSO-*d*$_6$) δ: 12.5 (CH_3), 27.9 (CH_2), 58.8 (CH), 103.9, 120.7, 121.0, 122.9, 129.7, 131.3, 131.7, 135.1, 137.9, 142.8, 142.9, 147.2 (Ar-C), 164.1 (C-S).

2-Cyclopentylsulfanyl-4-phenyl-4,5-dihydro-1H-indeno[1,2-d]pyrimidine (5c). White solid, (88 %), m.p. >300 °C, Anal.Calcd for $C_{22}H_{22}BrN_2S$: C 76.26, H 6.40, N 8.08% Found: C 76.39, H 6.30, N 7.99%. IR (KBr, cm^{-1}): 3251 (NH), 2964 (ArC-H), 1622 (C=C). ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 1.44 (m, 4H, CH_2), 2.3-2.5 (m, 5H, CH & CH_2), 3.21-3.25 (d, 2H, CH_2), 5.62 (s, 1H, CH), 7.21-7.43 (m, 8H, Ar-H), 10.4 (s, 1H, NH), ^{13}C NMR (400 MHz, DMSO-d_6) δ: 21.5 (CH_2), 27.7 (CH_2), 32.4 (CH_2), 32.9 (CH), 58.9 (CH), 103.2, 125.2, 125.7, 126.3, 127.8, 128.1, 129.4, 129.9, 135.9, 136.5, 136.9, 141.8 (Ar-C), 163.1 (C-S), MS: (M+1) 347.15.

RESULTS AND DISCUSSION

The tetrahydro-indeno[1,2-d]pyrimidinone derivatives **4a-h** was synthesized by Antimony(III)chloride ($SbCl_3$) catalyzed Biginelli reaction of (un)substituted indanone **1a-c,** (thio)urea **2a-b** and (un)substituted aldehyde **3a-f** in refluxing acetonitrile in high yield**.** In order to improve the yields, we performed reactions using different quantities of reagents. The best results were obtained with a 0.2:1:1:1.5 ratio of $SbCl_3$, aldehyde, cyclic ketone compound and urea or thiourea. After completion of the reaction, as indicated by TLC, the reaction mixture was poured onto crushed ice from which the dihydropyrimidinones were isolated by filtration and recrystallized from hot ethanol.

The dihydro-1H-indeno[1,2-d]pyrimidine derivatives **5a-c** have been synthesized by the reaction between corresponding tetrahydro-indeno[1,2-d]pyrimidinone **4a-h** derivatives and alkyl bromide in ethanol at reflux temperature. After completion of the reaction, as indicated by TLC, the reaction mixture was poured onto water from which the dihydro-1H-indeno[1,2-d]pyrimidine derivatives **5a-c** isolated by filtration and recrystallized from hot isopropyl alcohol to afford pure product.

The structure of compound **4a-h** was confirmed by IR, ^{1}H NMR, ^{13}C NMR spectra and mass spectra. IR spectra of **4a** exhibited absorptions at 3311, 3229 cm^{-1} for (NH), 3010, 3024 cm^{-1} for (aromatic C-H stretching), 1188 cm^{-1} for (thioketone group). The ^{1}H NMR of compound 4**a** showed singlet at δ 9.83 and 7.75 ppm for (NH) proton, it also showed singlet at δ 5.58 ppm for(CH), doublet at δ 2.73-2.80 and 3.21-3.29 ppm and aromatic protons resonate as multiplets at δ 7.10-7.59 ppm. The ^{13}C NMR spectrum of compound **4a** showed signals at δ 26.9, 60.4, for aliphatic carbon, δ 103.7, 122.1, 123.1, 124.0, 127.4, 128.2, 128.8, 135.2, ,135,9, 139.5, 141.7, 142.4 for aromatic carbon and the thioketone carbon was observed at δ 179.4. The structure was further confirmed by its mass spectral studies. It gave molecular ion peak at m/z 279.09 (M+1) corresponding to molecular formula $C_{17}H_{14}N_2S$ (Scheme 1). The structure of compounds **5a-c** was confirmed by IR, ^{1}H NMR, ^{13}C NMR and mass spectra. IR spectra of **5a** exhibited absorptions at 3241 cm^{-1} for (NH), 3015 cm^{-1} for (aromatic C-H stretching), 1527 & 1344 cm^{-1} for (nitro group) and 580 cm^{-1} for (C-Br stretching). The ^{1}H NMR of compound **5a** showed singlet at δ 10.65 ppm for (NH) proton, it also showed singlet at δ 6.06 ppm for(CH), doublets at δ 2.98-3.06 and 3.23-3.28 for (CH) and quartet at δ 3.30-3.37 for (CH_2). Aromatic protons resonate as multiplets at δ 7.24-7.75 ppm. The ^{13}C NMR spectrum of compound **5a** showed signals at δ 15.5, 17.9, 27.9, 58.8 for aliphatic carbon, δ 162.1 (C-S) and δ 103.2, 120.2, 121.3, 122.8, 130.7, 131.7, 131.9, 136.5, 136.9, 141.8, 142.9, 146.2 for aromatic carbon. The structure was further confirmed by its mass spectral studies. It gave molecular ion peak at m/z 431.01 (M+1) corresponding to molecular formula $C_{19}H_{16}BrN_3O_2S$ (Scheme 1). Similarly, all these compounds were characterized on the basis of spectral studies. All the compounds were screened for their antibacterial and antifungal activities using ampicillin, chloramphenicol and griseofulvin as standard drugs.

Antimicrobial activity

The *in vitro* antimicrobial activity of all the synthesized compounds was carried out by broth microdilution method. Mueller Hinton broth was used as nutrient medium to grow and dilute the compound suspension for the test bacteria and Sabouraud Dextrose broth used for fungal nutrition. Inoculum size for test strain was adjusted to 10^8 CFU [Colony Forming Unit] per milliliter by comparing the turbidity. The strains employed for the activity were procured from [MTCC – Micro Type Culture Collection] Institute of Microbial Technology, Chandigarh.

The compounds **4a-h** and **5a-c** were screened for their antibacterial activity against *Escherichia coli (E.coli), Pseudomonas aeruginosa (P.aeruginosa)*, *Staphylococcus aureus (S.aureus)*, *Streptococcus pyogenes (S.pyogenes)* as well as antifungal activity against and *Candida albicans (C.albicans)*. DMSO was used as vehicle to get desired concentration of compounds to test upon microbial strains. The lowest concentration, which showed no visible growth after spot subculture was considered as MIC for each compound. The standard antibiotics used for comparison in the present study were ampicillin, chloramphenicol for evaluating antibacterial activity as well as griseofulvin for antifungal activity. The protocols are summarized in (Table-2).

An examination of the data (Table-2) reveals that amongst all the synthesized compounds **4a-h**, compound **4c** exhibited excellent activity against Gram positive bacteria *Staphylococcus aureus (S.aureus)*. Except compound **4f**, all other compounds are found to be more potent against Gram positive bacteria *Staphylococcus aureus (S.aureus)* as compared to standard antibiotic ampicillin, while compounds **4d, 5a, 5b** and **5c** are found to be highly active against Gram negative bacteria *Escherichia coli* as compared to standard antibiotic ampicillin. Most of the compounds were not found sufficiently potent to inhibit *Streptococcus pyogenes (S.pyogenes)* and *Pseudomonas aeruginosa (P.aeruginosa)*.

Antifungal study revealed that compounds **4c**, **4h**, **4j**, **5b** and **5c** are more potent as compared to standard fungicidal griseofulvin against *Candida albicans (C.albicans)*.

Table-2: Antimicrobial activity of compounds 4a-h and 5a-c

Comp.No.	Minimal inhibitory concentration µg/ml				
	Gram-negative bacteria		Gram-positive bacteria		Fungi
	E.coli	***P.aeruginosa***	***S.aureus***	***S.pyogenus***	***C.albicans***
4a	250	250	200	250	1000
4b	200	100	100	200	>1000
4c	100	100	62.5	125	**250**
4d	62.5	250	100	200	1000
4e	125	100	200	250	>1000
4f	100	100	250	200	1000
4g	125	62.5	100	125	500
4h	200	125	125	200	**250**
5a	62.5	100	200	250	1000
5b	62.5	100	100	100	**200**
5c	62.5	100	100	100	**250**
Ampicillin	100	--	250	100	--
Chloramphenicol	50	50	50	50	--
Griseofulvin	--	--	--	--	500

(--) No inhibition zone.

CONCLUSION

A series of some new derivatives **4a-h** has been synthesized through a facile one-pot multicomponent reaction by using Antimony(III)chloride as a catalyst. This strategy provides better results with more sterically hindered substrates with high yield. It can be concluded from Table-2 that compound **4c** is highly active against Gram positive bacteria *Staphylococcus aureus (S.aureus)*. Compounds **4d, 5a, 5b** and **5c** are found to be highly active against Gram negative bacteria *Escherichia coli* as compared to standard antibiotic ampicillin.

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