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Synthesis of 3-amino-2-methyl/ethyl-5,6,7,8-tetrahydro[1]benzothieno[2,3-*d*] pyrimidin-4(3*H*)-one and its Schiff bases as possible antimicrobial and non-steroidal antiinflammatory agents

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Ethyl 2-amino-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate **1** has been converted into ethyl 2-(acetylamino)-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate **2a** and ethyl 2-(propionylamino)-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate **2b**. Compounds **2a** and **2b** on treatment with hydrazine hydrate give 3-amino-2-methyl-5,6,7,8-tetrahydro[1]benzothieno[2,3-*d*]pyrimid-4(3*H*)-one **3a** and 3-amino-2-ethyl-5,6,7,8-tetrahydro[1]benzothieno[2,3-*d*]pyrimid-4(3*H*)-one **3b** respectively. Compounds **3a** and **3b** have been treated with aromatic aldehydes to get Schiff bases **4a-l** and **5a-l**. The compounds have been characterized by spectral analysis and screened for antibacterial and antifungal activity. Eight compounds have also been screened for their antiinflammatory activity. A few of the compounds exhibit promising biological activity.

Keywords: Synthesis, thienopyrimidine, Schiff bases, antibacterial, non-steroidal antiinflammatory

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Thiophene derivatives are known to exhibit an array of biological activity such as antibacterial and antifungal[1-3], analgesic and anti-inflammatory[4,5]. Synthesis and biological studies on various thienopyrimidine derivatives have been reported in the literature[6-10]. Mahas *et al.*[11] first reported the anti-inflammatory activity of substituted thienopyrimi-*d*ines. A number of derivatives of 2-methyl-3-aryl-4-oxo-5, 6, 7, 8-tetramethylenethieno[2, 3-*d*]pyrimidine were prepared by them and screened for their anti-inflammatory activity.

Condensed thienopyrimidines exhibit interesting biological activity like antibacterial[12,13], antihistamic[14], anticancer[15], anti-inflammatory[16] and anticonvulsant[17]. Recent literature[18] describes the investigation of a few derivatives of thienopyrimi-*d*ines as possible non-steroidal antiinflammatory agents and neurotropic agents. These literature reports led to the synthesis of the hitherto unreported 3-amino-2-methyl-5, 6, 7, 8-tetrahydro[1]benzothieno [2,3-*d*]pyrimid-4(3*H*)-one and 3-amino-2-ethyl-5,6,7,8-tetrahydro[1]benzothieno[2,3-*d*]pyrimid-4(3*H*)-one and evaluation of their antimicrobial and antiinflammatory activity.

Ethyl-2-amino-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate **1** was prepared from cyclohexanone, sulphur and ethyl cyanoacetate in a one-pot thiolation-heterocyclisation reaction[6]. Ethyl-2-amino-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate **1** was treated with zinc and acetic anhydride to get ethyl 2-(acetylamino)-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate **2a**. In the same way ethyl 2-amino-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate **1** was treated with zinc and propionic anhydride to get ethyl 2-(propionylamino)-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate **2b**. Both the products were confirmed by ^{1}H NMR, mass, and IR spectral studies. Both ethyl 2-(acetylamino)-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate **2a** and ethyl 2-(propionylamino)-4, 5, 6, 7-tetrahydro-1-benzothiophene-3-carboxylate **2b** on refluxing with 80% hydrazine hydrate in methanol yielded 3-amino-2-methyl-5,6,7,8-tetrahydro[1]benzothieno[2,3-*d*] pyrimid-4(3*H*)-one **3a** and 3-amino-2-ethyl-5,6,7,8-tetrahydro [1]benzothieno[2,3-*d*]pyrimid-4(3*H*)-one **3b** respectively. Both the compounds were purified by recrystallisation from methanol and characterized by elemental analysis, ^{1}H and ^{13}C NMR, mass and IR spectral studies. The compounds **3a** and **3b** were then treated

with different aromatic aldehydes in chloroform with catalytic amount of acetic acid to yield the corresponding Schiff bases **4a-l** and **5a-l** (**Table I**). Synthetic route is outlined in **Scheme I**.

Biological Activity

Anti-inflammatory Activity

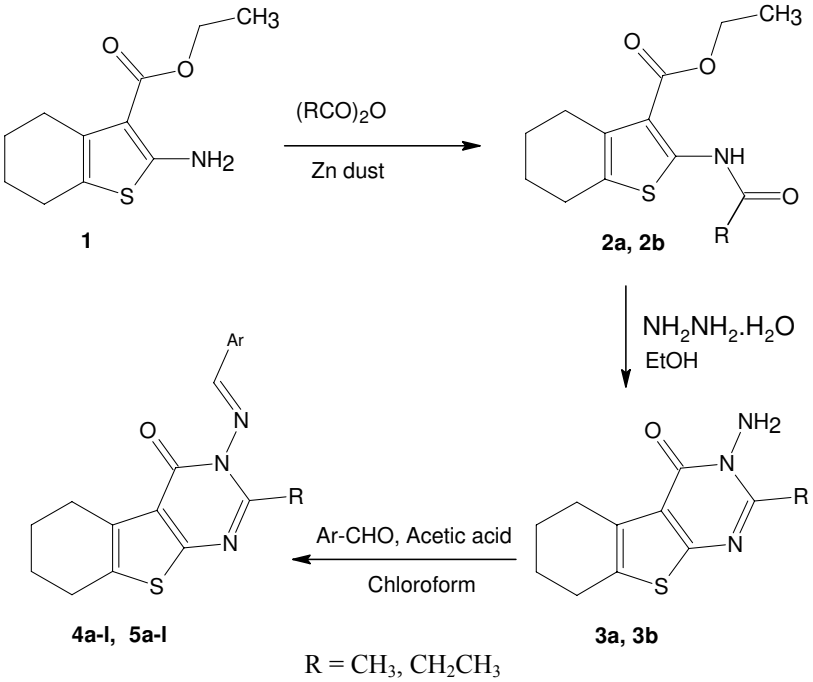
A few compounds among **4a-l** such as **4c**, **4j**, **4k** and **4l** and among **5a-l** such as **5b**, **5d** and **5g** were evaluated for their anti-inflammatory activity by cotton pellets induced granuloma in rats weighing 150- 200 g[19]. Results of the study are given in **Table II**.

An insight into the anti-inflammatory activity with respect to the chemical structure reveals that compound **4k** bearing 2-chlorophenyl moiety, **4l** bearing 2-hydroxy-4-methoxyphenyl moiety and **5b** bearing 6-methoxy-2-napthyl exhibited good anti-inflammatory activity at a dose of 100 mg/kg in comparison with standard drug ibuprofen. Compounds **4c** bearing 4-methoxyphenyl moiety, **4j** bearing 3,4,5-trimethoxyphenyl moiety and **5g** bearing 4-methoxyphenyl moiety have shown mild to moderate anti-inflammatory activity. The compound **5d** bearing 4-(N,N-*d*iethylamino) phenyl moiety is the least active among the seven tested compounds. Structure-activity relationship study reveals that the higher activity of **4k** and **5b** may be due to the presence of 2-chlorophenyl and 6-methoxy-2-naphthyl moieties, which are the major structural units of known anti-inflammatory agents diclofenac and nebumetone respectively. These inferences are based on screening test only, further tests using larger samples have to be performed for obtaining conclusive results.

Antibacterial Activity

The newly synthesized compounds **3a, 3b**, **4a-l** and **5a-l** were screened for their antibacterial activity against *Escherichia coli* (ATTC-25922), *Staphyllococcus aureus* (ATTC-25923), *Psuedomonus aeruginosa* (ATTC-27853), and *Klebsiella pneumoniae* (recultered) bacterial strains by disc diffusion method[20-22]. Furacin was used as standard drug. Solvent and growth controls were kept for comparison and the zones of inhibition and minimum inhibitory concentrations [MIC] were noted. The results of such studies are given in **Table III**.

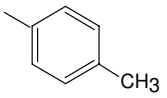
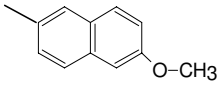
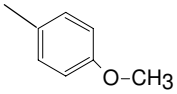
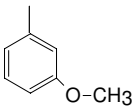
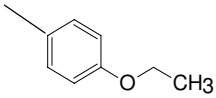
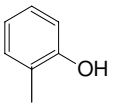
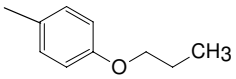
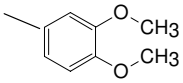
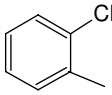
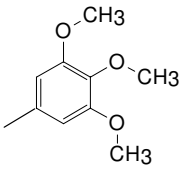
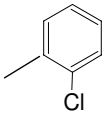
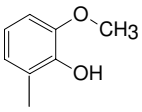
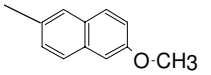
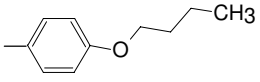
Antibacterial studies reveal that in addition to **3b** the compounds **5f** and **5j** containing 2,3,5-trichlorophenyl and quinolinyl moieties respectively were found to be the most active amongst all the tested compounds. Compounds **5b, 5c, 5d** and **5h** exhibited moderate activity in comparison with the other compounds. The presence of trichlorophenyl and quinolinyl moiety may be the reason for the enhanced activity of **5f** and **5j**. More studies have to be carried out to obtain conclusive results.



R = CH_3, CH_2CH_3

Scheme I

Table I — Characterization data of **4a-l** and **5a-l**

Compd	-Ar	Yield * (%)[a]	m.p. °C	% N Found	% N Calcd
4a		38	164-66	12.89	12.99
4b		68	230 (dec)	10.38	10.41
4c		52	206-08	11.80	11.89
4d		38	128-30	11.80	11.89
4e		34	165-68	11.34	11.44
4f		38	212-15	12.30	12.38
4g		38	138-39	10.90	11.01
4h		52	224-29	10.89	10.96
4i		33	160-64	11.28	11.37
4j		54	168-71	10.08	10.16
4k		58	160-62	11.71	11.74
4l		85	212-14	11.30	11.37
5a		65	136-38	12.41	12.45
5b		72	166-68	9.96	10.06
5c		80	146-48	10.24	10.26

Contd —

Table I — Characterization data of **4a-l** and **5a-l** — *Contd*

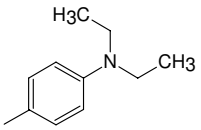
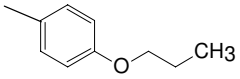
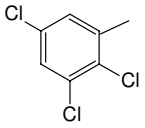
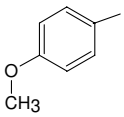
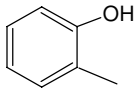
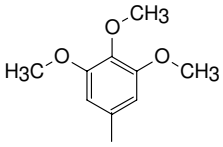
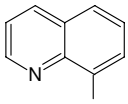
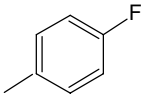
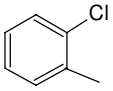
Compd	-Ar	Yield * (%)[a]	m.p. °C	% N Found	% N Calcd
5d		76	157-58	13.68	13.71
5e		82	144-45	10.59	10.62
5f		83	168-70	9.50	9.53
5g		62	153-54	11.40	11.44
5h		67	159-60	11.80	11.89
5i		67	174-76	9.79	9.83
5j		58	211-12	14.36	14.42
5k		78	183-84	11.79	11.82
5l		76	186-87	11.28	11.30

Table II — Effect of **4c, 4j, 4k, 4l, 5b, 5d** and **5g** on cotton pellet granuloma in rats

Group	Drug	Dose mg/kg p.o.	Weight of granuloma (mg)				Mean	% Inhibition
1	Control (2% gum acacia)	10 mL/kg	460	475	600	525	515	-
2	Ibuprofen	100	353	365	345	350	353.75	31.3
3	**4c**	100	440	438	429	460	441.75	14.2
4	**4j**	100	479	468	470	430	461.75	10.3
5	**4k**	100	372	395	332	380	369.75	28.2
6	**4l**	100	389	386	395	394	391.5	24.0
7	**5b**	100	370	385	330	390	368.75	28.3
8	**5d**	100	470	400	500	560	482.5	06.3
9	**5g**	100	479	470	465	430	461.0	10.4

N=3 in each group, $p < 0.05$ *vs* Ibuprofen

Table III — Antibacterial activity of **3a, 3b**, **4a-l** and **5a-l** (MIC in μg/mL)

Compd	*E. coli*	*P. aeruginosa*	*S. aureus*	*Klebseilla sps.*
3a	--	--	--	--
3b	12.5	12.5	12.5	12.5
4a	--	--	--	--
4b	--	--	--	--
4c	--	--	--	--
4d	--	--	--	--
4e	6.25	--	--	100
4f	--	--	--	--
4g	--	-	--	--
4h	--	--	--	--
4i	6.25	--	10	--
4j	12.5	100	10	100
4k	12.5	100	10	100
4l	12.5	100	50	100
5a	--	10	10	-
5b	10	--	10	10
5c	--	10	20	10
5d	10	--	10	10
5e	--	--	--	--
5f	10	10	20	10
5g	--	--	--	--
5h	--	10	10	10
5i	--	100	--	--
5j	12.5	12.5	10	10
5k	--	--	--	--
5l	10	10	--	--
Furacin	12.5	6.0	12.5	12.5

Antifungal study

Newly prepared compounds **3a, 3b**, **4a-l** and **5a-l** were screened for their antifungal activity against *Aspergilus flavus* (NCIM No.524)*, Aspergilus fumigatus* (NCIM No.902)*, Candida albicans* (NCIM No.3100)*, Penicillium marneffei* (recultered) and *Trichophyton mentagrophytes* (Recultered) in DMSO by serial plate dilution method[20-22]. Diameter of the inhibition zone and minimum inhibitory concentrations [MIC] were noted. The results of such studies are given in **Table IV**. Activity of each compound was compared with Itraconozole as standard drug. The minimum inhibitory concentration (MIC) for the Itraconazole in DMSO is <10 μg/mL against the tested species.

The antifungal studies reveal that the compound **5e** bearing 4-propoxybenzene was found to be most active amongst all the tested compounds. Compounds **4b** and **4d** bearing 6-methoxy-2-naphthyl and 3-methoxyphenyl moiety have exhibited moderate activity in comparison with other compounds. Since the compound **3b** exhibited more antifungal activity than **3a** most of the Schiff bases derived from **3b** have shown good activity. The exact reason why **5e** emerged as most active amongst all is not clear from the present studies. More studies have to be carried out to obtain conclusive results.

Experimental Section

Melting points were taken in open capillary tubes and are uncorrected. The homogeneity of the compounds were determined by thin layer chromatography using Merck silica gel 60 F_{254} coated aluminium plates. IR spectra were recorded on Shimadzu-FTIR infrared spectrometer in KBr pellets. ^{1}H NMR spectra were recorded in $CDCl_3$ and in DMSO-d_6 on a Varian 300 MHz spectrometer using TMS as internal standard and the FAB mass spectra were recorded on a JEOL SX 102/DA-600 mass spectrometer/data system using Argon/Xenon (6 kV, 10 mA) as FAB gas.

Synthesis of ethyl 2-(acetylamino)-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate 2a. Ethyl 2-amino-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate[6] (3.5 g, 0.0155 mole), acetic anhydride(14 mL) and zinc dust (0.883 g, 0.015 mole) was refluxed for 2 h. The reaction mixture was then cooled to RT and the precipitated product was filtered. The crude product was dissolved in methanol (35 mL) and filtered over celite. The filtrate was slowly cooled to RT and filtered to collect the solid. The product was obtained as white crystals with a yield of 3.5 g (84.3%), m.p. 148°C, Molecular formula, $C_{13}H_{17}NO_3S$; IR (KBr): 3436 and 3244 (-NH-), 2931 and 2873 (-CH-), 1666 and 1546 (-C=O) and 1250 cm^{-1} (C-O).

Synthesis of ethyl 2-(propionylamino)-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate 2b. Prepared in the same way as above from ethyl 2-amino-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate[6] (3.5 g, 0.0155 mole), propionic anhydride (10.5 mL) and zinc dust (0.883 g, 0.015 mole). The product was obtained as white crystals with yield of 2.5 g (58.1%), m.p. 79-80°C, Molecular formula, $C_{14}H_{19}NO_3S$; IR (KBr): 3436 and 3244 (-NH-), 2931 and 2873 (-CH-), 1666 and 1546 (-C=O) and 1250 cm^{-1} (C-O).

Synthesis of 3-amino-2-methyl-5,6,7,8-tetrahydro[1]benzothieno[2,3-*d*] pyrimidin-4 (3*H*)-one 3a. Ethyl 2-(acetylamino)-4,5,6,7-tetrahydro-1-benzthiophene-3-carboxylate (3 g, 0.011 mole), hydrazine hydrate (12.6 mL) in methanol (15 mL) was refluxed for 8 h.The reaction mixture was then cooled to RT and the product filtered. The crude product was then purified by recrystallisation from

Table IV — Antifungal activity of **3a, 3b**, **4a-l** and **5a-l** (MIC in μg/mL)

Compd	*Trichophton*	*Penicillium*	*As. fumigatus*	*As. Flavus*
3a	--	--	--	--
3b	--	100	100	10
4a	--	--	--	--
4b	--	6.25	10	10
4c	--	--	--	--
4d	--	6.25	10	10
4e	--	--	--	--
4f	--	--	--	--
4g	--	--	--	--
4h	--	--	--	--
4i	--	10	10	--
4j	--	--	--	--
4k	--	--	--	--
4l	--	--	--	--
5a	--	--	--	--
5b	10	10	100	--
5c	10	10	100	--
5d	--	100	--	10
5e	10	6.25	6.25	6.25
5f	10	10	100	--
5g	--	--	--	--
5h	10	100	100	--
5i	10	20	100	--
5k	--	--	--	--
5l	--	--	--	--
Itraconozole	<10	<10	<10	<10

methanol to get white micro crystals with yield of 1.2 g (45.45%), m.p. 190-94°C. IR (KBr): 3433 and 4286 (-NH_2), 2931 and 2931 (-CH), 1666 (-C=O) and 1608 cm^{-1} (C=N); ^{1}H NMR ($CDCl_3$): δ 1.79-1.90 (m, 4H, $2CH_2$), 2.75 (t, *J*=-5.3 Hz, 2H,CH_2), 2.97 (t, 2H, *J*=-4.3Hz, 2H,CH_2), 2.65 (s, 3H, -CH_3) and 4.87 (s, 2H, -NH_2); MS: *m/z* 235 (M^+, 100%), 219 (M-NH_2, 60%), 207 (M-(NH_2+CH_3), 18%), 177 ($C_{11}H_{15}NO$, 21%).

Synthesis of 3-amino-2-ethyl-5, 6,7,8-tetrahydro[1]benzothieno[2,3-*d*]pyrimidin-4(3*H*)-one 3b. Prepared in the same way mentioned for **3a** from ethyl 2-(propionyl amino)-4,5,6,7-tetrahydro-1-benzothiophene-3-carboxylate. The product was isolated as white needles with yield of 61.5%, m.p. 116-18°C. IR (KBr): 3277 and 3196 (-NH_2), 2935 (-CH) 1663 (-C=O) and 1549 cm^{-1} (-C=N); ^{1}H NMR ($CDCl_3$): δ 1.80- δ1.85 (m, 4H, $2CH_2$), 2.72 (t, *J*=-4.5 Hz, 2H, CH_2), 2.94 (t, *J*=-5.1 Hz, 2H, CH_2), 1.31 (t, *J*=-5.9 Hz, 3H, -CH_3), 2.98 (q, 2H, -CH_2) and 4.82 (s, NH_2); ^{13}C NMR ($CDCl_3$): δ 11.81, 23.06, 23.76, 25.98, 26.21, 28.53, 120.69, 131.74, 133.91, 158.95, 159.15 and 162.56; MS: *m/z* 250 (M+1, 100%), 249 (M^+, 85%).

Synthesis of 2-methyl/ethyl-3-{[(aryl)methyl-ene]amino}-5,6,7,8-tetrahydro[1]benzothieno [2,3-*d*]pyrimidin-4(3*H*)-ones 4a-l and 5a-l. 3-Amino-2-methyl/ethyl-5,6,7,8-tetrahydro[1] benzothieno[2,3-*d*]pyrimidin-4(3*H*)-one (0.01 mole) and aromatic aldehyde (0.01 mole) were refluxed in chloroform (25 mL) in presence of catalytic amount of acetic acid for 8 h. The reaction mixture was cooled and filtered. The crude product was then purified by recrystallisation from ethanol to get the Schiff bases as pure crystals.

4a: IR (KBr): 2939.3 and 2869 (-CH), 1670 (-C=O) and 1612 cm^{-1} (C=N); ^{1}H NMR ($CDCl_3$): δ 1.78- 1.81 (m, 4H, $2CH_2$), 2.37 (s, 3H, -CH_3), 2.51 (s, 3H, -CH_3), 2.7 (t, *J*=-4.0 Hz, 2H, CH_2), 2.93 (t, *J*=-4.0 Hz, 2H, CH_2), 7.21 (d, *J*=-8.0 Hz, 2H, -ArH), 7.7 (d, *J*=-8.0 Hz, 2H, -ArH), 8.77 (s, 1H, =CH-); MS: *m/z* 338 (M+1,28%), 220 ($C_{11}H_{12}N_2OS$, 100%), 192 ($C_{10}H_{10}NOS$), 64%), 177 ($C_{11}H_{15}NO$, 8%).

4d: IR (KBr): 2939.3 and 2869 (-CH), 1670 (-C=O) and 1612 cm^{-1}(C=N); ^{1}H NMR ($CDCl_3$): δ 1.5- 1.90 (m, 4H, $2CH_2$), 2.36 (s, 3H, -CH_3), 3.89 (s, 3H, -OCH_3), 2.77 (t, *J*=-4.0 Hz, 2H, CH_2), 2.98 (t, *J*=-4.0 Hz, 2H, CH_2), 6.99 (d, *J*=-8.0 Hz, 2H, -ArH), 7.84 (d, *J*=-10.0 Hz, 2H, -ArH), 8.75 (s, 1H, =CH-); MS: *m/z* 354 (M^+, 38%), 221 ($C_{11}H_{12}N_2OS$, 100%), 192 ($C_{10}H_{10}NOS$), 64%), 177 ($C_{11}H_{15}NO$, 12%).

4f: ^{1}H NMR (DMSO-d_6): δ 1.83-1.90 (m, 4H, CH_2), 2.59 (s, 3H, -CH_3), 2.75 (t, *J*=5.61Hz, 2H, CH_2), 2.97 (t, *J*=-5.76Hz, 2H, CH_2), 6.96-7.49 (m, 4H,ArH), 8.97 (s, 1H, N=CH), 10.36 (s, 1H, Ar-OH); MS: *m/z* 340 (M^+, 38%), 220 ($C_{11}H_{12}N_2OS$, 100%), 192 ($C_{10}H_{10}NOS$, 46%), 177 ($C_{11}H_{15}NO$, 6%).

4i: IR (KBr) : 2935.5 and 2862.2 (-CH), 1670 (-C=O) and 1612 cm^{-1} (C=N); ^{1}H NMR (DMSO- d_6): δ 1.82-1.97 (m, 4H, $2CH_2$), 2.76 (t, *J*=4.63Hz, 2H, CH_2), 2.99 (t, *J*=5.8Hz , 2H, CH_2), 2.56 (s, 3H, -CH_3), 3.95 (s, 3H, -OCH_3), 6.38 (s, 1H, -OH), 6.98 (d, *J* = 8.12Hz, 1H, Ar-H), 7.26 (dd, *J*=1.8,8.1Hz,1H, Ar-H), 7.53 (d, *J* = 1.8Hz, 1H, Ar-H)) and 8.64 (s, 1H, N=CH).

4k: IR (KBr): 2931.6 and 2854.5 (-CH), 1678 (-C=O), 1554 (C=N), 759.9 cm^{-1} (Ar-Cl); ^{1}H NMR (DMSO-d_6) δ 1.82-1.88 (m, 4H, $2CH_2$), 2.74 (t, *J*=5.62Hz, 2H, CH_2), 3.00 (t, *J*=5.79Hz 2H, CH_2), 2.61 (s, 3H, -CH_3), 7.34 - 7.40 (m, 2H, Ar-H), 7.45 (d, *J* = 3.79, 1H, Ar-H), 8.21 (d , *J*=7.52, 1H,Ar-H), 9.0 (s, 1H, N=CH).

5b: IR (KBr): 2933.5 and 2886.4 (-CH), 1676 (-C=O), 1554.5 (C=N), 864.1 and 825.5 cm^{-1} (Ar-Cl); ^{1}H NMR (DMSO-d_6): δ 1.26 (t, 3H, -CH_3), 1.78 (m, 4H, $2CH_2$), 2.7 (t, 2H,CH_2), 2.89 (m, 4H, CH_2), 3.87 (3H, -OCH_3), 7.07 (m, 2H, Ar-H), 7.69 (m, 2H, Ar-H), 7.99 (m, 2H, Ar-H), 8.88 (s, 1H, =CH-); ^{13}C NMR (DMSO-d_6): δ 10.88, 22.28, 22.94, 25.19, 25.52, 28.21, 55.27, 96.12, 106.01, 119.55, 123.60, 127.57, 128.10, 131.70, 132.14, 132.66, 136.98, 155.48, 156.52, 159.40, 160.84, 167.60.

5d: ^{1}H NMR (DMSO-d_6): δ 1.22 (t, 9H, -$3CH_3$), 1.86 (m, 4H, $2CH_2$), 2.70 (m, 6H, $3CH_2$), 3.43 (m, 4H, $2CH_2$), 6.67 (d, *J*=10 Hz, 2H, Ar-H), 7.71 (d, *J*=10 Hz 2H, Ar-H), 8.48 (s, 1H, =CH-); ^{13}C- NMR (DMSO-d_6): δ 10.92, 12.59, 22.38, 23.04, 25.25, 25.58, 28.21, 44.62, 110.54, 110.99, 131.06, 131.71,132.3, 150.86, 155.84, 156.72, 160.92, 168.08.

5f. ^{1}H NMR (DMSO- d_6): δ 1.21 (t, 3H, -CH_3), 1.79 (m, 4H, $2CH_2$), 2.70 (t, 2H, CH_2), 2.90 (m, 4H, $2CH_2$), 7.54 (s, 1H, Ar-H), 7.96 (s, 1H, Ar-H), 9.47 (s, 1H, =CH-); ^{13}C NMR (DMSO- d_6): δ 20.29, 22.52, 55.18, 58.32, 60.43, 61.16, 75.93, 114.54, 130.13, 130.9, 159.62, 169.29, 170.08, 172.56.

5i: ^{1}H NMR (DMSO-d_6): δ 1.25 (t, *J*=6.0, 3H, -CH_3), 1.78 (m, 4H, $2CH_2$), 2.70 (t, 2H, CH_2), 2.85 (m, 4H, $2CH_2$), 3.84 (s, 9H, OCH_3), 7.06 (s, 2H, Ar-H), 8.68 (s, 1H, =CH-); ^{13}C NMR (DMSO-d_6): δ 10.84, 22.27, 22.92, 25.19, 25.52, 28.19, 56.13, 60.93, 105.96, 106.63, 120.96, 127.72, 131.70, 132.88, 141.92, 153.5, 155.42, 156.33, 160.94, 167.98, 190.78.

5j: ^{1}H NMR (DMSO-d_6): δ 1.33 (t, *J*=7.41 Hz, 3H, -CH_3), 1.85 (m, 4H, $2CH_2$) 2.72 (t, *J*=5.76 Hz, 2H, CH_2) 2.93 (q, *J*=7.38 Hz, 2H, -CH_2), 3.03 (t, *J*=5.76 Hz, 2H, CH_2), 7.49 (dd, *J*=4.2 and 8.2, 1H, ArH), 7.69 (t, 7.7Hz, 1H, Ar-H), 8.05 (d, *J*=7.98Hz, 1H, Ar-H), 8.23 (dd, *J*= 1.05, 9.12 Hz, 1H, Ar-H), 8.67 d, *J*=7.28 Hz, 1H, Ar-H), 8.96 (t, *J*=2.56 Hz, 1H, Ar-H), 10.14, (s, 1H, =CH-).

5k: IR (KBr): 2945.1 and 2871.8 (-CH), 1668.3 (-C=O), 1546.8 (C=N), 864.1 and 1236.3 (Ar-F); MS: *m/z* 356 (M+1,100%), *m/z* 355 (M^+,40%), *m/z* 234 (M-C_7H_6FN).

Conclusion

Hitherto unreported 3-amino-2-methyl-5,6,7,8-tetrahydro[1]benzothieno[2,3-*d*]pyrimid-4 (3*H*)-one **3a** and 3-amino-2-ethyl-5,6,7,8-tetrahydro[1]benzo-thieno[2,3-*d*]pyrimid-4(3*H*)-one **3b** have been prepared. These compounds on treatment with aromatic aldehydes yield Schiff bases **4a-l** and **5a-l**. All the compounds have been screened for antibacterial and antifungal activity. Eight compounds have also been screened for their anti-inflammatory activity. The compounds **4k** and **5b** have emerged as promising anti-inflammatory agents. Compounds **5f** and **5j** have exhibited promising antibacterial activity and the compound **5e** has exhibited promising anti-fungal activity. Therefore, the compounds **4k, 5b, 5e, 5f** and **5j** can be recommended for further studies.

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References

1 Devani M B, Shishoo C J, Pathak U S, Parikh S H, Shah G G & Pandya A C, *J Pharm Sci*, 65, **1976**, 660.
2 Chambhare R V, Bobade A S & Khadse B G, *Indian J Heterocycl Chem,* 12, **2002**, 67.
3 Swamy V A, Pathak U S, Rajasolomon V, Meena S, Ramseshu K V & Rajesh R, *Indian J Hetercycl Chem,* 13, **2004**, 347.
4 Cannito A, Perissin M, Luu Duc C, Huguer F, Gaultier C & Narcisse G, *Eur J Med Chem*, 25, **1990**, 635.
5 Colin J & Drayton, *Comprehensive Medicinal Chemistry*, 1st edn, (Pergamon Press, Oxford, U.K.), 6, **1990**, 877.
6 Gewald K, Schinke E & Bottcher H, *Chem Ber* 99, **1996**, 94.
7 Tserng K Y & Bauer L, *J Org Chem,* **1975**, 40**,** 172.

8 Taylor E C & Berger J G, *J Org Chem*, 32, **1976**, 2375.
9 Nielsen K E & Pedersen E B, *Acta Chem Scand*, B32, **1978**, 303.
10 Robba M, Lemcomte J M & Cugnon de Servicourt M, *Tetrahedron*, 27, **1971**, 487.
11 Manhas M S, Sharma S D & Amin S G, *J Med Chem*, 15, **1972**, 106.
12 El-Bahaie S, Kadry A M, Assy M G & Ibrahim Y A, *Pharmazie,* 43**, 1988**, 537.
13 Bagoumy B E & Yousaf S, *J Pharm Sci*, 31, **1917**, 67.
14 Modica S & Santagati R, *J Med Chem*, 40, **1997**, 573.
15 Piazza G & Pamukeu R, *US Patent* 472 804, **1995**.
16 Russo F & Santagati S, *Farmaco Ed Sci,* 38, **1983**, 762.
17 Moneer A, Ahmed K & Omneya M, *Bull Fac Pharm*, 40, **2002**, 31.
18 Kh Oganisyan A, Noravyan A S, Dzhagatspanyan I A & Melikyan G G, *Pharm Chem J,* 37, **2003***,* 13.
19 Turner R A, *Screening Methods in Pharmacology*, (Academic Press, New York), **1965**.
20 Cruickshank R, Duguid J P, Marmion B P & Swain R H A, *Medicinal Microbiology*, 12th edn, Vol II, (Churchill Livingstone, London), **1975**.
21 Collins A H, *Microbiological Methods*, 2nd edn, (Butterworth, London) **1976**.
22 Arthington-Skaggs B A, Motley M, Warnock D W & Morrison C J, *J Clin Microbiology*, 38, **2000**, 2254.