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Synthesis, Characterization and Biological screening of some new Bis-1,4-dihydropyrimidines

KEYWORDS: Bis-1,4-dihydropyrimidines, S-alkylation, Anti-bacterial, Bordetella bronchiseptica.

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ABSTRACT *Bis-1,4-dihydropyrimidines (5a-k, 6a-k) were synthesized by S-alkylation of tetrahydropyrimidines using 1,4-dibromobutane and 1,5-dibromopentane. All the synthesized compounds were characterized using elemental analysis analytical (C, H and N) and spectral (FT-IR, ^{1}H-NMR, ^{13}C-NMR and MS) data. Some of the titled compounds evaluated for in vitro antibacterial activity against Bordetella bronchiseptica (MTCC 6837) and also screened for their antioxidant activity. The tested compounds exhibited potent antibacterial activity against Bordetella bronchiseptica (gram negative bacteria) and it was found that synthesized compounds are better antibacterial agents and mild antioxidants.*

INTRODUCTION

Among a wide variety of heterocycles that have been explored for developing pharmaceutically important molecules, pyrimidines[1] have played an important role in medicinal chemistry. The pyrimidines nucleus[2-4] occurs in a considerable number of natural products of vital importance to living organisms. Further, pyrimidine derivatives possessing anti-inflammatory and analgesic activities have been reported in the literature[5-11]. In addition to above mentioned activities pyrimidines derivatives possessing anti-hypertensive[12], antitumour[13], anti-microbial[14], anti-bacterial[15] and antifungal[16] and anti-infective[17] activities have been reported in the literature.

Dihydropyrimidines (DHPMs, popularly known as Biginelli's Compounds[18]) are associated with broad spectrum of biological activities ever since 4-aryl-1, 4-dihydropyridines of nifedipine type were first introduced into clinical medicines in 1975. Even today they are the most potent calcium channel modulators available for the treatment of various cardiovascular diseases and also several calcium channel blockers including nifedipine are reported with anti-ulcer activity[19-20]. From the literature it was observed that a lot of work has been done on DHPMs and its mono derivatives. So, in view of these observations it was considered worthwhile to synthesize some biological active bis-1,4-dihydropyrimidines via S-alkylation in which two pyrimidine moieties were joined through suitable alkylating reagents. Earlier we have synthesized such compounds using 1,3-dibromopropane as an alkylating reagent and these compounds showed potent antimicrobial activity and antioxidant activity[21].

In the present study, we have used 1,4-dibromobutane and 1,5-dibromopentane as alkylating reagents. Some of the synthesized compounds were screened for their biological activities i.e. antibacterial and antioxidant. The tested compounds showed potent activity against *Bordetella bronchiseptica* which is a gram negative bacteria. It is an upper respiratory tract pathogen which infects a wide variety of host species including domestic, laboratory and wild animals and may also opportunistically infect human being[22-23]. *Bordetella bronchiseptica* is involved in diseases such as kennel cough in dogs and atrophic rhinitis in swine[23].

RESULTS AND DISCUSSION

Synthesis and Characterization

As wide range of biological activities is associated with dihydropyrimidines, in view of this, synthesis of bis-1,4-dihydropyrimidines were considered for the synthesis of biologically active molecules. Bis-1,4-dihyropyrimidines are the compounds in which two tetrahydropyrimidine moieties are linked through a linker and in our case 1,4-dibromobutane and 1,5-dibromopentane act as a linkers. We report the alkylation of tetrahydropyrimidines **4(a-k)** (0.003 mole) using 1,4-dibromobutane and 1,5-dibromopentane (0.0015 mole) as alkylating reagents under refluxing conditions in alcoholic medium which yielded bis-1,4-dihydropyrimidines **5(a-k)-6(a-k) (Scheme-1).** The tetrahydropyrimidines **4(a-k)** were synthesized by acid catalysed condensation of aromatic aldehydes, ethylacetoacetae and thiourea. Ethanol was used as energy transfer media and the reaction mixture was irradiated in a domestic microwave oven for some time. The reaction conditions were optimized.

Scheme-1: Synthesis of bis-1,4-dihydropyrimidines insert here

The structure of the synthesized compounds **5(a-k)-6(a-k)** were characterized from spectral analysis (IR, ^{1}H-NMR, ^{13}C-NMR and Mass). IR spectra showed absorption bands at 3200-3338 cm^{-1}, 1640-1709 cm^{-1}, 1527-1597 cm^{-1} due to N-H, C=O and C=N stretching vibrations. In ^{1}H-NMR, N-H appeared as a singlet at δ 8.9-10.4, multiplets at δ 6.7-8.1 for aromatic protons. The proton at H-4 which confirms the ring closing appeared at δ 4.8-5.4. A quartet and triplet was observed at δ 4.0-4.3 and 1.0-1.3 for CH_2 and CH_3 of ester moiety in the compounds. CH_3 positioned at C-6 appeared as a singlet at δ 2.1-2.3 also confirms the structure. It is interesting to note that the CH_2 protons of the linker which attached to sulphur show non equivalence of two hydogens (δ 2.6-3.6) due to the slow rotation around

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C-S single bond. Further -CH_2-CH_2- protons of the linker appeared as multiplets at δ 2.1-1.5. Similarly ^{13}C-NMR analysis also confirms the structure of compounds. In this the most downfield resonance appeared at δ 174.5-167 (C=O), 165.2-161.0 (C-6) and 152-156 (C-2). The aromatic carbons appeared at their respective positions at δ 144.7-110.0. The characteristic carbon of the compounds **5(a-k)-6(a-k)** appeared at δ 31-24 (S-***C***H_2), 27-22 (S-CH_2-***C***H_2) and 23.8-26.5 (S-CH_2-CH_2-***C***H_2). The elemental analysis of compounds was found to be in good agreement with calculated values (± 0.4%). The characterization data of the synthesized compounds are given in experimental section.

BIOLOGICAL STUDIES

Some of the synthesized compounds were screened for their anti-bacterial and anti-oxidant studies using Agar well diffusion method and DPPH-Radical method respectively. Amoxicillin and Ascorbic acid were used as standard drug. The observed zone of inhibition at conc. 500 µg/ml of synthesized compounds were measured using strain namely *Bordetella bronchiseptica* (Table-1). Also, percentage inhibition was also measured for antioxidant activity (Table-2).

The antibacterial data of present study indicated that gram negative bacterial strain is most sensitive against compounds under investigation. This could be explained by the presence of lypophilic moieties in the bis-1,4-dihydropyrimidnes scaffold. It is revealed from the data presented in Table-1 that the compounds **5b**, **6b**, **5c**, **6f**, **5j** and **5k** exhibited higher antibacterial activity (Inhibition zone = 12-17 mm) against *Bordetella bronchiseptica* as compared to the standard drug used Amoxicillin while rest of the compounds except **6k** (Inactive) showed moderate activity (Inhibition zone = 07-11 mm). Thus compounds with 4-OCH_3, 3-NO_2, 4-OH, 2,4-Cl and 3,4-OCH_3 substitution to the phenyl nucleus showed much better inhibition of growth comparable with Amoxicillin. Whereas the compounds having 4-OH, 3-OCH_3 (Vanillin) and 2,3-OCH_2O substitution on the 4-phenyl nucleus were found to be less active as compared to the other substituted compounds.

On the other hand same compounds were screened for their anti-oxidant activity also and found to be mild anti-oxidant agents (**Table-2**).

Table-1: Zone of Inhibition (mm) of tested compounds at conc. 500 µg/ml

Sr. No.	Compounds	Zone of Inhibition (mm)
		Bordetella bronchiseptica
1.	5b	13
2.	6b	15
3.	5c	17
4.	6c	10
5.	5f	11
6.	6f	13
7.	5h	9
8.	6h	7
9.	5i	8
10.	6i	10
11.	5j	12
12.	5k	14
13.	6k	----
14.	Amoxicillin	12

(----)= showing no activity

Table-2: Percentage Inhibition of tested compounds at Conc. 500 µg/ml

Sr. No.	Compounds	Percentage Inhibition (%)
1.	5b	34
2.	6b	28
3.	5c	30
4.	6c	39
5.	5f	16
6.	6f	34
7.	5h	32
8.	6h	17
9.	5i	18
10.	6i	40
11.	5j	38
12.	5k	39
13.	6k	32
14.	Ascorbic acid	85

EXPERIMENTAL

Instrumentation

Melting points were taken in open end capillaries and were uncorrected. The purity of the synthesized compounds was checked by thin layer chromatography on Silica gel G (Merck) plates and spots were located by iodine vapours. ^{1}H-NMR spectra were recorded on BRUKER ADVANCE II 400 (400 MHz) NMR spectrometer using tetramethyl silane (TMS) as internal standard. All chemical shifts were reported as δ (ppm) values. The IR spectra were recorded on Perkin Elmer spectrum RX IFT-IR System using KBr pellets. The mass spectra were obtained on a JEOL 5 × 102/DA-6000 mass spectrometer. The elemental analysis was recorded on VARIO MICRO CHNS ANALYZER. All the compounds gave satisfactory results within ±0.4% of theoretical values.

General Procedure for the synthesis of 6-methyl-4-(substitutedphenyl)-2-thioxo-1, 2, 3, 4-tetrahydropyrimidin-5-carboxylic acid ethyl ester (4a-k): The compounds 4(a-k) were synthesized as per method reported in literature[12] and were confirmed by comparing melting points and spectral data with authentic samples.

General procedure for the synthesis of diethyl 2,2′-(butane-1,4-diyl bis (sulfanediyl)) bis (4-(substitutedphenyl)-6-methyl-1,4-dihydropyrimidin-5-carboxlate 5(a-k):

The compounds **4(a-k)** (0.003 mole) were dissolved in absolute alcohol and after complete dissolution 1,4-dibromobutane (0.0015 mole) was added. The reaction mixture was refluxed till completion of the reaction. Progress of the reaction was checked by TLC and product obtained was recrystallized from methanol. The structure of the synthesized compounds was characterized on the basis of melting point, IR, NMR, Mass and elemental analysis spectra. The spectral data of the compounds are given below:

diethyl 2,2′-(butane-1,4-diyl bis(sulfanediyl)) bis(6-methyl-4-phenyl)-1,4-dihydropyrimidin-5-carboxlate 5a: Yellow solid; m.p. 158-160°C; IR (KBr): υ_{max} (cm^{-1}) 3328 (N-H), 3070 (aromatic C-H), 2979, 2872 (methylene C-H), 1669 (C=O), 1574 (C=N); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 10.1 (2H, s, N-H), 7.38 (10H, m, Ar-H), 5.28 (2H, s, H-4), 4.07 (4H, q, O-C***H***$_2$-CH_3), 3.40 (4H, m, S-C***H***$_2$-CH_2-), 2.32 (6H, s, CH_3-6), 1.22 (4H, m, S-CH_2-C***H***$_2$), 1.19 (6H, t, O-CH_2-C***H***$_3$); ^{13}C-

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NMR (100 MHz): 174.23 (C=O), 165.26 (C-6), 152.25 (C-2), 144.71 (C-1'), 128.79 (C-3',5'), 126.38 (C-2',6'), 100.78 (C-5), 59.35 (OCH_2), 54.1 (C-4), 26.1 (S-***C***H_2), 23.9 (S-CH_2-***C***H_2), 17.7 (CH3-6), 13.8 (***C***H_3-CH_2-O); MS: m/z 607 (M+1), 608 (M+2), 609 (M+3); Anal Calcd for $C_{32}H_{38}N_4O_4S_2$: C 63.36, H 6.27, N 9.24; Found: C 63.61, H 6.25, N 9.24.

diethyl 2,2'-(butane-1,4-diyl bis (sulfanediyl)) bis (4-(4-methoxyphenyl)-6-methyl-1,4-dihydropyrimidin-5-carboxlate 5b: Yellow solid; m.p. 52-52°C; IR (KBr): υ_{max} (cm^{-1}) 3329 (N-H), 3070 (aromatic C-H), 2979, 2899 (methylene C-H), 1670 (C=O), 1537 (C=N); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 10.14 (2H, s, N-H), 7.18-6.82 (8H, m, Ar-H), 5.16 (2H, d, H-4), 4.01 (4H, q, O-C***H***$_2$-CH_3), 3.7 (6H, s, OCH_3), 3.24 (2H,m, S-C***H***$_2$-CH_2-), 2.94 (2H, m, S-C***H***$_2$-CH_2-), 2.33 (6H, s, CH_3-6), 1.68 (4H, m, S-CH_2-C***H***$_2$), 1.13 (6H, t, O-CH_2-C***H***$_3$); ^{13}C-NMR (100 MHz): δ 174.02 (C=O), 165.07 (C-6), 158.60 (C-2), 144.39 (C-1'), 135.0 (C-4'), 127.58 (C-2',6'), 113 (C-3',5'), 101 (C-5), 59.39 (OCH_2), 54.8 (OCH_3), 26.8 (S-***C***H_2), 24.1 (S-CH_2-***C***H_2),17.0 (CH_3-6), 13.0 (***C***H_3-CH_2-O), MS: m/z (M^+) 666; Anal Calcd for $C_{34}H_{482}N_4O_6S_2$: C 61.26, H 6.30, N 8.40; Found: C 61.50, H 6.32, N 8.43.

diethyl 2,2'-(butane-1,4-diyl bis (sulfanediyl)) bis (4-(3-nitrophenyl)-6-methyl-1,4-dihydropyrimidin-5-carboxlate 5c: Yellow solid; m.p. 177-180°C; IR (KBr): υ_{max} (cm^{-1}) 3332 (N-H), 3109 (aromatic C-H), 2969, 2899 (methylene C-H), 1709 (C=O), 1527 (C=N); ^{1}H-NMR (400 MHz, DMSO): δ 10.41 (2H, s, N-H), 8.12-7.57 (8H, Ar-H), 5.36 (2H, d, H-4), 4.1 (4H, q, C***H***$_2$-O-), 2.66-2.44 (4H, m, S-C***H***$_2$), 2.3 (6H, CH_3-6), 1.78-1.67 (4H, m, S-CH_2-C***H***$_2$-), 1.1 (6H, t, OCH_2-CH_3); ^{13}C-NMR (100 MHz): δ174.58 (C=O), 164.95 (C-2), 151.90 (C-2), 147.7 (C-3'), 145.4 (C-1'), 132.77 (C-6'), 129.7 (C-5'), 122.3 (C-2'), 121.2 (C-4'), 99.8 (C-5), 59.57 (O***C***H_2), 53.5 (C-4), 24.1 (S-***C***H_2), 22.1 (S-CH_2-***C***H_2), 17.8 (CH_3-6), 13.9 (***C***H_3-CH_2-O); MS: m/z (M^+) 696; Anal Calcd for $C_{32}H_{36}N_6O_8S_2$: C 55.17, H 5.17, N 12.0; Found: C 54.95, H 5.15, N 12.03.

diethyl 2,2'-(butane-1,4-diyl bis (sulfanediyl)) bis (4-(4-nitrophenyl)-6-methyl-1,4-dihydropyrimidin-5-carboxlate 5d: Yellow solid; m.p. 52-55°C ; IR (KBr): υ_{max} (cm^{-1}) 3328 (N-H), 3103 (aromatic C-H), 2922, 2889 (methylene C-H), 1640 (C=O),1537 (C=N); ^{1}H-NMR (400 MHz, DMSO): δ 9.7 (2H, s, N-H), 8.12-7.45 (8H,m, Ar-H's), 5.40 (2H, d, H-4), 4.13 (4H, q, CH_2-O-), 2.60 (4H, m, S-C***H***$_2$), 2.30 (6H, CH_3-6), 1.87-1.75 (4H, m, S-CH_2-C***H***$_2$-), 1.15 (6H, t, OCH_2-CH_3); ^{13}C-NMR (100 MHz): δ174.63 (C=O), 163.95 (C-6), 153.90 (C-2), 149.6 (C-1'), 145.3 (C-4'), 130.77 (C-2',6'), 122.9 (C-3',5'), 100.1 (C-5), 61.17 (O***C***H_2), 53.4 (C-4), 24.5 (S-***C***H_2), 23.1 (S-CH_2-***C***H_2), 17.5 (CH_3-6), 14.1 (***C***H_3-CH_2-O); MS: m/z (M^+) 696; Anal Calcd for $C_{32}H_{36}N_6O_8S_2$: C 55.17, H 5.17, N 12.0; Found: C 55.17, H 5.17, N 12.0.

diethyl 2,2'-(butane-1,4-diyl bis (sulfanediyl)) bis (4-(2-nitrophenyl)-6-methyl-1,4-dihydropyrimidin-5-carboxlate 5e: Yellow solid; m.p. ; IR (KBr): υ_{max} (cm^{-1}) 3276 (N-H), 3103 (aromatic C-H), 2975, 2889 (methylene C-H), 1657 (C=O),1537 (C=N); ^{1}H-NMR (400 MHz,CDCl3): δ 9.63 (2H, s, N-H), 8.1-7.50 (8H, m, Ar-H's), 5.53 (2H, s, H-4), 4.20 (4H, q, O-C***H***$_2$-CH_3), 3.60 (2H, m, S-C***H***$_2$), 3.24 (2H, m, S-C***H***$_2$-), 2.28 (6H, s, CH_3-6), 2.1 (m, S-CH_2-C***H***$_2$), 1.13 (6H, t, O-CH_2-C***H***3); ^{13}C-NMR (100 MHz, DMSO): 174.6 (C=O), 161.30 (C-6), 159.6 (C-2), 149.1 (C-2'), 133.55 (C-1'), 134.6 (C-5'), 129.61 (C-6'), 125.21 (C-4'), 120.3 (C-3'), 101.8 (C-5), 60.72 (O***C***H2), 58.5 (C-4), 26.70 (S-***C***H2-), 24.8 (S-CH_2-***C***H_2-), 18.0 (***C***H_3-6), 13.90 (O-CH_2-***C***H_3), Mass (m/z): MS: m/z (M^+) 696; Anal Calcd for $C_{32}H_{36}N_6O_8S_2$: C 55.17, H 5.17, N 12.0; Found: C 55.37, H 5.12, N 12.03.

diethyl 2,2'-(butane-1,4-diyl bis (sulfanediyl)) bis (4-(4-hydroxyphenyl)-6-methyl-1,4-dihydropyrimidin-5-carboxlate 5f: Yellow solid; m.p. 204 - 206°C; IR (KBr): υ_{max} (cm^{-1}) 3497 (OH), 3236 (N-H), 3124 (aromatic C-H), 2979, 2935 (methylene C-H), 1685 (C=O), 1597 (C=N); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 9.8 (2H, s, N-H), 7.7-6.8 (8H, m, Ar-H), 5.01 (2H, s, OH), 5.41 (2H, s, H-4), 4.24 (4H, q, C***H***$_2$-O-), 3.13 (2H, m, S-C***H***$_2$), 3.0 (2H, m, S-C***H***$_2$), 2.3 (6H, s, CH_3-6), 1.9 (4H, m, S-CH_2-C***H***$_2$-), 1.3 (6H, t, OCH_2-C***H***$_3$); ^{13}C-NMR (100 MHz): δ 167.27 (C=O), 163.09 (C-6), 156.56 (C-2), 152.3 (C-4'), 136.3 (C-1'), 130.50 (C-2', 6'), 116.4 (C-3', 5'), 99.5 (C-5), 59.30 (OCH_2), 53.4 (C-4), 29.8 (S-***C***H_2), 24.90 (S-CH_2-***C***H_2), 17.15 (CH_3-6), 13.84 (***C***H_3-CH_2-O); MS m/z : 638 (M^+), 639 (M+1), 640 (M+2); Anal Calcd for $C_{32}H_{38}N_4O_6S_2$: C 60.18, H 5.95, N 8.77; Found: C 60.43, H 5.97, N 8.74.

diethyl 2,2'-(butane-1,4-diyl bis (sulfanediyl)) bis (4-(2-hydroxyphenyl)-6-methyl-1,4-dihydropyrimidin-5-carboxlate 5g: Yellow solid; m.p. 77-81°C; IR (KBr): υ_{max} (cm^{-1}) 3497 (OH), 3236 (N-H), 3124 (aromatic C-H), 2979, 2935 (methylene C-H), 1685 (C=O), 1597 (C=N), ^{1}H-NMR (400 MHz, $CDCl_3$): δ 10.83 (2H, s, N-H), 7.5-6.7 (8H, m, Ar-H), 5.38 (2H, s, H-4), 4,7 (2H, s, OH), 4.24 (4H, q, C***H***$_2$-O-), 3.20 (2H, M, S-C***H***$_2$), 2.9 (2H, m, S-C***H***$_2$), 2.1 (6H, s, CH_3-6), 1.9 (4H, m, S-CH_2-C***H***$_2$-), 1.3 (6H, t, OCH_2-C***H***$_3$); ^{13}C-NMR (100 MHz): δ 167.27 (C=O), 165.09 (C-6), 156.16 (C-2), 150.1 (C-2'), 130.40 (C-6'), 127.9 (C-4'), 125.0 (C-1'), 122.3 (C-5'), 116.4 (C-3'), 81.70 (C-5), 62.30 (OCH_2), 50.4 (C-4), 31.00 (S-***C***H_2), 22.90 (S-CH_2-***C***H_2), 17.8 (CH_3-6), 14.1 (***C***H_3-CH_2-O); MS m/z : 638 (M^+), 639 (M+1), 640 (M+2); Anal Calcd for $C_{32}H_{38}N_4O_6S_2$: C 60.18, H 5.95, N 8.77; Found: C 60.40, H 5.93, N 8.75.

diethyl 2,2'-(butane-1,4-diyl bis (sulfanediyl)) bis (4-(4-hydroxy-3-methoxyphenyl)-6-methyl-1,4-dihydropyrimidin-5-carboxlate 5h: Yellow solid; m.p. 78-80°C; IR (KBr): υ_{max} (cm^{-1}) 3380 (OH), 3208 (N-H), 3071 (aromatic C-H), 2979, 2935 (methylene C-H), 1670 (C=O), 1597 (C=N); ^{1}H-NMR (400 MHz, DMSO): δ 10.0 (2H, s, N-H), 6.62-6.34 (6H, m, Ar-H), 5.17 (2H, s, OH), 4.84 (2H, d, H-4), 3.84 (4H, q, C***H***$_2$-O-), 3.70 (6H, s, OCH_3), 3.6 (2H, m, S-C***H***$_2$), 3.23 (2H, m, S-C***H***$_2$), 2.0 (4H, m, S-CH_2-C***H***$_2$), 2.27 (6H, s, CH_3-6), 1.27 (6H, t, O-CH_2-C***H***$_3$); ^{13}C-NMR (100 MHz): δ 173.97 (C=O), 165.2 (C-6), 150.9 (C-2), 147.3 (C-3'), 146.10 (C-4'), 134.52 (C-1'), 118.85 (C-6'), 115.36 (C-5'), 110.9 (C-2'), 100.93 (C-5), 59.6 (OCH_2), 55.5 (OCH_3), 53.6 (C-4), 27.81 (S-***C***H_2), 24.0 (S-CH_2-***C***H_2-), 17.71 (CH_3-6), 14.05 (***C***H_3-CH_2-O); MS (m/z): 699 (M+1), 700 (M+2); Anal Calcd for $C_{34}H_{42}N_4O_8S_2$: C 58.45, H 6.01, N 8.02; Found: C 58.67, H 5.99, N 8.05.

diethyl 2,2'-(butane-1,4-diyl bis (sulfanediyl)) bis (4-(2,3-methylenedioxyphenyl)-6-methyl-1,4-dihydropyrimidin-5-carboxlate 5i: Yellow solid; m.p. 44-47°C; IR (KBr): υ_{max} (cm^{-1}) 3200 (N-H), 3071 (aromatic C-H), 2979, 2935 (methylene C-H), 1680 (C=O), 1585 (C=N); ^{1}H-NMR (400 MHz, DMSO): δ 10.32 (2H, s, N-H), 6.7-6.6 (6H, Ar-H), 5.5 (4H, s, OCH_2O), 5.0 (2H, d, H-4), 4.1 (4H, q, C***H***$_2$-O-), 3.4-3.1 (4H, m, S-C***H***$_2$), 2.4 (6H, s, CH_3-6), 2.2 (4H, m, S-CH_2-C***H***$_2$), 1.1 (6H, t, O-CH_2-C***H***$_3$); ^{13}C-NMR (100 MHz): δ 173.98 (C=O), 165.2 (C-6), 163 (C-2), 152.0 (C-2'), 148.29 (C-3'), 137.4 (C-1'), 120.6 (C-6'), 119.6 (C-5'), 108 (C-4'), 101.0 (OCH_2O), 100.9 (C-5), 60.5 (OCH_2), 53.6 (C-4), 30.5 (S-***C***H_2), 27.05 (S-CH_2-***C***H_2), 17.1 (CH_3-6), 14.08 (***C***H_3-CH_2-O); MS m/z(M^+): 694; Anal Calcd for $C_{34}H_{38}N_4O_8S_2$: C 58.78, H 5.47, N 8.06; Found: C 58.34, H 5.49, N 8.10.

diethyl 2,2'-(butane-1,4-diyl bis (sulfanediyl)) bis (4-(2,4-dichlorophenyl)-6-methyl-1,4-dihydropyrimidin-

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5-carboxlate 5j: Yellow solid; m.p. 226-228°C; IR (KBr): υ_{max} (cm^{-1}) 3238 (N-H), 3059 (aromatic C-H), 2959, 2835 (methylene C-H), 1697 (C=O), 1528 (C=N); ^{1}H-NMR (400 MHz, DMSO): δ 8.9 (2H, s, N-H), 7.3-7.8 (6H, Ar-H), 5.4 (2H, d, H-4), 4.0 (4H, q, C***H***$_2$-O-), 3.4-3.1 (4H, m, S-C***H***$_2$), 2.34 (6H, s, CH_3-6), 1.91 (4H, m, S-CH_2-C***H***$_2$), 1.2 (6H, t, O-CH_2-C***H***$_3$); ^{13}C-NMR (100 MHz): δ 170.3 (C=O), 163.1 (C-6), 153.4 (C-2), 138.2 (C-1′), 136.7 (C-2′), 134.1 (C-4′), 131.9 (C-6′), 131.5 (C-3′), 128.4 (C-5′), 100.9 (C-5), 60.9 (OCH_2), 53.4 (C-4), 26.8 (S-***C***H_2), 24.5 (S-CH_2-***C***H_2), 17.6 (CH_3-6), 13.08 (***C***H_3-CH_2-O); MS m/z(M$^+$): 744; Anal Calcd for $C_{32}H_{34}Cl_4N_4O_4S_2$: C 51.61, H 4.56, N 7.52; Found: C 51.85, H 4.59, N 7.48.

diethyl 2,2′-(butane-1,4-diyl bis (sulfanediyl)) bis (4-(3,4dimethoxyphenyl)-6-methyl-1,4-dihydropyrimidin-5-carboxlate 5k: Yyellow solid; m.p. 100-106°C; IR (KBr): υ_{max} (cm^{-1}) 3338 (N-H), 3070 (aromatic C-H), 2959, 2835 (methylene C-H), 1686 (C=O), 1522 (C=N); ^{1}H-NMR (400 MHz, DMSO): δ 8.2 (2H, s, N-H), 6.89-6.76 (6H, Ar-H), 5.3 (4H, d, H-4), 4.1 (4H, q, C***H***$_2$-O-), 3.9 (6H, s, OCH_3), 3.6 (2H, m, S-CH_2), 2.6 (2H, m, S-C***H***$_2$), 2.3 (6H, s, CH_3-6), 2.1 (4H, m, S-CH_2-C***H***$_2$), 1.26 (6H, t, O-CH_2-C***H***$_3$); ^{13}C-NMR (100 MHz): δ 173.2 (C=O), 165.4 (C-6), 152.0 (C-2), 149.07 (C-3′), 149.0 (C-4′), 135.08 (C-1′), 119.0 (C-6′), 111.0 (C-2′), 109.9 (C-5′), 101.9 (C-5), 60.45 (OCH_2), 55.9 (OCH_3), 55.8 (C-4), 27.9 (S-***C***H_2), 25.05 (S-CH_2-***C***H_2), 18.6 (CH_3-6), 14.1 (***C***H_3-CH_2-O); MS m/z(M$^+$): 726; Anal Calcd for $C_{36}H_{46}N_4O_8S_2$: C 59.50, H 6.33, N 7.71; Found: C 59.73, H 6.29, N 7.74

General procedure for the synthesis of diethyl 2,2′-(pentane-1,5-diyl bis (sulfanediyl)) bis (4-(substitutedphenyl)-6-methyl-1,4-dihydropyrimidin-5-carboxlate 6(a-k): The compounds **4(a-k)** (0.003 mole) were dissolved in absolute alcohol and after complete dissolution 1,5-dibromopentane (0.0015 mole) was added. The reaction mixture was refluxed till completion of the reaction. Progress of the reaction was checked by TLC and product obtained was recrystallized from methanol. The structure of the synthesized compounds was characterized on the basis of melting point, IR, NMR, Mass and elemental analysis spectra. The spectral data of the compounds are given below:

Diethyl2,2′-(pentane-1,5-diylbis(sulfanediyl))bis(6-methyl-4-phenyl)-1,4-dihydro pyrimidin-5-carboxlate 6a: Yellow solid; m.p. 178-180°C; IR (KBr): υ_{max} (cm^{-1}) 3129 (N-H), 3170 (aromatic C-H), 2969, 2879 (methylene C-H), 1685 (C=O), 1544 (C=N); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 10.04 (2H, s, N-H), 7.38-7.23 (10H, m, Ar-H), 5.2 (2H, s, H-4), 4.1 (4H, q, O-C***H***$_2$-CH_3), 3.3 (2H, m, S-C***H***$_2$-CH_2-), 2.6 (2H, m, S-C***H***$_2$-CH_2), 2.3 (6H, s, CH_3-6), 2.1 (4H, m, S-CH_2-C***H***$_2$-), 1.5 (2H, m, S-CH_2-CH_2-C***H***$_2$-), 1.2 (6H, t, O-CH_2-C***H***$_3$); ^{13}C-NMR (100 MHz): 165.4 (C=O), 163.9 (C-6), 152.8 (C-2), 144.0 (C-1′), 128.37 (C-3′,5′), 127.59 (C-4′), 126.4 (C-2′,6′), 101.24 (C-5), 59.35 (OCH_2), 54.2 (C-4), 31.0 (S-***C***H_2), 28.4 (S-CH_2-***C***H_2), 26.5 (S-CH_2-CH_2-***C***H_2), 17.8 (CH_3-6), 13.9 (***C***H_3-CH_2-O); MS: m/z (M$^+$) 620; Anal Calcd for $C_{33}H_{40}N_4O_4S_2$: C 63.87, H 6.45, N 9.03; Found: C 64.15, H 6.47, N 9.07.

diethyl 2,2′-(pentane-1,5-diyl bis (sulfanediyl)) bis (4-(4-methoxyphenyl)-6-methyl-1,4-dihydropyrimidin-5-carboxlate 6b: Yellow solid; m.p. 98-100°C; IR (KBr): υ_{max} (cm^{-1}) 3329 (N-H), 3170 (aromatic C-H), 2979, 2899 (methylene C-H), 1670 (C=O), 1537 (C=N); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.93 (2H, s, N-H), 7.37-6.8 (8H, m, Ar-H), 5.3 (2H, d, H-4), 4.1 (4H, q, O-C***H***$_2$-CH_3), 3.7 (6H, s, OCH_3), 3.4 (2H,m, S-C***H***$_2$-CH_2-CH_2), 2.6 (2H, m, S-C***H***$_2$-CH_2-CH_2), 2.1 (4H, m, S-CH_2-C***H***$_2$-CH_2), 2.3 (6H, s, CH_3-6), 1.42 (2H, m, S-CH_2-CH_2-C***H***$_2$-), 1.1 (6H, t, O-CH_2-C***H***$_3$); ^{13}C-NMR (100 MHz): δ 174.3 (C=O), 161.80 (C-6), 159.2 (C-2), 153.1(C-4′), 134.0 (C-1′), 131.9 (C-2′,6′), 114.12 (C-3′,5′), 103.08 (C-5), 61.0(OCH_2), 55.4 (OCH_3), 54.1 (C-4), 32.5 (S-***C***H_2), 26.8 (S-CH_2-***C***H_2), 27.15 (S-CH_2-CH_2-***C***H_2-), 18.2 (CH_3-6), 14.1 (***C***H_3-CH_2-O), MS: m/z (M$^+$) 680; Anal Calcd for $C_{35}H_{44}N_4O_6S_2$: C 61.76, H 6.47, N 8.23; Found: C 61.54, H 6.43, N 8.19.

diethyl 2,2′-(pentane-1,5-diyl bis (sulfanediyl)) bis (4-(3-nitrophenyl)-6-methyl-1,4-dihydropyrimidin-5-carboxlate 6c: Brown solid; m.p. 75-80°C; IR (KBr): υ_{max} (cm^{-1}) 3329 (N-H), 3109 (aromatic C-H), 2969, 2889 (methylene C-H), 1699 (C=O), 1521 (C=N); ^{1}H-NMR (400 MHz, DMSO): δ 9.4 (2H, s, N-H), 7.6-6.4 (8H,m, Ar-H), 5.3 (2H, d, H-4), 4.0 (4H, q, C***H***$_2$-O-), 2.9 (2H, m, S-C***H***$_2$$CH_2$-$CH_2$), 2.6 (2H, m, S-C***H***$_2$-CH2-CH_2), 2.2 (4H, m, S-CH_2-C***H***$_2$-CH_2), 2.3 (6H, CH_3-6), 1.37 (2H, m, S-CH_2-CH2-C***H***$_2$-), 1.1 (6H, t, OCH_2-C***H***$_3$); ^{13}C-NMR (100 MHz): δ174.1 (C=O), 163.9 (C-2), 152.90 (C-2), 147.7 (C-3′), 145.8 (C-1′), 133.77 (C-6′), 129.3 (C-5′), 123.1 (C-2′), 121.2 (C-4′), 100.5 (C-5), 59.9 (O***C***H_2), 54.6 (C-4), 29.8 (S-***C***H_2), 26.4 (S-CH_2-***C***H_2), 23.5 (S-CH_2-CH_2-***C***H_2), 17.6 (CH_3-6), 13.7 (***C***H_3-CH_2-O); MS: m/z (M$^+$) 710; Anal Calcd for $C_{33}H_{38}N_6O_8S_2$: C 55.77, H 5.35, N 11.83; Found: C 55.51, H 5.38, N 11.80.

diethyl 2,2′-(pentane-1,5-diyl bis (sulfanediyl)) bis (4-(4-nitrophenyl)-6-methyl-1,4-dihydropyrimidin-5-carboxlate 6d: Yellow solid; m.p. 166 - 170°C ; IR (KBr): υ_{max} (cm^{-1}) 3330 (N-H), 3109 (aromatic C-H), 2917, 2886 (methylene C-H), 1647 (C=O),1537 (C=N); ^{1}H-NMR (400 MHz, DMSO): δ 9.3 (2H, s, N-H), 8.1-7.2 (8H,m, Ar-H), 5.1 (2H, d, H-4), 4.1 (4H, q, CH_2-O-), 3.1 (2H, m, S-C***H***$_2$$CH_2$-$CH_2$), 2.6 (2H, m, S-C***H***$_2$$CH_2$-$CH_2$), 2.30 (6H, s, CH_3-6), 2.1 (4H, m, S-CH_2-C***H***$_2$-CH_2), 1.4 (2H, m, S-$CH_2$$CH_2$-C***H***$_2$), 1.1 (6H, t, O-$CH_2$-$CH_3$); ^{13}C-NMR (100 MHz): δ169.0 (C=O), 163.4 (C-6), 152.90 (C-2), 148.2 (C-1′), 143.7 (C-4′), 130.7 (C-2′,6′), 124.5 (C-3′,5′), 101.8 (C-5), 60.5 (O***C***H_2), 54.1 (C-4), 31.0 (S-***C***H_2), 27.2 (S-CH_2-***C***H_2), 26.1 (S-CH_2-CH_2-***C***H_2), 18.1 (CH_3-6), 13.9 (***C***H_3-CH_2-O); MS: m/z (M$^+$) 710; Anal Calcd for $C_{33}H_{38}N_6O_8S_2$: C 55.77, H 5.35, N 11.83; Found: C 55.90, H 5.37, N 11.84.

diethyl 2,2′-(pentane-1,5-diyl bis (sulfanediyl)) bis (4-(2-nitrophenyl)-6-methyl-1,4-dihydropyrimidin-5-carboxlate 6e: Yellow solid; m.p. ; IR (KBr): υ_{max} (cm^{-1}) 3273 (N-H), 3071 (aromatic C-H), 2975, 2889 (methylene C-H), 1653 (C=O), 1537 (C=N); ^{1}H-NMR (400 MHz,CDCl3): δ 8.9 (2H, s, N-H), 7.9-7.50 (8H, m, Ar-H's), 5.3 (2H, s, H-4), 4.2 (4H, q, O-C***H***2-CH_3), 3.4 (2H, m, S-C***H***$_2$), 3.2 (2H, m, S-C***H***$_2$-), 2.3 (6H, s, CH_3-6), 2.1 (4H, m, S-CH_2-C***H***$_2$), 1.4 (2H. m, S-CH_2-CH_2-***C***H_2-), 1.13 (6H, t, O-CH2-C***H***$_3$); ^{13}C-NMR (100 MHz, DMSO): 172.1 (C=O), 162.7 (C-6), 159.6 (C-2), 148.3 (C-2′), 133.2 (C-1′), 134.8 (C-5′), 129.4 (C-6′), 125.9 (C-4′), 119.8 (C-3′), 101.8 (C-5), 60.8 (O***C***H_2), 58.5 (C-4), 29.4 (S-***C***H_2), 26.2 (S-CH_2-***C***H_2-), 24.7 (S-CH_2-CH_2-***C***H_2), 18.0 (***C***H_3-6), 13.90 (O-CH_2-***C***H_3), Mass (m/z): MS: m/z (M$^+$) 710; Anal Calcd for $C_{33}H_{38}N_6O_8S_2$: C 55.77, H 5.35, N 11.83; Found: C 55.90, H 5.37, N 11.84.

diethyl 2,2′-(pentane-1,5-diyl bis (sulfanediyl)) bis (4-(4-hydroxyphenyl)-6-methyl-1,4-dihydropyrimidin-5-carboxlate 6f: Yellow solid; m.p. 110-112°C; IR (KBr): υ_{max} (cm^{-1}) 3497 (OH), 3234 (N-H), 3124 (aromatic C-H), 2979, 2935 (methylene C-H), 1685 (C=O), 1597 (C=N); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 9.8 (2H, s, N-H), 7.5-6.8 (8H, m, Ar-H), 5.0 (2H, s, OH), 5.4 (2H, s, H-4), 4.1 (4H, q, C***H***$_2$-O-), 3.2 (2H, m, S-C***H***$_2$), 2.9 (2H, m, S-C***H***$_2$), 2.2 (6H, s, CH_3-6), 1.9 (4H, m, S-CH_2-C***H***$_2$-), 1.39 (2H, m, S-CH_2-CH_2-C***H***$_2$), 1.2 (6H, t, OCH_2-C***H***$_3$); ^{13}C-NMR (100 MHz): δ 168.4

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(C=O), 162.09 (C-6), 158.56 (C-2), 152.3 (C-4'), 136.3 (C-1'), 131.50 (C-2', 6'), 116.4 (C-3', 5'), 100.6 (C-5), 60.30 (OCH_2), 53.4 (C-4), 29.8 (S-***C***H_2), 27.90 (S-CH_2-***C***H_2), 25.9 (S-CH_2-CH_2-***C***H_2), 17.15 (CH_3-6), 13.84 (***C***H_3-CH_2-O); MS m/z (M^+): 652; Anal Calcd for $C_{33}H_{40}N_4O_6S_2$: C 60.73, H 6.13, N 8.58; Found: C 60.50, H 6.09, N 8.55.

diethyl 2,2'-(pentane-1,5-diyl bis (sulfanediyl)) bis (4-(2-hydroxyphenyl)-6-methyl-1,4-dihydropyrimidin-5-carboxlate 6g: Yellow solid; m.p. 100-104°C; IR (KBr): υ_{max} (cm^{-1}) 3497 (OH), 3236 (N-H), 3124 (aromatic C-H), 2979, 2935 (methylene C-H), 1685 (C=O), 1597 (C=N), ^{1}H-NMR (400 MHz, $CDCl_3$): δ 10.8 (2H, s, N-H), 7.4-6.7 (8H, m, Ar-H), 5.2 (2H, s, H-4), 4.9 (2H, s, OH), 4.2 (4H, q, C***H***$_2$-O-), 3.3 (2H, m, S-C***H***$_2$), 3.1 (2H, m, S-C***H***$_2$), 2.2 (6H, s, CH_3-6), 2.1 (4H, m, S-CH_2-C***H***$_2$-), 1.4 (2H, m, S-CH_2-CH_2-C***H***$_2$), 1.1 (6H, t, OCH_2-C***H***$_3$); ^{13}C-NMR (100 MHz): δ 167.1 (C=O), 163.05 (C-6), 152.16 (C-2), 151.1 (C-2'), 130.20 (C-6'), 128.9 (C-4'), 124.9 (C-1'), 122.8 (C-5'), 115.4 (C-3'), 99.0 (C-5), 62.30 (OCH_2), 50.4 (C-4), 30.3 (S-***C***H_2), 27.9 (S-CH_2-***C***H_2), 25.49 (S-CH_2-CH_2-***C***H_2), 18.0 (CH_3-6), 14.1 (***C***H_3-CH_2-O); MS m/z (M^+): 652; Anal Calcd for $C_{33}H_{40}N_4O_6S_2$: C 60.73, H 6.13, N 8.58; Found: C 60.93, H 6.15, N 8.60.

diethyl 2,2'-(pentane-1,5-diyl bis (sulfanediyl)) bis (4-(4-hydroxy-3-methoxyphenyl)-6-methyl-1,4-dihydropyrimidin-5-carboxlate 6h: Orange solid; m.p. 82-83°C; IR (KBr): υ_{max} (cm^{-1}) 3380 (OH), 3208 (N-H), 3071 (aromatic C-H), 2979, 2935 (methylene C-H), 1670 (C=O), 1597 (C=N); ^{1}H-NMR (400 MHz, DMSO): δ 9.02 (2H, s, N-H), 7.05-6.60 (6H, m, Ar-H), 5.58 (2H, s, OH), 5.07 (2H, d, H-4), 4.1 (4H, q, C***H***$_2$-O-), 3.8 (6H, s, OCH_3), 3.4 (2H, m, S-C***H***$_2$), 3.2 (2H, m, S-C***H***$_2$), 2.23 (6H, s, CH_3-6), 1.4-1.0 (12H, m, S-CH_2-C***H***$_2$, S-CH_2-CH_2-C***H***$_2$ & O-CH_2-C***H***$_3$); ^{13}C-NMR (100 MHz): δ 163.80 (C=O), 160.84 (C-6), 152.9 (C-2), 147.5 (C-4'), 147.1 (C-3'), 135.96 (C-1'), 130.53 (C-6'), 118.83 (C-5'), 115.43 (C-2'), 105.9 (C-5), 60.39 (OCH_2), 55.65 (OCH_3), 53.7 (C-4), 32.1 (S-***C***H_2), 28.51 (S-CH_2-***C***H_2-), 24.52 (S-CH_2-CH_2-***C***H_2), 16.83 (CH_3-6), 13.85 (***C***H_3-CH_2-O); MS (m/z): (M^+): 712; Anal Calcd for $C_{35}H_{44}N_4O_8S_2$: C 58.98, H 6.17, N 7.86; Found: C 59.21, H 6.15, N 7.89.

diethyl 2,2'-(pentane-1,5-diyl bis (sulfanediyl)) bis (4-(2,3-methylenedioxyphenyl)-6-methyl-1,4-dihydropyrimidin-5-carboxlate 6i: Yellow solid; m.p. 158-160°C; IR (KBr): υ_{max} (cm^{-1}) 3208 (N-H), 3071 (aromatic C-H), 2979, 2935 (methylene C-H), 1685 (C=O), 1570 (C=N); ^{1}H-NMR (400 MHz, DMSO): δ 9.67 (2H, s, N-H), 6.7-6.6 (6H, Ar-H), 5.8 (4H, s, OCH_2O), 5.1 (2H, d, H-4), 4.1 (4H, q, C***H***$_2$-O-), 3.2 (2H, m, S-C***H***$_2$), 3.1 (2H, m, S-C***H***$_2$), 2.4 (6H, s, CH_3-6), 2.2 (4H, m, S-CH_2-C***H***$_2$), 1.4 (2H, m, S-CH_2-CH_2-CH_2), 1.1 (6H, t, O-CH_2-C***H***$_3$); ^{13}C-NMR (100 MHz): δ 173.4 (C=O), 165.1 (C-6), 163.4 (C-2), 151.9 (C-2'), 148.7 (C-3'), 137.4 (C-1'), 121.5 (C-6'), 119.8 (C-5'), 110 (C-4'), 101.8 (OCH_2O), 100.9 (C-5), 61.3 (OCH_2), 53.9 (C-4), 31.1 (S-***C***H_2), 27.05 (S-CH_2-***C***H_2), 25.7 (S-CH_2-CH_2-***C***H_2), 17.4 (CH_3-6), 13.9 (***C***H_3-CH_2-O); MS m/z (M^+): 708; Anal Calcd for $C_{35}H_{40}N_4O_8S_2$: C 59.32, H 5.64, N 7.90; Found: C 59.55, H 5.67, N 7.93.

diethyl 2,2'-(pentane-1,5-diyl bis (sulfanediyl)) bis (4-(2,4-dichlorophenyl)-6-methyl-1,4-dihydropyrimidin-5-carboxlate 6j: Yellow solid; m.p. °C; IR (KBr): υ_{max} (cm^{-1}) 3238 (N-H), 3059 (aromatic C-H), 2959, 2835 (methylene C-H), 1697 (C=O), 1528 (C=N); ^{1}H-NMR (400 MHz, DMSO): δ 8.9 (2H, s, N-H), 7.2-7.5 (6H, m, Ar-H), 5.3 (2H, d, H-4), 3.9 (4H, q, C***H***$_2$-O-), 3.4-3.1 (4H, m, S-C***H***$_2$), 2.34 (6H, s, CH_3-6), 2.1 (4H, m, S-CH_2-C***H***$_2$), 1.5 (2H, m, S-CH_2-CH_2-C***H***$_2$), 1.3 (6H, t, O-CH_2-C***H***$_3$); ^{13}C-NMR (100 MHz): δ 170.3 (C=O), 163.1 (C-6), 153.4 (C-2), 138.2 (C-1'), 136.7 (C-2'), 134.1 (C-4'), 131.9 (C-6'), 131.5 (C-3'), 128.4 (C-5'), 100.9 (C-5), 60.9 (OCH_2), 53.4 (C-4), 26.8 (S-***C***H_2), 24.5 (S-CH_2-***C***H_2), 23.8 (S-CH_2-CH_2-***C***H_2), 18.0 (CH_3-6), 13.8 (***C***H_3-CH_2-O); MS m/z(M^+): 758; Anal Calcd for $C_{33}H_{36}Cl_4N_4O_4S_2$: C 52.24, H 4.74, N 7.38; Found: C 52.50, H 4.76, N 7.41.

diethyl 2,2'-(pentane-1,5-diyl bis (sulfanediyl)) bis (4-(3,4dimethoxyphenyl)-6-methyl-1,4-dihydropyrimidin-5-carboxlate 6k: Yellow solid; m.p. 59-60°C; IR (KBr): υ_{max} (cm^{-1}) 3338 (N-H), 3070 (aromatic C-H), 2959, 2835 (methylene C-H), 1686 (C=O), 1522 (C=N); ^{1}H-NMR (400 MHz, DMSO): δ 9.07 (2H, s, N-H), 7.14-6.72 (6H, m, Ar-H), 5.5 (4H, d, H-4), 4.1 (4H, q, C***H***$_2$-O-), 3.8 (12H, s, OCH_3), 3.2 (4H, m, S-CH_2), 2.4 (6H, s, CH_3-6), 2.2 (4H, m, S-CH_2-C***H***$_2$), 1.4-1.0 (8H, m, S-CH_2-CH_2-C***H***$_2$ & O-CH_2-C***H***$_3$); ^{13}C-NMR (100 MHz): δ 165.3 (C=O), 163.9 (C-6), 149.10 (C-2), 148.8 (C-3'), 148.39 (C-4'), 137.37 (C-1'), 119.0 (C-6'), 111.0 (C-2'), 109.9 (C-5'), 99.35 (C-5), 60.43 (OCH_2), 55.4 (OCH_3), 53.7 (C-4), 31.0 (S-***C***H_2), 27.89 (S-CH_2-***C***H_2), 27.89 (S-CH_2-CH_2-***C***H_2), 17.73 (CH_3-6), 14.0 (***C***H_3-CH_2-O); MS m/z(M^+): 740; Anal Calcd for $C_{37}H_{48}N_4O_8S_2$: C 60.00, H 6.48, N 7.56; Found: C 59.76, H 6.51, N 7.59.

BIOLOGICAL STUDIES

Antibacterial studies:

Screening of compounds for antibacterial activity was done by Agar well diffusion method. A lawn of culture was prepared by spreading the 100 µl culture broth having 10^6 CFU/ml of test organism on plates and left standing for 10-15 min to let the culture absorbed. The wells of 8 mm size punched into the agar with the help of sterile micropipette tips and sealed with one drop of molten agar (0.8 % nutrient agar) to prevent leakage of compound from the bottom of plate. The wells were filled with 100 µl of test compounds (concentration 500 µg/ ml, prepared in 1 % DMSO). DMSO was used as negative control. Plates were incubated at 37°C for 24 hrs and diameter of inhibition zone wµere recorded in Table-1.

Antioxidant Activity

DPPH Radical Scavenging Assay

Free radical scavenging activity of different fractions against stable DPPH (1, 1- Diphenyl-2- picryl-hydrazyl) was determined spectrophotometrically by the modified method of Gyamfi et al[24]. When DPPH reacts with an antioxidant, which can donate hydrogen, it is reduced. The changes in color (from deep violet to light yellow) were measured at 517 nm on a UV-Vis spectrophotometer (Spectronic 20 D+, USA). A 50 µl of the test compounds (conc. 500 µg/ml) was mixed with 1 ml of 0.1 mM DPPH in methanol solution and 450 µl of 50 mM Tris-HCl buffer (pH 7.4). Absorbance of the DPPH radical without antioxidant *i.e.* the control was measured at 517 nm. Methanol was used as a solvent blank in the experiment. After 1 hr of incubation under dark at room temperature, the reduction of the DPPH free radicals was measured spectrophotometrically at 517 nm. Ascorbic acid was used as positive control. Percent inhibition of the DPPH radical by the samples was calculated according to the formula of Yen & Duh[25] (Table-2)

$$\% \text{ inhibition} = ((A_{C(o)} - A_{A(t)}) / A_{C(o)}) \times 100$$

Where $A_{C(o)}$ is the absorbance of the control at t = 0 min and $A_{A(t)}$ is the absorbance of the antioxidant at t = 1 h.

CONCLUSION

In this paper, we report the synthesis of bis-1,4-dihydropyrimidines derivatives and the structures of the newly

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synthesized compounds were established on the basis of different spectral and analytical techniques. The *in vitro* antibacterial activities of some novel compounds were evaluated against Gram-negative bacteria namely *Bordetella Bronchiseptica* and antioxidant activity also evaluated. Moreover, antibacterial study was more fruitful than antioxidant activity.

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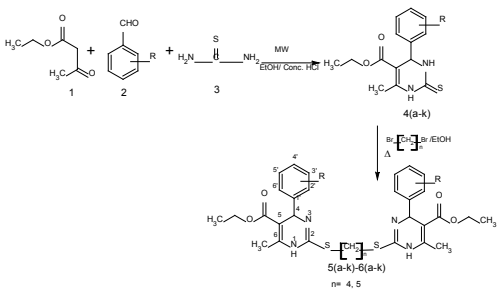
Scheme-1: Synthesis of bis-1,4-dihydropyrimidines



R: a. H; b. 4-OCH_3; c. 3-NO_2; d. 4-NO_2; e. 2-NO_2; f. 4-OH; g. 2-OH; h. 4-OH,3-OCH_3, i. 2,3 (OCH_2O); j. 2,4-Cl; k. 3,4-OCH_3

REFERENCE 1. Folkers, K.; Harwood, H. and Johnson, T. Synthesis of 2-keto-1,2,3,4-tetrahydropyrimidines 1932, 54, 3751. | 2. Siddiqui, A. U.; Siddiqui, A. H. and Ramaiah, T. S. J. Ind. Chem. Soc. 1994, 71, 107. | 3. Kumar, P. and Kumar, K. Ind. J. Chem. 1997, 36B, 782. | 4. Udupi, R. H.; Suresh,G. U.; Ramachandaran, S. R. and Bhart, A. R. J. Ind. Chem. Soc. 2000, 77, 302. | 5. Hill, M. R.; Holland, S. J.; Pearson, S. L. and Yeates, K. T. PCT Int. Appl. WO 2004048344 Chem. Abstr. 2003, 138, 187783. | 6. Carter, M. C.; Naylor, A.; Payne, J. J. and Pegg, N. A. PCT. Int. Appl. WO 2003014091 Chem. Abstr. 2003, 138, 187783. | 7. Aggarwal, S. K.; Tadiparthi, R.; Aggarwal, P. and Shivakumar, S. PCT. Int. Appl. WO 2003084936, Chem. Abstr. 2003, 139, 323529. | 8. Bahekar, S. S. and Shinde, D. B. Bioorg. Med. Chem. Lett. 2004, 14, 1733. | 9. Liu, L.; Lopez, P; Bajpai, M.; Siegmud, A. C. U.S. Pat. Appl. Publ. US-2004-923067 Chem. Abst. 2005, 142, 261550. | 10. Clare, M.; Hagen, T. J.; Houdek, S. C.; Lennon, P. J.; Wier, R. M. and Xu, X. PCT. Int. Appl. WO 2005040133 Chem. Abstr. 2005, 142, 463736. | 11. Earthen, A. J.; Giblin, G. M. P.; Mitchell, W. L.; Rawlings, D. A. and Wall, I. D. PCT. Int. Appl. WO 2005075440 Chem. Abstr. 2005, 143, 211924. | 12. Rana, K.; Kaur, B. and Kumar, B. Ind. J. Chem. 2004, 43B, 1553. | 13. Gangjee, A.; Jain, H. D.; Phan, J.; Lin, X.; Song, X; Mc GUIRE, J.J. and Kislink, R.L. J. Med. Chem. 2006, 49, 1055. | 14. Alam, O.; Imran, M. and Khan, S. A. Ind. J. Hetecycl. Chem. 2005, 14, 293. | 15. Hazarika, J. and Kataky, J. C .S. Ind. J. Chem., Sect B 2001, 40B, 255. | 16. Buurmann, E. T.; Blodgett, A. E.; Hull, K. G. and Carcanague, D. Antimicrob. Agents Chemother. 2004, 48, 313. | 17. Kidwai, M.; Saxena, S.; Rastogi, S. and Venkataramanan, R. Curr. Med. Chem.: Anti-Infect. Agents 2003, 2, 269. | 18. Biginelli, P. Gazz. Chem. Ital. 1893, 23, 360. | 19. Subudhi, B. B.; Panda, P. K. and Batta, D. Synthesis and antiulcer activity of 1,4-dihydropyrimidines Ind. J. Chem. 2009, 48B, 725. | 20. Patil, A.; Gangualy, S. and Surana, S. J. Chem. Sci. 2010, 122, 443. | 21. Samdhian, V.; Kaur, R.; Kaur, B. and Cameotra, S.S. Journal of Applicable Chemistry 2013, 2(6), 1721. | 22. Cotter, P.A. and Miller, J.F. Principles of Bacterial Pathogenesis 2001, 621. | 23. Goodnow, R.A. Microbiol Rev. 1980, 44, 722. | 24. Gyamfi, M.A., Yonamine, M. and Aniya, Y. General Pharmacology 1999, 32(6) 661. | 25. Yen, G.C. and Duh, P.D. J. Agric. Food Chem. 1994, 42, 629. |