Synthesis of Some Novel Methylene-bis-pyrimidinyl-spiro-4-thiazolidinones as Biologically Potent Agents

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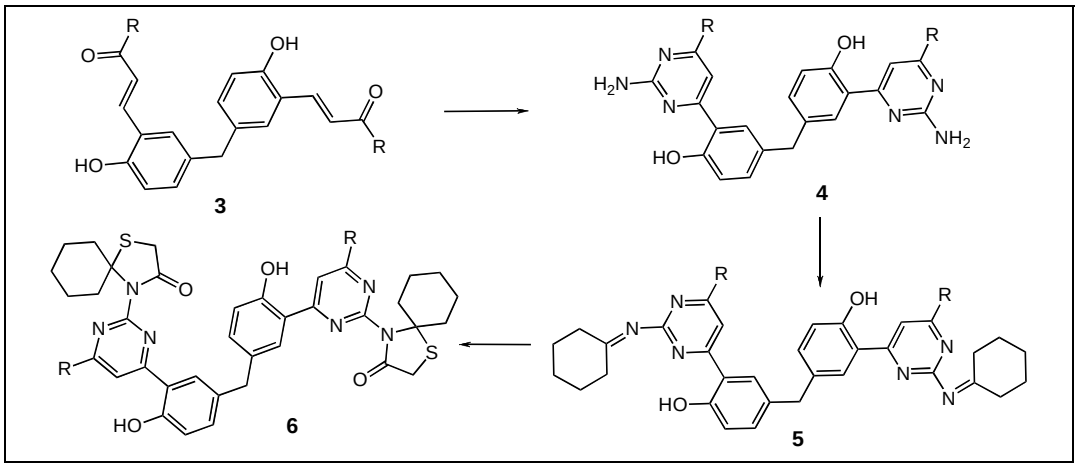

A series of novel methylene-bis-pyrimidinyl-spiro-4-thiazolidinones **6a-h** have been synthesized by cyclocondensation of thioglycolic acid with methylene-bis-(*N*-cyclohexylidene-*N*-pyrimidine) **5a-h**, which in turn have been prepared by the reaction of cyclohexanone with methylene-bis-2-aminopyrimidines **4a-h**, which are prepared by the reaction of guanidine hydrochloride with methylene-bis-chalcones **3a-h**. The compounds **3a-h** have been synthesized by the reaction of 5-(3-formyl-4-hydroxybenzyl)-2-hydroxy-benzaldehyde **2** with various acetophenones in presence of KOH. The compound **2** is prepared by the reported method. The structures of the compounds synthesized have been confirmed by their elemental analysis and spectral data. Their antibacterial and antifungal activities have also been evaluated.

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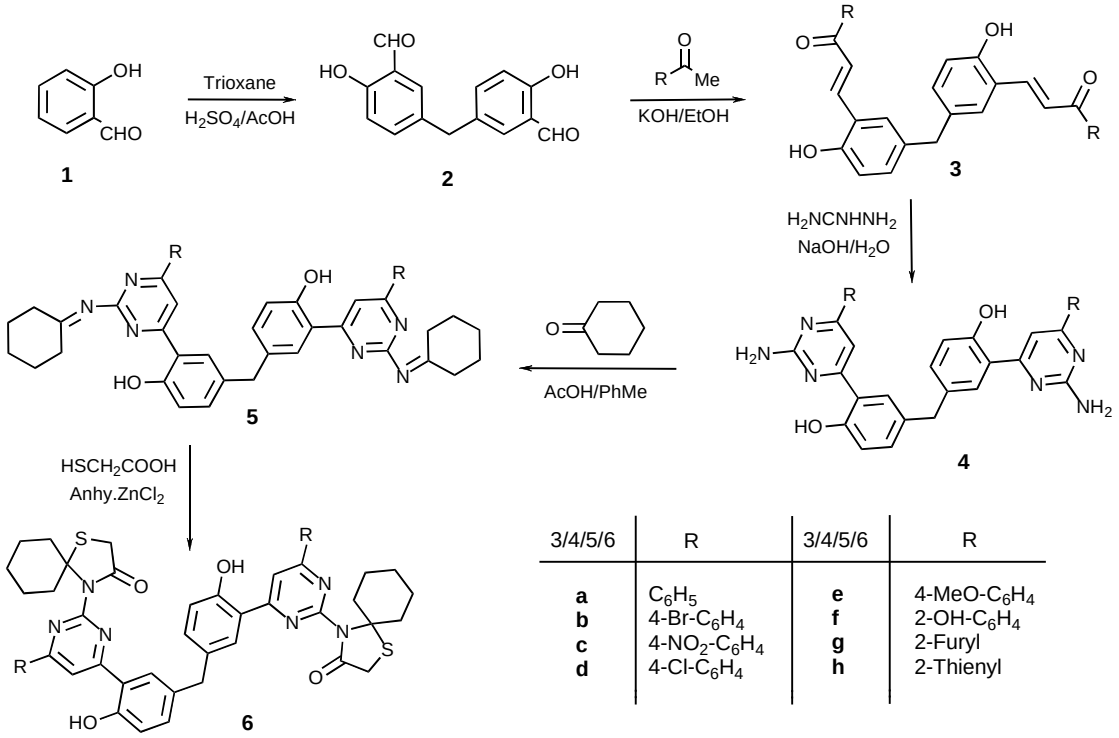
INTRODUCTION

In the course of work on new pharmacologically active thiazolidinones extensive efforts have been made to find more potent agents. The utility of 4-thiazolidinone/ thiazole as clinical agents and industrial intermediates is well established [1]. The 4-thiazolidinone/thiazole nucleus also frequently appears in the structure of various natural products and biologically active compounds, notably thiamine, penicillin, antibiotics such as micrococcin [2a], compounds possessing cardiac and glycemic benefit such as troglitazone [2b] and many metabolic products of fungi and primitive marine animals, including 2-(aminoalkyl)-thiazole-4-carboxylic acids [2c]. Recently more attention has been directed towards the synthesis of thiazolidinone bearing heteryl pharmacophores [3] as some of the deriva- tives have displayed significant pharmacological [4], and biological activities [5] including sedative [6], antiinflam-matory [7], antibacterial [8], antifungal [9], antitubercu- lar [10], analgesic and hypothermic [11], local [12a] and spinal [12b] anesthetic, CNS stimulant [13], anti-HIV [14] and nematicidal [15]. Further, thiazolidinones have also been used for the treatment of cardiac diseases [16], diabetic complications like cataracts, nephropathy and neuropathy [17], and selective anti-platelet activating factor [18]. Inspite of wide applications, it has been observed that there is scant information on the synthesis of thiazolidinones possessing heteryl substituted pyrimidinyl moiety in the literature.

On the other hand the pyrimidines have a unique place and have contributed significantly to biological and medicinal fields [19] such as antitubercular [20], and calcium channel blockers [21], and also many pyrimidines [22] have displayed diverse pharmaceutical activities depending upon the geometry and type of substituents attached to the ring [23]. 3-Azido-3-deoxythymidine (AZT) [24] a pyrimidine derivative has been found to be a potent antiviral agent against HIV type 1 *in vitro*, and has been found to decrease mortality and opportunistic infections in patients with AIDS. Inspired by the biological profile of thiazolidinones and pyrimidine derivatives and their increasing importance in pharmaceutical and biological fields, and in continuation of our work on the synthesis of biologically active heterocycles [25] considering the scope to introduce pyrimidinyl moiety into thiazolidinones, it was thought

Scheme 1



3/4/5/6	R	3/4/5/6	R
a	C_6H_5	**e**	4-MeO-C_6H_4
b	4-Br-C_6H_4	**f**	2-OH-C_6H_4
c	4-NO_2-C_6H_4	**g**	2-Furyl
d	4-Cl-C_6H_4	**h**	2-Thienyl

worthwhile to undertake the synthesis of the title compounds with the view to obtain certain new chemical entities with both active pharmacophores in a single molecular framework for the intensified biological activities.

In this article, we wish to report the synthesis of novel methylene-bis-pyrimidinyl-spiro-4-thiazolidinones **6** in good yields, from methylene-bis-(*N*-cyclohexylidene-*N*-pyrimidine) **5** and thioglycolic acid (Scheme 1). The antibacterial and antifungal activities of the compounds **6a-h** have also been evaluated.

RESULTS AND DISCUSSION

The title methylene-bis-pyrimidinyl-spiro-4-thiazolidinones **6** were synthesized from the methylene-bis-(*N*-cyclohexylidene-*N*-pyrimidine) **5**. For the synthesis of the target compounds, the 5-(3-formyl-4-hydroxybenzyl)-2-hydroxybenzaldehyde **2** was prepared by the reaction of salicylaldehyde **1** with trioxane in the presence of a mixture of acetic acid and conc. sulfuric acid [26], subsequent condensation with acetophenones in the presence of 60% aqueous KOH at room temperature [25e] yields methylene-bis-chalcones **3**. The reaction times, and the yields, vary depending on the corresponding reagents. The crude products, contaminated by some starting materials, were purified by extracting with ether. The methylene-bis-chalcones **3** were reacted with guanidine hydrochloride in the presence of aqueous NaOH to get the corresponding methylene-bis-2-amino-pyrimidines **4** in excellent yields [25g]. These compounds have low solubility in the most common solvents, hence were purified in small quantities by crystallizing the solid products in appropriate amounts of ethyl alcohol/benzene. The methylene-bis-2-aminnopyrimidine **4** was reacted with cyclohexanone in toluene in the presence of acetic acid to give the corresponding methylene-bis-(*N*-cyclo-hexylidene-*N*-pyrimidine) **5** in good yields. The one-pot synthesis of novel methylene-bis-pyrimidinyl-spiro-4-thi-azolidinones **6a-h** was carried out by the cyclocondensa-tion reaction between compound **5** and thioglycolic acid in *N*,*N*-dimethylformamide in the presence of anhy. $ZnCl_2$ under conventional heating. The structures of all the new compounds were confirmed by IR, ^{1}H NMR, ^{13}C NMR, MS and elemental analyses and further screened for their antibacterial and antifungal activities.

Antibacterial Activity. The compounds **6a-h** were screened for their antibacterial activity against human pathogenic bacteria *Escherichia coli*, *Klebseilla pneumoniae*, *Shigella dysentriae* and *Shigella flexnei*. The zone of inhibition in mm at concentration 100 μg was determined using the cup plate method [27]. Standard antibacterial agents such as streptomycin and neomycin, were also screened under similar conditions for the comparison and the results are given in Table 1.

The antibacterial screening of the compounds **6a-h** showed that compounds **6b**, **6d** and **6f** were highly active against *K. pneumoniae* and *S. dysentriae*. The compounds **6d**, **6e** and **6g** showed significant activity against *S. flexnei*. Compound **6d** is highly active against all the test organisms employed. The other compounds showed either moderate or less activity against these organisms. In case of *E. coli* all the compounds have displayed significant activity.

Table 1

Antimicrobial activity of compounds **6a-h.**

Compd	Antibacterial activity (zone of inhibition in mm at 100 μg)				Antifungal activity (zone of inhibition in mm at 500 μg)			
	E.coli	*K.pneumoniae*	*S.dysentriae*	*S. flexnei*	*A.niger*	*C.albicans*	*A.flavus*	*R.oryzae*
6a	21	17	17	19	18	17	18	14
6b	19	20	21	17	22	16	15	19
6c	23	19	24	19	25	27	23	19
6d	27	26	27	26	24	20	21	26
6e	19	11	20	25	18	17	19	16
6f	20	21	22	19	24	24	22	20
6g	23	18	23	19	19	24	16	24
6h	20	17	15	16	26	22	20	26
SM	30	30	30	30	--	--	--	--
NM	20	20	20	20	--	--	--	--
GF	--	--	--	--	32	32	30	32

SM = Streptomycin; NM = Neomycin; GF = Griseofulvin.

Note: <16mm, inactive; 17-23mm, moderately active; 23-27mm, highly active.

Antifungal Activity. The compounds **6a-h** were also screened for their antifungal activity against *Aspergillus niger*, *Candida albicans*, *Aspergillus flavus* and *Rhizopus oryzae* at concentration of 500 μg using cup plate method [27]. The antifungal activity of the compounds was compared with the standard drug griseofulvin, the zones of inhibition formed were measured in mm and are shown in Table 1.

The antifungal screening of the compounds **6a-h** showed that compounds **6d** and **6f** were significantly active and **6h** is highly active against all the test organisms. Compound **6c** is highly active against *A. niger*, *C. albicans* and *A. flavus*, compound **6g** is also highly active against *C. albicans* and *R. oryzae*. The other compounds showed either moderate or less activity against these organisms.

In conclusion, we have described the synthesis of novel methylene-bis-pyrimidinyl-spiro-4-thiazolidinones **6** in good to excellent yields by the reaction of methylene-bis-(*N*-cyclohexylidene-*N*-pyrimidine) **5** and thioglycolic acid. Some of these compounds exhibit excellent antibacterial and antifungal activities and can be evaluated as antimicrobial agents.

EXPERIMENTAL

The melting points were determined on a Fisher-Johns melting points apparatus and were uncorrected. The purity of the compounds was checked using precoated TLC plates. IR spectra were obtained on a Perkin-Elmer BX serried FTIR 5000 spectrophotometer, using KBr pellet. ^{1}H NMR, ^{13}C NMR spectra were obtained on a Varian Gemini spectrometer at 300 MHz, and 100 MHz , the chemical shifts ware reported as ppm down field using TMS as an internal standard and J values are quoted in Hz. Mass spectra were recorded on a VG-Micromass 7070H spectrometer operat- ing at 70 eV. Satisfactory elemental analyses was obtained using a Perkin-Elmer CHN analyzer. All solvents and chemicals were purchased from Sigma Aldrich chemical company and used without further purification.

Synthesis of methylene-bis-chalcones (3a-h). A solution of **2** (2.56 g, 0.01 mol) and 4-bromoacetophenone (0.02 mol) in absolute ethyl alcohol (20 mL) was treated with 60% KOH solution (20 mL) at 5-10 °C. The reaction mixture was stirred at room temperature for 4 hours. It was then diluted with water (50 mL) and extracted with diethyl ether (3x20 mL). The aqueous solution was acidified with dilute HCl. The solid obtained was collected by filtration, washed thoroughly with water, dried and purified by crystallization from toluene:MeOH (3:2) to give pure **3b** as yellow solid (91%), mp 160-62 °C; ^{1}H NMR (DMSO-d_6): 10.21 (2H, s, OH), 8.18-7.82 (6H, m, ArH), 8.05 (4H, d, J = 9.0 Hz, ArH), 7.70 (2H, d, J = 16.4 Hz, β-H), 7.18 (4H, d, J = 9.0 Hz, ArH), 6.84 (2H, d, J = 16.4 Hz, α-H), 3.84 (2H, s, CH2); IR (KBr): υ 3440, 3056, 1640, 1571, 1482, 1224 cm^{-1}; MS: m/z 616 (M^+). *Anal.* calcd. for $C_{31}H_{22}Br_2O_4$: C, 60.22; H, 3.59; Br, 25.85. Found: C, 60.12; H, 3.59; Br, 25.61. The other chalcones **3** were prepared by the similar procedure and characterized by IR, ^{1}H NMR, MS and elemental analyses [25e].

Synthesis of methylene-bis-2-aminopyrimidines (4a-h). A solution of **3b** (0.01 mol) and guanidine hydrochloride (0.03 mol) in ethyl alcohol (20 mL) was added aq. NaOH (0.02 mol) solution (5 mL). The reaction mixture was refluxed, TLC (EtOAc: Pet-ether, 2:1) showed that the reaction was complete after 6 hours. Then it was poured in cold 10% HCl (50 mL) solution and the precipitate obtained was collected by filtration, washed with water until free from acid and recrystallized from toluene-ethanol (3:2) to give pure **4b** as brown solid (83%), mp 123-25 °C; ^{1}H NMR (DMSO-d_6): δ 7.72 (4H, d, J = 8.1 Hz, ArH), 7.69 (4H, d, J = 8.1 Hz, ArH), 6.89-7.59 (8H, m, ArH),

7.10 (2H, s, OH), 7.03 (4H, s NH_2), 4.06 (2H, s, CH_2); IR (KBr): υ 3392, 3047, 2587, 1627, 1471 cm^{-1}; MS: m/z 694 (M^+). *Anal.* calcd. for $C_{33}H_{24}Br_2N_6O_2$: C, 56.92; H, 3.47; N, 1207. Found: C, 56.83; H, 3.41; N, 12.01. The other methylene-bis-2-amino-pyrimidines **4** were prepared by the similar procedure and their structures and biological activities are also evaluated [25g].

Synthesis of methylene-bis-(*N*-cyclohexylidene-*N*-pyrimidine) (5a-h). A mixture of compound **4b** (0.01 mol), cyclohexanone (0.02 mol) and acetic acid (0.5 mL) was refluxed in toluene using a Dean-Stark apparatus and the water formed was removed azeotropically. The progress of the reaction was checked by TLC using toluene: ethyl acetate (4:1) as an eluent. After completion of the reaction (5 hours), solvent was removed by distillation to give solid, which was collected by filtration, and recrystallized from absolute ethyl alcohol to give pure **5b** as brown solid (74%), mp 172-74°C; ^{1}H NMR (DMSO-d_6): δ 10.2 (2H, s OH), 7.72 (4H, d, J = 8.1 Hz, ArH), 7.69 (4H, d, J = 8.1 Hz, ArH), 7.59-6.89 (8H, m ArH), 4.06 (2H, s, CH_2), 2.50-2.40 (8H, m, CH_2), 2.34-2.28 (8H, m, CH_2), 1.62-1.59 (4H, m, CH_2); IR (KBr): υ 3410, 3062, 1625, 1471, 584 cm^{-1}; MS: m/z 856 (M^+). *Anal.* calcd. for $C_{45}H_{40}Br_2N_6O_2$: C, 63.09; H, 4.71; N, 9.81. Found: C, 62.94; H, 4.65; N, 9.77.

General procedure for the synthesis of compounds (6a-h). A mixture of compound **5** (0.01 mol) and thioglycolic acid (2.1 mL, 0.03 mol) in *N*,*N*-dimethylformamide (40 mL) with a pinch of anhydrous $ZnCl_2$, was refluxed for 6 hours. The progress of the reaction was checked by TLC using toluene:ether (3:1) as an eluent. The reaction mixture was cooled to room temperature and then poured into crushed ice. It was set-aside at room temperature overnight. The solid thus separated was filtered, washed several times with water, dried and purified by recrystallization from alcohol.

4-[4-(2-Hydroxy-5-{4-hydroxy-3-[2-(3-oxo-1-thia-4-azaspiro[4.5]dec-4-yl)-6-phenyl-4-pyrimidinyl]benzyl}phenyl)-6-phenyl-2-pyrimidinyl]-1-thia-4-azaspiro[4.5]decan-3-one (6a). Mp 143-45°C; Yield 83%; ^{1}H NMR (DMSO-d_6): δ 10.40 (2H, s, OH), 7.70-7.60 (10H, m, ArH), 7.40-7.32 (6H, m, ArH), 6.72 (2H, d, J = 9.2 Hz, ArH), 4.10 (2H, s, CH_2), 3.77 (4H, s, CH_2), 2.10-1.50 (20H, m, CH_2); ^{13}C NMR (DMSO-d_6): δ 175.6, 163.9, 158.6, 152.7, 152.0, 144.3, 136.4, 133.1, 131.0, 129.3, 128.7, 125.6, 111.0, 117.1, 115.9, 87.7, 47.3, 42.1, 36.7, 30.0, 26.3; IR (KBr): ν 3340, 3027, 2980, 1670, 1610, 1480, 1470, 1410, 688 cm^{-1}; MS: m/z 846 (M^+). *Anal.* calcd. for $C_{49}H_{46}N_6O_4S_2$: C, 69.48; H, 5.47; N, 9.92. Found: C, 69.36; H, 5.50; N, 9.86.

4-[4-(4-Bromophynyl)-6-(5-{3-[6-(4-bromophenyl)-2-(3-oxo-1-thia-4-azaspiro[4.5]dec-4-yl)4-pyrimidinyl]-4-hydroxybenzyl}-2-hydroxyphenyl)-2-pyrimidinyl]-1-thia-4-azaspiro[4.5]-decan-3-one (6b). Mp 148-50°C; Yield 81%; ^{1}H NMR (DMSO-d_6): δ 10.40 (2H, s, OH), 7.70 (4H, d, J = 8.4 Hz, ArH), 7.62 (4H, d, J = 8.4 Hz, ArH), 7.40-7.32 (6H, m, ArH), 6.72 (2H, d, J = 9.2 Hz, ArH), 4.10 (2H, s, CH_2), 3.78 (4H, s, CH_2), 2.10-1.50 (20H, m, CH_2); ^{13}C NMR (DMSO-d_6): δ 175.6, 163.2, 158.6, 152.6, 152.0, 144.3, 137.9, 133.7, 133.4, 131.2, 129.0, 124.1, 116.2, 115.6, 113.3, 87.6, 47.1, 42.1, 36.7, 30.1, 26.3; IR (KBr): ν 3340, 3020, 2995, 1676, 1595, 1480, 1470, 790, 686 cm^{-1}; MS: m/z 1004 (M^+). *Anal.* calcd. for $C_{49}H_{46}Br_2N_6O_4S_2$: C, 58.57; H, 4.41; N, 8.36. Found: C, 58.46; H, 4. 39; N, 8.29.

4-[4-(2-Hydroxy-5-{4-hydroxy-3-[6-(4-nitrophenyl)-2-(3-oxo-1-thia-4-azaspiro[4.5]dec-4-yl)-4-pyrimidinyl]benzyl}phenyl)-6-(4-nitrophenyl)-2-pyrimidinyl]-1-thia-4-azaspiro[4.5]decan-3-one (6c). Mp 169-71°C; Yield 78%; ^{1}H NMR (DMSO-d_6): δ 10.40 (2H, s, OH), 8.20 (4H, d, J = 8.7 Hz, ArH), 8.00 (4H, d, J = 8.7 Hz, ArH), 7.40-7.32 (6H, m, ArH), 6.72 (2H, d, J = 9.2 Hz, ArH), 4.10 (2H, s, CH_2), 3.78 (4H, s, CH_2), 2.10-1.50 (20H, m, CH_2); ^{13}C NMR (DMSO-d_6): δ 176.2, 162.6, 158.4, 152.6, 152.0, 147.3, 144.7, 141.3, 132.6, 130.7, 128.1, 124.7, 116.7, 115.2, 109.0, 87.3, 47.3, 42.1, 36.3, 30.1, 26.4; IR (KBr): ν 3340, 3015, 2985, 1670, 1610, 1510, 1475, 1415, 1318, cm^{-1}; MS: m/z 936 (M^+). *Anal.* calcd. for $C_{49}H_{44}N_8O_8S_2$: C, 62.81; H, 4.73; N, 11.96. Found: C, 62.37; H, 4.70; N, 11.82.

4-[4-(4-Chlorophenyl)-6-(5-{3-[6-(4-chlorophenyl)-2-(3-oxo-1-thia-4-azaspiro[4.5]dec-4-yl)-4-pyrimidinyl]-4-hydroxybenzyl}-2-hydroxyphenyl)-2-pyrimidinyl]-1-thia-4-azaspiro[4.5] decan-3-one (6d). Mp 165-67°C; Yield 76%; ^{1}H NMR (DMSO-d_6): δ 10.40 (2H, s, OH), 7.84 (4H, d, J = 8.4 Hz, ArH), 7.40-7.32 (6H, m, ArH), 7.15 (4H, d, J = 8.4 Hz, ArH), 6.72 (2H, d, J = 9.2 Hz, ArH), 4.12 (2H, s, CH_2), 3.80 (4H, s, CH_2), 2.10-1.50 (20H, m, CH_2); ^{13}C NMR (DMSO-d_6): δ 175.4, 162.0, 157.6, 152.7, 152.0, 143.9, 140.1, 134.6, 132.9, 132.1, 129.1, 126.6, 116.3, 115.0, 112.1, 87.1, 47.4, 42.1, 36.5, 30.0, 26.1; IR (KBr): ν 3340, 3027, 2985, 1675, 1610, 1480, 1470, 1410, 746, 686 cm^{-1}; MS: m/z 916 (M^+). *Anal.* calcd. for $C_{49}H_{44}Cl_2N_6O_4S_2$: C, 64.25; H, 4.84; N, 9.18. Found: C, 64.16; H, 4.72; N, 9.10.

4-[4-(2-Hydroxy-5-{4-hydroxy-3-[6-(4-methoxyphenyl)-2-(3-oxo-1-thia-4-azaspiro[4.5]dec-4-yl)-4-pyrimidinyl]benzyl}phenyl)-6-(4-methoxyphenyl)-2-pyrimidinyl]-1-thia-4-azaspiro[4.5]decan-3-one (6e). Mp 180-82°C; Yield 88%; ^{1}H NMR (DMSO-d_6): δ 10.40 (2H, s, OH), 7.90 (4H, d, J = 8.3 Hz, ArH), 7.40-7.32 (6H, m, ArH), 7.00 (4H, d, J = 8.3 Hz, ArH), 6.72 (2H, d, J = 9.2 Hz, ArH), 4.12 (2H, s, CH_2), 3.80 (4H, s, CH_2), 3.70 (6H, s, OCH_3), 2.10-1.50 (20H, m, CH_2); ^{13}C NMR (DMSO-d_6): δ 175.3, 162.3, 160.1, 157.9, 152.3, 152.0, 144.0, 139.3, 132.7, 131.7, 126.8, 116.2, 113.2, 111.7, 114.2, 87.8, 47.0, 42.0, 36.7, 30.1, 26.0; IR (KBr): ν 3344, 3027, 2980, 1672, 1600, 1480, 1472, 1410, 1224, 688 cm^{-1}; MS: m/z 906 (M^+). *Anal.* calcd. for $C_{51}H_{50}N_6O_6S_2$: C, 67.53; H, 5.56; N, 9.26. Found: C, 67.42; H, 5.50; N, 9.21.

4-[4-(2-Hydroxy-5-{4-hydroxy-3-[6-(2-hydroxyphenyl)-2-(3-oxo-1-thia-4-azaspiro[4.5]dec-4-yl)-4-pyrimidinyl]benzyl}-phenyl)-6-(2-hydroxyphenyl)-2-pyrimidinyl]-1-thia-4-azaspiro[4.5]decan-3-one (6f). Mp 162-64°C; Yield 86%; ^{1}H NMR (DMSO-d_6): δ 10.40 (2H, s, OH), 7.50-6.80 (16H, m, ArH), 4.10 (2H, s, CH_2), 3.78 (4H, s, CH_2), 2.10-1.50 (20H, m, CH_2); ^{13}C NMR (DMSO-d_6): δ 175.1, 162.4, 160.7, 156.3, 154.1, 152.0, 144.0, 132.0, 131.6, 130.1, 128.7, 122.0, 118.7, 118.1, 117.1, 116.2, 87.6, 47.9, 42.3, 36.3, 30.4, 26.2; IR (KBr): ν 3541, 3015, 2985, 1670, 1600, 1472, 1415, 688 cm^{-1}; MS: m/z 878 (M^+). *Anal.* calcd. for $C_{49}H_{46}N_6O_6S_2$: C, 66.95; H, 5.27; N, 9.56. Found: C, 66.82; H, 5.19; N, 9.43.

4-[4-(2-Furyl)-6-(5-{3-[6-(2-furyl)-2-(3-oxo-1-thia-4-azaspiro[4.5]dec-4-yl)-4-pyrimidinyl]-4-hydroxybenzyl}-2-hydroxyphenyl)-2-pyrimidinyl]-1-thia-4-azaspiro[4.5]decan-3-one (6g). Mp 201-03°C; Yield 71%; ^{1}H NMR (DMSO-d_6): δ 10.40 (2H, s, OH), 8.21 (2H, s, ArH), 7.40-6.30 (12H, m, ArH), 4.10 (2H, s, CH_2), 3.87 (4H, s, CH_2), 2.10-1.50 (20H, m, CH_2); ^{13}C NMR (DMSO-d_6): δ 176.7, 175.6, 161.7, 156.7, 152.0, 150.2, 147.1, 143.7, 132.2, 131.0, 118.3, 116.7, 116.0, 117.4, 111.7, 87.9, 47.6, 42.2, 36.4, 30.1, 26.3; IR (KBr): ν 3342, 3027, 2982, 1672, 1600, 1480, 1470, 1410, 686 cm^{-1}; MS: m/z 826 (M^+). *Anal.* calcd. for $C_{45}H_{42}N_6O_6S_2$: C, 65.36; H, 5.12; N, 10.16. Found: C, 65.22; H, 5.10; N, 10.10.

4-[4-(2-Hydroxy-5-{4-hydroxy-3-[2-(3-oxo-1-thia-4-azaspiro-[4.5]dec-4-yl)-6-(2-thienyl)-4-pyrimidinyl]benzyl}phenyl)-6-(2-thienyl)-2-pyrimidinyl]-1-thia-4-azaspiro[4.5]decan-3-one (6h).

Mp 192-94°C; Yield 74%; ^{1}H NMR (DMSO-d_6): δ 10.40 (2H, s, OH), 8.21 (2H, s, ArH), 7.40-6.30 (12H, m, ArH), 4.10 (2H, s, CH_2), 3.87 (4H, s, CH_2), 2.10-1.50 (20H, m, CH_2); ^{13}C NMR (DMSO-d_6): δ 183.3, 175.5, 156.6, 152.4, 152.0, 146.0, 137.6, 134.7, 133.9, 132.3, 132.0, 123.4, 117.1, 115.2, 112.0, 87.0, 47.6, 42.3, 36.7, 30.5, 26.1; IR (KBr): ν 3345, 3062, 2985, 1680, 1595, 1480, 1472, 1410, 688 cm^{-1}; MS: m/z 860 (M^+). *Anal.* calcd. for $C_{45}H_{42}N_6O_4S_4$: C, 62.91; H, 4.93; N, 9.79. Found: C, 62.88; H, 4.81; N, 9.67.

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