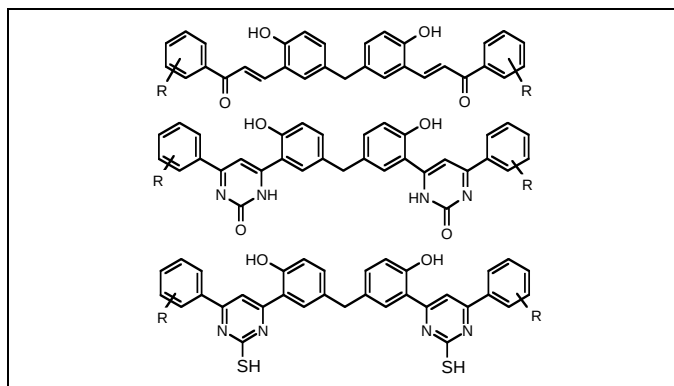


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A series of novel methylene-bis-chalcones was prepared by the reaction of 5,5'-methylene-bis-salicylaldehyde with different acetophenones, subsequent treatment of methylene-bis-chalcones with urea/thiourea gave the corresponding methylene-bis-pyrimidinones/ methylene-bis-mercaptopyrimidines in good yields. Characterization of the new compounds has been done by means of IR, ^1H NMR, MS and elemental analysis. The antibacterial, antitubercular and antifungal activity of the compounds has also been evaluated.

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INTRODUCTION

Heterocycles are abundant in nature and are of great significance to life [1], hence have attracted considerable attention in the design of biologically active molecules [2] and advanced organic materials [3]. Pyrimidine ring systems containing substituted six membered ring exhibit anticancer and herbicidal activities [4,5]. In recent years pyrimidine derivatives have received significant attention owing to their diverse range of biological properties, particularly being antitubercular [6] and calcium channel blockers [7]. Many classes of chemotherapeutic agents containing pyrimidine nucleus are in clinical use such as antibacterial, anticancer, antiviral, antifungal, antimalarial and antihypertensive agents. Apart from this, chalcones and their derivatives have been reported to possess various biological activities such as antibacterial [8], antifungal [8b] anti-inflammatory [9], antitumor [10], anticancer [11] and prostaglandin binding [11b].

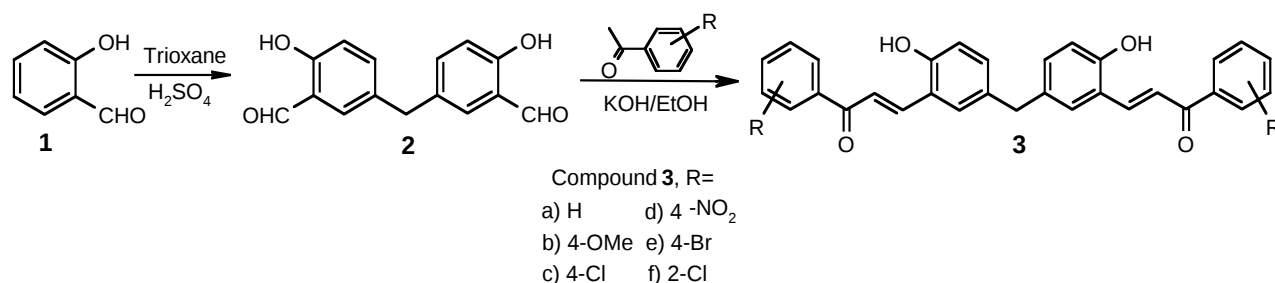
The most general and widely employed synthetic route to pyrimidine [12] involves the combination of a reagent containing the N-C-N skeleton with C-C-C unit. There are typical examples of bis nucleophile with bis electrophile method of constructing heterocycles. Both the nitrogen atoms of the N-C-N reagent act as nucleophiles and both the terminal carbon atoms of C-C-C reagent are electrophiles. Urea and thiourea are the most commonly used N-C-N reagents and chalcones are typically C-C-C reagents.

Inspired with the biological profile of pyrimidine derivatives and their increasing importance in pharmaceutical and biological fields, and in continuation of our work on biologically active heterocycles [13] it was considered worthwhile to synthesize certain new chemical entities incorporating two active pyrimidine/pyrimidinone nuclei in a single molecular frame work and to get them evaluated for their antibacterial, antitubercular and antifungal activity.

RESULTS AND DISCUSSION

The 5,5'-methylene-bis-salicylaldehyde **2** was prepared by the reaction of salicylaldehyde **1** with trioxane in the presence of a mixture of acetic acid and concentrated sulfuric acid [14]. The methylene-bis-chalcones **3a-f** were synthesized by the Claisen condensation of substituted acetophenones and 5,5'-methylene-bis-salicylaldehyde **2** in ethanol in the presence of 60% aqueous KOH at room temperature [15] (Scheme 1). The reaction times as well as the yields vary depending on the corresponding reagents. The crude product contaminated by some starting materials was purified by extracting with ether. The methylene-bis-chalcones **3** were reacted with urea [16] or thiourea [17] in presence of aqueous NaOH to get the corresponding methylene-bis-pyrimidinones **4a-f** and methylene-bis-mercaptopyrimidines **5a-f** (Scheme 2). These compounds have low solubility in the most

Scheme 1



common solvents hence purified in small quantities by crystallizing the solid products in appropriate amounts of ethanol/benzene. The structures of the synthesized compounds were confirmed by ir, ¹H nmr, ms and elemental analysis. The compounds were subject to antibacterial, antitubercular and antifungal activity testing.

Antimicrobial Activity. The compounds **4a-f** and **5a-f** were screened for their antibacterial activity against human pathogenic bacteria *Escherichia coli*, *Staphylococcus aureus* and *Bacillus subtilis*. The minimum inhibition concentration (MIC) was determined using the tube dilution method [18]. DMF was used as a blank and streptomycin/neomycin was used as antibacterial standard. An examination of the data reveals that all the compounds showed antibacterial activity ranging from 25 to 100 µg/mL. The antibacterial activity was compared with the known antibiotic streptomycin/neomycin and the results are given in Table 1.

The compounds **4b** and **5b** were highly active against all the three organisms employed. Compounds **4d**, **4e**, **5e** and **5f** were highly active against *E.coli* and *S.aureus*, compound **4f** was highly active against

E.coli and *S.subtilis* and the compound **5c** was highly active against *S.aureus* and *B.subtilis*. The compound **4a** did not show any promising results. From the screened results, it is evident that the presence of methoxy/chloro group at the phenyl ring enhances the antibacterial activity.

Antitubercular screening of the compounds **4a-f** and **5a-f** were carried out using Almar blue assay procedure [19], INH was used as a standard drug. Antitubercular screening revealed that the compounds **4b**, **4d**, and **4f** exhibited equipotent activity with the standard at both the tested conc. 1.0 µg/mL and 0.1 µg/mL. The compounds **5b**, **5d** and **5f** exhibited moderate activity.

Antifungal Activity. The compounds **4a-f** and **5a-f** were also screened for their antifungal activity against *Candida albicans* at 160, 320, 480 and 640 µg/mL concentration using Agar plate technique [20]. The compounds **4e** and **5b** were highly active against *Candida albicans*. Other compounds showed moderate to good activity. The antifungal activity of the compounds was compared with the known antibiotic fluconazole and the results are presented in Table 1.

Scheme 2

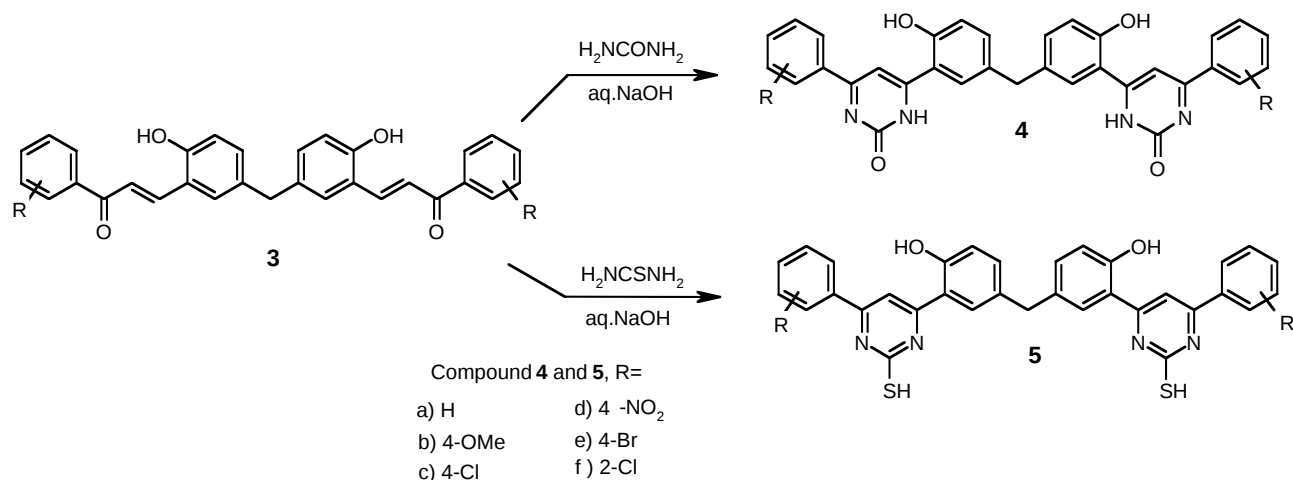


Table 1
Antibacterial and Antifungal Activity of **4a-f** and **5a-f**

Compound	Antibacterial activity			Antifungal activity			
	Minimum inhibition conc. µg/mL			Spore germination inhibition (in%) at different conc. (µg/mL) against <i>Candida albicans</i>			
	<i>E.coli</i>	<i>S.aureus</i>	<i>B.subtilis</i>	160	320	480	640
4a	100	Inactive	Inactive	32.1	23.0	29.1	26.3
4b	25	25	25	49.4	79.1	89.7	91.0
4c	50	75	50	46.0	43.1	81.7	86.9
4d	25	25	75	19.6	29.0	29.7	33.1
4e	25	25	50	79.0	87.3	89.0	90.1
4f	25	50	25	77.1	79.3	81.0	86.5
5a	75	100	Inactive	68.7	75.2	83.0	86.7
5b	25	25	25	83.1	86.4	87.6	93.3
5c	50	25	25	72.7	78.6	79.4	87.6
5d	75	50	Inactive	59.2	66.1	69.9	72.1
5e	25	25	50	76.2	78.1	82.3	84.0
5f	25	25	75	75.1	78.2	80.3	84.1
Streptomycin	10	10	10				
Neomycin	30	30	30				
Fluconazole				84.0	87.0	95.0	98.0

EXPERIMENTAL

Melting points were determined on a Fisher-Johns melting point apparatus and were uncorrected. The purity of the compounds was checked using precoated TLC plates (Merck, 60_{F-254}). IR spectra were obtained on a Perkin-Elmer BX series FTIR 5000 spectrophotometer, using KBr pellet. ¹H NMR spectra were obtained with a Varian Gemini 200 MHz spectrometer and the chemical shifts were reported as parts per million (δ ppm) downfield using TMS as an internal standard. Mass spectra were obtained on a VG micromass 7070H spectrometer operating at 70 eV. UV spectra were obtained on a UV-2401 spectrometer. Elemental analyses were performed on a Perkin-Elmer 240 CHN elemental analyzer. All solvents and chemicals were purchased from Sigma-Aldrich chemical company and used without further purification.

General procedure for the synthesis of methylene-bis-chalcones (3a-f). A solution of **2** (2.56 g, 0.01 mol) and the corresponding acetophenone (0.02 mol) in 20 mL of ethanol was treated with 20 mL of 60% KOH solution 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 (3 x 20 mL). The aqueous solution was acidified with dilute HCl. The solid obtained was filtered, washed thoroughly with water, dried the crude product and purified by crystallization from benzene: MeOH (3:2).

(E)-3-(2-Hydroxy-5-{4-hydroxy-3-[(E)-3-oxo-3-phenyl-1-propenyl]benzyl}phenyl)-1-phenyl-2-propen-1-one (3a). This compound was obtained as yellow solid, yield 92%; mp 108-109°C; ir (KBr): δ 3440, 3058, 1574, 1640, 1487, 1224 cm⁻¹; uv: λ_{max} (EtOH) 372, 302, 266 nm; ¹H nmr: δ 3.84 (2H, s, -CH₂-), 7.01 (2H, d, J=16.4 Hz, α-H), 7.85 (2H, d, J=16.4 Hz, β-H), 10.24 (2H, s, OH), 7.34- 8.34 (16H, m, aromatic); ms: m/z 460; (M⁺). Anal. Calcd. For C₃₁H₂₄O₄: C, 80.85; H, 5.20. Found: C, 80.80; H, 5.21.

(E)-3-(2-Hydroxy-5-{4-hydroxy-3-[(E)-3-(4-methoxyphenyl)-3-oxo-1-propenyl]benzyl}phenyl)-1-(4-methoxyphenyl)-2-propen-1-one (3b). This compound was obtained as orange solid, yield 95%; mp 95-97°C; ir (KBr): δ 3380, 3058, 1563, 1646, 1482, 1223 cm⁻¹; uv: λ_{max} (EtOH) 373, 304, 266 nm; ¹H nmr: δ 3.82 (6H, s, OCH₃), 3.84 (2H, s, -CH₂-), 6.94 (2H, d, J=16.4 Hz,

α-H), 7.70 (2H, d, J=16.4 Hz, β-H), 10.10 (2H, s, OH), 6.97-7.10 (4H, d, J=9 Hz, 3'-H, 5'-H), 8.0- 8.1 (4H, d, J=9 Hz, 2'-H, 6'-H), 7.82-8.18 (6H, m, aromatic); ms: m/z 520 (M⁺). Anal. Calcd. for C₃₃H₂₈O₆: C, 76.14; H, 5.42. Found: C, 76.11; H, 5.39.

(E)-1-(4-Chlorophenyl)-3-(5-{3-[(E)-3-(4-chlorophenyl)-3-oxo-1-propenyl]-4-hydroxybenzyl}-2-hydroxyphenyl)-2-propen-1-one (3c). This compound was obtained as yellow solid, yield 82%; mp 101-103°C; ir (KBr): ν 3420, 3054, 1576, 1640, 1487, 1223 cm⁻¹; uv : λ_{max} (EtOH) 370, 306, 269 nm; ¹H nmr: δ 3.84 (2H, s, -CH₂-), 6.90 (2H, d, J=16.4 Hz, α-H), 7.85 (2H, d, J=16.4 Hz, β-H), 10.20 (2H, s, OH), 7.26 (4H, d, J=9 Hz, 3'-H, 5'-H), 8.0 (4H, d, J=9 Hz, 2'-H, 6'-H), 7.82-8.18 (6H, m, aromatic); ms: m/z 529 (M⁺). Anal. Calcd. for C₃₁H₂₂Cl₂O₄: C, 70.33; H, 4.19. Found: C, 70.23; H, 4.13.

(E)-3-(2-Hydroxy-5-{4-hydroxy-3-[(E)-3-(4-nitrophenyl)-3-oxo-1-propenyl]benzyl}phenyl)-1-(4-nitrophenyl)-2-propen-1-one (3d). This compound was obtained as red solid; yield 95%; mp 130-132°C; ir (KBr): ν 3420, 3054, 1574, 1640, 1487, 1452, 1523, 1347, 852, 1222 cm⁻¹; uv: λ_{max} (EtOH) 370.4, 303.9, 266.4 nm; ¹H nmr: δ 3.84 (2H, s, -CH₂-), 7.85 (2H, d, J=16.4 Hz, α-H), 8.23 (2H, d, J=16.4 Hz, β-H), 10.20 (2H, s, OH), 8.20 (4H, d, J=9 Hz, 3'-H, 5'-H), 8.0 (4H, d, J=9 Hz, 2'-H, 6'-H), 7.82-8.18 (6H, m, aromatic); ms: m/z 550 (M⁺). Anal. Calcd. for C₃₁H₂₂N₂O₈: C, 67.63; H, 4.03; N, 5.09. Found: C, 67.60; H, 4.0; N, 5.01.

(E)-1-(4-Bromophenyl)-3-(5-{3-[(E)-3-(4-bromophenyl)-3-oxo-1-propenyl]-4-hydroxybenzyl}-2-hydroxyphenyl)-2-propen-1-one (3e). This compound was obtained as yellow solid; yield 91%; mp 160-161°C; ir (KBr): ν 3440, 3056, 1571, 1640, 1482, 1224 cm⁻¹; uv: λ_{max} (EtOH) 370.5, 304.9, 268.1 nm; ¹H nmr: δ 3.84 (2H, s, -CH₂-), 6.84 (2H, d, J=16.4 Hz, α-H), 7.70 (2H, d, J=16.4 Hz, β-H), 10.21 (2H, s, OH), 7.18 (4H, d, J=9 Hz, 3'-H, 5'-H, 3''-H, 5''-H), 8.05 (4H, d, J=9 Hz, 2'-H, 6'-H, 2''-H, 6''-H) 7.82-8.18 (6H, m, aromatic); ms: m/z 618 (M⁺). Anal. Calcd. for C₃₁H₂₂Br₂O₄: C, 60.22; H, 3.59; Br, 25.85. Found: C, 60.12; H, 3.59; Br, 25.61.

(E)-1-(2-Chlorophenyl)-3-(5-{3-[(E)-3-(2-chlorophenyl)-3-oxo-1-propenyl]-4-hydroxybenzyl}-2-hydroxyphenyl)-2-propen-1-one (3f). This compound was obtained as brown solid; yield 90%; mp 96-97°C; ir (KBr): ν 3420, 3056, 1568, 1640,

1489, 1224 cm^{-1} ; uv: λ_{max} (EtOH) 372, 305.2, 268.2 nm; ^1H nmr: δ 3.84 (2H, s, $-\text{CH}_2-$), 6.90 (2H, d, $J=16.4$ Hz, α -H), 7.85 (2H, d, $J=16.4$ Hz, β -H), 10.24 (2H, s, OH), 7.82–8.18 (14H, m, aromatic); ms: m/z 529 (M^+). *Anal.* Calcd. for $\text{C}_{31}\text{H}_{22}\text{Cl}_2\text{O}_4$: C, 70.33; H, 4.19. Found: C, 70.26; H, 4.17.

General procedure for the synthesis of methylene-bis-pyrimidinones (4a-f). A solution of **3** (0.01 mol) and urea (0.03 mol) in 20 mL ethanol was treated with 3 mL of NaOH (0.02 mol). The reaction mixture was refluxed. Tlc (EtOAc: Pet-ether, 2:1) showed that the reaction was complete after 6 hours. The reaction mixture was poured in 50 mL of cold 10% HCl solution and the precipitate was filtered, washed with water until it was free from acid and on recrystallization from benzene-ethanol gave **4**.

6-{2-Hydroxy-5-[4-hydroxy-3-(2-oxo-6-phenyl-2,3-dihydro-4-pyrimidinyl)benzyl]phenyl}-4-phenyl-1,2-dihydro-2-pyrimidinone (4a). This compound was obtained as brown solid; yield 93%; mp 125–126°C; ir (KBr): ν 3235, 3040, 2920, 1685, 1615, 1594, 1471 cm^{-1} ; ^1H nmr: δ 4.20 (2H, s, $-\text{CH}_2-$), 6.23 (2H, s, OH), 7.20 (2H, s, 4-H, 4'-H), 7.22–8.24 (16H, m, aromatic), 8.31 (2H, s, NH); ms: m/z 540 (M^+). *Anal.* Calcd. for $\text{C}_{33}\text{H}_{24}\text{N}_4\text{O}_4$: C, 73.32; H, 4.47; N, 10.36. Found: C, 73.06; H, 4.42; N, 10.27.

6-(2-Hydroxy-5-{4-hydroxy-3-[6-(4-methoxyphenyl)-2-oxo-2,3-dihydro-4-pyrimidinyl]benzyl}phenyl)-4-(4-methoxyphenyl)-1,2-dihydro-2-pyrimidinone (4b). This compound was obtained as brown solid; yield 94%; mp 132–133°C; ir (KBr): ν 3230, 3030, 2920, 1690, 1626, 1596, 1480, 1122 cm^{-1} ; ^1H nmr: δ 3.81 (6H, s, OCH_3), 4.10 (2H, s, $-\text{CH}_2-$), 6.10 (2H, s, OH), 6.9–7.0 (4H, d, $J=9$ Hz, 3-H, 3'-H, 5-H, 5'-H), 7.10–7.91 (6H, m, aromatic), 7.19 (2H, s, 4-H, 4'-H), 7.7–8.80 (4H, d, 2-H, $J=9$ Hz, 2'-H, 6-H, 6'-H), 8.31 (2H, s, NH); ms: m/z 600 (M^+). *Anal.* Calcd. for $\text{C}_{35}\text{H}_{28}\text{N}_4\text{O}_6$: C, 69.99; H, 4.70; N, 9.33. Found: C, 73.06; H, 4.42; N, 10.27.

4-(4-Chlorophenyl)-6-(5-{3-[6-(4-chlorophenyl)-2-oxo-2,3-dihydro-4-pyrimidinyl]-4-hydroxybenzyl}-2-hydroxyphenyl)-1,2-dihydro-2-pyrimidinone (4c) This compound was obtained as brown solid; yield 91%; mp 137–139°C; ir (KBr): ν 3225, 3035, 2922, 1690, 1624, 1590, 1486 cm^{-1} ; ^1H nmr: δ 4.20 (2H, s, $-\text{CH}_2-$), 6.10 (2H, s, OH), 7.10–7.17 (4H, d, $J=9$ Hz, 3-H, 3'-H, 5-H, 5'-H), 7.6–8.0 (4H, d, $J=9$ Hz, 2-H, 2'-H, 6-H, 6'-H), 7.0–8.10 (6H, m, aromatic), 7.21 (2H, s, 4-H, 4'-H), 8.30 (2H, s, NH); ms: m/z 609 (M^+). *Anal.* Calcd. for $\text{C}_{33}\text{H}_{22}\text{Cl}_2\text{N}_4\text{O}_4$: C, 65.03; H, 3.64; N, 9.19. Found: C, 64.92; H, 3.60; N, 9.14.

6-(2-Hydroxy-5-{4-hydroxy-3-[6-(4-nitrophenyl)-2-oxo-2,3-dihydro-4-pyrimidinyl]benzyl}phenyl)-4-(4-nitrophenyl)-1,2-dihydro-2-pyrimidinone (4d). This compound was obtained as red solid; yield 94%; mp 144–145°C; ir (KBr): ν 3230, 3042, 2922, 1690, 1626, 1592, 1482, 1347 cm^{-1} ; ^1H nmr: δ 4.18 (2H, s, $-\text{CH}_2-$), 6.0 (2H, s, OH), 7.21 (2H, s, 4-H, 4'-H), 7.90 (4H, d, $J=9$ Hz, 2-H, 2'-H, 6-H, 6'-H), 7.82–8.16 (6H, m, aromatic), 8.21 (4H, d, $J=9$ Hz, 3-H, 3'-H, 5-H, 5'-H), 8.30 (2H, s, NH); ms: m/z 630 (M^+). *Anal.* Calcd. for $\text{C}_{33}\text{H}_{22}\text{N}_6\text{O}_8$: C, 62.86; H, 3.52; N, 13.33. Found: C, 62.80; H, 3.48; N, 13.26.

4-(4-Bromophenyl)-6-(5-{3-[6-(4-bromophenyl)-2-oxo-2,3-dihydro-4-pyrimidinyl]-4-hydroxybenzyl}-2-hydroxyphenyl)-1,2-dihydro-2-pyrimidinone (4e). This compound was obtained as yellow solid; yield 91%; mp 147–148°C; ir (KBr): ν 3230, 3038, 2920, 1695, 1620, 1590, 1470 cm^{-1} ; ^1H nmr: δ 4.22 (2H, s, $-\text{CH}_2-$), 6.02 (2H, s, OH), 7.19 (4H, d, $J=9$ Hz, 3-H, 3'-H, 5-H, 5'-H), 7.21 (2H, s, 4-H, 4'-H), 7.80–8.18 (6H, m, aromatic), 8.09 (4H, d, $J=9$ Hz, 2-H, 2'-H, 6-H, 6'-H), 8.30 (2H, s, NH); ms: m/z

698 (M^+). *Anal.* Calcd. for $\text{C}_{33}\text{H}_{22}\text{Br}_2\text{N}_4\text{O}_4$: C, 56.76; H, 3.18; N, 8.02; Br, 22.88. Found: C, 56.70; H, 3.15; N, 8.01; Br, 22.62.

4-(2-Chlorophenyl)-6-(5-{3-[6-(2-chlorophenyl)-2-oxo-2,3-dihydro-4-pyrimidinyl]-4-hydroxybenzyl}-2-hydroxyphenyl)-1,2-dihydro-2-pyrimidinone (4f). This compound was obtained as brown solid; yield 90%; mp 145–146°C; ir (KBr): ν 3233, 3035, 2920, 1690, 1621, 1592, 1482 cm^{-1} ; ^1H nmr: δ 4.22 (2H, s, $-\text{CH}_2-$), 6.10 (2H, s, OH), 7.16–8.21 (14H, m, aromatic), 7.20 (2H, s, 4-H, 4'-H), 8.31 (2H, s, NH); ms: m/z 609 (M^+). *Anal.* Calcd. for $\text{C}_{33}\text{H}_{22}\text{Cl}_2\text{N}_4\text{O}_4$: C, 65.03; H, 3.64; N, 9.19. Found: C, 64.96; H, 3.58; N, 9.13.

General Procedure for the synthesis of methylene-bis-mercaptopyrimidine (5a-f). A solution of **3** (0.01 mol) and thiourea (0.03 mol) in 20 mL ethanol was treated with 3 mL of NaOH (0.02 mol). The reaction mixture was refluxed. Tlc (EtOAc: Pet-ether, 2:1) showed that the reaction was complete after 6 hours. The reaction mixture was poured in 50 mL of cold 10% HCl solution and the precipitate was filtered, washed with water until it was free from acid and on recrystallization from benzene-ethanol gave **5**.

4-{4-Hydroxy-3-(6-phenyl-2-sulfanyl-4-pyrimidinyl)benzyl}-2-(6-phenyl-2-sulfanyl-4-pyrimidinyl)phenol (5a). This compound was obtained as brown solid; yield 86%; mp 119–120°C; ir (KBr): ν 3326, 3040, 2590, 1620, 1595, 1470, 1216, 795 cm^{-1} ; ^1H nmr: δ 3.31 (2H, s, SH), 4.20 (2H, s, $-\text{CH}_2-$), 6.17 (2H, s, OH), 7.10–8.24 (16H, m, aromatic), 7.60 (2H, s, 4-H, 4'-H); ms: m/z 572 (M^+). *Anal.* Calcd. for $\text{C}_{33}\text{H}_{24}\text{N}_4\text{O}_2\text{S}_2$: C, 69.21; H, 4.22; N, 9.78. Found: C, 69.14; H, 4.19; N, 9.73.

4-{4-hydroxy-3-[6-(4-methoxyphenyl)-2-sulfanyl-4-pyrimidinyl]benzyl}-2-[6-(4-methoxyphenyl)-2-sulfanyl-4-pyrimidinyl]phenol (5b). This compound was obtained as brown solid; yield 91%; mp 170–171°C; ir (KBr): ν 3326, 3035, 2590, 1630, 1592, 1470, 1216, 795 cm^{-1} ; ^1H nmr: δ 3.30 (2H, s, SH), 3.92 (6H, s, OCH_3), 4.20 (2H, s, $-\text{CH}_2-$), 6.10 (2H, s, OH), 6.9–7.20 (4H, d, $J=9$ Hz, 3-H, 3'-H, 5-H, 5'-H), 7.10–7.91 (6H, m, aromatic), 7.60 (2H, s, 4-H, 4'-H), 7.7–8.60 (4H, d, $J=9$ Hz, 2-H, 2'-H, 6-H, 6'-H); ms: m/z 632 (M^+). *Anal.* Calcd. for $\text{C}_{35}\text{H}_{28}\text{N}_4\text{O}_4\text{S}_2$: C, 66.44; H, 4.46; N, 8.85. Found: C, 67.21; H, 3.18; N, 8.88.

2-[6-(4-Chlorophenyl)-2-sulfanyl-4-pyrimidinyl]-4-{3-[6-(4-chlorophenyl)-2-sulfanyl-4-pyrimidinyl]-4-hydroxybenzyl}-phenol (5c). This compound was obtained as brown solid; yield 89%; mp 142–143°C; ir (KBr): ν 3035, 2580, 1634, 1590, 1216, 795 cm^{-1} ; ^1H nmr: δ 3.30 (2H, s, SH), 4.19 (2H, s, $-\text{CH}_2-$), 6.17 (2H, s, OH), 7.10–7.18 (4H, d, $J=9$ Hz, 3-H, 3'-H, 5-H, 5'-H), 7.57 (2H, s, 4-H, 4'-H), 7.67–8.0 (4H, d, $J=9$ Hz, 2-H, 2'-H, 6-H, 6'-H), 7.0–8.10 (6H, m, aromatic); ms: m/z 641 (M^+). *Anal.* Calcd. for $\text{C}_{33}\text{H}_{22}\text{Cl}_2\text{N}_4\text{O}_2\text{S}_2$: C, 61.78; H, 3.46; N, 8.73. Found: C, 61.71; H, 3.42; N, 8.70.

4-{4-Hydroxy-3-[6-(4-nitrophenyl)-2-sulfanyl-4-pyrimidinyl]benzyl}-2-[6-(4-nitrophenyl)-2-sulfanyl-4-pyrimidinyl]phenol (5d). This compound was obtained as red solid; yield 94%; mp 135–136°C; ir (KBr): ν 3040, 2580, 1634, 1590, 1216, 795 cm^{-1} ; ^1H nmr: δ 3.31 (2H, s, SH), 4.22 (2H, s, $-\text{CH}_2-$), 6.22 (2H, s, OH), 7.60 (2H, s, 4-H, 4'-H), 7.96 (4H, d, $J=9$ Hz, 2-H, 2'-H, 6-H, 6'-H), 7.70–8.20 (6H, m, aromatic), 8.22 (4H, d, $J=9$ Hz, 3-H, 3'-H, 5-H, 5'-H); ms: m/z 662 (M^+). *Anal.* Calcd. for $\text{C}_{33}\text{H}_{22}\text{N}_6\text{O}_6\text{S}_2$: C, 59.81; H, 3.35; N, 12.68. Found: C, 59.74; H, 3.31; N, 12.62.

2-[6-(4-Bromophenyl)-2-sulfanyl-4-pyrimidinyl]-4-{3-[6-(4-bromophenyl)-2-sulfanyl-4-pyrimidinyl]-4-hydroxybenzyl}-phenol (5e). This compound was obtained as brown solid; yield

92%; mp 123-124°C; ir (KBr): ν 3324, 3027, 2587, 1627, 1595, 1471, 1216, 790 cm^{-1} ; ^1H nmr: δ 3.31 (2H, s, SH), 4.21 (2H, s, $-\text{CH}_2-$), 6.02 (2H, s, OH), 7.15 (4H, d, $J=9$ Hz, 3-H, 3'-H, 5-H, 5'-H), 7.62 (2H, s, 4-H, 4'-H), 7.80-8.16 (6H, m, aromatic), 8.05 (4H, d, $J=9$ Hz, 2-H, 2'-H, 6-H, 6'-H); ms : m/z 730 (M^+). *Anal.* Calcd. for $\text{C}_{33}\text{H}_{22}\text{Br}_2\text{N}_4\text{O}_2\text{S}_2$: C, 54.26; H, 3.04; N, 7.67; Br, 21.88. Found: C, 54.20; H, 3.0; N, 7.61; Br, 21.64.

2-[6-(2-Chlorophenyl)-2-sulfanyl-4-pyrimidinyl]-4-[3-[6-(2-chlorophenyl)-2-sulfanyl-4-pyrimidinyl]-4-hydroxybenzyl]-phenol (5f). This compound was obtained as red solid; yield 91%; mp 130-131°C; ir (KBr): ν 3040, 2585, 1630, 1590, 1470, 795 cm^{-1} ; ^1H nmr: δ 3.32 (2H, s, SH), 4.20 (2H, s, $-\text{CH}_2-$), 6.16 (2H, s, OH), 7.10-8.15 (14H, m, aromatic), 7.60 (2H, s, 4-H, 4'-H); ms: m/z 641 (M^+). *Anal.* Calcd. for $\text{C}_{33}\text{H}_{22}\text{Cl}_2\text{N}_4\text{O}_2\text{S}_2$: C, 61.78; H, 3.46; N, 8.73. Found: C, 61.70; H, 3.41; N, 8.69.

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