

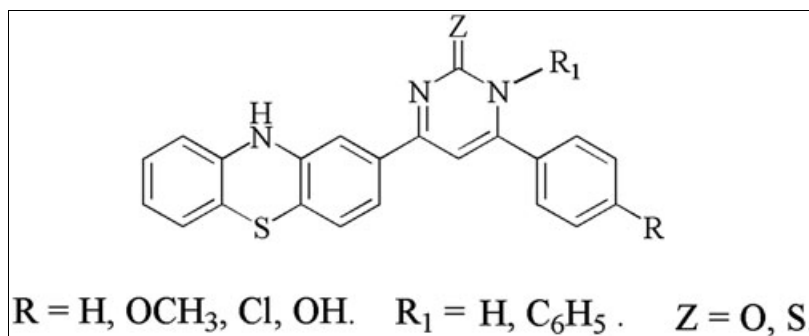
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A series of chalcones **3a–d** containing phenothiazine nucleus were prepared by Claisen–Schmidt condensation. The chalcones on treatment with urea, thiourea, phenyl urea, and phenyl thiourea in alcoholic KOH yielded compounds **4a–p**, and the structures of these compounds were confirmed by spectral and elemental analyses. The newly synthesized compounds were evaluated for antimicrobial activity.

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INTRODUCTION

Heterocyclic compounds particularly five- or six-membered ring compounds have occupied the first place among various classes of organic compounds for their diverse biological activities [1]. Pyrimidine rings have received significant attention owing to their diverse range of biological properties [2,3]. Pyrimidine derivatives are of interest because of their pharmacological properties including antibacterial [4], anticancer [5], antitubercular [6], antifungal [7], antimalarial [8], analgesic [9], antihypertensive [10], and anti-inflammatory activity [11,12].

Phenothiazine and related compounds have shown diverse biological activities including tranquilizers [13], anti-inflammatory [14], antimalarial [15], antipsychotropic [16], antimicrobial [17], antitubercular [18–20], antitumor [21–23] antihistamine [24], and analgesic [25,26] properties. These observations prompted us to synthesize the Phenothiazine derivatives containing pyrimidine ring and evaluate their antimicrobial activities.

RESULT AND DISCUSSION

Chalcones **3a–d** were obtained by Claisen–Schmidt reaction, that is, by treating 2-acetylphenothiazine with methanolic KOH (40%) and various aldehydes **2a–d**

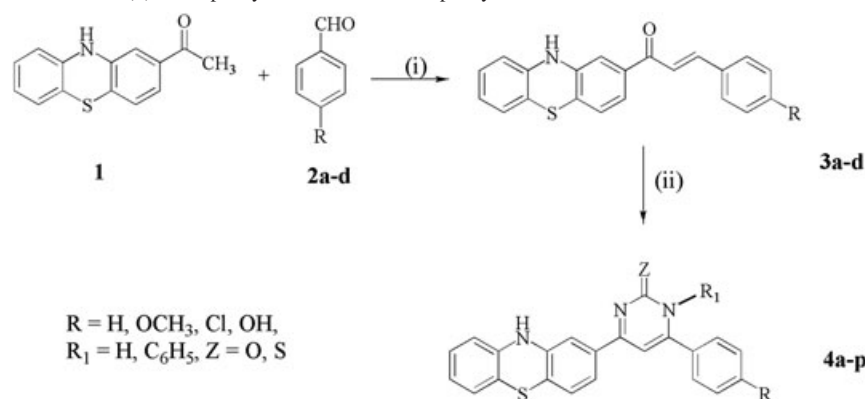
gave above 90% yield. The cyclization of chalcones **3a–d** with urea, thiourea, phenyl urea, and phenyl thiourea under basic condition led to the formation of new pyrimidine derivatives **4a–p**. The reaction sequences are outlined in Scheme 1.

Formation of substituted (10H-phenothiazin-2-yl) pyrimidin-2(1H)-one/thione derivatives (**4**) was confirmed on the basis of elemental analysis, IR, ¹H NMR, and mass. Compounds **4** showed IR absorption bands in the regions 3331–3360 cm^{−1} (NH Stretching), 1576–1593 cm^{−1} (C=N stretching), and 1463–1469 cm^{−1} (C=C pyrimidine). The ¹H NMR spectrum of compounds **4a–p** showed singlet at δ 8.11–8.79 due to phenothiazine NH proton. In case of compounds, **4a–d** and **4i–l** showed additional singlet at 8.02–8.08 due to pyrimidine NH protons. It showed multiplets at 7.87–6.66 due to aromatic protons and one singlet at δ 5.68–5.36 due to pyrimidine ring protons in all compounds. The ¹³C NMR spectrum of **4** showed signals at δ 115.3–144.7 due to aromatic carbons and at δ 104.7–109.8, 157.1–181.4 due to pyrimidine ring carbons. The physical data of compounds **4a–p** are recorded in Table 1.

CONCLUSIONS

In conclusion, we have described a mild, efficient, and convenient method for the synthesis of new 6-(10H-

Scheme 1. Synthetic route of compounds **4a–p**, R = H, OCH₃, Cl, OH, R₁ = C₆H₅, Z = O, S. Reaction reagents and conditions (i) 40% methanolic KOH, reflux 70°C, 2–3 h, 90%. (ii) Urea, phenyl urea, thiourea, and phenyl thiourea, reflux in methanolic KOH 70°C, 3–4 h, 67%.



phenothiazine 2-yl)-pyrimidin-2(1H)-one/thione derivatives from corresponding chalcones. All compounds of the series showed moderate to good biological activity. Hence, it is concluded that there is ample scope for further developing this field.

EXPERIMENTAL

General procedures. All chemicals were purchased from Aldrich and Merck chemicals, Mumbai (India) and were used without further purification. Melting points were determined in open capillaries using a Toshniwal melting point apparatus and are uncorrected. Formation of compound was routinely checked by TLC using Silica G, and the spots were exposed to iodine vapor for visualization. The IR spectra in KBr were recorded on a Perkin-Elmer FTIR spectrometer (ν_{max} in cm^{-1}); ^1H NMR and ^{13}C NMR spectra were obtained in DMSO- d_6 on a Bruker 300 MHz instrument using TMS as internal standard (chemical shifts in δ , ppm), mass spectra on LCQ Advantage Thermo Finiger spectrometer. Elemental analysis was performed on Carlo Erba 1108 analyzer.

General Procedure for synthesis of compounds 3a–d. To a solution of 2-acetyl phenothiazine **1** (0.01 mol) in absolute methanol (50 mL), benzaldehyde **2a** (0.01 mol) in 40% methanolic KOH (10 mL) was added and refluxed for 2–3 h at 70°C. The reaction mixture was then cooled to room temperature and poured on to crushed ice containing few drops of conc. HCl. The solid, thus, obtained was filtered and recrystallized from methanol to give **3a**.

Similarly, chalcones **3b–d** were synthesized by condensing 2-acetyl phenothiazine with various aldehydes **2b–d**.

(E)-1-(10H-Phenothiazin-8-yl)-3-phenyl-2-en-1-one (3a). Yield 90%, m.p. 201–203°C, IR (KBr) cm^{-1} : 3352 (NH), 3056 (Ar-H), 1653 (C=O), 1606 (C=C); ^1H NMR (DMSO- d_6): δ 8.11 (s, 1H, NH), 7.88 (d, $J = 3.8$ Hz, 1H, =CH-Ar), 7.56 (d, $J = 3.6$ Hz, 1H, =COCH=), 7.38–6.69 (m, 12H, Ar-H); ^{13}C NMR (DMSO- d_6): δ 118.5, 119.8, 120.8, 127.1, 127.9, 129.5, 131.9, 132.8, 133.9, 135.2, 136.8, 140.3, 141.6, 143.9, 144.9, 146.1, 147.6 (Ar-C, =CH=CH=C=O), 151.3 (=CH=CH=C=O); ^1H NMR (DMSO- d_6): δ 8.11 (s, 1H, NH), 7.88 (d, $J = 3.8$ Hz, 1H, =CH-Ar), 7.56 (d, $J = 3.6$ Hz, 1H, =COCH=), 7.38–6.69 (m, 12H, Ar-H); ^{13}C NMR (DMSO- d_6): δ 118.5, 119.8, 120.8, 127.1, 127.9, 129.5, 131.9, 132.8, 133.9, 135.2, 136.8, 140.3, 141.6, 143.9, 144.9, 146.1, 147.6 (Ar-C, =CH=CH=C=O), 151.3 (=CH=CH=C=O); ^1H NMR (DMSO- d_6): δ 8.11 (s, 1H, NH), 7.88 (d, $J = 3.8$ Hz, 1H, =CH-Ar), 7.56 (d, $J = 3.6$ Hz, 1H, =COCH=), 7.38–6.69 (m, 12H, Ar-H); ^{13}C NMR (DMSO- d_6): δ 118.5, 119.8, 120.8, 127.1, 127.9, 129.5, 131.9, 132.8, 133.9, 135.2, 136.8, 140.3, 141.6, 143.9, 144.9, 146.1, 147.6 (Ar-C, =CH=CH=C=O), 151.3 (=CH=CH=C=O); 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^1H NMR (DMSO- d_6): δ 8.11 (s, 1H, NH), 7.88 (d, $J = 3.8$ Hz, 1H, =CH-Ar), 7.56 (d, $J = 3.6$ Hz, 1H, =COCH=), 7.38–6.69 (m, 12H, Ar-H); ^{13}C NMR (DMSO- d_6): δ 118.5, 119.8, 120.8, 127.1, 127.9, 129.5, 131.9, 132.8, 133.9, 135.2, 136.8, 140.3, 141.6, 143.9, 144.9, 146.1, 147.6 (Ar-C, =CH=CH=C=O), 151.3 (=CH=CH=C=O); ^1H NMR (DMSO- d_6): δ 8.11 (s, 1H, NH), 7.88 (d, $J = 3.8$ Hz, 1H, =CH-Ar), 7.56 (d, $J = 3.6$ Hz, 1H, =COCH=), 7.38–6.69 (m, 12H, Ar-H); ^{13}C NMR (DMSO- d_6): δ 118.5, 119.8, 120.8, 127.1, 127.9, 129.5, 131.9, 132.8, 133.9, 135.2, 136.8, 140.3, 141.6, 143.9, 144.9, 146.1, 147.6 (Ar-C, =CH=CH=C=O), 151.3 (=CH=CH=C=O); ^1H NMR (DMSO- d_6): δ 8.11 (s, 1H, NH), 7.88 (d, $J = 3.8$ Hz, 1H, =CH-Ar), 7.56 (d, $J = 3.6$ Hz, 1H, =COCH=), 7.38–6.69 (m, 12H, Ar-H); ^{13}C NMR (DMSO- d_6): δ 118.5, 119.8, 120.8, 127.1, 127.9, 129.5, 131.9, 132.8, 133.9, 135.2, 136.8, 140.3, 141.6, 143.9, 144.9, 146.1, 147.6 (Ar-C, =CH=CH=C=O), 151.3 (=CH=CH=C=O); ^1H NMR (DMSO- d_6): δ 8.11 (s, 1H, NH), 7.88 (d, $J = 3.8$ Hz, 1H, =CH-Ar), 7.56 (d, $J = 3.6$ Hz, 1H, =COCH=), 7.38–6.69 (m, 12H, Ar-H); ^{13}C NMR (DMSO- d_6): δ 118.5, 119.8, 120.8, 127.1, 127.9, 129.5, 131.9, 132.8, 133.9, 135.2, 136.8, 140.3, 141.6, 143.9, 144.9, 146.1, 147.6 (Ar-C, =CH=CH=C=O), 151.3 (=CH=CH=C=O); ^1H NMR (DMSO- d_6): δ 8.11 (s, 1H, NH), 7.88 (d, $J = 3.8$ Hz, 1H, =CH-Ar), 7.56 (d, $J = 3.6$ Hz, 1H, =COCH=), 7.38–6.69 (m, 12H, Ar-H); ^{13}C NMR (DMSO- d_6): δ 118.5, 119.8, 120.8, 127.1, 127.9, 129.5, 131.9, 132.8, 133.9, 135.2, 136.8, 140.3, 141.6, 143.9, 144.9, 146.1, 147.6 (Ar-C, =CH=CH=C=O), 151.3 (=CH=CH=C=O); ^1H NMR (DMSO- d_6): δ 8.11 (s, 1H, NH), 7.88 (d, $J = 3.8$ Hz, 1H, =CH-Ar), 7.56 (d, $J = 3.6$ Hz, 1H, =COCH=), 7.38–6.69 (m, 12H, Ar-H); ^{13}C NMR (DMSO- d_6): δ 118.5, 119.8, 120.8, 127.1, 127.9, 129.5, 131.9, 132.8, 133.9, 135.2, 136.8, 140.3, 141.6, 143.9, 144.9, 146.1, 147.6 (Ar-C, =CH=CH=C=O), 151.3 (=CH=CH=C=O); ^1H NMR (DMSO- d_6): δ 8.11 (s, 1H, NH), 7.88 (d, $J = 3.8$ Hz, 1H, =CH-Ar), 7.56 (d, $J = 3.6$ Hz, 1H, =COCH=), 7.38–6.69 (m, 12H, Ar-H); ^{13}C NMR (DMSO- d_6): δ 118.5, 119.8, 120.8, 127.1, 127.9, 129.5, 131.9, 132.8, 133.9, 135.2, 136.8, 140.3, 141.6, 143.9, 144.9, 146.1, 147.6 (Ar-C, =CH=CH=C=O), 151.3 (=CH=CH=C=O); ^1H NMR (DMSO- d_6): δ 8.11 (s, 1H, NH), 7.88 (d, $J = 3.8$ Hz, 1H, =CH-Ar), 7.56 (d, $J = 3.6$ Hz, 1H, =COCH=), 7.38–6.69 (m, 12H, Ar-H); ^{13}C NMR (DMSO- d_6): δ 118.5, 119.8, 120.8, 127.1, 127.9, 129.5, 131.9, 132.8, 133.9, 135.2, 136.8, 140.3, 141.6, 143.9, 144.9, 146.1, 147.6 (Ar-C, =CH=CH=C=O), 151.3 (=CH=CH=C=O); ^1H NMR (DMSO- d_6): δ 8.11 (s, 1H, NH), 7.88 (d, $J = 3.8$ Hz, 1H, =CH-Ar), 7.56 (d, $J = 3.6$ Hz, 1H, =COCH=), 7.38–6.69 (m, 12H, Ar-H); ^{13}C NMR (DMSO- d_6): δ 118.5, 119.8, 120.8, 127.1, 127.9, 129.5, 131.9, 132.8, 133.9, 135.2, 136.8, 140.3, 141.6, 143.9, 144.9, 146.1, 147.6 (Ar-C, =CH=CH=C=O), 151.3 (=CH=CH=C=O); ^1H NMR (DMSO- d_6): δ 8.11 (s, 1H, NH), 7.88 (d, $J = 3.8$ Hz, 1H, =CH-Ar), 7.56 (d, $J = 3.6$ Hz, 1H, =COCH=), 7.38–6.69 (m, 12H, Ar-H); ^{13}C NMR (DMSO- d_6): δ 118.5, 119.8, 120.8, 127.1, 127.9, 129.5, 131.9, 132.8, 133.9, 135.2, 136.8, 140.3, 141.6, 143.9, 144.9, 146.1, 147.6 (Ar-C, =CH=CH=C=O), 151.3 (=CH=CH=C=O); ^1H NMR (DMSO- d_6): δ 8.11 (s, 1H, NH), 7.88 (d, $J = 3.8$ Hz, 1H, =CH-Ar), 7.56 (d, $J = 3.6$ Hz, 1H, =COCH=), 7.38–6.69 (m, 12H, Ar-H); ^{13}C NMR (DMSO- d_6): δ 118.5, 119.8, 120.8, 127.1, 127.9, 129.5, 131.9, 132.8, 133.9, 135.2, 136.8, 140.3, 141.6, 143.9, 144.9, 146.1, 147.6 (Ar-C, =CH=CH=C=O), 151.3 (=CH=CH=C=O); ^1H NMR (DMSO- d_6): δ 8.11 (s, 1H, NH), 7.88 (d, $J = 3.8$ Hz, 1H, =CH-Ar), 7.56 (d, $J = 3.6$ Hz, 1H, =COCH=), 7.38–6.69 (m, 12H, Ar-H); ^{13}C NMR (DMSO- d_6): δ 118.5, 119.8, 120.8, 127.1, 127.9, 129.5, 131.9, 132.8, 133.9, 135.2, 136.8, 140.3, 141.6, 143.9, 144.9,

Anal. Calcd for $C_{21}H_{14}ClNOS$: C, 69.32; H, 3.88; N, 3.85. Found: C, 69.19; H, 3.64; N, 3.73%.

(E)-3-(4-Hydroxyphenyl)-1-(10H-phenothiazin-8-yl)prop-2-en-1-one (3d). Yield 92%, m.p. 175–178°C, IR (KBr) cm^{-1} : 3353 (NH), 3054 (Ar-H), 1660 (C=O), 1611 (C=C); 1H NMR (DMSO- d_6): δ 8.11 (s, 1H, NH), 7.91 (d, J = 3.8 Hz, 1H, =CH-Ar), 7.55 (d, J = 3.6 Hz, 1H, =COCH=), 7.18–6.69 (m, 11H, Ar-H), 5.23 (s, 1H); ^{13}C NMR (DMSO- d_6): δ 114.3, 116.9, 119.3, 120.4, 120.9, 121.8, 124.9, 125.4, 128.6, 129.7, 132.9, 138.4, 141.2, 142.5, 143.6, 144.1 (Ar-C, =CH=CH=C=O), 147.3 (=CH=CH=C=O), 160.3 (Ar-C=OH), 191.1 (C=O); MS: m/z (%): 345 (80), 226 (68), 198 (50), 119 (48). Anal. Calcd for $C_{21}H_{15}NO_2S$: C, 73.02; H, 4.38; N, 4.06. Found: C, 72.86; H, 4.08; N, 3.93%.

General procedure for synthesis of compounds 4a–p. A mixture of chalcone **3a** (0.01 mol) and urea/phenyl urea/thiourea/phenyl thiourea (0.03 mol) in methanolic KOH (10 mL) was refluxed for 4 h at 70°C. The solid, thus, obtained was washed with water and recrystallized from methanol to give **4a–d**.

Similarly, **4e–p** were synthesized by using chalcones **3b–d**.

4-(10H-Phenothiazin-2-yl)-6-phenylpyrimidin-2(1H)-one (4a). IR (KBr) cm^{-1} : 3331 (NH), 3056 (Ar-H), 1593 (C=N), 1466 (C=C pyrimidine); 1H NMR (DMSO- d_6): δ 8.75 (s, 1H, NH, phenothiazine), 8.28 (d, J = 8.4 Hz, 2H, Ar-H), 8.06 (s, 1H, NH, pyrimidine), 7.69–6.66 (m, 12H, Ar-H), 5.50 (s, 1H); ^{13}C NMR (DMSO- d_6): δ 118.1, 119.8, 120.6, 120.9, 121.8, 127.1, 128.2, 128.9, 130.6, 134.6, 134.9, 135.3, 136.4, 137.1, 144.9, 145.1 (Ar-C), 109.2, 154.3, 166.4, 166.9 (pyrimidine-C); MS: m/z (%): 368 [M^+ -1] (98), 340 (74), 312 (46), and 238 (32). Anal. Calcd for $C_{22}H_{15}N_3OS$: C, 71.52; H, 4.09; N, 11.37. Found: C, 71.37; H, 4.01; N, 11.29%.

6-(4-Methoxyphenyl)-4-(10H-phenothiazin-2-yl)pyrimidin-2(1H)-one (4b). IR (KBr) cm^{-1} : 3341 (NH), 3056 (Ar-H), 1577 (C=N), 1468 (C=C pyrimidine); 1H NMR (DMSO- d_6): δ 8.79 (s, 1H, NH, phenothiazine), 8.28 (d, J = 8.4 Hz, 2H, Ar-H), 8.02 (s, 1H, NH, pyrimidine), 7.71 (d, J = 8.1 Hz, 2H, Ar-H), 7.63–6.67 (m, 7H, Ar-H), 5.61 (s, 1H), 3.68 (s, 3H); ^{13}C NMR (DMSO- d_6): δ 55.8 (OCH₃), 115.4, 118.1, 119.3, 120.6, 121.2, 122.6, 127.1, 127.8, 128.5, 129.6, 130.1, 130.3, 139.4, 140.1, 142.7 (Ar-C), 105.4, 162.3, 163.6, 165.4, 166.2 (pyrimidine-C, Ar-C=OCH₃); MS: m/z (%): 398 [M^+ -1] (99), 370 (78), 328 (15), 300 (50), and 240 (48); Anal. Calcd for $C_{23}H_{17}N_3O_2S$: C, 69.15; H, 4.29; N, 10.52. Found: C, 69.01; H, 4.11; N, 10.40%.

6-(4-Chlorophenyl)-4-(10H-phenothiazin-2-yl)pyrimidin-2(1H)-one (4c). IR (KBr) cm^{-1} : 3339 (NH), 3056 (Ar-H), 1583 (C=N), 1466 (C=C pyrimidine); 1H NMR (DMSO- d_6): δ 8.77 (s, 1H, NH, phenothiazine), 8.29 (d, J = 8.4 Hz, 2H, Ar-H), 8.04 (s, 1H, NH, pyrimidine), 7.74 (d, J = 8.1 Hz, 2H, Ar-H), 7.23–6.89 (m, 7H, Ar-H), 5.68 (s, 1H); ^{13}C NMR (DMSO- d_6): δ 118.2, 120.2, 120.8, 121.3, 122.5, 123.1, 128.5, 128.8, 129.6, 133.8, 134.3, 135.3, 135.8, 136.1, 141.6, 141.9 (Ar-C), 107.7, 157.1, 166.8, 167.5 (pyrimidine-C); MS: m/z (%): 402 [M^+ -1] (100), 374 (60), 344 (38), 314 (52) and 238 (28); Anal. Calcd for $C_{22}H_{14}N_3OSCl$: C, 65.45; H, 3.49; N, 10.40. Found: C, 65.59; H, 3.31; N, 10.22%.

6-(4-Hydroxyphenyl)-4-(10H-phenothiazin-2-yl) pyrimidin-2(1H)-one (4d). IR (KBr) cm^{-1} : 3340 (NH), 3048 (Ar-H), 1575 (C=N), 1466 (C=C pyrimidine); 1H NMR (DMSO- d_6): δ 8.71 (s, 1H, NH, phenothiazine), 8.26 (d, J = 8.3 Hz, 2H,

Ar-H), 8.05 (s, 1H, NH, pyrimidine), 7.73 (d, J = 8.1 Hz, 2H, Ar-H), 7.33–6.69 (m, 7H, Ar-H), 5.61 (s, 1H), 5.56 (s, 1H); ^{13}C NMR (DMSO- d_6): δ 116.8, 119.5, 120.3, 121.6, 122.1, 122.8, 123.5, 124.8, 128.3, 128.9, 129.4, 130.8, 131.3, 139.8, 140.4, (Ar-C), 108.7, 158.1, 159.7, 167.6, 168.5 (pyrimidine-C, Ar-C=OH); MS: m/z (%): 384 [M^+ -1] (98), 356 (66), 330 (40), and 328 (28); Anal. Calcd for $C_{22}H_{15}N_3O_2S$: C, 68.55; H, 3.92; N, 10.90. Found: C, 68.48; H, 3.82; N, 10.99%.

4-(10H-Phenothiazin-2-yl)-1,6-diphenylpyrimidin-2(1H)-one (4e). IR (KBr) cm^{-1} : 3343 (NH), 3050 (Ar-H), 1591 (C=N), 1467 (C=C pyrimidine); 1H NMR (DMSO- d_6): δ 8.35 (s, 1H, NH, phenothiazine), 7.87–6.69 (m, 17H, Ar-H), 5.39 (s, 1H); ^{13}C NMR (DMSO- d_6): δ 117.8, 118.5, 119.6, 120.4, 120.8, 121.6, 122.1, 125.3, 127.4, 128.1, 129.3, 129.8, 130.6, 132.4, 134.1, 134.9, 135.3, 136.2, 142.1, 142.8 (Ar-C), 103.2, 153.1, 156.2, 162.5 (pyrimidine-C); MS: m/z (%): 444 [M^+ -1] (88), 416 (60), 326 (48), 312 (20), and 238 (38); Anal. Calcd for $C_{28}H_{19}N_3OS$: C, 75.48; H, 4.30; N, 9.43. Found: C, 75.57; H, 4.51; N, 9.32%.

6-(4-Methoxyphenyl)-4-(10H-phenothiazin-2-yl)-1-phenylpyrimidin-2(1H)-one (4f). IR (KBr) cm^{-1} : 3336 (NH), 3048 (Ar-H), 1593 (C=N), 1469 (C=C pyrimidine); 1H NMR (DMSO- d_6): δ 8.11 (s, 1H, NH, phenothiazine), 7.78 (d, J = 8.4 Hz, 2H, Ar-H), 7.46 (d, J = 8.2 Hz, 2H, Ar-H), 7.35–6.69 (m, 12H, Ar-H), 5.37 (s, 1H), 3.73 (s, 3H); ^{13}C NMR (DMSO- d_6): δ 56.7 (OCH₃), 116.3, 118.6, 119.6, 120.8, 121.5, 122.3, 123.1, 124.3, 126.1, 128.3, 129.7, 130.3, 131.8, 134.4, 134.9, 135.5, 136.3, 143.8, 144.2 (Ar-C), 104.7, 158.1, 161.6, 168.3 (pyrimidine-C, Ar-C=OCH₃); MS: m/z (%): 474 [M^+ -1] (96), 446 (70), 356 (54), 342 (30), and 238 (42); Anal. Calcd for $C_{29}H_{21}N_3OS$: C, 73.14; H, 4.55; N, 8.84. Found: C, 73.27; H, 4.41; N, 8.89%.

6-(4-Methoxyphenyl)-4-(10H-phenothiazin-2-yl)pyrimidine-2(1H)-thione (4j). IR (KBr) cm^{-1} : 3349 (NH), 3056 (Ar-H), 1577 (C=N), 1468 (C=C pyrimidine), 1270 (C=S); 1H NMR (DMSO- d_6): δ 8.59 (s, 1H, NH, phenothiazine), 8.08 (d, J = 8.1 Hz, 2H, Ar-H), 8.02 (s, 1H, NH, pyrimidine), 7.86 (d, J = 8.0 Hz, 2H, Ar-H), 7.47–6.60 (m, 7H, Ar-H), 5.38 (s, 1H), 3.65 (s, 3H); ^{13}C NMR (DMSO- d_6): δ 56.2 (OCH₃), 115.3, 118.2, 119.4, 120.7, 121.4, 122.8, 123.6, 127.4, 128.6, 129.5, 134.5, 135.6, 136.4, 144.4, 144.7 (Ar-C), 104.9, 160.3, 165.8, 178.6, 181.2 (pyrimidine-C, Ar-C=OCH₃); MS: m/z (%): 415 [M^+] (100), 371 (70), 342 (40) and 238 (22); Anal. Calcd for $C_{23}H_{17}N_3OS_2$: C, 66.48; H, 4.12; N, 10.11. Found: C, 66.59; H, 3.90; N, 10.19%.

6-(4-Chlorophenyl)-4-(10H-phenothiazin-2-yl)pyrimidine-2(1H)-thione (4k). IR (KBr) cm^{-1} : 3347 (NH), 3050 (Ar-H), 1576 (C=N), 1465 (C=C pyrimidine), 1273 (C=S); 1H NMR (DMSO- d_6): δ 8.52 (s, 1H, NH, phenothiazine), 8.18 (d, J = 8.1 Hz, 2H, Ar-H), 7.93 (s, 1H, NH, pyrimidine), 7.86 (d, J = 8.0 Hz, 2H, Ar-H), 7.26–6.63 (m, 7H, Ar-H), 5.36 (s, 1H); ^{13}C NMR (DMSO- d_6): δ 118.3, 120.4, 121.3, 121.9, 122.6, 123.3, 128.3, 128.8, 129.7, 133.5, 134., 135.6, 135.5, 136.2, 143.6, 143.8 (Ar-C), 105.7, 166.3, 178.5, 181.4 (pyrimidine-C); MS: m/z (%): 419 [M^+] (96), 375 (78), 346 (24), and 238 (28); Anal. Calcd for $C_{23}H_{14}N_3S_2Cl$: C, 62.92; H, 3.36; N, 10.01. Found: C, 63.04; H, 3.49; N, 9.89%.

6-(4-Chlorophenyl)-4-(10H-phenothiazin-2-yl)-1-phenylpyrimidine-2(1H)-thione (4o). IR (KBr) cm^{-1} : 3366 (NH), 3048 (Ar-H), 1591 (C=N), 1463 (C=C pyrimidine), 1272 (C=S); 1H NMR (DMSO- d_6): δ 8.19 (s, 1H, NH, phenothiazine), 8.08 (d,

Table 2
Antibacterial activity of the compounds **4a–p**.

Compound	Antibacterial activity			
	<i>Bacillus subtilis</i>	<i>Escherichia coli</i>	<i>Staphylococcus aureus</i>	<i>Pseudomonas aeruginosa</i>
4a	10(25)	18(10)	12(5)	12(25)
4b	14(5)	16(5)	12(25)	12(25)
4c	12(25)	18(5)	12(5)	22(5)
4d	18(25)	19(10)	17(15)	20(25)
4e	16(20)	20(15)	18(10)	21(20)
4f	17(15)	22(15)	16(20)	15(20)
4g	15(20)	21(10)	20(20)	17(25)
4h	20(15)	20(15)	21(15)	19(25)
4i	13(5)	19(5)	15(5)	10(10)
4j	16(25)	20(5)	15(5)	8(10)
4k	17(25)	24(5)	12(25)	10(25)
4l	18(15)	24(10)	14(20)	11(15)
4m	17(15)	26(15)	19(20)	14(10)
4n	14(20)	25(20)	20(15)	17(15)
4o	11(20)	24(20)	21(10)	14(15)
4p	12(15)	21(20)	22(20)	10(20)
Ampicillin	24(5)	26(5)	24(5)	23(5)

MIC values are given in brackets; MIC ($\mu\text{g/mL}$) = minimum inhibitory concentration, that is, lowest concentration to completely inhibit bacterial growth; zone of inhibition is expressed in mm.

$J = 8.2$ Hz, 2H, Ar-H), 7.66 (d, $J = 8.0$ Hz, 2H, Ar-H), 7.25–6.66 (m, 12H, Ar-H), 5.37 (s, 1H); ^{13}C NMR (DMSO- d_6): δ 117.9, 119.6, 120.5, 120.9, 121.7, 122.3, 125.6, 127.6, 128.3, 129.2, 130.2, 130.7, 133.5, 134.2, 134.4, 135.3, 136.2, 137.4, 142.1, 142.8 (Ar-C), 104.6, 157.3, 168.5, 181.2 (pyrimidine-C); MS: m/z (%): 495 [M^+] (99), 451 (66), 360 (36), 347 (52), and 238 (22); Anal. Calcd for $\text{C}_{28}\text{H}_{18}\text{N}_3\text{S}_2\text{Cl}$: C, 67.80; H, 3.66; N, 8.47. Found: C, 67.97; H, 3.51; N, 8.29%.

6-(4-Hydroxyphenyl)-4-(10H-phenothiazin-2-yl)-1-phenylpyrimidine-2(1H)-thione (4p). IR (KBr) cm^{-1} : 3360 (NH), 3052 (Ar-H), 1578 (C=N), 1465 (C=C pyrimidine), 1272 (C=S); ^1H NMR (DMSO- d_6): δ 8.13 (s, 1H, NH, phenothiazine), 8.04 (d, $J = 8.2$ Hz, 2H, Ar-H), 7.69 (d, $J = 8.0$ Hz, 2H, Ar-H), 7.28–6.67 (m, 12H, Ar-H), 5.57 (s, 1H), 5.37 (s, 1H); ^{13}C NMR (DMSO- d_6): δ 116.6, 118.6, 120.8, 121.5, 122.3, 123.1, 124.4, 127.9, 128.8, 129.7, 131.3, 132.2, 133.7, 134.5, 135.8, 136.3,

Table 3
Antifungal activity of the compounds **4a–p**.

Compound	Antifungal activity			
	<i>Aspergillus niger</i>	<i>Aspergillus fumigatus</i>	<i>Aspergillus flavus</i>	<i>Candida albicans</i>
4a	17(5)	18(5)	14(15)	10(15)
4b	18(5)	18(5)	16(15)	13(15)
4c	12(5)	18(5)	20(15)	10(15)
4d	17(10)	22(10)	13(10)	13(15)
4e	16(15)	22(10)	17(15)	12(10)
4f	15(10)	19(10)	13(15)	20(20)
4g	18(20)	16(10)	19(10)	21(20)
4h	17(20)	20(25)	17(15)	20(25)
4i	14(15)	18(5)	21(5)	12(20)
4j	12(15)	18(5)	18(5)	12(20)
4k	12(15)	10(5)	10(5)	12(20)
4l	23(10)	18(10)	20(10)	14(15)
4m	25(20)	19(15)	25(15)	12(15)
4n	24(20)	21(20)	26(15)	14(20)
4o	25(20)	20(20)	22(15)	13(20)
4p	22(20)	19(15)	24(20)	14(20)
Fluconazole	24(5)	22(5)	16(5)	19(5)

MIC values are given in brackets, MIC ($\mu\text{g/mL}$) = minimum inhibitory concentration, that is, lowest concentration to completely inhibit fungal growth; zone of inhibition is expressed in mm.

137.6, 143.8, 144.2 (Ar-C), 104.1, 158.2, 165.6, 181.3 (pyrimidine-C, Ar-C=OH); MS: m/z (%): 477 [M^+] (96), 433 (74), 342 (28), 329 (40), and 238 (28); Anal. Calcd for $C_{28}H_{19}N_3S_2O$: C, 70.41; H, 4.01; N, 8.80. Found: C, 70.59; H, 4.06; N, 8.90%.

BIOLOGICAL ACTIVITY

Antibacterial activity. The newly synthesized compounds were screened for their antibacterial activity against *Bacillus subtilis* (ATCC-11774), *Escherichia coli* (ATCC-25922), *Staphylococcus aureus* (ATCC-25923), and *Pseudomonas aeruginosa* (ATCC-27853) bacterial strains by disc diffusion method [27, 28]. The test compounds were prepared with different concentrations using dimethylsulphoxide. The discs of each concentration were placed in triplicate in nutrient agar medium seeded with fresh bacteria separately. The incubation was carried out at 37°C for 24 h. Ampicillin was used as a standard drug. Solvent and growth controls were prepared and kept. Zones of inhibition and minimum inhibitory concentrations (MICs) were noted. The results of antibacterial studies are given in Table 2.

Antifungal activity. Newly prepared compounds were screened for their antifungal activity against *Aspergillus niger* (NCIM no. 617), *Aspergillus flavus* (NCIM no. 524), *Aspergillus fumigatus* (NCIM no. 902), and *Candida albicans* (NCIM no. 300) in DMSO by serial plate dilution method [29, 30]. Sabouraud agar media were prepared by dissolving peptone (1 g), D-glucose (4 g) and agar (2 g) in distilled water (100 mL) and adjusting pH to 5.7. A particular fungal strain was transferred to 3-mL saline to get a suspension of corresponding species. Agar media (20 mL) were poured into each Petri dish. The plates were dried by placing in an incubator at 37°C for 1 h. Using an agar punch, wells were made and each well was labeled. A control was also prepared in triplicate and maintained at 37°C for 2 to 3 days. Zone of inhibition and MIC were noted. The activity of each compound was compared with fluconazole as the standard drug. The results of antifungal studies are given in Table 3.

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