This section deals with the synthesis, antimicrobial and cytotoxic activities of 2-(2-((benzoxazol-2-yl)methylthio)-6-methylpyrimidin-4-ylthio)benzoxazole, 2-(2-((benzothiazol-2-yl)methylthio)-6-methylpyrimidin-4-ylthio)benzothiazole, 2-(2-((1H-benzimidazol-2-yl)methylthio)-6-methylpyrimidin-4-ylthio)-1H-benzimidazole, 2-(4-((benzoxazol-2-yl)methylthio)-6-methylpyrimidin-2-ylthio)methyl)benzoxazole, 2-(4-((benzothiazol-2-yl)methylthio)-6-methylpyrimidin-2-ylthio)methyl)benzothiazole, 2-((4-((1H-benzimidazol-2-yl)methylthio)-6-methylpyrimidin-2-ylthio)methyl)-1H-benzimidazole, 

N-(2-((benzoxazol-2-yl)methylthio)-6-methylpyrimidin-4-yl)benzoxazol-2-amine, N-(2-((benzothiazol-2-yl)methylthio)-6-methylpyrimidin-4-yl)benzothiazol-2-amine, N-(2-((1H-benzimidazol-2-yl)methylthio)-6-methylpyrimidin-4-yl)-1H-benzimidazol-2-amine.

The synthon 4-chloro-6-methylpyrimidine-2-thiol (43) was prepared as follows. The reaction of ethyl acetoacetate with thiourea in the presence of sodium methoxide produced 6-methyl-2-thioxo-2,3-dihydropyrimidin-4(1H)-one. This on treatment with POCl3 resulted in compound 43 (Scheme III.1). The IR spectrum of 43 displayed an absorption band at 1564 cm⁻¹ corresponding to C=N. The 1H NMR spectrum of 43 showed three singlets at δ 2.34, 6.94 and 11.04 ppm due to CH₃, C₅-H and SH. The signal of SH disappeared on deuteration.

The benzoxazol-2-ylmethanethiol (44), benzothiazol-2-ylmethanethiol (45) and 1H-benzimidazol-2-ylmethanethiol (46) were obtained by the reaction of 2-aminophenol, 2-aminothiophenol and o-phenylenediamine with thioglycolic acid in the presence of 5N HCl (Scheme III.2). The IR spectra of the compounds 44, 45 and 46 exhibited an
absorption band in the region 1557-1562 (C=N). The compound 46 showed an additional band at 3348 cm\(^{-1}\) due to NH. The \(^1\)H NMR spectra of 44, 45 and 46 presented two singlets at \(\delta\) 4.19, 4.23, 4.13 and 11.08, 11.12, 11.07 corresponding to CH\(_2\) and SH. The compound 46 displayed another broad singlet at 11.24 ppm due to NH. The signals of SH and NH disappeared on deuteration. The benzoaxazol-2-amine (47) and 1H-benzimidazol-2-amine (49) were prepared by the treatment of \(o\)-aminophenol or \(o\)-phenylenediamine with cyanogen bromide. However, benzothiazol-2-amine (48) was obtained from aniline and ammonium thiocyanate in the presence of bromine in acetic acid (Scheme III.2). The IR spectra of 47, 48 and 49 exhibited absorption bands in the regions 1559-1568 and 3353-3359 & 3441-3447 cm\(^{-1}\) due to C=N and NH\(_2\). The compound 49 presented an additional band at 3341 cm\(^{-1}\) due to NH. The \(^1\)H NMR spectra of 47, 48 and 49 displayed a broad singlet at \(\delta\) 7.06, 7.11, 7.02 ppm due to NH\(_2\) in addition to the signals of aromatic protons. The compound 49 showed another broad singlet at 11.31 ppm due to NH of benzimidazole. The signals of highly acidic protons disappeared on deuteration (Scheme III.2).

![Scheme III.2](image)

The reaction of compound 1 with 43 in the presence of triethylamine in tetrahydrofuran resulted in 2-((4-chloro-6-methylpyrimidin-2-ythio)methyl)benzoxazole (50). Similarly, 2-((4-chloro-6-methylpyrimidin-2-ythio)methyl)benzothiazole (51) and 2-((4-chloro-6-methylpyrimidin-2-ythio)methyl)-1H-benzimidazole (52) were prepared by treating the compounds 2 and 3 with 43 (Scheme III.3 & Table III.1). In the IR
spectra of the compounds 50, 51 and 52 the absorption band observed in the region 1561-1568 was attributed to C=N. Besides the compound 52 showed an additional band at 3353 cm$^{-1}$ due to NH (Table III.2). The $^1$H NMR spectra of 50, 51 and 52 (Fig. III.1) exhibited three singlets at $\delta$ 2.39, 2.43, 2.36; 4.21, 4.26, 4.19 and 7.61, 7.64, 7.60 due to methyl, methylene and C$_5$-H protons (Table III.3). The compound 52 displayed another singlet at 11.69 ppm due to NH which disappeared on deuteration. The $^{13}$C NMR spectra of 50, 51 and 52 (Fig. III.2) showed signals at $\delta$ 24.5, 24.9, 24.3 (CH$_3$), 36.8, 38.5, 36.1 (CH$_2$), 111.5, 111.7, 111.2 (C-5), 154.5, 170.2, 143.6 (C-2'), 161.5, 161.8, 161.1 (C-4), 169.4, 169.7, 169.0 (C-6) and 174.5, 174.9, 174.2 ppm (C-2) (Table III.3). The HRMS mass spectra of 50, 51 and 52 (Fig. III.3) presented M+Na peaks at m/z 314.7452, 330.8109 and 313.7603 corresponding to the chemical compositions C$_{13}$H$_{10}$ClN$_3$OS+Na, C$_{13}$H$_{10}$ClN$_3$S$_2$+Na and C$_{13}$H$_{11}$ClN$_4$S+Na.

The pyrimidinyl benzazoles 50, 51 and 52 were exploited to prepare pyrimidinyl bis benzazoles. The reaction of compound 22 with 50 in the presence of methanesulfonic acid resulted in 2-(2-((benzoxazol-2-yl)methylthio)-6-methylpyrimidin-4-ylthio)benzoxazole (53). The 2-(2-((benzothiazol-2-yl)methylthio)-6-methylpyrimidin-4-ylthio)benzothiazole (54) and 2-(2-((1H-benzimidazol-2-yl)methylthio)-6-methylpyrimidin-4-ylthio)-1H-benzimidazole (55) were also prepared by the treatment of 23 with 51 and 24 with 52 under similar reaction conditions (Scheme III.4 & Table III.1). The IR spectra of 53, 54 and 55 displayed an absorption band in the region 1578-1586 due to C=N. The compound 55 exhibited another band at 3367 cm$^{-1}$ due to NH (Table III.2). The $^1$H NMR spectra of 53 (Fig. III.4), 54 and 55 exhibited three singlets at $\delta$ 2.45, 2.48,
2.41; 4.30, 4.35, 4.28 and 7.13, 7.17, 7.10 ppm due to methyl, methylene and C5-H protons (Table III.3). The compound 55 displayed another broad singlet at 11.75 ppm due to NH which disappeared when D2O was added. The 13C NMR spectra of 53 (Fig. III.5) presented signals at δ 26.6, 36.6, 113.3, 154.8, 155.6, 166.4, 173.5, 188.5, 54 at 26.8, 38.7, 113.7, 157.9, 170.5, 166.7, 173.8, 188.7 and 55 at 26.3, 36.3, 113.1, 143.4, 144.9, 166.1, 173.1, 188.1 ppm which are accounted for CH3, CH2, C-5, C-2’, C-2”, C-6, C-2 and C-4, respectively (Table III.3).

![Scheme III.4](image)

In a much similar way, 2-((4-((benzoxazol-2-yl)methylthio)-6-methylpyrimidin-2-ylthio)methyl)benzoxazole (56) was obtained by treating 44 with 50 in the presence of a catalytic amount of methanesulfonic acid. Likewise, 2-((4-((benzothiazol-2-yl)methylthio)-6-methylpyrimidin-2-ylthio)methyl)benzothiazole (57) and 2-((4-((1H-benzimidazol-2-yl)methylthio)-6-methylpyrimidin-2-ylthio)methyl)-1H-benzimidazole (58) were prepared by the reaction of 45 with 51 and 46 with 52 (Scheme III.5 & Table III.1). The IR spectra of these compounds exhibited an absorption band in the region 1566-1577 for C=N. The compound 58 showed another absorption band for NH at 3361 cm⁻¹ (Table III.2). The 1H NMR spectra of 56, 57 and 58 (Fig. III.6) displayed four singlets at δ 2.44, 2.49, 2.42 (CH3), 4.20, 4.24, 4.18 (CH2-C2’), 4.23, 4.26, 4.22, (CH2-C2”) and 7.07, 7.09,
7.04 ppm (C5-H) (Table III.3). The 13C NMR spectra of 56 showed signals at δ 26.5, 36.4, 36.7, 116.5, 154.7, 155.3, 165.6, 172.4, 173.3, 57 at 26.9, 38.9, 39.2, 116.9, 170.3, 170.8, 165.9, 172.7, 173.6 and 58 at (Fig. III.7) 26.2, 36.2, 36.5, 116.3, 143.5, 144.1, 165.4, 172.1, 172.9 ppm which were attributed to CH3, CH2-C2, CH2-C2', C-5, C-2', C-2'', C-6, C-4, C-2, respectively (Table III.3).

On the other hand, methanesulfanyl and amino linked pyrimidinyl bis benzazoles-
N-(2-((benzoxazol-2-yl)methylthio)-6-methylpyrimidin-4-yl)benzoxazol-2-amine (59),
N-(2-((benzothiazol-2-yl)methylthio)-6-methylpyrimidin-4-yl)benzothiazol-2-amine (60)
and
N-(2-((1H-benzimidazol-2-yl)methylthio)-6-methylpyrimidin-4-yl)-1H-benzimidazol-2-amine (61) were prepared by the reaction of 47 with 50, 48 with 51 and 49 with 52 in the presence of methanesulfonic acid in ethanol (Scheme III.6 & Table III.1).

In the IR spectra of these compounds the absorption bands observed in the regions
1573-1584 and 3348-3372 cm⁻¹ were assigned to C=N and NH (Table III.2). The 1H NMR spectra of 59, 60 and 61 (Fig. III.8) displayed three singlets at δ 2.54, 2.56, 2.51; 4.33, 4.37, 4.32 and 7.01, 7.05, 6.99 ppm due to methyl, methylene and C5-H protons (Table III.3). Besides, a broad singlet was observed at 8.56, 8.58, 8.52 due to NH. The compound 61 displayed another abroad singlet at 11.82 ppm due to NH of benzimidazole. The signals of NH disappeared on deuteration. The 13C NMR spectra of
59, 60 and 61 (Fig. III.9) exhibited signals at δ 26.9, 27.2, 26.5 (CH₃), 37.3, 39.5, 37.1 (CH₂), 101.6, 101.9, 101.2 (C-5), 154.9, 170.6, 143.6 (C-2′), 160.4, 176.3, 144.9 (C-2″), 168.3, 168.7, 168.1 (C-6), 169.5, 169.8, 169.3 (C-4) and 172.7, 172.9, 172.5 (C-2) (Table III.3). In the HRMS mass spectra of 59, 60 and 61 (Fig. III.10) the M+Na peaks observed at m/z 412.4196, 444.5501 and 410.4501 are in agreement with their chemical compositions C₂₀H₁₅N₅O₂S+Na, C₂₀H₁₅N₅S₃+Na and C₂₀H₁₇N₇S+ Na.