Synthesis and Biological Activity of Some 3,5-Diaryl-1-benzothiazolopyrazoline Derivatives: Reaction of Chalcones with 2-Hyrazinobenzothiazoles

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Abstract: A series of 3,5-diaryl-1-benzothiazolopyrazoline derivatives were synthesized by the reaction of appropriately substituted chalcones and 2-hyrazinobenzothiazole in ethanol. The synthesized heterocycles have been characterized on the basis of their chemical properties and spectroscopic data. These compounds were tested for biological activity against a variety of test organisms.

Keywords: Chalcones, 2-Hyrazinobenzothiazole, 3,5-Diaryl-1-benzothiazolopyrazoline, Biological activity

Introduction

Heterocycles bearing nitrogen, sulphur and thiazole moieties constitute the core structure of a number of biologically interesting compounds. Pyrazolines are an interesting group of compounds, many of which possess wide-spread pharmacological properties such as analgesic, antipyretic, antidepressant and antirheumatic activities^{1,2} and are also known for their pronounced anti-inflammatory activity³ and are used as potent antidiabetic agents^{4,5}. Recently, pyrazolines were reported as a DP-IV inhibitors and antitumor agents⁶⁻⁸. Some nitrogen heterocyclic compounds were reported to be antiparkinsonian⁹, anticancer^{10,11}, antimicrobial¹²⁻¹⁵ and anti-inflammatory agents^{16,17}. Due to the interesting activity of various substituted pyrazolines as biological agents considerable attention has been focused on this class. In addition, pyrazolines have played a crucial part in the development of theory in heterocyclic chemistry and also used extensively in organic synthesis¹⁸⁻²². Benzothiazole and its derivatives²³⁻²⁷ have been recognized as a class of medicinal importance. Benzothiazoles have also been screened for their antituberculosic activity²⁸. Benzothiazole derivatives represent an extensive group of heterocyclic compounds, several of which have already

found application in the medical sphere as medicines²⁹ as well as in agriculture^{30, 31}. Many of 2-R substituted benzothiazoles are known as substances with antibacterial and antifungal activities³²⁻³⁴ and are reported also to be active as antineoplastics³⁵ agent. Keeping in view the biological and clinical importance of benzothiazoles and pyrazolines, in this paper we report the synthesis and biological activity of new 3,5-diaryl-1-benzothiazolopyrazoline derivatives.

Experimental

General procedures

Melting points were determined by the open tube capillary method and are uncorrected. The purity of the compounds was controlled by thin layer chromatography (TLC). IR spectra were recorded as KBr pellets on Perkin-Elmer spectrum RX1 spectrophotometer. Carbon, hydrogen, nitrogen and sulphur were estimated by Thermo Finnigan FLASH EA 1112 elemental analyzer. ¹H-NMR spectra were recorded on Bruker DRX-300 spectrometer at room temperature. Mass spectra were measured on JEOL SX 102/DA-6000 mass spectrometer. Substituted chalcones (**1-20**) were prepared according to the reported methods.

Synthesis of 2-hydrazinobenzothiazole

To a suspension of 2-aminobenzothiazole (7.5 g) in ethylene glycol (40 mL), hydrazine hydrate (100%, 10 mL) and concentrated hydrochloric acid (10 mL) was added at 5-6 °C. The reaction mixture was refluxed for 2-3 h and cooled to room temperature. The reaction mixture was filtered and resulting precipitate was washed with distilled water. The resulting crude was crystallized from ethanol to obtained brownish black crystalline product.

General procedure for the preparation of compounds(21-40)

A mixture of substituted chalcone (**1-20**, 10.00 m mol) and 2-hydrazinobenzothiazole (10.00 m mol) in ethanol (50 mL) was refluxed for 5 h and then cooled to room temperature. The precipitate was separated by filtration, washed with water and crystallized from a mixture of alcohol and chloroform (1:1) to obtained 3, 5-diaryl-1-benzothiazolopyrazoline derivatives (Scheme 1).

3,5-Diphenyl-1-benzothiazolopyrazoline(21)

Obtained as white crystals in 70% yield, m.p. 174-175 °C; ¹H NMR (δ): 3.25 (1H,dd, CH₂(Pyraz)), 3.90 (1H,dd, CH₂(Pyraz)), 5.80 (1H,dd, CH(Pyraz)), 7.00-7.90(14H, m, ArH); IR(ν) max: 3400, 3030, 1600, 1490, 1440, 1400, 1320, 1280, 1230, 1120, 1020, 880, 810 760, 730 700, 670, 540 and 430 cm⁻¹; MS, *m/z*: 355, 354, 278, 233, 154, 126, 112, 100, 86. Anal. Calcd. for C₂₂H₁₇N₃S: C, 74.36; H, 4.78; N, 11.83; S, 9.02. Found: C, 74.43; H, 4.72; N, 11.90; S, 9.01%.

3(2'-Hydroxyphenyl)-5-phenyl-1-benzothiazolopyrazoline(22)

Obtained as white crystals in 80% yield, m.p. 187-188 °C; ¹H NMR (δ): 3.40 (1H,dd, CH₂(Pyraz)), 4.00 (1H, dd, CH₂(Pyraz)), 5.75 (1H,dd, CH(Pyraz)), 6.90-7.80 (13H, m, ArH); 10.11 (1H, s, OH); IR (ν) max: 3400, 3210, 3030, 3000-2500 (Stretching vibrations), 1610, 1590, 1490, 1460, 1440, 1400, 320, 1300, 1250, 1140, 1040, 1020, 880, 830, 760, 700, 660, 570, 500 and 440 cm⁻¹; MS, *m/z*: 371, 370, 354, 294, 277, 170, 153, 128, 111, 102, 85. Anal. Calcd. for C₂₂H₁₇N₃OS: C, 71.15; H, 4.58; N, 11.32; S, 8.62. Found: C, 71.25; H, 4.45; N, 11.32; S, 8.63%.

3(4'-Chlorophenyl)-5-phenyl-1-benzothiazolopyrazoline(23)

Obtained as white crystals in 75% yield, m.p. 165-166 °C; ¹H NMR (δ): 3.26 (1H, dd, CH₂(Pyraz)), 3.91 (1H, dd, CH₂(Pyraz)), 5.81 (1H,dd, CH(Pyraz)), 7.01-7.91 (14H,m, ArH); IR (ν) max: 3400, 3030, 2900, 1600-1490, 1440, 1400, 1320, 1280, 1240, 1140, 1090, 880, 820, 750, 720, 700, 610, 530

and 430 cm^{-1} ; MS, m/z : 389, 388, 352, 312, 276, 188, 152, 146, 120, 110, 84. Anal. Calcd. for $\text{C}_{22}\text{H}_{16}\text{ClN}_3\text{S}$: C, 67.86; H, 4.11; N, 10.79; S, 8.23 Found: C, 67.95; H, 4.21; N, 10.79; S, 8.22%.

3(4'-Methylphenyl)-5-phenyl-1-benzothiazolopyrazoline (24)

Obtained as white crystals in 78% yield, m.p. 160-161 $^{\circ}\text{C}$; ^1H NMR (δ): 3.24 (1H, dd, $\text{CH}_2(\text{Pyraz})$), 3.88 (1H, dd, $\text{CH}_2(\text{Pyraz})$), 5.82 (1H, dd, $\text{CH}(\text{Pyraz})$), 7.00-7.88 (14H, m, ArH); IR (ν) max: 3400, 3030, 2900, 1600, 1490, 1440, 1400, 1330, 1280, 1230, 1120, 1040, 1020, 880, 810, 750, 690, 530 and 430 cm^{-1} ; MS, m/z : 369, 368, 354, 292, 277, 168, 153, 126, 111, 100, 85. Anal. Calcd. for $\text{C}_{23}\text{H}_{19}\text{N}_3\text{S}$: C, 74.79; H, 5.14; N, 11.38; S, 8.67. Found: C, 74.96; H, 5.08; N, 11.37; S, 8.68%.

3(4'-Methoxyphenyl)-5-phenyl-1-benzothiazolopyrazoline(25)

Obtained as white crystals in 71% yield, m.p. 149-150 $^{\circ}\text{C}$; ^1H NMR (δ): 3.30 (1H, dd, $\text{CH}_2(\text{Pyraz})$), 3.90 (1H, dd, $\text{CH}_2(\text{Pyraz})$), 5.75 (1H, dd, $\text{CH}(\text{Pyraz})$), 6.80-7.80 (13H, m, ArH); 3.80 (1H, s, $-\text{OCH}_3$); IR (ν) max: 3400, 3220, 3030, 1660, 1600, 1500, 1440, 1310, 1250, 1170, 1120, 1050, 880, 830, 760, 700, 580, 530 and 430 cm^{-1} ; MS, m/z : 385, 384, 354, 308, 277, 184, 153, 142, 126, 111, 85. Anal. Calcd. for $\text{C}_{23}\text{H}_{19}\text{N}_3\text{OS}$: C, 71.68; H, 4.93; N, 10.90; S, 8.31. Found: C, 71.73; H, 4.87; N, 10.93; S, 8.29%.

3-Phenyl-5-(2-hydroxyphenyl)-1-benzothiazolopyrazoline(26)

Obtained as white crystals in 65% yield, m.p. 230-231 $^{\circ}\text{C}$; ^1H NMR (δ): 3.60 (1H, dd, $\text{CH}_2(\text{Pyraz})$), 3.95 (1H, dd, $\text{CH}_2(\text{Pyraz})$), 6.20 (1H, dd, $\text{CH}(\text{Pyraz})$), 6.80-7.90 (13H, m, ArH); 11.15 (1H, s, $-\text{OH}$); IR (ν) max: 3400, 3030, 3000, 2500, 1600, 1530, 1490, 1450, 1280, 1230, 1130, 1100, 1020, 890, 750, 690, 530 and 430 cm^{-1} ; MS, m/z : 371, 370, 354, 294, 277, 170, 153, 128, 111, 102, 85. Anal. Calcd. for $\text{C}_{22}\text{H}_{17}\text{N}_3\text{OS}$: C, 71.15; H, 4.58; N, 11.32; S, 8.63 Found: C, 71.23; H, 4.52; N, 11.41; S, 8.65%.

3(2'-Hydroxyphenyl)-5-(2-hydroxyphenyl)-1-benzothiazolopyrazoline(27)

Obtained as white crystals in 72% yield, m.p. 242-243 $^{\circ}\text{C}$; ^1H NMR (δ): 3.62 (1H, dd, $\text{CH}_2(\text{Pyraz})$), 3.92 (1H, dd, $\text{CH}_2(\text{Pyraz})$), 6.21 (1H, dd, $\text{CH}(\text{Pyraz})$), 6.81-7.92 (13H, m, ArH); 11.16 (1H, s, $-\text{OH}$); IR (ν) max: 3100, 3030, 3000-2500, 1600, 1540, 1450, 1280, 1120, 1100, 1020, 890, 870, 750, 730, 690, 680, 540 and 430 cm^{-1} ; MS, m/z : 387, 386, 370, 293, 169, 127, 101. Anal. Calcd. for $\text{C}_{22}\text{H}_{17}\text{N}_3\text{O}_2\text{S}$: C, 68.21; H, 4.39; N, 10.8; S, 8.27 Found: C, 68.28; H, 4.39; N, 10.85; S, 8.28%.

3(4'-Chlorophenyl)-5-(2-hydroxyphenyl)-1-benzothiazolopyrazoline(28)

Obtained as white crystals in 76% yield, m.p. 250-251 $^{\circ}\text{C}$; ^1H NMR (δ): 3.60 (1H, dd, $\text{CH}_2(\text{Pyraz})$), 3.95 (1H, dd, $\text{CH}_2(\text{Pyraz})$), 6.20 (1H, dd, $\text{CH}(\text{Pyraz})$), 6.80-7.90 (13H, m, ArH); 11.14 (1H, s, $-\text{OH}$); IR (ν) max: 3400, 3030, 3000-2500, 1600, 1540, 1490, 1450, 1400, 1320, 1280, 1240, 1130, 1100, 1010, 890, 830, 750, 530 and 430 cm^{-1} ; MS, m/z : 405, 404, 369, 334, 392, 257, 168, 133, 126, 100, 91, 65. Anal. Calcd. for $\text{C}_{22}\text{H}_{16}\text{ClN}_3\text{OS}$: C, 65.18; H, 3.95; N, 10.37; S, 7.90. Found: C, 65.23; H, 3.93; N, 10.42; S, 7.92%.

3(4'-Methylphenyl)-5-(2-hydroxyphenyl)-1-benzothiazolopyrazoline(29)

Obtained as white crystals in 65% yield, m.p. 229-230 $^{\circ}\text{C}$; ^1H NMR (δ): 3.59 (1H, dd, $\text{CH}_2(\text{Pyraz})$), 3.94 (1H, dd, $\text{CH}_2(\text{Pyraz})$), 6.22 (1H, dd, $\text{CH}(\text{Pyraz})$), 6.80-7.89 (13H, m, ArH); 11.15 (1H, s, $-\text{OH}$); IR (ν) max: 3400 3030, 3000-2500, 600, 1550, 1490, 1450, 1380, 1320, 1280, 1230, 1180, 1100, 1050, 1030, 890, 810, 750, 720, 690, 530 and 430 cm^{-1} ; MS, m/z : 385, 384, 370, 368, 293, 291, 169, 167, 127, 125, 101, 99. Anal. Calcd. For $\text{C}_{23}\text{H}_{19}\text{N}_3\text{OS}$: C, 71.68; H, 4.93; N, 10.90; S, 8.31. Found: C, 71.78; H, 4.89; N, 10.92; S, 8.35%.

3(4'-Methoxyphenyl)-5-(2-hydroxyphenyl)-1-benzothiazolopyrazoline(30)

Obtained as white crystals in 65% yield, m.p. 247-248 °C; ¹H NMR (δ): 3.64 (1H,dd, CH₂(Pyraz)), 3.96(1H,dd, CH₂(Pyraz)), 6.21 (1H,dd, CH(Pyraz)), 6.82-7.90 (13H,m,ArH); 11.16 (1H,s,-OH); IR(ν)_{max}: 3400, 3030, 3000-2500, 1600, 1540, 1450, 1320, 1250, 1170, 1120, 1030, 880, 830, 750, 630, 530 and 430 cm⁻¹; MS, *m/z*: 401, 400, 384, 370, 307, 293, 183, 169, 141, 127, 115, 101. Anal. Calcd. for C₂₃H₁₉N₃O₂S: C, 68.93; H, 4.73; N, 10.47; S, 7.98. Found: C, 68.93; H, 4.71; N, 10.43; S, 7.99%.

3(2'-Hydroxyphenyl)-5-(4-methoxyphenyl)-1-benzothiazolopyrazoline(31)

Obtained as white crystals in 78% yield, m.p. 185-186 °C; ¹H NMR (δ): 3.35 (1H,dd, CH₂(Pyraz)), 3.75(3H,s,-OCH₃); 3.95(1H,dd, CH₂(Pyraz)), 5.70 (1H,dd, CH(Pyraz)), 6.80-7.80 (12H,m,ArH); 10.10(1H,s,-OH); IR(ν)_{max}: 3200, 3030,3000-2500, 1610, 1590, 1490, 1450, 1400, 1320, 1290, 1240, 1170, 1140, 1100, 1030, 880, 830, 820, 760, 730, 660, 640, 570, 550, 500 and 430 cm⁻¹; MS, *m/z*: 401, 400, 384, 370, 307, 293, 183, 169, 141, 127, 115, 101. Anal. Calcd. for C₂₃H₁₉N₃O₂S: C, 68.82; H, 4.73; N, 10.47; S, 7.98. Found: C, 68.93; H, 4.71; N, 10.43; S, 7.95%.

3(4'-Chlorophenyl)-5-(4-methoxyphenyl)-1-benzothiazolopyrazoline(32)

Obtained as white crystals in 65% yield, m.p. 158-159 °C; ¹H NMR (δ): 3.35 (1H,dd, CH₂(Pyraz)), 3.75(3H, s, -OCH₃); 3.94(1H,dd, CH₂(Pyraz)), 5.71 (1H,dd CH(Pyraz)), 6.80-7.82 (12H,m,ArH);10.12(1H,s,-OH); IR(ν)_{max}: 3400, 3040, 2900, 1610, 1510, 1430, 1250, 1180, 1090, 1030, 880, 820, 75, 630, 540 and 430 cm⁻¹; MS, *m/z*: 419, 418, 388, 383, 306, 264, 187, 182, 147, 140, 119, 114. Anal. Calcd. for C₂₃H₁₈ClN₃OS: C, 65.87; H, 4.53; N, 10.02; S, 7.64. Found: C, 65.90; H, 4.51; N, 10.10; S, 7.62%.

3(4'-Methylphenyl)-5-(4-methoxyphenyl)-1-benzothiazolopyrazoline(33)

Obtained as white crystals in 68% yield, m.p. 175-176 °C; ¹H NMR (δ): 3.36 (1H,dd, CH₂(Pyraz)), 3.76 (3H, s,-OCH₃); 3.96 (1H,dd CH₂(Pyraz)), 5.73 (1H,dd, CH(Pyraz)), 6.82-7.80(12H,m,ArH); 10.14(1H,s,-OH); IR(ν)_{max}: 3400, 3030, 2940, 2820, 1600, 1530, 1490, 1440, 1320, 1250, 1180, 1120, 1030, 880, 830, 750, 720, 690, 670, 530 and 430 cm⁻¹; MS, *m/z*: 399, 398, 384, 383, 368, 306, 219, 182, 167, 140, 125, 114, 99. Anal. Calcd. for C₂₄H₂₁N₃OS: C, 72.18; H, 5.26; N, 10.52 S, 8.02. Found: C, 72.20; H, 5.23; N, 10.52 S, 8.04%.

3-Phenyl-5-(4-chlorophenyl)-1-benzothiazolopyrazoline(34)

Obtained as white crystals in 74% yield, m.p. 145-146 °C; ¹H NMR (δ): 3.25 (1H,dd, CH₂(Pyraz)), 3.90(1H,dd, CH₂(Pyraz)), 5.75(1H,dd, CH(Pyraz)),7.00-7.80 (13H,m,ArH); IR(ν)_{max}: 3400, 3030, 2900, 1650, 1600, 1530, 1490, 1440, 1400, 1320, 1280, 1230, 1130, 1100, 1080, 1030, 1000, 880, 820, 780, 750, 730, 690, 670, 560 and 430 cm⁻¹; MS, *m/z*: 389, 388, 353, 312, 311, 276, 190, 154, 148, 122, 112, 86. Anal. Calcd. for C₂₂H₁₆ClN₃S: C, 67.86; H, 4.11; N, 10.79;S, 8.23. Found: C, 68.02; H, 4.09; N, 10.76; S, 8.20%.

3(2'-Hydroxyphenyl)-5-(4-chlorophenyl)-1-benzothiazolopyrazoline(35)

Obtained as white crystals in 71% yield, m.p. 149-150 °C; ¹H NMR (δ): 3.26 (1H,dd, CH₂(Pyraz)), 3.91(1H,dd, CH₂(Pyraz)), 5.76(1H,dd, CH(Pyraz)),7.02-7.84 (13H,m,ArH); 11.15(1H,s,-OH); IR(ν)_{max}: 3400, 3030, 3000-2500, 1600, 1530, 1490, 1440, 1400, 1320, 1280, 1230, 1130, 1100, 1080, 1000, 880, 830, 780, 750, 720, 690, 670, 550 and 430 cm⁻¹; MS, *m/z*: 405, 404, 388, 387, 293, 265, 223, 171, 197, 129, 103. Anal. Calcd. for C₂₂H₁₆ClN₃OS: C, 65.18; H, 3.95; N, 10.37; S, 7.90. Found: C, 68.20; H, 3.98; N, 10.42; S, 7.88%.

3-(4'-Chlorophenyl)-5-(4-chlorophenyl)-1-benzothiazolopyrazoline(36)

Obtained as white crystals in 72% yield, m.p. 155-156 °C; ¹H NMR (δ): 3.24 (1H,dd, CH₂(Pyraz)), 3.95(1H,dd, CH₂(Pyraz)), 5.77(1H,dd, CH(Pyraz)), 7.04-7.85 (13H,m,ArH); IR(ν)_{max}: 3400, 3030, 2900, 1880, 1660, 1240, 1210, 1150, 1020, 880, 840, 780, 750, 730, 700, 630, 600, 530, 520, 480 and 430 cm⁻¹; MS, *m/z*: 423, 422, 387, 310, 186, 144, 118. Anal. Calcd. for C₂₂H₁₅Cl₂N₃S: C, 62.41; H, 3.54; N, 9.92; S, 7.57. Found: C, 62.49; H, 3.58; N, 9.92; S, 7.55%.

3-(4'-Methylphenyl)-5-(4-chlorophenyl)-1-benzothiazolopyrazoline(37)

Obtained as white crystals in 78% yield, m.p. 195-196 °C; ¹H NMR (δ): 3.23 (1H,dd, CH₂(Pyraz)), 3.89(1H,dd, CH₂(Pyraz)), 5.75(1H,dd, CH(Pyraz)), 7.00-7.85 (13H,m,ArH); IR(ν)_{max}: 3400, 3030, 2900, 1600, 1530, 1490, 1440, 1400, 1330, 1280, 1230, 1130, 1100, 1080, 1040, 1010, 880, 820, 780, 750, 720, 690, 670, 600, 560 and 430 cm⁻¹; MS, *m/z*: 403, 402, 388, 368, 311, 310, 291, 187, 169, 145, 127, 119, 101. Anal. Calcd. For C₂₃H₁₈ClN₃S: C, 68.48; H, 4.46; N, 10.42; S, 7.94. Found: C, 68.52; H, 4.49; N, 10.49; S, 7.93%.

3-(4'-Methoxyphenyl)-5-(4-chlorophenyl)-1-benzothiazolopyrazoline(38)

Obtained as white crystals in 68% yield, m.p. 128-129 °C; ¹H NMR (δ): 3.24 (1H,dd, CH₂(Pyraz)), 3.93(1H,dd, CH₂(Pyraz)), 5.76(1H,dd, CH(Pyraz)), 7.05-7.86 (13H,m,ArH); 3.76 (3H, s, -OCH₃); IR(ν)_{max}: 3400, 3030, 1650, 1600, 1510, 1440, 1400, 1250, 1180, 1090, 1040, 880, 750, 690, 670, 550 and 430 cm⁻¹; MS, *m/z*: 419, 418, 388, 383, 306, 264, 222, 196, 182, 140, 114. Anal. Calcd. For C₂₃H₁₈ClN₃OS: C, 65.87; H, 4.29; N, 10.11; S, 7.64. Found: C, 65.91; H, 4.32; N, 10.13; S, 7.65%.

3-(4'-Chlorophenyl)-5-(3,4-dimethoxyphenyl)-1-benzothiazolopyrazoline(39)

Obtained as white crystals in 78% yield, m.p. 144-145 °C; ¹H NMR (δ): 3.28 (1H,dd, CH₂(Pyraz)), 3.96(1H,dd, CH₂(Pyraz)), 5.27(1H,dd, CH(Pyraz)), 6.85-7.76 (11H,m,ArH), 3.85(6H, 2-s, -OCH₃); IR(ν)_{max}: 3400, 3030, 2920, 2820, 1600, 1530, 1490, 1440, 1260, 1230, 1140, 1090, 1030, 900, 830, 750, 730, 700, 640, 590 and 430 cm⁻¹; MS, *m/z*: 449, 448, 417, 414, 386, 337, 309, 213, 185, 171, 145, 143, 117, 114. Anal. Calcd. For C₂₄H₂₀ClN₃O₂S: C, 64.14; H, 4.45; N, 9.35; S, 7.13. Found: C, 64.18; H, 4.44; N, 9.42; S, 7.15%.

3-Phenyl-5-(3,4-dimethoxyphenyl)-1-benzothiazolopyrazoline(40)

Obtained as white crystals in 80% yield, m.p. 162-163 °C; ¹H NMR (δ): 3.30 (1H,dd, CH₂(Pyraz)), 3.90(1H,dd, CH₂(Pyraz)), 5.25(1H,dd, CH(Pyraz)), 6.70-7.80 (11H,m,ArH), 3.80(6H, 2-s, -OCH₃); IR(ν)_{max}: 3400, 3030, 2920, 2820, 1600, 1530, 1490, 1440, 1320, 1260, 1230, 1140, 1030, 900, 820, 760, 690, 670, 640, 540 and 430 cm⁻¹; MS, *m/z*: 415, 414, 399, 384, 338, 307, 214, 183, 172, 146, 141, 115. Anal. Calcd. For C₂₄H₂₁N₃O₂S: C, 69.42; H, 5.05; N, 10.18; S, 7.71. Found: C, 69.39; H, 5.06; N, 10.12; S, 7.70%.

Results and Discussion

Formation of 3,5-diarylpyrazoline derivatives by the reaction of α, β-unsaturated ketones and hydrazines may take place under various reaction conditions using ethanol³⁶ as solvent. In our present case to obtain 3,5-diaryl-1-benzothiazolopyrazoline derivatives (**21-40**) a mixture of substituted chalcone (**1-20**, 10.00 m mol) and 2-hydrazinobenzothiazole (10.00 m mol) in ethanol (50 mL) was refluxed for 5 h and then cooled to room temperature. The precipitate was separated by filtration, washed with water and crystallized from a mixture of alcohol and chloroform (1:1) (Scheme 1). Substituted chalcones (**1-20**) were prepared

according to the reported methods. Structures of all new compounds (**21-40**) have been elucidated by elemental analyses, ^1H NMR, Mass spectral and IR measurements. In the IR spectra of 3,5-diaryl-1-benzothiazolopyrazoline derivatives (**21-40**) there is no carbonyl absorption but absorption bands in the region $1600\text{--}1450\text{ cm}^{-1}$ due to the presence of $\text{C}=\text{C}$ and $\text{C}=\text{N}$ stretching vibrations. Stretching vibrations due to the intramolecular hydrogen bonding of $-\text{OH}$ group gave absorption in the region $3000\text{--}2500\text{ cm}^{-1}$.

In addition to aromatic protons, the ^1H NMR spectra of these compounds exhibit double doublets for each $-\text{CH}_2$ proton between δ 3.23 to 3.64 and δ 3.88 to 4.00 and double doublet between δ 5.25 to 6.22 for $-\text{CH}$ proton of the pyrazoline nucleus (ABX) system.

3,5-Diaryl-1-benzothiazolopyrazoline (**21-40**)

21: $\text{R}_1 = \text{R}_2 = \text{R}_3 = \text{R}_4 = \text{R}_5 = \text{H}$	31: $\text{R}_1 = \text{R}_3 = \text{R}_4 = \text{H}, \text{R}_2 = \text{OH}, \text{R}_5 = \text{OCH}_3$
22: $\text{R}_2 = \text{OH}, \text{R}_1 = \text{R}_3 = \text{R}_4 = \text{R}_5 = \text{H}$	32: $\text{R}_1 = \text{Cl}, \text{R}_2 = \text{R}_3 = \text{R}_4 = \text{H}, \text{R}_5 = \text{OCH}_3$
23: $\text{R}_1 = \text{Cl}, \text{R}_2 = \text{R}_3 = \text{R}_4 = \text{R}_5 = \text{H}$	33: $\text{R}_1 = \text{CH}_3, \text{R}_2 = \text{R}_3 = \text{R}_4 = \text{H}, \text{R}_5 = \text{OCH}_3$
24: $\text{R}_1 = \text{CH}_3, \text{R}_2 = \text{R}_3 = \text{R}_4 = \text{R}_5 = \text{H}$	34: $\text{R}_1 = \text{R}_2 = \text{R}_3 = \text{R}_4 = \text{H}, \text{R}_5 = \text{Cl}$
25: $\text{R}_1 = \text{OCH}_3, \text{R}_2 = \text{R}_3 = \text{R}_4 = \text{R}_5 = \text{H}$	35: $\text{R}_1 = \text{R}_3 = \text{R}_4 = \text{H}, \text{R}_2 = \text{OH}, \text{R}_5 = \text{Cl}$
26: $\text{R}_3 = \text{OH}, \text{R}_2 = \text{R}_3 = \text{R}_4 = \text{R}_5 = \text{H}$	36: $\text{R}_1 = \text{R}_5 = \text{Cl}, \text{R}_2 = \text{R}_3 = \text{R}_4 = \text{H}$
27: $\text{R}_1 = \text{R}_4 = \text{R}_5 = \text{H}, \text{R}_2 = \text{R}_3 = \text{OH}$	37: $\text{R}_1 = \text{CH}_3, \text{R}_2 = \text{R}_3 = \text{R}_4 = \text{H}, \text{R}_5 = \text{Cl}$
28: $\text{R}_1 = \text{Cl}, \text{R}_2 = \text{R}_4 = \text{R}_5 = \text{H}, \text{R}_3 = \text{OH}$	38: $\text{R}_1 = \text{OCH}_3, \text{R}_2 = \text{R}_3 = \text{R}_4 = \text{H}, \text{R}_5 = \text{Cl}$
29: $\text{R}_1 = \text{CH}_3, \text{R}_2 = \text{R}_4 = \text{R}_5 = \text{H}, \text{R}_3 = \text{OH}$	39: $\text{R}_1 = \text{Cl}, \text{R}_2 = \text{R}_3 = \text{H}, \text{R}_4 = \text{R}_5 = \text{OCH}_3$
30: $\text{R}_1 = \text{OCH}_3, \text{R}_2 = \text{R}_4 = \text{R}_5 = \text{H}, \text{R}_3 = \text{OH}$	40: $\text{R}_1 = \text{R}_2 = \text{R}_3 = \text{H}, \text{R}_4 = \text{R}_5 = \text{OCH}_3$

Scheme 1. Synthesis of 3,5-diaryl-1-benzothiazolopyrazoline derivatives.

Biological activity

The synthesized 3,5-diaryl-1-benzothiazolopyrazoline derivatives (**21-40**) have been subjected to *in vitro* antimicrobial activity against various plant and human pathogenic bacteria and fungi.

Antimicrobial activity was carried out against Gram negative rod *P. fluorescence*, *E. coli*, *P. vulgaris* and *A. faecalis*, gram positive rod *B. subtilis* and gram positive coccus *S. epidermidis*, *C. albicans*, *C. cladosporoides*, *A. niger* and *C. lunata* all are soil fungi obtained from standard cultures. The results are summarized in the Table 1.

Table 1. Antimicrobial activity of 3,5-diaryl-1-benzothiazolopyrazoline derivatives.

Comp No	Culture									
	A	B	C	D	E	F	G	H	I	J
21	-	-	-	-	-	-	-	-	-	-
22	-	-	-	-	-	-	6	-	-	-
23	22	15	10	14	14	8	9	9	7	8
24	-	-	-	-	-	-	-	20	-	21
25	-	-	-	-	-	-	-	-	-	-
26	-	-	-	-	-	-	-	-	-	-
27	-	-	-	-	-	-	8	-	-	-
28	20	13	10	13	12	6	8	8	10	10
29	-	-	-	-	-	-	9	21	-	20
30	-	-	-	-	-	-	8	20	-	20
31	-	-	-	-	-	-	7	13	-	-
32	21	14	11	12	13	7	10	14	8	7
33	-	-	-	-	-	-	-	20	-	20
34	-	-	-	-	-	-	-	-	-	-
35	-	-	-	-	-	-	9	8	-	8
36	20	13	10	13	12	6	8	7	8	7
37	21	14	11	12	13	7	9	8	7	9
38	22	15	10	14	14	6	9	8	8	7
39	20	13	11	13	13	8	8	8	8	8
40	-	-	-	-	-	-	-	-	-	-

(Diameter of inhibition zone measured in mm, paper disc 5 mm, inhibition zone measured excluding paper disc diameter)

A = *P. fluorescence*; B = *E. Coli*; C = *P. vulgaris*; D = *A. faecalis*; E = *B. subtilis*;
F = *S. epidermidis*; G = *C. albicans*; H = *C. cladosporoides*; I = *A. niger*; J = *C. lunata*

The compounds **23**, **28**, **32**, **36**, **37**, **38**, **39** showed broad range of activity as inhibition zones were found against all plant and human bacteria and fungi. Compound **22**, **26**, **29**, **30**, **31** and **35** possess moderate activity against *C. albicans* but compound **24**, **29**, **30** and **33** shows higher activity against *C. cladosporoides* and *C. lunata*.

It can be concluded from the observation that these 3,5-diaryl-1-benzothiazolopyrazoline derivatives (**21-40**) have antimicrobial activity. Out of twenty compounds **23**, **28**, **32**, **36**, **37**, **38** and **39** possessed wide range of activity. Compounds **22**, **24**, **27**, **29**, **30**, **31**, and **33** showed only antifungal activity. In general these 3,5-diaryl-1-benzothiazolopyrazoline derivatives showed sufficient antimicrobial activity.

In conclusion, we have synthesized a systematically substituted series of new 3,5-diaryl-1-benzothiazolopyrazoline derivatives for structure-activity relationship studies. These substituted benzothiazolopyrazolines are very stable compounds, which renders them beneficial substances for biological or pharmacological trials.

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