Chemistry of Heterocyclic Compounds, Vol. 40, No. 2, 2004

SYNTHESIS OF SOME BIOLOGICALLY ACTIVE PYRAZOLE, THIAZOLIDINONE, AND AZETIDINONE DERIVATIVES

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Pyrazole, thiazolidinone, and azetidinone derivatives were synthesized from chalcones of 4-hydroxycoumarin. The structures of all the synthesized compounds were confirmed on the basis of spectral and analytical data. The compounds were screened in vitro for their antibacterial activity against various bacterial strains.

Keywords: azetidinones, biologically active pyrazoles, thiazolidinones.

1-Benzopyran-2-(2H)-ones are well known for their various biological activities [1, 2]. Pyrazoles and several N-substituted pyrazoles are known to possess neuroleptic [3], analgesic and anti-inflammatory, antipyretic [4], antiarrhythmic [5], sedative-hypnotic effect [6], and antimicrobial activity [7]. They are inhibitors and deactivators of liver alcohol dehydrogenase [8], while 3,5-substituted pyrazoles are known for hypoglycemic activity [4] in glucose primed and diabetic rats. 4-Thiazolidinones have been reported to demonstrate a wide range of pharmacological activities such as hypnotic-sedative, analgesic activity, anticonvulsant [9], antifungal [10], antibacterial [11], and antitubercular activity against *M. tuberculosis* $H_{37}Rv$ [12]. β-Lactamase is generally considered to be responsible for microbial resistance against a broad spectrum of β-lactam antibiotics [13].

In continuation of our work [14] we report here for the first time on the synthesis of some dihydropyrazole, thiazolidinone, and azetidinone derivatives, and on estimation of their biological properties. For this purpose chalcones of 4-hydroxy-1-benzopyran-2-(2H)-one and 3-(2H-4-hydroxy-2-oxobenzopyran-3-yl)-ω-arylethenyl ketones **1a**,**b** were treated with hydrazine hydrate in the presence of piperidine to yield dihydropyrazole derivatives **2a**,**b**. The ^{1}H NMR spectrum of compound **2a** showed the presence of a doublet at δ 1.95 (J = 7 Hz) for two protons at C(4) and a triplet at δ 2.48 for one proton at C(5). It showed the presence of a singlet at δ 3.68 for three protons of OCH_3 along with signals at 7.18–8.41 for eight aromatic protons. It also exhibited singlets at δ 8.74 and 10.04 for one proton each for the N–H and O–H groups, which were D_2O exchanged. Dihydropyrazoles **2a**,**b** were treated with chloroacetyl chloride in the presence of triethylamine in 1,4-dioxane to give N-chloroacetyl derivatives **3a**,**b**. The ^{1}H NMR spectra of **3a**,**b** did not show the signal at δ 8.74 for N–H, but a singlet at δ 4.11 for two protons of CH_2–CI was present along with other signals. Chlorides **3a**,**b** were treated with hydrazine hydrate in ethanol in the presence of piperidine to give N-acetylhydrazines **4a**,**b**. The ^{1}H NMR spectra of **4a** and **4b** showed a signal at δ 4.46 for two protons of CH_2–NH and a broad signal at δ 4.30 for two protons of NH_2 and δ 8.50 for one proton of NH, which are D_2O exchanged. Compounds **4a**,**b** when treated with benzaldehyde gave the corresponding hydrazones **5a**,**b** which

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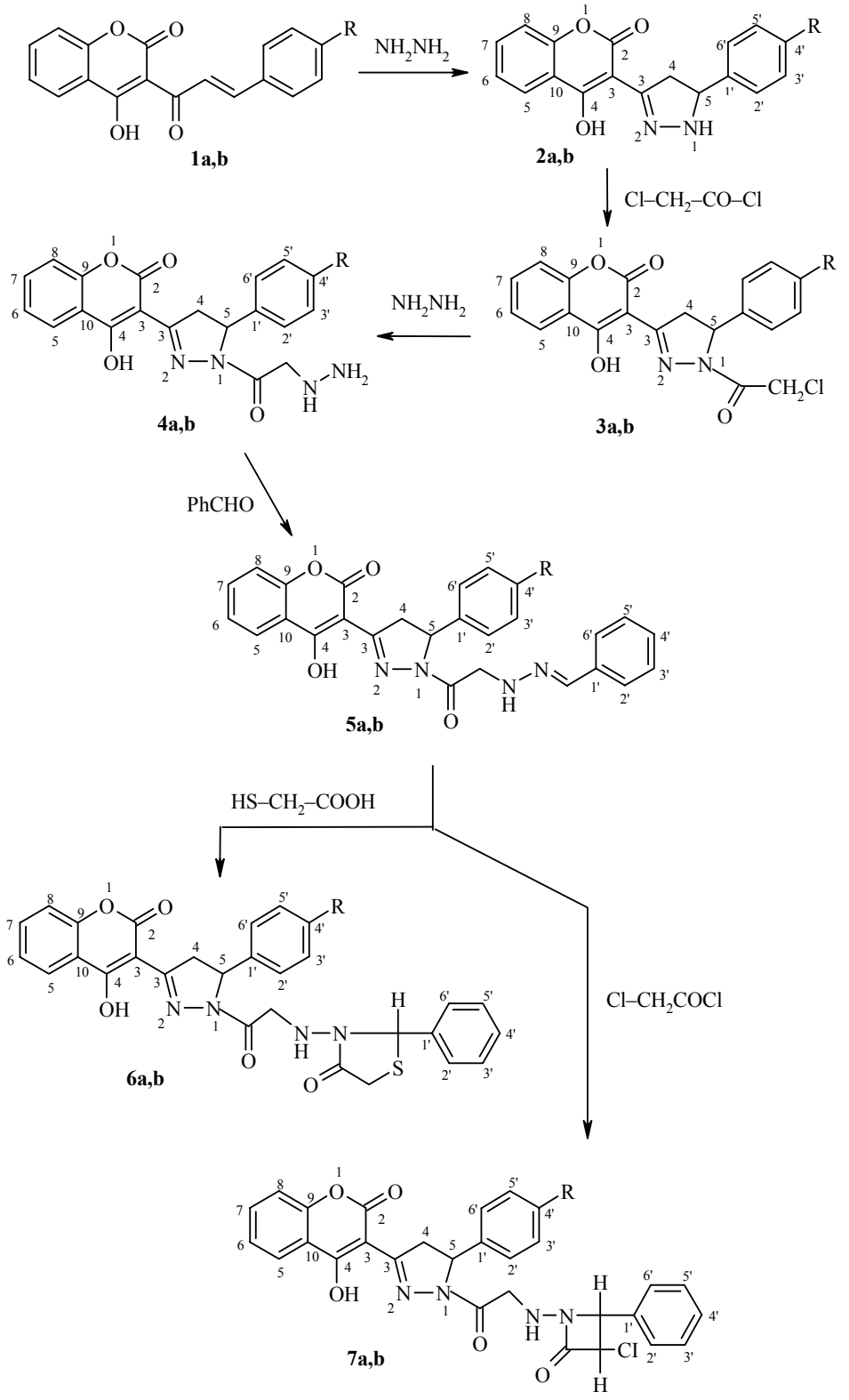
Scheme 1



2–**7 a** R = OMe, **2**–7 **b** R = H

TABLE 1. Spectral Data of Compounds **2a,b-7a,b**

Com-pound	IR spectra, ν, cm^{-1}, KBr	^1H NMR spectra (δ, ppm), DMSO-d_6 (*J*, Hz)	^{13}C NMR spectra (δ, ppm), DMSO-d_6	Mass spectra, *m/z* (%)
1	2	3	4	5
2a	3426 (O–H and N–H), 2927 (C–H), 1724 (C=O), 1620 (C=N), 1544, 1440, 1373, 1257, 1027, 778	1.95 (2H, d, *J* = 7, 4-, 4-H_2); 2.48 (1H, t, 5-H, CH–NH), 3.68 (3H, s, OCH_3); 7.18 (1H, d, *J* = 6, 8-H); 7.40 (2H, d, *J* = 8, 2'- and 6'-H); 7.59 (2H, d, *J* = 8.5, 3'- and 5'-H); 7.80 (1H, d, *J* = 7.5, 5-H), 8.11 (1H, t, 6-H); 8.41 (1H, t, 7-H); 8.74 (1H, s, NH, D_2O exchanged); 10.04 (1H, s, OH, D_2O exchanged)	41.3 (C(4)), 53.8 (OCH_3), 56.1 (C(5), 100.2 (C(3)), 111.9 (C(10)), 116.4 (C(2')), 118.2 (C(8)), 119.9 (C(6')), 127.6 (C(5)), 128.6 (C(6)), 132.7 (C(7)), 136.0 (C(3')), 137.1 (C(1')), 151.2 (C(9)), 154.3 (C-4')), 158.1 (C(3)), 162.0 (C(4)), 166.2 (C(2))	M^+ 336 *m/z* 319, 305, 292, 280, 265, 254, 240, 223, 216, 200, 185, 176, 161, 152, 144, 135, 121, 105, 91, 77, 65,43, 42
2b	3420 (O–H and N–H), 2928 (C–H), 1723 (C=O), 1614 (C=N), 1511, 1459, 1380, 1250, 1177, 1031, 823	1.90 (2H, d, *J* = 7, 4-, 4-H_2); .42 (1H, t, 5-H); 7.05 (3H, m, 3'-, 4'- and 5'-H); 7.32 (2H, d, *J* = 8.5, 2'- and 6'-H); 7.50 (1H, d, *J* = 7, 8-H); 7.67 (1H, t, 6-H); 7.80 (1H, d, *J* = 7, 5-H); 8.60 (1H, s, NH, D_2O exchanged); 10.40 (1H, s, OH, D_2O exchanged)	42.0 (C(4)), 51.2 (C(5)), 103.9 (C(3)), 111.9 (C(10)), 117.0 (C(2')), 118.2 (C(8)), 119.8 (C(6')), 120.9 (C(2')), 124.0 (C(6')), 127.4 (C(5)), 128.6 (C(6)), 132.5 (C(7)), 136.0 (C(3')), 137.0 (C(5')), 145.0 (C(1')), 151.2 (C(9)), 158.0 (C(3)), 163.6 (C(4)), 166.8 (C(2))	M^+ 306, *m/z* 278, 270, 229, 221, 207, 201, 175, 161, 145,133, 121, 104, 90, 85, 77, 67, 57
3a	3300 (OH), 2959 (CH), 1707 (C=O), 1621 (C=N), 1510, 1447, 1253, 1099, 1027, 806	2.01 (2H, d, *J* = 6, 4-, 4-H_2); 2.50(1H, t, H(5)), 3.56 (3H, s, OCH_3); 4.11 (2H, s, Cl–CH_2–C=O); 6.49 (2H, d, *J* = 6, 2'- and 6'-H); 6.73 (1H, t, 6-H), 6.91(1H, t, 7-H); 7.13(1H, d, *J* = 7, 8-H); 7.16 (2H, d, *J* = 6, 3'- and 5'-H); 7.39 (1H, d, *J* = 6, 5-H); 10.92 (1H, s, OH, D_2O exchanged)	43.0 (C(4)), 54.2 (OCH_3), 57.7 (C(5)), 61.0 (Cl–<u>C</u>H_2–C=O), 100.5 (C(3)), 111.0 (C(10)), 116.5 (C(2')), 118.2 (C(8)), 119.9 (C(6')), 127.6 (C(5)), 128.6 (C(6)), 132.7 (C(7)), 136.0 (C(3')), 137.1 (C(1')), 151.2 (C(9)), 154.3 (C(4')), 158.1 (C(3), 162.0 (C(4)), 166.2 (C(2)), 169.1 (N–C=O)	M^+ 412, M^{+2} 414, *m/z* 384, 353, 335, 323, 305, 290, 268, 251, 237, 223, 204, 175, 161, 144, 121, 107
3b	3432 (OH), 3017 (CH), 1721 (>C=O), 1623 (C=N), 1553, 1442, 1249, 1136, 1111, 996, 833	2.20 (2H, d, *J* = 6.5, 4-, 4-H_2); 2.75 (1H, t, 5-H); 4.15 (2H, s, CH_2–C=O); 6.60 (2H, t, 6- and 7-H); 6.75 (1H, d, *J* = 7, H-8); 6.85 (1H, d, *J* = 7.5, 5-H); 7.15 (2H, d, *J* = 7, 2'- and 6'-H); 7.35 (3H, m, 3'-, 4'-H and 5'-H); 10.40 (1H, s, OH, D_2O exchanged)	41.2 (C(4)), 56.0 (C(5)), 61.0 (Cl–<u>C</u>H_2–C=O), 99.5 (C(3)), 111.9 (C(10)), 117.2 (C(2')), 118.2 (C(8)), 119.8 (C(6')), 120.9 (C(3')) and C(5')), 127.5 (C(5)), 128.6 (C(6)), 132.6 (C(7)), 136.0 (C(4')), 137.1 (C(1')), 151.2 (C(9)), 158.0 (C(3)), 161.8 (C(4)), 163.5 (C(2)), 166.9 (N–C=O)	M^+ 382, M^{+2} 384, *m/z* 354, 339, 315, 305, 276, 270, 247, 227, 221, 207, 199, 175, 161, 145, 133, 121, 105, 90, 85, 77, 67, 56

TABLE 1 (continued)

1	2	3	4	5
4a	3433 (OH, NH and NH_2), 2955(CH), 1727 (C=O), 1617, 1541, 1444, 1378, 1259, 1159, 1115, 992, 778	2.34 (2H, d, *J* = 6, 4,- 4-H_2); 2.77 (1H, t, 5-H); 3.48 (3H, s, OCH_3); 4.30 (2H, b, NH_2); 4.46 (2H, s, CH_2–C=O); 7.06 (2H, d, *J* = 8.5, 2'- and 6'-H); 7.10 (1H, t, 6-H); 7.27 (1H, t, 7-H); 7.90 (2H, d, *J* = 7.5, 3- and 5'-H); 7.82 (1H, d, *J* = 7, 8-H); 8.00 (1H, d, *J* = 7.5, 5-H); 8.50 (1H, s, NH, D_2O exchanged); 10.42 (1H, s, OH, D_2O exchanged)	43.2 (C(4)), 54.7 (OCH_3), 56.9 (C(5)), 58.9 (NH–$\underline{C}H_2$–C=O), 104.1 (C(3)), 111.5 (C(10)), 118.0 (C(8)), 120.7 (C(6')), 120.8 (C(2')), 123.9 (C(5)), 124.3 (C(6)), 132.2 (C(7)), 137.6 (C(3') and C(5')), 140.5 (C(1')), 150.0 (C(9)), 154.0 (C(4'), $\underline{C}$–OCH_3), 159.4 (C(3)), 163.4 (C(4)), 164.6 (C(2)), 170.0 (N–C=O)	M^+ 408, *m/z* 380, 354, 331, 305, 287, 270, 247, 241, 227, 221, 175, 161, 133, 121, 104, 90, 84, 77, 67, 56
4b	3420 (OH, NH and NH_2), 2928 (CH), 1725 (>C=O), 1613, 1511, 1459, 1250, 1177, 1031, 823	2.10 (2H, d, *J* = 6, 4-, 4-H_2); 2.42 (1H, t, 5-H, CH–NH); 4.20 (2H, b, NH_2); 4.45 (2H, s, CH_2–C=O); 7.04 (2H, d, *J* = 8.5, 6- and 7-H); 7.25 (1H, d, 8-H); 7.49 (3H, m, 3'-H, 4'- and 5'-H); 7.75 (1H, d, *J* = 7, 5-H); 8.00 (2H, d, 2'- and 6'-H); 8.80 (1H, s, NH, D_2O exchanged); 10.43 (1H, s, OH, D_2O exchanged)	42.0 (C(4)), 56.8 (C(5)), 60.0 (Cl–$\underline{C}H_2$–C=O), 98.8 (C(3)), 112.0 (C(10)), 117.3 (C(2')), 118.3 (C(8)), 119.9 (C(6')), 121.0 (C(3') and C(5')), 127.5 (C(5)), 128.6 (C(6)), 132.6 (C(7)), 135.9 (C(4')), 137.0 (C(1')), 151.3 (C(9)), 158.0 (C(3)), 161.9 (C(4)), 163.6 (C(2)), 167.0 (N–C=O)	
5a	3479 (OH and NH), 2877 (CH), 1719 (>C=O), 1623, 1556, 1453, 1313, 1213, 999, 784	2.09 (2H, d, *J* = 8, 4-, 4-H_2); 2.75 (1H, t, 5-H); 3.48 (3H, s, OCH_3); 4.33 (2H, s, CH_2–C=O); 6.55 (1H, s, N=CH–Ph); 7.02 (2H, d, *J* = 7.5, 2"- and 6"-H); 7.07 (3H, m, 3"-, 4"- and 5"-H); 7.19 (2H, d, *J* = 9, 2'- and 6'-H); 7.34 (2H, t, 6- and 7-H); 7.45 (1H, d, *J* = 7.5, 8-H); 7.57 (1H, d, *J* = 7, 5-H); 7.69 (2H, d, *J* = 8, 3'- and 5'-H); 8.27 (1H, s, NH, D_2O exchanged), 10.30 (1H, s, OH, D_2O exchanged)	42.5 (C(4)), 52.9 (OCH_3), 53.9 (C(5)), 55.4 (NH–$\underline{C}H_2$–C=O), 98.1 (C(3)), 111.5 (C(10)), 112.2 (C(3") and C(5")), 117.3 (C(4")), 118.0 (C(8)), 120.7 (N=CH–Ph), 120.8 (C(2'), C(6'), C(2") and C(6")), 123.9 (C(5)), 124.3 (C(6)), 132.2 (C(7)), 137.6 (C(3') and C(5')), 140.5 (C(1')), 152.0.0 (C(9)), 154.2 (C(4')), 159.4 (C(3)), 160.0 (C(4)), 165.0 (C(2)), 172.0 (N–C=O)	
5b	3440 (OH and NH), 3081 (CH), 1711 (>C=O), 1613, 1546, 1438, 1380, 1207, 1135, 1021, 824	2.05 (2H, d, *J* = 8, 4-, 4-H_2); 2.49 (1H, t, 5-H); 4.38 (2H, s, CH_2–C=O); 6.60 (1H, s, N=CH–Ph); 7.35 (2H, t, 6- and 7-H); 7.57 (3H, m, 3"-, 4"- and 5"-H); 7.73 (2H, d, *J* = 8.5, 2"- and 6"-H); 8.00 (3H, m, 3'-, 4'- and 5'-H); 8.25 (3H, d, *J* = 8.5, 2'-, 6'- and 8-H); 8.55 (1H, d, *J* = 7, 5-H); 9.04 (1H, s, NH, D_2O exchanged); 10.41 (1H, s, OH, D_2O exchanged)	41.3 (C(4)), 53.8 (OCH_3), 56.1 (C(5)), 59.9 (NH–CH_2–C=O), 100.2 (C(3)), 111.9 (C(10)), 116.4 (C(2') and C(6')), 118.2 (C(8)), 119.9 (C(2") and C(6")), 121.0 (N=CH–Ph), 127.6 (C(5)), 128.6 (C(6)), 132.7 (C(7)), 136.0 (C(3'), C(4') and C(5')), 137.1 (C(3"), C(4") and C(5")), 140.2 (C(1') and C(1")), 151.2.0 (C(9)), 158.1 (C(3)), 162.0 (C(4)), 166.2 (C(2)), 169.1 (N–C=O)	M^+ 466, *m/z* 434, 300, 280, 251, 238, 228, 204, 190, 175, 145, 135, 121, 105, 91, 77, 43

TABLE 1 (continued)

1	2	3	4	5
6a	3464 (OH and NH), 2897 (CH), 1710 (>C=O), 1607, 1511, 1442, 1251, 1176, 1031, 829	2.31 (2H, d, *J* = 7, 4-, 4-H_2); 2.76 (1H, t, 5-H); 3.48 (3H, s, OCH_3); 3.73 (2H, s, S–CH_2–C=O); 4.53 (2H, s, N–CH_2–C=O); 4.90 (1H, s, N–CH–S); 6.82 (2H, d, *J* = 7.5, 2'- and 6'-H); 6.87 (2H, d, *J* = 7.5, 2"- and 6"-H); 7.00 (2H, d, *J* = 7, 3'- and 5'-H); 7.17 (1H, t, 6-H); 7.44 (3H, t, 3"-, 4"- and H-5"); 7.58 (1H, d, *J* = 7, 8-H); 7.76 (1H, t, 7-H); 8.06 (1H, d, *J* = 8, 5-H); 8.67 (1H, s, NH, D_2O exchanged); 10.52 (1H, s, OH, D_2O exchanged)	41.6 (N–CH–S), 45.1 (C(4)), 53.5 (OCH_3), 55.4 (C(5)), 59.0 (S–CH_2–C=O), 62.5 (NH–$\underline{C}H_2$–C=O), 102.8 (C(3)), 111.5 (C(10)), 112.2 (C(2'), C(6'), C(2"") and C(6"")), 117.3 (C(3""), C(4"") and C(5"")), 118.0 (C(8)), 123.9 (C(5)), 124.3 (C(6)), 132.2 (C(7)), 137.7 (C(3') and C(5')), 140.5 (C(1') and C(1"")), 150.2 (C(9)), 152.2 (C(4'), $\underline{C}$–OCH_3), 158.0 (C(3)), 162.4 (C(4)), 163.0 (C(2)), 166.0 (S–C=O), 172.0 (N–C=O)	M^+ 570, *m/z* 550, 493, 450, 392, 361, 284, 252, 232, 204, 190, 175, 144, 134, 115, 105, 91, 77
6b	3431 (OH and NH), 2928 (CH), 1727 (C=O), 1607, 1542, 1445, 380, 1260, 1159, 1023, 779	1.99 (d, 2H, *J* = 7, 4-, 4-H_2); 2.53 (1H, t, 5-H); 3.80 (2H, s, S–CH_2–C=O); 4.42 (2H, s, N–CH_2–C=O); 4.80 (1H, s, N–CH–S); 7.42 (3H, m, 3'-, 4'- and 5'-H); 7.72 (2H, d, *J* = 7.5, 2'- and 6'-H); 8.00 (2H, m, 6- and 7-H); 8.20 (1H, d, *J* = 7, 8-H); 8.40 (3H, m, 3"-, 4"- and 5"-H); 8.60 (2H, d, 2"- and 6"-H); 8.80 (1H, d, *J* = 7.5, 5-H); 9.61 (1H, s, NH, D_2O exchanged); 10.85 (1H, s, OH, D_2O exchanged)	41.9 (N–CH–S), 45.5 (C(4)), 53.3 (C(5)), 56.8 (S–CH_2–C=O), 61.0 (NH–$\underline{C}H_2$–C=O), 99.0 (C(3)), 111.9 (C(10)), 117.2 (C(2') and C(6')), 118.2 (C(8)), 119.8 (C(2"") and C(6"")), 127.5 (C(5)), 128.6 (C(6)), 132.6 (C(7)), 136.0 (C(3'), C(4') and C(5')), 137.1 (C(3""), C(4"") and C(5"")), 142.2 (C(1') and C(1"")), 151.3 (C(9)), 158.0 (C(3)), 161.9 (C(4)), 163.6 (C(2)), 166.7 (S–C=O), 170.0 (N–C=O)	
7a	3464 (OH and NH), 2897 (CH), 1710 (>C=O), 1607, 1511, 1442, 1251, 1176, 1031, 829	2.20 (2H, d, *J* = 7, 4-, 4-H_2); 2.63 (1H, t, 5-H); 3.38 (1H, d, *J* = 6, Cl–CH–C=O); 3.55 (3H, s, OCH_3); 4.46 (2H, s, N–CH_2–C=O); 4.47 (1H, d, *J* = 6, N–CH–Ar); 6.68 (1H, d, *J* = 7.5, 8-H); 6.95 (2H, d, *J* = 7.5, 2"-H, 6"-H); 7.10 (2H, m, 6- and 7-H); 7.27 (3H, t, 3"-, 4"- and 5"-H); 7.49 (2H, d, *J* = 7.5, 2'- and 6'-H); 7.85 (1H, d, *J* = 7, 5-H); 7.91 (2H, d, *J* = 7, 3'- and 5'-H); 8.67 (1H, s, NH, D_2O exchanged); 10.52 (1H, s, OH, D_2O exchanged)	31.6 (N–$\underline{C}$H–Ph), 40.5 (Cl–$\underline{C}$H–C=O), 45.1 (C(4)), 53.5 (OCH_3), 55.4 (C(5)), 59.0 (S–CH_2–C=O), 62.5 (NH–CH_2–C=O), 102.8 (C(3)), 111.5 (C(10)), 112.2 (C(2'), C(6'), C(2"") and C(6"")), 117.3 (C(3""), C(4"") and C(5"")), 118.0 (C(8)), 123.9 (C(5)), 124.3 (C(6)), 132.2 (C(7)), 137.7 (C(3') and C(5')), 140.5 (C(1') and C(1"")), 150.2 (C(9)), 152.2 (C(4')), 158.0 (C(3)), 162.4 (C(4)), 163.0 (C(2)), 166.0 (S–C=O), 172.0 (N–C=O)	M^+ 572 M^{+2} 574 *m/z* 550, 495, 464, 434, 392, 361, 300, 284, 251, 232, 204, 190, 175, 145, 134, 115, 105, 91, 77, 43
7b	3433 (OH and NH), 2927 (CH), 1726 (>C=O), 1606, 1541, 1445, 1375, 1261, 1115, 1025, 779	1.80 (2H, d, *J* = 7, 4-, 4-H_2); 2.60 (1H, t, 5-H); 3.40 (1H, d, *J* = 6, Cl–CH–C=O); 4.20 (2H, s, N–CH_2–C=O); 4.49 (1H, d, *J* = 6, N–CH–Ph); 7.05 (2H, t, 6-H and 7-H); 7.22 (3H, m, 3'-, 4'- and 5'-H); 7.38 (1H, d, *J* = 8, 8-H); 7.50 (1H, d, *J* = 7.5, 5-H); 7.67 (3H, m, 3"-, 4"- and 5"-H); 7.80 (4H, m, 2'-H, 6'-, 2"- and 6"-H); 8.50 (1H, s, NH, D_2O exchanged); 10.51 (1H, s, OH, D_2O exchanged)	29.9 (N–$\underline{C}$H–Ph), 39.1 (Cl–$\underline{C}$H–C=O), 45.0 (C(4)), 53.0 (C(5)), 62.3 (NH–CH_2–C=O), 102.5 (C(3)), 113.4 (C(10)), 114.2 (C(2'), C(6'), C(2"") and C(6"")), 119.2 (C(8)), 119.3 (C(3"), C(4") and C(5")), 122.8 (C(3'), C(4') and C(5')), 125.0 (C(5)), 125.4 (C(6)), 133.0 (C(7)), 140.1 (C(1"")), 142.2 (C(1')), 151.1 (C(9)), 162.6 (C(3)), 164.0 (C(4)), 167.3 (C(2)), 172.2 (N–C=O)	

did not show signals at δ 4.46 for NH_2 but showed the presence of a signal at δ 6.55 for one proton of N=CH–Ph. Hydrazones **5a**,**b** on further treatment with either mercaptoacetic acid or chloroacetyl chloride gave thiazolidinones **6a**,**b** or azetidinones **7a**,**b** respectively. The ^{1}H NMR spectra of **6a**,**b** showed the presence of signals at δ 3.73 for two protons of S–CH_2 and at δ 4.90 for S–CH–N, which confirm the formation of the thiazolidinone ring. Also the ^{1}H NMR spectra of **7a**,**b** showed the presence of doublets at δ 3.38 (J = 6 Hz) for one proton of Cl–CH and δ 4.47 (J = 6 Hz) for one proton of N–CH–Ph along with other signals, which confirm the formation of the azetidinone ring. The structures of all the above-synthesized compounds are confirmed on the basis of spectral (Table 1) and analytical data (Table 2). All compounds were screened *in vitro* for their antibacterial activity against a variety of bacterial strains (Table 3).

Antimicrobial activity. The minimum inhibition concentration (MIC) was determined using the Tube Dilution method according to the standard procedure [15]. All the compounds were screened *in vitro* for their antimicrobial activity against a variety of bacterial strains such as *Staphylococcus aureus, Salmonella paratyphi,* and *Escherichia coli* (Table 3). The standard drugs used for comparison were ciprofloxacin (MIC 5 μg/ml), cloxacillin (MIC 10 μg/ml), and gentamycin (MIC 5 μg/ml).

The antimicrobial data of the above compounds reveal that compounds having the methoxy group have increased antibacterial activity while azetidinones are found to be more biologically active than thiazolidinones.

TABLE 2. Physical and Analytical Data of Compounds **2a,b-7a,b**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, %
		C	H	N		
2a	$C_{19}H_{16}N_2O_4$	68.10 / 67.85	8.43 / 8.33	4.76 / 4.55	190	75
2b	$C_{18}H_{14}N_2O_3$	70.15 / 70.58	4.69 / 4.69	9.15 / 9.45	168	70
3a*	$C_{21}H_{17}N_2O_5Cl$	60.87 / 61.16	4.33 / 4.12	6.85 / 6.79	238	72
3b*[2]	$C_{20}H_{15}N_2O_4Cl$	63.10 / 62.82	4.05 / 3.92	7.15 / 7.32	225	68
4a	$C_{21}H_{20}N_4O_5$	61.95 / 61.76	5.05 / 4.90	13.85 / 13.72	256	76
4b	$C_{20}H_{18}N_4O_4$	63.85 / 63.49	4.70 / 4.76	14.90 / 14.81	265	80
5a	$C_{28}H_{24}N_4O_5$	67.87 / 67.74	4.55 / 4.83	11.36 / 11.29	213	79
5b	$C_{27}H_{22}N_4O_4$	69.86 / 69.52	4.50 / 4.72	11.86 / 12.01	226	77
6a*[3]	$C_{30}H_{26}N_4O_6S$	63.40 / 63.15	4.65 / 4.56	9.70 / 9.82	245	67
6b*[4]	$C_{29}H_{24}N_4O_5S$	64.67 / 64.44	4.23 / 4.44	10.25 / 10.37	>300	70
7a*[5]	$C_{30}H_{25}N_4O_6Cl$	63.05 / 62.93	4.49 / 4.37	9.53 / 9.79	>300	65
7b*[6]	$C_{29}H_{23}N_4O_5Cl$	64.35 / 64.20	4.15 / 4.24	10.21 / 10.33	287	63

* Found, %: Cl 9.03. Calculated, %: Cl 9.16.
*[3] Found, %: S 5.43. Calculated, %: S 5.61.
*[4] Found, %: S 5.98. Calculated, %: S 4.81.
*[5] Found, %: Cl 6.13. Calculated, %: Cl 6.11.
*[6] Found, %: Cl 6.30. Calculated, %: Cl 6.45.

TABLE 3. Antibacterial Activity of **2a,b-7a,b**

Compound	Activity, μg/ml			Compound	Activity, μg/ml		
	S. aureus	*S. typhi*	*E. coli*		*S. aureus*	*S. typhi*	*E. coli*
2a	50	50	100	**5a**	25	50	50
2b	100	100	150	**5b**	50	100	100
3a	50	100	50	**6a**	50	25	100
3b	50	100	100	**6b**	100	50	100
4a	50	50	100	**7a**	25	25	50
4b	100	50	50	**7b**	50	25	50

EXPERIMENTAL

Melting points were taken in open capillaries and are uncorrected. IR spectra (ν_{max}, cm^{-1}) were recorded on Perkin–Elmer FTIR, and NMR (^1H and ^{13}C) were recorded on Bruker AMX (500 MHz) and AC (200 MHz) using TMS as standard. Mass spectra were recorded on Shimadzu GC-MS.

5-Aryl-3-[2H-4-hydroxy-2-oxobenzopyran-3-yl]-4,5-dihydropyrazole (2a,b). Chalcones of 4-hydroxybenzopyran-2-one **1a**,**b** (0.01 mol) and hydrazine hydrate (0.01 mol, 0.5 ml) in the presence of piperidine (1.0 ml) in alcohol were refluxed for 7-8 h. The reaction was monitored on TLC. On the completion of the reaction the reaction mixture was poured onto crushed ice and neutralized with dilute HCI to give a solid product, which was then crystallized from alcohol to afford **2a**,**b** in 70-75% yield.

5-Aryl-1-chloroacetyl-3-[2H-4-hydroxy-2-oxobenzopyran-3-yl]-4,5-dihydropyrazole (3a,b). 5-*p*-Methoxyphenyl-3-[2H-4-hydroxy-2-oxobenzopyran-3-yl]-4,5-dihydropyrazoles **2a**,**b** (0.01 mol) were taken in hot benzene, and chloroacetyl chloride (0.015 mol, 1.68 ml) was added dropwise. The reaction mixture was stirred at room temperature for 8 h and was then cooled to give a pale yellow solid. This solid was recrystallized from methanol to give **3a**,**b** in 65-72% yield.

5-Aryl-1-hydrazinoacetyl-3-[2H-4-hydroxy-2-oxobenzopyran-3-yl]-4,5-dihydropyrazole (4a,b). A mixture of compound **3a**,**b** (0.01 mol) and hydrazine hydrate (0.01 mol, 1.40 ml) in alcohol was refluxed for 7-8 h. The reaction mixture was then poured onto crushed ice to give a solid product, which was then recrystallized from alcohol to give hydrazines **4a**,**b** in 75-80% yield.

5-Aryl-1-[(benzylidenehydrazino)acetyl]-3-[2H-4-hydroxy-2-oxobenzopyran-3-yl]-4,5-dihydro-pyrazole (5a,b). An equimolar mixture of hydrazines **4a**,**b** (0.01 mol) and benzaldehyde (0.01 mol, 1.06 ml) in ethanol (30 ml) containing acetic acid (0.5 ml) was refluxed for 6 h. The excess solvent was distilled off and the residue was poured onto crushed ice to give a solid. The separated solid was filtered off and recrystallized from methanol to give hydrazones **5a**,**b** in 77-79% yield.

5-Aryl-3-[2H-4-hydroxy-2-oxobenzopyran-3-yl]-1-[(2-phenyl-4-oxothiazolidin-3-ylamino)-acetyl]-4,5-dihydropyrazole (6a,b). A mixture of hydrazones **5a**,**b** (0.01 mol) and thioglycolic acid (0.02 mol, 1.84 ml) in DMF was refluxed for 12 h. The reaction mixture was cooled and poured into ice-cold sodium bicarbonate solution to remove traces of acid, if any. Finally the solid obtained was filtered off, dried, and recrystallized from alcohol to give **6a**,**b** in 65-70% yield.

5-Aryl-N-[(3-chloro-2-oxo-4-phenylazetidin-1-ylamino)acetyl]-3-[2H-4-hydroxy-2-oxo-benzopyran-3-yl]-4,5-dihydropyrazoles (7a,b). To the hydrazones **5a**,**b** (0.01 mol) in 1,4 dioxane (40 ml) was added chloroacetyl chloride (0.01 mol, 1.12 ml) and triethylamine (0.01 mol, 1 ml) while stirring at 0-5°C. The reaction mixture was stirred at this temperature for 1 h and then refluxed for 7 h. The excess solvent was removed and the residue was poured onto crushed ice to afford a solid product. The solid was filtered off, washed, and recrystallized from methanol to give **7a**,**b** in 77-82% yield.

The authors are thankful to Mumbai University for financial assistance. The authors are grateful to National Facility for High Field NMR, TIFR Mumbai. The authors are also grateful to the Padmaja Occupational Hygiene & Diagnostic Centre, Navi Mumbai, and Prof. Vaidya, Head of the Microbiology Dept., Institute of Science, Mumbai for biological testing. The authors are also thankful to Mr. S. V. Chiplunkar, UDCT, Mumbai for elemental analysis.

REFERENCES

1. M. A. Stahmann, M. Ikawa, and K. P. Link, US Pat. 2427579; *Chem. Abstr*., **42**, 603 (1948).
2. R. B. Arora and C. N. Mathur, *Brit. J. Pharmacol*., **20**, 29 (1963).
3. *Burger's Medicinal Chemistry*, Wiley, N. Y. (1980), p. 291.
4. *The Merck Index*, ed. M. Windholz, Merck and Co., Rahway, New Jersey, 11th ed. (1989), p. 161.
5. R. W. Hamilton, *J. Heterocycl. Chem*., **13**, 545 (1976).
6. L. S. Goodman and A. Gilman, *The Pharmacological Basis of Therapeutics*, Macmillan, N. Y. (1980), p. 295.
7. K. Ramalingam, G. X. Thyvelikakath, K. D. Berlin, R. W. Chesnul, R. P. Brown, N. N. Durham, S. E. Ealick, and D. Vander Helm, *J. Med. Chem*., **20**, 847 (1977).
8. R. W. Fries, D. P. Bohlken, and B. V. Plapp, *J. Med. Chem*., **22**, 356 (1979).
9. E. Ylhan and N. Ergenc, *Arch. Pharm*. (Weinheim), **325**, 453 (1992).
10. N. Cesur, Z. Cesur, N. Ergenc, M. Uzun, M. Kiraz, and O. Kasymodlu, D. Kaya, *Arch. Pharm*. (Weinheim), **327**, 271 (1994).
11. The Merck Index, 11th Edition, 6233 (1989).
12. Z. Cesur, H. Guner, and G. Otuk, *Eur. J. Med. Chem*., **29**, 981 (1994).
13. Eunhee Kim, Jongsook Bang, Han-Young Kang, Ae Nim Pae, Hun Yeong Kob, and Moon HO Chang, *Korean J. Med. Chem.*, **2**, 45 (1992).
14. V. V. Mulwad and R. B. Pawar, *Ind. J. Het. Chem*., **10**, 241 (2001).
15. S. Frankle, S. Reitman, and A. C. Sonnenwirth, *Gradwol's Clinical Laboratory Methods and Diagnosis*, **II**, 7th ed., C. V. Mosby Company, Germany (1970), p. 1406.