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SUPPLEMENTARY MATERIAL TO

Synthesis and SAR studies of pyrazole-3-carboxamides and -3-carbonyl thioureides including chiral moiety: Novel candidates as antibacterial agents

ISHAK BILDIRICI[1], ADNAN CETIN[2]*, NURETTIN MENGES[1] and YUSUF ALAN[3]

[1]*Van Yuzuncu Yil University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Van, Turkey,* [2]*Muş Alparslan University, Faculty of Education, Department of Science, 49250, Muş, Turkey and* [3]*Muş Alparslan University, Faculty of Science and Arts, Department of Biology, 49250, Muş, Turkey*

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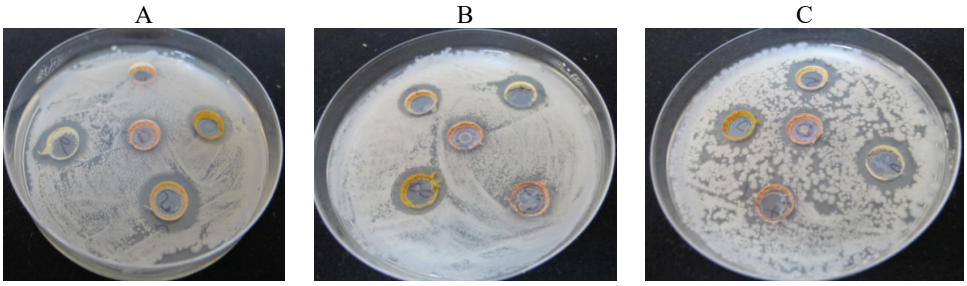

Fig. S-1. Inhibition zone images of the **6a** against A: *Staphylococcus aureus* ATCC 6538, B: *Enterobacter aerogenes* ATCC 13048, C: *Bacillus megaterium* DSM 32.

CHARACTERIZATION DATA FOR THE PREPARED COMPOUNDS

*(*R*)-4-Benzoyl-1-(2,5-dimethylphenyl)-*N*-(2-hydroxy-1-phenylethyl)-5-phenyl-1*H*-pyrazole-3-carboxamide (**3a**)*. Yield: 88 %; R_f: 0.38; m.p.: 210–212 °C; Anal. Calcd. for $C_{33}H_{29}N_3O_3$ (*FW*: 515.22): C, 76.87; H, 5.67; N, 8.15 %. Found: C, 76.71; H, 5.59; N, 8.30 %; IR (cm^{-1}): 3275, 3154, 3056, 2865, 1692, 1664, 1603, 1548, 1476, 1434, 1274; ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 8.42 (1H, *d*, *J* = 9.4 Hz, NH), 7.91–7.82 (3H, *m*, Ar-H), 7.61–7.52 (5H, *m*, Ar-H), 7.24–7.15 (6H, *m*, Ar-H), 6.63–6.56 (4H, *m*, Ar-H), 4.55 (1H, *m*, CH), 3.53–3.50 (3H, *m*, OH & CH_2), 2.17 (3H, *s*, CH_3), 1.76 (3H, *s*, CH_3); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 192.4, 166.2, 145.3, 143.6, 141.3, 139.5, 137.6, 136.2, 134.5, 133.6, 132.3, 121.2, 129.7, 128.1, 123.6, 121.4, 116.5, 111.4, 63.2, 54.7,

* Corresponding author. E-mail: adnankimya@gmail.com

21.6, 17.4; (+)ESI-HRMS (*m*/*z*) Calcd. for [$C_{33}H_{29}N_3O_3$+H^+]: 516.2287. Found: 516.2271; $[\alpha]_D^{23}$ (*c*: 0.001 mg mL^{-1}, EtOH): +142.0.

*(*R*)-4-Benzoyl-1-(2,5-dimethylphenyl)*-N-*(1-hydroxy-3-methylbutan-2-yl)-5--phenyl-1*H*-pyrazole-3-carboxamide (**3b**)*. Yield: 85 %; R_f: 0.38; m.p.: 191–193 °C; Anal. Calcd. for $C_{30}H_{31}N_3O_3$ (*FW*: 481.24): C, 74.82; H, 6.49; N, 8.73 %. Found: C, 74.69; H, 6.61; N, 8.92 %; IR (cm^{-1}): 3312, 3168, 3040, 2818, 1696, 1668, 1576, 1482, 1401, 1370, 1315; ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 8.35 (1H, *d*, *J* = 9.2 Hz, NH), 7.90–7.88 (2H, *m*, Ar-H), 7.78–7.77 (2H, *m*, Ar-H), 7.26–7.16 (5H, *m*, Ar-H), 6.76–6.52 (4H, *m*, Ar-H), 3.71–3.58 (3H, *m*, CH & CH_2), 2.50 (2H, *m*, CH & OH), 2.17 (3H, *s*, CH_3), 1.61 (3H, *s*, CH_3), 1.34 (6H, *d*, *J* = 7.2 Hz, CH_3); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm: 194.2, 162.5, 144.1, 142.7, 141.5, 140.1, 138.6, 136.4, 135.3, 133.1, 132.0, 130.5, 129.1, 128.4, 127.6 122.3, 121.1, 109.2, 63.3, 55.3, 30.1, 21.0, 18.4, 12.2; (+)ESI--HRMS (*m*/*z*) Calcd. for [$C_{30}H_{31}N_3O_3$+H^+]: 482.2444. Found: 482.2441; $[\alpha]_D^{23}$ (*c*: 0.001 mg mL^{-1}, EtOH): –204.0.

*(*R*)-4-Benzoyl-1-(2,5-dimethylphenyl)*-N-*(1-hydroxy-butan-2-yl)-5-phenyl--1*H*-pyrazole-3-carboxamide (**3c**)*. Yield: 85 %; R_f: 0.39; m.p.: 199–201 °C; Anal. Calcd. for $C_{29}H_{29}N_3O_3$ (*FW*: 467.22): C, 74.50; H, 6.25; N, 8.99 %. Found: C, 74.71; H, 6.42; N, 8.73 %; IR (cm^{-1}): 3362, 3156, 3066, 1576, 1489, 1385, 1310; ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 8.34 (1H, *d*, *J* = 9.2 Hz, NH), 7.88–7.74 (2H, *m*, Ar-H), 7.52–7.45 (5H, *m*, Ar-H), 7.25–7.14 (5H, *m*, Ar-H), 6.77 (1H, *m*, Ar-H), 3.82 (2H, *m*, CH_2), 3.51 (1H, *m*, CH), 2.68 (1H, *s*, OH), 2.13 (3H, *s*, CH_3), 1.87 (3H, *s*, CH_3), 1.62 (2H, *m*, CH_2), 1.35 (3H, *t*, *J* = 7.1 Hz, CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 198.3, 164.7, 146.3, 143.2, 141.5, 134.1, 133.9, 132.9, 131.6, 130.8, 130.0, 129.5, 129.1, 128.1, 126.3,125.4, 121.1, 108.2, 58.6, 55.3, 30.1, 22.1, 17.3, 14.6; (+)ESI-HRMS (*m*/*z*): Calcd. for [$C_{29}H_{29}N_3O_3$+H^+]: 468.2287. Found: 468.2287; $[\alpha]_D^{23}$ (*c*: 0.001 mg mL^{-1}, EtOH): +186.3

*4-Benzoyl-1-(2,5-dimethylphenyl)-N-{[(2-hydroxy-1-phenylethyl)amino]--thioxomethyl}-5-phenyl-1*H*-pyrazole-3-carboxamide (**6a**)*. Yield: 61 %; R_f: 0.37; m.p.: 231–233 °C; Anal. Calcd. for $C_{34}H_{30}N_4O_3S$ (*FW*: 574.20): C, 71.06; H, 5.26; N, 9.75 %. Found: C, 71.23; H, 5.34; N, 9.79 %; IR (cm^{-1}): 3355, 3212, 3054, 2925, 1712, 1686, 1674, 1572, 1494, 1442, 1323; ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 8.29 (1H, *m*, NH), 8.21–7.04 (16H, *m*, Ar-H), 6.57 (2H, *m*, Ar-H), 3.95 (2H, *m*, CH_2), 3.13 (1H, *m*, CH), 2.30 (1H, *m*, OH), 2.17 (3H, *s*, CH_3), 1.18 (3H, *s*, CH_3); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 198.3, 188.6, 166.7, 143.1, 141.2, 136.7, 135.4, 132.6, 132.2, 131.5, 131.1, 130.4, 130.2, 130.0, 129.9, 129.8, 129.6, 129.3, 129.2, 129.1, 128.7, 128.5, 128.1, 127.2, 122.5, 109.1, 64.2, 50.3, 21.4, 16.8; (+)ESI-HRMS (*m*/*z*) Calcd. for [$C_{34}H_{30}N_4O_3S$+H^+]: 575.2117. Found: 575.2111; $[\alpha]_D^{23}$ (*c*: 0.005 mg mL^{-1}, EtOH): +192.3.

*4-Benzoyl-1-(2,5-dimethylphenyl)-N-{[(1-hydroxy-3-methylbutan-2-yl)--amino]thioxomethyl}-5-phenyl-1H-pyrazole-3-carboxamide (**6b**).* Yield: 56 %; R_f: 0.37; m.p.: 207–209 °C; Anal. Calcd. for $C_{31}H_{32}N_4O_3S$ (*FW*: 540.22): C, 68.87; H, 5.97; N, 10.36 %. Found: C, 68.95; H, 5.89; N, 10.42 %; IR (cm^{-1}): 3365, 3151, 3062, 2957, 1704, 1686, 1671, 1568, 1498, 1444, 1321; ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 8.12 (1H, *m*, NH), 8.05–7.20 (12H, *m*, Ar-H), 6.64 (1H, *m*, Ar-H), 3.93 (2H, *m*, CH_2), 2.88 (1H, *m*, CH), 2.41 (1H, *bs*, OH), 2.21 (3H, *s*, CH_3), 1.95 (1H, *m*, CH), 1.79 (3H, *s*, CH_3), 1.64 (3H, *m*, CH_3), 1.18 (3H, *s*, CH_3); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 196.8, 180.3, 165.9, 144.7, 142.3, 141.8, 137.5, 135.2, 134.4, 133.2, 132.1,131.7, 129.8, 129.1, 128.6, 127.5, 126.3, 125.4, 124.2, 121.7, 108.2, 64.1, 59.7, 32.1, 21.4, 18.4, 17.2; (+)ESI-HRMS (*m*/*z*) Calcd. for $[C_{31}H_{32}N_4O_3S+H^+]$: 541.2273. Found: 541.2269; $[\alpha]_D^{23}$ (*c*: 0.005 mg mL^{-1}, EtOH): +125.4.

*4-Benzoyl-1-(2,5-dimethylphenyl)-N-{[(1-hydroxybutan-2-yl)amino]--thioxomethyl}-5-phenyl-1H-pyrazole-3-carboxamide (**6c**).* Yield: 50 %; R_f: 0.37; m.p.: 215–217 °C; Anal. Calcd. for $C_{30}H_{32}N_4O_3S$ (*FW*: 512.19): C, 67.95; H, 5.51; N, 10.93 %. Found: C, 68.56; H, 5.91; N, 10.51 %; IR (cm^{-1}): 3435, 3165, 3058, 2895, 1711, 1685, 1667, 1572, 1498, 1442, 1323; ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 8.67 (1H, *bs*, NH), 8.23–6.97 (13H, *m*, NH & Ar-H), 6.83 (1H, *m*, Ar-H), 3.74 (2H, *m*, CH_2), 2.81 (1H, *m*, CH), 2.25 (4H, *m*, OH & CH_3), 2.13 (3H, *s*, CH_3), 1.66–1.63 (2H, *m*, CH_2), 1.13 (3H, *m*, CH_3); ^{13}C-NMR (100 MHz, DMSO-d_6, δ / ppm): 194.5, 181.0, 167.1, 144.4, 141.6, 139.5, 137.2, 136.7, 135.3, 131.5, 130.3, 129.9, 129.4, 129.1, 128.8, 128.6, 128.4, 128.0, 127.5, 124.3, 108.8, 62.3, 55.7, 27.3, 22.6, 17.1, 10.6; (+)ESI-HRMS (*m*/*z*) Calcd. for $[C_{30}H_{30}N_4O_3S+H^+]$: 527.2117. Found: 527.2110; $[\alpha]_D^{23}$ (*c*: 0.005 mg mL^{-1}, EtOH): +153.2.