

Supplementary Materials: Synthesis and Biological Activity

Evaluation of Novel Heterocyclic Pleuromutilin Derivatives

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14-O-(p-toluene sulfonyloxyacetyl) mutilin(2):

A 5 mL of NaOH aqueous solution (2 g, 50 mmol) was added dropwise to a mixture of pleuromutilin (7.57 g, 20 mmol) and p-toluenesulfonyl chloride (4.2 g, 22 mmol) in methyl isobutyl ketone (10 mL) and water (5 mL). The mixture was vigorously stirred for 45min at 60 °C, then the reaction mixture was cooled to 10 °C and separated. The organic layer was washed with 5 mL water and 5 mL saturated sodium carbonate solution. The organic phase was dried overnight with anhydrous sodium sulfate. After filtration, the solvent was concentrated in vacuo to give 10.56 g of yellow oil. It was used in the next step without further purification. Yield: 93%. IR (KBr): 3446 (OH), 2924 (CH₂), 2863 (CH₂), 1732 (C=O), 1633 (C-C), 1597 (C=C), 1456 (C=C), 1371 (CH₃), 1297 (C-O-C), 1233 (CH), 1117 (C-(C=O)-C), 1035 (C-O-C), 832 (CH), 664 (CH₂=), 560 (CH₂=) cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.74 (d, J = 8.3 Hz, 2H), 7.26 (t, J = 13.3 Hz, 2H), 6.34 (dd, J = 17.4, 11.0 Hz, 1H), 5.70 (d, J = 8.5 Hz, 1H), 5.19 (dd, J = 55.1, 14.2 Hz, 2H), 4.47 – 4.33 (m, 2H), 3.28 (s, 1H), 2.38 (s, 3H), 2.25 – 2.09 (m, 3H), 2.01 (s, 1H), 1.99 – 1.88 (m, 1H), 1.71 – 1.62 (m, 1H), 1.61 – 1.51 (m, 2H), 1.46 – 1.38 (m, 2H), 1.35 (d, J = 7.8 Hz, 3H), 1.27 (d, J = 11.5 Hz, 1H), 1.18 (dd, J = 11.6, 4.5 Hz, 2H), 1.12 – 1.00 (m, 4H), 0.80 (d, J = 7.0 Hz, 3H), 0.55 (d, J = 7.0 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 215.71 (C=O), 163.87 (C=O), 144.29 (benzene-C), 137.70 (CH=), 131.63 (benzene-C), 128.91 (benzene-C), 127.09 (benzene-C), 116.38 (CH₂=), 73.54 (CH), 69.29 (CH), 64.03 (CH), 57.02 (CH), 44.39 (C), 43.51 (CH₂), 42.97 (C), 40.84 (C), 35.54 (CH), 35.03 (CH), 33.40 (CH₂), 29.34 (CH₃), 25.77 (CH₂), 25.39 (CH₂), 23.81 (CH₂), 20.68 (CH₃), 15.53 (CH₃), 13.76 (CH₃), 10.47 (CH₃). HRMS (ESI) calcd [M+H]⁺ for C₂₉H₄₀O₇S 533.250, found 533.2507.

14-O-(acetic acidthioacetyl) mutilin(4):

Compound 3 was prepared by stirring a mixing of compound 2 (10 mmol), potassium thioglycolate (20 mmol), methyl isobutyl ketone (30ml) in room temperature, and the mixture

was stirred for 2h. The mixture was extracted with water (10ml). The organic were combined, dried over Na₂SO₄, and concentrated to give compound 3. Yield: 80%. IR (KBr): 3448 (OH), 2967 (CH₂), 2924 (CH₃), 2865 (CH₂), 1731 (C=O), 1702 (C=O), 1453 (C-C), 1419, 1384 (CH₃), 1295 (C-O-C), 1183 (CH), 1154 (C-O), 1115 (C-(C=O)-C), 1017 (C-O-C) cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 6.58 – 6.30 (m, 1H), 5.72 (d, J = 8.4 Hz, 1H), 5.43 – 5.14 (m, 2H), 3.63 (s, 2H), 3.36 (d, J = 6.4 Hz, 1H), 2.36 (dd, J = 13.5, 3.5 Hz, 3H), 2.35 – 2.27 (m, 1H), 2.21 (dd, J = 17.4, 7.9 Hz, 1H), 2.13 (d, J = 14.9 Hz, 1H), 2.04 (dd, J = 26.1, 17.5 Hz, 1H), 1.73 (dd, J = 31.8, 10.6 Hz, 2H), 1.68 – 1.62 (m, 2H), 1.62 – 1.41 (m, 6H), 1.41 – 1.24 (m, 2H), 1.24 – 0.99 (m, 4H), 0.89 (t, J = 8.4 Hz, 3H), 0.78 – 0.61 (m, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 216.90 (C=O), 193.45 (C=O), 167.32 (C=O), 138.92 (CH=), 117.19 (CH₂=), 74.60 (CH), 70.09 (CH), 58.13 (CH), 45.45 (C), 44.71 (CH₂), 44.01 (C), 41.89 (C), 36.74 (CH), 36.00 (CH₃), 34.45 (CH₂), 32.20 (CH₂), 30.42 (CH₂), 30.06 (CH₂), 26.84 (CH₂), 26.41 (CH₃), 24.82 (CH₂), 16.74 (CH₃), 14.81 (CH₃), 11.43 (CH₃). HRMS (ESI) calcd [M+H]⁺ for C₂₄H₃₆O₅S 437.2356, found 437.2339.

(R)-5-ChloroMethyl-2-oxazolidinone(5):

The title compound was prepared by stirring a mixing of magnesium sulphate (10 mmol), Sodium Cyanate (10 mmol), water (50ml) in room temperature. (R)-(-)-Epichlorohydrin to the solution (5mmol) was added dropwise to the mixture. The result mixture was stirred under 60° C for 1h. The reaction mixture was concentrated in vacuo and extracted by ethyl acetate. The two layers were separated, and the organic layer was dried over Na₂SO₄, filtered, and concentrated to dryness. Yield: 57%. IR (KBr): 3365 (NH), 1744 (C=O), 1429 (C-N), 1240 (C-C(=O)-O), 736 (C-Cl) cm⁻¹. ¹H NMR (400 MHz, DMSO) δ 7.60 (s, 1H), 4.84 (dd, J = 9.6, 4.7 Hz, 1H), 4.04 – 3.73 (m, 2H), 3.59 (t, J = 9.0 Hz, 1H), 3.25 (dd, J = 9.0, 6.2 Hz, 1H). ¹³C NMR (101 MHz, d₆-DMSO) δ 158.68 (C=O), 74.35 (CH), 46.66 (CH₂), 43.03 (CH₂). HRMS (ESI) calcd [M+H]⁺ for C₄H₆ClNO 136.0159, found 136.0150.

General Procedure for Synthesis of Compounds 3a-3g

A mixing of thiols (1mmol), sodium hydroxide (1.1mmol), water (0.5ml) and methanol (3ml) were stirred in room temperature. After 30 minute, compound 2 (1.1mmol) in 5ml CH₂Cl₂ was added dropwise to the mixture for 36h-42h. The mixture was concentrated in vacuo. The residue was dissolved by CH₂Cl₂. The solution was extracted three times with water. The organic phase was dried overnight with anhydrous sodium sulfate. The solvent was concentrated in vacuo to give

crude products. The crude product was purified by silica gel column chromatography.

14-O-[(4-amino-pyrimidinone-2-yl) thioacetyl] mutilin (3a):

Compound **3a** was prepared according to the general procedure from 14-O-(p-toluene sulfonyloxyacetyl) mutilin(**2**) and 4-amino-2-Pyrimidinone. The crude product was purified over silica gel column chromatography to give 4.09 g. Yield: 84%. IR (KBr): 3448 (OH), 2933 (CH₂), 1730 (C=O), 1629 (C-C), 1583 (C=N), 1543 (C=C), 1467 (C=C), 1372 (CH₃), 1249(C-C(=O)-O), 1153(C-O), 1117 (C-(C=O)-C), 1018 (C-O-C) cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.89 (d, *J* = 5.1 Hz, 1H), 6.42 (dd, *J* = 17.1, 11.2 Hz, 1H), 6.04 (d, *J* = 5.2 Hz, 1H), 5.68 (d, *J* = 7.9 Hz, 1H), 5.17 (dd, *J* = 51.9, 14.0 Hz, 2H), 4.94 (s, 2H), 3.72 (dd, *J* = 32.8, 16.1 Hz, 2H), 3.28 (s, 1H), 2.24 (d, *J* = 6.5 Hz, 1H), 2.14 (dd, *J* = 14.8, 9.1 Hz, 2H), 2.02 (s, 1H), 1.94 (dd, *J* = 15.6, 8.5 Hz, 1H), 1.69 (d, *J* = 13.7 Hz, 1H), 1.61 – 1.52 (m, 2H), 1.48 (d, *J* = 12.0 Hz, 2H), 1.37 (s, 4H), 1.32 – 1.22 (m, 2H), 1.07 (s, 4H), 0.79 (d, *J* = 6.2 Hz, 3H), 0.68 (d, *J* = 6.2 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 216.11 (C=O), 168.72 (pyrimidine-C), 167.20 (C=O), 161.35 (pyrimidine-C), 154.88 (pyrimidine-C), 138.26 (CH=), 116.02 (CH₂=), 100.18 (pyrimidine-C), 73.60 (CH), 68.51(CH), 57.36 (CH), 57.21(CH₂), 44.46 (CH₂), 43.47 (C), 42.93 (C), 40.87 (CH), 35.81 (CH), 35.02 (CH), 33.48 (CH₂), 33.06 (CH₂), 29.45(CH₂), 25.89 (CH₃), 23.84 (CH₂), 15.74 (CH₃), 13.92 (CH₃), 10.44 (CH₃). HRMS (ESI) calcd [M+H]⁺ for C₂₆H₃₇N₃O₄S 488.2578, found 488.2570.

14-O-[(4-methylpyrimidine-2-yl) thioacetyl] mutilin (3b):

Compound **3b** was prepared according to the general procedure from 14-O-(p-toluene sulfonyloxyacetyl) mutilin(**2**) and 4-methy-2-pyrimidinone. The crude product was purified over silica gel column chromatography to give 3.55 g. Yield: 73%. IR (KBr): 3439 (OH), 2935 (CH₂), 1733 (C=O), 1658 (C-C), 1580 (C=N), 1535 (C=C), 1458 (C=C), 1396 (CH₃), 1285 (C-O-C), 1118 (C-(C=O)-C) cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 6.37 (dt, *J* = 33.7, 16.8 Hz, 1H), 5.99 (s, 1H), 5.69 (d, *J* = 8.4 Hz, 1H), 5.19 (dd, *J* = 56.5, 14.2 Hz, 2H), 3.88 – 3.73 (m, 2H), 3.29 (d, *J* = 5.6 Hz, 1H), 2.27 – 2.15 (m, 2H), 2.11 (d, *J* = 13.1 Hz, 3H), 2.02 (d, *J* = 6.4 Hz, 1H), 1.96 (d, *J* = 10.9 Hz, 1H), 1.69 (d, *J* = 14.2 Hz, 1H), 1.58 (dd, *J* = 21.0, 10.8 Hz, 2H), 1.49 (dd, *J* = 26.7, 13.3 Hz, 2H), 1.43 – 1.26 (m, 6H), 1.20 (dd, *J* = 17.5, 11.2 Hz, 2H), 1.05 (d, *J* = 20.9 Hz, 4H), 0.80 (d, *J* = 6.9 Hz, 3H), 0.67 (d, *J* = 6.9 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 215.94 (C=O), 165.80(C=O), 164.69 (pyrimidine-C), 164.11 (pyrimidine-C), 157.85 (pyrimidine-C), 137.90 (CH=), 116.27 (CH₂=), 107.63 (pyrimidine-C), 73.55 (CH), 69.14 (CH), 57.08 (CH), 44.43 (C),

43.49 (CH₂), 42.94 (C), 40.87 (C), 35.70 (CH), 35.00 (CH₃), 33.44 (CH₂), 32.23 (CH₂), 29.39 (CH₂), 25.84(CH₃), 25.36(CH₂), 23.82 (CH₂), 23.09 (CH₂), 15.84(CH₃), 13.84 (CH₃), 10.46 (CH₃). HRMS (ESI) calcd [M+H]⁺ for C₂₇H₃₈N₂O₄S 487.2625, found 487.2623.

14-O-[(benzimidazole-2-yl) thioacetyl] mutilin (3c):

Compound **3c** was prepared according to the general procedure from 14-O-(p-toluene sulfonyloxyacetyl) mutilin(**2**) and 2-mercaptobenzothiazole. The crude product was purified over silica gel column chromatography to give 3.54 g. Yield: 67%. IR (KBr): 3442 (OH), 2929 (CH₂), 1731 (C=O), 1458 (C=C), 1429 (C-C), 1274 (C-O-C), 1153 (C-O), 1117 (C-(C=O)-C) cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.77 (dd, *J* = 19.9, 8.0 Hz, 2H), 7.39 (t, *J* = 7.7 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 6.42 (dd, *J* = 17.4, 11.0 Hz, 1H), 5.76 (d, *J* = 8.5 Hz, 1H), 5.19 (dd, *J* = 57.6, 14.2 Hz, 2H), 4.08 (dd, *J* = 41.4, 16.2 Hz, 2H), 3.31 (d, *J* = 6.4 Hz, 1H), 2.29 (dd, *J* = 14.1, 7.2 Hz, 1H), 2.20 (dd, *J* = 11.6, 6.3 Hz, 1H), 2.06 (s, 1H), 1.98 (dd, *J* = 16.0, 8.5 Hz, 1H), 1.82 – 1.64 (m, 2H), 1.64 – 1.51 (m, 2H), 1.50 – 1.33 (m, 6H), 1.24 (dd, *J* = 14.3, 7.4 Hz, 2H), 1.13 – 0.97 (m, 4H), 0.85 (d, *J* = 7.0 Hz, 3H), 0.77 (d, *J* = 6.9 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 215.94 (C=O), 165.84 (C=O), 163.54 (benzothiazole-C), 151.74 (benzothiazole-C), 137.76 (CH=), 134.49(benzothiazole-C), 125.02 (benzothiazole-C), 123.46 (benzothiazole-C), 120.68 (benzothiazole-C), 120.05 (benzothiazole-C), 116.21 (CH₂=), 73.57 (CH), 69.20 (CH), 57.10 (CH), 44.42 (C), 43.41 (CH₂), 42.90 (C), 40.86 (C), 35.74 (CH), 34.98 (CH), 34.67 (CH₂), 33.43(CH₂), 29.40 (CH₂), 25.84 (CH₂), 25.28 (CH₃), 23.81 (CH₂), 15.80(CH₃), 13.81 (CH₃), 10.44 (CH₃). HRMS (ESI) calcd [M+H]⁺ for C₂₉H₃₇NO₄S 528.2237, found 528.2234.

14-O-[(benzothiazole-2-yl) thioacetyl] mutilin (3d):

Compound **3d** was prepared according to the general procedure from 14-O-(p-toluene sulfonyloxyacetyl) mutilin(**2**) and 2-mercaptobenzimidazole. The crude product was purified over silica gel column chromatography to give 3.68 g. Yield 72%. IR (KBr): 3423 (OH), 2925 (CH₂), 1726 (C=O), 1458 (C=C), 1439 (C-C), 1271 (C-O-C), 1152 (C-O), 1117 (C-(C=O)-C) cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.50 (dd, *J* = 5.8, 3.1 Hz, 2H), 7.20 (dd, *J* = 6.0, 3.2 Hz, 2H), 6.41 (dd, *J* = 17.4, 11.0 Hz, 1H), 5.79 (d, *J* = 8.4 Hz, 1H), 5.18 (dd, *J* = 43.7, 14.2 Hz, 2H), 3.91 (s, 2H), 3.73 (q, *J* = 7.0 Hz, 1H), 3.35 (d, *J* = 6.4 Hz, 1H), 2.35 – 2.28 (m, 1H), 2.27 – 2.17 (m, 1H), 2.08 (s, 1H), 2.03 (dd, *J* = 16.1, 8.6 Hz, 1H), 1.82 – 1.65 (m, 2H), 1.64 – 1.52 (m, 2H), 1.49 – 1.32 (m, 6H), 1.24 (t, *J* = 7.0 Hz, 2H), 1.16 – 1.05 (m, 4H), 0.88 (d, *J* = 6.9 Hz, 3H), 0.72 (d, *J* = 7.0 Hz,

3H). ^{13}C NMR (101 MHz, CDCl_3) δ 215.89 (C=O), 167.78 (C=O), 147.20 (benzimidazole-C), 137.75 (CH=), 121.68 (benzimidazole-C), 116.28 (CH_2 =), 73.61 (CH), 69.82 (CH), 57.43 (CH), 57.09 (benzimidazole-C), 44.42 (CH_2), 43.52 (C), 42.97 (C), 40.84 (C), 35.68 (CH), 35.04 (CH_2), 34.16 (CH_2), 33.42, 29.38 (CH_2), 25.84 (CH_2), 25.44 (CH_3), 23.83 (CH_2), 17.42 (CH_2), 15.80 (CH_3), 13.80 (CH_3), 10.50 (CH_3). HRMS (ESI) calcd $[\text{M}+\text{H}]^+$ for $\text{C}_{29}\text{H}_{38}\text{N}_2\text{O}_4\text{S}$ 511.2526, found 511.2531.

14-O-[(5-benzimidazolesulfonate-2-yl) thioacetyl] mutilin (3e):

Compound **3e** was prepared according to the general procedure from 14-O-(p-toluene sulfonyloxyacetyl) mutilin(**2**) and sodium 2-mercapto-5-benzimidazolesulfonate dihydrate. The crude product was purified over silica gel column chromatography to give 3.2 g. Yield: 54.2%. IR (KBr): 3448 (OH), 2940 (CH_2), 1732 (C=O) 1298 (C-O-C), 1190 (S=O), 1178 (S=O) cm^{-1} . ^1H NMR (400 MHz, DMSO) δ 7.80 (s, 1H), 7.69 (d, J = 8.5 Hz, 1H), 7.60 (d, J = 8.5 Hz, 1H), 6.04 (dd, J = 17.8, 11.2 Hz, 1H), 5.50 (d, J = 8.1 Hz, 1H), 4.96 (dd, J = 38.2, 14.5 Hz, 2H), 4.38 (d, J = 4.4 Hz, 1H), 3.36 (d, J = 5.5 Hz, 1H), 2.51 (s, 1H), 2.35 (s, 1H), 2.13 (dd, J = 21.0, 10.7 Hz, 1H), 2.08 – 1.96 (m, 2H), 1.90 (dd, J = 16.0, 8.1 Hz, 1H), 1.60 (s, 2H), 1.44 (d, J = 6.9 Hz, 1H), 1.33 (d, J = 7.6 Hz, 2H), 1.27 – 1.12 (m, 6H), 1.10 – 1.02 (m, 1H), 1.02 – 0.90 (m, 4H), 0.78 (d, J = 6.8 Hz, 3H), 0.58 (t, J = 9.3 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 217.48 (C=O), 166.34 (C=O), 150.52 (benzimidazole-C), 145.67 (benzimidazole-C), 141.16 (benzimidazole-C), 133.41 (CH=), 128.59 (benzimidazole-C), 125.97 (benzimidazole-C), 123.22 (benzimidazole-C), 115.68 (CH_2 =), 113.22 (CH_2), 110.71 (benzimidazole-C), 72.92 (CH), 71.44 (CH), 57.42 (CH), 45.35 (C), 44.58 (CH_2), 41.95 (C), 36.89 (CH), 36.64 (CH), 35.03 (CH_2), 34.40 (CH_2), 30.53 (CH_2), 29.06 (CH_2), 26.99 (CH_2), 24.85 (CH_2), 16.47 (CH_3), 14.64 (CH_3), 11.96 (CH_3). HRMS (ESI) calcd $[\text{M}+\text{H}]^+$ for $\text{C}_{29}\text{H}_{38}\text{N}_2\text{O}_7\text{S}_2$ 591.2193, found 591.2192.

14-O-[(pyrazolo[3,4d]pyrimidine-4-yl) thioacetyl] mutilin (3f):

Compound **3f** was prepared according to the general procedure from 14-O-(p-toluene sulfonyloxyacetyl) mutilin(**2**) and 4-mercaptopyrazolo[3,4-d]pyrimidine. The crude product was purified over silica gel column chromatography to give 4.30g. Yield: 84%. IR (KBr): 3431 (OH), 2934 (CH_2), 1732 (C=O), 1567 (C=C), 1456 (C=C), 1406 (C-C), 1271 (C-O-C), 1152 (C-O), 1117 (C-(C=O)-C), 981 (CH) cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 8.65 (d, J = 37.7 Hz, 1H), 8.29 – 8.08 (m, 1H), 6.43 (dt, J = 21.8, 10.9 Hz, 1H), 5.80 (d, J = 8.4 Hz, 1H), 5.38 – 5.29 (m, 1H), 5.24 (dd, J

= 33.0, 14.5 Hz, 2H), 4.18 – 4.02 (m, 2H), 3.38 (d, J = 6.3 Hz, 1H), 2.31 (dd, J = 13.9, 7.1 Hz, 1H), 2.22 (dd, J = 13.0, 7.5 Hz, 1H), 2.11 (t, J = 8.4 Hz, 1H), 2.04 (d, J = 7.9 Hz, 1H), 1.73 (dd, J = 31.9, 9.2 Hz, 2H), 1.65 (dd, J = 17.1, 7.1 Hz, 2H), 1.58 – 1.37 (m, 6H), 1.36 – 1.22 (m, 2H), 1.19 – 1.06 (m, 4H), 0.88 (t, J = 11.3 Hz, 3H), 0.79 (t, J = 12.6 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 216.06 (C=O), 166.18 (C=O), 162.56 (pyrimidine-C), 153.05 (pyrimidine-C), 151.46 (pyrimidine-C), 137.88 (CH=), 131.82 (pyrazolo-C), 116.28 (CH₂=), 110.65 (pyrimidine-C), 73.59 (CH), 69.22 (CH), 57.14 (CH), 44.46 (C), 43.57 (CH₂), 42.92 (C), 40.88 (C), 35.75 (CH), 35.01 (CH₂), 33.46 (CH₂), 31.11 (CH₂), 29.41 (CH₂), 25.44 (CH₃), 23.83 (CH₂), 17.40 (CH₂), 15.74 (CH₃), 13.86 (CH₃), 10.47 (CH₃). HRMS (ESI) calcd $[\text{M}+\text{H}]^+$ for $\text{C}_{27}\text{H}_{36}\text{N}_4\text{O}_4\text{S}$ 513.2530, found 513.2527.

14-O-[(furfuryl-2-yl) thioacetyl] mutilin (3g):

Compound **3g** was prepared according to the general procedure from 14-O-(p-toluene sulfonyloxyacetyl) mutilin (**2**) and furfuryl mercaptan. The crude product was purified over silica gel column chromatography to give 3.53 g. Yield: 74%. IR (KBr): 3547 (OH), 2933 (CH₂), 2882 (CH₂), 1731 (C=O), 1455 (C=C), 1281 (C-O-C), 1150 (C-O), 1115 (C-(C=O)-C) cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.29 (s, 1H), 6.42 (dd, J = 17.4, 11.0 Hz, 1H), 6.31 – 6.06 (m, 2H), 5.71 (d, J = 8.4 Hz, 1H), 5.23 (dd, J = 57.0, 14.2 Hz, 2H), 3.75 (s, 2H), 3.30 (s, 1H), 3.02 (s, 2H), 2.29 (dd, J = 13.7, 6.8 Hz, 1H), 2.15 (dt, J = 19.6, 8.8 Hz, 2H), 2.09 – 1.98 (m, 2H), 1.75 – 1.66 (m, 1H), 1.64 – 1.55 (m, 2H), 1.53 – 1.35 (m, 6H), 1.30 (t, J = 14.9 Hz, 2H), 1.17 – 1.05 (m, 4H), 0.82 (d, J = 7.0 Hz, 3H), 0.68 (d, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 215.99 (C=O), 167.67 (C=O), 149.27 (furan-C), 141.51 (furan-C), 138.12 (CH=), 116.19 (CH₂=), 109.37 (furan-C), 107.39 (furan-C), 73.65 (CH), 68.31 (CH), 57.21 (CH), 44.46 (C), 43.85 (CH₂), 42.94 (C), 40.77 (C), 35.78 (CH), 35.04 (CH), 33.45 (CH₂), 32.11 (CH₂), 29.44 (CH₂), 27.36 (CH₂), 25.85 (CH₃), 25.42 (CH₂), 23.86 (CH₂), 15.81 (CH₃), 13.92 (CH₃), 10.49 (CH₃). HRMS (ESI) calcd $[\text{M}+\text{H}]^+$ for $\text{C}_{27}\text{H}_{38}\text{O}_5\text{S}$ 475.2513, found 475.2522.

14-O-[(1-methylimidazole -2-yl) thioacetyl] mutilin (3h):

Compound **3h** was prepared according to the general procedure from 14-O-(p-toluene sulfonyloxyacetyl) mutilin(**2**) and 2-mercapto-1-methylimidazole. The crude product was purified over silica gel column chromatography to give 3.46 g. Yield: 73%. IR (KBr): 3423 (OH), 2924 (CH₂), 2863 (CH₂), 1717 (C=O), 1455 (C=C), 1410 (C-C), 1280 (C-O-C), 1145 (C-O), 1117

(C-(C=O)-C) cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 6.88 (d, J = 49.1 Hz, 2H), 6.35 (dd, J = 17.4, 11.0 Hz, 1H), 5.63 (d, J = 8.5 Hz, 1H), 5.32 – 5.01 (m, 2H), 3.92 – 3.62 (m, 2H), 3.56 (d, J = 11.0 Hz, 3H), 3.27 (s, 1H), 2.22 (dt, J = 13.8, 7.0 Hz, 1H), 2.19 – 2.07 (m, 2H), 2.03 (d, J = 21.6 Hz, 1H), 1.93 (dd, J = 16.0, 8.6 Hz, 1H), 1.77 – 1.61 (m, 1H), 1.58 – 1.46 (m, 3H), 1.45 – 1.35 (m, 2H), 1.31 (d, J = 14.3 Hz, 3H), 1.26 – 1.13 (m, 2H), 1.12 – 0.97 (m, 4H), 0.80 (d, J = 7.0 Hz, 3H), 0.59 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 215.93 (C=O), 166.75 (C=O), 139.06 (imidazole-C), 138.01 (CH=), 128.55 (imidazole-C), 121.39 (imidazole-C), 116.07 (CH₂=), 73.57 (CH), 68.77 (CH), 57.12 (CH), 44.42 (C), 43.48 (CH₂), 42.94 (C), 40.77 (C), 36.08 (CH), 35.70 (CH₂), 35.00 (CH₃), 33.44 (CH₂), 32.35 (CH₂), 29.40 (CH₂), 25.83 (CH₂), 25.41 (CH₃), 23.82 (CH₂), 15.61 (CH₃), 13.79 (CH₃), 10.44 (CH₃). HRMS (ESI) calcd $[\text{M}+\text{H}]^+$ for $\text{C}_{26}\text{H}_{38}\text{N}_2\text{O}_4\text{S}$ 475.2625, found 475.2630.

14-O-(2-oxazolidinone, 5-(methyl)-) (thioacetyl) mutilin(3i):

A mixing of (R)-5-chloromethyl-2-oxazolidinone (**5**) (1mmol), Sodiumiodide (0.1mmol), Acetone (10ml) were stirred in room temperature. After 30 minute, the reaction solution was filtered and concentrated. Compound **4** (1.1mmol) and triethylamine (20ml) was added under N_2 . The solvent was stirred in 40 °C for 10h. The mixture was extracted with water (10ml) and HCl (2N, 10ml). The organic layers were concentrated in vacuo to give crude products. The crude product was purified by silica gel column chromatography. Yield: 62%. IR (KBr): 3422 (O), 2933 (CH₂), 1735 (C=O), 1686 (C=O), 1458 (C=C), 1420 (C-C), 1284 (C-O-C), 1151 (C-O), 1117 (C-(C=O)-C) cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 6.63 – 6.35 (m, 1H), 6.17 (d, J = 8.2 Hz, 1H), 5.75 (d, J = 8.2 Hz, 1H), 5.27 (dd, J = 51.9, 14.2 Hz, 2H), 4.92 – 4.67 (m, 1H), 3.82 – 3.62 (m, 1H), 3.45 – 3.32 (m, 2H), 3.30 – 3.07 (m, 2H), 2.99 (ddd, J = 9.9, 8.9, 4.4 Hz, 1H), 2.87 (dt, J = 12.8, 5.2 Hz, 1H), 2.34 (s, 1H), 2.28 – 2.17 (m, 2H), 2.11 (s, 1H), 2.08 (d, J = 8.6 Hz, 1H), 1.77 (d, J = 14.3 Hz, 1H), 1.65 (d, J = 10.4 Hz, 2H), 1.52 (dd, J = 25.3, 6.7 Hz, 2H), 1.44 (d, J = 1.0 Hz, 4H), 1.39 (s, 1H), 1.35 – 1.26 (m, 1H), 1.16 (d, J = 14.9 Hz, 4H), 0.89 (d, J = 6.8 Hz, 3H), 0.73 (d, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 216.99 (C=O), 168.63 (C=O), 159.41 (C=O), 139.16 (CH=), 117.14 (CH₂=), 75.66 (CH), 74.61 (C), 69.70 (CH), 58.17 (CH), 45.46 (C), 45.06 (CH₂), 44.88 (CH₂), 43.95 (C), 41.78 (C), 36.75 (CH), 36.03 (CH), 35.99, 34.81 (CH), 34.45 (CH₂), 30.42 (CH₂), 26.86 (CH₃), 26.41 (CH₂), 24.84 (CH₂), 16.82 (CH₃), 14.88 (CH₃), 11.48 (CH₃). HRMS (ESI) calcd $[\text{M}+\text{Na}]^+$ for $\text{C}_{26}\text{H}_{39}\text{NO}_6\text{S}$ 516.2395, found 516.2394.







































































