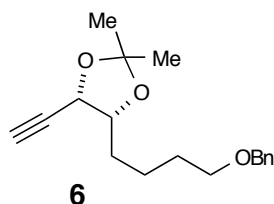


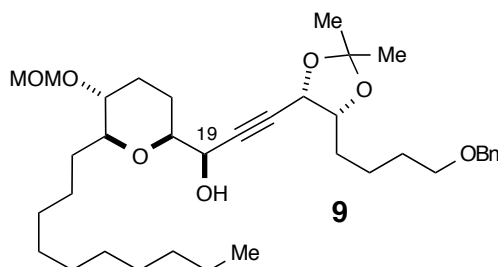
Total Synthesis of a New Cytotoxic Acetogenin, Jimenezin, and the Revised Structure

Shunya Takahashi, Katsuya Maeda, Shinsuke Hirota, and Tadashi Nakata

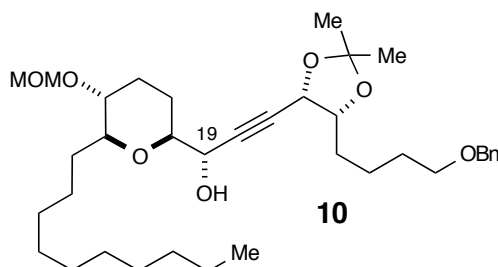
Supporting Information for Total Synthesis of a New Cytotoxic Acetogenin, Jimenezin, and the Revised Structure



Acetylene 6. $[\alpha]_D^{27} -30.6^\circ$ (*c* 0.98, CHCl_3); IR (neat) 3287, 2986, 2938, 2865, 2149, 1456, 1371, 1227, 1164, 1101, 1042, 863, 737, 698, 668 cm^{-1} ; $^1\text{H-NMR}$ (300MHz, CD_2Cl_2): δ 1.34 (3H, s), 1.41-1.89 (6H, m), 1.51 (3H, s), 2.55 (1H, d, $J = 2.4$ Hz), 3.51 (2H, t, $J = 6.3$ Hz), 4.08 (1H, ddd, $J = 7.8, 6.0, 5.4$ Hz), 4.50 (2H, s), 4.72 (1H, dd, $J = 5.4, 2.4$ Hz), 7.24-7.39 (5H, m); $^{13}\text{C-NMR}$ (75MHz, CD_2Cl_2): δ 23.13, 26.22, 27.98, 30.10, 30.80, 69.40, 70.55, 73.12, 75.60, 78.17, 80.71, 109.90, 127.74, 127.93, 128.61, 139.35; HRMS calcd for $\text{C}_{18}\text{H}_{25}\text{O}_3$ $[\text{M}+\text{H}]^+$ 289.1804, found 289.1790.

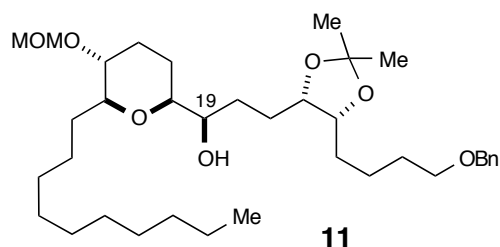


Acetylene alcohol 9. $[\alpha]_D^{29} -60.3^\circ$ (*c* 0.99, CHCl_3); IR (neat) 3444, 2927, 2856, 1497, 1455, 1370, 1226, 1104, 1039, 918, 862, 736, 698 cm^{-1} ; $^1\text{H-NMR}$ (300MHz, CD_2Cl_2): δ 0.88 (3H, t, $J = 6.8$ Hz), 1.20-1.87 (27H, m), 1.31 (3H, s), 1.48 (3H, s), 2.22 (1H, dddd, $J = 11.7, 3.9, 3.6, 3.0$ Hz), 2.52 (1H, d, $J = 7.2$ Hz), 3.12-3.24 (2H, m), 3.33 (3H, s), 3.39-3.46 (1H, m), 3.49 (2H, t, $J = 6.3$ Hz), 4.05 (1H, ddd, $J = 7.2, 6.0, 5.7$ Hz), 4.37 (1H, ddd, $J = 7.2, 3.6, 1.5$ Hz), 4.48 (2H, s), 4.57 (1H, d, $J = 6.8$ Hz), 4.69 (1H, d, $J = 6.8$ Hz), 4.74 (1H, dd, $J = 5.7, 1.5$ Hz), 7.24-7.38 (5H, m); $^{13}\text{C-NMR}$ (75MHz, CD_2Cl_2): δ 14.27, 23.08, 23.09, 25.65, 25.75, 26.26, 28.10, 29.73, 29.89, 30.03, 30.06, 30.08, 30.11, 30.19, 30.98, 32.31, 32.41, 55.68, 65.11, 69.60, 70.53, 73.09, 75.73, 78.38, 79.29, 81.20, 82.40, 85.71, 95.63, 109.74, 127.75, 127.93, 128.61, 139.30; Anal. calcd for $\text{C}_{36}\text{H}_{58}\text{O}_7$: C, 71.73; H, 9.70, found: C, 71.64; H, 9.80.

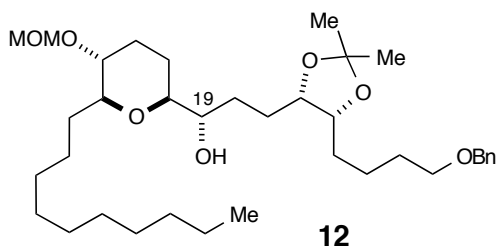


Acetylene alcohol 10. $[\alpha]_D^{27} -46.7^\circ$ (*c* 1.01, CHCl_3); IR (neat) 3447, 2926, 2855, 1456, 1379, 1370, 1226, 1103, 1039, 918, 862, 736, 698 cm^{-1} ; $^1\text{H-NMR}$ (300MHz, CD_2Cl_2): δ 0.88 (3H, t, $J = 6.8$ Hz), 1.20-1.91 (27H, m), 1.31 (3H, s), 1.47 (3H, s), 2.18-2.26 (1H, m), 2.68 (1H, d, $J = 3.5$ Hz), 3.14-3.24 (2H, m), 3.29-3.39 (1H, m), 3.33 (3H, s), 3.49 (2H, t, $J = 6.3$ Hz), 4.06 (1H, ddd,

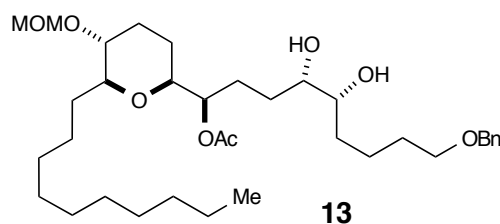
$J = 7.2, 6.0, 5.5$ Hz), 4.20 (1H, ddd, $J = 7.3, 3.5, 1.7$ Hz), 4.48 (2H, s), 4.58 (1H, d, $J = 6.8$ Hz), 4.69 (1H, d, $J = 6.8$ Hz), 4.74 (1H, dd, $J = 5.5, 1.7$ Hz), 7.23-7.39 (5H, m); $^{13}\text{C-NMR}$ (75MHz, CD_2Cl_2): δ 14.26, 23.07, 25.71, 26.17, 27.02, 28.08, 29.72, 29.87, 30.02, 30.06, 30.10, 30.18, 31.05, 32.30, 32.38, 55.69, 65.92, 69.57, 70.51, 73.09, 75.63, 78.30, 80.01, 81.05, 82.52, 85.52, 95.64, 109.74, 127.74, 127.93, 128.61, 139.30; Anal. calcd for $\text{C}_{36}\text{H}_{58}\text{O}_7$: C, 71.73; H, 9.70, found: C, 71.73; H, 9.78.



Alcohol 11. $[\alpha]_{\text{D}}^{24} -31.1^\circ$ (c 1.01, CHCl_3); IR (neat) 3477, 2925, 2856, 1455, 1378, 1368, 1306, 1245, 1217, 1102, 1041, 919, 863, 736, 698 cm^{-1} ; $^1\text{H-NMR}$ (300MHz, CD_2Cl_2): δ 0.88 (3H, t, $J = 6.8$ Hz), 1.20-1.85 (31H, m), 1.29 (3H, s), 1.38 (3H, s), 2.16-2.25 (2H, m), 3.13-3.26 (3H, m), 3.34 (3H, s), 3.48 (2H, t, $J = 6.3$ Hz), 3.59 (1H, ddd, $J = 8.1, 4.5, 3.6$ Hz), 3.98-4.10 (2H, m), 4.47 (2H, s), 4.57 (1H, d, $J = 6.8$ Hz), 4.70 (1H, d, $J = 6.8$ Hz), 7.23-7.37 (5H, m); $^{13}\text{C-NMR}$ (75MHz, CD_2Cl_2): δ 14.31, 23.10, 23.47, 24.95, 25.75, 26.08, 26.69, 28.76, 29.76, 29.90, 29.94, 30.05, 30.09, 30.11, 30.15, 30.17, 32.34, 32.52, 55.66, 70.68, 73.14, 73.63, 76.09, 78.34, 78.32, 79.98, 81.02, 95.59, 107.62, 127.74, 127.95, 128.62, 139.38; HRMS calcd for $\text{C}_{36}\text{H}_{63}\text{O}_7$ $[\text{M}+\text{H}]^+$ 607.4574, found 607.4568.

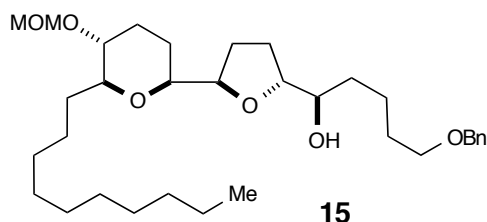


Alcohol 12. $[\alpha]_{\text{D}}^{25} -35.4^\circ$ (c 1.18, CHCl_3); IR (neat) 3525, 2927, 2855, 1456, 1377, 1368, 1245, 1217, 1101, 1040, 918, 863, 735, 698 cm^{-1} ; $^1\text{H-NMR}$ (300MHz, CD_2Cl_2): δ 0.88 (3H, t, $J = 6.8$ Hz), 1.22-1.72 (30H, m), 1.29 (3H, s), 1.38 (3H, s), 1.73-1.88 (1H, m), 2.15-2.27 (1H, m), 2.61 (1H, brd), 3.09-3.23 (3H, m), 3.33 (3H, s), 3.36-3.46 (1H, m), 3.48 (2H, t, $J = 6.3$ Hz), 3.97-4.08 (2H, m), 4.47 (2H, s), 4.57 (1H, d, $J = 6.8$ Hz), 4.70 (1H, d, $J = 6.8$ Hz), 7.23-7.38 (5H, m); $^{13}\text{C-NMR}$ (75MHz, CD_2Cl_2): δ 14.28, 23.08, 23.45, 25.83, 25.84, 26.11, 27.05, 28.75, 29.73, 29.77, 29.87, 30.03, 30.06, 30.15, 30.16, 32.31, 32.48, 55.67, 70.67, 73.12, 73.76, 75.99, 78.14, 78.33, 80.42, 80.87, 95.64, 107.59, 127.72, 127.93, 128.61, 139.39; HRMS calcd for $\text{C}_{36}\text{H}_{63}\text{O}_7$ $[\text{M}+\text{H}]^+$ 607.4574, found 607.4581.

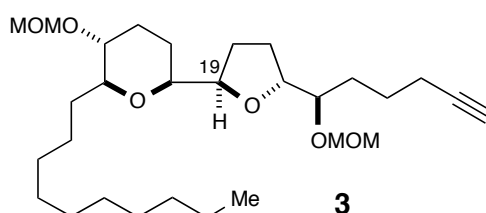


Diol 13. m.p. 77.5-78.0 $^\circ\text{C}$; $[\alpha]_{\text{D}}^{25} -17.7^\circ$ (c 0.28, CHCl_3); IR (KBr) 3360, 2923, 2853, 1732, 1462, 1456, 1443, 1379, 1362, 1323, 1260, 1208, 1125, 1111, 1092, 1049, 982, 914, 884, 870, 750 cm^{-1} ; $^1\text{H-NMR}$ (300MHz, CD_2Cl_2): δ 0.88 (3H, t, $J = 6.8$ Hz), 1.22-1.94 (31H, m), 1.95 (1H, d, $J = 4.2$ Hz), 2.01 (3H, s), 2.13 (1H, d, $J = 4.5$ Hz), 2.15-2.23 (1H, m), 3.10 (1H, ddd, $J = 9.0, 7.5, 2.4$ Hz), 3.18 (1H, ddd, $J = 9.3, 9.0, 4.5$ Hz), 3.31 (1H, ddd, $J = 10.5, 6.0, 2.1$ Hz), 3.33

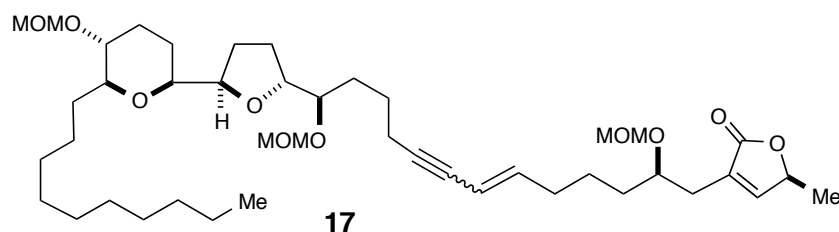
(3H, s), 3.48 (2H, t, $J = 6.3$ Hz), 3.53 (2H, m), 4.48 (2H, s), 4.56 (1H, d, $J = 6.8$ Hz), 4.69 (1H, d, $J = 6.8$ Hz), 4.79 (1H, ddd, $J = 7.8, 6.9, 3.9$ Hz), 7.23-7.37 (5H, m); $^{13}\text{C-NMR}$ (75MHz, CD_2Cl_2): δ 14.28, 21.31, 23.08, 23.13, 25.66, 27.20, 27.29, 27.78, 29.75, 30.04, 30.08, 30.11, 31.51, 32.31, 55.65, 70.73, 73.12, 74.82, 75.03, 75.74, 75.98, 78.14, 81.07, 95.55, 127.75, 127.95, 128.62, 139.27, 171.03; Anal. calcd for $\text{C}_{35}\text{H}_{60}\text{O}_8$: C, 69.05; H, 9.93, found: C, 69.05; H, 10.02.



Tetrahydrofuran alcohol 15. $[\alpha]_{\text{D}}^{24} -20.3^\circ$ (c 1.02, CHCl_3); IR (neat) 3482, 2925, 2855, 1455, 1362, 1306, 1212, 1152, 1105, 1040, 919, 735, 697 cm^{-1} ; $^1\text{H-NMR}$ (300MHz, CDCl_3): δ 0.88 (3H, t, $J = 6.8$ Hz), 1.18-2.10 (31H, m), 2.16-2.25 (1H, m), 2.26 (1H, brd), 3.06-3.24 (3H, m), 3.32-3.41 (1H, m), 3.36 (3H, s), 3.47 (2H, t, $J = 6.3$ Hz), 3.77 (1H, ddd, $J = 6.6, 6.6, 6.6$ Hz), 3.79 (1H, ddd, $J = 6.6, 6.6, 6.6$ Hz), 4.49 (2H, s), 4.59 (1H, d, $J = 6.8$ Hz), 4.72 (1H, d, $J = 6.8$ Hz), 7.22-7.38 (5H, m); $^{13}\text{C-NMR}$ (75MHz, CDCl_3): δ 14.17, 22.38, 22.72, 25.47, 27.92, 28.14, 28.84, 29.38, 29.65, 29.68, 29.71, 29.81, 29.87, 31.95, 32.09, 33.30, 55.49, 70.29, 72.83, 73.87, 75.91, 79.58, 80.57, 81.25, 82.74, 95.18, 127.30, 127.46, 128.17, 138.46; HRMS calcd for $\text{C}_{33}\text{H}_{57}\text{O}_6$ $[\text{M}+\text{H}]^+$ 549.4155, found 549.4156.

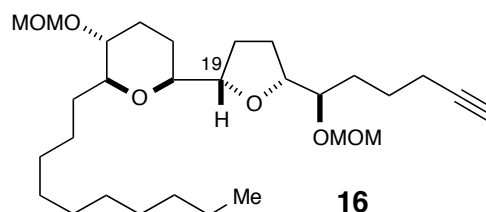


Acetylene 3. $[\alpha]_{\text{D}}^{25} -2.4^\circ$ (c 0.79, CHCl_3); IR (neat) 3345, 2926, 2855, 1733, 1456, 1361, 1298, 1214, 1151, 1104, 1039, 919 cm^{-1} ; $^1\text{H-NMR}$ (300MHz, CDCl_3): δ 0.88 (3H, t, $J = 6.8$ Hz), 1.18-2.10 (29H, m), 1.94 (1H, t, $J = 2.7$ Hz), 2.15-2.26 (3H, m), 3.06-3.24 (3H, m), 3.37 (3H, s), 3.39 (3H, s), 3.45-3.53 (1H, m), 3.78 (1H, ddd, $J = 6.9, 6.6, 6.6$ Hz), 3.97 (1H, ddd, 8.4, 6.3, 6.0 Hz), 4.59 (1H, d, $J = 6.8$ Hz), 4.67 (1H, d, $J = 6.8$ Hz), 4.72 (1H, d, $J = 6.8$ Hz), 4.82 (1H, d, $J = 6.8$ Hz); $^{13}\text{C-NMR}$ (75MHz, CDCl_3): δ 14.08, 18.39, 22.65, 24.33, 25.40, 28.19, 28.23, 28.70, 29.31, 29.59, 29.62, 29.65, 29.81, 30.15, 31.89, 32.04, 55.47, 55.72, 68.45, 76.01, 78.96, 79.83, 80.54, 81.29, 81.66, 84.18, 95.23, 96.62; HRMS calcd for $\text{C}_{28}\text{H}_{49}\text{O}_5$ $[\text{M}+\text{H}-\text{CH}_3\text{OH}]^+$ 465.3580, found 465.3572.

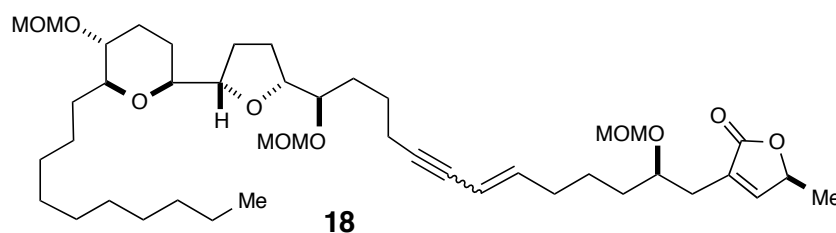


Enyne 17 ($E/Z = 94/6$ mixture). IR (neat) 2925, 2360, 2343, 1760, 1457, 1374, 1319, 1211, 1149, 1035, 958, 918, 721, 668 cm^{-1} ; $^1\text{H-NMR}$ E -isomer (270MHz, CDCl_3): δ 0.88 (3H, t, $J = 6.8$ Hz), 1.15-2.35 (38H, m), 1.41 (3H, d, $J = 6.8$ Hz), 2.49 (2H, d, $J = 5.7$ Hz), 3.05-3.23 (3H, m), 3.34 (3H, s), 3.36 (3H, s), 3.39 (3H, s), 3.44-3.53 (1H, m), 3.78 (1H, ddd, $J = 7.0, 7.0, 6.5$ Hz), 3.82 (1H, m), 3.97 (1H, ddd, $J = 7.8, 7.8, 6.5$), 4.59 (1H, d, $J = 6.8$ Hz), 4.61 (1H, d, $J =$

6.8 Hz), 4.65 (1H, d, $J = 6.8$ Hz), 4.67 (1H, d, $J = 6.8$ Hz), 4.72 (1H, d, $J = 6.8$ Hz), 4.81 (1H, d, $J = 6.8$ Hz), 5.02 (1H, dq, $J = 1.1, 6.8$ Hz), 5.44 (1H, d, $J = 15.7$ Hz), 6.00 (1H, ddd, $J = 15.7, 8.4, 7.0$ Hz), 7.15 (1H, d, $J = 1.1$ Hz); $^{13}\text{C-NMR}$ *E*-isomer (68MHz, CDCl_3): δ 14.15, 19.09, 19.42, 22.70, 24.45, 24.71, 25.44, 28.24, 28.76, 29.35, 29.65, 29.85, 30.06, 30.39, 31.91, 32.08, 32.74, 33.72, 55.45, 55.63, 55.70, 75.17, 75.96, 78.93, 79.28, 79.76, 80.47, 81.21, 81.59, 88.35, 95.14, 95.51, 96.52, 110.22, 130.25, 142.34, 151.29, 173.54; HRMS calcd for $\text{C}_{42}\text{H}_{69}\text{O}_9$ $[\text{M}+\text{H}-\text{CH}_3\text{OH}]^+$ 717.4942, found 717.4962.



Acetylene 16. $[\alpha]_{\text{D}}^{26} +3.2^\circ$ (c 0.93, CHCl_3); IR (neat) 3338, 2926, 2855, 1735, 1457, 1375, 1305, 1214, 1151, 1104, 1040, 982, 919 cm^{-1} ; $^1\text{H-NMR}$ (400MHz, CDCl_3): δ 0.87 (3H, t, $J = 6.8$ Hz), 1.20-1.91 (29H, m), 1.93 (1H, t, $J = 2.4$ Hz), 2.16-2.25 (3H, m), 3.09 (1H, ddd, $J = 8.8, 8.8, 2.4$ Hz), 3.19 (1H, ddd, $J = 9.8, 8.8, 4.4$ Hz), 3.22 (1H, ddd, $J = 10.7, 4.4, 2.0$ Hz), 3.36 (3H, s), 3.39 (3H, s), 3.53 (1H, ddd, $J = 7.8, 7.3, 2.4$ Hz), 3.83-3.95 (2H, m), 4.59 (1H, d, $J = 6.8$ Hz), 4.66 (1H, d, $J = 6.8$ Hz), 4.71 (1H, d, $J = 6.8$ Hz), 4.92 (1H, d, $J = 6.8$ Hz); $^{13}\text{C-NMR}$ (100MHz, CDCl_3): δ 14.10, 18.37, 22.68, 24.36, 25.53, 26.77, 27.83, 29.35, 29.64, 29.69, 29.73, 29.76, 30.09, 30.25, 31.92, 32.16, 55.49, 55.76, 68.41, 75.83, 79.35, 80.55, 80.95, 82.58, 84.31, 95.31, 96.88; HRMS calcd for $\text{C}_{28}\text{H}_{49}\text{O}_5$ $[\text{M}+\text{H}-\text{CH}_3\text{OH}]^+$ 465.3580, found 465.3585.



Enyne 18 (*E/Z* = 96 / 4 mixture). IR (neat) 2925, 2855, 1759, 1652, 1456, 1373, 1319, 1211, 1150, 1102, 1038, 956, 918, 722 cm^{-1} ; $^1\text{H-NMR}$ *E*-isomer (400MHz, CDCl_3): δ 0.86 (3H, t, $J = 6.8$ Hz), 1.20-1.90 (33H, m), 1.39 (3H, d, $J = 6.8$ Hz), 2.03-2.12 (2H, m), 2.15-2.22 (1H, m), 2.25-2.33 (2H, m), 2.47 (2H, d, $J = 5.9$ Hz), 3.04-3.12 (1H, m), 3.13-3.24 (2H, m), 3.32 (3H, s), 3.35 (3H, s), 3.38 (3H, s), 3.50 (1H, ddd, $J = 7.8, 7.3, 2.4$ Hz), 3.75-3.93 (3H, m), 4.58 (1H, d, $J = 6.8$ Hz), 4.59 (1H, d, $J = 6.8$ Hz), 4.63 (1H, d, $J = 6.8$ Hz), 4.65 (1H, d, $J = 6.8$ Hz), 4.70 (1H, d, $J = 6.8$ Hz), 4.90 (1H, d, $J = 6.8$ Hz), 5.00 (1H, dq, $J = 1.5, 6.8$ Hz), 5.42 (1H, d, $J = 15.6$ Hz), 5.97 (1H, ddd, $J = 15.6, 7.3, 6.8$ Hz), 7.14 (1H, d, $J = 1.5$ Hz); $^{13}\text{C-NMR}$ *E*-isomer (100MHz, CDCl_3): δ 14.06, 19.02, 19.33, 22.64, 24.41, 24.66, 25.47, 26.70, 27.72, 27.87, 29.30, 29.60, 29.64, 29.68, 29.71, 30.02, 30.06, 30.52, 31.88, 32.10, 32.71, 33.69, 55.44, 55.63, 55.69, 75.21, 75.80, 77.48, 79.24, 79.30, 79.39, 80.49, 80.92, 82.56, 88.50, 95.28, 95.59, 96.79, 110.37, 130.39, 142.41, 151.44, 173.75; HRMS calcd for $\text{C}_{43}\text{H}_{72}\text{O}_{10}\text{Na}$ $[\text{M}+\text{Na}]^+$ 771.5023, found 771.4988.