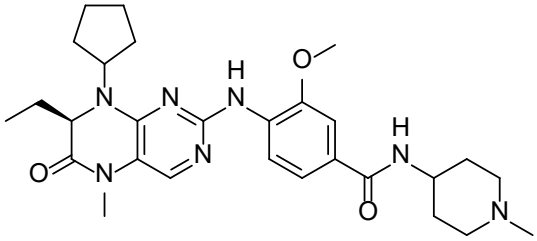
PLK1 Inhibitor | BI-2536

Synthesis of BI-2536 (Patent No. US 2006/35902)

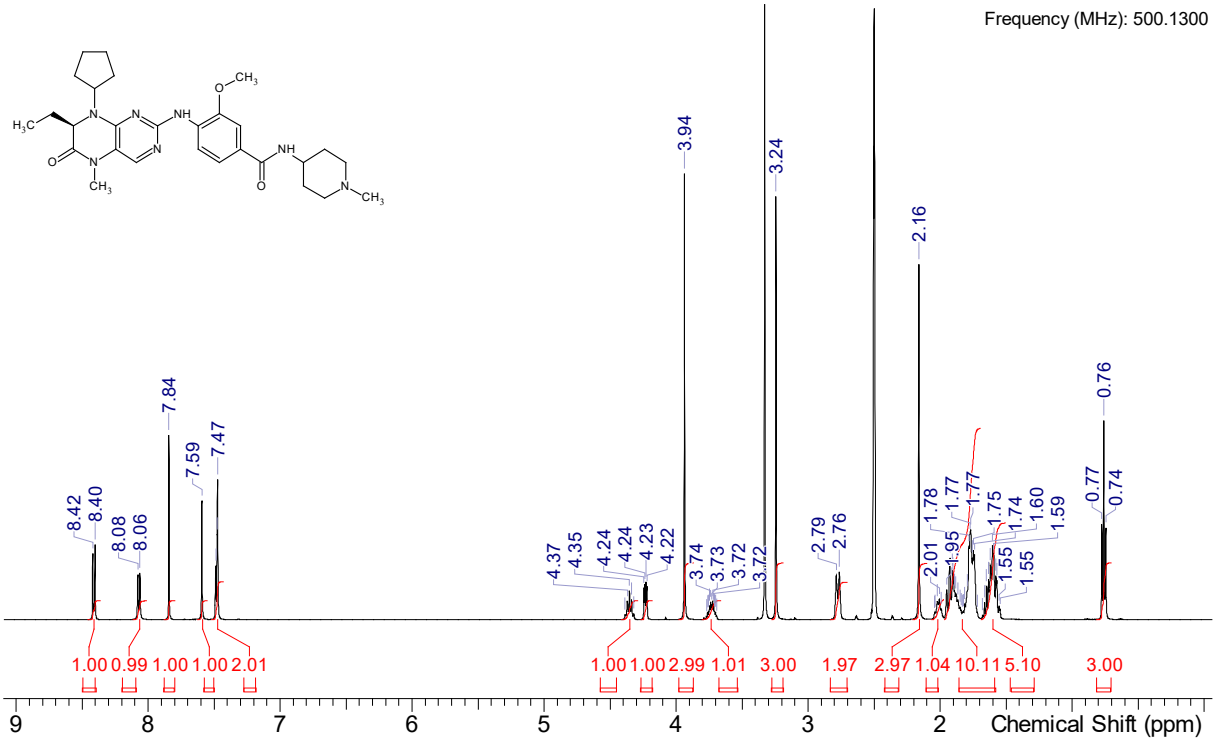
The compound numbers mentioned herein are a reference to the numbering system employed in: Gollner A., Heine C., Hofbauer K. S. Kinase Degraders, Activators, and Inhibitors: Highlights and Synthesis Routes to the Chemical Probes on opnMe.com, Part 1. *ChemMedChem* **2023**, 18, e202300031. DOI: 10.1002/cmdc.202300031, PubMed.

PLK1 Inhibitor, BI-2536 (Compound 67)



0.15 g of the 4-{[(7R)-8-cyclopentyl-7-ethyl-5-methyl-6-oxo-5,6,7,8-tetrahydropteridin-2-yl]amino}-3-methoxybenzoic acid, 0.12 g TBTU, 0.12 mL DIPEA were dissolved in 5 mL dichloromethane and stirred for 30 minutes at 25°C. 50 mg 1-methyl-4- aminopiperidin were added and the mixture was stirred for a further 2.5 hours at 25°C. The solution was extracted with water and evaporated. The residue was dissolved in warm ethyl acetate and crystallised from ether and petroleum ether. Yield: 25 mg of white crystals.

^{1}H NMR (DMSO-d6, 500 MHz) δ 8.41 (d, 1H, J=8.8 Hz), 8.07 (d, 1H, J=7.6 Hz), 7.84 (s, 1H), 7.59 (s, 1H), 7.4-7.5 (m, 2H), 4.35 (quin, 1H, J=8.3 Hz), 4.23 (dd, 1H, J=3.6, 7.7 Hz), 3.94 (s, 3H), 3.73 (tdt, 1H, J=4.1, 7.7, 11.4 Hz), 3.24 (s, 3H), 2.77 (br d, 2H, J=11.7 Hz), 2.16 (s, 3H), 2.0-2.1 (m, 1H), 1.7-2.0 (m, 10H), 1.5-1.7 (m, 5H), 0.76 (t, 3H, J=7.4 Hz)
^{13}C NMR (DMSO-d6, 125 MHz) δ 165.1, 162.9, 154.3, 151.5, 146.6, 138.3, 132.1, 126.7, 120.1, 116.1, 115.9, 109.2, 59.7, 58.3, 56.0, 54.7, 46.5, 46.0, 31.6, 28.7, 28.4, 27.8, 26.4, 23.2, 23.0, 8.8
HRMS (m/z): [M+H]+ calculated for C28H39N7O3, 522.31871; found, 522.31954;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3.73
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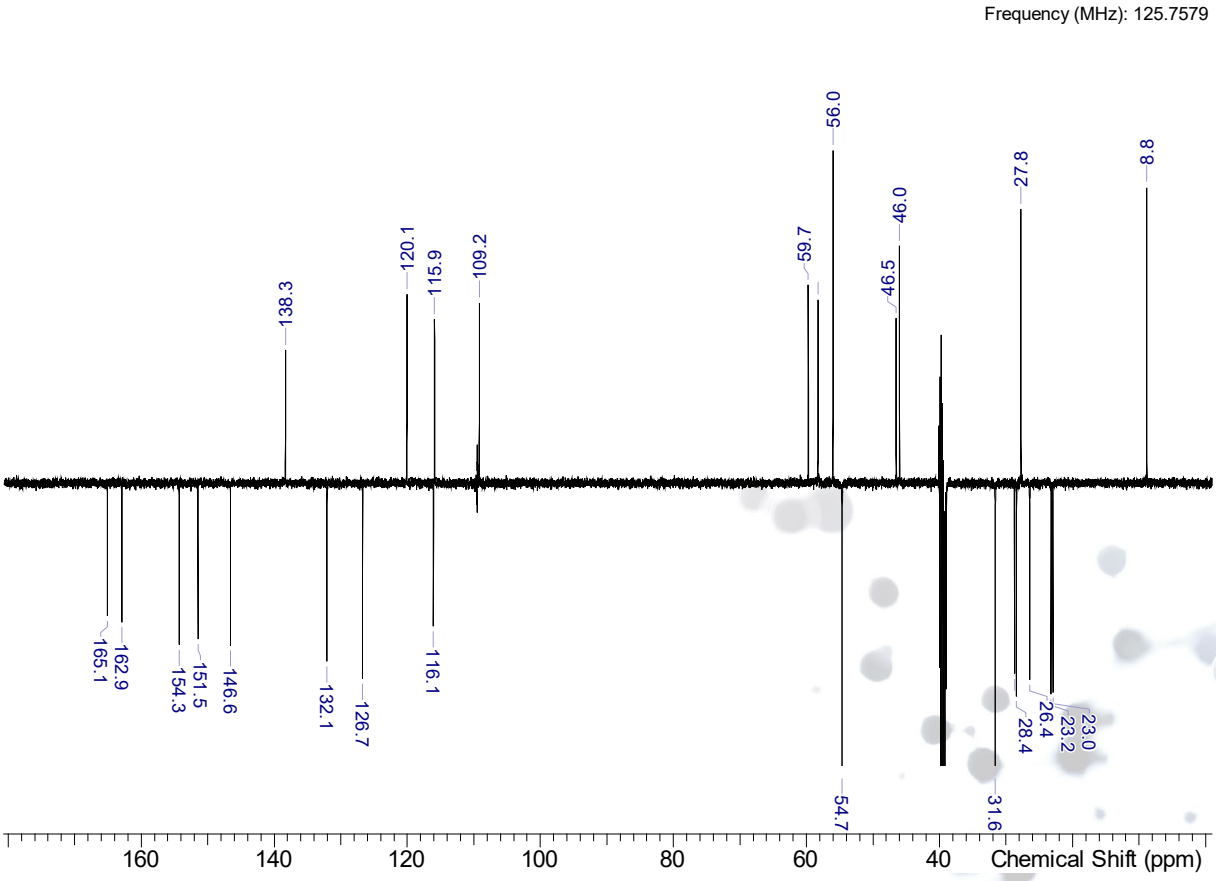
2.76
2.16
2.01
1.95
1.78
1.77
1.77
1.75
1.74
1.60
1.59
1.55
1.55
0.79
0.77
0.74
1.00 0.99 1.00 1.00 2.01
1.00 1.00 2.99 1.01 3.00 1.97 2.97 1.04 10.11 5.10 3.00
9 8 7 6 5 4 3 2
Chemical Shift (ppm)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138.3
132.1
126.7
120.1
115.9
116.1
109.2
59.7
56.0
54.7
46.5
46.0
31.6
28.4
27.8
26.4
23.2
23.0
8.8
160 140 120 100 80 60 40
Chemical Shift (ppm)