Supporting Information

Identification, Synthesis and Biological Evaluation of 6-[(6R)-2-(4-fluorophenyl)-6-(hydroxymethyl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrimidin-3-yl]-2-(2-methylphenyl)pyridazin-3(2H)-one, A Potent p38 MAP Kinase Inhibitor

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Combustion Analysis Data (C,H,N)

Compound	Calcd	Found
1	C,71.98; H,6.04; N,13.99	C,71.95; H,6.06; N,14.04
2a	C,67.85; H,5.18; N,17.98	C,67.22; H,5.26; N,17.59
2b	C,65.86; H,5.29; N,16.70	C,65.75; H,5.27; N,16.68
3b	C,65.50; H,5.54; N,15.53.	C,65.55; H,5.22; N,15.34.
3d	C,66.00; H,4.78; N,16.88.	C,66.18; H,4.83; N,16.78.
3e	C,66.15; H,4.79; N,16.98.	C,66.18; H,4.87; N,16.78.
3f	C,67.10; H,5.28; N,16.43.	C,66.81; H,5.14; N,16.23.
3g	C,67.01; H,5.33; N,16.36.	C,66.81; H,5.14; N,16.23.

3h	C,53.89; H,5.96; N,15.17.	C,54.22; H,5.98; N,14.80.
3i	C,63.83; H,4.91; N,15.38.	C,63.85; H,4.94; N,15.37.
3j	C,66.75; H,5.16; N,16.05.	C,66.81; H,5.14; N,16.23.
3k	C,64.97; H,4.50; N,15.79.	C,65.11; H,4.64; N,15.35.

Docking study

To date, more than 150 crystal structures of p38 MAP inhibitors have been published in the Protein Data Bank (PDB). Five crystal structures (PDB id: 3K3J, 2I0H, 3FI4, 1OVE, and 2GFS) were selected as docking templates based on ligand similarity to compound **2a**, which was calculated using FCFP_6 fingerprint in pipeline pilot version 8.0 (Accelrys Inc., San Diego). Hydrogen atoms were added to each structure using molecular modeling software Molecular Operation Environment version 2009.10 (Chemical Computing Group Inc., Montreal). Six compounds (**3d**, **3e**, **3f**, **3g**, and **3j**) with closely similar activities and chemical structures were docked into each structure using the docking program GOLD version 3.2. Only in the case of 1OVE were the docking poses of the six compounds conserved. Because it is reasonable to consider that docking poses are conserved among similar compounds with closely similar activities, docking models using 1OVE as a docking template were selected for this study.