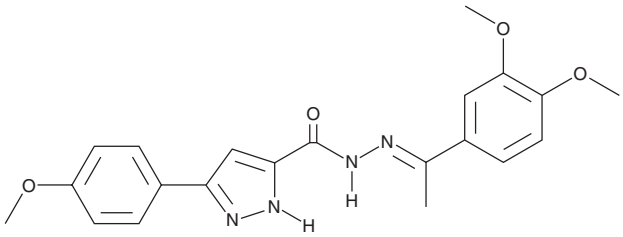
PRODUCT INFORMATION

SKI 178

Item No. 24880

CAS Registry No.:	1259484-97-3
Formal Name:	3-(4-methoxyphenyl)-1H-pyrazole-5-carboxylic acid, 2-[1-(3,4-dimethoxyphenyl) ethylidene]hydrazide
MF:	$C_{21}H_{22}N_4O_4$
FW:	394.4
Purity:	≥98%
UV/Vis.:	λ_{max}: 314 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

SKI 178 is supplied as a crystalline solid. A stock solution may be made by dissolving the SKI 178 in the solvent of choice. SKI 178 is soluble in organic solvents such as DMSO and dimethyl formamide, which should be purged with an inert gas. The solubility of SKI 178 in these solvents is approximately 25 mg/ml.

SKI 178 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, SKI 178 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. SKI 178 has a solubility of approximately 0.2 mg/ml in a 1:4 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

SKI 178 is an inhibitor of sphingosine kinase 1 (SPHK1) and SPHK2.[1] Though previously thought to be selective for SPHK1, cellular thermal shift assay results demonstrate direct target engagement of both SPHK1 and SPHK2 in HEK293 cells overexpressing either SPHK1 or SPHK2. It inhibits SPHK1 by 59.6% when used at a concentration of 10.7 µM and inhibits the production of sphingosine-1-phosphate (S1P; Item No. 62570) in A549 cells.[2] SKI 178 is cytotoxic to a variety of cancer cell lines including PANC-1, A549, U251, and MCF-7 cells (IC_{50}s = 0.1, 0.3, 0.5, and 1.3 µM, respectively). It prolongs mitosis and induces cell death through the intrinsic apoptotic pathway in a CDK1-dependent manner.[3] SKI 178 (20 mg/kg every other day) reduces the number of white blood cells to a normal range and increases survival in an MLL-AF9 acute myeloid leukemia (AML) mouse xenograft model.[1] It also destabilizes and inhibits microtubule polymerization in an SPHK-independent manner.

References

1. Hengst, J.A., Dick, T.E., Sharma, A., *et al.* SKI-178: A multitargeted inhibitor of sphingosine kinase and microtubule dynamics demonstrating therapeutic efficacy in acute myeloid leukemia models. *Cancer Transl. Med.* **3(4)**, 109-121 (2017).
2. Hengst, J.A., Wang, X., Sk, U.H., *et al.* Development of a sphingosine kinase 1 specific small-molecule inhibitor. *Bioorg. Med. Chem. Lett.* **20(24)**, 7498-7502 (2010).
3. Dick, T.E., Hengst, J.A., Fox, T.E., *et al.* The apoptotic mechanism of action of the sphingosine kinase 1 selective inhibitor SKI-178 in human acute myeloid leukemia cell lines. *J. Pharmacol. Exp. Ther.* **352(3)**, 494-508 (2015).

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