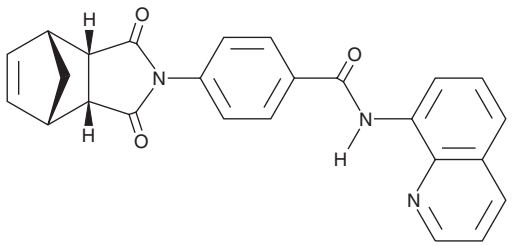
PRODUCT INFORMATION

IWR-1-endo

Item No. 13659

CAS Registry No.:	1127442-82-3
Formal Name:	4-[(3aR,4S,7R,7aS)-1,3,3a,4,7,7a-hexahydro-1,3-dioxo-4,7-methano-2H-isoindol-2-yl]-N-8-quinolinyl-benzamide
MF:	$C_{25}H_{19}N_3O_3$
FW:	409.4
Purity:	≥98%
UV/Vis.:	λ_{max}: 240, 320 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

IWR-1-endo is supplied as a crystalline solid. A stock solution may be made by dissolving the IWR-1-endo in the solvent of choice, which should be purged with an inert gas. IWR-1-endo is soluble in organic solvents such as DMSO and dimethyl formamide. The solubility of IWR-1-endo in these solvents is approximately 20 mg/ml.

IWR-1-endo is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, IWR-1-endo should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. IWR-1-endo has a solubility of approximately 0.25 mg/ml in a 1:3 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

Wnt signaling proteins are small secreted proteins that are active in embryonic development, tissue homeostasis, and tumorigenesis.[1-3] Wnt proteins bind to receptors on the cell surface, initiating a signaling cascade that leads to β-catenin activation of gene transcription. IWR-1-endo is a potent inhibitor of the Wnt response, blocking a cell-based Wnt/β-catenin pathway reporter response with an IC_{50} value of 180 nM.[4] It inhibits, at 10 µM, Wnt-induced accumulation of β-catenin, leading to proteasomal degradation of this protein through a destruction complex which consists of Apc, Axin2, Ck1, and GSK3β. IWR-1-endo stabilizes the destruction complex, increasing the level of Axin2 protein without changing the levels of Apc or GSK3β.[4] The IWR compound does not change the *de novo* synthesis of Axin2, alter the affinity of Axin2 for β-catenin, or inhibit the proteasome. It has a half-life of 60 minutes in murine whole blood and 20 minutes in intact murine hepatocytes.[5] In *in vivo* tests, IWR-1-endo inhibits zebrafish tail fin regeneration with a minimum inhibitory concentration of 0.5 µM.[5] The IWR-1-exo diastereomer exhibits much less activity against the Wnt/β-catenin pathway and has been used as a control.[4]

References

1. Clevers, H. *Cell* **127(3)**, 469-480 (2006).
2. Polakis, P. *Genes Dev.* **14(15)**, 1837-1851 (2000).
3. Reya, T. and Clevers, H. *Nature* **434(7035)**, 834-850 (2005).
4. Chen, B., Dodge, M.E., Tang, W., *et al. Nat. Chem. Biol.* **5(2)**, 100-107 (2009).
5. Lu, J., Ma, Z., Hsieh, J.C., *et al. Bioorg. Med. Chem. Lett.* **19(14)**, 3825-3827 (2009).

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