

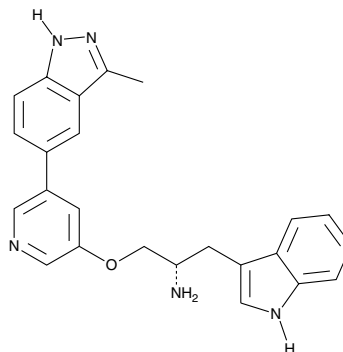
Product Information



A-443654

Item No. 16499

CAS Registry No.: 552325-16-3
Formal Name: α S-[[[5-(3-methyl-1H-indazol-5-yl)-3-pyridinyl]oxy]methyl]-1H-indole-3-ethanamine
MF: C₂₄H₂₃N₅O
FW: 397.5
Purity: ≥98%
Stability: ≥2 years at -20°C
Supplied as: A crystalline solid
UV/Vis.: λ_{max} : 222, 291 nm



Laboratory Procedures

For long term storage, we suggest that A-443654 be stored as supplied at -20°C. It should be stable for at least two years.

A-443654 is supplied as a crystalline solid. A stock solution may be made by dissolving the A-443654 in the solvent of choice. A-443654 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas. The solubility of A-443654 in these solvents is approximately 10, 15, and 20 mg/ml, respectively.

A-443654 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, A-443654 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. A-443654 has a solubility of approximately 0.5 mg/ml in a 1:1 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Three related forms of the kinase Akt (1, 2, 3, also known as protein kinase B isoforms PKB α , β , γ) modulate cell proliferation, metabolism, and survival as well as angiogenesis. A-443654 is an inhibitor of Akt (K_i = 160 pmol/L for all three isoforms) that interferes with mitotic progression and bipolar spindle formation.^{1,2} It induces G₂/M accumulation, defects in centrosome separation, and formation of either monopolar arrays or disorganized spindles.² A-443654 has been reported to slow the progression of Akt-dependent tumors in *in vivo* mouse models.¹ In response to an A-443654-induced decrease in phosphorylation of Akt targets, a concomitant increase in Thr³⁰⁸ and Ser⁴⁷³ phosphorylation of Akt has been observed in human cancer cell lines.³ A-443654 has been used to examine the mechanism of this rapid feedback reaction.

References

1. Luo, Y., Shoemaker, A.R., Liu, X., *et al.* Potent and selective inhibitors of Akt kinases slow the progress of tumors *in vivo*. *Mol. Cancer Ther.* **4**(6), 977-968 (2005).
2. Liu, X., Shi, Y., Woods, K.W., *et al.* Akt inhibitor A-443654 interferes with mitotic progression by regulating Aurora A kinase expression. *Neoplasia* **10**(8), 828-837 (2008).
3. Han, E.-K., Levenson, J.D., McGonigal, T., *et al.* Akt inhibitor A-443654 induces rapid Akt Ser-473 phosphorylation independent of mTORC1 inhibition. *Oncogene* **26**(38), 5655-5661 (2007).

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