

Product Data Sheet

Product Name: TMP778
Cat. No.: GC31163

Chemical Properties

Cas. No. 1422171-08-1

SMILES O=C(N[C@H](C1=CC=C(C)C=C1C)C2=CC=CC=C2)CC3=CC=C(OC(C(C4=C(C)ON=C4C)O)=C5)C5=C3

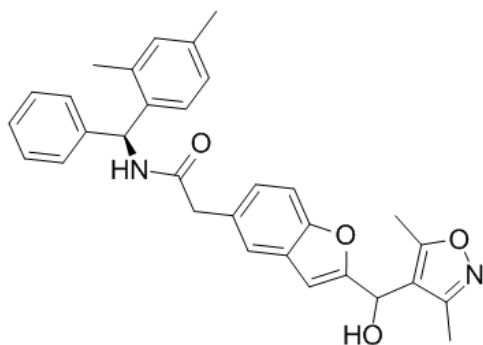
Formula $C_{31}H_{30}N_2O_4$ M.Wt 494.58

Solubility Soluble in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Background

TMP778 is a potent and selective ROR γ t inverse agonist, with an IC₅₀ of 7 nM in FRET assay.

It is found that TMP778 at >2.5 μ M starts to show toxic effects on cell growth, which however is not ROR γ t-dependent, since the proliferation of ROR γ t-deficient T cells cultured under Th17 cell-polarizing conditions is also decreased. Otherwise, these inhibitors do not show inhibitory effects on

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cell proliferation or ROR γ t expression or its nuclear translocation, but efficiently inhibited IL-17 production. TMP778 has a much broader dose range and efficiently decreased IL-17 production, consistent with its higher binding affinity for ROR γ t. These data indicate that TMP778 is the ROR γ t inhibitor that most potently reduced IL-17 production[2].

All three compounds (e.g., TMP778) delay the onset of disease and substantially reduce the severity of disease progression compared to control-treated mice. Consistent with in vitro results, TMP778 treatment causes the most pronounced effect on the disease phenotype. This treatment not only decreases the number of mononuclear cells infiltrating the central nervous system (CNS), but also most strongly reduces the percentage of IL-17+ T cells in the CNS (including IL-17+ IFN γ +). There is no significant change in the percentage IFN γ + IL-17-T cells in the CNS among all groups, indicating that none of the inhibitors affects Th1 responses. TMP778 strongly inhibits Th17 cell generation, reduces IL-17 production from differentiated Th17 cells, and also dramatically ameliorates the progression of EAE[2].

[1]. Skepner J, et al. Pharmacologic inhibition of ROR γ t regulates Th17 signature gene expression and suppresses cutaneous inflammation in vivo. J Immunol. 2014 Mar 15;192(6):2564-75. [2]. Xiao S, et al. Small-molecule ROR γ t antagonists inhibit T helper 17 cell transcriptional network by divergent mechanisms. Immunity. 2014 Apr 17;40(4):477-89.

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