

# MRK-990: A chemical probe for PRMT9/5

Version 1.0 (15<sup>th</sup> October 2022)

Web link for more details: <https://www.thesgc.org/chemical-probes/MRK-990>

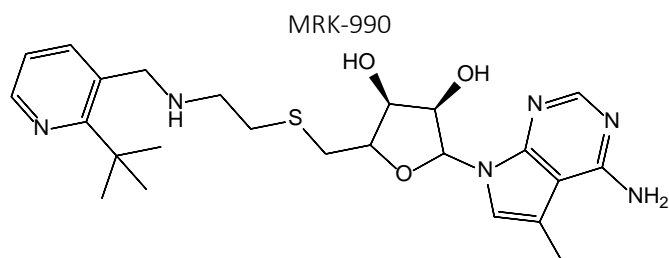
## Overview

MSD in collaboration with the SGC has developed a dual activity chemical probe MRK-990 for PRMT9 and PRMT5. When used in parallel with selective chemical probes for PRMT5 (e.g., GSK591 and LLY-283), MRK-990 can be used to study the biological role of PRMT9.

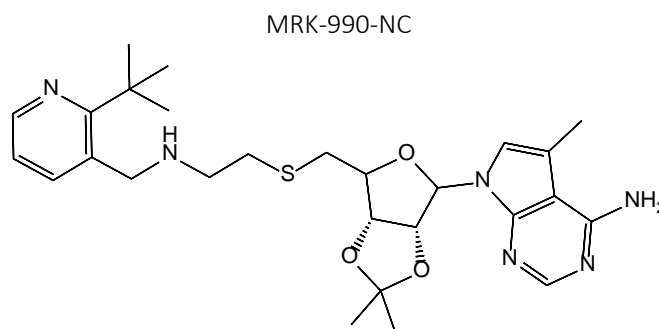
## Summary

Chemical Probe Name	MRK-990
Negative control compound	MRK-990-NC
Target(s) (synonyms)	PRMT9/PRMT5
Recommended <i>in vitro</i> assay concentration	< 0.1 $\mu$ M; use with negative control, and orthogonal controls for PRMT5 for best interpretation of data
Suitability for <i>in vivo</i> use and recommended dose	This chemical probe was not tested for <i>in vivo</i> use.
Publications	
Orthogonal chemical probes	GSK591, LLY-283
<i>In vitro</i> assay(s) used to characterise	Radioactivity (methyltransferase), SPR
Cellular assay(s) for target-engagement	NanoBRET, in cell western
ChemicalProbes.org	

## Chemical Probe & Negative Control Structures and Use



SMILES:  
Cc1cn(C2[C@@H]([C@@H](C(CSCCNc3cccnc3C(C)(C)O)O)c2c1c(N)ncn2  
InChiKey: PYMRXCFAOAFGR-VROYJQPTSA-N  
Molecular weight: 486.2  
Storage: As a dry powder or as DMSO stock solutions (10 mM) at -20 °C.  
DMSO stocks beyond 3-6 months or 2 freeze/thaw cycles should be tested for activity before use  
Dissolution: Soluble in DMSO up to 50 mM; use only 1 freeze/thaw cycle per aliquot



SMILES:  
Cc1cn(C2[C@H]3[C@@H](C(CSCCNc4cccnc4C(C)(C)O)OC(C)(C)O3)c2c1c(N)ncn2  
InChiKey: AOTRDGXOHNXERF-DHYJKAKLSA-N  
Molecular weight: 526.3  
Storage: As a dry powder or as DMSO stock solutions (10 mM) at -20 °C.  
DMSO stocks beyond 3-6 months or 2 freeze/thaw cycles should be tested for activity before use  
Dissolution: Soluble in DMSO up to 50 mM; use only 1 freeze/thaw cycle per aliquot

## Chemical Probe Profile

***In vitro* Potency & Selectivity:** In a radioactivity-based methyltransferase assay, MRK-990 inhibits PRMT9 with  $IC_{50}$  = 10 nM and PRMT5 with  $IC_{50}$  = 30 nM.

***Potency in Cells and Cellular Target Engagement:*** In an in-cell western, MRK-990 inhibits the symmetric dimethylation of SAP145 (PRMT9) with  $IC_{50}$  = 145 nM, and dimethylarginine (PRMT5) with  $IC_{50}$  = 519 nM.