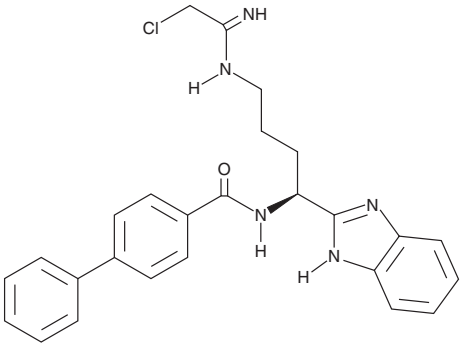
PRODUCT INFORMATION

BB-Cl-Amidine

Item No. 17079



CAS Registry No.: 1802637-39-3
Formal Name: N-[(1S)-1-(1H-benzimidazol-2-yl)-4-[(2-chloro-1-iminoethyl)amino]butyl]-[1,1'-biphenyl]-4-carboxamide
MF: $C_{26}H_{26}ClN_5O$
FW: 460.0
Purity: ≥95%
UV/Vis.: λ_{max}: 274, 281 nm
Supplied as: A crystalline solid
Storage: -20°C
Stability: ≥1 year

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

Laboratory Procedures

BB-Cl-Amidine is supplied as a crystalline solid. A stock solution may be made by dissolving the BB-Cl-Amidine in the solvent of choice. BB-Cl-Amidine is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide, which should be purged with an inert gas. The solubility of BB-Cl-Amidine in ethanol is approximately 25 mg/ml and approximately 20 mg/ml in DMSO and DMF.

BB-Cl-Amidine is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, an ethanolic solution of BB-Cl-amidine should be diluted with the aqueous buffer of choice. BB-Cl-Amidine has a solubility of approximately 0.5 mg/ml in a 1:1 solution of ethanol:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

BB-Cl-Amidine is a modified version of Cl-amidine (Item No. 10599) that retains the functional components but possesses a C-terminal benzimidazole group designed to limit proteolysis of the C-terminal amide.[1] BB-Cl-Amidine irreversibly inactivates all four PAD subtypes (k_{inact}/K_I = 16,100, 4,100, 6,800, and 13,300 $M^{-1}min^{-1}$ for PAD1-4, respectively) by covalently modifying an active site cysteine that is important for its catalytic activity.[2,3] The cellular potency of BB-Cl-amidine against PAD4 is increased 20-fold over the parent compound (EC_{50} = 8.8 µM *versus* >200 µM for Cl-amidine). BB-Cl-Amidine also has a significantly longer *in vivo* half-life than Cl-amidine (1.75 h *versus* ~15 min, respectively). Both compounds inhibit the formation of neutrophil extracellular traps without altering H_2O_2 production by neutrophils.[1] BB-Cl-Amidine is effective *in vivo*, improving endothelial function while downregulating the expression of type I interferon-regulated genes in MRL/*lpr* mice.

References

1. Knight, J.S., Subramanian, V., O'Dell, A.A., *et al.* Peptidylarginine deiminase inhibition disrupts NET formation and protects against kidney, skin and vascular disease in lupus-prone MRL/lpr mice. *Ann. Rheum. Dis.* **74(12)**, 2199-2206 (2015).
2. Luo, Y., Arita, K., Bhatia, M., *et al.* Inhibitors and inactivators of protein arginine deiminase 4: Functional and structural characterization. *Biochem.* **45(39)**, 11727-11736 (2006).
3. Muth, A., Subramanian, V., Beaumont, E., *et al.* Development of a selective inhibitor of protein arginine deiminase 2. *J. Med. Chem.* **60(7)**, 3198-3211 (2017).

CAYMAN CHEMICAL
1180 EAST ELLSWORTH RD
ANN ARBOR, MI 48108 · USA
PHONE: [800] 364-9897
[734] 971-3335
FAX: [734] 971-3640
CUSTSERV@CAYMANCHEM.COM
WWW.CAYMANCHEM.COM