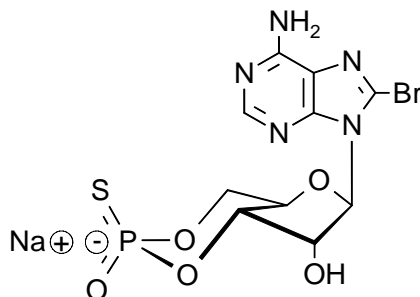


Technical Information about Sp-8-Br-cAMPS

Potent membrane-permeant, metabolically stable activator of cAMP-dependent protein kinases

Update: April 30, 2009 HU



Abbreviation: Sp-8-Br-cAMPS

Formula	CAS No.	Molecular Weight	UV	BIOLOG Cat.No.
C ₁₀ H ₁₀ BrN ₅ O ₅ PS·Na	[127634-20-2]	446.2	λ _{max} 264 nm / ε 17000 / pH 7	B 002

Name: 8- Bromoadenosine- 3', 5'- cyclic monophosphorothioate, Sp- isomer

Description: Sp-8-Br-cAMPS is an analogue of the parent compound cyclic AMP in which the hydrogen in position 8 of the nucleobase is replaced by bromine and the axial one of the two exocyclic oxygen atoms in the cyclic phosphate moiety is modified by sulfur. The suffix "p" indicates that R/S nomenclature refers to phosphorus.

Properties: Sp-8-Br-cAMPS combines the structures of the two well known protein kinase activators Sp-cAMPS and 8-Br-cAMP yielding a novel membrane permeant cyclic AMP mimetic^{1-5, 6, 7} which is not degraded by mammalian cyclic nucleotide phosphodiesterases.

Sp-8-Br-cAMPS is about 2 times more lipophilic compared to 8-Br-cAMP and Sp-cAMPS and 4 times more compared to cAMP, respectively⁸. If you have good or moderate results with 8-Br-cAMP or Sp-cAMPS, you can be sure that Sp-8-Br-cAMPS will be membrane-permeant in your system as well.

Application: Applicable concentrations of Sp-8-Br-cAMPS strongly depend on the type of biosystem, its membrane properties and kinase content.

Since Sp-8-Br-cAMPS is hydrolytically stable in mammalian and many other systems, there is no danger of degradation during incubation periods. Sp-8-Br-cAMPS is a good choice, if unwanted side effects of metabolites of hydrolyzable cyclic AMP analogues, e.g. 8-Br-cAMP or 8-CPT-cAMP, must be excluded and solely the effect of an intact protein kinase A agonist is desired⁹.

Specification: Lyophilized or crystallized sodium salt. The free acid or other salt forms are available upon request. Equal concentrations of Sp-8-Br-cAMPS can appear very different in volume due to sensitivity of the lyophilized form to humidity. The compound can even contract to small volume droplets. Normally the compound is located in the conical bottom of the tube. Micromolar quantities are determined by UV at λ_{max}.

Purity: Typical analysis is better than 98% (HPLC / UV / 264 nm). The product is not sterile and has not been tested for endotoxins.

Stability and Storage: Sp-8-Br-cAMPS has sufficient stability at room temperature and does not need special care during handling or shipment. Nevertheless, we recommend that the compound should be stored in the freezer, for longer storage periods preferably in freeze-dried form.

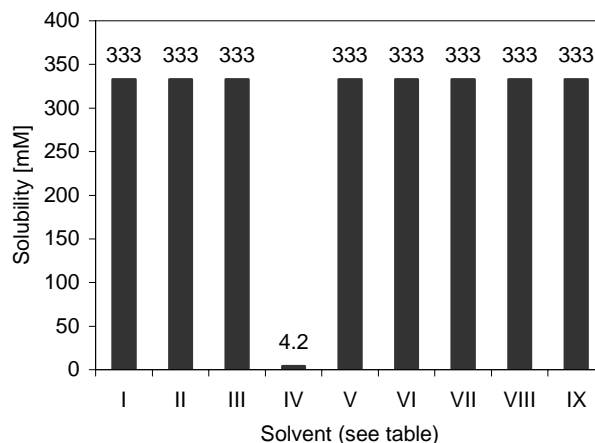
Toxicity and Safety: Since cyclic AMP has multiple tasks in every organism it is very likely that lipophilic cAMP analogues will interfere with many cell regulation processes *in vivo*. However, due to the rather small quantities to work with no health hazards have been reported. Nevertheless please keep in mind that the *in vivo* properties of these compounds are not sufficiently characterized up to now. Avoid skin contact or ingestion and allow only trained personnel to handle the product.

Our products are designed, developed and sold for research purposes only! They are intended for *in vitro* and nonhuman *in vivo* laboratory applications. Any other use requires approval of health authorities.

Not for drug, household or related uses!

Solubility: Detailed information on the solubility of Sp-8-Br-cAMPS in water and various buffers are listed in the solubility chart below. Concentrations have been tested at ambient temperature and can be considered as minimum concentrations usually obtainable, however, slight batch-to-batch variations cannot be ruled out. When opening the tube please make sure that no substance is lost within the cap. Please rinse tube walls carefully and preferably use ultrasonic or vortex to achieve total and uniform mixing.

No.	Solvent	Solubility [mM]
I	H ₂ O	333
II	DMSO	333
III	DMF	333
IV	Ethanol 96%	4.2
V	Methanol	333
VI	PBS, pH 7.4	333
VII	100 mM Na ₂ HPO ₄ , pH 7.0	333
VIII	25 mM Hepes/NaOH, pH 7.2	333
IX	25 mM Tris/HCl, pH 7.4	333



Selected References for Sp-8-Br-cAMPS:

For a comprehensive and updated list please visit our website (<http://www.biolog.de>).

Ouyang, M.; Zhang, L.; Zhu, J.; Schwede, F.; Thomas, S.A., *PNAS*, **105**, 11993 - 11997 (2008): "Epac Signaling is Required for Hippocampus-dependent Memory Retrieval"

Bryn, T.; Mahic, M.; Aandahl, E.M.; Froland, S.S.; Aukrust, P.; Tasken, K., *AIDS Res. Hum. Retroviruses*, **24**, 1013 - 1015 (2008): "Inhibition of Protein Kinase A Improves Effector Function of Monocytes from HIV-Infected Patients"

Bryn, T.; Mahic, M.; Enserink, J.M.; Schwede, F.; Aandahl, E.M.; Tasken, K., *J. Immunol.*, **176**, 7361 - 7370 (2006): "The cyclic AMP-Epac1-Rap1 Pathway is Dissociated from Regulation of Effector Functions in Monocytes but Acquires Immunoregulatory Function in Mature Macrophages"

Kang, G.X.; Chepurny, O.G.; Malester, B.; Rindler, M.J.; Rehmann, H.; Bos, J.L.; Schwede, F.; Coetzee, W.A.; Holz, G.G., *J. Physiol.-London*, **573**, 595 - 609 (2006): "cAMP Sensor Epac as a Determinant of ATP-sensitive Potassium Channel Activity in Human Pancreatic Beta Cells and Rat INS-1 Cells"

Moll, D.; Prinz, A.; Gesellchen, F.; Drewianka, S.; Zimmermann, B.; Herberg, F.W., *J. Neural. Transm.*, **113**, 1015 - 1032 (2006): "Biomolecular Interaction Analysis in Functional Proteomics"

Pacheco, M.A.; Pastoor, T.E.; Wecker, L., *Mol. Brain. Res.*, **114**, 65 - 72 (2003): "Phosphorylation of the Alpha 4 Subunit of Human Alpha 4 Beta(2) Nicotinic Receptors: Role of cAMP-dependent Protein Kinase (PKA) and Protein Kinase C (PKC)"

Morgan, E.E.; Stader, S.M.; Hodnichak, C.M.; Mavrich, K.E.; Folkesson, H.G.; Maron, M.B., *Am. J. Physiol.-Lung. Cell. Mol. Physiol.*, **285**, L 578 - L583 (2003): "Postreceptor Defects in Alevolar Epithelial Beta-adrenergic Signaling after Prolonged Isoproterenol Infusion"

Matuszyk, J.; Cebrat, M.; Kalas, W.; Strzadala, L., *Int. Immunopharmacol.*, **2**, 435 - 442 (2002): "HA1004, an Inhibitor of Serine/Threonine Protein Kinases, Restores the Sensitivity of Thymic Lymphomas to Ca²⁺-mediated Apoptosis through a Protein Kinase A-independent Mechanism"

Johansson, C.C.; Bryn, T.; Yndestad, A.; Eiken, H.G.; Bjerkeli, V.; Frøland, S.S.; Aukrust, P.; Tasken, K., Abstracts of the 13th Protein Kinase Symposium, Oslo/Norway, 2002: "Cytokine Networks are Pre-activated in T Cells from HIV-infected Patients and under Control of cAMP as Assessed by Cytokine Arrays"

Aandahl, E.M.; Moretto, W.J.; Haslett, P.A.; Vang, T.; Bryn, T.; Tasken, K.; Nixon, D.F., *J. Immunol.*, **169**, 802 - 808 (2002): "Inhibition of Antigen-specific T Cell Proliferation and Cytokine Production by Protein Kinase A Type I"

Spicuzza, L.; Belvisi, M. G.; Birrell, M. A.; Barnes, P. J.; Hele, D. J.; Giembycz, M. A., *Br. J. Pharmacol.*, **133**, 1201 - 1212 (2001): "Evidence that the Anti-Spasmogenic Effect of the Beta-Adrenoceptor Agonist, Isoprenaline, on Guinea-Pig Trachealis is not Mediated by Cyclic AMP-dependent Protein Kinase"

Suzuki, Y.; Saitoh, M.; Suzumori, K.; Kajikuri, J.; Itoh, T., *Br. J. Pharmacol.*, **131**, 37 - 42 (2000): "Characterization of Changes in Mechanical Responses to Histamine in Omental Resistance Arteries in Pre-Eclampsia"

Myklebust, J.H.; Josefsen, D.; Blomhoff, H.K.; Levy, F.O.; Naderi, S.; Reed, L.C.; Smeland, E.B., *J. Cell. Physiol.*, **180**, 71 - 80 (1999): "Activation of the cAMP Signaling Pathway Increases Apoptosis in Human Beta-Precursor Cells and is Associated with Downregulation of Mcl-1 Expression"

Boulanger, L.; Poo, M.-M., *Science*, **284**, 1982 - 1984 (1999): "Gating of BDNF-Induced Synaptic Potentiation by cAMP"

Aukrust, P.; Aandahl, E.M.; Skallehegg, B.S.; Nordoy, I.; Hansson, V.; Tasken, K.; Froland, S.S.; Müller, F., *J. Immunol.*, **162**, 1178 - 1185 (1999): "Increased Activation of Protein Kinase A Type I Contributes to the T Cell Deficiency in Common Variable Immunodeficiency"

Takeuchi, T.; Kishi, M.; Hirayama, N.; Yamaji, M.; Ishii, T.; Nishio, H.; Hata, F.; Takewaki, T., *J. Physiol.*, **514**, 177 - 188 (1999): "Tyrosine Kinase Involvement in Apamin-sensitive Inhibitory Responses of Rat Distal Colon"

Keryer, G.; Alsat, E.; Tasken, K.; Evain-Brion, D. J., *Cell Sci.*, **111**, 995 - 1004 (1998): "Cyclic AMP-dependent Protein Kinases and Human Trophoblast Cell Differentiation in Vitro"

Aandahl, E. M.; Aukrust, Pal, Skalhegg, B.S.; Müller, F.; Froland, S.S.; Hansson, V.; Tasken, K., *FASEB J.*, **12**, 855 - 862 (1998): "Protein Kinase A Type I Antagonists Restores Immune Responses of T Cells from HIV-infected Patients"

Torgersen, K.M.; Vaage, J.T.; Levy, F.O.; Hansson, V.; Rolstad, B.; Tasken, K., *J. Biol. Chem.*, **272**, 5495 - 5500 (1997): "Selective Activation of cAMP-Dependent Protein Kinase Type I Inhibits Rat Natural Killer Cell Cytotoxicity"

Hatton, C.J.; Peers, C., *Pflugers Arch.-Europ. J. Physiol.*, **433**, 129 - 135 (1996): "Hypoxic Inhibition of K⁺ Currents in Isolated Rat Type I Carotid Body Cells - Evidence Against the Involvement of Cyclic Nucleotides"

Levin, G.; Peretz, T.; Chikvashvili, D.; Jing, J.; Lotan, I., *J. Mol. Neurosci.*, **7**, 269 - 276 (1996): "Deletion of the N-Terminus of a K⁺Channel Brings About Short-Term Modulation By cAMP and Beta-1-Adrenergic Receptor Activation"

Stella, N.; Magistretti, P.J., *J. Biol. Chem.*, **271**, 23705 - 23710 (1996): "Vasoactive Intestinal Peptide (VIP) and Pituitary Adenylate Cyclase-activating Polypeptide (PACAP) Potentiate the Glutamate-evoked Release of Arachidonic Acid from Mouse Cortical Neurons- Evidence for a cAMP-independent Mechanism"

Yokozaki, H.; Tortora, G.; Pepe, S.; Maronde, E.; Genieser, H.-G.; Jastorff, B.; Cho-Chung, Y.S., *Cancer Res.*, **52**, 2504 - 2508 (1992): "Unhydrolysable Analogs of Cyclic Adenosine-3', 5'-Monophosphate Demonstrating Growth Inhibition and Differentiation in Human Cancer Cells"

References cited in this Technical Information:

- 9 Sandnes, D.; Jacobson, F.W.; M. Refsnes; T. Christoffersen, *Pharmacol. Toxicol.*, **79**, 15 - 22 (1996): "8-Bromo-cAMP and 8-CPT-cAMP Increase the Density of β -Adrenoceptors in Hepatocytes by a Mechanism Not Mimicking the Effect of cAMP"
- 8 Genieser, H.-G., Proc. 9. Int. Conf. Second Mess. & Phosphoprot., Nashville, TN, USA, 1995: "Lipophilic Ranking of Biologically Important Cyclic Nucleotides"
- 7 Schaap, P.; van Ments-Cohen, M.; Soede, R.D.M.; Brandt, R.; Firtel, R.A.; Dostmann, W.; Genieser, H.-G.; Jastorff, B.; van Haastert, P.J.M., *J. Biol. Chem.*, **268**, 6323 - 6331 (1993): "Cell-permeable Non-hydrolyzable cAMP Derivatives as Tools for Analysis of Signaling Pathways Controlling Gene Regulation in Dictyostelium"
- 6 Jastorff, B., Proceedings of the 8th. Internatl. Conference on Second Messengers & Phosphoproteins, Glasgow, UK 1992: "A New Generation of Cyclic Nucleotide Analogues: Site Specific, Enzyme Selective, Agonistic or Antagonistic and Resistant to Hydrolysis"
- 5 Kessin, R.H.; Fleischmann, R.D.; Gottesmann, M.M.; Jastorff, B.; van Lookeren Campagne, M.M. in Adv. in Second. Mess. Phosphoprot. Res., **25**, (eds. S.J. Strada, H. Hidaka), Raven Press, NewYork, 1991: "Use of the Yeast Low Km cAMP Phosphodiesterase Gene to Control Cyclic AMP Levels in Mammalian Cells"
- 4 Jastorff, B.; Maronde, E.; van Bemmelen, M.X.P.; Zorn, M.; Störmann, R.; Proc. 3rd Int. Symp. Mol. Aspects Chemother., Gdansk, Poland 1991, pp.73 - 104: "Cyclic Nucleotide Metabolism as a Target in Chemotherapy"
- 3 Van Ments-Cohen, M., Dissertation University of Leiden, Leiden 1990, The Netherlands: "cAMP Receptors and Signal Transduction in Dictyostelium Discoideum. A Comparative Study With cAMP Derivatives"
- 2 Van Lookeren Campagne, M.M.; Diaz, F.V.; Jastorff, B.; Winkler, E.; Genieser, H.-G.; Kessin, R.H., *J. Biol. Chem.*, **265**, 5847 - 5854 (1990): "Characterization of the Yeast Low Km cAMP-Phosphodiesterase With cAMP Analogues"
- 1 Dostmann, W.R.G.; Taylor, S.S.; Genieser, H.-G.; Jastorff, B.; Døskeland, S.O.; Øgreid, D., *J. Biol. Chem.*, **265**, 10484 - 10491 (1990): "Probing the Cyclic Nucleotide Binding Sites of cAMP-Dependent Protein Kinase I and II With Analogs of Adenosine 3', 5'- Cyclic Phosphorothioates"