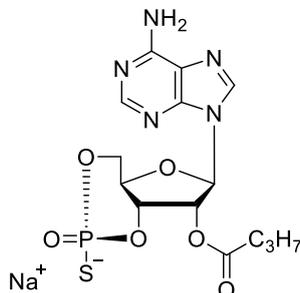


Technical Information about Rp-2'-O-Monobutyryl-cAMPS

Lipophilic, metabolically activated precursor of the PDE-resistant protein kinase A inhibitor Rp-cAMPS

Update: June 15, 2017 HU



Abbreviation: Rp-2'-O-MB-cAMPS

| Formula | CAS No. | Molecular Weight | UV | BIOLOG Cat.No. |
|---|---------------|------------------|--|----------------|
| C ₁₄ H ₁₇ N ₅ O ₆ PS·Na | [152218-23-0] | 437.3 | λ _{max} 258 nm / ε 15200 / pH 7 | M 004 |

Name: 2'-O-Monobutyryladenine-3',5'-cyclic monophosphorothioate, Rp-isomer

Description: Rp-2'-O-MB-cAMPS is an analogue of the parent compound cyclic AMP where the equatorial 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). In addition, the 2'-hydroxy group of the ribose is esterified by butyric acid.

Properties: Rp-2'-O-MB-cAMPS is a lipophilic prodrug of the phosphodiesterase-stable protein kinase A inhibitor Rp-cAMPS which releases Rp-cAMPS and butyrate after metabolic degradation by intracellular esterases. **Caution:** Butyrate was shown to have distinct biological effects, thus control experiments with sodium butyrate are necessary.

Rp-2'-O-MB-cAMPS is about 7 times more lipophilic compared to Rp-cAMPS.

By occupying cAMP binding sites Rp-cAMPS prevents the kinase holoenzyme from dissociation and thus from activation. Due to this working principle preincubation of the inhibitor prior to the activation step is necessary for optimal results.

Application: Experience shows that applicable concentrations of Rp-2'-O-MB-cAMPS depend on the type of biosystem, its membrane properties and kinase content. A main application for Rp-2'-O-MB-cAMPS is to eliminate the first messenger-stimulated phosphorylation by cyclic AMP-dependent protein kinase. For this purpose preincubation (e.g. 20 min) is important, since the production of intracellular cyclic AMP initiated by a first messenger is much faster than the antagonist can penetrate the membrane when given extracellularly. Since Rp-cAMPS is metabolically stable in mammalian and many other systems, there is no danger of degradation during incubation periods. However, if the medium contains serum or other potential sources of esterases, Rp-cAMPS could be released already in the medium and the advantage of better membrane permeability is lost.

Specification: Lyophilized or crystallized sodium salt. The free acid or other salt forms are available upon request. Equal concentrations of Rp-2'-O-MB-cAMPS can appear very different in volume due to high sensitivity of the lyophilized form to humidity. The compound is hygroscopic and can even contract to small volume droplets. Normally, the product is located in the conical bottom of the tube. Micromolar quantities are determined by UV at λ_{max}.

Purity: Typical analysis is better than 97% (HPLC / UV / 258 nm). The product is not sterile and has not been tested for endotoxins.

Caution: Since even minor impurities of 2'-O-MB-cAMP/cAMP (0.2%) or Sp-cAMPS and Sp-2'-O-MB-cAMPS, respectively, can already activate protein kinase and compete with the antagonistic effect of the Rp-isomer, it is very important to work with strictly pure compounds concerning cyclic nucleotide contaminants. Therefore, Rp-2'-O-MB-cAMPS is specially checked for absence of both activators Sp-cAMPS/Sp-2'-O-MB-cAMPS and 2'-O-MB-cAMP/cAMP (0.05% when packed).

However, we cannot guarantee total absence of 2'-O-MB-cAMP/cAMP due to its formation during prolonged storage.

Solubility: Rp-2'-O-MB-cAMPS is readily soluble in water or buffer. Please rinse tube walls (and cap if necessary) carefully and preferably use ultrasonic or vortex to achieve total and uniform mixing. When opening the tube please make sure that no substance is lost within the cap.

Stability and Storage: Rp-2'-O-MB-cAMPS has sufficient stability at room temperature and does not need special care during handling or shipment. Nevertheless the compound and its solutions should be stored in the refrigerator and should be lyophilized and frozen for longer storage periods since desulfurization yielding 2'-O-MB-cAMP can occur slowly. This normally rather slow sulfur/oxygen exchange is accelerated by oxidizing agents. Please note that some cell culture media contain esterases which can already release the active inhibitor.

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!

References for Rp-2'-O-MB-cAMPS:

Cousin, S.P.; Hügl, S.R.; Myers, M.G.; White, M.F.; Reifel-Miller, A.; Rhodes, C. J., *Biochem. J.*, **344**, 649 - 658 (1999): "Stimulation of Pancreatic β -Cell Proliferation by Growth Hormone is Glucose-dependent: Signal Transduction via Janus Kinase 2 (JAK2)/Signal Transducer and Activator of Transcription 5 (STAT5) with no Crosstalk to Insulin Receptor Substrate-mediated Mitogenic Signalling"

Hügl, S.R.; White, M.F.; Rhodes, C.J., *J. Biol. Chem.*, **273**, 17771 - 17779 (1998): "Insulin-like Growth Factor I (IGF-I)-stimulated Pancreatic β -Cell Growth is Glucose-dependent - Synergistic Activation of Insulin Receptor Substrate-mediated Signal Transduction - Pathways by Glucose and IGF-I in INS-1 Cells"

Vischer, U.M.; Wollheim, C.B., *Blood* **91**, 118 - 127 (1998): "Purine Nucleotides Induce Regulated Secretion of von Willebrand Factor - Involvement of Cytosolic Ca^{2+} and Cyclic Adenosine Monophosphate-dependent Signaling in Endothelial Exocytosis"

Selected References for Rp-cAMPS:

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

Dostmann, W.R.G.; Taylor, Susan 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"

Van Haastert, P.J.M.; Kesbeke, F.; Konijn, T.M.; Baraniak, J.; Stec, W.; Jastorff, B., *Bioact. Mol.*, **3**, 469 - 483 (1987): "(Rp)-cAMPS, an Antagonist of cAMP in Dictyostelium Discoideum"

Scheinman, S.J.; Stec, W.J.; Coulson, R., *Miner. Electrolyte Metab.*, **11**, 85 - 90 (1985): "Effects of (Sp)- and (Rp)-Adenosine Cyclic 3',5' Phosphorothioates on Electrolyte Excretion by the Isolated Perfused Rat Kidney"

Scholübbbers, H.-G.; Van Knippenberg, P.H.; Baraniak, J.; Stec, W.J.; Morr, M.; Jastorff, B., *Eur. J. Biochem.*, **138**, 101 - 109 (1984): "Investigations on Stimulation of Lac Transcription in Vivo in Escherichia Coli by cAMP Analogs. Biological Activities and Structure-Activity Correlations"

Botelho, L.H.P.; Rothermel, J.D.; Coombs, R. V.; Jastorff, B., *Methods Enzymol.*, **159**, 159 - 172 (1988): "cAMP Analog Antagonists of cAMP Action"

Rothermel, J.D.; Jastorff, B.; Botelho, L.H.P.; *J. Biol. Chem.*, **259**, 8151 - 8155 (1984): "Inhibition of Glucagon-Induced Glycogenolysis in Isolated Rat Hepatocytes by the Rp-Diastereomer of Adenosine Cyclic 3',5'-Phosphorothioate"